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Posters

P1-1

Long-term effect of donepezil for Alzheimer's disease in Japan

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Background: Alzheimer's disease (AD) became as a generic disease to Japanese people, and donepezil was authorized in Japan as a drug of AD at 1999. Because a day is comparatively short since it was authorized, there are a still few reports about the long-term effect of donepezil for the Japanese AD patients.
Methods: In this study, clinical features of 72 patients of AD treated at Juntendo University Urayasu Hospital were examined in order to study the long-term effect of donepezil. 62 cases had been administrated donepezil and 10 cases had no medication.
Results: The duration of medication was divided into 4 groups which were half a year (16 cases, 25%), one year (16 cases, 25%), two years (13 cases, 21%) and more than 3 years (11 cases, 18%). 6 cases (10%) were canceled prescription for adverse effects. The effect of donepezil was categorized as follow: 27 cases (48%) were improved dementia, 5 cases (9%) were inhibited progress of dementia, and 24 cases (43%) were turned worse. The difference of effect was not seen in sexuality, apolipoprotein E genotype, and medical history. Comparative studies for age of onset and points of the Revised Hasegawa Dementia Scale (HDS-R) before administration, donepezil was effective in the cases developed at 71–80 years old and taken 16–20 points of HDS-R. The cognition of cases with effect of donepezil returned to a state before the treatment at 2 years later. However, the remarkable degradation of cognition was not accepted for the cases. On the other hand, a difference was not seen in long term consequence of the cases that donepezil was not effective after half a year and the cases that treatment was not done.
Conclusion: Donepezil improved dementia symptoms of the effective cases for the long-term. It was thought that presence of drug efficacy after half a year became the index of the necessity of long-term administration of donepezil. In particular, donepezil was effective for cases with mild to moderate AD.

P1-2

The relationship between the severity of Alzheimer type dementia and hippocampal atrophy and laterality

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Objective: To investigate the relationship between the severity of dementia (Functional Assessment Staging: FAST) and hippocampal volume (H) and its laterality in Alzheimer type dementia (AD).
Method: H and intracranial volume (C) were measured, based on images obtained by means of volumetric MRI scans, in 80 subjects (26 males and 54 females), of whom 17 were FAST2 (non-dementia), 10 were FAST3 (borderline), 34 were FAST4 (mild AD), and 19 were FAST5 (moderate AD), and whose mean age was 75.8 ± 8.1. H and C were segmented manually in T2-weighted axial slices horizontal to the AC-PC line and T1-weighted coronal slices perpendicular to the AC-PC line. 3D-Slicer Ver. 1.3 was used as the image analysis software, and the H that was adjusted for by means of the C was designated the adjusted hippocampal volume (H/C). The FAST assessments and H measurements were conducted under a blind.
Results: 1. H/C values and the severity: 1) Both left and right H/C values were large in the order to FAST2, 3, 4, 5. 2) Left H/C values were significantly lower ($p < 0.01$) in the FAST3, 4, or 5 groups than those in the FAST2 group. 3) Right H/C values were significantly lower ($p < 0.01$) in the FAST5 group than those in the FAST2, 3 or 4 groups. 2. Laterality: 1) Left H/C values were lower than right H/C values in every group. 2) Significant differences ($p < 0.05$, $p = 0.0009$, $p < 0.0001$) were observed between the left and right H/C values in the FAST2,

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FAST3 and FAST4 groups respectively. However, no statistically significant differences were observed between the left and right H/C values in the FAST5 group. 3) In right to left rate (L/R) of H/C values, significant differences ($p < 0.01$) were observed between the FAST2 and 3 groups, the FAST4 and 5 groups. However, no statistically significant differences were observed between FAST2 and 5 groups, the FAST3 and 4 groups.

Conclusion: 1. H/C values both on the left and on the right are small along with increases in FAST severity. 2. H/C values are smaller on the left than those on the right. 3. Left H/C values decrease markedly in the initial stages of cognitive impairment (from FAST2 to FAST3), while right H/C values decrease markedly in the intermediate stage (from FAST4 to FAST5) of AD. These results suggest that H/C laterality is observed in the initial stage of AD, and disappears in the intermediate stage of AD.

P1-3

A case report: Complication of Guillain-Barre syndrome in Alzheimer's disease

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We experienced Alzheimer's disease male patient with complication of Guillain-Barre syndrome (GBS) during admission. Diagnosis of GBS was difficult because of impairment of verbal communication ability and aspects of a GBS-related mimicking gait apraxia occurring in dementia. When the patient was 61 years old, memory impairment was observed with depressive mood, irritability and persecutory delusion. He was admitted to Yokohama City University Medical Center for treatment of psychotic symptoms. Quetiapine was effective for improvement his irritability. On the day 67th after admission, he showed dysbasia shortly after lumbago. He was subsequently unable to stand up and lay down for almost all days. 2 weeks later, his legs came to present excycloducted position with areflexia. The nerve conduction test showed a sign of peripheral neuropathy. Data of cerebrospinal fluid (CSF) showed increased protein concentration, and contains few mononuclear leukocytes. Therefore, he was diagnosed having acute GBS because of peripheral neuropathy and alubuminocytologic dissociation. He was immediately treated with a course of intravenous immunoglobulins. Subsequently, steroid pulse therapy was applied with methylpredonisolone sodium succinate due to deterioration of CSF data. Lumbago as well as protein level in CSF were improved while rehabilitation program was performed since his leg paresis remained unimproved. Then, he was able to sit up with minimal help although he was still unable to stand up or walk at all. Cognitive impairments gradually progressed. He discharged from the hospital on day 245th, and transferred to a geriatric hospital for the purpose of continuous rehabilitation. Despite presumably unrelated etiologies, concurrence of these diseases is interesting in view of possible participation of cytokine and complement complexes in the pathophysiology of both AD and GBS.

P1-4

Everyday function in early stage of Alzheimer's disease

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Objective: This study examined what aspects of everyday function (EF) are impaired in early stage of Alzheimer's disease (AD).

Subject: Subjects of this study were 82 AD patients (mean age = 74.43, SD = 8.86, 55–89; mean number of years of education = 12.92, SD = 2.73, 6–18) judged to be CDR 0.5 (n = 28) or CDR1.0 (n = 57). Their mean MMSE score was 21.13 (SD = 4.06, 13–29). Everyday Function (EF) was assessed by using a relative/carer rated scale which covered various everyday activities which were important for independent living. To examine the nature of EF in early stage of AD, we calculated rate of decline in EF (rDEF) for each of activities by following formula: (rDEF = the number of subject who could not perform the activity independently)/(the number of subjects who did the activity independently before). Cognitive function was assessed by the Japanese version COGNISTAT.

Results: On 18 of 34 activities (i.e. using E-mail, driving, bargaining, administering property, utilize train, subway, bus and taxi, application for social care, cleaning, planning meals, ordering one's

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affaire, going to hospital, managing a bank account, preparing meals, using a card, taking medicine properly, writing letter, gifting), rDEF exceeded 50%. When rDEF was calculated by the CDR stages, at stage of CDR0.5 (very mild AD), rDEF exceeded 50%, on 18 of 34 activities (e.g. using E-mail, driving, bargaining, administering property, utilize train, subway, bus and taxi). At stage of CDR1.0 (mild AD), on another 10 activities (e.g. exercising care regard to fire and gas valves, using washing machine), in addition to the 18 activities, rDEF exceeded 50%. To examine underlying cognitive factors of disturbance in EF, we conducted a discriminant analysis with independence of each activities as an independent variables and with demographic and COGNISTAT subtest-score as dependent variables. The majority of EF activities were accounted for by patient's age and cognitive abilities such as orientation, constructional abilities, and confrontational naming.

Conclusion: These result suggested that patient with AD had impairments in many aspects of EF activities even in the very mild stage, and that these impairments may be accounted for the age and the several cognitive deficits.

P1-5

Psychosocial care for severe Alzheimer patients based on their reserved cognitive function: The Tajiri Osaki-Tajiri Project (5)

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Objective: The aim of this study is to evaluate reserved cognitive function in patients with severe Alzheimer's disease (AD) for applying adequate psychosocial care based on their functions.

Methods: We retrospectively analyzed data of demographic, cognitive function and physical function for 29 AD patients whose MMSE score were 10 or less. Psychosocial care included personal reminiscence, occupational therapy, and group work including reminiscence and reality orientation (RO). Their reserved cognitive functions were assessed using domains of Cognitive Abilities Screening Instrument (CASI).

Results: Using factor analysis, the patients were significantly classified to four groups, according to the CASI domains. Namely, the first group (G1, n = 7), the second group (G2, n = 9), the third group (G3, n = 6), the fourth group (G4, n = 7). The mean MMSE scores were 7.4, 6.7, 6.7 and 7.2 for G1-G4, respectively. There were no significant differences on MMSE score, education year and age among the four groups. The ANOVA showed that G1 had higher score on CASI domain *language*, G3 had higher score on CASI domain *orientation*, and G4 had good scores on CASI domain *long-term memory* and *orientation*. Regarding the relationship between such reserved cognitive functions and psychosocial care, we found that personal reminiscence was adequately carried out for three of seven patients in G1, and group work including reminiscence and RO was applied for two of seven patients in G4.

Comment: Even severe AD patients can be further classified to four groups by their reserved cognitive functions. The G1 patients had reserved language function. Thus, they were considered to be fit for individual reminiscence, which mainly used language. On the other hand, the G4 patients remained long-term memory and orientation, thus they were thought to be good for group reminiscence and RO.

P1-6

The transition of prevalence of dementia in Japan: A population based epidemiological study

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Background and objectives: Nakayama study has been conducted on all people aged over 65 years old residing in Nakayama town. The first Nakayama study was done in 1997, and the second study was done in 2001. The third study was carried out between

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April 2004 and April 2006. The aim of this study is to evaluate the transition of the prevalence of dementia in rural area in Japan.

Methods: The third Nakayama study was carried out among 1521 residents of Nakayama town and they were selected from same population of the first study. As the same way of the first Nakayama study, a door-to-door three-phase population survey was carried out in the third Nakayama study. Senior neuropsychiatrists administered the Mini-Mental State Examination (MMSE), standard physical and neurological examination to subjects. All subjects who were suspected of dementia were asked to undergo a cranial computed tomography (CT), and some of them were checked with a blood test and/or a brain single photon emission computed tomography (SPECT) when necessary. The diagnosis of dementia was established according to DSM-Third Edition-Revised criteria. Alzheimer's disease (AD) was defined according to the NINCDS-ADRDA criteria; Vascular Dementia (VaD) according to the DSM-Fourth edition criteria; other dementia, according to the standard criteria of each dementia. Written informed consent was obtained from all participants (or relatives when necessary), with a full explanation of the procedures.

Results: Of 1521 inhabitants, 1290 (84.8%) completed the protocol. The prevalence of dementia was 6.0% (92 subjects). Of the 92 subjects with dementia, 50(54%) had AD, 27(29%) had VaD, and 15(16%) had dementia resulting from other causes.

Conclusions: In the first Nakayama study, the prevalence of dementia was 4.8%. In the third study, the prevalence of dementia was 6.0% and it was higher than the first study. However the prevalence of VaD (the third study: 1.7%) decreased in comparison with the first study (1.9%), and the prevalence of AD (3.3%) increase in comparison with the first study (1.5%). As for this result, there is a possibility that old-old have increased, and we thought that enlightenment in educational activities on dementia was associated with decrease of the prevalence of VaD although we did not intervene directly.

P1-7

Uncinate fasciculus-correlated cognition in Alzheimer's disease: A diffusion tensor imaging study by tractography

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Several researchers show increased diffusivity and decreased anisotropy in Alzheimer's disease (AD) by diffusion tensor imaging (DTI), but only few reports have been able to show a correlation with cognitive function. The reason for this may be the study method, such as a region of interest (ROI), used to calculate parameters for DTI. Because the ROI method includes various neuronal fiber tracts, isolating specific tracts for analysis is difficult. To resolve these problems and confirm a relationship between cognitive function and DTI parameter values in AD, we measured mean diffusion anisotropy and diffusivity of co-registered voxels along the tracking lines (i.e. tract of interest) of the uncinate fasciculus by using tractography. The subjects were 30 patients (11 males and 19 females; mean age, 76.2 years) with probable AD (NINCDS-ADRDA criteria), recruited from Nara Medical University. Assessment of global cognitive function was carried out according to a standardised battery, including the mini-mental state examination (MMSE) and the Alzheimer's disease assessment scale-cognitive component-Japanese version (ADAS-Jcog.) Informed consent for the imaging study was obtained from all patients or their families. A 1.5-T clinical MR unit (Magnetom Sonata, Siemens AG, Erlangen, Germany) was used to obtain diffusion tensor images. Diffusion tensors were computed and fiber-tract maps were created using a PC workstation with "dTV II" diffusion tensor imaging software developed by Masutani et al. (University of Tokyo, diffusion tensor visualizer ver. 2). We measured mean fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values along the bilateral uncinate fasciculus. The relationships were investigated by Pearson's correlation coefficient test. The MMSE scores of patients with probable AD ranged from 7 to 23 (mean = 15.2), and the ADAS-Jcog. score ranged from 13 to 57 (mean = 27.6). The mean FA value along the uncinate fasciculus was 0.35 and mean ADC value was 0.46×10^{-3} seconds/mm^2. FA values were positively correlated with MMSE score ($r = 0.67$, $P < 0.001$) and were negatively correlated with ADAS-Jcog. score ($r = -0.62$, $P < 0.001$), while ADC values were negatively correlated with MMSE score ($r = -0.58$, $P < 0.001$) and were positively correlated with ADAS-Jcog. score ($r = 0.59$, $P < 0.001$). FA and ADC values may

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reflect the severity of cognitive dysfunction. The tract-of-interest method might be a useful tool for objectively evaluating DTI parameters in AD.

P1-8

Comparison of performance in word recall among the normal elderly and patients with cognitive disorder

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Although there is no known cure for Alzheimer's disease (AD), early detection and treatment may improve cognitive function and retard its progression in many patients. Therefore to diagnose the mild cognitive impairment (MCI), which is transitional state between normal ageing and early AD, is important and attracts attention. Wechsler Memory Scale-Revised is widely used as a diagnostic assistance of MCI, but the examination is unsuitable for screening in a large-scale senior citizen because of taking a long time in surveys. Word recall which is the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-J.cog) is one of the Word List Learning tasks standardized in Japan and can be performed in a short time. The subtest consists of 10 words administered over three trials. In this study, we used this task and compared the number of correct answers (recall) among the patients with mild memory impairment/no dementia (MMI/ND), mild AD and the normal elderly (NE), classified by Mini-Mental State Examination (MMSE) score. The subjects were 12 (3 males and 9 females) patients with probable AD and 14 patients (6 males and 8 females) with MMI/ND, recruited from the Department of Psychiatry, Nara Medical University. For comparison, 28 (16 males and 12 females) cognitively intact subjects (NE group) were selected from a local feasibility study of senior citizen older than 65 years old. Probable AD was diagnosed according to the NINCDS-ADRDA criteria. MMSE scores of mild AD were between 21 and 23. MMI/ND was basically defined by MMSE score (>23) and delayed recall score, subscale of MMSE (0 or 1/3). Informed consent was obtained from all patients or participants. The results were analyzed by one-way ANOVA or Mann-Whitney test. The number of recall of NE (6.6 ± 1.2: mean $\pm$ SD) was significantly larger than that of MildAD (4.0 ± 1.4, $p < .01$) and MMI/ND (4.7 ± 1.3, $p < .01$). In terms of the number of recall increased between trials, for MildAD, the increased from trial1 to trial2 and trial3 were smaller than that of NE ($p < .01$), while for MMI/ND, the number of recall increased was significantly smaller only from trial1 to trial3 than that of NE ($p < .05$). These results are suggesting that the performance of MildAD and MMI/ND were worse than that of NE. In addition, the difference in performance would appear by repeating some trials between NE and MMI/ND, while between NE and MildAD, the clear difference would arise in earlier trial than MMI/ND.

P1-9

Risk of conversion from mild memory impairment to Altzhemier's disease in a Japanese community (from the Nakayama Study)

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Background and aims: Previously we have estimated the rate that subjects with Mild Memory Impairment/Not Dementia (MMI/ND) shifted to Altzheimer's disease (AD) in a population-based cohort study [1]. In the present study, we have assessed whether the risk of conversion (from MMI/ND to AD) was affected by several established and emerging risk factors.

Methods: Subjects in a community-based elderly cohort of MMI/ND were followed longitudinally. Subjects were selected from the participants in the first Nakayama study [2]. MMI/ND was defined as memory deficit with objective memory assessment, without dementia, impairment of general cognitive function, or disability in activities of daily living.

Result and comment: At baseline, the MMI/ND group consisted of 104 subjects (59 female; 45 male) selected from 1162 community dwellers aged over 65 year. During the five-year follow-up, eleven (10.6%) subjects were diagnosed as AD. The risk of conversion (from MMI/ND to AD) was associated

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with Diabetes Mellitus and family history of AD. On the other hand, this risk of conversion was not associated with hypertension, hyper-cholesteremia, the Geriatric Depression Scale (GDS) and history of both drinking and smoking. These findings have implications for developing preventive strategies of AD.

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P1-10

Neuroanatomical predictor of cognitive effects of donepezil

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Background and objective: Although donepezil is widely used as cholinesterase inhibitor to slow the progress of Alzheimer's disease (AD), the neuroanatomical predictors of its effects in AD remain unclear. The major reason for this lies in the method of cognitive outcome assessment, namely the Mini Mental State Examination (MMSE), among almost all the previous studies. However, the Alzheimer's Disease Assessment Scale Japan cognitive subscale function test (ADAS-J cog) is more sensitive to detect subtle cognitive changes in AD. Therefore, we aimed to determine whether pre-treatment regional cerebral blood flow (rCBF) might predict a cognitive change in response to donepezil treatment in terms of the ADAS-J cog.
Method: Forty-one patients with mild to moderate AD participated in this study. They underwent single photon emission computed tomography (SPECT) using 99mTc-ECD before receiving donepezil, and ADAS-J cog was performed at baseline and after twenty-four weeks of donepezil therapy. We analyzed the correlation between baseline rCBF and changes in ADAS-J cog score by using statistical parametric mapping 2 (SPM2).
Results: We found a significant correlation between the baseline rCBF in the orbitofrontal cortex (OFC) (Brodmann 11) and the change in ADAS-J cog score in AD patients receiving donepezil treatment.
Conclusion: Our results suggest that donepezil therapy may affect the neural activity of the OFC in AD patients. Such effect may reflect the choline acetyltransferase activity associated with OFC.

P1-11

The increase of hydrolase activity for I2PP2A in AD brain

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The activity of protein phosphatase 2A (PP2A) is compromised and is believed to be a cause of the abnormal hyperphosphorylation of tau in Alzheimer's disease (AD) brain. The intracellular PP2A activity is regulated by two inhibitor proteins, called I1PP2A and I2PP2A in mammalian tissue. Previously we have reported 1) an increase in the mRNA expressions of I1PP2A and I2PP2A in temporal and in entorhinal cortices of AD as compared to age-matched control cases; 2) a shift in the intracellular distribution of I2PP2A from its primarily nuclear location to the cytoplasm in neurons and as well as a cleavage of full length 39 kDa protein to a ~20 kDa fragment in AD brains; 3) a co-localization of the two inhibitors with PP2A in neuronal cytoplasm and with the abnormally hyperphosphorylated tau in neurons. Based on these data, we further investigated the cleavage of I2PP2A in AD brain. 1. Recombinant I2PP2A was digested with AD or control brain extract *in vitro*. Though several cleavage products of recombinant I2PP2A were seen in both AD and control, they were generated significantly earlier on digestion with AD brain extract than control brain extract. 2. To further confirm that the cleavage products of I2PP2A with AD brain extract, digested products were analyzed by mass spectrometry. The results of mass spectrometry analysis of several digested polypeptides revealed a complete match to that of I2PP2A and showed that those polypeptides were from the amino terminal half or greater half of I2PP2A. 3. Amino terminal sequencing of these products of the recombinant I2PP2A

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with AD brain extract were also analyzed. Interestingly, one result revealed that I2PP2A was cleaved at the position between amino acid 175 and 176 of I2PP2A (the sequence from amino acid 168 to181 of I2PP2A is considered as a nuclear localization signal). These data suggest an increased activity of specific hydrolase, which break the sequence of nuclear localization signal in I2PP2A, in AD brain. As a result, amino terminal half of I2PP2A, which also has PP2A inhibitory activity, translocate from neuronal nucleus to cytoplasm and possibly involve in the abnormal hyperphosphorylation of tau through the inhibition of PP2A activity in neuronal cytoplasm.

P1-12

A cerebral blood flow study on verbal fluency in patients with Alzheimer's disease

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The aim of this study was to clarify the characteristics of verbal fluency and regional cerebral blood flow (rCBF). Subjects were 82 senile patients having amnesia as a complaint including 51 Alzheimer's disease (AD), 17 mild cognitive impairment (MCI) and 17 control subjects (CS). We examined cognitive function using the category fluency test (CFT) and the letter fluency test (LFT). The rCBF was measured with using the three-dimensional stereotaxic ROI template method (3DSRT) that was a quantitative method simplified and less invasive for 99mTc-labeled bicisate (ECD) single-photon emission tomography (SPECT). It was composed of 259 regions of interest (ROIs) in 11 segments on each side. As results, the score of AD was lower than those of MCI and CS in both CFT and LFT. Those scores were correlated with severity of dementia. CFT scores were correlated with rCBF in left thalamus, right precentral region and hippocampus. LFT scores correlated highly with rCBF in left precentral and pericallosal regions, hippocampus and thalamus. In conclusion, we suggested that verbal fluency with CFT may be caused in a mechanism different from that caused with LFT. The verbal fluency is efficient tool to distinguish the process of cognitive impairment.

P1-13

The difference between amino acid metabolism and cerebral perfusion in early Alzheimer's disease patients: L-[methyl-11C] methionine PET study

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Backgrounds: Hypometabolism or hypoperfusion in posterior cingulate cortex(PCC) in Alzheimer's disease (AD) is thought to be characteristic to AD and useful for the early diagnosis. But this abnormality in PCC is earlier and more severe than in the medial temporal cortex and inferior temporal cortex, where pathologic changes is more severe than in PCC in AD patients. It is considered that the functional or structural deafferentation, or both, from neural degenerations occurred in the other brain areas cause this discrepancy between this finding and the pathological change in the PCC, in which there is various neural connections with other limbic structures. Recently it is revealed that L-[methyl-11C] Methionine (MET) uptake was not affected in the crossed cerebellar diaschisis, which defined as a depression of blood flow and metabolism of glucose in the cerebellum contralateral to a supratentorial brain lesion. This result indicates that MET uptake is independent of depression of neuronal activity through neural connections without direct neuronal damage. So we assumed that the neuronal loss in AD patients is directly assessed by using Met-PET.

Objectives: To examine the difference between N-isoprpyl-p-[123I] iodoamphetamine (IMP) SPECT images and Met-PET images in PCC and the other region.

Method: We performed both IMP SPECT and MET PET to 8 outpatients who were diagnosed probable AD by using National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders

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Association (NINCDS-ADRDA) criteria and had apolipoprotein E epsilon 4 allele. Individual SPECT or PET scans were stereotactically standardized with NEUROSTAT software, and subsequently, cortical activity of each data set extracted to a set of predefined surface pixels (three-dimensional stereotactic surface projection, 3D-SSP). We set volume of interest (VOI) on bilateral PCC, frontal lobe, parietal lobe, medial temporal lobe, parahippocampus, and amygdala full automatically with VOI classic software, and analyzed by paired t-test in each area with the global regional normalization.
Results: Compared with the MET PET images, IMP SPECT images were significantly more decreased in PCC, medial temporal lobe, parahippocampus, and amygdale bilaterally and right parietal lobe.
Conclusions: This present study may indicate that amino acid metabolism in PCC and limbic structures was spared than cerebral perfusion in AD patients.

P1-14

Cognitive profile that predicts the rate of cognitive decline in Alzheimer's disease

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The number of those with dementia is expected to increase sharply due to the aging population. Delaying the progression of disease is very important for the well-being of the patient as well as his/her family members. Among Alzheimer's disease (AD) patients, their progression of the cognitive decline has been shown to be heterogeneous. It is useful that we could differentiate the group of patients who expect to show increased declines and need vigorous pharmacological and social intervention from those who retain relatively stable cognitive functions over time. This type of information will also contribute to clarify pathophysiological mechanism of the disease, most of which is largely unknown. In this study, we analyzed cognitive domains at baseline which predict the rate of cognitive declines using the data where AD patients were followed over three years, most of them were under a pharmacological treatment. Clinical course of 130 AD patients (Male/Female 41/89) who visited outpatient memory clinic of Kyoto University Hospital at least for 2 years were included in this study. Their mean age (SD), education (SD) and MMSE (SD) in the first visit were 74.5 (8.0), 10.9 (2.7) and 22.8 (4.5), respectively. AD diagnosis was made according to DSM-IV criteria. One hundred and fifteen patients received cholinesterase inhibitor medication and the other 15 patients stopped taking the medication during the. In the initial diagnostic session, patients underwent series of cognitive examinations which includes episodic memory, executive and visuospacial functions. After the session, follow-up examinations were performed at 6 month, 1, 2 and 3 years. Patients who showed more than 6 points decline in MMSE were classified as a decliner. Multiple logistic regression models were used to find the cognitive tests which predict decliners, after controlling for age, sex, education and initial MMSE score. Mean (SD) MMSE scores at the initial, 6 months and 1, 2 and 3 years follow-up were 22.8 (4.5), 22.5 (4.0), 21.6 (4.3), 20.0 (5.5) and 18.4 (5.4), respectively. Logistic regression analysis showed that the Clock Drawing test and the Block Design test were predictors of decliners at both second and third year. Lower executive and visuospacial functions at baseline predicted increased decline in a general cognitive. These data might indicate existence of subgroup of patients who need for intense intervention, although further research is needed.

P1-15

A study on the short-term and long-term effect of donepezil for cognitive functions in Alzheimer's disease

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Donepezil was effective in maintenance of cognitive functions in mild to moderate Alzheimer's disease (AD). On the other hand, prediction of treatment efficacy was difficult before treatment. In the previous study, we reported short-term effect for cognitive functions may predict long-term effect at 1 year after donepezil treatment. We examined short-term effect for cognitive functions may predict long-term effect at 2 year after donepezil treatment.

Subject was 69 outpatients (11 male, 58 female) of AD who took donepezil over 2 years and received periodic evaluation of cognitive function (mini mental state examination: MMSE, Rorschach test: R-T) and Clinical Dementia Rating (CDR), before and 4 months intervals after donepezil treatment. All patients fulfilled the diagnostic criteria of probable

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AD of NINCDS-ADRDA. Responses of the R-T were appraised to the cognitive score (RCT) that may be indicator of abstract thinking or recognition (Hoshino et al 1996). Agreement for treatment and periodic evaluation was confirmed by all subjects or their caregiver before treatment.

During the treatment period, 17 patients showed deterioration on the CDR compare with before treatment (ineffective group: IG) and 52 patients maintained on the CDR during the time point of 4–24 months after donepezil treatment (effective group: EG). Out of 17 patients, 1 at 4 months, 1 at 8 months, 3 at 12 months, 4 at 16 months, 4 at months and 4 at 24 months showed deterioration on the CDR. On the clinical evaluation before treatment, average age was 77.0 ± 7.4 in EG vs 76.5 ± 4.8 in IG, CDR was 1.2 ± 0.4 vs 1.1 ± 0.5, MMSE was 19.4 ± 3.2 vs 19.6 ± 4.0, RCT was -1.9 ± 2.4 vs -2.0 ± 3.4. There were no statistical differences between two groups. On the evaluation 4 months after treatment, CDR was 1.1 ± 0.3 in EG vs 1.1 ± 0.5 in IG, MMSE was 20.2 ± 2.8 vs 17.8 ± 3.4, RCT was -1.0 ± 2.4 vs -1.6 ± 2.8. Though, there were no statistical differences on the CDR and RCT, EG showed higher score on MMSE ($p = 0.005$) than IG. EG showed higher score on MMSE ($p = 0.03$) and RCT ($p = 0.009$) than score of the before treatment. IG showed lower score on MMSE ($p = 0.05$) than score of the before treatment. These results suggest that short-term effect for cognitive functions may predict long-term effect on the donepezil treatment. Periodic clinical evaluation and examination of cognitive function is indispensable for effective donepezil treatment.

P1-16

Increased expression of toll like receptor 3 in Alzheimer's disease brain

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Alzheimer's disease (AD) is characterized by senile plaques, which are predominantly composed of amyloid beta (Aβ) peptide, and neurofibrillary tangles, composed of filamentous aggregates of hyperphosphorylated tau protein. In addition, immunological and inflammatory changes including microgliosis, atrogliosis, complement activation, cytokine elevation and acute phase protein changes are also common phenomena in AD. These changes are thought to represent, at least in part, a response to the early accumulation of Aβ in the brain. However the precise mechanism is yet to be revealed. In this study the involvement of innate immune activation in AD was investigated in relation to Toll like receptor 3 (TLR3). TLR3 is a receptor working in innate immune system, and its expression in brain was already reported. Real time PCR revealed that mRNA of TLR3 expression in AD brain significantly increased compared to control brain. And by immunohistochemical analysis significant increased TLR3-positive cells in AD brain around the amyloid plaque were observed. Our study suggests that innate immunity might be involved in neurodegenerative processes in AD brain.

P1-17

A case of Alzheimer's disease with amygdala Lewy bodies (AD/ALB) presenting with visual hallucination

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It is well known that visual hallucination is one of the core features in dementia with Lewy bodies (DLB). The cause of visual hallucinations in DLB is thought to be severe LB pathology in the temporal cortex, including the amygdala (Harding AJ 02), an area which is extremely vulnerable in DLB. Recently, one of the authors (Uchikado H 06) proposed a distinct form of Lewy body disease, Alzheimer's disease with amygdala LBs (AD/ALB), which is characterized by both advanced AD pathology and α-synuclein-immunoreactive neuronal lesions that are relatively restricted to the amygdala. The α-synucleinopathy resembles cortical-type LBs at light and electron microscopic levels. Clinical features of AD/ALB, in particular, differences from AD, have not been described well. We here report a 67-year-old, right-handed, Japanese male patient of AD/ALB. He had no family history of neurological disorders. His past history was not contributory. He died 3 years after the onset of visual hallucination, memory disturbance and disorientation. At age 64, he consulted us

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for vivid visual hallucination of an unknown person. The Mini-Mental State Examination score was 4/30 and the revised Hasegawa dementia scale score 6/30. Dressing and constructional apraxia, agraphia and acalculia were seen. He also had fluctuating cognition but no Parkinsonism. Brain CT demonstrated mild cerebral atrophy, predominantly in the temporal and parietal lobes. SPECT showed decreased blood flow in the parietal and occipital lobes. His clinical diagnosis was either AD or DLB. The postmortem examination revealed advanced AD pathology (NFT stage V and senile plaque stage C by Braak H 91) and severe LB pathology in the amygdala. Macroscopically, pigmentation of the substantia nigra and locus ceruleus were preserved. No neuronal loss or extraneuronal neuromelanin was seen in the substantia nigra. The locus ceruleus had mild neuronal loss with gliosis. LBs were not found in the brainstem regions and were limited to the limbic area, especially the amygdala. This case was neuropathologically compatible for AD/ALB. We speculate that visual hallucination is associated with LB pathology in the amygdala not only in DLB but also in AD/ALB. A number of patients who present rigorous hallucination but are otherwise more likely to be AD than DLB may be AD/ALB.

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P1-18

The effect of anticholinergic burden on cognitive performance in Alzheimer's disease patients

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Because cholinergic deficiency is prominent in Alzheimer's disease (AD), patients with AD are especially vulnerable to anticholinergic burden. In fact, medications with anticholinergic properties are associated with variety of adverse events, including cognitive impairment in patients with AD. However, there have been inconclusive results to date on the relationships between the anticholinergic burden using and the global cognitive performance in patients with AD. Therefore, we evaluated the association between serum anticholinergic activity (SAA) and various cognitive domains of Mini-Mental State Examination (MMSE) score in patients with AD. All subjects were met the diagnostic criteria for probable AD developed by the working group of the National Institute of Neurological and Communicative Disorders and Stroke in collaboration with the Alzheimer's Disease and Related Disorders Association. We evaluated the educational level, the age at dementia onset, duration and severity of dementia, global cognitive performance. The severity of dementia was evaluated using FAST. Global cognitive function was evaluated with MMSE. The level of SAA was measured according to the protocol of Tune and Coyle. The level of SAA was expressed as equivalents of atropine and was reported in nM of atropine equivalents. We measured SAA in 76 consecutively referred AD patients and compared various cognitive domains of MMSE scores between in the SAA positive (SAA (+)) group and in the SAA negative (SAA (−)) group using the Mann-Whitney U test. $P < 0.05$ was accepted as a statistically significant value. We obtained informed consents at the study entry (the first referential day) from all participants and their proxies, after explaining their involvement in this study. This study was approved by the Ethical Committee at the National Shimofusa Hospital. words) was only significantly lower in the SAA (+) group than in the SAA (−) group. The scores the mean (SD) SAA value in the SAA (+) ($n = 36$) group was 3.19 (2.91) nM. The score of recall domain of in MMSE (recall three of other domains of MMSE including the total scores of MMSE were not significantly differences between in the SAA (+) group and in the SAA (−) group. Our result indicated that contribution of anticholinergic burdens to the cognitive performance in AD was only limited domain of cognitive functions.

P1-19

Changes in a precision of S3 cleavage by presenilin/gamma-secretase regulate Notch signaling

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Notch signaling, essential for development, is a type of local-cell signaling that participates in neurodegeneration and tumorigenesis. The canonical Notch pathway is mediated by the RIP (regulated intramembrane proteolysis) pathway, in which Notch receptors undergo ligand-dependent sequential endoproteolysis via a series of enzymes, including Presenilin (PS)/γ-secretase. The Notch-1 ICD (NICD), which is produced by PS/γ-secretase-mediated cleavage at site-3 (S3), translocates to the nucleus and participates in transactivation of target genes. Whether the site of S3 cleavage can vary has not been examined previously. In this study, we show that there is diversity in the site of S3 cleavage, resulting in the production of two different types of NICD with apparently distinct stability and ability to transmit intracellular Notch signaling. Moreover, we found that the precision of S3 cleavage depends on where in the cell it occurs. Collectively, our results suggest that the precision of PS/γ-secretase-mediated cleavage is important for determining the intensity of Notch signaling.

P1-20

Enhancement of Abeta degradation by BACE1

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Since the ectodomain shedding of β APP by γ-secretase is prerequisite for Aβ generation, cleavage by BACE is the first step in Aβ cascade. Enhanced BACE1 activity is considered to increase the amount of Aβ secretion and it is suggested that BACE1 activity was up-regulated in Alzheimer disease brain. However, we observed that the amount of secreted Aβ was rather reduced when BACE1 was overexpressed in cultured cells. In order to clarify the mechanism that BACE1 overexpression reduces the level of secreted Aβ, the conditioned media of BACE1 expressing cell lines were analyzed by combined immunoprecipitation and MALDI-TOF MS. In vitro assay using synthetic Aβ peptides and purified BACE1 was also performed. Surprisingly, we observed that BACE1 cleaved Aβ40 at more than one site which was previously reported. Moreover, we found that pathogenic Aβ42 is also degraded by BACE1. These results suggest that modification of BACE1 may be of use to enhance Aβ degradation.

P1-21

A novel process to reduce Abeta production without directly affecting secretases and Notch signaling

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Aβ is generated in the process of sequential endoproteolysis of βAPP. Mainly three secretases, α-β-, and γ-secretase are involved in the process. Modulation of these secretase activities is a general approach to inhibit Aβ generation. However, it may cause unexpected side effects since many other substrates undergo proteolysis by the enzymes which have the secretase activities. γ-Secretase inhibitors, for instance, inhibit Aβ production but down regulate Notch signaling, which is involved in cell differentiation as well as neurodegeneration. In this study, we tried to obtain compounds which inhibit Aβ generation but less affect Notch signaling. We performed screening to find natural compounds which modify Aβ generation. Dual-luciferase reporter assay was used for measuring Notch signaling. Cell-based, cell-free and *in vitro* secretase assays were established for further analysis to investigate the effects of screened compounds on α-β-, and γ-secretase activities. We found Compound X can modify Aβ generation without affecting Notch signaling. Moreover, Compound X does not directly inhibit/stimulate α-β-, and γ-secretase activities. We expect that Compound X acts a new target for knocking-down Aβ production.

P1-22

Reduction of calbindin D28K and parvalbumin gene expression in the frontal cortex in patients with Alzheimer's disease

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Purpose: Disturbances in calcium homeostasis have been observed to be associated with Alzheimer's and other neurodegenerative diseases. Increased total calcium levels and decreased levels of calcium binding proteins have been found in Alzheimer's disease (AD) brain tissue. However, the mechanism behind these disturbances remains unknown. We investigated the gene expression of calcium binding proteins in the prefrontal cortex (Brodmann area 9, 10, 11) in patients with AD.
Methods: Brain tissues from 6 patients with AD and 6 elderly patients without dementia who died in hospital were obtained at autopsy. The written consent of the study was obtained. In situ hybridization with antisense probes for the calcium binding proteins, calbindin D28K (CB) and parvalbumin (PV), was used to examine the expression of genes coding for these proteins in AD brain tissues matched for age, agonal process and autopsy interval.
Results: mRNA levels for CB and PV were reduced in the frontal cortex in patients with AD, as compared to controls.
Conclusion: These findings strongly suggest that change in calcium homeostasis may be involved in the pathogenesis of AD.

P1-23

Genetic risk candidates of late-onset Alzheimer's disease at chromosome 12p

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Late-onset Alzheimer's disease (LOAD), the most frequent cause of degenerative dementia in the elderly, is genetically classified as polygenetic disorder, differently from the representative and monogenic disorder of familial early-onset Alzheimer's disease. The $\epsilon 4$ allele of apolipoprotein E gene (APOE-$\epsilon 4$) was confirmed as the genetic risk of LOAD, but risk genes in non-APOE-$\epsilon 4$ carriers remains undetermined, because of the difficulty of replication in multiple ethnic backgrounds. Chromosome 12 has been noted to harbor a risk locus of non-APOE-$\epsilon 4$ LOAD, and the short arm of chromosome 12 (12p) was noted by affected sib-pair analysis. However, the exact genome research of this locus remains obscure. To screen risk genes for this locus, we performed a genome scan using 387 SNPs spanning 34Mb mapped at 12p. Association was evaluated by chi square method, and p values < 0.05 were judged significant. Exploratory scan using 188 LOAD and 375 control subjects noted associations with more than 30 SNPs, and these SNPs were further evaluated in confirmatory scan using the cases with additional 186 LOAD and the control data in the exploratory scan. We identified 17 risk loci, and 10 risk genes, in total, were proposed as candidate risk genes. While no association was found with $\alpha 2$-macroglobuin and oxidated LDL receptor gene, Von Willebrand factor (VWF) gene indicated a risk effect. Subjects with the risk allele of the VWF gene showed the decreased amount as well as the decreased activity of VWF, suggesting the propensity to be resistant of cerebral infarction. One wide region close to centromere, spanning about 500 kb, indicated a cluster of significantly associated SNPs, and this region contains more than 3 genes. Those candidate risk genes should be warranted in large-scale association studies, and could be targeted to study functional relation with the development of LOAD.

P1-24

Functional memory disorder: Effects of a pilot group therapy program

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Non-organic, functional memory disorders (FMD) represent a large and under researched diagnostic subgroup among patients attending memory clinics. This study assessed a new group therapy program of FMD in a randomized controlled trial with a follow-up period of six months. FMD patients had to fulfill the following inclusion criteria: – complaint of acquired dysfunction of memory that significantly affects the level of functioning at patients job and/or private life, – absence of a recognisable organic cause, – verbal memory and attention test performances in the normal range (better than minus 1.5 SD, – Beck depression inventory below

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18 points, – at least five points on a ten-point FMD questionnaire (Schmidtke, 1995, 2005). 40 FMD patients were randomly assigned to either the experimental (EG) or a wait-list control group (WLC). The 13-week intervention consisted of psychoeducation, cognitive restructuring, stress management strategies, relaxation techniques and mindfulness exercises, and was designed to increase patient's memory self-efficacy. Data were collected at baseline, immediately after the intervention (3 months) and at follow-up (3 months after the intervention) on the Metamemory in Adulthood questionnaire (MIA), the Perceived Stress Questionnaire (PSQ) and the SCL-90-R. At follow-up, the EG showed a significantly higher improvement on the primary outcome measure (i.e., memory self-efficacy; MIA-MSE) than the WCG (effect size: 0.88 SD). Immediately after the intervention, there was a smaller (effect size: 0.19 SD) which did not become significant. We also found a significant reduction of memory-related achievement motivation (MIA-achievement) at three months ($d = 0.95$), but not at 6 months ($d = 0.56$). There were no significant effects on the PSQ and the SCL-90-R. In summary, this new psychotherapeutic group treatment of FMD was effective in reducing FMD-related complaints, while perceived stress or general psychiatric complaints did not change significantly.

P1-25

Development and clinical utility of the geriatric anxiety inventory

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Although anxiety disorders are highly prevalent in older people, there is no generally accepted scale to measure generalized anxiety symptoms in later life. Accordingly, we undertook the development and initial clinical testing of a new scale that we have called the Geriatric Anxiety Inventory (GAI). We developed the GAI with the intention that it would be able to measure anxiety symptoms in both normal older people and those with anxiety disorders. We generated a large number of potential items de novo and by reference to existing anxiety rating scales. Items were chosen to represent fearfulness, worry, meta-worry (i.e., worry about worry), cognitions about anxiety, somatic symptoms of anxiety, anxious mood and anxiety sensitivity. Through consultation with a reference group of psychiatrists, psychologists and normal older people we reduced the number of draft items to 60. We deliberately minimised the number of somatic anxiety items to avoid confounding by the symptoms of chronic health problems commonly experienced by older people. To maximise usability, we applied a one-week self-rating perspective and a dichotomous response scale. We then tested the psychometric properties of the 60 items in a group of 452 community-residing normal older people and 46 patients attending a psychogeriatric service. Items were eliminated from this pool of 60 draft items if they had low item-total correlations, if they were considered potentially confusing to cognitively impaired people, if they were redundant, and if they were reverse scored. By these means, we were able to reduce the number of items to 20. These items all had item-total correlations of 0.39 or above. Test-retest reliability (Pearsons r) after a one-week interval was 0.91 ($p < 0.0000$). In the normal community sample the mean (SD) GAI score was 2.3 (3.8), whereas in the psychogeriatric sample it was 5.2 (5.8). The GAI was able to discriminate quite well between patients with and without any anxiety disorder [$F(1,44) = 16.87$, $p = 0.0002$] and with and without Generalized Anxiety Disorder in particular [$F(1,44) = 10.56$, $p = 0.0022$]. Receiver operating characteristic (ROC) analysis indicated that the GAI was able to detect Generalized Anxiety Disorder using a cutting score of 10/11 with an area under the curve of 0.80. This cut point correctly classified 83%. Further clinical applications are being tested in patients with Parkinson's disease and in patients with phobic disorders.

P1-26

IADL and everyday memory abilities in elderly women

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Background: To demonstrate the characteristics of the Instrumental Activities of Daily Living (IADL), assessed by the Assessment of Motor and Process Skills (AMPS), and everyday memory functions (memory necessary function for daily life) assessed by the Rivermead Behavioral Memory Test (RBMT) in elderly women.

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Participants: The subjects were 102 women divided into two groups. Subjects were over 68 and under 92 years old. One group consisted of 52 women with dementia who lived in a health care facility or in three group homes for dementia patients. The second group consisted of 50 women living independently in their own homes.
Ethical considerations: This study was approved by the ethical committees of our university.
Research methods: AMPS is a standardized tool that assesses IADL ability and is based on the evaluation of the quality of the performance skills displayed in the individual actions in IADL two tasks. The RBMT was originally designed for rehabilitation of adults who have everyday memory problems and it also has norms for elderly people. The highest score for the RBMT is 24. There are three prospective memory (PM) tasks and five retrospective memory (RM) tasks. The cut-off for Alzheimer's disease is 13/14. I divided the RBMT result into three categories, PM, RM and PM+RM.
Results: There were no associations between the AMPS motor skills and PM, RM, and PM+RM in both groups. There were associations between the AMPS process skills and RM in both groups, but no associations between the AMPS process skills and PM in either groups. The scatter chart revealed some subjects with a PM deficit even though they had a normal IADL performance ability level. From those results, it is founded that IADL performance ability and PM were not simultaneously damaged.
Discussion: For a patient with dementia to be able to live on his or her own, IADL and everyday memory ability are essential. The AMPS and RBMT can be used to determine the level of disability. I also discovered that some of the subjects had sufficient IADL abilities but suffered from deficits in PM, which affects daily activities, such as forgetting appointments or not taking prescribed drugs on time. In the future, I intend to study how IADL performance ability and PM ability affect some stages of dementia, and to develop an approach for Mild Cognitive Impairment.

P1-27

Influence of depression and apathy on executive function, as assessed using the Frontal Assessment Battery (FAB) and the dual task, in patients with Alzheimer's disease

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Background and objective: Both apathy and depression can interfere with executive function in patients with Alzheimer's disease (AD) because executive dysfunction, which is indicative of frontal lobe involvement, is correlated with these symptoms. The Frontal Assessment Battery (FAB) is a quick and easy battery for assessing executive function tasks like mental flexibility and sensitivity to interference. The dual task paradigm is also a clinically useful task for assessing divided attention. Both the FAB and the dual task test enable executive function tasks to be evaluated easily in patients with AD. However, the influence of neuropsychiatric symptoms on these tasks remains unclear. We hypothesized that both apathy and depression may influence task performance in patients with AD.
Method: Both the FAB and the dual task were used to evaluate patients with mild to moderate AD (n = 88). Neuropsychiatric symptoms were diagnosed using the Neuropsychiatric Inventory (NPI). A two-way analysis of variance (ANOVA) was conducted between the executive task scores (FAB and dual task) and the absence versus the presence of depression or the absence versus the presence of apathy.
Results: Among the 88 patients with AD, 26 had both apathy and depression, 26 had depression only, 18 had apathy only, and 18 had neither depression nor apathy. The total FAB scores and the dual task scores were significantly different between the AD patients with depression and those without depression and also between those with apathy and those without apathy. Also, a significant interaction between depression and apathy was noted for the total FAB scores and the dual task scores.
Conclusions: Our results suggest that the deficit in the total FAB and dual task scores is larger in AD patients with both depression and apathy, compared with either depression or apathy only. Careful interpretation of these task results may be required for AD patients with neuropsychiatric symptoms.

P1-28

Improvement of cerebral blood flow and depressive symptoms after cilostazol

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administration in a case of Alzheimer's disease

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Behavioral and Psychological Symptoms of Dementia (BPSD) have influences on QOL of patients with dementia. Psychiatrists are often consulted and required successful treatments for BPSD. Depression is one of the most frequent symptoms of PBSD. Alzheimer's disease (AD) is the most common cause of dementia. A large part of AD has concomitant cerebrovascular disorder. Depression after cerebrovascular attack (post-stroke depression, PSD), is reported to be occurred in 40% of post-apopletic patients. However, possibilities are also discussed that depression was caused after mild cerebrovascular disorders without medical history of cerebral apoplex. Therefore, conception of "Vascular Depression" was first reported in 1997. In geriatric patients with depression, treatment strategy may be different from patients of middle age although, antidepressants are sometimes effective on treatment to improve depression with dementia. We used the cilostazol to an AD patient with depression and mild cerebrovascular disorder without apoplexy. Regional cerebral blood flow (rCBF) was assessed by fully automated ROI analysis software (3DSRT). Cilostazol is a platelet aggregation inhibitor and effective in preventing the recurrence of cerebral infarction. In this case, a BDI score was recovered from 22 to 10 while rCBF in right thalamus was 18% increased probably due to cilostazol administration. This case showed the possibility that the primary rCBF increment may improve depressive symptoms as BPSD of dementia.

P1-29

The relationship between psychiatric symptoms and regional cerebral blood flow in the patients with mild dementia

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Background and purposes: The behavioral and psychological symptoms of dementia (BPSD) have been frequently seen in the patients with dementia and often bring serious problems. However, the cause of BPSD is not clarified. Moreover, the precise evaluation of BPSD in mild dementia has not been studied in depth. In this study, we investigated the relationships between psychiatric symptoms and regional cerebral blood flows (rCBF) in the patients with early stage of dementia of Alzheimer type.

Methods: The participants were 65 patients (28 men; 37 women) who have been diagnosed with Dementia. The mean age of the participants was 74.0 (SD = 8.3). To those participants who signed the informed consent, Brain MRI and Single Photon Emission Computed Tomography (SPECT) were performed. The SPECT data was analyzed using 3-Dimensional Stereotactic Region of interest Template (3DSRT), which evaluated CBF of 12 Regions on Interest. Based on the semi-quantified evaluation method of cerebral vessel disease on brain MRI, we divided the patients into two groups according to the presence of severe cerebral vessel disease; V group (i.e. presence of vessel disease; N = 39) and A group (i.e. absence of vessel disease; N = 26). The severity of dementia was evaluated using Clinical Dementia Rating (CDR), and psychiatric symptoms were evaluated using Brief Psychiatric Rating Scale (BPRS). Each psychiatric symptom was designated positive in case the BPRS item score was more than 3. We compared the rCBF of positive BPSD patients with that of negative BPSD patients in each group.

Results: The mean score on CDR in the V group was significantly higher than that of the A group (0.8 ± 0.4 and 1.2 ± 0.6, $t = -2.5$, $p = 0.014$). In the A group, the conceptual disorganization was significantly associated with the reduction of right parietal CBF ($p < 0.05$). In contrast, the motor retardation in the V group was significantly related to the reduction of right central, right precentral, right-parietal and right-temporal CBF ($p < 0.05$), and the depression subscale of BRPS was significantly associated with reduction of bilateral callosomarginal, temporal, occipital, and pericallosal, and right parietal, angular, and hippocampal CBF ($p < 0.05$).

Conclusion: Reduction of frontal CBF has been reported to be seen in the patient with major depression. We could not find the relationships between the reduction of rCBF and depression in the A group, however, the reduction of frontal blood flow was recognized in the V group.

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P1-30

The use of antipsychotics for BPSD of oldest-old Alzheimer's disease patients

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Background: For BPSD of the AD (Alzheimer's disease) patients including oldest-old individuals (more than 90 years olds), a little antipsychotic drugs are used for medical therapy. However, there are little studies according the optimum dose and periods of use for oldest-old patients. We investigated the actual condition of the treatment for BPSD of oldest-old AD in the psychogeriatrics ward.
Methods: We examined the oldest-old AD patients (over 90 years old) who admitted in the psychogeriatrics ward of Tokyo metropolitan Matsuzawa Hospital between July 2002–March 2007. Sixteen patients were admitted in this period.
Results: The average hospitalization was 163 days. After the discharge except four death cases, seven individuals moved to the nursing-care facility institution, three individuals to the hospitals for the old, two individuals to own home. The average dose of antipsychotics in initial hospitalization was 101.6 mg (CP reduced quantity), the average dose of antipsychotics at the time of discharge was 45 mg (CP reduced quantity), and nine individuals was prescribed no psychiatric medication at the discharge. Concluding remarks: It was less doses of antipsychotic dugs needed than that of the previously recommended in the text for the treatment of BPSD of oldest-old AD patients. It was suggested that there needed the sparse dose or no psychiatric drugs under appropriate care settings after once BPSD was medicated by initial prescribed. There are more practical studies needed for the anti-psychotic drug treatment for BPSD of oldest-old AD.

P1-31

Anger management program for patients with mild AD and MCI

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Frustration and anger are common BPSD symptoms. Patients with Alzheimer's disease (AD) feel frustration or anger because of their cognitive impairment and/or lack of self efficacy. Even for healthy people it is not easy to learn to manage feelings of anger. It is much more difficult for patients with mild AD and mild cognitive impairment (MCI). Impaired insight of patients with AD or MCI limit capability of management of anger. They cannot identify antecedents, neither recognize their physical signs of anger, nor reflect on how they behaved and coped with that situation. Common anger management cannot be applied without modification. We have proposed anger management program modified for patients with mild AD.

Anger management program consisted of building therapeutic alliance, distraction techniques, self-talk, relaxation, and reframing. All these modules should be optimized for the patient's capacity. There were some areas especially necessary for modification. It is rather easy to build good relationship. They could not distance themselves from the situation, as the consequences the physiological response might increase, and they could not think more rationally and calmly. They sometimes forgot to state calming self-talk. Relaxation techniques seemed very helpful for coping with feelings of anger as well as anxiety. To teach patients to reduce the likelihood that a difficult situation will become threatening or anger-provoking was generally difficult. To deal with insults and criticisms was another important aspect. They occasionally could not distinguish between insults and criticisms. It was also helpful for them to learn more assertive and to express their own wishes and needs rather than going along with an attitude or behavior with which they disagreed and which would make them angry later.

Our preliminary program should develop into Anger management module for mild cognitive impairment. With proper psycho-education and training, patients with mild AD and MCI will manage their frustration and anger efficiently.

P1-32

Impact of living a life worth (ikigai) on burden among caregivers of the frail elderly in Japan

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To determine the relationship of caregiver burden to psychological factors and family support among caregivers, we conducted a self-administered questionnaire for 250 caregivers of frail elderly listed on a roster for utilization of day service or short stay service from two Home Visit Nursing Care Stations from June to July of 2006. A total of 111 caregivers without missing data were analyzed. Caregiver burden was assessed by Zarit Caregiver Burden Interview (J-ZBI). Family caregivers were defined as co-residents family members who provided a minimum of 1 hour of daily care for at least 3 months. Total score (0–32) of the J-ZBI was dichotomized into heavily burdened (ZBI > 21 points) and low burdened (ZBI < 21). Multiple stepwise logistic regression analysis was performed to detect factors associated with caregiver burden for disabled elderly at home. Heavily burdened caregivers were a significantly higher mean age, had less ikigai ($p = 0.0000$), and emotional expression ($p = 0.04$), striving to achieve to goal ($p = 0.04$) and family support ($p = 0.03$). In multivariate stepwise logistic regression analysis, only ikigai (adjusted OR = 3.8; 95% CI, 1.1 to 12.8) was associated with feeling of burden. The direct effect of ikigai with caregiver burden (92.9%) was much greater than the indirect effect (7.1%). The findings of the present study suggest that living a life worth (ikigai) may play an effectively role in reducing feeling of burden among family caregivers.

P1-33

Factors related to institutionalization among disabled older people; a two-year longitudinal study

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Objective: The purpose of the present study was to examine factors related to institutionalization among disabled older people in a longitudinal study.
Methods: Four hundred and twelve pairs of community-dwelling disabled older adults and their co-residing family caregivers participated in the study. At Time 1, the caregivers were asked to complete questionnaires in relation to their potentially harmful behaviors (PHB) towards their older family members, caregiver burden, patient-caregiver kinship, age and sex, behavioral disturbances and cognitive impairment of their older adults. Visiting nurses obtained the following information regarding the older adults: the severity of dementia, the severity of physical impairment, problems in vision, problems in hearing, age and sex. Data from 398 pairs of disabled older adults and their caregivers were subjected to analyses. The factors related to institutionalization at Time 2 (two years later) among disabled older people were examined by χ^2 tests. Subsequently, relative risk (RR) and its 95% confidential interval (95%CI) were calculated.
Ethics: Written informed consent was obtained from all subjects. This study was endorsed by the ethical committee of the National Institute for Longevity Sciences.
Results: At Time 2, 6.8% (n = 27) of the older people were institutionalized and 52.6% (n = 209) were community-dwelling (with or without their caregiver). Only PHB by family caregiver at Time 1 has found to be related with institutionalization of the disabled older adult ($\chi^2 = 4.31$, RR = 2.43, 95%CI = 1.02–5.78). The other variables at Time 1 did not have any correlations with institutionalization of the disabled older adult.
Conclusions: In the present study, only PHB towards the disabled older people by family caregivers at the previous time point was associated with institutionalization of the disabled older people at the follow-up. In order to allow disabled older people to stay their own home, it is necessary to provide interventions in order to prevent family caregivers from engaging in PHB. The factors related to PHB should be taken into account when the interventions are planned.
Acknowledgement: The authors wish to thank the participants of this study, which was in part supported by research grants provided by the Ministry of Health, Labor and Welfare (Grant No. H17-C029, H19-C025, principal investigator: YA). The authors are grateful for support from Mrs. Junko Nitta for her administrative support for this project.

P1-34

Comparative study of the perceived difficulties of caring for relatives with early and late onset dementia

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Background: Despite the abundance of findings on family caregivers of patients with late onset dementia (LOD), few reports have indicated the problems faced by caregivers of early onset dementia (EOD) patients.
Objective: To compare family caregiving situations for patients with EOD and late onset dementia LOD, and to identify the specific problems experienced by relatives caring for EOD patients.
Methods: The participants were chosen from 92 consecutive caregiver-patient dyads, comprising coresiding family caregivers and outpatients who fulfilled the diagnostic criteria for dementia. The patients were assessed according to cognitive function, neuropsychiatric disturbances and the severity of dementia. The caregivers completed a self-administered questionnaire that included items on their sociodemographic status and caregiving situation.
Results: In total, 68 dyads were eligible for the analysis, 14 of which included patients with EOD and 54 of which included patients with LOD. There were no significant differences between the two groups in terms of patient clinical features, duration of caregiving, number of hours during which caregivers were relieved per day or number of hours of caregiving per day. No significant associations were detected between the type of dementia and caregiver characteristics (such as health status), patient difficulties due to activities of daily living (ADL) or caregiver burden. However, the caregivers of EOD patients had greater perceived difficulties due to patient behavioural disturbances than did the caregivers of LOD patients, even after adjusting for confounding variables.
Conclusions: This is one of only a few studies to compare the psychosocial effects of the onset of dementia on patients and their family caregivers. Our findings demonstrated that additional resources, such as care services, should be provided for sufferers of EOD, in order to allow family caregivers to cope with difficulties associated with patient behavioural problems.
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P1-35

The experience of burnout among home caregivers of patients with dementia: the relation to depression and quality of life

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Background and purpose: In Japan, it has been estimated that 1.6 million people suffer from dementia and 67% of those patients receive care at home. It is generally recognized that caregivers of patients with dementia may experience chronic and emotional strain. Therefore, caregivers of patients with dementia may prone to burnout. The objective of the present study was to examine the relationships between burnout, quality of life, and depression in the home caregivers of patients with dementia.
Methods: Participants were caregivers of patients with dementia (39 male; 45 female), who first visited for the Kitasato University East Hospital between November 2001 and December 2006. Total of 84 caregivers participated in the study, and the mean age of the caregivers was 59.6 (SD = 14.0). Those participants who were interested in participating and signed the informed consent completed 3 questionnaires: Beck Depression Inventory Second Edition (BDI-II), WHO Quality of Life 26 (WHO-QOL26), and Pines Burnout Measure (BM). These measures assessed the severity of depressive symptoms, quality of life (QOL), and the levels of burnout. In addition, the burnout scores were classified as 4 groups: no burnout (N = 49), risk of burnout (N = 19), burnout present (N = 16), and clinically depressed (N = 0).
Results: The Peasons correlation coefficients were calculated, and the scores on BM were significantly correlated with the scores on BDI-II ($r = .67$, $p < .01$) and WHO-QOL26 ($r = -.53$, $p < .01$). The scores on all subscales of WHO-QOL26, especially psychological subscale had significant negative correlations with the score on BM. A one-way analysis

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of variance was conducted for 4 groups of burnout, and revealed that there were significant differences between the groups of burnout in the score on BDI-II and WHO-QOL26 ($F(2, 81) > 10.45$, $p < .01$). Post hoc comparison revealed that there were significant differences between each group of burnout in the scores on BDI-II. For the scores on WHO-QOL26, there were significant differences between no burnout group and risk of burnout group, and between no burnout group and burnout present group.

Conclusion: The results from the present study indicated that caregivers who experienced higher levels of burnout were more likely to have severe depressive symptoms and poor QOL. These findings suggested that caregiver intervention, which aimed to reduce burnout, may benefit from the incorporated strategies to reduce depression and increase QOL.

P1-36

Roles and outcomes of training to foster senior dementia care leaders in Japanese dementia care training system

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Dementia care training has been implemented since 2001 in Japan based on the standard curriculum of the Ministry of health, labour and welfare with the aim of improving dementia care in quality. This dementia care training consists of training for Dementia care practitioners and training for Dementia care leaders both organized by local prefectural governments, and training to foster senior Dementia care leaders conducted in the three Dementia care research and training centers located in Sendai, Tokyo and Obu. Training for Dementia care practitioners targets people with basic knowledge about dementia care, nearly equal to certified care workers, etc. as well as with experience of long term care over 2 years, aiming to provide practical knowledge and skill which enables them to support people with dementia to lead an independent life according to each ability. Meanwhile, the goal of training for Dementia care leaders is to educate trainees so that they could promote qualitative improvement of dementia care through guiding and supporting care workers in addition to coordinating team care as dementia care leaders. Further, training to foster senior Dementia care leaders is developed with a view to train dementia care leaders in each region, who are able to draw up or plan curriculum and also take charge of lectures, seminars and training in training for Dementia care practitioners and training for Dementia care leaders. The training program is well conceived to accomplish the purposes; the capacity is about 20 people, the period is 10 weeks, and trainees are able to learn training methodology concerning dementia care chiefly by way of seminars and training. The program involves general views and systematic understanding of Dementia care training, planning method to foster human resources, understanding of method of educational guidance and seminars and training to cultivate practical skill. In this study, the purpose, curriculum and methods of training, attribute of trainees and the results are reported in detail, while the significance of the training with the aim of improving quality of dementia care is examined.

P1-37

Effect of mindfulness-based psychotherapy on burden of caregivers of Alzheimer's disease patients

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Introduction: In Japan, the majority of patients with Alzheimer's disease (AD) live outside institutions, and this creates a serious psychological morbidity among their caregivers. Mindfulness is well known to be effective for treatment of depressed patients, but no study has yet examined whether mindfulness-based psychotherapy intervention is effective for reduction of depression in caregivers.

Aims: To evaluate whether mindfulness-based psychological intervention reduces the depression in caregivers of patients with AD and increases the quality of life (QOL) of the patients.

Participants: Ten Japanese patients with AD (7 males and 3 females, mean age 76.0 y, SD 6.6 y) and their 10 caregivers(3 males and 7 females, mean age 63.9 y, SD 11.0 y). The patients are living in the community with their caregivers.

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Method: Psychological intervention was done for twenty weeks. The first 10 weeks were the baseline phase, and supportive psychotherapy and psychoeducation were given. The second 10 weeks were the intervention phase, and mindfulness-based psychotherapy was conducted in addition to the same supportive psychotherapy.
Measures: We used POMS and Zarit8 for caregivers, and MMSE, QOL for dementia scale (QOL-D), and dementia happy check (DHC) for patients with AD. Statistical analyses were performed by SPSS 10J.
Results: The caregivers showed significantly lower scores on the POMS depression scale at the 20-weeks than at 0 and the end of 10 weeks ($p < 0.05$). The MMSE scores of patients showed no significant change, but the QOL-D and DHC scores showed a significant increase ($p < 0.05$).
Discussion: The present study revealed that mindfulness-based psychological intervention contributed to reduction of depression scores on the POMS in caregivers. It was also found that the QOL of patients improved as a result of the intervention.

P1-38

Degradation of tau protein in cultured cells

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Neurofibrillary tangles (NFTs) are neuropathological hallmarks of Alzheimer's disease (AD) and abnormally hyperphosphorylated and ubiquitinated tau is the major protein component of NFTs. However, the mechanisms of degradation of tau protein are still unclear. The ubiquitin proteasome system is the major protein quality control system in eukaryotic cells and neurodegenerative diseases including AD, are characterized by aggregates and inclusions of aberrant proteins. Therefore proteasome might be the most important key player in degradation of aberrant proteins. Therefore the mechanisms of degradation of tau protein were investigated employing several protease inhibitors including proteasome inhibitors. SH-SY5Y cells were treated with MG-132 and lactacystin and tau protein was analyzed by western blot. After treatment of cell with MG-132 or lactacystin, ubiqitinated protein products were increased however tau protein levels were unaltered. This study suggests that tau might be degraded by other mechanisms than proteasome in cultured cells, and other degradation pathways should be analyzed.

P1-39

Cell cycle re-entry induces intraneuronal amyloid-β accumulation in CaMKII-MYC mice: pathogenic implication for the mitotic abnormality in Alzheimer's disease

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Recently, cell cycle re-entry (CCRE), namely, aberrant re-expression of a series of cell cycle-related proteins has been reported in vulnerable neurons in Alzheimer's disease (AD). On the other hand, growing evidence suggests an initial role of intraneuronal amyloid-β (Aβ) accumulation in the pathogenesis of AD. A possible connection between the mitotic abnormality and the Aβ pathology is worth investigating under a hypothesis that AD is a disease of inappropriate cell cycle control. To elucidate involvement of CCRE in neurodegeneration accompanied by Aβ pathology, we have developed a double transgenic mouse model that expresses a powerful cell cycle inducer, human c-MYC, specifically in forebrain neurons. We used two lines of animals: CaMKII-tTA mice that were applied the tetracycline-controlled transactivator (tTA) system under the control of forebrain specific promoter, calcium-calmodulin-dependent kinase II (CaMKII); and tetO-MYC mice that were applied the Tet system to obtain a tightly controlled MYC gene expression, in which the MYC gene was inserted behind the tet operator (tetO). We crossed these two lines of mice to obtain the double transgenic CaMKII-MYC mice. The CaMKII-MYC mice express MYC by deprivation of a tetracycline analog, doxycycline, from diet (MYC-On), while those mice repress MYC expression by continuation of doxycycline treatment (MYC-Off). After the treatment, the animals were sacrificed and the brains were

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processed for immunocytochemistry. The brain sections were immunostained with C-terminal specific antibodies for Aβ1–42 after the treatment with formic acid. After 4 or 8-weeks of MYC induction, brain sections of MYC-On mice displayed robust expression of MYC and CCRE markers such as proliferating cell nuclear antigen and incorporation of bromodeoxyuridine in the hippocampal neurons in comparison to the basal levels in MYC-Off mice. Of particular interest, in MYC-On mice, but not MYC-Off mice, intraneuronal Aβ immunoreaction was detected in the hippocampal neurons predominantly in the CA1 region. Relative immunointensity measurements of the intraneuronal Aβ in the hippocampal CA1 region revealed a significant deference between MYC-On mice [36.0 (12.0); mean (SD), arbitrary unit] and MYC-Off mice [13.5 (4.8)] ($p < 0.05$). No apparent Aβ immunoreaction was observed in the cerebellar Purkinje cells of both MYC-On/Off animals. These results suggest that CCRE may be one of the basic mechanisms underlying the neurodegeneration in AD.

P1-40

Effect of reading aloud and arithmetic calculation on inhibitory function in the elderly

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Recent investigations demonstrated that reading aloud and solving simple arithmetic activated prefrontal lobe more than other many tasks. Such investigations also indicated that by repeating such tasks for half year in the aged with dementia, function of pre-frontal lobe as measured by FAB(A frontal assessment battery at bedside) and general intelligence score (MMSE) improved significantly. Therefore, the purpose of this study was to examine whether repeating these tasks improve inhibitory function (measured by stroop test and SRC) as well as intellectual one in the aged. 35 individuals in a nursing home for elderly were randomly assigned to one of experimental ($N = 20$) or control ($N = 15$) groups. The materials for the training program were two tasks in the arithmetic and Japanese language, which were systematized basic problems in reading and arithmetic. The problems were printed on both sides of A4-size paper. The participants completed at least four or five sheets of each task prepared for each individual for a day and their work would be assessed by the staff. The mistakes were corrected by the participants. The daily learning time for the two tasks was approximately 15 to 20 minutes. They were given the training program three times a week over half a year. To estimate the change in inhibitory function, stroop test, SRC task, FAB, and FAB were measured in all participants prior to the start of the training program and 6months after the program had taken place. As results, error rate in the stroop test for the experimental group decreased significantly after 6 months although control group did not show significant change. The same tendency was obtained in error rate in SRC task. However, reaction time in SRC one significantly decreased in both the experimental and control groups. The FAB score of the experimental group showed significant improvement after 6 months of training. But, the control group did not show significant change after 6 months. These results indicate that learning tasks of reading aloud and arithmetic calculation can be used for cognitive rehabilitation of the aged with dementia.

P1-041

A proposal of modified method for cognitive rehabilitation for patients with *frontal cognitive dysfunction*

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Patients with *frontal cognitive dysfunction* (FCD) suffer from aggressiveness, disinhibition, apathy, stereotyped behaviors, ideomotor apraxia, disability of abstract thinking and judgment. FCD symptoms involve frontal vascular lesion, Alzheimer's disease, frontotemporal lobar degeneration, and related diseases. Kawashima et al. proposed the learning therapy as a cognitive rehabilitation (CR) on the basis of SPECT studies, but patients with FCD cannot

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follow procedures of this CR because, in particular, their stereotyped behaviors, apraxia and incapability in abstraction prevent them from following the therapy tasks even when their aggressiveness and disinhibition are well controlled on medications. A study was help with this problem in which patients with FCD appear to be mentally in well condition when the therapy program accepts fully their stereotyped behaviors. In the present study, we hypothesized that frontal cognitive function related to work operations could be grouped into two functions: *abstractive ability* and *executive function* for work operations. For example, to think meanings of materials or colors is performed by abstractive ability, while stereotyped behaviors or constant schedule is related to executive function. Based on this hypothesis, we analyzed the processes of every task of CR according to occupational therapy theory and divided work operations into abstractive ability or executive function. Then we designed tasks which guaranteed behaviors by motor thought and also gave the patients assignments that needed abstraction. Finally, we provided a feedback to patients' abstractive achievements using *"praises"*, to be concrete, cheering and clapping or skin ship. With this feedback model, improvement of their behaviors such as enhanced activities of daily life and a decrease in frequency of stereotyped behaviors, were availed. Three patients (Case 1: 58-year-old woman with corticobasal degeneration, Case 2: 63-year-old man with severe semantic dementia, Case 3: 63-year-old man with early onset Alzheimer's disease with the frontal lobe atrophy) enrolled in our trial study. We present three cases that could follow the modified CR program and could take satisfactory clinical course maintaining abstractive ability for more than eight months and that this feedback model of modified method for CR was effective for behavioral change of FCD.

P1-42

Thiamine administration for reducing post-ECT confusion

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Electroconvulsive therapy (ECT) is often used in elderly patients with depression. The main side effect of ECT, or cognitive impairment such as retrograde amnesia and confusion, is usually transient in self-remitting courses. In elderly patients, post-ECT confusion is occasionally delayed, so that ECT is forced to be discontinued. Various psychotropic medicines have been prescribed for preventing post-ECT confusion, and their beneficial effect is controversial. Recently, Linton et al. reported the beneficial possibility of thiamine on post-ECT confusion, and we report a case of major depression, whose post-ECT confusion was successfully improved with thiamine supplementation. A 74-year-old man presented with a severe delusional depression and tried a suicidal attempt. He was assigned to have bilateral modified ECT 3 times a week. Soon after the first ECT, he developed confusion with psychomotor excitement. He consistently showed severe confusion with agitation throughout the course of ECT. His confusion became insidiously worse with the course of ECT. The therapy was stopped after five trials. He was partly improved, and antidepressants were prescribed after ECT. Thereafter, he relapsed into depression within a year, and again assigned to take ECT of 3 trials a week. He exhibited severe confusion with disorientation, agitation, insomnia and excitement after three trials. These symptoms persisted for more than 24 hours. Thiamine was medicated orally at 100 mg/day. His confusion was improved within 24 hours on the next day, and he was cooperative and fully orientated. Thiamine of 100mg a day was continued. Further five trials were completed without post-ECT confusion, and he remitted well in his mood. In the present case, a series of modified ECT consistently developed severe confusion. Thiamine administration immediately resolved post-ECT confusion, and prevented further post-ECT confusion. This result suggests that post-ECT confusion observed in this case may be associated with thiamine deficiency. Thiamine supplementation has a beneficial effect on treating post-ECT confusion.

P1-43

Identification of preventable factors in post-operative care associated with delirium

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Post-operative delirium (POD) occurs in up to 53% patients undergoing orthopedic hip or knee surgery. Peri-operative clinical pathways designed to reduce morbidity in hip fracture patients have shown

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successful reduction in delirium risk. This study builds upon the results of the Delirium at Risk (DEAR) studies which indicate that POD is associated with predisposing factors such as age, cognition, substance abuse, and function. This study examines whether preventable factors in post-operative care may also contribute to POD in arthroplasty patients. We conducted a retrospective chart review of 201 elective and hip fracture patients enrolled in the DEAR studies. Factors associated with POD in published studies were examined for association with POD in this population using Chi-squared and t-tests. Association between specific factors and POD was examined using univariate and stepwise logistic regression models. The number of factors and the DEAR score were examined in a multiple logistic regression model. Forty-five (23%) patients had POD. 97% of those with POD had preventable factors of care that are have shown previous association with POD, but the number of factors did not differ significantly between those with POD and those without. 31% of those with POD had no bloodwork, medreview, physical exam, or reason for their delirium noted, and only 2% of individuals with POD had a full work-up for their delirium. POD was significantly associated with DEAR score. Poor PO intake (RR 2.45), elevated post-void residual volumes (RR 1.58), and insomnia (RR 3.42) were associated with delirium in univariate analyses. The majority of patients with POD did not receive optimal therapy for these factors. In stepwise regression models, insomnia and poor oral intake remained significantly associated with POD ($p < 0.02$) when controlling for the number of delirium risk factors. Although this study did not indicate significant association between deviation from optimal care and occurrence of POD in this population, it does indicate that most patients experience multiple preventable factors of post-operative care which have shown association with POD in the published literature, This abundance of preventable factors of post-operative care could contribute to the risk of delirium and the treatment of this patient population should therefore be further optimized.

P1-44

Incidence and predictors of postcardiotomy delirium

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The high rates of postcardiotomy (PC) delirium, its incidence variability, and the uncertainty of its risk factors have led us to carry out this prospective, observational study in PC patients at the Minneapolis Veterans Affairs Medical Center. Our objective was to determine the incidence and predictors of delirium after cardiac surgery. Operative procedures included 1) heart valve replacement or repair, 2) coronary artery bypass graft surgery, 3) closure of patent foramen ovale, or 4) all three or any of the combinations of the three. Patients were given a pre-operative delirium assessment battery that was also performed daily from postoperative day 1 to 7. Pre-operative variables included demographics; burden of medical comorbidity; pain assessment; history of dementia, delirium, stroke, brain injury, myocardial infarction, chronic pulmonary disease; history of alcohol and other substance abuse; visual and hearing impairment; presence of psychiatric symptoms or diagnoses; medications; creatinine levels; and average and peak 24-hour troponin levels. Intraoperative factors included durations of anesthesia, surgery, and intubation; cardiopulmonary bypass time; and ischemic time. For the initial three days postoperatively, an average morphine equivalent of administered opiates was calculated. Postoperative pain was assessed daily. Of the 59 patients enrolled in the study, 53 (mean age = 64 y/o; age range = 46 to 81 y/o) completed it. Twelve of the 53 patients (23%) met criteria for a diagnosis of PC delirium using the Confusion Assessment Method. A history of stroke ($p = 0.006$), mildly increased preoperative pain rating ($p = 0.03$), higher mean preoperative medical comorbidity score ($p = 0.05$), and an increased pre-operative creatinine level ($p = 0.03$) were significant predictors of PC delirium. Eighteen of the 53 patients (34%) met criteria for PC subsyndromal delirium. When these patients were combined with those with delirium, a history of stroke ($p = 0.001$) and diabetes ($p = 0.04$) emerged as predictors. We found that delirium after cardiac surgery was significantly associated with a history of stroke, high

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medical comorbidity, and an increased preoperative creatinine level. History of stroke and diabetes also predicted the development of delirious symptoms. Neuroimaging may be beneficial in identifying the location and extent of infarction that correlates with PC delirium and may assist surgeons in identifying patients who may be at increased risk for PC delirium.

P1-45

Osteosynthesis or prosthesis for demented patients with femoral neck fracture?

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Background: Hip fracture is a global and a growing public health problem. More women than men sustain hip fractures, the incidence increases exponentially with age and mean age is above 80. The mental state can predict survival and functional outcome for hip-fracture patients. Some studies however, have either not specified the mental status or excluded patients with dementia, confusion or severe cognitive dysfunction. About one third of hip-fracture patients suffer from dementia and are prone to develop delirium and may have difficulties adhering to postoperative instructions. How should this affect the choice of surgical method?

Methods: A total of 180 patients ? 70 years, were operated on using Internal Fixation (IF) when they had an undisplaced femoral neck fracture and Hemiarthroplasty (HAP) if the fractures were displaced. Their mental state was assessed according to the Mini Mental State Examination, Organic Brain Syndrome Scale and dementia and delirium were diagnosed according to the DSM-IV criteria. Their personal Activities of Daily Living (P-ADL), walking ability, use of a walking aid and hip pain were also assessed. All survivors were reassessed at four and twelve months after surgery.

Results: A higher proportion of patients with and without dementia, operated on using HAP regained their prefracture mobility at the one-year follow up compared to those operated on using IF. Six out of 111 patients dislocated their HAP during hospitalization and during an episode of delirium, non of them had dementia.

Interpretation: The presence of dementia is not a reason for disqualifying patients from the surgical method most appropriate for their fracture type. Postoperative delirium has to be prevented and treated in all patients to minimize the complication rate after surgery.

P1-46

Causes of drug induced delirium in a medical ward in India

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Delirium is a commonly encountered medical condition in different wards of a hospital, especially in older patients (over 65 years). Causes of delirium in old age is multi-various metabolic causes like ureamia, hypertensive enchephalopathy, other viral meningo-enchephalopathy, delirium in dementia and other degenarative disorders, even in AIDS delirium in dementia may occur. Drug induced delirium accounts for a sizeable proportion of all delirium cases in a medical ward. A total of 124 delirium cases those were sought for psychiatrist's referral in one calender year in medical ward of midnapore medical college hospital were analysed. Later on investigation was made as to their possible etilogies on history, clinical and laboratory examination. 42 cases of which 29% were diagnosed as delirium arisen out of drug used in the course of treatment of the basic disease most commonly encountered drugs, here, were- 1) ciprofloxacin, ofloxacin type quinolones. 2) inj. metchormide (anti emetic) either alone or in combination with inj.ranitidine 3) inj. atropine used in huge doses in treating organophosphorous insecticide poisoning cases 4) choloroquine and quinine in malaria 5) digoxin, 6) anti-parkinson's drugs like trihexyphinidyl, 6) steroids like prednisolone in high doses 7) sedative and hypnotics-zolpidem etc. 8) isoniazid used in long duration in treating tuberculosis, 9) inj. morphin, pethidine etc, 10) anti hypertensive beta blockers like propanalol hydrochloride, diuratics etc. advance age is a risk factor for devoloping delirium in both sexes. Delirium is also a bad prognostic sign for course of outcome and a significant portion of delirious cases die in 1st year of follow up. An awareness and caution in drug use and its doses building is necessary to prevent delirium. 10–15% of patients older than 65 years develop delirium after admission. An all round vigilance on drug use in elderly

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will give rich dividends in delirium prevention. One up study of those delirium cases shows a relapse of delirium in those elderly as 35% and 3 cases were noted in 1 year period that constitutes 8% of drug induced delirium cases.

P1-47

The comparison of the efficacy between risperidone and quetiapine in elderly patients with delirium

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Object: Many studies showed that risperidone and olanzapine in treatment of delirium were similar to haloperidol, in side effects were superior to that. Quetiapine is frequently used in delirium because of lower risk of side effects and sedative effect. However, the studies of quetiapine are very few. This study was designed to evaluate difference of risperidone and quetiapine in treatment of delirium.
Methods: We divided 2 groups of delirious patients(risperidone and quetiapine). 42 subjects were randomly assigned to receive a flexible dose regimen of risperidone or quetiapine by double-blind design. The initial dose of each drug was 0.5 mg (risperidone) or 50 mg (quetiapine) twice a day. The dosage was increased depending on the status of delirium during the 7 days. We compared the risperidone group and the quetiapine group by DRS and MMSE at baseline and after 1 week. At the end of the study (7th day), the mean dose of the risperidone group was 1.95 mg (SD = 0.84), and the mean dose of the quetiapine group was 154.76 mg (SD = 41.55). Paired and unpaired Student's t tests, Fisher's exact test, Mann-Whitney U test, and two-way anaylsis of variance with repeated measures were used as appropriate.
Results: There were no differences in socio-demographics, baseline Delirium Rating Scale (DRS), baseline MMSE. The mean initial DRS score for all subjects at screening was 23.43 (SD = 5.79). There were no significant differences in mean DRS scores between the risperdone group (mean = 24.33, SD = 4.90) and the quetiapine group (mean = 22.52, SD = 6.55) (t = 1.013, p = 0.317). There were no significant differences in mean MMSE scores between the risperdone group (mean = 6.38, SD = 3.49) and the quetiapine group (mean = 6.24, SD = 4.45) (t = 0.116, p = 0.908). After 1 week, There were no significant differences in mean MMSE, DRS score between the risperidone group (mean DRS score = 14.57, SD = 4.28; mean MMSE score = 13.19) and the quetiapine group (mean DRS score = 12.19, SD = 3.31; mean MMSE score = 12.43, SD = 3.92).
Conclusion: The treatment of delium was effective both in risperidone group and quetiapine group by DRS and MMSE. Therefore our results showed that the risperidone and quetiapine were effacious in the treatment of delirious patients. There were no significant differences in the degree of effects in both drugs. The quetiapine was as effacious as risperidone in the treatment of delirious patients. In future, the sample size needs to be increased in the studies of delirium.

P1-48

Sundown syndrome in elderly patients with dementia is ameliorated by showing the DVD of fashionable stories in their younger days

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Background: It has been demonstrated that "sundown syndrome" is associated with increased agitation and confusion that occurs in the late afternoon, and induces disturbances of sleep in elderly patients with dementia. Some reports suggest that the mention of fashionable stories in the younger days is as effective therapy on sundown syndrome in demented patients. To explore whether showing the DVD of fashionable stories in the younger days ameliorates sundown syndrome in elderly patients with dementia, we showed the DVD to them in the every evening during a month in our hospital.
Methods: We showed the DVD of fashionable stories in the younger days to 48 elderly patients with dementia (23 male and 25 female, 58 to 99 years) in the every evening (16 to 18 o'clock) during a month (January 4 to 31, 2007), and investigated their conditions during and after showing the DVD.
Results: Of 48 patients, we could show the DVD to 40 patients, and 34 patients were interested in the DVD in these 40 patients. Showing the DVD indicated the significant decrease of agitation, confusion and antipsychotic therapy in these patients.
Conclusions: We suggest that showing the DVD of fashionable stories in the younger days significantly

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decreases agitation, confusion and antipsychotic therapy, and that DVD therapy can ameliorate sundown syndrome in elderly patients with dementia.

P1-49

Intramuscular olanzapine versus intravenous haloperidol for the elderly patients with delirium: A randomized, open prospective study

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Purpose: The present study aimed to provide preliminary data on the effectiveness and tolerability of atypical antipsychotics, intramuscular (IM) olanzapine and intravenous(IV) haloperidol for the elderly patients with delirium.
Methods: Fourty-two elderly patients with delirium were randomly assigned to either olanzapine IM or haloperidol IV groups, with a flexible dosing schedule for 7days. The Delirium Rating Scale-revised-98(DRS-R-98), the Korean version of mini mental status examination (K-MMSE) and clinical global impression-severity (CGI-S) were assessed daily. The Simpson Angus Rating Scale, the Barnes Akathisia Rating Scale and the Abnormal Involuntary Movement Scale were used for the assessment of side effects.
Results: The DRS-R-98 and CGI-S scores were significantly decreased over time in both treatment groups without any significant group difference and time by the group interaction effect ($P < 0.0001$). The mean duration of stabilization were 6.4 ± 3.2 days for the olanzapine IM group and 6.9 ± 2.3 days for the haloperidol IV group without group differences. Both treatments were well tolerated and there were no serious adverse events in both groups.
Conclusions: This study showed that either olanzapine IM or haloperidol IV would be effective and tolerable for treating patients with delirium. Adequately powered studies with a head-to-head comparison design will be mandatory to draw any definite conclusion.

P1-50

Open-trial of risperidone for the treatment in the elderly

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Delirium is a common disorder in the elderly, who are more prone to antipsychotic-related adverse effects. A two-week open-label trial of risperidone for delirium treatment was conducted to assess the efficacy and tolerance of this medication in elderly patients. Twenty-two patients with DSM-IV defined delirium were investigated. All patients were hyperactivity-hyperalert variant of delirium. They received a fixed-dose of risperidone (0.5–3 mg). Delirium was assessed using the Delirium Rating Scale (DRS) at baseline and days 1, 3, 5, 7 and 14 after initiation of risperidone treatment. Clinical and demographic data, risperidone therapy-related information were also collected. Delirium resolved in all patients over the course of treatment. The mean period of delirium resolution was 4.0 ± 2.9 days. The mean DRS score at baseline was 20.7 ± 3.0. The DRS score significantly improved from baseline to day 1 of treatment. Delirium improvement was even greater on day 3, and continued to improve until the endpoint. Mild side effects were present in 27.3% of the patients. A stepwise logistic regression model identified that a decrease in 2 points or higher on the DRS on day 1 was associated with side effects. Our findings suggest that fixed low-dose risperidone may be effective and safe for the treatment of delirium in elderly patients.

P1-51

Usefulness of Korean version of Mini-Cog in people with low education

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Background: In Korea, the dementia is a main public health problem, and mini-cog is expected to be used as a rapid and easy-to-use screening tool which can be routinely used by primary care physicians to detect the problem. As there are many elderly people

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with low education in Korea, the evaluation of the usefulness of this test in these people is needed.

Objective: To test the usefulness of the Korean version of the Mini-Cog in people with low education, by analyzing its performance in people with high and low educational level.

Methods: The Mini-Cog-K was applied to elderly people who are living in community. All subjects underwent the evaluation procedure composed of the clinical assessment, neuropsychological test battery, and the diagnosis of dementia based on the DAT criteria of DSM-IV. The subjects were divided in two groups by the level of education. In each group, ROC curve analysis was performed to test the sensitivity and specificity, and to obtain optimal cut-off value.

Results: There was no remarkable difference in the cut-off value, the sensitivity and the specificity of the Min-cog between the low education and high education group. Mini-cog can be applied usefully to the low education group.

P1-52

Relationship between mini mental state examination (MMSE), clock drawning test, confusion assessment method and delirium rating scale (DRS) at elderly patients submitted a coronary artery bypass graft: A prospective study

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Objectives: Delirium is a common organic psychiatric disorder with high prevalence and incidence rates in elderly patients at general hospital. The essentials features include widespread cognitive impairment, abnormal psychomotor behaviour, relatively rapid onset and a fluctuating course, usually of brief duration. In the context of cardiac surgery, the incidence of delirium is high, with recent literature reporting values as high as 72%. As the etiology of delirium after cardiac surgery remains largely unknown, only few causative factors are established.

Methods: We conducted a study in the cardiothoracic surgery department of Coimbra University Hospital, a 1500-bed, university-affiliated hospital. The study design was a prospective and observational study. Every patient, in a total of 160 patients, admitted for coronary artery bypass graft (CABG) was screened for cognitive impairment (CDT; MMSE; IADL), depression (GDS) and after surgery a specialized psychiatry observed the patients until discharge. The diagnosis of delirium was based on the psychiatric assessment and the Confusion Assessment Method (CAM).

Results: A total of 15 cases of delirium were reported. We are now under statistical evaluation, combining preoperative measures (CDT; MMSE; IADL; GDS) with a total of 58 measures normally obtained from the cardiothoracic surgery database, reporting peri and postoperative variables. The influence of pre-cognitive impairment measured with MMSE and DRS are presented.

P1-53

Bender-gestalt test as a screening measure for dementia with Lewy bodies showing mild to moderate dementia

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A clinical differentiation of dementia with Lewy bodies (DLB) from Alzheimer's disease (AD) is often difficult, even if diagnostic criteria of DLB are applied. In this study, we examined an utility of the Bender-gestalt test (BGT) as a screening measure for DLB, comparing BGT scores between DLB and AD patients.

Twenty DLB patients (DLB group) and 30 AD patients (AD group) met the consensus criteria for the clinical diagnosis of probable DLB (McKeith et al., 2005) and the NINCDS-ADRDA criteria for the clinical diagnosis of probable AD, respectively. A DLB group, AD group, and 21 non-demented elderly participants (control group) were subjected to the BGT, Global Deterioration Scale (GDS), Clinical Dementia Rating (CDR), and Mini-Mental State Examination (MMSE). The BGT performance was scored according to the Pascal-Suttell

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method. In the statistical analysis, continuous variables were compared with the t-test or ANOVA and Tukey's HSD post-hoc tests, and categorical variables were compared with the chi-square test. Differences with p values less than 0.05 were considered significant in all tests.

As the results, there were no significant differences between the three groups for the age, years of education, the GDS, CDR, or MMSE score, except for GDS, CDR, and MMSE scores in the control group. On the BGT, the DLB group showed significantly higher (that is worse) scores than the other groups (mean score ± SD was 148.5 ± 40.0 in the DLB group, 71.4 ± 19.4 in the AD group, and 58.2 ± 19.5 in the control group, respectively). When a cutoff point of 98 was used to differentiate DLB from AD, the patients exceeding 98 were 19 of 20 (95%) in the DLB group, one of 30 (3%) in the AD group, and none of 21 (0%) in the control group. The sensitivity and specificity of this cut off point for differentiation of DLB from AD were 0.95 and 0.97, respectively.

The DLB group more frequently and prominently showed the destroying gestalt than the other groups. In addition, the DLB group occasionally showed unacceptable performances, for example, dots like the waxing and waning of the moon, numerals, or lines like a box.

In conclusion, the BGT is a useful clinical measure to differentiate DLB from AD. Further studies about the quality of the BGT performance are needed to clarify the relationship between the visuoperceptual disability in DLB patients and DLB-related findings in DLB brains, including hypoactivity in the occipital lobe and Lewy pathology in the secondary visual pathway.

P1-54

The prevalence of DLB among consecutive cases referred as patients with depression in the psychiatric ward of a university hospital

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It is not always easy to distinguish depression from dementia and vice versa. Regarding this issue, it has been well known that depression may coexist with Alzheimer's disease (AD) and exaggerate the intellectual deterioration, and thus clinicians can misdiagnose depression-associated dementia (so called pseudo dementia) as AD. On the other hand, increasing attention has been paid to Dementia with Lewy Bodies (DLB) because of its unexpectedly higher prevalence rate among dementia causing illnesses. In addition, many reports have showed that patients with DLB often develop depression during its clinical course. Some previous study noted that sometimes patients with DLB had been misdiagnosed as depression, especially therapy refractory one. In fact, we have encountered several cases whose diagnosis had been refractory depression was changed to DLB. Therefore, we attempted to retrospectively estimate the prevalence of DLB among consecutive clinical cases referred as patients with depression in our psychiatric ward of university hospital. The subjects of the present study fulfilled the following criteria: inpatients of our ward; having diagnosis of certain mood or related disorder at admission; aged 50 years or older, and availability of a set of clinical examination. The set included a battery of neuropsychological tests, Single Photon Emission Tomography, MIBG scintigraphy, and Magnetic Resonance Imaging, and a series of autonomic assessment. The diagnosis of probable and possible DLB was made best on the clinical diagnosis criteria of the consortium of dementia with Lewy bodies. Besides the two diagnoses, we set a diagnosis of supportive DLB which has some characteristic features but fall short of the two. We examined the data of 175 inpatients who fulfilled above noted criteria. The mean (SD) length of hospitalization for the subjects was 71 days (± 48). The examination revealed that 2 cases (1.2%) were diagnosed as having probable DLB, 8 cases (4.7%) were possible DLB, and 2 cases (1.2%) were supportive DLB. In summary, we found an unexpectedly high prevalence of DLB among consecutive clinical cases referred as patients with depression in our psychiatric ward. When we encounter case with apparently refractory depression, we should call DLB to our mind.

P1-55

An attempt to screen mild cognitive impairment: Usefulness of 50 second screening

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Since mild cognitive impairment (MCI) proposed by Petersen and colleagues is considered as an omen of dementia, it has been necessary to diagnose MCI. We made a method to screen MCI, 50 Second Screening (50SS), and investigated whether 50SS correlates closely with Mini-Mental State Examination (MMSE) and whether 50SS is useful for diagnosis of MCI.

One hundred twenty four out-patients aged 54–97 (mean ± SD, 78.6 ± 9.1) were diagnosed by using a neuropsychiatric examination, a blood test, neuropsychological tests (MMSE, Clinical Dementia Rating, Wechsler Memory Scale-Revision logical memory, 50SS) and radiological examinations. On the other hand, as a control, 101 volunteers aged 65–87 (72.7 ± 5.7) spontaneously participated a lecture meeting and readily agreed to the examination of 50SS. Total scores of 50SS were compared between patients and controls. Statistical analyses were used Mann-Whitney U test and ANCOVA. As a post hoc test, multiple comparisons among each groups were used Scheffe's test. And the analysis of correlation between MMSE and 50SS was used Spearman Rank-Order Correlation Coefficient. We explained the purpose of this study to the participants or their families and got their agreements.

We found a significant correlation between scores of 50SS and MMSE ($rs = 0.647$, $P < 0.0001$). The patients consisted of 20 MCI, 20 Alzheimer's disease (AD), 8 vascular dementia (VD), 30 frontotemporal dementia (FTD) and 46 dementia with Lewy bodies (DLB). The mean 50SS scores in control and patient groups were 6.85 ± 1.44 and 1.81 ± 1.68, respectively. The score in controls was significantly higher than that in patient group ($p < 0.0001$). The mean 50SS scores in MCI, AD, VD, FTD and DLB groups were 3.50 ± 1.76, 1.55 ± 1.47, 1.63 ± 1.30, 1.67 ± 1.54 and 1.30 ± 1.46, respectively. The score in controls was significantly higher than that in each patient group ($p < 0.0001$) and the score in MCI group was significantly higher than those in other dementia groups ($p < 0.0001$). When we established a point during 4 and 5 to cut-off between control and patient groups, the sensitivity and specificity were 93.5% and 93.1%, respectively.

In this study, the sensitivity and specificity in screening MCI and dementia were 93%, indicating a high precision of 50SS. It takes less than one minute to examine one person in 50SS. Based on these findings, it is considered that 50SS is useful for screening MCI.

P1-56

Epilepsy with memory impairment misdiagnosed as dementia

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Purpose: Late onset epilepsy may be misdiagnosed as dementia due to disruption of memory and cognitive performance. We report four cases of progressive memory disturbances which clinically resembled early-stage dementia.

Methods: The patients consisted of 2 males and 2 females, aged 56–76 years old. Both the patients and their families had been aware of memory disturbances for approximately one year. Recent memories showed the greatest disturbance, whereas remote memories and orientations were relatively intact. MMSEs were 19–27/30. No apraxia, agnosia or aphasia was seen in any of the patients. Three had no history of overt seizures, although one exhibited occasional episodes of a brief loss of consciousness. MRI revealed left or bilateral temporal lobe atrophy in three patients. SPECT showed areas of hypoperfusion in the left frontal and/or temporal lobe in all patients. EEG revealed spikes in the left temporal region in three patients, and the left central regions in the other patient.

Results: The patients were diagnosed with epilepsy on the basis of the EEG findings and clinical symptoms. Carbamazepine was prescribed, and daily life activities and memory disturbances showed a rapid improvement in three patients, of which one patient showed a marked improvement on the MMSE (19 to 26/30). Poor memory performances, however, persisted in the other patient.

Conclusions: Patients with rapidly progressive memory disturbances should be carefully examined to rule out the possibility of a treatable condition such as epilepsy. A discrepancy between MMSE score and complaints of memory disturbance, unilaterally localized areas of hypoperfusion on SPECT, EEG abnormalities and trials of antiepileptic drugs may point to a diagnosis of epilepsy.

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P1-57

The study on the correlations between the Z-score of VSRAD and the results of neuropsychological tests in the patients with Alzheimer's disease

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Introduction: The early diagnosis of Alzheimer's disease (AD) is important for estimating the prognosis and determining the management. VASRAD(Voxel-based Specific Regional Analysis System for AD), a newly developed software for analysis of brain MRI, would have made it possible to diagnose AD at early stage. It transforms morphological information of parahippocampal gyrus into a numerical value as a Z-score which means the degree of atrophy.
Objective: To examine the clinical usefulness of VASRAD, correlations between the Z-scores and the results of neuropsychological tests are investigated.
Subjects: Subjects were comprised of 14 patients including 4 males and 10 females. Thirteen patients met the ICD-10 criteria for AD including two patients of early onset and one patient diagnosed as Mild Cognitive Impairment (MCI). Mean age of subjects was 74.1 (range: 57–83) years. And mean of HDS-R scores was 15.1 (range: 9–23). Eleven of 14 patients having AD were judged as probable AD and three were judged as possible AD with Cerebral Vascular Disease (CVD). No patient had neurological deficits and history of stroke.
Methods: Neuropsychological tests consisted of ADAS-J cog., WAIS-R (or WAIS-3rd) and WMS-R. Subjects were evaluated within one month before or after cranial MRI investigation conducted.
Ethical considerations: Patients and their families were given an explanation of the objectives of this research and their approval was obtained. As a part of clinical investigation, results were used for the benefit of individual patients.
Results: Mean of the Z-scores was 1.9 ± 1.0 ($\pm$SD). Mean scores of neuropsychological tests were as follows; FIQ; 70.2 ± 15.5, VIQ; 73.7 ± 11.3, PIQ; 71.2 ± 18.6, GMI; 56.4 ± 9.6, score of ADAS; 20.8 ± 9.3. There were no significant correlations between the Z-scores and results of these neuropsychological tests including HDS-R. Comment: Reportedly, the Z-scores correlates with score of HDS-R, MMSE and ADAS in the studies comprising approximately 50 subjects. In this study, there were no significant correlations between the Z-scores and results of neuropsychological tests at the present, because the sample size is too small. This study is now in progress recruiting subjects. At the convention, we are going to demonstrate the results of the analysis of the data from larger number of subjects and, additionally, of the data on SPECT.

P1-58

Regional cerebral blood flow in the patients with dementia – Is the analysis tool of rCBF useful or not to diagnose dementia?

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Objective: In aged society of late years, we have many times to diagnose dementia. Availability of the assessment of the regional cerebral blood flow (rCBF) for Alzheimer's disease (AD) is recognized broadly. In previous report, AD patients have hypoperfusion in posterior cingulate, cuneus, parietal lobe (that is interest domains of AD). A new analysis method named as Specific VOI analysis (SVA) which assists for diagnosing AD was reported. We assessed the rCBF in various types of dementia and investigated the usefulness of SVA to diagnosis dementia. Methods-Subjects were 88 patients with amnesia including 27 with Alzheimer's disease (AD), 7 with frontotemporal dementia (FTD), 22 with vascular dementia (VaD), 4 with dementia with Levy bodies (DLB), 17 with mild cognitive impairment (MCI) and 12 control subjects. We assessed rCBF of the patients included interest domain of AD. And the severity, extent, and ratio of the SVA were measured by using a three-dimensional stereotaxic ROI template method that was a quantitative method composed of 259 regions of interest (ROIs) for 99mTc-labeled bisucate (ECD) single photon emission CT (SPECT). Neuropsychological tests were also evaluated using the Mini-mental State (MMS), an auditory verbal learning test (AVLT), a word fluency test (WFT) and Raven's Coloured Progressive Matrices (RCPM).
Results: Severity of SVA in AD and DLB were higher than in MCI and Control Subjects (CS). Extent of SVA in AD was higher than in MCI, CS and VD. Ratio of SVA in AD was higher than in CS, MCI and VD. In MMSE and AVLT-delayed, there are

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significant differences among the dementia group and non-dementia group.

Conclusion: Close coupling was evident between reduced rCBF and cognitive dysfunction in patients with dementia. In this study, SVA is useful as a supplementary means for diagnosis dementia. However, we recognize the importance of traditional tool, for example detailed question about their symptoms, neurological/neuropsychological tests and neuroradiological examination. We suggest the combination of traditional tools and new method that should enhance diagnostic accuracy.

P1-59

Early diagnosis of dementia: Assessment of kana-picking test and MMSE sub-item

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We examined the effectiveness of kana-picking test and sub-item of MMSE as screener for the preclinical dementia. The subjects of this study were 602 individuals (mean age, 76.4 ± 7.2 years). MMSE and Kana-picking test were used as a cognitive disorder test and performed by a trained examiner to avoid score variability between examiners. The percentage of kana-picking test rejecters were 46.8% (282/602) among the patients whose MMSE score more than 15 points. Even among the patients those more than 24 points, 28.8% (92/320) failed kana-picking test. The correct answer rate for each MMSE item was determined in the subjects who scored 15 or higher. The item with the lowest rate was recall (35.2%), followed by calculation (55.6%) and time orientation (79.9%). Among the sub-items of MMSE, recall, calculation, time orientation items had significant negative correlation with kana-picking test. The kana-picking test combined with the correct answer rate for recall and calculation items in MMSE allows early clinical diagnosis of dementia. This combination is a simple technique that can be used routinely in clinical practice.

P1-60

Neuropsychological test for the evaluation of dementia in the elderly: The Nishimura dementia test (ND Test)

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Objective: Progression of the core and accessory symptoms of dementia can be slowed if drug therapies and psychosocial interventions are administered at an early stage of dementia. The purpose of this study is to develop and standardize a neuropsychological test for the elderly that can detect dementia at an early stage with high sensitivity and can evaluate a wide range of severities of dementia based on assessment of various cognitive functions.

Methods: A preliminary test consisting of 23 items and the Nishimura Mental State Scale for the Elderly (NM Scale), which evaluates the mental functions of elderly individuals by observing their actual behaviors in daily life, were administered to 448 elderly subjects. After applying Hayashi quantification theory type I to the results, we revised the preliminary test to construct a neuropsychological test for the elderly, which we named the Nishimura Dementia Test (ND Test), and standardized it. Then, we examined its validity and test-retest reliability

Ethical considerations: Prior to the study, consent in writing was obtained from all of the subjects and their families after a full explanation of the nature of the study was provided.

Results: The ND Test showed a good general agreement rate for the discrimination of the severity of dementia, and good sensitivity and specificity of discrimination of dementia when compared with the actual NM Scale. In addition, the ND Test showed validity and test-retest reliability.

Discussion: Referring to the maximum scores of the groups of the items, story recall, which requires logical memory that is often examined for screening for mild cognitive impairment (MCI), has relatively large contribution to the total score of the ND Test, suggesting that the ND Test is more suitable for examining MCI than the Revised Hasegawa Dementia Scale and the Mini-Mental State Examination.

Conclusion: The ND Test is based on assessment of a variety of cognitive functions and can evaluate a wide range of severities of dementia with good validity and reliability.

P1-61

A new one-minute dementia screening test (automated quantification of the drawing tests replaced by CPU-assisted plotting)

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Table Correlation between the CADS and the Cognitive function tests(1992)

	r =	p =
HDS-R	0.5338	<0.0001
WAIS-R		
Full-scale IQ score	0.3587	<0.0001
Performance IQ score	0.3741	<0.0001
Kohs'Block-Design Test	0.3949	0.0045
Bender-Gestalt Test	-0.3261	0.0007

P1-61

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We improved and developed the CADS (Computer Applied Dementia Scale) from quite different aspect from other screening tests that detect the early stage of dementia. The purpose of this study was to introduce the excellent feature of the CADS. The CADS is the system that hits 30 points with the electronic pen on the touch panel include the lattice chart (12 rows in side and 20 lines in length), and the data was analyzed with the computer. This study tried to quantify the feature of the dementia patients shown in the drawing tests such as Baum test. In 1992, the CADS and various cognitive function tests were completed by 201 older adults. In 2004, 20 patients alive out of 201 took the same tests. Then, the results of these data were compared. The results obtained in 1992 found that there were positive correlations between the CADS and the HDS-R, the WAIS-R, the full-scale IQ score, the performance IQ score, and the Kohs Block-Design Test. There was a negative correlation between the CADS and the Bender-Gestalt Test(Table). Additionally, test-retest reliability was assessed in a sample of 30 patients, and high correlation was indicated (r = .880). Thus, the CADS are thought to have enough validity and reliability and are useful screening test for dementia. Furthermore, the positive correlation between the CADS and the HDS-R in 2004 (r = .8963) as well as 1992 (r = .5338) was found. Therefore, it is thought that the CADS is a useful tool to observe cognitive function. The CADS is a simple test that hit only 30 points and extremely short compared with the HDS-R and the MMSE that take the average of 5 to 10 minutes. The implementation is also easy and patients do not notice being tested, so it will not hurt the pride and self-respect of older adults. Thus, the CADS excels as a screening test for dementia because it has an excellent feature that does not exist in current tests.

P1-62

Utility of cognitive screening with "what's the latest news on TV or papers?" in Japanese community

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Background: Dementia is a significant public health problem that is under recognized in primary care

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settings. This study examined the usefulness of 3 brief questionnaires in detecting dementia and mild cognitive impairment (MCI) by their home doctors in the Japanese community.

Methods: Consecutive outpatients of 75 Alzheimer's disease (AD), 15 MCI and 73 normal cognitive aging controls were recruited. Three neurologists classified into several answer types for each question according to the record on videotape.

Results: For "What's the latest news on TV or papers?", the correct answer was 3% in AD, 33% in MCI; not remember or no answer was 45% in AD, 27% in MCI; a vague or outdated answer was 13% in AD, 20% in MCI; saving appearances answer was 45% in AD, 27% in MCI, while, 99% of aging controls were classified as correct answer. Using this question, AD patients were identified from controls with 97% sensitivity and 99% specificity and MCI with 67% and 97%. In 56% and 7% of AD and MCI, saving appearances answer was given for "What season is it now?": an incorrect season was answered immediately.

Conclusions: "What's the latest news on TV or papers?" was highly effective in identifying AD and MCI in Japanese community. This result would be closely connected with the popularization of TV and abundant tabloid TV talk shows in Japanese society, and national characteristics of the standardization in cultural level, religion, and interest in Japanese community.

P1-63

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P1-64

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P1-65

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P1-66

Development of a computer-based testing system and its application for screening of patients with dementia and mild cognitive impairment

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For the screening of community-dwelling elderly people with dementia, we have developed a computer-based test system in which two test programs are executed, one for primary screening and the other for close examination.

Description of the computer-based system: The system was assembled with a touch-panel display and computer devices unified into one case. The primary screening program was made with reference to the Hasegawa dementia rating scale and

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consisted of 4 test tasks, all procedures usually being completed within 5 minutes. The total number of points on this test is 15. The close examination program was made with reference to the Alzheimer's Disease Assessment Scale and consists of 10 tasks, usually completed within 30 minutes. In this procedure, a perfect score is 0 which increases according to the number and value of false answers. The score reaches 107 when all answers are incorrect.

Materials and methods: Nine hundred ninety-eight elderly residents aged over 65 participated in the testing survey. The screening process was done using the system as follows: first, we screened any person whose primary test score was 13 or less as hi-risk; then, we asked those hi-risk participants to take the close examination test. We regarded a person whose score on the close examination to be 14 or more as suspicious of suffering from dementia and recommended them to have a medical examination. Also we regarded a person whose score on the close examination to be from 7 to 13 as mild cognitive impairment (MCI).

Results: Two hundred ninety-five people were screened as hi-risk based on the primary test. Subsequently, they were asked to take the close examination and 151 of them took the examination. Finally, we detected 55 persons as MCI and 74 persons as suspicious of suffering dementia respectively. The suspicious 74 persons were recommended a medical examination. Out of the 74 persons, 48 had received a medical examination by the writing of this paper. Final diagnosis by the medical specialist was as follows: 41 were diagnosed with Alzheimer's, 2 with vascular dementia and 5 with other diseases.

Conclusion: We have developed a computer-based test system to screen for dementia. Out of 998 elderly residents, we initially screened 295 people as hi-risk. Finally, our testing system resulted in 74 persons as suspicious of suffering from dementia. We think our system seems to be useful in screening for community-dwelling elderly people with dementia.

P1-67

A predictive validity of the tropicamide-induced pupil dilation for Alzheimer's disease: Prospective study

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Background: A rate of pupil dilation after instillation of a diluted tropicamide solution was proposed as a noninvasive neurobiologic diagnostic test for Alzheimer's disease (AD) by Scinto et al., (1994). We have performed the tropicamide drop test and the mini mental state examination (MMSE) to 149 elderly subjects, aged 75.7 ± 6.1,living in a local community or 18 AD patients in 1995–1997 (Time A, Imamura, 1995).

Objective: To evaluate a predictive validity of the tropicamide drop test for the diagnosis of AD.

Method: Forty four subjects out of 149 normal subjects who have been performed the tropicamide drop test in Time A were examined MMSE in 2004–2006(Time B).The predictive validity of the tropicamide drop test for the diagnosis of AD was examined by an analysis of co-valience using the rate of pupil dilation after tropicamide (%) as an independent valuable and changes in MMSEscore during 9years as a dependent valuable.

Results: The tropicamide drop caused a 4.96 ± 6.7% pupil dilation in normal subjects and 13.2 ± 9.8 in patients with AD at Time A. The mean MMSE score was 26.2 ± 2.4 at Time A which was reduced to 24.8 ± 5.5 at Time B in 44 normal subjects. An analysis of co-valiance revealed that the rate of pupil dilation after tropicamide has no significant relationship with a decline of MMSE score during 9 years ($F(1,42) = 1.91$, $P = 0.281$) nor MMSE score at B ($F(1,42) = 0.65$, $P = 0.88$).The data indicate that the tropicamide drop test has no predictive validity for early diagnosis of AD.

P1-68

Exploratory study with memory tests global cognitive decline in elderly: A Portuguese study

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The purpose is to proceed to the cognitive evaluation in people with more than 60 years and to inquire the existence of differences according to education level, sex and age. In the current study, three participant groups were recruited in a total

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of 250 people: patients with Dementia (D), patients meeting criteria for MCI, and normal elderly controls (NC). The detection of MCI and Dementia, with clinical diagnosis in a Psychiatric Clinic of Coimbra University Hospital was the criterion standard. All subjects live in Coimbra, some of them living in a community (community day center or nursing home residence).The aim of this exploratory study is to correlate the global cognitive decline in elderly assessed by the Clock Drawing Test (CDT) Faces Recognition Test (FRT; Simoes, Pinho and Lopes, 2004), Semantic Verbal Fluency Test, the Montreal Cognitive Assessment (MoCA; Z. Nasreddine, 2004) and Mini Mental State Examination (MMSE; Folstein et al., 1975) at the Portuguese population. Subjects also answered to the Geriatric Depression Scale (GDS; Yesavage et al., 1983), after informed consent, in the context of a personal interview. All subjects live in Coimbra, some of them living in a community (community day center or nursing home residence). The findings provide additional support for the clinical utility of these tests for use in detection and evaluation of cognitive handicaps.

P1-69

Assessing apraxia in patients with senile dementia of Alzheimer type: A comparative study

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Many patients with Alzheimer's disease suffer from apraxia. Apraxia is a major cognitive deficit leading to severe consequences in activities of daily living. The aim of this study was to examine the type and extent of apraxia in patients with senile dementia of Alzheimer type (SDAT) compared to the elderly without dementia. In this descriptive- analytic study, 14 patients with (SDAT) were compared with 20 elderly without dementia matched for age and education. The patients were selected among Iranian Alzheimer's Association members. They all had confirmed neuron-psychiatric diagnosis and their MMSE scores ranged between15 to 27. The range of MMSE scores for control group was 25–30. Apraxia Test designed by Nilipour (2005) was administered on both groups. The test included 4 subtests: conceptual movements, gestured conceptual movements, oral and respiratory movements, and pantomime of movements of object manipulations. Gathered data were analyzed, using SPSS software, version 11/5. Results showed that apraxia scores were significantly different between 2 groups ($p = 0.000$), regarding that(SDAT) patients were diagnosed as having apraxia and the controls were not. Additionally, comparison of subtests scores of (SDAT) patients revealed that conceptual movements scores were significantly higher ($p = 0.000$) than other subtests, which means less apraxia. It is concluded that neuropsychological evaluation of praxis may have some implications in the diagnosis of (SDAT) and subgroup scoring could be used for understanding and categorization of the observed defects and possibly designing new rehabilitation methods.

P1-70

Reliability and validity of Zung depression rating scale in elderly population of Iran

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Zung depression rating scale (ZDRS) is a well-known and world widely used self-rating scale for the measurement of depression in elderly population. The aim of the current study was to assess the reliability and validity of ZDRS in Iranian elderly. In this cross-sectional study, 400 patients (236 males and 164 females) aged 60 years or more selected randomly from four different regions of Tehran city. Data regarding validity were gathered, using psychiatric diagnosis according to DSM-IV criteria and Beck depression inventory, and analyzed by the software SPSS, version 10th. The results revealed that criterion validity of ZDRS as compared with Beck depression inventory was equal to 0.62(0.50 for men and 0.67 for women) and objective validity as compared to the psychiatric diagnosis was 0.664 (0.665 for men and 0.667 for women). Sensitivity and specificity exceeded 88 and 80 respectively at 60/65 level. Cronbach's alpha coefficient for the total scale was 0.73(0.64 for men and 0.55 for women). There was no significant relationship between age and ZDRS scores. It is concluded that ZDRS is a valid and reliable tool for the assessment of

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depression in Farsi-speaking depressed elderly people.

P1-71

Usefulness of EASI in screening for cognitive disorders in the community

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Background: Identification of cognitive disorders among community resident older people is important for service development.
Objective and hypothesis: Everyday Abilities Scale for India (EASI) may be useful in identifying older people with cognitive impairment in the community.
Methods: We identified people aged 65 years and above from the voters list. Trained interviewers administered EASI to the key informants of 302 individuals aged 65 years and above. Individuals with a score of 3 or above in the 11 item EASI underwent detailed evaluation by the clinician. Subjects were then classified as cases of dementia or mild cognitive impairment (MCI) and non-cases.
Results: We identified 14 cases of dementia and 8 cases of MCI from the test positives. EASI had a positive predictive value of 50%.
Conclusion: Health workers can use EASI to identify potential cases of dementia. It can also help in identifying cases of MCI. This is an interesting finding that merits further study.

P1-72

Cognitive disorders prevalence study from Thrissur, Kerala

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Background: Dementia and mild cognitive impairment are important causes of disability in the elderly. Prevalence of cognitive disorders has implications for long-term care.
Objective and hypothesis: We investigated the prevalence of dementia and Mild Cognitive Impairment (MCI) in the community.
Method: We identified people aged 65 years and above in a specified geographical area. Trained interviewers administered EASI to the key informants. A clinician evaluated all those who received a score of 3 or above in the 11 item EASI. We classified subjects as cases of dementia, mild cognitive impairment (MCI) and non cases.
Results: We identified 302 individuals aged 65 years and above. The prevalence of dementia and MCI in the community was 4.64% (95% CI 4.08 to 5.2) and 2.65% (95% CI 2.4 to 2.9) respectively. Alzheimer's disease was the most common type (50%). Vascular dementia accounted for 14% of the cases. 36% cases were other types of dementia.
Conclusion: About 7% older people had dementia or MCI. They need assistance in activities of daily living and would make enormous demand on home-based care.

P1-73

The study of cognitive impairment in neurodegenerative disease using a semantic paradigm: An on-line approach

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The study of anomia in dementia diagnosis is of particular interest as it is often one of the first sign of cognitive decline even when no other objective evidence of memory deficit can be found. In clinical practice the methods of choice for assessing anomia are standardised neuropsychological off-line tests requiring effortful retrieval but not considering automated processing. Nevertheless recent studies have shown that patients with Mild Cognitive Impairment (MCI) show cognitive impairment only in tasks involving intentional processing in comparison to patients suffering from Alzheimer's disease (AD) who are impaired in both intentional and automated processing tasks. The aim of this study is o develop a new, non-invasive, fast and low cost test

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inquiring automated processing to introduce in clinical practice in order to distinguish in a more precise way age related cognitive impairment from MCI and AD. The method of choice is an on-line semantic test with both discrimination tasks and lexical decision tasks build on a semantic paradigm and characterized by phonetic manipulation administered to age- and gender-matched healthy elderly, MCI patients and patients suffering from mild AD. The test battery is constituted by semantic related and semantic unrelated word pairs together with pairs of nonwords used as distractors. The test is administered through headphones and response accuracy together with reaction time registered on an ordinary computer. Preliminary results from a study involving 21 trail persons with Swedish as their mother tongue show that the test battery has been formulated correctly. Results from a pilot study involving accuracy and reaction time from healthy elderly, AD and MCI patients will be presented. Preliminary results suggest that the test battery as been formulated correctly and that it could be used as a new diagnostic tool. The pilot study to be initiated soon will show the sensitivity and specificity of the test battery in differentiating the three groups.

P1-74

Use of a gene expression signature in blood for an accurate and early detection of Alzheimer's disease

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Alzheimer's disease (AD) is today the leading cause of dementia. An accurate, convenient and objective test to detect AD is much desired but currently, no definitive diagnostic test for AD exists. An accurate test based on peripheral blood as the clinical sample would be in line with the desired criteria. We have previously presented results from a pilot study suggesting that a blood-based gene expression test can be developed for AD [Abstract number: 162960, 2005 12th IPA, Stockholm, Sweden]. We have recently also shown results from a large-scale study on ABI Human Whole Genome microarrays that confirm our initial findings. The test set validated results from this study identifies a blood-based gene expression signature that classify patients with AD with high specificity (91%), sensitivity (84%) and accuracy (87%) [Abstract number: O3-01-01, 2006, 10th ICAD Conference, Madrid, Spain]. The signature also distinguished AD from Parkinson disease. Initial results from a non-optimised test with a subset of the gene expression signature using the RT-PCR based TaqMan Low Density Arrays (LDA) (ABI) did show that LDA potentially can be used as a diagnostic platform. This has now been confirmed in a more extensive validation of an expression signature using a limited set of genes on LDA and using an independent cohort of more than 100 patients and controls. With a very much reduced number of genes in the model it is still retaining a high accuracy. Based on a set of less than 96 genes including all controls the model is able to predict AD with a sensitivity of 73.5%, a specificity of 84.1%, and an accuracy of 79.5%. Data showing that the proteins encoded by the genes used in this model are involved in several interesting biological processes will also be presented.

P1-75

Screening of cognitive and social functioning in medically elderly

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Study objectives: We determine mental status impairment of elderly patients attending geriatric clinic for medical problems and assess their social functioning.

Methods: We performed a prospective cross-sectional study. Patients were 60 years of age or older and presented to geriatric clinic of an urban teaching hospital over a period of one year. Mental status impairment screening comprised of Mini-Mental State Examination (MMSE). The social functioning of the elders assessed with Social and

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Occupational Functioning Assessment Scale (SOFAS) – the Social component of DSM IV. Results of mental status impairment screens were then given to physicians working in geriatric clinic so that they could incorporate any change in care.

Results: One hundred patients randomly selected from geriatric clinic. On MMSE, 5 patients scores' (mean 21.20, SD 1.30, SE 0.581) differed significantly than rest other patients (mean 28.75, SD 1.20, SE 0.142) suggesting impaired mental status. On SOFAS, those five patients showed significantly lower scores than rest of the patients ($p < 0.05$). Physicians altered management in three of the study patients based on survey results.

Conclusion: Mental status impairment is highly prevalent in medically elderly patients. There is a lack of recognition by physicians of mental status impairment in this group. There is a need to incorporate screening tools for mental status impairment in the medical settings to alter the care of elderly patients with mental status impairment.

P1-76

Applicability of tests of cognitive evaluation in healthy old people and patients with Alzheimer's disease and mild cognitive impairment

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Objective: To evaluate three different tests of cognitive evaluation in healthy volunteers and in patients with Alzheimer's disease (AD) in different stages.

Patients and methods: We studied 21 healthy old volunteers (CDR:0), 7 with Mild Cognitive Impairment (MCI), 20 with mild AD (CDR:1), 16 with moderate AD (CDR:2) and 14 with severe AD (CDR:3). The diagnosis of probable Alzheimer's disease was accomplished with the DSM-IV and CID 10 criteria; MCI with Petersen criteria. All volunteers were submitted to the Mini-Mental State Examination (MMSE), clock drawing test (CDT) and the structured interview for the diagnosis of dementia of the Alzheimer type, multi-infarct dementia and dementias of other etiology (SIDAM) in its cognitive section.

Results: (Table) Means (SD)* $p < 0.05$ compared with control group. The sensibility, specificity, positive and negative predictive values seems to be better when we used SIDAM (93%, 90%, 96% and 83%) in comparison with MMSE (91%, 76%, 91% e 76%) and the clock drawing test (89%, 52%, 84% e 65%).

Conclusions: SIDAM seems to be a good evaluation instrument for older people with Alzheimer's disease and educational status between 1 and 8 years, with good sensibility and specificity including MCI in the diseased group.

	Control	MCI	Mild AD	Moderate AD	Severe AD
Age	74.2 (1.9)	75.1 (2.7)	75.3 (3.7)	75.3 (3.2)	75.0 (3.2)
Education	3.7 (1.4)	4.0 (1.5)	4.3 (1.9)	4.9 (2.6)	4.7 (2.4)
MMSE	27.6 (2.2)	25.6 (1.3)	18 (3.6)*	11 (3.9)*	1.5 (2.6)*
SIDAM	46.8 (4.6)	40.1 (4.4)*	26.0 (6.4)*	14.7 (7.3)*	1.6 (2.7)*
CDT	8 (1.7)	7.9 (2.0)	5.7 (1.8)*	3.3 (1.9)*	1.1 (0.4)*

P1-76

P1-77

Clinical utility of the clock drawing test in the memory disorders clinic

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Background: In a clinical setting of screening early-stage dementia, the Hasegawa's Dementia Scale-Revised (HDS-R) and the Mini-Mental State Examination (MMSE) are widely used in Japan. The cut-off points of HDS-R and MMSE have been set as 20–21/30 and 23–24/30, respectively. The Clock Drawing test (CDT) is another candidate for screening dementia. The primary interest in the present study is focused on the utility of CDT as a tool for screening dementia.

Methods: The participants were 140 consecutive outpatients (50 male, 90 female) who first consulted the Memory Disorders Clinic in Musashi Hospital, National Center of Neurology and Psychiatry. The clinical diagnosis given to participants included healthy (12 persons), Mild Cognitive Impairment (17), Alzheimer's disease (AD)(81), Dementia with Lewy Bodies (5), vascular dementia (VD)(8), AD+VD (11) and others. HDS-R and MMSE as well as the Clock Drawing test

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(CDT) were given to participants for screening dementia. The Wechsler Memory Scale-Reviced (WMS-R) was also given as the additional test to further explore memory deficits. We examined the utilities of the screening tests with a retrospective review of a database.

Results: Fifty participants scored above the cut-off points in the two standard dementia screening test (i.e., $\geq$21 in HDS-R and $\geq$24 in MMSE), thus indicating that they were not demented. However, 32 among such 50 participants scored 1SD below average (i.e., <85) in the delayed recall index of WMS-R. Those who scored <85 in the delayed recall index were more impaired in CDT as compared to those whose delayed memory scored $\geq$85. Performance in CDT was significantly correlated with the delayed recall index of WMS-R (Rho = .39, $p < .01$). No significant correlations were observed between CDT performance and the attention/concentration index of WMS-R (Rho = .18, $p > .10$).

Conclusions: HDS-R and MMSE are widely used as the screening tests for dementia, but more detailed memory examinations including WMS-R are necessary to further explore slight memory deficits and mild cognitive impairment. Although CDT is regarded to be a test for visuospatial and executive functions, its performance showed a robust correlation with delayed memory activities as indexed by WMS-R. Since CDT is handy and is easily given to an individual with questionable dementia, we consider it is clinically useful for exploring subtle cognitive impairment in the Memory Disorders Clinic.

P1-78

Feelings in the elderly suffering chronic pain

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Circumlex model, a brief diagnostics instrument for anxiety and depression, provides patients an opportunity to gain insight into themselves. It was successfully used in a chronic pain assessment in the elderly as a part of multidimensional questionnaires. The aim of this cross-sectional study was to assess the patient's emotions, satisfactions and level of mental activation and their interplay according the presence of long-lasting pain. Data was obtained by interviewing patients in their homes and analyzed on a PC (SPSS). The study has been conducted on the 179 patients (134f/45m), very old (mean 78.6y; st.dev.8.5y), suffering chronic pain 6 months and more (Pain group, PG), and control group (CG) of 24 pts (18f/6m) without pain, mean 77.9 $\pm$ st.dev.10.9 years old. All was functionally totally disabled, depending on others help. Patients in both groups underline the dominant feelings of unsatisfactions (30% PG; 34.3% CG), high activated negative affect (15%PG; 16.5% CG) and low positive affect (15%PG; 5.1%CG). It was found high statistical difference between pts in pain and without pain in the expression of low positive affects, $p < 0.01$. Also, according the Circumplex model, in the PG the four pts was in depression and in CG only the two was depressed.

Conclusion: It could be simply concluded that pain increases level of patients affect. These results have broader implications as well by pointing out the necessity to estimate level of other entities influence like as mental declining, personal, sociological and environmental factors.

P1-79

Frequency of previously unknown dementia in elderly patients admitted to a geriatric clinic for emergencies not primarily related to mental health

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Frequently relatives and even the family doctors are surprised by the diagnosis of dementia in patients admitted to a geriatric clinic for emergencies not primarily related to mental health. Since limited awareness of dementia may cause a delay in an adequate approach to these patients we studied the frequency of previously not suspected dementia in all patients admitted to a geriatric clinic in 2005–2006. Besides the routine diagnostic procedure (patient history, physical examination, exploration, laboratory, imaging if indicated) all patients underwent a comprehensive geriatric assessment including Minimental State Examination (MMSE), Barthel index, handgrip test, timed up and go test, and Geriatric Depression Scale. In patients with suspected dementia further psychometric and neuropsychological tests and cranial CT and/or MRT were performed. 4365 geriatric patients admitted to a

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geriatric clinic were included in the study (mean age 82.2, SD 4.1 years; mean duration of stay in hospital 18.2, SD 1.9 days; 63% females, 37% males). In 375 patients previously unknown dementia (D.) of various causes (Alzheimer D. 39%, vascular D. 30%, mixed D. 12%, Parkinson D. 5%, Lewy-body D. 2%, and other D. 12%) and stages (mild [21–25 pts. MMSE] 39%, moderate [11–20 pts. MMSE] 46%, severe [0–10 pts. MMSE] 15%) was diagnosed. Whenever possible, the relatives were contacted and underwent a standardized educational program on dementia. Anti-dementic therapy depending on the type of D. including galantamine, rivastigmin (especially in Parkinson D.), and memantine was initiated in 211 of the patients. Further medication for behavioural disturbances during stay in hospital included atypical neuroleptics (risperidon, clozapin), and antidepressants besides other drugs in 252 of the patients. It is not unusual that a sudden change of environment like an admission to hospital may unmask dementia in geriatric patients. However, in about one third of the patients rather substantial symptoms of dementia had been ignored by relatives or other caregivers. Our findings emphasize that relatives and sometimes family doctors are frequently unaware of dementia. This may cause various problems like a substantial risk of decompensation in the activities of daily living and otherwise preventable admission to a hospital. More awareness of the problem of dementia in the elderly and education is required in the public and even in the medical community.

P1-80

Heat shock protein level changes in normal elderly, mild cognitive impairment, vascular cognitive impairment and Alzheimer's dementia patients

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Objectives: The purpose of this study was to compare the level of plasma Hsp70 and Hsp27 in normal elderly, mild cognitive impairment, vascular cognitive impairment, and Alzheimer's disease.

Method: All 73 participants were evaluated by K-MMSE, Clinical Dementia Rating (CDR), Global Deterioration Scale (GDS), Korean version Neuropsychiatric Inventory(CGA-NPI), Seoul Instrumental Activity of Daily Living(S-IADL), SNSB-D. Plasma Hsp70 and Hsp27 were assayed by Hsp immunoassay plate. Informed consent was obtained by all participants and caregivers and this study was approved by IRB of Severance Mental Health Hospital.

Results: Compared with the level of plasma Hsp70 and Hsp27 among 4 groups, only the level of plasma Hsp70 (0.27 ± 0.13) in VCI was significantly higher than that (0.20 ± 0.04) in MCI ($F = 3.61$, $p = 0.017$), and there was no difference of level of plasma Hsp27 among 4 groups.

Conclusion: Plasma Hsp70 may be not related with cognitive impairment but stoke or vascular factors.

Keywords: Heat shock protein, mild cognitive impairment, vascular cognitive impairment, Alzheimer's disease, biomarker.

P1-81

Correlation between head circumference and cognition in the elderly by ApoE genotype

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Purpose of this study is to find out the effect of ApoE genotype on correlation between head circumference and cognition of the elderly in community. A total of 1,807 subject (575 men and 1232 women) aged 60–91 years were analyzed from data of Gwangju Dementia and MCI Study (GDEMCIS). The study questionnaire consisted of demographic characteristics, current and past illness history, alcohol, smoking, drug history and K-MMSE(Korean version-Mini Mental Status Examination). We measured head circumference and examined ApoE genotype. On regression analysis, as head circumference of participants become larger, K-MMSE scores become increased adjusted by age, sex, educational level, Apo E ϵ allele, smoking, and alcohol ($\beta = 0.15$, $p = 0.038$). In individuals with a head circumference in the lowest quartile, presence of ApoE $\epsilon 4$ allele reduced K-MMSE scores

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($\beta = 1.40$, $p = 0.007$). These results suggest that head circumference may have influence on cognitive functions in the elderly by the presence of ApoE $\epsilon 4$ allele.

P1-82

Anamnestic and demographic data as determinants of plasma homocysteine in subjects with dementia or non-dementia

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We have set up a database for monitoring the efficacy of various diagnostic markers and anamnestic data in differentiating between clinical dementia (D) and non-dementia (ND) conditions in our memory unit. In recent years, homocysteine has been proposed as an independent risk factor for dementia and Alzheimer's disease. The present report therefore focuses on Hcy and its determinants. We included 1149 persons (507 men; 642 women) attending the Memory Unit of Örebro University Hospital between 1996 and 2000. Clinical and psychological findings, EEG and selected biochemical markers in the blood and serum were analyzed. Computed tomography examination of the brain was done in approximately 60% (693/1149) of the cases. Patients were classified as demented or as non-demented according to the DSM-III-R criteria. In all, 689 subjects were classified as having D, and 460 as ND subjects. Total P-Homocysteine (tHcy) was significantly higher (20.4 vs. 16.9 μmol/L) and S-folate significantly lower (10.7 vs 13.2 nmol/L) in D than in ND subjects, but S-B12 did not differ. Furthermore we astonishingly found that subjects taking B-12 supplement had significantly higher tHcy. Patients living in sheltered housing also had significantly higher Hcy levels ($p < 0.001$ in Chi-2 test with tHcy ≤ 14 μmol/L as cut-off). ND subjects, without community-provided home service, had significantly lower tHcy ($p < 0.001$ in Chi-2 test with tHcy ≤ 14 μmol/L as cut-off) than those ND subjects who were provided such service. In a multivariate regression model where ln tHcy was the dependent variable, D/ND and EEG background activity was the independent variables, we found a significant negative correlation with reduced background rhythm on EEG ($p = 0.012$; adj R-sq = 0.081). In summary, we propose that tHcy levels were elevated among D subjects along two different pathways. One pathway is the poor nutritional status of D subjects, but also of ND subjects who are in need of community-provided home service: the latter seems to be unsatisfactory in terms of adequate nutrition. Another pathway would be the D process itself, as suggested by the significant association between pathological EEG background rhythm and elevated tHcy. The findings bring into attention the needs for better home-care as well as better sheltered housing care of both D and ND elderly subjects.

P1-83

Portuguese psychometric studies with raven coloured progressive matrices at the elderly

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Raven Coloured Progressive Matrices, consists of three sets of 12 items. Each one has an incomplete figure (above). The patient is required to select the missing part (the right item) among the six alternative responses given below the figure. The difficulty increases as the patient solves each item. The sum of the number of correct responses for each set is defined as the RCPM score. With the aim of obtaining norms for the Portuguese elder population with RCPM (that evaluates mainly fluid intelligence and abstract reasoning), we used this instrument and MMSE, in a sample with more than 60 years old. Also, we tried to explore possible age, education and gender effects in answering to RCPM test. The sample includes 250 subjects aged from 60 to 98 years. All subjects live in Center and North Region of Portugal, some of them living in a community (some at Day Center) and others living in a nursing home.3 groups are constituted (normal, with cognitive decline and with dementia) and sex and educational level are studied. The findings provide additional support for the clinical utility of these tests for use in detection and evaluation of cognitive handicaps.

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P1-84

Portuguese psychometric studies with Montreal Cognitive Assessment (MoCA)

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The Montreal Cognitive Assessment (MOCA) is a cognitive screening test designed to assist Health Professionals for detection of mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation. The authors attempted to correlate the global cognitive decline in elderly assessed by the Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE – Folstein et al.) at a Portuguese population. The sample includes 250 subjects aged from 60 to 92 years. All subjects live in Center and North Region of Portugal, some of them living in a community (some at Day Center) and others living in a nursing home. The findings provide additional support for the clinical utility of these tests for use in detection and evaluation of cognitive handicaps.

P1-85

Portuguese psychometric studies with Mini Mental State Examination (MMSE)

Horácio Firmino[1]; Mario Simoes[2]; Fatima Almeida[2]; Sofia Andrade[2]; Monica Martins[2]; Joana Martins[2]; Joana Araujo[2]; Manuela Vilar[2]; Joana Noronha[2]; Maria Salome Pinho[2]

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The Mini-Mental State Examination (MMSE) is arguably the most widely used screening measure for cognitive impairment. The objectives of the present study is to proceed to the cognitive evaluation in people with more than 60 years and to determine whether the Mini-Mental State Examination (MMSE) could be use to discriminate the existence of differences according to education level, sex and age in a Portuguese population. The sample included 200 persons, patients meeting MCI clinical criteria, patients with Dementia (D), and healthy elderly controls (NC).

P1-86

Portuguese psychometric studies with geriatic depression scale (GDS)

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The principal purpose of this study is to screen Depression in subjects with more than 60 years and to inquire the existence of differences according to education level, sex and age; secondly, to verify the existence of depression at cognitive impairment. The sample (N = 180) of our study was recruited at the Gerontopsychiatry Consultation, Nurses Home, Daily Care Centers and Community. A team of psychologists applied the GDS (30 items) and the MMSE. The diagnostic of cognitive impairment was based on a clinic interview by a psychiatrist in a Psychiatric Clinic of Coimbra University Hospital and on the scores of the MMSE. The existence and level of Depression was based on the score of the GDS.

P1-87

Portuguese psychometric studies with Clock Drawing Test(CDT)

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Clock Drawing Test (CDT) is a widely used instrument for cognitive assessment and screening of dementia as well as other neuropsychiatric disorders. As it recruits simultaneously visuospacial and language abilities, numeric knowledge, work memory and executive functions, CDT is a rapid method

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of cognitive scrutiny. However, these characteristics also challenge test interpretation and scoring. In the last two decades a number of studies have proposed some variants of the test and have characterized its psychometric proprieties, establishing its usefulness as a screening method to dementia. In a recent international survey, Shulman reported that CDT is the second most popular screening cognitive test used at a regular basis by geriatric specialists. Data concerning to Portuguese population is limited, however. Interpretation and scoring of the test have encountered some difficulties regarding educational and cultural factors. The authors attempted to correlate the global cognitive decline in elderly assessed by the Clock Drawing Test (CDT) and Mini Mental State Examination (MMSE – Folstein et al.). The sample includes 200 subjects aged from 60 to 92 years. All subjects live in Center and North Region of Portugal, some of them living in a community (Day Center) and others living in a nursing home. The findings provide additional support for the clinical utility of these tests for use in detection and evaluation of cognitive handicaps.

P1-88

False recognition in the word recognition task of the Alzheimer's disease assessment scale

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Background: The Alzheimer's Disease Assessment Scale (ADAS) includes the word recall and word recognition tasks for evaluating the severity and the progression of the memory disturbance. In the ADAS, the standard scoring method for the word recognition task gave no points to an incorrect response to a dummy word. However, recently, this standard method has been considered to be insufficient for precisely evaluating the memory disturbance, and a modified scoring method, which assesses incorrect responses due to false recognition to dummy words, has been proposed and sometimes used. The purpose of this study is to examine the usefulness and the validity of the modified scoring method in the word recognition task of the ADAS for evaluating the severity and the progression of the memory disturbance in the elderly.

Methods: One hundred elderly subjects have been followed up for more than 2 years using several clinical assessment scales including the ADAS and the Mini-Mental State Examination (MMSE). The assessment scales were performed more than two times in the follow-up periods. We examined 1) the relationship between incorrect responses due to false recognition in the word recognition task and the performances in the other subtest items of the ADAS; 2) the relationship between the MMSE scores and the ADAS scores obtained by either the standard or modified scoring method; 3) whether the assessment of the incorrect responses due to false recognition can predict more accurately the progression of the memory disturbance in the elderly than the MMSE or not.

Results and discussion: The results show a high internal correlation between the incorrect responses due to false recognition and the performances of the subtest items of the ADAS, suggesting that false recognition is related with disturbances of various cognitive functions. The ADAS scores obtained by the modified scoring method show higher correlation with the MMSE scores than the standard method, suggesting the validity of the modification of the standard scoring. In the subjects who obtained more than 23 points of the MMSE in the first clinical assessment, the subjects who made incorrect responses due to false recognition at that time have shown more severe progression of dementia than those who did not, indicating that the assessment of the incorrect responses due to false recognition can be useful for predicting the progression of dementia of the elderly in the stage of the mild cognitive impairment.

P1-89

CAMCOG as a screening tool for the diagnosis of mild cognitive impairment and dementia in Brazil

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Background: The CAMCOG is a brief cognitive assessment battery included in the CAMDEX

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(Cambridge Examination for Mental Disorders of the Elderly) designed to evaluate cognitive functions in the screening for dementia. The maximum (normal) score is 107, and the threshold score to dementia in the original European studies is 79/80. Like other cognitive screening tests, the performance on the CAMCOG is influenced by the educational level, rendering less educated individuals prone to a false positive result. Moreover, the current cut-off values lacks sensitivity for the detection of less impaired patients.

Objective: To evaluate the cut-off values and the diagnostic accuracy of the CAMCOG in the identification of mild cognitive impairment (MCI) and dementia in a cross-section of highly educated elderly Brazilians.

Methods: 157 individuals were included (mean age: 69.6 ± 7.4 years). They had at least 8 years of formal education (mean schooling 14,2 ± 3,8 years). Subjects were divided into 3 groups according to cognitive profile: 62 were unimpaired (controls), 65 had MCI and 30 had mild or moderate dementia (DSM-IV). The cut-off values were established by the analysis of ROC curves.

Results: Comparing controls with subjects with dementia, the cut-off value was 92 (AUC = 0,99: sensitivity: 100%, specificity: 95%) and the subscales most relevant to differentiation were orientation, (AUC = 0,86), language (AUC = 0,96), memory (AUC = 0,89) and abstraction (AUC = 0,85). Comparing subjects with MCI and dementia the cut-off score was 86 (AUC = 0,91, sensitivity: 81%, specificity: 88%) and the subscales most relevant were orientation (AUC = 0,83), language (AUC = 0,82) and memory (AUC = 0,92). Comparing controls with MCI the cut-off score was 96 (AUC = 0,83, sensitivity: 64%, specificity: 88%) and no subscale gave a good discrimination. The Mini-mental State Examination, Verbal Fluency (animals) and the Clock Drawing Test alone (which are part of the CAMCOG) were less accurate than the total CAMCOG score.

Conclusion: The cut-off value of 93 points to discriminate controls from dementia was higher than the originally described (79/80). One possible reason was the diagnosis of dementia in the current sample corresponded mostly to mild or initial stages of Alzheimer s disease. The CAMCOG had limited value to discriminate subjects with MCI from controls. The discrimination of MCI and dementia can be optimised using not only the total CAMCOG score but also the subtests memory and language.

P1-90

To tell or not to tell: Mild demented patients' attitude on disclosing of AD diagnosis

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The diagnosis of Alzheimer's disease (AD) is an emotional issue with profound impacts on patients and family. From patients' perspective, to disclose AD diagnosis is a complicated issue and remains as an ethical dilemma. In Asian culture, affected by AD is ashamed and people often withhold the facts from the public, preferring to confining the information to the family. It is hypothesized that demented patients are unwilling to disclose their diagnosis to others. We interviewed 51 mild AD patients and their caregivers for their attitudes on disclosing of AD diagnosis, using a semi-structured questionnaire. Among 51 patients, 32 were males and 19 were females with age ranges from 50 to 94 years old (Mean = 77.9; SD = 8.3) and year of education ranges from 0 to 16 (Mean = 9.02; SD = 5.03). Among 51 caregivers, 15 were males and 36 were females with age ranges from 30 to 85 (Mean = 59.5; SD = 14.4). Twenty-seven caregivers (52.9%) were patients' spouses; 21 (41.2%) were patients' children; 3 (5.9%) were the patients' daughters-in-law. According to the caregivers, half of the patients (49.0%) were aware, 29.4% were not sure, and 21.6% were not aware of their diagnosis. Contrary to our hypothesis, more than half of the demented patients (70.6%) and their caregivers (56.9%) favor truth felling and prefer to disclose their diagnosis of AD. The same amount (60.8%) of the patients and their caregivers favor truth felling and prefer to disclose their relatives' diagnosis of AD to the public. The majority of the patients and caregivers prefer doctor to disclose the diagnosis to themselves (92.1%; 94.1%) and to their affected family (86.2%; 82.4%). Main reasons for disclosure were to understand their disease, receive treatment earlier, plan for the future, and patient's right to know. Worrying about patient's emotional disturbance, embarrassing the patients, and causing deterioration of the disease were main reasons for favoring non-disclosure. Whether or not patients' awareness of their disease did not affect their understanding of the disease; the disclosure of their

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diagnosis; the disclosure of their affected family's diagnosis; caregivers' disclosure of their diagnosis; caregivers' disclosure of affected family's diagnosis (χ^2 tests, $p \geq 0.05$). Disclosing of AD diagnosis is no longer considered as ashamed and something not respectable to their family, indicating that our society has become more open-minded and civilized in disclosing of AD diagnosis.

P1-91

Dementia and driving; Why does the driver with dementia not stop driving?

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Introduction: Drivers with dementia continuing driving is present in spite of a doctor and familial advice a lot while dementia is diagnosed. Therefore, as for determining background of the psychosocial of the patient stopping neither the diagnosis of the dementia nor driving, it is thought that it is important when we perform management of the psychiatry of the dementia patient.

Methods: We determine the psychosocial background of the dementia driver who does not stop purpose driving. We intended for 101 patients we had a checkup in 1995 or more 2005, and it was given a hospital attached to the subject Kochi University School of Medicine a diagnosis of dementia. In addition, we investigated it about the age of the method subject, sex, clinical diagnosis, having driving interruption advice or not, driving continuation and a cancellation success reason.

Results: Driving interruption person 87 of 101 who recommended were from results chief physician or a family (86%).Nine successful people urged (8.9%), an interruption on a driving interruption out of 87, but continued driving even if evaluation in itself of the driving ability urged seven difficult people (7%), 71 (70.3%) and advised it. As for nine interruption winners, a middle-class dementia level or a spouse maintained a license by an advice/advice, and a child acted for need tide of the times change. Seven reasons that an evaluation of the ability for driving had difficulty with were patients with extremely minor dementia level or meaning dementia. Because 17 (21.5%), the driving that we cannot stop in 49 rejection (62%) of the patient person himself, life were a hobby/definite aims, for the reason why the advice back of the driving interruption did not stop driving, it was 10 (12.7%).On the other hand, as for 14 of 101 people without an interruption advice and the advice, two people (1.9%) stopped driving in (13.8%) spontaneously, and 4 (3.9%) stopped driving by familial persuasion.

Conclusion: Though a driving interruption advice was accomplished for most patients after a diagnosis of the discussion dementia, many patients refused a driving interruption and continued driving afterwards. It is not only the correspondence of the doctor for the driving interruption of the dementia driver and will think that we require the disorder measures that considered severity of psychosociology and the dementia that do not accept the advice of the doctor and causative disease in future.

P1-92

Terminal care for dementia patients in Matsubara hospital

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We think that how to spend the last days of life is important for dementia patients as same as for patients without dementia. What makes the problem difficult is that most of the dementia patients are unable to express their will. Here we show how we did for dementia patients-IVH? or PEG? or taking an operation or chemotherapy when they get cancer? We also show the results of interviews with their families.

P1-93

The relationship between activeness toward notifying diagnosis, tendency of treatment decision, and a severity of dementia in the primary care physician

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Background and purpose: In recent years, medical treatment for elderly people or demented patients has been a controversial issue in Japan. A recent survey revealed that although many people do not want life-prolonging treatments for themselves, they

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want to continue life-prolonging treatments for their families. The present study examined whether a severity of dementia and activeness toward notifying diagnoses were associated with the primary care physicians' treatment decision for the patients living in a local area.

Methods: Total of 83 doctors (63 male, 8 female, and 12 unspecified) agreed to participate in this study. The average age of the doctors was 52.8. Those doctors who signed the informed consent were asked to complete the questionnaire in terms of notifying diagnosis, active therapies to malignancy, fracture, renal failure and sudden death, and continuation of life-prolonging treatments for demented patients.

Results: Around 80% doctors notified the patient his/her diagnosis in case of mild dementia, and 40–50% doctors notified diagnosis even in case of severe or moderate dementia. When making the treatment decision, around 15% doctors gave priority to patients' own wishes, and 55% doctors took balance of wishes between patients and their families. In addition, female doctors had a tendency to respect both patients' and familial wishes. Moreover, those doctors who actively notified the patients' diagnoses tended to give priority to patients' wishes ($r = 0.22$). The ratio of recommendation for active treatment to malignancy, fracture, renal failure, and sudden death were negatively corresponded to a severity of dementia. Although patients did not wish for life-prolonging treatments at the end of their life stage, the rates of doctors who applied cardiac massage to the mild demented patients and severe demented patients were 40% and 25% respectively. Whether or not the medical doctors provided life-prolonging treatments to the patients with dementia had similar trends in different stages of dementia ($r = 0.63$–0.85).

Conclusion: We found that the doctors had different opinions in terms of the notification of dementia, the recommendation for active therapy, and life-prolonging treatments of demented patients. We have to respect both patients' and familial wishes when making treatment decisions, and hope that guideline for the end stage therapy of demented patients as well as elderly people will be made.

P1-94

Cognitive function and psychiatric symptom in early onset frontotemporal dementia and late onset frontotemporal dementia

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Several recent studies mentioned late-onset FTD patients were more common than previously assumed. Despite many researches on FTD, there are no systematic studies which compared clinical characteristics of early-onset FTD and late-onset FTD. The aim of this study was to compare cognitive function and psychiatric symptoms in patients with early and late onset FTD in consecutive patients of the university memory clinic in Japan. Study participants were consecutive outpatients of the Higher Brain Function Clinic of the Department of Neuropsychiatry, Ehime University Hospital, with a diagnosis of FTD between January 1997 and September 2005. We examined difference in sex, education, duration from onset to consultation, CDR score, MMSE score, RCPM score, and NPI sore at first consult between early and late onset FTD patient. There were totally 35 FTD patients, mean onset age was 63.0 years old, and 40% of them were late-onset FTD patients. There were no significant differences between the two groups in sex, education, CDR, and duration from disease onset to consultation. There were significant differences in the total MMSE score, "recall of three words" item, "construction" item and RCPM score between two groups; late-onset FTD groups scored significantly lower than early-onset FTD groups. There were significant differences in apathy domain of NPI and total NPI score between two groups; late-onset FTD groups scored significantly higher than early-onset FTD groups. Late-onset FTD patients may have memory and visuospatial deficit in addition to their behavioural changes, even they are clinically diagnosed according to consensus diagnostic criteria. They also present more apathy compared to early-onset FTD patients. They may have different histolopathological background.

P1-95

Key symptom in semantic dementia; difference between 'Gogi aphasia' and memory disturbance

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Semantic dementia (SD) is characterized by selective loss of the semantic memory, especially the profound loss of a word sense called 'Gogi aphasia', which is now classified into a type of frontotemporal lobar degeneration. One of the core features of the aphasia is a severe impairment of the aspect of word meaning with relatively well preserved phonological processing, so the patient could not retrieve phonological and semantic fragments of the target word or proverbs, and they show quite impressive 'I don't know' responses. We previously investigated initial symptoms of patients with degenerative dementias, such as frontotemporal dementia (FTD), SD, and Alzheimer's disease (AD). In that report, although language impairments were observed in all the three groups, language impairments were significantly more common in patients with SD as the initial symptom, than changes in social behavior, affection, and daily activities. If patients had begun to speak the same phrases repeatedly, clinicians have to ascertain whether this repetitive questioning is caused by the context of a memory disorder or a stereotypic catch-phrase usage. Likewise, if patients whose language become rough and/or blunt it should be considered whether this crude speech is due to the lack of social awareness or aspontaneity in speech or word finding difficulty. Clinicians may often misinterpret the aspect of aphasia as a symptom of memory disturbance and make a diagnosis of AD or Fading our exploration of outpatients, some sets of language tests are examined to detect 'Gogi aphasia' of SD. We apply confrontation naming test for detecting the loss of the word sense, reading aloud some sets of Kanji for surface dyslexia, in other words, legitimate alternative reading of components (LARC) error associated with semantic impairments, and proverb completion task for the loss of meaning representations for the language unit. We report a case of SD presenting relatively mild 'Gogi aphasia' with apparent symptoms of a social breakdown.

P1-96

Two cases of frontotemporal dementia preceded by a long-term clinical course of bipolar affective disorder

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Background: Affective disorder, particularly depression, has been documented as a precursory or early symptom of dementia. We report here two cases of frontotemporal dementia (FTD;Neary:1998) preceded by a long-term clinical course of bipolar affective disorder.

Cases: The present study took into account the protection of privacy and anonymity. Case 1: A 63-year-old man. At 36-years-old, he developed mania, and after a period of remission, again experienced mania at 42-years-old. From 48- to 50-years-old, he experienced two manic phases and a depressive phase. Starting at 57-years-old, he started to exhibit disinhibited behaviors and failure to dress appropriately. At 60-years-old, cerebral blood flow single photon emission computed tomography (SPECT) showed reduced blood flow in the frontotemporal region, and at 61-years-old, brain magnetic resonance imaging (MRI) confirmed atrophy of the frontotemporal region. At 62-years-old, spontaneity is reduced and mini-mental state examination (MMSE) score is 14 (diagnosis: frontotemporal degeneration (FTD)). Case 2: A 61-year-old man. He first developed mania at 30-years-old, and again experienced mania at 34-years-old after a period of remission. Up to 47-years-old, he experienced three manic phases and a depressive phase. Starting at 59-years-old, he began to exhibit disinhibited behaviors, loss of insight. At 58-years-old, cerebral blood flow SPECT showed reduced flow in the frontotemporal region, and head CT confirmed atrophy in the frontotemporal region. At 60-years-old, disinhibition is marked.

Conclusion: The above two patients first experienced bipolar affective disorder at 30- to 36-years-old and developed FTD at 57-years-old. Bipolar affective disorder thus occurred about 20 years before FTD. Since FTD symptoms occurred after long-term bipolar affective disorder, bipolar affective disorder was not a early symptom of FTD, but rather, onset of FTD was secondary to bipolar affective disorder. The above findings suggest the existence of a subgroup of bipolar affective disorder patients who eventually develop FTD.

P1-97

Common and uncommon clinical features between semantic dementia(SD) and

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Alzheimer's disease (AD): A case presentation of late-onset SD

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Semantic dementia (SD) shows selective and progressive loss of semantic memory associated with focal atrophy of the temporal lobes. The clinical features of SD are distinct from those of Alzheimer's disease (AD) in the pattern of cognitive deficits and behavioral symptoms associated with the anatomical dysfunctions. We report a case of late-onset SD who was given a diagnosis of AD of his first examination. A 78-year-old right handed man presented with two years history of gradual changes in memory and personality noticed by his family. At the 1st examination he had no insight about these problems and some responses similar to saving appearance behavior quite common to typical AD patients. Total score of the MMSE was 28 points; recall score was two point lost. These features were often observed in mild AD patients. However, in another occasion he could flawlessly perform delayed recall of real objects and revealed word finding difficulty in middle or low frequency words with poor cue effects. Furthermore completion phenomena in proverbs were sometimes absent though idiomatic kanji reading (e.g. samisen/sya-mi-se-n/ prawn/eb-i/) was preserved different from SD patients. His day-to-day memory, intelligence or ADL were relatively preserved compared with his semantic impairment. The latest MRI revealed left predominant anterobasal temporal lobe atrophy and he was diagnosed as having SD though it was in an early stage. In this case, the age of onset later than usual onset of SD, saving appearances behavior and results of neuropsychological screening tests might mislead us to diagnosis of early AD. We would discuss about the most distinctive symptoms of SD through this case.

P1-98

An autopsy case of fronto-temporal dementia without family history, who shows an atypical tau neuropathology

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Clinical history: At the age of 25, the patient began to show progressive impaired spontaneous speech and activities. She had no family history of any other dementia and neurological disease. Her Brain CT demonstrated severe frontotemporal atrophy. At the age of 29, she showed gait disturbances and went to almost bedridden. At the age of 41, she died, due to pneumonia.

Neuropathological findings: The formalin fixed brain weight was 700g. Macroscopically, severe atrophy of frontal lobe and pyramidal tract in midbrain and pons were revealed. Microscopically, Hematoxylin/eosin sections showed profound neuronal loss and gliosis throughout neocortices and subcortical white matters, predominantly in the frontal and temporal lobes. We did not found any Pick bodies, ballooned neurons, basophilic inclusion bodies, Lewy bodies, senile plaques, astrocytic plaques, and tufed astrocytes. A lot of Tau and Gallyas-Braak stained positive coiled bodies and atypical thick threads were detected in the subcortical white matters. Tau and Gallyas-Braak stained positive but bodian stain negative neurons were found in the cortices and subcortical gray nuclei. Neurons of substantia nigra and hypoglossal nucleus were almost preserved.

Summary: Our case was fronto-temporal dementia without family history. The autopsied brain showed severe frontal atrophy and atypical tau neuropathology without pick bodies.

P1-99

Five cases of frontotemporal lobar degeneration (FTLD) presenting with visual simultanagnosia

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Impairment at recognition of two objects is called simultanagnosia. Simultanagnosia is being considered to be disturbance of processing the second item. Patients with simultanagnosia can recognize each object by visual or auditory perception but cannot detect them at the same time. Visual agnosia is closely associated with posterior cortical atrophy (PCA) irrespective of underlying diseases and has been rarely reported in corticobasal degeneration (CBD). We report here five cases of FTLD with some being clinically diagnosed CBD and they showed visual simultanagnosiain which frontotemporal lobar atrophy (FTLA) was in common to all cases on MRI study. Case 1: A 73-year-old woman showed personality change at age 66 years old and developed aphasia at age 72. She featured frontal lobe syndrome, alien hand, and visual simultanagnosia without agnosia. MRI disclosed left-sided atrophy of the motor cortex. Case 2: A 67-year-old man developed parkinsonian features when he was 63 years old. He showed alien hand at age 68. He had visual simultanagnosia without agnosia and dementia. Case 3: A 58-year-old woman suffered from insomnia at age 55 years old. She showed dysfunction of initiation about thinking and visual simultanagnosia without agnosia. SPECT study revealed hypoperfusion of the parietal lobe with left-sided predominance. Case 4: A 57-year-old woman was unable to go through with center line of roads by car and began excessive intake of sweets at age 50 years old. One year later she showed difficulty in calculation with both visual simultanagnosia and agnosia. On MRI, she showed FTLA and PCA at age 52. She developed alien hand and myoclonus at age 54. Case 5: A 63-year-old man was unable to use his tools of for his work at age 59 years old. He became aggressive and showed difficulty in writing at age 61. MRI revealed FTLA with the mild PCA at age 63. He developed alien hand and visual simultanagnosia without agnosia. Five cases of FTLD presented here showed visual simultanagnosia and MRI imaging study showed brain morphological change relevant to FTLA. PCA causes difficulty in calculation and writing, and visual agnosia as well as simultanagnosia, but PCA, observed in Case 4 and 5, was not in common to all cases. The lateral temporal pole was shown to be a locus of visual information neuronal pathway and was involved in the present cases of FTLD. In consequence, the lateral temporal pole atrophy was attributable to another locus for visual simultanagnosia.

P1-100

Efficacy of fluvoxamine and tiapride as a treatment for streotypyed eating behaviors in frontotemporal lobar degeneration

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Patients with frontotemporal lobar degeneration (FTLD) present several behavioral symptoms. The Stereotypy Rating Inventory (SRI) was developed to assess the wide range of stereotyped behaviors. In SRI eating and cooking behavior is one of the five distinctive stereotyped behavioral disturbances. The present study reports a 67-year-old man with FTLD who manifested severe stereotyped eating behaviors. At the age of 65 he was hospitalized as a traffic accident, then his behavioral abnormalities and personality change were found: throwing away important documents from the window or going away without permission. After leaving hospital his stereotyped behavior started: taking the same route for a walk for over 6 hours every day. At 66 he sometimes stole or spent money. At 67 he ate sweets too much, pointed out hyperglycemia and diagnosed diabetes. He took a cake away from his grandchildren, but he didn't seem to have repented at all for what he did. His wife made him have psychiatric examination. Brain magnetic resonance image showed slight atrophy of bilateral medial frontal and anterior temporal lobes, and several small ishemic lesions in subcortical area. He was diagnosed as FTLD and entered our hospital. On admission, his SRI score was 29/60 (eating and cooking: 12/12). We caught diabetes/hyperglycemia for an index of the stereotyped eating behaviors, and treated with fluvoxamine-75mg/day and tiarpide-75mg/day with a dietary cure-1600Kcal/day. Fluvoxamine is one of the selective serotonine reuptake inhibitors (SSRIs) and reported effective for the stereotyped behaviors in FTLD. The latter is a selective D2 antagonist to treat disinhibition. He took two kinds of

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oral hypoglycemic agents: glibenclamide 2.5mg/day and voglibose 0.6mg/day to control diabetes. On 35th day, blood sugar level became within normal limit without oral hypoglycemic agents and then SRI score was 13/60. At last on 100th, his SRI score became 11/60 (eating and cooking: 2/12), he left our hospital and entered the geriatric institution. It is suggested that the stereotyped behaviors of FTLD are associated with a decrease in serotonergic activity of brain. Therefore SSRIs might raise serotonergic discharge and improve the symptoms on FTLD. On the present case, we regarded overeating sweets/diabetes as the result of stereotyped eating behaviors and treated them with fluvoxamine. In addition administration of tiapride from the early days was also effective on tendency to disinhibition.

P1-101

IDE gene polymorphism influences on BPSD in mild dementia of Alzheimer's type

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Background: The lower activity of insulin degrading enzyme (IDE), which divides amyloid β proteins (Aβ), is regarded as one of the factors that may inhibit the accumulation of Aβ in a brain affected with dementia of Alzheimer's type (DAT). The cognitive symptoms and psychiatric symptoms in DAT may be affected by the changes of glucose utilization in the brain that are caused by the lower activity of the enzyme. We examined an association of IDE gene polymorphism with DAT and behavioral and psychological symptoms of dementia (BPSD) in mild DAT.

Methods: We collected 163 patients who met the criteria for probable Alzheimer's disease of NINCDS-ADRDA and who were followed during FAST stage 4 at the Department of Neuropsychiatry in Hyogo College of Medicine. As a control, we collected 186 age- and sex-matched non-demented controls who had neither mental disorder nor family medical history. The genomic DNA was extracted from the peripheral whole blood of all examinees, and the genotyping for IDE and apolipoprotein E (ApoE) was determined using restriction fragment length polymorphism. Appearance of BPSD in the course of the mild dementia was determined using the behavioral pathology in Alzheimer's disease rating scale (BEHAVE-AD).

Results: No significant differences in IDE genotype distribution or allele frequency were identified between DAT patients and the controls (genotype distribution: $\chi^2 p = 0.4447$, allele frequency: $\chi^2 p = 0.8833$) regardless of ApoE $\epsilon 4$ allele. However, among the DAT patients with BPSD, significant association was observed between presence of IDE allele C and affective disturbance (after Bonferroni correction, $\chi^2 p = 0.0112$). This association was independent of the presence of the ApoE ϵ 4 allele (after Bonferroni correction, $\chi^2 p = 0.0063$). IDE polymorphism influences the risk of developing affective disturbance.

Conclusion: IDE gene polymorphism is unlikely to play a substantial role in conferring susceptibility to DAT. It may be involved in the development of affective disturbance through the course of mild degree DAT.

P1-102

Genetic variations in the dysbindin gene are associated with human memory performance

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There are few studies investigating underlying mechanism of cognitive ability in genetic basis. Cognitive decline is observed in Alzheimer's disease and

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in normal aging. ApoE gene, a risk gene for developing Alzheimer's disease, is reported to be associated with memory function. Patients with Alzheimer's disease often show delusions and hallucinations, which are major symptoms of schizophrenia. A genetic variation of the dysbindin gene (DTNBP1), a susceptibility gene for schizophrenia, has been reported to be associated with general cognitive ability and cognitive decline in schizophrenia. Although profound disturbance of memory performance is observed in schizophrenia, no study has reported the relationship between this gene and memory. We examined the possible association between two genetic variants, a protective haplotype and a risk neutral polymorphism for developing schizophrenia, in the dysbindin gene and memory and IQ (intelligence quotient) in 165 healthy volunteers and 70 patients with schizophrenia. Healthy controls, who did not carry the protective haplotype, had lower performance in several memory domains measured by the Wechsler Memory Scale-Revised (WMS-R), although this haplotype did not affect IQ measured by the Wechsler Adult Intelligence Scale-Revised (WAIS-R). A risk neutral polymorphism influences both memory and sub-categories of IQ in the opposite direction. These data suggest that the dysbindin gene may have impact on the cognitive function such as memory and IQ. Further examination such as association analysis between the dysbindin gene and Alzheimer's disease could be helpful to understand the shared mechanisms of developing Alzheimer's disease and schizophrenia.

P1-103

The center of evaluation of the psychological troubles linked to ageing of Sainte-Anne hospital (Paris, France): First assessment of activity

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Since May 2006, the Center of evaluation of the psychological troubles connected to ageing has opened in the University Department of Psychiatry, in Sainte-Anne Hospital (Paris, FRANCE).This functional unit of ambulatory evaluation is devoted to more than 50 year-aged patients. It has two main objectives: diagnostic and therapeutic assessment of psychopathological situations including both psychic, cognitive and behavioral symptoms, and orientation in care system. The addressing is made by a psychiatrist in half of the cases, more rarely by a general practitioner or another specialist. The current active line of the first author counts more than about seventy patients, average age 71 years [47–95]. The sex ratio is 2 women for 1 man. The patients essentially consult in ambulatory, on average twice, for symptoms arising on a pre-existent psychiatric pathology in more than two thirds of the cases. Personal antecedents of depression are present in 80% of the cases and in 70% of the cases, in the family. The average age of the first symptom is of 51.6 years [15–88]; it is a depressive episode in more half of the cases, a psychotic symptom in 10% of the cases, and a cognitive complaint in less than 5% of the cases. The average MMSE is 25.9 [21–30]. Sixty percents of the patients are treated by antidepressants at the time of the consultation, mainly in monotherapy, 40% are on a neuroleptic, 25% a mood stabilizer and 20% receive an acetylcholine esterase inhibitor. The use of minor tranquilizers is frequent in 30% of the cases. The diagnosis in the international classification of the diseases (CIM-10) is a mood disorder in 45% of the cases, a psychosis in 10% of the cases. Near half of the patients come back at home, only 2% will be hospitalized to complete the cognitive and psychocomportemental evaluation, either in psychiatric hospitalization for the week, or in geriatrics or in neurology. We present the main social, demographical and anamnestic characteristics, the existential events, the vascular comorbidities and the profile of therapeutic received by the patients of this troop.

P1-104

Liaison psychiatry for older people in Hong Kong

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Introduction: The ageing population and increasing healthcare expenditure have led to shifting of healthcare resources from hospital to community. Geriatric day hospital is one of the important components of community care. Overseas studies show that comprehensive psychiatric management can alleviate the burden of inpatient care and lead to better outcomes of patients in the community. However, there is limited information concerning the liaison psychiatric service for older people in the geriatric day hospital.

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Objective: To compare two groups of geriatric patients who were attended by liaison psychiatrists before and after the introduction of liaison psychiatric service to the geriatric day hospital of a regional hospital in Hong Kong.
Method: The consultation records from September 2002 to August 2004 and from September 2004 to August 2006 were compared basing on the fact that liaison psychiatric service to the geriatric day hospital was started since 1st September 2004 on top of the existing psychogeriatric consultation service to the geriatric ward of the hospital. The demographic characteristics, source and reasons of referral, clinical diagnoses and recommended management of the two groups of geriatric patients were analyzed.
Results: A total of 343 consultation records were identified from the period September 2002 to August 2006. One hundred and sixty six patients were referred by the geriatric ward and 177 patients were referred by the geriatric day hospital. There was a significant increase in the number of referrals after the introduction of liaison service to the geriatric day hospital. The commonest reasons for referral among inpatients and day patients are mood, cognitive, and behavioral symptoms. The commonest psychiatric diagnosis among inpatients is dementia (45.8%), followed by depressive disorders (27.7%) and delirium (15.1%). Depressive disorders (68.4%) and dementia (23.7%) are the most prevalent psychiatric diagnoses among day patients. Significantly more day patients required psychiatric reassessment (35%) and early outpatient psychiatric follow-up (44.6%).
Conclusion: The growing need for liaison psychiatric service for older people comes hand in hand with the ageing populations and changing service provisions in healthcare sector. Further research, appropriate training and sustainable service development are required so as to meet the need and expectation of the stakeholders.

P1-105

Cognitive impairment adversely affects functional muscle performance: An element of frailty in old age

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Cross-sectional studies have demonstrated the association between muscle loss and cognitive impairment but the mediating mechanism is unclear. It is possible that those with cognitive deficits might be less active in physical activities, resulting in disuse atrophy. Another explanation is that neurodegenerative disease and muscle degeneration may share the same factors, namely sex hormone decline and inflammatory markers increase. Though impairment in muscle strength and cognition are increasingly being recognized separately as features of frailty in old age, the effect of cognitive impairment on functional muscle performance has seldom been investigated.

To test the hypothesis that impaired cognition adversely affects functional muscle strength independent of muscle mass.

4000 community dwelling Chinese elderly aged 65 or above were recruited. Functional muscle performance was measured by average grip strength of both hands. Muscle mass was measured using dual-energy X-ray absorptiometry (DXA). Appendicular skeletal mass (ASM) was calculated by the summation of muscle mass measured in the 4 limbs, with the operator adjusting the cut lines of the limbs according to specific anatomical landmarks. Cognitive part of Community Screening Instrument of Dementia (CSI-D) was administered to the subjects. CSI-D score less than 28.40 was classified as cognitive impairment. Relationships between grip strength, cognitive impairment and muscle mass were analyzed using univariate and then multivariate analyses for each gender. Possible confounding factors which may affect grip strength such as arthritis, diabetes mellitus, stroke and heart disease were also included in the multivariate analysis.

The cognitive impairment group was older in both genders. In men, the muscle mass was lower in the cognitive impairment group whereas no difference was found in women. However, grip strength was significantly lower in cognitively impaired subjects in both genders. (Table 1 and 2) The prevalence of conditions that may affect grip strength were tabulated in Table 3. After adjustment to age, appendicular skeletal mass, arthritis, diabetes mellitus, stroke and heart disease, significant differences in grip strength still exists between the cognitively impaired and non-impaired group. (Table 4)

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Table 1 Comparison between the Cognitively Impaired and the Non-impaired Group in Men

	Impaired Group	Non-impaired Group	p-value
	Mean ± SE N = 99	Mean ± SE N = 1901	
Age (year)	76.43 ± 0.59	72.18 ± 0.11	0.000
Whole Body Muscle Mass (kg)	42.14 ± 0.56	44.34 ± 0.12	0.000
Appendicular Skeletal Mass	18.12 + 0.27	19.23 + 0.06	0.000
Grip Strength (kg)	26.36 + 0.71	31.46 + 0.14	0.000

Table 2 Comparison between the Cognitively Impaired and the Non-impaired Group in Women

	Impaired Group	Non-impaired Group	p-value
	Mean ± SE N = 506	Mean ± SE N = 1493	
Age (year)	74.64 ± 0.26	71.87 ± 0.13	0.000
Whole Body Muscle Mass (kg)	33.69 ± 0.19	33.88 ± 0.12	0.380
Appendicular Skeletal Mass (kg)	13.73 + 0.08	13.84 + 0.05	0.264
Grip Strength (kg)	19.44 + 0.19	20.52 + 0.11	0.000

Table 3 Prevalence of chronic illness that may affect grip strength

	Men N = 2000	Women N = 2000
Arthritis	24.3%	21.8%
Diabetes Mellitus	14.7%	14.3%
Stroke	5.5%	3.3%
Heart disease	18.3%	16.5%

Table 4 Grip strength difference between the cognitively impaired and the non-impaired group

	Men Mean (95% CI)	p-value	Women Mean (95% CI)	p-value
Crude difference (kg)	5.10 (3.82, 6.39)	0.000	1.08 (0.66, 1.50)	0.000
Adjusted* difference (kg)	2.69 (1.58, 3.81)	0.000	0.52 (0.14, 0.91)	0.007

*Adjusted to age, appendicular skeletal mass, arthritis, diabetes mellitus, stroke and heart disease

P1-105

Cognitive impairment adversely affects functional muscle strength independent of muscle mass. Cognitive impairment and muscle loss contribute synergistically to frailty in old age.

P1-106

Gender differences in psychiatric morbidity among elderly in-patients at an African General Hospital

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Introduction: Psychiatric illness often affects the elderly due to inherent biological factors of the ageing process, the multiplicity of physical illnesses, polypharmacy; but also as a result of different gender roles and expectations. For example some disorders like depression and suicide occur more in one sex than the other.

Objective: This study aimed to establish the sex differences in mental health morbidity among elderly in-patients at a general hospital in Uganda.

Method: In a cross sectional study we enrolled 127 elderly participants admitted in a general hospital in Uganda. In a 2 stage process, we administered a standardized demographic questionnaire and the Self Reporting Questionnaire SRQ-25 to screen for general psychological distress. In the second stage, for all patients we administered the Mini Mental State Examination (MMSE) to assess cognitive impairment and the Structured Clinical Interview for the Diagnostic and Statistical Manual IV (SCID) for specific psychiatric diagnosis.

Results: The sex ratio was 1:1. The males were more likely to be married or cohabiting and the females were widowed or living alone ($p = 0.00$). Males had more children and more social (family) support. The mean SRQ score for the females was 4.1 and for the males 3.5. The mean MMSE score for the females was 23.6 and 22.87 for the males. More female 35 (54%) had a psychiatric diagnosis most of whom were suffering from depression 13 (20.3%).

Conclusion: There were gender differences in psychiatric morbidity among the elderly in-patients of Mulago General Teaching Hospital in Uganda with females being more represented. However, there were no gender specific interventions for these elderly patients calling for more awareness.

P1-107

Memory training increases platelet PLA2 activity

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Background: PLA2 is a ubiquitous enzyme involved with membrane fatty acid metabolism and intracellular signalling pathways. PLA2 activity is decreased in patients with Alzheimer's disease (both in brain

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and in platelets), and this abnormality is associated with certain neuropathological and clinical findings of the disease. In addition, the inhibition of cerebral PLA2 leads to memory impairment in adult rats. Recent evidence suggest that cognitive stimulation may trigger intracellular signaling cascates, including GSK inactivation and favoring long-term potentiation. We investigated the effects of memory training on platelet PLA2 activity in healthy individuals.
Methods: Twenty-three cognitively unimpaired older individuals were selected to this study. Eleven received a four-session memory training intervention (experimental group – EG) and twelve completed the same evaluation as the EG and received standard outpatient care only (control group – CG). Training included information on memory aging and instruction and practice on organization of grocery lists and underlining of main ideas in short texts. Pre and post test measures included prose and list recall, WAIS-R digit symbol, and strategy use measures. Platelets were isolated from peripheral blood of the subjects at baseline and after the training intervention, and the activity of the three main PLA2 groups (sPLA2, cPLA2, and iPLA2) was determined by a radio-enzymatic assay.
Results: After memory training, the EG showed significant improvement in speed of processing (digit symbol, $p = .004$), prose recall ($p = .009$), and the strategy use measures (categorization, $p = .006$). In addition, patients in the EG group had significant changes in PLA2 activity, namely a significant increase in total PLA2, cPLA2, sPLA2 activity ($p = .01$), and significant decrease in iPLA2 activity ($p < .001$). Patients in the CG did not show differences neither in cognitive measures nor PLA2 activity between pre and post test.
Discussion: Our results suggest that memory training may have a modulating effect in certain biological systems associated with cognitive functions and neurodegenerative diseases, e.g. Alzheimer's disease, and this putative cerebral effect can be detected in platelets. The increments observed in PLA2 activity after training may be associated to better cognitive performance and to a potentially protective effect against this disorder (or cognitive decline).

P1-108

Social and cultural representation of madness, mental disorder and depression in elderly aged 65 and more, during a community survey in Haute-Vienne (France)

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Psychiatry is still quite often stained with discrediting representations. The main purpose was to assess beliefs, behaviour and knowledge while dealing with madness, mental disorders, depression and the psychiatric treatments for the elderly in Haute-Vienne (France).
Method: An analysis of the answers given by 190 persons aged 65 and more, during a face to face interview using a questionnaire which explores the representations of madness, mental disorder and depression in a sample of 902 adults selected with the method of quota. The interview was done in 2003 during the local step of an international multicentric community survey entitled: Mental disorders: Image and Realities in community sample.
Results: For people aged 65 and more, these tree expressions were connected with different images. Madness was incurable and was strongly associated with notions of violence, danger and exclusion. The image of Mental Disorder though closed to that of Madness was more oriented towards psychiatric symptoms and its specificity seemed to be the notion mental deficiency (49.2% of answers). As for Depression, this concept was clearly separated of the two others and was better known by the elderly. A depressed people was described as someone who really suffers: he or she cries quite often (88.5%), is isolated (67.9%), does suicidal attempts (74.7%); he or she can be healed through the use of well known and appropriate treatments.
Discussion: This study was interesting in that it was coupled with an international multicentric community survey which had a valid methodology. It showed that those aged 65 and more in Haute-Vienne had similar representation as those collected in elderly in the national sample, however generally more pessimistic than those of the persons aged less than 65. The limits of this study could be those of the method of quota and those of anthropological survey in mental health.

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Conclusion: The study of social and cultural representation of Madness, Mental disorder and Depression in 190 elderly aged 65 and more in Haute-Vienne (France) confirmed a decrease in the stigma of the depressed. Information and education regarding health should be intensified in order to better the image of psychiatry in the population.

Keywords: Elderly, social and cultural representation, mental health, community survey.

P1-109

Correlation between metabolic syndrome and cognition in the Korean elderly

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Recently, it has been found that the presence of metabolic syndrome in elderly is associated with risk of cognitive decline, and also known that the genotype of ApoE is related with more cognitive impairment accompanying metabolic disturbances. Thus, we investigated the effect of ApoE genotype in correlation between metabolic syndrome and cognition of the elderly in the community. We hypothesized that cognitive function would be more impaired by factors of metabolic syndrome in the presence of ApoE ϵ 4 allele. A total of 1,305 subjects (440 men and 865 women) aged 60 to 98 were analyzed from preliminary data of Gwangju Dementia and MCI Study (GDEMCIS). The study questionnaire consisted of demographic characteristics, current and past history, drug history, family history of dementia and stroke, and Korean version-Mini Mental State Examination (K-MMSE). We also examined ApoE genotype and analyzed associated factors with metabolic syndrome as defined according to the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).Metabolic syndrome was present in 28.6% of the subjects (13.4% of men and 36.3% of women). On multiple logistic regression analysis, low serum HDL cholesterol was associated with an increased risk for cognitive impairment (K-MMSE score $\leq$ 17) adjusted by age, sex, educational level, and smoking in the presence of ApoE ϵ 4 allele (OR 0.95, 95% CI 0.92–0.99).These results suggest that serum HDL cholesterol may affect cognitive function in the elderly in the presence of ApoE ϵ 4 allele.

P1-110

Mental and physical health factors in relation to falls amongst very old people- prospective follow-up of over-90-year-olds in the CC75C study

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Falling in advanced old age is one of the most complex co-morbidities that affect the oldest old. Common psychogeriatric conditions have been linked to falling but their aetiological role is unclear. Intensive 1-year follow-up of over-90-year-olds in a UK population-based study revealed potential fall predictors – both mental health (cognitive impairment, depressive symptoms, self-rated health) and physical factors (walking mobility, ADL impairment, other co-morbidities) – and allowed examination of their relative importance.

At Year 17 of Cambridge City Over-75s Cohort (CC75C) participants from general practices, all over 90 years old, were visited by the project nurse and followed-up for a year. Structured interviews covered general health, well-being, ADLs, self-rated health, Depressive Symptom Scale and cognitive assessment by CAMCOG, including MMSE. Falls data from participants/informants were collected by calendars, phone-calls and visits.

84% of survivors took part: 90 women + 20 men aged 91–106 years, mean and median age 94. 60% fell during the year following interview. Cognition was impaired in ~2/3: 32% severely and a further 32% moderately. Depressive Symptom Scale results were skewed to lower, less depressed scores: only 1/3 scored >4 (mean of 0–11 scale). 2/3 rated their health as good/very good compared with others of the same age, and only 20% rated it fair/poor/very poor, but those unable to respond gave no rating.

Severe cognitive impairment (RR 1.9, 95% CI 1.0–3.5), higher depression scores (RR 2.1, 95% CI 1.1–4.3) and lower self-rated health (RR 6.0, 95% CI 2.8–12.8) were amongst many suggested risk factors shown to predict falls in univariate analyses. Physical health factors that also showed a 2–3 fold increased risk of falling included the number of co-morbid conditions, incontinence, ADL disability and mobility limitations. Clearly many of these factors are inter-related and it is important to consider possible confounding effects. Multiple variable

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negative binomial regression modeling with likelihood ratio testing assessing the effect of covariates reduced the significance of all mental health associated relative risks (Table).

In advanced old age falling is extremely common and the interplay of physical and mental health contributory factors is complex. Higher fall rates amongst the cognitively impaired and depressed may not be inevitable if other factors are considered and addressed.

P1-112

Depressive state, physical symptoms and irregular daily life are associated with poor perceived health of old inhabitants of Japan

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Background: Perception of health status is regulated by several factors. Quality of life is strongly associated with it.
Objective: Perceived health or self-rated subjective health of the old inhabitants of Japan was studied to identify its association to several physical and mental illness.
Methods: The target subjects were interviewed by using health questionnaire. A health questionnaire including the Todai Health Index (THI) was applied to 529 inhabitants of Gunma Prefecture, Japan, aged 85 years or older. THI is a symptom checklist composed of 130 questions. Twelve scale scores; (1) physical symptoms, (2) respiratory complaints, (3) eye and skin complaints, (4) mouth and evacuation complaints, (5) digestive complaints, (6) impulsiveness, (7) lie scale, (8) mental instability, (9) depressive state, (10) aggressiveness, (11) nervousness, (12) irregular daily life, were calculated. Response rate was 99.8% (528/529). Other items included sex, age, prevalence of chronic disease and its treatment, marital status, academic career, and friendship. A question "How is your health?" with five ordinal response options was used to assess perceived health, which is a comprehensive rating scale.
Results: The mean values of other THI scale scores of poor perceived health except eye and skin complaints, impulsiveness, lie scale, mental instability and nervousness in male subjects were significantly higher than those of good perceived health. Spearman's rank correlation coefficients between perceived health score and THI scale scores were all statistically significant. Furthermore, multiple logistic regression analysis was conducted to identify significant factors predicting poor perceived health. Twelve THI scores; sex; age; suffering from chronic illnesses; receiving medications; not having attended schools after compulsory education; single, and not having friends were used as independent variables. THI scale scores of physical symptoms, depressive state, and irregular daily life were selected as significant factors. Odds ratios and 95% confidence intervals in parentheses on each factor were 1.15 (1.07–1.23), 1.14 (1.02–1.30), and 1.15 (1.02–1.30), respectively.
Conclusions: Poor perceived health was significantly associated with irregular lifestyle, physical and mental complaints. Perceived health reflects the health status of the older inhabitants of Japan.

P1-113

Neuroanatomical characteristics of geriatric apathy and depression: An MRI study

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Background: Apathy is one of the most common late-life neuropsychiatric syndromes. The objective of our study was to examine the neuroanatomical correlates of apathy in older subjects with and without geriatric major depression (MDD).
Methods: Eighty-four subjects (43 patients with MDD and 41 controls) underwent comprehensive neuropsychiatric and physical examinations, and the high-resolution MRI brain scans on a 1.5T GE MRI scanner. Apathy was assessed using the Apathy Evaluation Scale. MRI image analyses included cortical surface extraction, tissue segmentation, and cortical parcellation methods to measure the gray and white matter volumes in two prefrontal subregions: the anterior cingulate and orbitofrontal cortex.
Results: Depressed group had smaller orbitofrontal gray matter volumes compared to the controls. The severity of apathy was associated with the decreased gray matter volume in the right and left anterior cingulate gray matter volumes using partial correlation and regression analyses after controlling for age, sex, and the diagnosis.
Conclusions: Apathy and depression were associated with different anatomical correlates in the prefrontal

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regions implicated in the regulation of cognition and emotion. Our findings offer new understanding of the neuroanatomical characteristics of apathy and depression in late-life, and have broad implications for the neurobiology of behavior.

P1-114

Screening for depression and assessing change in severity of depression. Is the geriatric depression scale (30, 15 and 8-item version) useful for both purposes in nursing home patients?

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Background: Depression is a common psychiatric disorder in nursing home patients. Recognition and management of depression by nursing home staff is reported to be poor. It would facilitate the management of depressive disorders in nursing homes, if one instrument could be used both for screening and assessment of (change in) severity of depression.
Objectives: determining the ability of three versions of the GDS for screening and assessing change in severity of depression in nursing home (NH) patients.
Method: In 350 elderly NH-patients the GDS and the MADRS were administered by trained interviewers. The presence of major (MaD) or minor depression (MinD) was evaluated with the Schedules for Clinical Assessment in Neuropsychiatry. Receiver Operator Characteristic (ROC) curves of the GDS-versions were performed to measure the ability to screen on depression. The ability to measure change in severity of depression was measured by differences in mean GDS-scores and mean MADRS-scores between patients with MaD, MinD and no depression, and expressed in terms of effect sizes.
Results: In ROC-curves all three GDS-versions performed well. The MADRS showed larger effect sizes for the differences between MaD, MinD and no depression than the GDS-versions. The effect sizes of the three GDS versions were comparable.
Conclusion: All three versions of the GDS can be used for screening on depression among NH-patients. The MADRS is superior to the GDS for assessment of (changes in) severity of depression, but the GDS also appears to be an acceptable instrument for this purpose and is less time-consuming.

P1-115

Depression in people with dementia

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The recognition of depression in elderly people with dementia can be problematic as many of the symptoms of depression are also symptoms of dementia. To improve the diagnosis of depression, we identified and quantified the behavioural and psychological symptoms of dementia which are indicative of depression and are likely to respond to the use of anti-depressants. Thirty-five subjects with dementia from the Home Care program of the CLSC Cotedes-Neiges, in Montreal were assessed for depression by a psychiatrist in their homes. Other tools such as the Cornell Depression Scale validated for people with dementia, and the Neuropsychiatric Inventory were completed by an interviewer with the primary care-giver. Since we do not have a gold standard, we used two reasonable assessments of depression: the continuous value of the Cornell scale and the binary variable indicating the psychiatrist diagnosis of depression (1 if the psychiatrist diagnoses depression, 0 otherwise). Then the analytic task consists of studying the association between these two outcomes and ten items of the neuropsychiatric inventory (NPI). Our analysis was exploratory and relied on Partial Least Squares (PLS) regression, a regression method used on a relatively small number of cases. Most of the subjects (32) were severely demented with a score on the FASS (Functional Assessment Staging Scale) at 6 or 7. Five were diagnosed as depressed by the psychiatrists and 40% obtained a high score on the Cornell Depression Scale (9). Further results are based on the index known as Variable Influence on Projection (VIP), a standard tool in PLS regression. We consider a variable important in defining outcome

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if VIP > 1. We found that delusional symptoms are most strongly and positively associated with both outcomes. Disinhibition is also positively associated to both outcomes but less strongly so. Other variables positively associated to the Cornell Depression Scale are depression, apathy and aberrant behaviour.

P1-116

Body mass index, waist circumference, waist-hip ratio and depressive symptoms in Chinese elderly: A population-based study

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Background: Studies that investigated the relationship between obesity and depression in the elderly have generated conflicting findings, partly because of the use of body mass index (BMI) alone to measure obesity in the elderly. The use of BMI fails to account for varying proportions of muscle, fat and bone, and few studies have used other measures of central obesity, such as waist-hip ratio (WHR) and waist circumference (WC).
Objectives: The aim of this study was to examine whether individually BMI, WHR and WC were consistently associated with depressive symptoms in the elderly.
Methods: Analysis of cross sectional data of 2604 community dwelling Chinese elderly aged 55 and above, including socio-emotional characteristics, self-rated health and functional status, anthropometric measurements and Geriatric Depression Scale (GDS).
Results: There was a negative trend in the prevalence of depressive symptoms (GDS greater or equal to 5) across increasing BMI categories: 16.9% in low BMI, 14.2% in normal weight, 12.1% in moderate to high BMI. The associations for moderate to high BMI (OR, 0.77; $p = 0.04$) relative to normal BMI, were statistically significant after controlling for confounding variables. However, no consistent trends in the prevalence of depression and its odds of association were observed for increasing WHR and WC categories.
Conclusion: Our results suggest that waist-hip and circumference measures of central obesity did not support an inverse relationship of obesity and depressive symptoms. An inverse relationship of BMI with depressive symptoms may indicate greater physiologic and functional reserve from greater muscle mass that protects against depression.

P1-117

The course of adverse effects of nortriptyline and venlafaxine during 3-year treatment in elderly patients with major depression

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Rationale: Suboptimal treatment of depression in elderly patients may be partly the result of the greater vulnerability of elderly patients to adverse effects. However, few studies have investigated the course of adverse effects in elderly patients and data are lacking about the relation between the number and severity of adverse effects and antidepressant dose, physical comorbidity and age.
Methods: The frequency and severity of 43 individual adverse effects were assessed during a 12-week double-blind randomized controlled trial comparing venlafaxine with nortriptyline, followed by an open treatment phase of 3 years.
Results: No difference could be demonstrated in tolerability between venlafaxine and nortriptyline, both in the double-blind and in the open treatment phase. Both antidepressants were tolerated well by elderly patients. The number of adverse effects showed an initial increase followed by a decrease, the global severity of adverse effects followed a non-linear decline from the start of the trial medication. We found no relationship between antidepressant dose and serum levels with the number of adverse effects and a relation of borderline significance with the global severity of adverse effects. A decrease in depression severity was associated with a decrease in the number of adverse effects, and depression severity was also related with the global severity of adverse effects. The number and global severity of adverse effects was not related age and gender, physical comorbidity, or with type of depression (first or recurrent).
Conclusion: Venlafaxine and nortriptyline are tolerated well by elderly patients, and most adverse effects decreased with time as the depression improved. Age and physical comorbidity are not related with number and severity of adverse effects.

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P1-118

Volumetric correlates of cognitive functions in depressed elderly patients

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Depression, especially in elderly, is associated with structural abnormalities of cortical and subcortical regions, as well as cognitive deficts. Several voxel-based-morphometry (VBM) studies have often detected gray and white matter abnormalities in patients with late life depression. However, VBM studies that investigated correlations between brain volumes and scores of cognitive measurements have been scarce. The purpose of this study was to determine the correlation between VBM brain volumes and scores in neuropsychological tests and psychiatric scales in elderly depressed patients and health controls. Statistical parametric mapping was used to analyze magnetic resonance imaging scans from 18 depressed patients and 11 nondepressed subjects. A comprehensive neuropsychological battery was used to evaluated memory, executive function and speed processing information. Depressed patients had significant white matter volumetric reduction in frontal regions than nondepressed subjects. Depressed patients with more atrophy in the brain white matter demonstrated worse performance in verbal fluency test; and when the atrophy was in the gray matter, more alteration was observed in Activities of Daily Living Scale and verbal fluency tests. The control group demonstrated less depressive symptoms when they had less atrophy in the brain white matter; and less atrophy in the gray matter showed better performance in verbal fluency, processing speed and memory tests. These preliminary results corroborate that elderly depressed present neuropsychological deficits and suggest possible neuroanatomical correlations for these findings.

P1-120

Abstract withdrawn

P1-121

Loneliness, depression and hopelessness in older people

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Loneliness is associated with poor health outcomes in older people, increasing the risk of depression,

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suicide, poor physical health and all cause mortality. The aim of this study was to examine the relationship between loneliness and depression in a large sample of community dwelling elderly. 1337 individuals over the age of 65 were recruited from 5 local GP practices and interviewed at home using GMS AGECAT. Loneliness, depression and hopelessness was measured using GMS self report items. One third of participants admitted to feeling lonely. Loneliness was more common in women and was associated with widowhood, depression and hopelessness. The risk of depression was independently associated with the degree of loneliness. Loneliness is common in community dwelling elderly. It is a significant risk factor for depression and independently contributes to hopelessness in older people over and above the effect of depression. Loneliness should be inquired about in older people and where it co-exists with depression warrants targeted and individualized intervention.

P1-122

Stressful life events and susceptibility genes (5-HTTLPR and BDNF) for depression in Korean elders

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Objective: It has been reported that the functional polymorphism in the serotonin transporter gene linked promoter region (5-HTTLPR) modifies the association between stressful life events (SLEs) and depression in child, adolescent and adult populations. We sought to replicate this finding in elders and, additionally, to test modifying effects of the brain-derived neurotrophic factor (BDNF) val66met polymorphism.

Methods: In 732 Korean community residents aged 65+, diagnosis of depression (Geriatric Mental State Schedule), information on SLEs, and genotypes for 5-HTTLPR and BDNF val66met were ascertained. Of those without depression at baseline 521 (88%) were followed up 2.5 years later. Interactions between SLEs and the two genotypes were investigated for both prevalent depression at baseline and incident depression at follow-up.

Results: Significant interactions of SLEs with both 5-HTTLPR and BDNF genotypes were observed on risk of depression after adjustment for age, sex, education and disability. A significant three-way interaction between 5-HTTLPR, BDNF, and SLEs was also found. The same findings were observed for predictors of incident depression in the prospective analysis.

Conclusions: These findings suggest that environmental risk of depression is modified by at least two genes, and that gene-environment interactions are found even into old age.

P1-123

Depressive status as a risk factor of functional decline among Japanese rural community-dwelling elderly: An 8-year prospective cohort study

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Objectives: Maintenance of functional capacity among the elderly has become a major issue in geriatrics and gerontology. It has been reported that depressive status is a risk factor of functional decline among the elderly. However, there are few community-based data on this relationship for Asian populations. We therefore examined the relationship between depressive status and functional decline among Japanese rural community-dwelling elderly, using an 8-year prospective cohort study design.

Methods: The study population included 192 men and 315 women aged 65 years and over at the baseline. Functional capacity was measured using self-reported basic activities of daily living (BADL) (walking, eating, bathing, and dressing) and instrumental ADL (IADL) (measured by the 13-item Tokyo Metropolitan Institute of Gerontology Index of Competence, with a cut-off score of 10/11), and then functional decline (i.e. BADL-decline and IADL-decline) was defined as new onset of functional dependency during the 8-year follow-up period. Depressive status was assessed using the 30-item Geriatric Depression Scale with a cut-off score of 10/11 (meaning that scores of 11 and above were classified as indicating depressive symptoms). The baseline data for gender, age, history of chronic diseases (defined as having at least one disease among stroke, heart disease, and diabetes), smoking, and physical activity, were collected as covariates. Logistic regression analysis adjusted for the potential

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confounders cited above was performed to test the association between depressive status and functional decline.

Results: One hundred seventeen persons (23.1%) were classified as having depressive symptoms at the baseline. Multiple logistic regression analysis showed that depressive status was associated significantly and independently with both BADL-decline and IADL-decline (odds ratio [OR] = 1.87, 95% confidence intervals [CI]: 1.01 to 3.50; OR = 1.99, 95% CI: 1.09 to 3.62, respectively).

Conclusion: Our results suggest that depressive status is a reliable predictor of functional decline. Early intervention strategies for late life depression are needed urgently to prevent or slow functional decline among community-dwelling elderly.

P1-124

Biochemical abnormalities detected with 3-T proton magnetic resonance spectroscopy in late-life major depression

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Background: Neuroimaging studies have consistently shown structural abnormalities in late-life depression, but little functional brain study has been done.

Objective: The goal of this study was to examine the biochemical abnormalities of late-life major depression in the frontal white matter, per ventricular white matter, basal ganglia and pons by using 3-T proton magnetic resonance spectroscopy (MRS).

Method: Twenty-seven elderly patients with major depressive disorder and 19 comparison elders received 3-T MRS. MRS spectra were acquired from voxels which were placed in the frontal white matter, per ventricular white matter, basal ganglia and pons. Ratio levels of N-acetylaspartate (NAA), choline, and myo-inositol reference to creatine were calculated. Means of these biochemical levels between the depressed elders and the comparison subjects were compared.

Results: Patients with late-life major depressive disorder had a significantly lower NAA/creatine in the frontal white matter, and higher choline/creatine and myo-inositol/creatine in the basal ganglia as compared to the control subjects.

Conclusion: Biochemical differences at cortical and subcortical levels may reflect the different pathophysiology process at distinct regions involving emergence of late-life depression.

P1-125

The relationship between major depression and physical illnesses in older men: a survey in the aged care center

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Objectives: Physical illnesses are believed to be the risk factors of suicide and depressive disorder, especially in older men. However, major depression is often misdiagnosed or overlooked due to the mixed symptoms of aging and comorbid physical illness in this population. The study examined the relationship between major depression and physical illnesses.

Methods: Older (aged 70 years or older) men were recruited from the Veterans Home. Specialist physicians obtained past histories of the physical illnesses which were believed to be associated with depression (including hypertension, heart diseases, diabetes, arthritis, chronic pulmonary diseases and malignant diseases) through chart reviews and further history taking. Mini-International Neuropsychiatric Interview (MINI) was used to assess a current major depressive episode and the revised Geriatric Depression Scale Short Form (GDS) was used to measure the severity of depression.

Results: One hundred and fifty six older men (mean age: 79.19 ± 4.59 years, ranging from 75–95 years) were recruited at the Veterans Home in Taiwan between September 2004 and May 2006. They were divided into two groups based on the presence of major depressive disorder: 77 men were depressed (mean age: 79.22 ± 4.27 years) and 79 men were non-depressed (mean age: 79.16 ± 4.90 years). Among the physical illnesses we examined, only diabetes ($x2[1] = 6.989$; $p = 0.008$) and malignant diseases ($x2[1] = 4.988$; $p = 0.026$) had higher

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prevalence of major depression among the patient population than the non-patient population, and only the diabetic patients had higher GDS score than the non-diabetic ones ($t = -2.084$, $p = 0.039$). **Discussion:** Clinicians should pay more attention to the elder men with diabetes or malignant diseases for major depression screening. The diabetic men with major depression, who might had higher severity of depression should be diagnosed and treated early and properly to decrease the complication.

P1-126

Memory in depressive and alcoholic old patient

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Memory deficits are noted in both alcoholism and depressive illness old patients. Alcoholism and depressive illness appeared together as comorbidity. Alcohol and depressive symptom can be a risk factor for dementia, in which memory decreased mainly. We evaluate the memory function, especially verbal and nonverbal visuospatial memory in 15 alcoholism and 15 depressive illness old patients over 60 years of age, also comparing to 15 alcoholism patients below 50 years of age for investigate the age factor. We can differentiate 3 groups according to memory score, especially verbal and nonverbal memory by using one-way ANOVA statistically (0.01 significant interval). The 3 group is below 50 years old alcoholism, over 60 years' old alcoholism and over 60 years old depressive illness and total memory function decreased in above order. Age affects the memory function. Both Short term memory and long-term verbal memory decreased in depressive illness (0.01 significant interval). Nonverbal or visuospatial memory tasks which are more susceptible to CNS damage, are decrease in both alcoholism and depressive illness old patient. In our study depressive illness old patients showed more memory deficit than alcoholism old patients. Differentiating depression from dementia in the elderly is extremely complicated. This is a one point epidemiological study but we need follow-up over time for getting more detailed results.

P1-127

Latent factors of depressive symptoms differently associated with subsequent cognitive decline: A population-based cohort study

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It is expected that a portion of the aged non-demented population is in a precursor stage of dementia. They might manifest some depressive symptom and show a characteristic profile in response to questionnaires for depression screening. The present study empirically identified multiple latent factors of depressive symptoms (responses to the Japanese translation of the 15-item Geriatric Depression Scale: GDS-15) in an aged non-demented population and described how these factors were associated with the chance of subsequent cognitive decline in 2 years.

We conducted 2 rounds of community-based interview surveys for all the dwellers aged 65 or older with a 2-year interval (response rate: 97% and 91%, respectively). The study subjects were 864 persons (women: 64%, mean age: 73.1 years) who completed the GDS-15 in the first survey, completed the mini-mental state examination (MMSE) in both the surveys, scored 24 or over in the first MMSE, and were free from stroke history at the second survey. Factor analysis with a promax rotation was applied to the responses to the GDS-15 items. The occurrence of subsequent cognitive decline was defined as 3 points or more of decrease in the MMSE score, and its chance was related to the estimated scores of latent factors of GDS-15 on a logistic regression model controlling for sex, age, and the first MMSE score. Likewise, we assessed the predictive value of the standard GDS-15 score.

The factor analysis yielded the following 4 interpretable factors: factor I corresponding to GDS-15 items #1, 5, 7, 11 labeled as positive items; factor II, #2, 4, 6, 8, 15, general depressive affects and thoughts; factor III, #3, 12, 14, hopelessness; factor IV, #9, 10, 13, loss of energy. Subsequent cognitive decline occurred in 15.4% of the subjects. Logistic regression analysis indicated that the chance of subsequent cognitive decline was associated with factor IV in the positive direction: odds ratio 1.78 per the estimated factor score (95% confidence interval: 1.3–2.5) and with the factor II in the negative direction: odds ratio 0.49 (0.32–0.76). Contrastingly, the standard GDS-15 score could not predict the cognitive decline.

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The findings suggest that the precursor or early stage of cognitive decline can be characterized by a subset of depressive symptoms (e.g., loss of energy, preferring to stay at home, and self-perceived memory decline) that is disproportionate to the limited manifestation of general depressive affects and thoughts.

P1-128

Psychological assessment of elderly depression outpatients with dementia

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Elderly depression is prone to reducing QOL and ADL due to loss of motivation in addition to psychiatric symptoms. Moreover, it is often associated with cognitive decline. For treatment of elderly depression, conventional drug therapy using antidepressants does not provide sufficient efficacy. Considering physical features of the elderly, it is necessary to develop comprehensive assessment and treatment with instructions on lifestyle taken into account. This study aimed to develop effective treatment for elderly depression from a psychological aspect of elderly depression with dementia.

Objectives: were 82 outpatients who visited the special clinic of elderly depression in the National Hospital for Geriatric Medicine, named "The Mental Vitality Clinic". They were 74.7 years old on average. The diagnoses were as follows: Alzheimer's disease (AD) with depression 31, major depression without dementia 51. With those depressive patients, 14 AD patients without depression were assessed for control study. The diagnosis of AD were based on the criteria of DSM-IV. Hippocampal atrophy on brain MRI was inclusion criteria for the diagnosis. All cases were assessed with Minimental examination (MMSE), Geriatric Depression Scale (GDS), Cornel Medical Index (CMI). The value of MMSE and GDS and subgroup of CMI were compared in 3 group. The CMI subgroup of inadequacy became significantly in AD patients without depression. The CMI subgroup of depression and the like other mental item showed significantly high score in major depression. Although not significant, AD patients without depression also showed the tendency of high inadequacy. It was the same pattern as those AD patients with depression. In depression cases associated with dementia due to AD, depression was milder but sense of inadequacy was felt significantly more strongly compared with the cases without dementia. The sense of inadequacy seems to be the key word for understanding of the AD with depression.

P1-129

Low free testosterone concentration is associated with depression in older men

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The serum concentration of gonadal hormones has been associated with various measures of well-being, but it is unclear if their association with mood is confounded by the presence of concurrent physical morbidity.

We designed this study to determine if the association between the serum concentration of testosterone and mood in older men is independent of physical comorbidity and, therefore, possibly causal.

We conducted a cross-sectional study of a community-derived sample of men aged 71 to 89 years, and used the Geriatric Depression Scale 15 items (GDS-15) to assess depressed mood. Clinically significant depression was defined a priori by a GDS-15 > 7. The concentration of free testosterone was calculated using the Vermeulen method. Physical health was assessed by measures of comorbidity which included the Charlson weighted index and Physical Component Summary score of the SF-36 Health Survey. We used logistic regression to determine the association between depression and quintiles of total and free testosterone.

3,987 men were included in the study, of whom 203 (5.1%, 95% CI: 4.4% to 5.8%) had depression. Participants with depression had significantly lower total and free testosterone than non-depressed men ($p < 0.001$ for both). However, they were also more likely to smoke and have low educational attainment, body mass index >30, Mini-Mental State Examination score < 24, prior or current history of antidepressant treatment and greater concurrent physical morbidity. After adjusting for these factors and for age, men with depression were 1.55

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(95%CI = 0.91, 2.63) and 2.71 (95%CI = 1.49, 4.93) times more likely to have total and free testosterone concentrations in the lowest quintile (<10.7 and < 0.2 nmol/L, respectively),

Free testosterone concentration below 0.2 nmol/L is associated with a significant increase in the risk of depression, and this association cannot be adequately explained by physical comorbidity. A randomised controlled trial is required to determine whether the link between low free testosterone and depression is causal, as older men with depression may benefit from systematic screening of free testosterone concentration and testosterone supplementation.

P1-130

Depression elderly profile between institutionalized care and home care in Makassar, Indonesia

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Recently, population of elderly is significantly increased not only in developed country but also in developing country. As many as 70% of institutionalized elderly experienced significant depression, and the incidence in community settings is approximately 18% in populations over 65 years old. Depression is a medical condition that affects not only quality of life but also the way in which people take care of themselves. It is a condition that could be easily resolved with you treatment, but untreated elderly could have dire consequences. This study was designed using cross sectional approached. We recruited 30 elderly with institutionalized care and 30 with home care. DSM IV TR criterion was used ti diagnose the depression. HDRS was used for grading depression each group. We found 36.7% depression in elderly with institutionalized care and 26.7% with home care. The result was significantly ($p < 0,05$) by continuous correction of X test. In institutionalized care was found 16.7% mild depression, 10.0% moderate depression, 10.0% severe depression. But in home care was found 16.8% mild depression, 6.7% moderate depression and 3.3% severe depression. First, depression may cause an overwhelmed burden on mental health service. Second, quite numbers of elderly suffer depression but undetected, so mental health system should provided service for elderly. Collaborative study is needed from other department to treat elderly physically and mentally.

P1-131

Late life depression treated by an algorithm

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The depression in elderly people configures a heterogeneous syndrome, not just about its etiology but about the responsive to the treatment too. The development of the depression in the elderly ones has a basically multifactor character. The success of the antidepressants treatment depends on the type and the gravity of: the depression, the others psychiatric or clinical illnesses; on the adequate choice of antidepressants, its effectiveness and profile of adverse effect; on the orientation supplied to the patient; and, finally, it depends on the adherence to the treatment.

Objective: To evaluate the effectiveness of the pharmacologic treatment in the late life depression, based on the use of an Algorithm treatment specify for depression

Methods: 48 Elderly people had been evaluated with diagnosis of depression according to diagnostic criteria of CID-10 and DSM-IV. The patients had been evaluated with scales and tests to investigate the cognition (Cambridge Cognitive Test – CAMCOG; Mini-examination of the Mental State), to investigate depression: Montgomery-Asberg Depression Rating Scale (MADRS), and Hamilton Rating Scale for Depression (HAM-D); and clinical global impression (CGI). All the patients had in agreement initiated pharmacologic treatment to a standardized Algorithm, independently of the description and gravity of the current depressive episode.

Results: Of the 48 patients, 79.2% were of the feminine sex, married 45.8%, age measured 72.15%. Of the 48 patients, 12 (25%) had had partial response, in accordance with scale (MADRS 15), and 36 patients (75%) had presented remission (MADRS 8).

Conclusion: The algorithm for the treatment of the depression in late life, demonstrated be a useful instrument, allowing treatment for patients independently of the gravity of the current episode, and its previous description to the treatment.

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P1-132

Frontal lobe dysfunction in senile depression in relation to cognitive function

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Background: The aim of the present study was to investigate frontal lobe dysfunction among elderly (over 65) patients with depression. The important issue for elderly persons with depression is that depression causes decreased quality of life and increases the nursing burden. Appropriate evaluation of senile depression must occur from both social and medical viewpoints in order to attempt prevention. Brain imaging studies that can aid in this evaluation, such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) have been reported in recent years.
Methods: We used near-infrared spectroscopy (NIRS) to evaluate functional changes in the frontal lobe of elderly depressed patients. The word fluency task (WFT) that we used consisted of a 30-s pre-task period, a 60-s task period consisting of three 20-s blocks, and a 70-s post-task period. The subject was two groups of depressed patients who met the diagnostic criteria defined in DSM-IV, an elderly group (N = 8, over 65 years old) and a non-elderly group (N = 15, under 65 years old). In addition, 127 healthy volunteers without psychiatric disorder participated in the study.
Results: The prefrontal regional brain blood volume changes during the task by patients with depression were remarkably smaller than those of healthy controls. Significant changes of both [oxy-Hb] and [deoxy-Hb] were observed between the elderly group and the non-elderly group. As a result, the decrease of activation during the WFT was admitted in senile depression. A significant correlation between the amount of average changes of [deoxy-Hb] and score of Zung Depression Scale (SDS) cognitive symptoms in the medial frontal lobe region was observed in the elderly group (N = 8) (Spearman rho = 0.823 (p = 0.023)). The cognitive symptom of SDS was estimated based on the sum of the score of items 14), 16), 17), and 18). The detail of each item is as follows; 14) I feel hopeful about the future, 16) I find it easy to make decisions, 17) I feel that I am useful and needed, and 18) My life is pretty full.
Conclusion: Our result suggests the utility of NIRS inspection in the evaluation of frontal lobe function in elderly depressed patients. We also believe that additional examinations other than the word fluency task should be applied, for example, a digit span test or visual search test. The development of an overall evaluation measure for elderly depression including the above-mentioned measurements is important.

P1-133

A patient with senile depression who suffered increased asymptomatic cerebral infraction after electroconvulsive therapy

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We encountered a 73-year-old female with major senile depressive disorder characterized by physical morbidity (concomitant diabetes and hypertension), brain organic vulnerability (multiple lacunar infarction) and brain functional vulnerability (compromised drug tolerability and mild cognitive impairment). The patient responded to electroconvulsive therapy (ECT) and the main effects were recognized. However, we obtained the following findings that might compromise assurance of the long-term safety of ECT: higher D-dimer values noticed before and after ECT, blood pressure surge associated with application of current and increased aggregation of minor infarctions in the region of the perforator artery, which was noticed in the comparison between the findings of MRI of the brain conducted before and after ECT. In view of these findings, we report the progress of this case along with the preliminary insight into the perioperative management of hypertension that is a risk factor of cerebral infarction and which frequently occurs after ECT. The summation of the areas of lacunar infarction and the ratio of the affected area to the cross-sectional area of brain parenchyma were calculated using the serial cross-sectional images from the MRI scan of the brain conducted before and after ECT. The post treatment data showed an increasing tendency when compared with the pretreatment data (452.17 mm2 vs 228.17 mm2; 0.447% vs 0.226%). Establishment of the prophylactic measure to control post-ECT hypertension in the

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above-mentioned subgroup of patients is urgently needed along with evaluation of the efficacy of secondary prevention of subsequent cerebrovascular disorder. The follow-up of the clinical course of this case suggested the following two possibilities. Pretreatment with nicardipine hydrochloride may prevent post-ECT hypertension, and post-ECT increase in asymptomatic cerebral infarction may aggravate the functional and organic prognoses.

P1-134

Short-term treatment outcome of severe depression among elderly patients in Japan

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Background: Many studies have reported that the outcome of depression was worse among the elderly than among the middle aged. Although the number of elderly with mental disorder has reportedly been increasing, reflecting the super-aging society in Japan, the outcome of severe depression is infrequently reported.
Objective and hypotheses: We investigated the short-term outcome of severe depression among the elderly. We hypothesized that aging had negative effects on the short-term treatment outcome of severely depressed elderly.
Methods: We reviewed the medical records of elderly patients with severe depression on DSM-IV consecutively admitted to our hospital between January 2005 and March 2007. Patients were excluded from our study if their age was under 60 and/or they had other comorbid psychiatric disorder. We investigated their background characteristics and the method of treatment. We also examined the frequency of severe adverse events (i.e., delirium), length of stay, and discharge to home or not to evaluate short-term treatment outcome. Then we compared the old-old group (age 70 or over) to the young-old group (age under 70) to determine treatment outcome. Statistical analyses were performed using Student's t-test (two-tailed) for parametric data and chi-square test and Fisher's exact test for non-parametric data.
Results: There were 30 patients (male 8, female 22, mean age 71.7 $\pm$ 5.9). Twenty of the patients had psychological factors on admission, and 19 of 30 patients were treated with ECT (mean number 10.5 $\pm$ 3.8). The mean number of complications on admission was 1.8 $\pm$ 1.7. Nineteen patients had severe adverse events, and 10 of them experienced delirium. The average length of hospitalization was 50.6 $\pm$ 21.2 days, and twenty of the patients were discharged to home. Although there were no significant differences in background characteristics between the old-old and young-old groups, the old-old group had significantly worse short-term outcome than the young-old group in frequency of delirium (47.4% vs. 9.1%, $p < 0.05$) and low rate of discharge to home (52.6% vs. 90.9%, $p < 0.05$).
Conclusions: Our study of elderly patients with severe depression revealed that aging had negative effects on their short-term treatment outcome. These results highlight the fact that we need to take into account the vulnerability of the aged, and that we should treat them both carefully and aggressively.

P1-135

Continuation ECT to prevent relapse of catatonia in relapse-prone middle-aged and elderly patients

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Objective: Electroconvulsive therapy (ECT) is known to be effective and safe in middle-aged and elderly patients with catatonia. However, relapse after response to acute ECT is a major problem in clinical psychogeriatrics. We conducted a prospective study of middle-aged and elderly patients with catatonia who relapsed after responding to a first acute ECT course to evaluate the effect of continuation ECT on prevention of relapse.
Background: We previously studied the short-term effect of a first course of acute ECT (phase 1) and the 6-month relapse rate (phase 2) after response to the acute ECT in catatonic patients. Subjects of the phase 1 study were 35 consecutive patients older than 45 years who had exhibited 2 and over signs on the Bush-Francis Catatonia Rating Scale (BFCRS) 14-item screening and had been referred for acute ECT after other treatments had failed. The patients were treated at Tohoku University Hospital between January 1998 and April 2007. Acute-ECT

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response was defined as resolving catatonic sighs to one or none of 14 BFCRS screening items for 1 week after the final ECT session. Relapse was defined as presenting 2 and over sings on the BFCRS 14-item screening. Thirty-two of the 36 patients (88.9%) responded to acute ECT. Of these 32 patients, 12 (42.9%) relapsed within 6 months after response to acute ECT. Four patients are being followed up at present.

Subjects and methods: The present study included 12 consecutive catatonic patients (4 men, 8 women) who relapsed within 6 months after response to the first acute ECT course and then responded to a second acute ECT course. Patients were given continuation ECT; four ECT sessions at weekly intervals, then four ECT sessions every 2 weeks, then three ECT sessions every 4 weeks. Clinical symptoms were evaluated by the BPCRS 14-item screening weekly for 24 weeks or until relapse. Relapse was defined as presenting 2 and over sings on the BFCRS 14-item screening. Adverse cognitive and physical effects resulting from the continuation ECT were evaluated and noted by each patient's attending physician.

Results: Relapse occurred in 3 of the 12 patients (25%) within the 6-month follow-up period. No patient experienced adverse cognitive or physical effects.

Conclusion: We believe that continuation ECT to be an efficacious and safe treatment for prevention relapse in middle-aged and elderly patients with catatonia who have relapsed after response to acute ECT.

P1-136

Determinants of excessive daytime sleepiness in a French community-dwelling elderly population

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Epidemiological studies have suggested that excessive daytime sleepiness (EDS) is associated with depression, but the association between EDS and other psychiatric disorders has not been investigated. The aim of the study was to investigate the association of EDS with psychiatric disorders and health-related conditions in the elderly population. 2259 non-institutionalised persons aged 65 years and over randomly recruited from the Montpellier district, France, were assessed by the Epworth sleepiness scale in regard to their EDS. Associations of EDS with psychiatric variables assessed by the Mini International Neuropsychiatric Interview and demographic and physical health-related variables were determined. This cross-sectional study was conducted from March 1999 to February 2001. Men were significantly more likely to report EDS as compared with women (12.0% versus 6.0% respectively). EDS was significantly associated in univariate analyses with chronic diseases, early awakening, snoring, severity of depression, and lifetime prevalence of manic and hypomanic episode. Multivariate analyse revealed that the lifetime prevalence of manic and hypomanic episode, snoring, and gender (male) were independently associated with EDS. No independent association with other psychiatric disorders was found.

P1-137

Lack of aging effect on prepulse inhibition and habituation of the acoustic startle response in patients with schizophrenia

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Prepulse inhibition (PPI) and Habituation (HAB) of the acoustic startle response (ASR) have been proposed as neurophysiologic measures of sensorimotor gating and discussed as trait-linked biological markers for information-processing deficits in patients with schizophrenia. Several studies have reported that the effect of aging is little on PPI and HAB of the ASR in healthy subjects. However, only few attempts have so far been made to examine the effect of aging on these neurophysiologic measures in patients with schizophrenia.

The objective of the present study is to characterize the effect of aging on PPI and HAB of the ASR in patients with schizophrenia and to

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examine the hypothesis that aging affect little on these neurophysiologic measures, which are considered to be trait-linked biological markers for patients with schizophrenia.

The subjects were 41 patients with schizophrenia (23 males and 18 females with an average ± SD age of 41.7 ± 12.5 years) and 60 healthy subjects (30 males and 30 females with a mean age of 35.0 ± 8.9). We measured ASR by using the Startle Eyeblink Reflex Analysis System Map1155SYS (NIHONSANTEKU Co., Osaka, Japan). Subjects were tested in a startle paradigm consisted of 3 blocks with continuously presented 70 dB background noise. In the first block, ASR for 115 dB startle pulse (40 msec) alone was recorded for 6 times. The second block consisted of 115 dB pulses with or without prepulses (20 msec) of 82, 86 and 90 dB (prepulse-to-pulse intervals 120 msec), 8 times for each condition. The last block was same as the first block to see the HAB. Inter-trial intervals randomly changed (20 sec on average, range 15 sec to 25 sec). A startle paradigm consisted of 44 trials and lasted approximately 15 minutes.

Patients had significantly decreased startle amplitude in the first block compared with normal subjects. Compared with normal subjects, patients exhibited significant deficits in startle habituation and in PPI at the 90 dB prepulse condition. However, in both patients and normal subjects, age did not correlate significantly with startle amplitude in the first block, PPI at neither prepulse condition and HAB.

Results suggest that, under the present paradigmatic conditions, deficits on PPI and HAB of the ASR, which are considered as trait-linked biological markers, might be affected little by aging in patients with schizophrenia.

P1-138

Late-onset catatonia responding to treatment with aripiprazole

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Catatonia is characterized as a specific disturbance in motor functioning that represents a phase in a progressive illness that includes stages mania, depression, and psychosis that typically ends in dementia. Sommer presented a clinical case report on late-onset catatonia first, and Jacobi reported that prognosis of late-onset catatonia was very poor. Regarding to treatment, it has been generally considered that the majority of late-onset catatonia does not respond to antipsychotic drugs, however, respond to electroconvulsive therapy (ECT) in some cases. In the present study, we demonstrated a case with late-onset catatonia responding to treatment with aripiprazole. The patient was a 56-year-old married housewife. Three years before, she became depressive state with depressive mood, anxiety, agitation, restlessness, psychomotor retardation. At that time, she was diagnosed as major depressive disorder and her depressive state was recovered treating with clomipramine. One year later, she had auditory hallucinations and persecutory delusions. Subsequently, catatonic symptoms, autism, mood liability, anxiety, agitation were elucidated. Her diagnosis was changed to late-onset catatonia. Brain CT and MRI scan, and EEG demonstrated no abnormality. Her SPECT images showed an area of irregular hyporperfusion areas in left temporal lobe. She did not respond to treatment with clomipramine, fluvoxamine, risperidone, lithium, and repetitive transcranial magnetic stimulation. She revealed a partial response to ECT, which was associated with the changing blood levels of catecholamine metabolites and brain-derived neurotrophic factor (BDNF). Her symptoms, however, relapsed after discontinuation of the ECT. Therefore, she was continuously treated with ECT in twice a week. The symptoms were waxing and warning in spite of maintaining the ECT. Then, aripiprazole was started at 6 mg/day and increased up to 30 mg/day in addition to the ongoing treatment with ECT. A month later, her verbal and nonverbal contact was improved, in addition, her activity was increased and her catatonic symptoms were disappeared. She keeps her improvement only treated with aripiprazole (30 mg/day) without the ECT. This case suggests that aripiprazole is a candidate drug for treating late-onset catatonia.

P1-139

The experience of quetiapine use for Japanese patients with psychotic symptoms

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In Japan, five atypical antipsychotics are distributed and recommended as first choice drugs for schizophrenia. However, methods for optimal selection in each case from five of them are not established. The purpose of this presentation is to summarize personal experience of quetiapine use for patients with psychotic symptoms and to make some suggestions for quetiapine use in daily clinical situations. Quetiapine was used for five Japanese patients with psychotic symptoms. The DSM-IV diagnosis of the patients included schizophrenia (3 patients), bipolar I disorder with psychotic features (1 patient), major depressive disorder with psychotic features (1 patient). Quetiapine was effective for three of the five cases prescribed. The common features of effective cases were 1) elderly or middle aged, 2) bipolar-like clinical course, 3) extrapyramidal symptoms by other atypical antipsychotics. It is notable that one of the patients exhibited severe lightheadness and somnolence by small dosage of quetiapine. In Japan, insurance coverage of atypical antipsychotics is limited to schizophrenia only. This experience suggests that quetiapine might be more suitable for the treatment of elderly schizphrenia prone to extrapyramidal side effects with bipolar-like clinical course than other atypical antipsychotics. Further clinical trial is required to test this suggestion.

P1-140

The hallucination without major psychological disorder in aged women

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Charles Bonnet syndrome was well-known visual hallucination observed in healthy aged person. Disturbed sensory input was thought to be one of the causes for pathogenesis. We presented here four such cases including one typical Charles Bonnet syndrome. Described were four cases we had experienced for two years in our institute. Case 1: A 72-year-old woman who had low vision can see a human face in her central visual field for 16 years. The face changes the expressions, and she recognized that the face was hallucination. A SPECT showed normal brain blood flow. Case 2: A 94-year-old woman she complained that she can see ticks around her for over 9 years. She always tries to remove the ticks using an adhesive tape. She denied that the ticks were hallucination. Psychologically she is healthy and active. She only embarrassed by that. Case 3: A 75-year-old woman experienced auditory hallucination. When she thinks something the part of it echoed in her ears for one year, without any major psychiatric problems. Although similar to a thought hearing, she never experienced as persecutive. She had mild hearing difficulty and the hallucination only bothering her. The hallucination was completely suppressed by listening music. She got full scale in MMSE. But SPECT showed mild decrease of blood flow in frontal lobe. Case 4: A 79-year-old woman heard neighbors shouting and which bothering her for one and a half year. The neighbors shouting was never heard by her family members and she denied her having hallucination. She had mild hearing difficulty but had good memory. All cases were woman. There was no major delusional development and all of them only annoyed or bothered by the hallucination. Some cases had sensory disturbance and which might be an inducing factor. In all cases drug therapy was ineffective. We can say that there is a cases group where the patients were aged woman with a continuing hallucination without major psychological disorders. Is this benign hallucination?

P1-141

Somatic hallucinations in Parkinson's disease resolved with electroconvulsive therapy

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Background: Hallucinations are common in Parkinson's disease(PD). Visual hallucinations(VHs) are the most common and auditory, tactile or olfactory hallucinations are less common. We here report on four PD patients with somatic hallucinations(SHs) besides VHs. Electroconvulsive therapy(ECT) were effective for these hallucinations and motor symptoms. SHs have been rarely mentioned in the past studies though the reason is unknown. Case report: All cases were admitted to the hospital. Hallucinations simultaneous with SHs were visual in all cases and auditory in the case 2 and 3. In the treatment of ECT the hallucinations

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were eliminated and the motor symptoms relieved in all cases. Case 1) 78-year-old woman of Yahr stage 4 or 5 with disease duration of 2.5 years. Daily levodopa dose is 200mg. She told her upper limbs were extending and her face stretching. She had the sensation that the bed was rugged on the back. Case 2) 65-year-old man of Yahr stage 5 with disease duration of 8 years. Daily levodopa dose is 300mg. He felt like his head was revolving or taken away from body and he had two heads. He often insisted there was somebody under his back on the bed. Case 3) 69-year-old woman of Yahr stage 5 with disease duration of 10 years. Daily levodopa dose is 600mg. She felt like she was falling out of her bed because the bed was leaning or shaking. Also She felt herself revolving and sometimes somebody clinging to her leg. Case 4) 82-year-old woman of Yahr stage 5 with disease duration of 2 years. No antiparkinsonian drugs have taken since she stopped them 1.5 years ago because of worsened VH. She insisted her upper limbs were getting shorter and complained that there was somebody under her back on the bed and had a pain. She felt her head pulled back and herself standing by the wall while she lay down on the bed.

Discussion: SHs are considered to be consist of three types. They are abnormality of the sense of equilibrium (case 3, 4), abnormality of body image of self (case 1, 2, 4) and abnormal sense of being touched (all cases). Whether these were induced by levodopa or intrinsic in PD is not clear. SHs in PD have been only rarely mentioned but couldn't be rare if the patients were carefully observed. ECT may be effective for SHs as well as for VHs and motor symptoms in PD.

P1-142

Quetiapine for elderly resistant schizophrenia patients

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We examined whether elderly chronic schizophrenia patients would clinically improve if switched to quetiapine from previous second generation antipsychotic (SGA) treatment. Ten hospitalized patients, aged 60–91 years, suffering from chronic schizophrenia who were exposed to a SGA and had not responded were switched to quetiapine. The Brief Psychiatric Rating Scale (BPRS) and the Abnormal Involuntary Movement Scale (AIMS) were completed while patients were on their previous medication regimen and again 6 months after the last patient had been started on quetiapine. The mean duration of quetiapine treatment was 188 days (SD = 114). Four patients discontinued the medication; 3 due to clinical exacerbation and 1 due to severe sedation. Mean end dose of quetiapine was 391 mg (SD = 245). Paired samples t-tests were used to test change on BPRS, AIMS and body weight. Clinical improvement as measured by the BPRS demonstrated statistically significant improvement ($p = 0.001$). There was no significant change in AIMS ($p = 0.04$) and body weight ($p = 0.46$). In conclusion, elderly patients with chronic resistant schizophrenia showed improvement after being switched to quetiapine with no weight gain or abnormal movements. Clinically meaningful changes were observed and tolerability was excellent.

P1-143

Aging and social functioning in people with mental illness

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With an increase in the number of older people in the general population, there are more elderly people with mental illness than ever before. In general, functional abilities decline with aging, which is the case also for people with mental illness. However, the details of the functional abilities of mentally ill people have not been fully investigated. Therefore, we explored the difference of functional status among age groups in people with mental illness to clarify the effects of aging on their functional abilities. The subjects were 74 outpatients (40 to 89 years old) who are participants in the Day-Night Care program at a psychiatric clinic in Hiroshima, Japan. The diagnoses of the participants were schizophrenia (60 persons) and other mental illnesses (14). To evaluate functional status, we used the Life Assessment Scale for the Mentally Ill. The mean scores of items in the scale were compared between the age groups (40s, 50s, 60s, and 70s and older) and within each domain in the scale. In the

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domain of Daily Living, the abilities in the use of transportation, in money management, and in the management of private items decline with aging. To maintain abilities in daily living, the balance of supportive care and independence is important. This might be attained if unnecessary cares were withheld from these subjects, and instead they were prompted to do what they can on their own. In the domain of Interpersonal Relations, overall status is relatively well preserved in all age groups, which is indicated by the mean scores of items in this domain being better than those of items in the domain of Daily Living. However, spontaneity, comprehension, and contacts with friends decline with aging, which may reflect the autistic nature of mental illness and may indicate the need to provide more opportunities to participate in various activities. In the domain of Self-Recognition, recognizing one's own disabilities and self-evaluation decline with aging, which may result from a low comprehension of and an indifference to one's own mental and physical states. Social interests and social contacts are very important for a better life in a person with mental illness. The programs provided in the Day-Night Care must aim at improving physical, mental, and social functions in persons with mental illness by nurturing their social interests and widening their social contacts, which may result in improving and maintaining overall social functioning.

P1-144

Amisulpride and cognition in schizophrenic elderly

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Background: Amisulpride, a substituted benzamide derivative, is second-generation antipsychotic that highly selective bindings to D2/D3 receptors in limbic rather than striatal structure. It is as effective as haloperidol, risperidone as well as olanzapine in schizophrenics. Amisulpride is not associated with impaired cognitive functions.

Objective: To evaluate the effect of amisulpride and risperidone on cognition in elderly patients of schizophrenia.

Method: In a 12 week study of twenty elderly (age 65 years SD $\pm$ 10) schizophrenic patients were randomly assigned to receive flexible dosages of Amisulpride n = 10 (100–200 mg.) or risperidone n = 10(1–3 mg.). cognitive test were administered at baseline, week 4, 8 and 12.

Results: Significant improvement at end point in the serial verbal learning test trials 1 to 3 occurred in both group, but only the amisulpride group showed significant improvement in the verbal fluancy examinations and trial making test B($p < 0.05$) as well as continuous performance test. No decrease in cognitive function occurred at any time point in either group.

Conclusion: After only twelve weeks both Amisulpride and risperidone were associated with improved cognitive function in elderly schizophrenics. Amisulpride appeared to provide wider ranging significant improvement in cognitive function compared with risperidone.

P1-145

SAGE study: Health management of elderly patients with psychotic disorders in France

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Elderly patients with psychotic disorders need specific medical care, but epidemiological studies addressed to evaluate such specific management are scarce in the literature. Here, we present the global results of an observational, transversal and multicentric study, denominated SAGE, concerning such subject in France. Patients were aged 60 years old or more and suffered psychotic disorders since at least 10 years. 123 physicians participated to the study, where 97 psychiatrists included 746 patients and 26 geriatrists included 184 patients. Of the 942 selected patients, data from 930 patients was finally used for analysis. Most patients (58.5%) suffered from schizophrenia (20.8% had paranoic delirium and 20.5% hallucinatory chronic psychosis). 67.5% of patients were ambulatory and 43.4% were institutional. Psychotic trouble severity was evaluated for 98.0% of patients. Conversely, only 41.6% of

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patients had an evaluation of cognitive function during the last 6 months. Antipsychotics were prescribed in monotherapy to 74.2% patients and in association to 25.8% patients. 36% patients were given antiparkinsonian medication, of whom only 17.3% as preventive treatment. Only 52.7% of patients had an ECG of less than 12 months. Glycemia of the last 12 months was available for only 58.2% patients, HDL-Cholesterol for 20.6% patients, triglycerides for 28.5% patients (and creatininemia for 54.8% patients. 475 patients had at least one somatic comorbidity. Of these: 72.8% presented cardiovascular disorders, 22.1% respiratory disorders, 11.6% type I diabetes, 17.6% type 2 diabetes, 4.4% renal failure and 38.1% obesity. In conclusion, antipsychotic and antiparkinsonian drugs prescription in aged french psychotic patients tends to follow the recommendations of guidelines and consensus conferences. Conversely, cognitive, cardiac and metabolic aspects are less well managed.

P1-146

Successful treatment of pseudohallucinations with venlafaxine

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A 90-year-old man with adult macular degeneration, insulin dependent diabetes mellitus without overt retinopathy, and previous cataract surgery, was seen because of vivid visual hallucinations, like horses with carriages, floating people with short legs, and colourful flowers in trees. The hallucinations started several weeks earlier, one day after a fall due to hypoglycaemia. He realised that the images were false, and there were no signs of cognitive impairment (MMSE score 25/27). A CT scan of the brain showed no abnormalities. A diagnosis of pseudohallucinations due to visual impairment, the Charles Bonnet Syndrome, was made. Treatment with venlafaxine 37.5 mg once daily was started. Within 1 week, the symptoms disappeared completely. The Charles Bonnet Syndrome is named after a Swiss philosopher, who described the complex visual hallucinations in his mentally healthy, but visually handicapped grandfather. Treatment with drugs is often unsuccessful; antipsychotics, anticonvulsants and antidepressants have all been tried. It is important to explain the patient that the hallucinations are not a symptom of psychosis or dementia. Venlafaxine is a serotonin and norepinephrine reuptake inhibitor, and registered as an antidepressant; Lang et al. recently described a similar case responding to venlafaxine after 4 days of treatment.

P1-147

SAGE study: Health management of elderly patients with psychotiac disorders in France

Vincent Camus[1]; Christopheh Arbus[2]; Jean-Pierre Clement[3]; Ahcene Hameg[4]; Thierry Bougerol[5]; Ricardo P. Garay[6]; Patrick Fremont[7]

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Elderly patients with psychotic disorders need specific medical care, but epidemiological studies addressed to evaluate such specific management are scarce in the literature. Here, we present the global results of an observational, transversal and multicentric study, denominated SAGE, concerning such subject in France. Patients were aged 60 years old or more and suffered psychotic disorders since at least 10 years. 123 physicians participated to the study, where 97 psychiatrists included 746 patients and 26 geriatrists included 184 patients. Of the 942 selected patients, data from 930 patients was finally used for analysis. Most patients (58.5%) suffered from schizophrenia (20.8% had paranoic delirium and 20.5% hallucinatory chronic psychosis). 67.5% of patients were ambulatory and 43.4% were institutional. Psychotic trouble severity was evaluated for 98.0% of patients. Conversely, only 41.6% of patients had an evaluation of cognitive function during the last 6 months. Antipsychotics were prescribed in monotherapy to 74.2% patients and in association to 25.8% patients. 36% patients were given antiparkinsonian medication, of whom only 17.3% as preventive treatment. Only 52.7% of patients had an ECG of less than 12 months. Glycemia of the last 12 months was available for only 58.2% patients, HDL-Cholesterol for 20.6% patients, triglycerides for 28.5% patients (and creatininemia for 54.8% patients. 475 patients had at least one somatic comorbidity. Of these: 72.8% presented cardiovascular disorders, 22.1% respiratory disorders, 11.6% type I diabetes, 17.6% type 2 diabetes, 4.4% renal failure and 38.1% obesity. In conclusion, antipsychotic and antiparkinsonian drugs prescription in aged french psychotic patients tends to follow the

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recommendations of guidelines and consensus conferences. Conversely, cognitive, cardiac and metabolic aspects are less well managed.

P1-148

One year weight change after switching to secondary generation antipsychotics in elderly psychotic patients

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Introduction: Most available antipsychotics have been reported associated with weight gain, especially second generation antipsychoitcs (SGAs). This study aims to evaluate weight change after switching from conventional antipsychotics to SGAs in elderly psychotic patients for one year.

Method: This study was a retrospective chart review of 64 hospitalized elderly (age more than 60 years old) patients with psychotic features, who were switched to SGAs from the conventional antipsychotics. Data on monthly weight change, gender, and dosage of antipsychotics were recorded after switching from conventional antipsychotic to SGAs for one year. Weight changes were analysis by repeated measure method.

Results: The demographic data of patients using SGA, including mean age and number of patients, were olanzapine (7 patients, 67.65 ± 6.49 years old), clozapine (7 patients, 66.12 ± 5.22 years old), quetiapine (14 patients, 74.75 ± 8.98 years old), and risperidone (36 patients, 73.62 ± 7.35 years old) respectively. The mean dosage of each SGAs was clozapine (203.13 ± 114.3 mg/day), olanzapine (6.88 ± 4.24 mg/day), quetiapine (178.4 ± 159.9 mg/day), and risperidone (3.25 ± 1.23 mg/day). Mean weight of each SGA on baseline and the end of one year were clozapine (53.43 ± 10.96 Kg; 57.79 ± 12.55 Kg), olanzapine (55.07 ± 12.86 Kg; 57.35 ± 13.61 Kg), quetiapine (58.07 ± 0.65 Kg; 58.61 ± 1.8 Kg), and risperidone (59.12 ± 9.51 Kg; 61.67 ± 11.31 Kg). The ratio of change weight from the end of one year to baseline was risperidone (2.35%), olanzapine (3.45%), clozapine (4.21%), and quetiapine (0.93%) respectively.

Discussion: Weight increase was found after switching to all type of SGAs in elderly psychotic patients. Clozapine showed the greatest weight gain in the elderly psychotic patients after switching to SGAs for one year. Quetiapine was the least weight change in these SGAs.

P1-149

Prevalence of psychotic symptoms in an old age community sample from Brazil

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Until now, four studies estimate the prevalence of psychotic symptoms in old age in developed countries. These studies evaluated the prevalence of one or more psychotic symptom, including delusions, hallucinations, thought insertion, unusual experiences and paranoid ideation. It ranges from 3.8% (in a population with mean 78 years in Australia) to 14% in a population with mean 67 years in US. Psychotic symptoms are robustly associated with depressive symptoms (OR 1.2 to 3.9), poor performance on daily activities (OR 4.9 to 5.9), and physical symptoms (OR 1.76 to 4.6). We made an epidemiological survey in the city of Sao Paulo, Brazil, with 1563 persons over 60 years old, stratified according to economical status. They were evaluated with MMSE, FOME, IQCODE, B-ADL, a sociodemographic, clinical and socioeconomic inventory and three questions about psychotic symptoms extracted from the Camdex. Patients with dementia, MCI and other psychiatric diseases were excluded and 1125 remained for the analysis. Mean age of the sample was 70.8 (SD 7.3), mean score at MMSE was 25.9 (SD3.8) and mean score in B-ADL was 1.6 (SD 0.8). The prevalence of one or more symptom was 13%, of delusions was 4.6%, of auditory hallucinations was 10.7% and other hallucinations was 10.7%. Test T showed no difference of age between patients without psychotic symptoms and with one or more psychotic symptoms (mean age 70.94 and 69.84, $p = 0.11$). On the other hand subjects with one or more psychotic symptom showed a

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worst performance on the scale MMSE (mean 22.7 versus 25.12, $p < 0.0001$) and on the scale B-ADL (mean 1.82 versus 2.13, $p = 0.003$). Using test qui a significant difference between the groups with and without psychotic symptoms was shown when we compared presence of stroke ($p = 0.01$), myocardial infarction ($p = 0.008$), depression ($p < 0.001$) and arthritis ($p = 0.003$). There was also a significant difference when economical status was compared ($p < 0.001$). A logistic regression was made with the above mentioned variables. The ones with remained significant were depression (OR 2.52, $p < 0.001$), score at MMSE (OR 0.94, $p < 0.05$) and at B-ADL (OR 1.29, $p < 0.01$). The association with depression may be due to psychotic symptoms as a manifestation of psychotic depression. But the association between cognitive deficit and disability in daily life activities and psychotic symptoms is noteworthy and may be evidence that psychotic symptoms in old age persons are part of incipient dementia.

P1-150

Neuropsychological rehabilitation on higher brain dysfunction with chief complaint of memory disturbance

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Neuropsychological assessment, that addresses the various symptoms caused by brain damage sustained through disease or accident, is essential in identifying the type and extent of impairment. First, results from diagnostic imaging, performed by a physician, showing the location and degree of brain damage are used to generate assumptions on the functional disorders that may arise from such damage. Subsequently, results from observations made in the hospital ward, recorded on the patient's chart, or information given in interviews with the patient's family are used identify an image of impairment. Through interviews, awareness of deficits (presence or lack thereof), degree of emotional stability, tension during interpersonal interactions and fatigue are assessed. Finally, a decision is made as to the type of neuropsychological assessment that needs to be implemented. In administering the assessment, it is important to fully explain the purpose (why the test is necessary) of the test to the patient in advance and obtain his/her consent. When the test is administered, it is indispensable the measures are taken to shorten the length of time required for testing (so as not to cause fatigue in patients) and that considerations are made (measures to alleviate tension) to provide a comfortable testing environment. In this report, by studying a case example of higher brain dysfunction, the following are discussed: 1)how to plan neuropsychological assessments 2) how to implement such tests 3) how to utilize the results of such tests 4) how to provide family support, etc. based on neuropsychological assessments.

P1-151

Effects of affective stimuli on cognitive function in subjects with MCI: comparison with healthy controls

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We examined the effects of differences in the affective on cognitive function in healthy controls previously. The present study was performed to examine the effects of affective stimuli (crying or smiling baby faces) in MCI subjects compared with healthy controls evaluation with P300 components and LORETA Analyses. MCI subjects (16: 68.8 ± 5.2 old)) and age matched healthy controls (16: 68.3 ± 3.5 old). The visual induction-related potential was measured using NeuroFax (Nihon Koden), and oddball tasks (target stimulation: photograph of a crying or smiling baby faces: 20% probability, non target stimulation: photograph of a neutral face: 80% probability) were used. Brain waves were recorded at 18 sites (F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, Pz, and Oz). The P300 component was analyzed using the maximal amplitude and latency of brain waves recorded at Fz, Cz, Pz, T3, and T4. LORETA analysis was performed using the LORETA Explorer by the paired test between groups (healthy controls vs. MCI subjects). Ethics Committee of Kurume University approved the present study. The P300 amplitude under crying condition was significantly larger than that under the smiling condition in healthy controls, but in MCI subjects there was not significant difference between the P300 amplitude under the crying and the smiling condition.

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The P300 amplitude in healthy controls was significantly larger than that in patients under crying condition. The P300 latency in MCI subjects was significantly prolonged than that in controls under the crying and smiling conditions. LORETA analysis demonstrated that there were significant differences of the activity in the and the 40, 7 area (Parietal Lobe) between the crying and smiling conditions in healthy controls, but the significant activity difference was not observed in MCI patients. Significant differences in the activity in the 39,22 area (temporal Lobe) between the task condition and non task condition in cry condition in healthy controls, but no significant difference under crying condition between task and non task in MCI subjects. Event-related potential and LORETA analyses can be used for the neurophysiological evaluation of cognitive dysfunction in patients with MCI, and it is important to diagnose such cognitive disorder secondarily and to determine the therapeutic strategy.

P1-152

The Ajimu project; prevention trail of dementia using nonpharmacological interventions in mild cognitive impairment (MCI) among the community dwelling elderly

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To conduct a three year follow up survey of 64 senior citizens aged 65 or over in Ajimu district who were diagnosed with amnestic MCI (MCI with memory loss only) from June 2003 to December 2006.

1251 elderly citizens aged 65 and over in Ajimu district were assessed for their cognitive functions using a method called "Five Cog", a neuropsychological assessment comprising the following five categories: memory, attention, verbal fluency, clock drawing test, and analogy. 64 seniors, who had been found to have memory deficits, were selected for the subjects of this study. The 64 subjects were separated by three groups; the intervention group (n = 18) attended the occupational therapy and aerobic therapy once a week for three years, the nonintervention group (n = 14) attended a dementia enlightenment lecture once a year and lived ordinary life, and the control group (n = 32) did not attend dementia prevention program at all and lived a conventional life.

After 3 years of follow up, 27 who could visit Ajimu health center underwent the Five Cog examination and were revaluated by a doctor. 37 who could not visit the center were revaluated in the doctor's individual visits and underwent MMSE examination.

A nonpharmacological intervention was given to 18 subjects to prevent dementia. In this group, 16 shifted to normal, 2 maintained the state of MCI and no one shifted to dementia. After 3 years of follow up, in the nonintervention group, 5 maintained the state of MCI and 2 were diagnosed as normal. 5 were diagnosed with dementia (Alzheimer's disease: 4, Dementia with Lewy bodies: 1). And 2 were dead, both of whom were considered to have developed Alzheimer's disease before their death by the interviews with their families. Also, in the control group, 14 maintained the state of MCI and 4 were diagnosed as normal. 13 were diagnosed with dementia (Alzheimer's disease: 12, Mixed dementia: 1). And one were dead (with Alzheimer's disease).

The nonpharmacological intervention appears effective to prevent MCI patients from developing dementia.

P1-153

Characteristics of visual cognitive function in MCI evaluating exploratory eye movements: comparison with healthy subjects

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The present study was performed to compare the effects of three types of S shape figures on exploratory eye movements in 30 MCI (mild cognitive impairments) subjects, age-matched 20 Alzheimer patients and 30 healthy subjects. Eye movements were recorded using an eye-mark recorder (Nac, EMR-8, Tokyo, Japan). Movement of more than 1° with duration greater than 0.1 s was scored as an eye movement. In the present study, exploratory eye movements were analyzed for three parameters: total eye scanning length for gazing points (TESL), total number of gaze points (TNGP) and response search score (RSS). All subjects were asked "look the front figure 1 carefully and memorize" because

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"I will ask you immediately after recording, what figure did you see" Session 1: All subjects were asked, "Are there any differences between the present figure and the former one" in the same figures (figure 1) as comparison condition. Session 2 and 3: All subjects were asked, "Are there any differences between the present figure 2 or 3 and the former one (figure 1)". After all subjects answered the differences, and then, all subjects were asked, "Are there any more differences between the present figure 2 or 3 and the former one (figure)" as re-comparison condition. Data were analyzed from the right eye and the left eye in the present study. There was no significant difference of analyzing elements in the eye movements between the right and left eyes. A one way (group) ANOVA was used to compute the main group effects in each measure. Post-hoc analyses were conducted using Scheffe tests. A level of $p < 0.05$ was accepted as statistically significant. Both TESL for controls and MCI subjects were significantly longer than those for patients but TESL for controls was similar to that for MCI subjects in all figures. Both TNGP for controls and MCI subjects were significantly larger than for patients but TEGP for controls was similar to that for MCI subjects in all figures. The RSS for controls was significantly larger than for patients in all figures. The RSS for controls was significantly larger than that for MCI subjects only in figure 3. There was significant difference among three groups in figure 3. These finding indicate that the impairments of visual cognitive function are characterized in MCI subjects.

P1-154

Decreased cortical glucose metabolism in converters from MCI to Alzheimer's disease in a community: The Osaki-Tajiri Project 3

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Using PET and the FDG method, there were several longitudinal studies on MCI for the effect of CMRglc for declining to AD. However, there are few research fields for follow MCI people in a community using PET. We performed a survey in 1998 and reported the prevalence of CDR 0.5 to be 30.1%. At that time, using FDG-PET, we had examined the glucose metabolism for 50 people and followed for 5 years. In this study, we examined the difference of glucose metabolism among healthy, CDR 0.5 decliners, non-decliners, and AD at baseline, for applying FDG-PET method for predicting further decline. For the prevalence study in 1998, 497 participants were randomly selected to receive MRI, finally consisting 346 CDR 0, 119 CDR 0.5, and 32 CDR 1+. For consecutive 100 participants in Study 1998, 11 CDR 0, 21 CDR 0.5, and 12 AD patients finally agreed to be examined with PET. The neuropsychological tests used included MMSE and CASI. The PET study was performed with a model PT-931 scanner, according to the FDG method. The CMRglc was calculated according to the method of Phelps and SPM2. For the CDR 0 group, they were all stable as CDR 0 after the 5-year period. For the CDR 0.5 group, 11 converted to AD, whereas 10 stayed as CDR 0.5 stage. For all the scores except for CASI item short-term memory, the AD group showed lower scores compared with three remaining groups (ANCOVA, $p = 0.008$). On top of the same pattern, the CDR 0.5 converters showed lower value compared with the non-converters regarding CASI item short-term memory (ANCOVA, $p = 0.008$). For CMRglc, most areas showed decreased values in the AD group. For the comparison between the CDR 0.5 converter vs the non-converter, the converters had lower (SPM2, $p < 0.0001$, uncorrected) CMRglc values at baseline in the right posterior cingulate, left angular gyrus, and left parahippocampal gyrus. Our findings showed that the decliners to AD had already manifest metabolic decline in the posterior cingulate and other areas which are specific to AD.

P1-155

Feasibility of online internet diagnostic tool for early detection of mild dementia

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Recent progress in pharmacological treatment of dementia yielded a great change of therapeutic strategy. Although early diagnosis and intervention in dementia has been needed in primary care settings, yet it is difficult for general practitioners to detect elderly patients with early stage of dementia or with mild cognitive impairments. One study showed that general practitioners recognized MCI in only 3.2% of cases and dementia in only 23.5% of cases. One of the reasons for this inaccuracy of diagnosing cognitive dysfunctions might be that the current definition of early stage of dementia such as MCI seems to be controversial. Another reason is that there are many factors affecting cognitive performance in elderly populations apart from neurodegenerative disorders, including education, vascular risk factors, genetic background, use of drugs, and psychiatric status. Several machine learning methods have been applied to diagnose patients with mild dementia in clinical settings. In this study, we used the online internet diagnostic system devised by the US Medical Care Corporation. This system includes neuropsychological battery and depression rating scale. Using this system combined with medical history, physical examination, and laboratory, cognitive, and neuroimaging results, we examined sixty non-institutionalised persons aged 65 years and over recruited from the Joetsu district, Japan. Dementia and depressive episodes were diagnosed according to the DSM-IV-criteria. We examined the feasibility of the online internet diagnostic system for mild dementia in primary care setting. We will present the characteristics of the population and the data of the first year of follow-up.

P1-156

1st year analysis of a 3-year mild cognitive impairment (MCI) study

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We recruited 28 patients who meet a modified version of the operational criteria for MCI as defined by the Alzheimer's disease cooperative study group. This modified criteria includes (1) memory complaint, corroborated by an informant; (2) abnormal memory function, documented by delayed recall of one paragraph from the Logical Memory 2 subtest of the Wechsler Memory Scale-revised; (3) normal general cognitive function, as determined by a clinician's judgment based on a structured interview with the patient and informant (Clinical Dementia Rating (CDR) and Mini-Mental State Examination (MMSE) score greater than or equal to 24); and (4) no or minimal impairment in activities of daily living. Patients had to be aged 55 to 90 years, be in good health with no significant cerebral vascular disease, have a Self Depression Scale (SDS) score less than or equal to 50, and undergo a magnetic resonance imaging (MRI) brain scan within 6 months before screening without indication of infection, infarction, or focal lesions. Patients were required to have a global CDR of 0.5, with at least a 0.5 in the memory domain. All patients and their representatives signed a written consent form. We launched a 3- year MCI study on April 1, 2006, and baseline data was collected. At study entry, participants were assessed using the MMSE, the Kana-pick up test, the Alzheimer's disease Assessment Scale-Cognitive Subscale (ADAS-Cog), the global CDR, and SDS. Caregivers were interviewed with the Burden interview. Participants underwent an MRI brain scan and electroencephalography (EEG). We analyzed the MRI brain scan using the textures analyze method, and analyzed EEG by using EEG alpha bipolarity method. We divided the participants into two groups, one with an active life style support system and the other without it. We have found some relation between cognitive decline and EEG and MRI investment.

P1-157

Screening and evaluation of MCI by Short Test of Mental Status-Japanese (STMS-J) and SPECT

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Mild cognitive impairment (MCI) was proposed by Petersen and colleagues and MCI is considered as an omen of dementia. The following studies have reported that amnestic MCI has been presumed to be a *prestage* of Alzheimer's disease (AD). Therefore,

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it has been proposed that clinicians should diagnose MCI correctly and begin the therapy of patients with the mild neuropsychological deterioration. In 2003, Petersen and colleagues devised Short Test of Mental Status (STMS). To evaluate the specificity and sensitivity of detection of MCI by STMS in Japan, we prepared STMS-Japanese (STMS-J), tried the screening of MCI by STMS-J and investigated the relationship between STMS-J and SPECT. We examined one hundred sixty six subjects who consulted our hospital by Mini-Mental State Examination (MMSE), STMS-J and I^{123}IMP-SPECT. The cut-off point between MCI and normal cognition was set to be 32/33 in STMS-J. The cut-off point in MMSE was defined to be 23/24 as dementia/non-dementia. There were nine subjects, averaged 79 years old, with more than 24 points in MMSE and less than 32 in STMS-J, and five of them showed AD pattern in SPECT, which demonstrated circulatory hypoperfusion in the posterior cingulate gylus. The radiological investigation concerning these five cases also showed the dilatation of the bilateral collateral sulcus in continuous three sections of MRI in four cases at the same time. Our hospital treat mainly already demented patients; nevertheless STMS-J caught MCI. Therefore, STMS-J could be the useful clinical tool to detect MCI. However, it is not evident whether SPECT could disclose MCI defined by STMS-J. On the other hand, all MCI cases defined by both STMS-J and SPECT showed the parahippocampal atrophy in this study, although it was not enough number. We need to incorporate the longitudinal study to confirm the correspondence among STMS-J, SPECT and MRI.

P1-158

Cognitive function in the elderly patients under hemodialysis

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The elderly patients with the renal insufficiency and under hemodialysis (HD) are getting increased in Japan. And cognitive function is supposed to be one of the important factors of QOL and therapeutic compliance among elderly patients. We have investigated the cognitive function of HD patients annually for three consecutive years. We discuss the relation between the cognitive function and HD. One hundred nine HD patients were examined in the first study, 129 in the second and 110 in the third in our cooperative clinic. We investigated all the patients using Mini-Mental State Examination (MMSE) for screening of the cognitive function. Sixty five patients, averaged 72 years old, were examined in the both first and second study. Approximately 40% of them showed the lower score less than 23 points in MMSE. However, the improvement more than 3 points between two investigations were recognized in 25% of them. Furthermore, 48 patients, averaged 70 years old, were examined three times for three years. Nineteen percent of them went worse from the normal score to less than 23 points in MMSE. The elderly HD patients demonstrated high frequency of the cognitive impairment. The important point concerning its frequency is that this impairment includes either reversible or irreversible factors. In addition, the rate of conversion from normal to abnormal cognitive function is higher than one of conversion from amnestic mild cognitive impairment (amnestic MCI) (Petersen et al., 2001) to dementia in general population[1]. Since the therapeutic condition under HD itself is stressful, the patients easily show depression and so called pseudodementia. This condition also makes the patients inactive in general and cognitive functions. In the other hand, the renal insufficiency produces increased toxic substances and HD causes the exchanges of circulatory dynamism. The high frequency or conversion in this study could be related to these specificities.

P1-159

Neural substrates of impaired emotional facial expression recognition in mild cognitive impairment

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Impairment of emotional facial expression recognition has been reported recently in patients with Alzheimer's disease (AD). This may cause

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interpersonal disturbance of patients with AD, and increase burden of their caregivers. However, it remains unclear whether such an impairment already exists at the prodromal stage of AD, i.e., in subjects with mild cognitive impairment (MCI). Since early AD pathology involves the amygdala, which is a key structure of emotional recognition, it could be suspected that pathology of the amygdala and its connection with other limbic structures would be the neural basis of such impairment in AD. Moreover, this could also be the case in subjects with MCI. In the present study, we investigated facial expression recognition ability, structural changes in the amygdala and uncinate faciculs, and interrelationship between them in MCI subjects. 16 subjects with MCI participated in the study. A facial expression recognition task was administered, and their performances were compared with those of age-and-gender-matched healthy subjects, separately for six basic emotions (happiness, fear, anger, sadness, disgust, and surprise). Amygalar volumes were measured by manually tracing the borders of the structure on high resolutional structural MRI. In addition, diffusion tensor imaging was performed, and the fractional anisotropy (FA) values in the uncinate fasciculus was obtained. Finally, the relationship between the task performance and structural measures were investigated. The subjects with MCI performed worse than the healthy controls in facial emotional recognition for the emotion of surprise, fear, anger and sadness. In the MRI studies, bilateral amygdalar volumes were significantly smaller and the FA values in the bilateral uncinate fasciculus were significantly lower in the MCI subjects compared with the matched healthy subjects. In the correlational analyses, the FA value of the left uncinate fasciculus was correlated with the performances of fear and surprise recognition in the MCI subjects. There was a trend for correlation between the left amygdalar volume and the fear recognition performance in the MCI subjects. The present study suggests existence of impaired recognition of emotional facial expression in the prodromal stage of AD. Very early pathology of the amygdala and the uncinate fascicus would be the possible neural substrates of such an impairment.

P1-160

α-synuclein promotes neuronal cell death through the activation of microglia

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Background and aims: α-synuclein gene mutations (A30P and A53T) are major underlying genetic defects known in familial juvenile onset Parkinson's disease (PD), and α-synuclein is a major constituent of Lewy bodies, the pathological hallmark of PD and dementia with Lewy bodies (DLB). The normal cellular function of α-synuclein has been elusive, and its exact etiological mechanism in causing neuronal death in PD and DLB is also not clearly understood [1]. Recently an increasing evidence points that neurodegeneration in PD and DLB is accompanied by a local immune reaction (such as the activation of microglia) in the affected brain regions [2]. Here we investigated the effect of α-synuclein overexpression and co-culture with microglia on neurons.

Methods and results: Recombinant adenovirus expressing α-synuclein wild type (Syn.Wt), two mutant types of α-synuclein (Syn.A30P and Syn.A53T) and LacZ were constructed as described previously [3]. Rat cultured neurons were exposed to adenovirus vector expressing Syn.Wt, Syn.A30P, Syn.A53T or LacZ for 2h and incubated with fresh medium up to 72h. Then, neurons were co-cultured with rat cultured microglia in two different ways. 1) direct co-culture: microglia were added directly to 24 well plates containing neurons. 2) insert co-culture: microglia were seeded into cell culture inserts that were placed on the top of the 24 well plates containing neurons. At 48 hr after co-culture, cells were homogenized in lysis buffer and immunoblotted with antibody against MAP2.

Results: Overexpression of the mutant type of α-synuclein (Syn.A53T) induced neuronal cell death while overexpression of Syn.Wt and Syn.A30P did not. In addition, overexpression of Syn.Wt and Syn.A30P induced cell death in neurons after direct co-culture with microglia but not after insert co-culture with microglia. These results suggested that direct contact of microglia with neurons expressing Syn.Wt and Syn.A30P induced cell death in neurons.

Conclusion: Our data revealed that overexpression of α-synuclein promoted neuronal cell death through activation of microglia. These results suggested that activation of microglia might play a crucial role in the neuronal cell death in PD and DLB.

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P1-161

Involvement of DYRK1A activation by oxidative stress in Alzheimer's disease

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Oxidative stress is a major feature in the pathophysiology of Alzheimer's disease (AD) and Down syndrome (DS). The dual specificity tyrosine regulated kinase 1A (*DYRK1A*) gene is located in the Down syndrome critical region on chromosome 21, which is thought to be responsible for neurological defects in DS. In the current study, we found an increased expression level of DYRK1A in AD brain tissue. Furthermore, studies on a human neuronal cell line showed that oxidative stress induced the expression and activation of DYRK1A. These results suggest that activation of DYRK1A by oxidative stress could be involved in the pathological process of AD.

P1-162

Phosphorylation of tau with or without FTDP-17 mutations similarly affects the interaction with 14-3-3 protein

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We have found that 14-3-3 protein is associated with microtubule associated protein tau at Ser214 in a phosphorylation-dependent manner. In addition to being required for cytoskeletal reorganization in neuronal development, 14-3-3 has been implicated in the pathogenesis of Alzheimer's disease (AD) as it binds to microtubule binding domain of tau independent of phosphorylation and promotes their aggregation into filament, one of pathological hallmarks in AD. Since tau is genetically linked to frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17) and tau pathology is found in FTDP-17 brain, we have investigated the effects of the phosphorylation of tau with FTDP-17 mutations on the tau-14-3-3 interaction. Real time surface plasmon resonance studies demonstrated that the phosphorylation induced interaction between tau and 14-3-3 was almost unaltered by FTDP-17 mutations, whereas the affinity between tau and 14-3-3 was increased 2–4 folds by FTDP-17 mutations. Our results suggest that this phosphorylation of tau affects an affinity of the different binding site on tau with 14-3-3 than the site when tau is unphosphorylated, and this mechanism might have implication in neurodegenerative processes.

P1-163

Neuroprotective effects of lithium

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Lithium is one of well known mood stabilizers employed for treatment of manic patients. Until now target mechanisms of biochemical action of lithium is characterized as an inhibitior to Glycogen Synthase Kinase-3 (GSK-3), and an inhibitior to inositol monophosphatase. Recently, neuroprotective action of lithium has been also focused on, and induction of Bcl-2, one of anti-apoptotic factors, by lithium has been reported, however its mechanisms are still unclear. We investigated the action of lithium to reveal its mechanisms of neuroprotection, especially for treatment of neurodegenerative disease including Alzheimer's disease (AD). We investigate the expression levels of X-chromosome-linked Inhibitor of Apoptosis (XIAP), one of major anti-apoptotic protein. In SH-SY5Y cells, lithium enhanced the expression level of XIAP protein, whereas expression level of mRNA was unaltered. Similar effects were observed in SH-SY5Y cells treated with GSK-3 inhibitors, suggesting this effect depends on inhibition of GSK-3. Lithium also increased the survival ratio in cells exposed by oxidative stress. Our study suggests that lithium may have actions on the induction of anti-apoptotic proteins, through inhibition of GSK-3. These findings might support therapeutics of neurodegenerative disease including AD.

P1-164

Application of "proteasome tolerance" to therapies for neurodegenerative diseases

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Aggregation of abnormal protein impairs the function of the ubiquitin-proteasome system, and it possibly leads neurodegenerative disease. To find the novel therapies we investigated the mean which can activate proteasome function. Here we reported a phenomenon proteasome tolerance: pretreated with low dose of proteasome inhibitor increase proteasome activity and resist to subsequent high dose of proteasome inhibitor treatment. We performed microarray analysis and revealed global expression changes while proteasome tolerance was induced. Among them we focused on Nrf2, a transcription factor and studied it effect on proteasome function. Overexpression of Nrf2 was found to induce proteasome subunit and activate proteasome function. Moreover Nrf2 overexpression reduced accumulation of tau protein induced by tau overexpression. These data suggest that Nrf2 is one of the factors which cause proteasome tolerance and could be therapeutic target of neurodegenerative disease.

P1-165

Voxel-based morphometry of entorhinal cortex in Alzheimer's disease and other dementias: Analysis by voxel-based specific regional analysis system for Alzheimer's disease (VSRAD)

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Volumetric MRI studies have demonstrated that atrophy of entorhinal cortex (ERC), where the tangle formation initially begins in Alzheimer's disease (AD), is a sensitive marker of early AD. However, atrophy of ERC in other types of dementia is not fully evaluated and its specificity remains unclear. The voxel-based specific region analysis for AD (VSRAD), developed by Hirata et al, is a software program which can automatically analyze three dimensional T1-weighted MRI data as a series of segmentation, anatomical standardization and smoothing using Statistical Parametric Mapping 2002 (SPM2) and Z-score analysis. Using 1.5T scanner (MAGNETOM Symphony, Siemens) and VSRAD, we examined normal medical control (n = 5), mild cognitive impairment (MCI) (n = 11), early-onset AD (n = 9), late-onset AD (n = 48), Dementia with Lewy bodies (DLB)(n = 11), and frontotemporal lobar degeneration (FTLD) (n = 10). A three dimensional volumetric acquisition of a T1-weighted gradient echo sequence produced a gapless series of 0.9mm sagittal sections. Normal data base The averaged value of positive Z-scores in bilateral entorhinal cortex (ERC atrophy index) and the percentage voxels of Z-score larger than 2 in the whole brain (general atrophy index) were compared among these subgroups. ERC atrophy index was significantly higher in late-onset AD compared to control. In MCI, early-onset AD and DLB, ERC atrophy index were higher than control but did not reach significant level. FTLD had highest ERC atrophy index. General atrophy index was not significantly different among groups except FTLD which had again higher index. In late-onset AD, ERC atrophy index did not significantly correlate with MMSE score, but general atrophy index did. ERC atrophy was present regardless of the stage of the disease. For discrimination of late-onset AD from MCI and DLB, ERC atrophy could be a diagnostic marker. However, in the case of very severe atrophy of ERC, a diagnosis of FTLD should be considered.

P1-166

Noninvasive detection of amyloid deposits in the patients with Alzheimer's disease using [11C]BF-227 PET

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For early diagnosis of Alzheimer's disease (AD), noninvasive detection of amyloid deposits using positron emission tomography (PET) is a potentially useful technique. To achieve successful in vivo imaging using PET, sensitive and selective contrast agents to amyloid deposits are needed. The purpose of this study is to evaluate the

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diagnostic utility of a novel PET imaging agent, 2-[2-(2-Dimethylaminothiazol-5-yl) ethenyl]-6-[2-(fluoro) ethoxy]benzoxazole (BF-227), in demented patients. Total 40 subjects, including 15 normal controls, 10 subjects with mild cognitive impairment (MCI), 14 patients with probable AD and one patient with frontotemporal dementia (FTD), underwent PET studies using [^{11}C]BF-227 and [^{18}F]fluorodeoxyglucose (FDG). Regions of interest were placed on individual axial MR images and copied onto PET images. Regional standardized uptake values (SUVs) were sampled and the ratio of regional to cerebellar SUV were calculated as the index of [^{11}C] BF-227 retention and regional glucose metabolism. Regional tracer distribution of AD patients was statistically compared with normal subjects on a voxel-by-voxel basis. The clinical PET study demonstrated the retention of [^{11}C]BF-227 in cerebral cortices of AD patients. When AD patients were compared with normal individuals, a significant difference in time activity curves was observed in the frontal, temporal and parietal cortices, but not in the cerebellum. All AD patients were clearly distinguishable from normal individuals using neocortical-to-cerebellar SUV ratio in [^{11}C]BF-227 PET. However, posterior cingulate glucose metabolism in FDG-PET showed overlap between AD patients and normal subjects. Six out of 10 MCI subjects showed elevated SUV ratio in the temporal and parietal cortices. However, these elevations in MCI subjects were milder than those in AD patients. Voxel-by-voxel analysis of PET images revealed cortical retention of BF-227 in mainly posterior association area of AD brain. In conclusion, current PET study demonstrated significant retention of [^{11}C]BF-227 in sites with predilection for the deposition of dense amyloid deposits and distinctly differentiated early AD patients from normal subjects. These findings suggest that [^{11}C]BF-227 PET is useful for early diagnosis of AD.

P1-167

Relationship between the mini-mental state examination (MMSE) score and regional cerebral blood flow

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The Mini-Mental State Examination (MMSE) is frequently used to assess the cognitive function of patients with neurological diseases. But there are few empirical researches concerning which part of the brain associates with the MMSE score. The purpose of this study is to investigate associations between regional cerebral blood flow (rCBF) and MMSE score in demented patients.

We studied sixty-five outpatients (thirty-two patients with Alzheimer's disease (AD), nine patients with frontotemporal dementia (FTD), seven patients with vascular dementia (VaD), five patients with dementia with Lewy bodies (DLB), three patients with other diseases and nine normal elderlies) retrospectively. Technetium-99m ethyl cysteinate dimer single photon emission computed tomography (^{99m}Tc-ECD SPECT) was performed within two weeks before or after the MMSE examination for all the subjects. The SPECT images were analyzed objectively using 3DSRT, fully automated rCBF quantification software based on the constant ROI (region of interest) template, and segmental CBF (sCBF, area-weighted mean rCBF value for each of the 24 segments) and sCBF ratio (each sCBF divided by the cerebellum sCBF) were calculated.

Mean MMSE score was 21.8 points and intergroup differences were found among AD, DLB and normal groups (AD < normal; $P < 0.01$, DLB < normal; $P < 0.01$). The MMSE scores showed significant correlation with age ($r = -0.337$, $P < 0.01$), years of education ($r = 0.269$, $P < 0.05$) and sCBF ratio as followings: bilateral parietal (right; $r = 0.454$, $P < 0.01$, left; $r = 0.523$, $P < 0.01$), bilateral angular (right; $r = 0.449$, $P < 0.01$, left; $r = 0.506$, $P < 0.01$), left temporal ($r = 0.523$, $P < 0.01$), left posterior cerebral ($r = 0.410$, $P < 0.01$), bilateral pericallosal (right; $r = 0.470$, $P < 0.01$, left; $r = 0.480$, $P < 0.01$), bilateral hippocampus (right; $r = 0.544$, $P < 0.01$, left; $r = 0.506$, $P < 0.01$). Additionally, stepwise multiple regression analysis revealed that right hippocampus sCBF ratio ($\beta = 0.373$, $P < 0.01$) and left parietal sCBF ratio ($\beta = 0.328$, $P < 0.01$) had significant contribution (adjusted $R^2 = 0.354$, $P < 0.01$) to the variance of the MMSE scores.

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In conclusion, a decrease of rCBF in right hippocampus and left parietal lobe correlated with the MMSE total score.

P1-168

Alterations in the prefrontal cortex activity in the course of treatment for late-life depression as assessed by near-infrared spectroscopy

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The pathophysiology of late-life depression is so complicated and, at present, there have been few functional neuroimaging methods to evaluate it. We therefore examined the alterations in the prefrontal cortex activity associated with mood disorders, as assessed by near-infrared spectroscopy (NIRS) in the course of treatment for late-life depression, to elucidate the alterations associated with the severity of depression and cognitive impairments.

We examined ten of eighteen subjects who were more than sixty years old and were hospitalized for major depressive disorders at our hospital from May, 2006 to February, 2007 consecutively. For seven of the ten subjects, we measured the hemoglobin concentration changes as assessed by NIRS using the rock, paper, scissors game as cognitive tasks for the prefrontal cortex on two days, including one day when the depressive symptoms had slightly improved due to the treatment, and then another day more than one month afterwards. We measured on only one day for three of the ten subjects. We also simultaneously assessed the severity of depression using the 17-item Hamilton Depression Rating Scale, and cognitive impairments using the Mini Mental State Examination.

The oxygenated hemoglobin concentration changes during a difficult task (intentionally lose task) were significantly larger than those of an easy task (try to win task) bilaterally (left, $P = 0.007$; right, $P = 0.022$). There were significant negative correlations between the proportion of oxygenated hemoglobin measurements on the second day to those on the first day, and the severity of depression on the second day bilaterally (left, $P = 0.003$; right, $P = 0.046$). Therefore, the more the prefrontal cortex activity tended to increase, the fewer depressive symptoms tended to be present on the second day.

In conclusion, we were able to evaluate the prefrontal cortex activity as assessed by NIRS using the rock, paper, scissors game in late-life depression, and our results show that it may be possible to examine the alterations in the prefrontal cortex activity in the course of treatment using NIRS. The pathophysiology of late-life depression is so complicated that the development of methodologies to evaluate it is urgently needed. NIRS may therefore be a potentially useful tool for evaluating late-life depression.

P1-169

Depressive symptoms and prefrontal hypoperfusion in patients with DAT

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Depressive symptoms are common in Alzheimer's disease (AD) and contribute to clinical morbidity. Previous studies have suggested that hypoperfusion in the prefrontal cortex and anterior cingulate gyrus are involved in the pathophysiology of depression. The etiology and pathologic mechanisms of depression in patients with DAT remain unclear, and few studies using neuroimaging or other techniques to examine the regional brain structure or function have been performed. Using eZIS, we investigated the relationship between depressive symptoms and prefrontal hypoperfusion in AD.

Tc-99m-ECD-SPECT and Neuropsychiatric Inventory (NPI) were performed in forty-four patients diagnosed as having Dementia of Alzheimer's Type (DAT) with DSM-IV. These patients were divided into Depression groups (D groups: $n = 26$) and Non depression groups (ND groups: $n = 18$) using the NPI depression items. All data from SPECT images were analyzed using eZIS software. Scores in four regions were determined by Z-values; these regions consisted of each side of the prefrontal cortex and anterior cingulate gyrus. When the highest Z-values in the region were greater than 5, the score of the region was defined as 2. When the highest Z-values in the region were between 2

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and 5, the score was defined as 1. When these Z-values were less than 2, the score was defined as 0. We compared mean scores between the D groups and ND groups.

The mean scores of the bilateral prefrontal cortex for the D groups were significantly higher ($p < 0.05$) than those of the ND groups. There were no significant differences in the scores of bilateral anterior cingulate gyrus between these two groups. (Mann-Whitney U-test).

These findings suggest that hypoperfusion in the prefrontal area contributes to the expression of depressive symptoms in patients with DAT.

P1-170

Neural correlates of different scoring systems of clock drawing test in Alzheimer's disease patients

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Clock drawing test (CDT) is a useful instrument to evaluate cognitive function. There have been various scoring systems, which emphasize visuospatial ability and executive function to different degrees. Although the difference of neuropsychological property of these scoring systems has been investigated, the difference of their neural correlates has remained unclear. The objective of this study is to identify the brain areas related with different scoring systems of CDT in Alzheimer's disease (AD). Twenty-nine patients who met the National Institute of Neurological and Communicative Disease and Stroke-Alzheimer's Disease and Related Disorders Association criteria for probable AD (6 men and 23 women, mean age: 73.8 ± 8.7) were participated in this study. Informed consent was obtained from all of the patients. Mean Mini-Mental State Examination score was 20.4 ± 4.7. The participants were asked to draw a clock set to 8:20. These clocks were scored according to two different systems that referred to Rouleau scoring system (CDT1) and Royall scoring system (CDT2) respectively. The CDT1 emphasized conceptual knowledge and visuospatial function, and the CDT2 emphasized executive function. Regional cerebral blood flow (rCBF) was measured by N-isopropyl-p-^{123}I iodoamphetamine single photon emission computed tomography. Image analysis was performed using SPM2 software (the Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College London) running in MATLAB 6.5 (Mathworks, Sherborn, MA). The images were spatially normalized to the Montreal Neurological Institute (MNI) template and were smoothed with a 12-mm full-width at half-maximum isotropic Gaussian kernel. Then simple regression analysis was performed between the CDT1 score, CDT2 score and rCBF. Voxels that had a t statistic greater than 3.42 ($p < 0.001$) were considered to be significant. The CDT1 score positively correlated with rCBF in the left parietal cortex (MNI coordinates: $X = -40$, $Y = -58$, $Z = 60$) and the CDT2 score positively correlated with rCBF in the right posterior temporal cortex (MNI coordinates: $X = 60$, $Y = -54$, $Z = -10$). The present result suggests that different scoring systems of CDT have distinct neural correlates. Although CDT2 emphasized executive function, it may also evaluated posterior cerebral function as a whole.

P1-171

Longitudinal MRI study of Alzheimer's disease using VSRAD(Voxel-based Specific Regional Analysis System for Alzheimer's disease)

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Voxel-based Specific Regional Analysis System for Alzheimer's disease (VSRAD), a voxel-based morphometry that employs MRI, has been reported to be clinically useful for the objective evaluation of atrophy in the parahippocampal gyri of Alzheimer's disease(AD). To examine the relationship between the progression of atrophy in parahippocampal gyri and the symptomatic progression in AD, we performed a longitudinal MRI study of AD using VSRAD. Methods: Seventeen patients with AD have undergone MRI studies at the first visit and 1 year

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later. VSRAD was performed for each MRI images and Z-score was calculated. These patients were clinically evaluated and divided into two groups according to the progression of the symptoms(cases symptomatically progressed and cases symptomatically stable). Changes of Z-score through 1 year follow-up in the two groups were compared.

Results: In 10 of 17 patients, clear progression of the symptoms were observed, and the other 7 patients were symptomatically stable. In progressed group (PG), the mean increase of Z-score ($\pm$SD) was 0.31 ± 0.20. On the other hand, in stable group (SG), the mean increase of Z-score ($\pm$SD) was 0.03 ± 0.32. Increase of Z-score in PG tends to be larger than that in SG, although there is no statistically significant difference ($p = 0.088$) between the mean increase of Z-score in the 2 groups.

Discussion: Increase of Z-score through 1 year follow-up tended to be larger in PG than that in SG. In this study, we could not get enough number of patients, however, our result suggests when the AD patients have rapid progression of symptoms, they may have rapid progression of atrophy in parahippocampal gyri.

P1-172

Magnetoencephalographic study of visual hallucination in Charles Bonnet syndrome

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Charles Bonnet syndrome (CBS) was first reported by a Swiss philosopher named Charles Bonnet in 1760 when he noticed his 89 year old otherwise healthy and cognitively sound grandfather, who was blinded by cataracts describing vividly seeing men, women, birds and buildings which were not there.

The clinical features are the occurrence of well formed, vivid, elaborate, and often stereotyped visual hallucinations in a partially sighted person who has insight into the unreality of what he or she is seeing. There should not be any feature of psychosis, impaired sensorium, dementia, intoxication, metabolic derangement, or focal neurological illness. The syndrome usually affects elderly people. These hallucinations, which are always outside the body, may last from a few seconds to most of the day. They may persist for a few days to years, changing in frequency and complexity.

These hallucinations are determined to identify its functional localization by the brain functional image as is functional Magnetic Resonance Imaging or Single Photon Emission Computed Tomography, but no trial to determine is done by Positron Emission Tomography or magneto encephalographic (MEG). The reports about the location of the hallucination showed some inconsistent results.

We report a case of 75 years old female with semi blindness by cataracts describing visual hallucination. She had seen us with complaining about seeing vividly cats-including black kitten and a tabby playful on a chest. She knew that these visions were not real and they did not bother her much. She had lived independent life and denied her amnesia. Haloperidol did not work for her hallucination. Since it persisted for a year and came to happen every day, she was admitted to psychiatric unit for close examination and medical treatment. She was recorded MEG signals and analyzed the change of basic rhythm by Synthetic Aperture Magnetometry between the visual hallucination states and non-hallucination states.

We found the reduction of the theta (4–8 Hz) activity at bilateral primary visual cortices and right visual associated cortex during visual hallucination status. We suggested that these areas might be involved in the pathophysiology of visual hallucination.

P1-173

The value of routine digital EEG recordings for elderly psychiatric patients

Ryouhei Ishii[1]; Masao Iwase[1]; Ryu Kurimoto[1]; Leonides Canuet[1]; Koji Ikezawa[1]; Michiyo Azechi[1]; Hidetoshi Takahashi[1]; Takayuki Nakahachi[1]; Nasatoshi Takeda[1]

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Since 1924 when Hans Berger made the first recordings of electroencephalography (EEG), EEG has been widely used in clinical practice of pediatrics, neurology, neurosurgery and psychiatry as a useful and non-invasive measure of brain function. EEG is an easy, convenient and inexpensive tool for monitoring and diagnosis in patients with

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cognitive dysfunction, either a general decline of overall brain function or a localized or lateralized deficit. Because of the increase of age-related diseases and the growing elderly population, clinical EEG evaluation of the elderly has received increasing attention. Here we reported the statistics of routine digital EEG recordings for elderly psychiatric patients at Osaka University Hospital. From November 2005 to April 2007, we have recorded digital EEG from 163 elderly psychiatric patients over 60 years old out of 627 psychiatric patients. Among them, 59 patients (36.2%) with dementia and related disorders, 49 patients (30.1%) of syncope and epilepsy and 33 patients (20.2%) of depression made up the major groups. Digital EEG recordings allow us to localize the abnormal brain activities by reformatting the original referential montage to bipolar montages and to analyze the current source density by using standardized low resolution brain electromagnetic tomography (sLORETA). We assumed that the clinical importance of digital EEG evaluation for elderly patients still remains, especially for dementias, epilepsy and depression.

P1-174

Neural correlates of interictal episodic psychosis in two elderly epilepsy patients

Ryouhei Ishii[1]; Leonides Canuet[1]; Masao Iwase[1]; Ryu Kurimoto[1]; Michiyo Azechi[1]; Hidetoshi Takahashi[1]; Takayuki Nakahachi[1]; Masatoshi Takeda[1]

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We used magnetoencephalography (MEG) to directly image the brain activity associated with delusions in the episodic interictal psychosis of two female elderly temporal lobe epilepsy patients aged 65 and 68 years. MEG was recorded using a 64-channel SQUID sensor array (NeuroSQUID Model 100, CTF Systems Inc.). Topographic images of the excess kurtosis (g2), the statistical index of spiky activities, were obtained from unaveraged MEG recordings using an analysis called Synthetic Aperture Magnetometry (SAM). In both patients the excess kurtosis (g2) images showed spiky activity running in the gamma-band as an index of activation in the right parietal region during the delusional state. A second MEG measurement after delusions were resolved with antipsychotic therapy showed no excess kurtosis activation in the right parietal area. Neither the previous EEG-detectable epileptic discharge nor excess kurtosis activity in temporal regions were observed. Although delusions are quite common symptoms among psychiatric patients, especially in those suffering from schizophrenia, dementia and epileptic psychosis, few studies have examined the neural correlates of delusions. Our results support association of the right parietal area with the experience of delusion in these patients. We suggest that MEG with SAM(g2) analysis is useful for the investigation and elucidation of the pathogenesis and anatomo-functional bases of psychotic symptoms.

P1-175

Functional connectivity of electroencephalogram in mild Alzheimer's disease

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The detection of early-stage Alzheimer's disease (AD) has become increasingly important for treatment. Electroencephalography (EEG) is an easy, non-invasive and inexpensive tool which directly measures cortical activity. In this study we used time-frequency analysis of EEG signals in patients with AD to quantify the relationships between brain areas and spectral peaks, according to the severity of the disease. A total of 42 patients diagnosed with AD were enrolled in this study. EEG recording were carried out using a 12-channel digital-EEG system (International 10–20 electrode placement system). The multi-channel EEG signal was recorded during resting states with eyes closed to minimize electromyography-related artifacts. A Mini-Mental State Examination (MMSE) was performed on all patients prior to EEG measurement. The patients were divided into 3 groups of severity according to the MMSE scores: mild (MMSE = 20–23, N = 13), moderate (MMSE = 14–19, N = 14), and severe (MMSE = 0–13, N = 15) AD patients. Spectral analysis was applied to the spontaneous brain rhythms. Patients with moderate to severe AD showed an increase of delta (1–4 Hz) and theta (4–8 Hz) activities in frontal regions, and a

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decrease of alpha (8–13 Hz) and beta (13–30 Hz) activities in occipital regions, as compared with the mild AD patients. Furthermore, coherence analysis indicated increased connectivity in low frequency bands, while decreased connectivity was observed in the high frequency bands. Our findings suggest that frequency analysis of EEG may be of value in the early detection of AD.

P1-176

Difference of brain activity between mild cognitive impairment and successful aging during verbal fluency task: an fMRI study

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Background: The human brain undergoes a series of degenerative changes during aging. Cognitive impairment, including deficits in various cortical functional domains, in the absence of clinically defined dementia, has been demonstrated by examination of cognitive function among elderly people. However, although many old people show cognitive decline, some may perform tests as well as younger adults. Thus, the cognitive status is variable within elderly people without dementia while the mechanisms underlying these heterogeneity are unclear.
Objective and hypotheses: To explore the disparity of neural activity within aging-sensitive regions between heterogeneous aged groups of successful aging (SA) and mild cognitive impairment (MCI). It is anticipated to show that SA would exhibit more frontal lobe activation, particularly in the left prefrontal and anterior cingulate gyri, and fewer extraneous areas of activation during VFTs than MCI.
Method: Verbal fluency task (VFT) was presented through auditory. Blood oxygenation level dependent functional magnetic resonance imaging (BOLD-fMRI) was performed in 10 subjects met with standard of successful aging and 9 subjects met with the criteria for MCI.
Results: (1) Generally, SA showed more intensive activation than MCI ($p < 0.000$); (2) The areas activated by VFTs in SA included left parietal lobe, prefrontal cortex, anterior cingulated cortex and bilateral occipital lobe, with the attendance of obviously centralizing in left hemisphere (laterality index, LI_s is 0.46); (3) MCI did not show this attendance (LI_s is −0.12) and except right prefrontal cortex, activation in other areas were very weak, occipital lobe was almost not activated.
Conclusion: (1) status of brain function in SA was still better maintained while in MCI has been obviously impaired; DLPFC may play an important role in their mechanisms; (2) The different model of learning and memory may be one of factors causing diverse cognitive status in the elderly.
Keywords: successful aging; mild cognitive impairment; functional magnetic resonance imaging (fMRI).

P1-177

Magnetic resonance imaging for unusually clinical course of dementia

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The objective of this article is to describe and discuss the clinical manifestations of rapidly progressive dementia in a patient with brain tumor. Rapid dementia was observed in a 65 years old man 4 months before hospitalization. Ability to perform instrumental activities of daily living and personal activities of daily living was deteriorated, and pure cognitive ability (immediate and recent memory) was impaired. The common features of dementia such as delusions, hallucinations, and depression were not observed. He was admitted to our geropsychiatric ward because he lost his way home twice in a week. Physical examination showed him to be drowsy. Neurological examination showed a widened gait. Findings of routine laboratory tests such as complete blood count, urinalysis, serum biochemistry (electrolytes, liver and renal function, vitamin B12, folic acid), thyroid function, serological tests for syphilis, and tests for human immunodeficiency antibodies were negative. However, hyponatremia (129 mEq/ L) was noted. Electroencephalography (EEG) showed moderate bilateral slowing. Computed tomography (CT) of the brain showed slightly generalized atrophic change of the brain parenchyma and an enlarged pituitary gland. For further survey of pituitary gland and rapidly dementing process, brain MRI was performed. On T2 weighted MR images of this patient, high

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signal lesions were revealed in the bilateral thalamus, brain stem, and white matter of the bilateral cerebral hemispheres. On T1 weighted images, lesions in the bilateral medial temporal regions, periventricular area, and the corpus callosum were also shown. The MRI findings and clinical manifestations of this patient were compatible. The lesions, like thalamus, medial temporal lobe, and corpus callosum, are all the key structures of the memory systems. The differential diagnosis of these lesions included: lymphoma, leukemia, tumor seedings (primary to be determined), and as yet unidentified infectious disease. This unusual case of dementia illustrates the importance of a thorough evaluation of anyone who experiences early rapidly progressive dementia with some neurological signs. When an elderly patient shows early rapid deterioration of cognitive function associated with the neurological signs, the geriatric psychiatrist should not assume a diagnosis of primary degenerative dementia, such as Alzheimer's disease. Imaging studies (like brain MRI) should be arranged.

P1-178

Association between parietal white matter hyperintensities and late-onset bipolar disorder in elderly subjects

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Background: There is strong evidence that white matter hyperintensities (WMH) in the elderly are related to cerebrovascular risk factors. Magnetic resonance imaging (MRI) studies have reported an increased frequency of WMH in association with late-onset (LO) depression. Recent clinical studies have also suggested a link between LO bipolar disorder (LO-BD) and cerebrovascular risk factors, but this has been little investigated with neuroimaging techniques.

Objective and hypotheses: We aimed to ascertain whether there is a specific association between WMH and LO-BD, when directly comparing WMH rates between LO-BD (onset 60 years or older) patients, early-onset BD (EO-BD, onset < 60 years) subjects and elderly healthy controls. We hypothesized that higher WMH rates would be found in the LO-BD group in the frontal lobe, parietal lobe and basal ganglia.

Methods: T2-weighted MRI data were acquired in LO-BD subjects ($n = 10$, age $= 73.60 \pm 4.09$), EO-BD patients ($n = 49$, age $= 67.78 \pm 4.44$) and controls ($n = 24$, age $= 69.00 \pm 7.22$). WMH rates were assessed using the Scheltens scale. Demographic and clinical characteristics were documented with regard to previous diseases, vascular risk factors and use of medication.

Results: There were significant differences in the prevalence of WMH in the LO-BD subgroup relative to EO-BD patients and controls in the parietal deep-WMH (D-WMH) ($\chi^2 = 8.07$, df $= 2$, $p = 0.018$) and basal ganglia WMH (both in the caudate nucleus, putamen and globus pallidus) ($\chi^2 > 6.20$, df $= 2$, $p < 0.045$). After correction for multiple comparisons (alpha $= 0.007$), significant higher WMH severity scores in the LO-BD group in comparison to both EO-BD and healthy subjects were observed in parietal D-WMH (analysis of covariance [ANCOVA], $p < 0.001$ and $p = 0.004$, respectively). Additionally, there were significantly higher WMH severity scores in frontal D-WMH in the direct comparison between LO-BD and healthy subjects ($p = 0.004$). There was a significant correlation between the severity of parietal D-WMH and the age of BD onset (Spearman rho $= 0.285$, $p = 0.028$).

Conclusions: These results provide preliminary evidence that vascular-related parietal WMH could be implicated in development of LO-BD; this reinforces the notion that there may be different pathophysiological mechanisms involved in BD according to age of onset of the disorder.

P1-180

Comparison of white matter anisotropy among Alzheimer's disease, mild cognitive impairment, and normal elderly: A Diffusion Tensor Imaging and voxel-based analysis study

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The aim of this study is to investigate microstructural changes of white matter among Alzheimer's disease, mild cognitive impairment, and normal elderly with Diffusion Tensor Imaging (DTI) in vivo. This study included thirty nine patients with Alzheimer's disease, age- and sex-matched twenty one with MCI, and twenty controls through clinical evaluation, the CERAD-K battery, MRI and DTI imaging. Fractional Anisotropy (FA) was measured in order to evaluate directionality of white matter microstructure, being transformed with spatial normalization and analyzed with SPM5 controlling for age, gender and education. The FA value decreased significantly in the sub-gyral white matter of temporal lobe and the fasciculus longitudinalis superior of frontal lobe in mild cognitive impairment, compared with normal controls. On the contrary, the FA value showed no significant difference between Alzheimer's disease and mild cognitive impairment. In conclusion, this study showed that the abnormality of directionality in temporal and frontal lobe white matter occurs at the level of mild cognitive impairment before onset of Alzheimer's disease.

P1-181

Hypoperfusion in the primary visual cortex of patients with Charles Bonnet Syndrome: A clue to exploring the mechanism of visual hallucinations

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We recently experienced two cases (Case1 and Case2) with Charles Bonnet Syndrome (CBS). The two patients underwent SPECT studies, after we diagnosed them as CBS according to the following criteria; (1) experiencing visual hallucinations which happens for the first time in old age, (2) having insight into visual hallucinations, (3) having no anamnesis of delirium, psychosis, or dementia. Case1 was a 76y.o. right-handed woman. She had had visual hallucinations of cats since one year ago. She was diagnosed as diabetic retinopathy. Moreover she had a history of binocular cataract and had operations of both eyes. Her neurological and neuropsychological findings were the following: eyesight(with glasses) 0.02 (right) 0.4(left), no parkinsonism, Mini-Mental State Examination (MMSE) 26/30 (Serial 7:-4), Alzheimer's Disease Assessment Scale-Cognition (ADAS) 7.0/70, Everyday Memory Checklist (EMC) 13/39 (by herself) 10/39 (by a family member), Physical Self-Maintenance Scale (PSMS) intact, Instrumental Activity of Daily Living (IADL) intact. Case 2 was a 65 y.o. right-handed woman. She had had visual hallucinations of woods, mountains, seashores, fields, or flowers since 12 years ago. She had a phacocystectomy twice, 7 years ago (right) and 8 years ago (left). Her neurological and neuropsychological findings were the following: eye sight(with glasses) 0.06(right) 0.04(left), no parkinsonism, MMSE 30/30, ADAS 3/70, PSMS almost intact, IADL intact. Cranial Magnetic Resonance Images are intact in both cases. SPECT images of both cases revealed that blood flow of Brodmann Area (BA) 17 and BA 18 was reduced, while blood flow of BA 19 and BA37 was preserved. BA17 is the primary visual cortex, and BA18, BA 19 and BA37 play an important role as association cortex. From this, we could suppose that because of dysfunction of the primary visual cortex, hyperactivity of the visual association cortex is caused, which results in visual hallucinations. Now we have got a clue to exploring the mechanism of visual hallucinations of CBS.

P1-182

Presynaptic dopaminergic dysfunction in "almost pure" freezing patients

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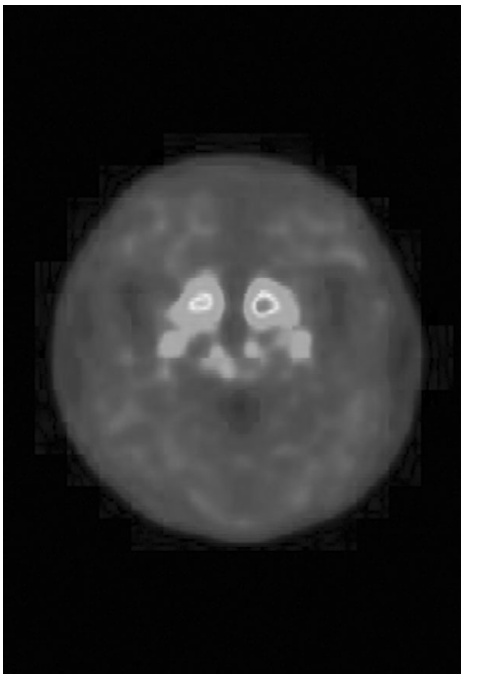
The syndrome of "almost pure" freezing patients was reported by Narabayashi et al in 1976. It has been called various names including gait ignition failure, primary progressive freezing gait, or pure akinesia. The characteristic features include the presence of freezing, loss of postural reflexes, bradykinesia in the absence of tremors and rigidity. The natural course of this syndrome is unknown although some turned out to be progressive supranuclear palsy (PSP), dementia with Lewy bodies (DLB) or idiopathic Parkinson's disease (IPD).

We aimed to investigate presynaptic dopaminergic function and glucose metabolism in "almost pure" freezing patients.

We retrospectively reviewed medical records, videotapes, results of speech evaluation, brain magnetic resonance imaging(B-MRI), [18F]fluorodeoxyglucose (FDG) positron emission tomography(PET), and [18F] N-(3-fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane (FP CIT) PET among patients presenting with prominent gait freezing.

Three patients were considered as having "almost pure" freezing syndrome. They had common features of gait freezing, especially in the form of start and turning hesitation, tachyphemia of speech, and postural instability. Rigidity and tremors were not present. The duration of the disease was between 6 and 8 years. The course was slowly progressive in terms of gait and speech, without bradykinesia or rigidity. Extra ocular movements and bulbar functions were normal. Speech evaluation revealed severe hypo kinetic type of dysarthria, harsh voice quality, and accelerated speech in all patients. Palilalia was found to be mild in two patients. The response to dopaminergic treatment was unremarkable. The B-MRI and [18F] FDG PET findings were unremarkable in all patients. [18F] FP CIT PET, presynaptic dopaminergic imaging, was done in 2 patients and showed markedly decreased uptake in both basal ganglia, which is reminiscent of Parkinson's disease.

The combination of motor blocks and acceleration of speech is unique and intriguing with this syndrome. Also, the presynaptic dopaminergic dysfunction shown in [18F] FP CIT PET suggests that the "almost pure" freezing syndrome could evolve to Parkinson's disease and may be considered a variant of idiopathic Parkinson's disease. Further large study will be needed to clarify the nature of the "almost pure" freezing syndrome.



P1-182

P1-183

Voxel-based investigation of regional cerebral blood flow abnormalities in neuro-psychiatric disorders: Application in studies using conventional single-detector SPECT systems

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Background: Automated methods of Single Photon Emission Computed Tomography (SPECT) have allowed the comparison of regional cerebral blood flow (rCBF) values in Alzheimer's disease (AD) patients performed on a voxel-by-voxel basis, using the *Statistical Parametric Mapping* (SPM) program. Conventional, single-detector SPECT systems provide rCBF data of lower spatial resolution and sensitivity compared to multiple-detector systems. However, it is not known whether it is possible to detect, using single-detector SPECT systems, statistically significant rCBF deficits with the

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SPM approach in studies comparing AD samples to healthy controls.

Objective and hypotheses: To evaluate the feasibility of using the SPM for voxel-by-voxel assessments of rCBF deficits in AD subjects relative to age-matched controls studied with a conventional, single-detector SPECT system and to compare the SPM results obtained with different forms of radioactive uptake normalization.

Methods: We used a databank of ^{99m}Tc-HMPAO images of patients with probable AD (n = 19) and elderly healthy volunteers (n = 15), acquired using an Orbiter-Siemens single-detector SPECT system. A customized SPECT template was created for the study and this was used for spatial normalization of the original volumes. Images were then re-sliced using tri-linear interpolation, and smoothed at 12mm FWHM. Comparisons between AD patients and controls were performed using t-tests.

Results: There were significant rCBF reductions in AD patients relative to controls in regions predicted *a priori* to be affected in AD, namely left temporal and parietal cortices, and posterior cingulate gyrus bilaterally ($p < 0.01$, uncorrected for multiple comparisons). The statistical significance and extent of voxel clusters showing reduced rCBF in AD patients were considerably larger when the global normalization method was employed compared to the method of normalization to the cerebellar uptake.

Conclusions: The location of rCBF reductions in AD subjects in our study is consistent with the deficits detected in previous functional imaging studies of AD. This suggests the potential usefulness of using SPM for the analysis of data acquired with single-detector SPECT systems, despite the limited sensitivity of such equipment. Compared to the normalization method using cerebellar radioactive counts, the method of global normalization showed greater sensitivity to detect foci of reduced rCBF in AD patients.

P1-184

Silent brain infarcts detected by magnetic resonance imaging in a neurological complaints-free elderly sample

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Background: Silent infarcts (SI) may be found on brain magnetic resonance imaging (MRI) scans of neurological complaints-free elderly persons. These findings have been associated with both mild cognitive impairment and dementia, and may be related to the degree of cardiovascular risk.

Objective and hypotheses: We investigated the prevalence of SI in neurological complaints-free elderly subjects selected to compose three subgroups with different degrees of cardiovascular risk using Framingham criteria.

Methods: MRI data were collected in 139 subjects (70.7 ± 2.9 years); 44 had low cardiovascular risk, 60 had moderate risk, and 35 had high risk. Exclusion criteria were: major psychiatric disorders according to ICD-10 criteria; history of head trauma, cancer, or other non-cardiovascular medical conditions that could affect brain function/structure; and contra-indications for MRI scanning.

Results: There were no significant socio-demographic differences between the three subgroups. A total of 31 SI were observed in 26 subjects (18.7% from the total sample). The most frequent findings were lacunar infarcts, present in 17 subjects (12.2% from the total sample). Most infarcts (n = 13, 41.9% from SI) were located in the basal ganglia (putamen, globus pallidus) and thalamus; five (16.1%) were located in the white matter (internal capsule, corona radiata, centrum semiovale, and subcortical parietal lobe), and four (12.9%) in the cerebellum and brainstem. Strokes were present in nine subjects (6.5% from the total sample), seen as simple lesions in the cortex (frontal [n = 1], parietal [n = 2] and temporo-occipital [n = 1]), basal ganglia (n = 3) and cerebellum (n = 2). The proportions of SI in the three subgroups were: 8 in the low cardiovascular risk subgroup (18.2%), 8 in the moderate risk subgroup (13.3%), and 10 in the high risk subgroup (22.9%), with no statistical difference between them ($p = 0.184$). The subjects that presented SI were significantly older than those without SI (72.4 ± 4.09

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and 70.3 ± 2.5, $p = 0.001$). There was also a significant association between the presence of SI and heart failure ($p = 0.020$). There was no difference between subjects with and without SI regarding to hypertension, diabetes, and gender ($p > 0.662$).

Conclusions: These findings confirm the high prevalence of SI in healthy asymptomatic elderly subjects and its association with older age. Our results also suggest a specific association of SI with heart failure, but not with overall cardiovascular risk.

P1-185

Decreased attenuation of basic rhythm in patients with early Alzheimer's disease: An MEG study

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In patients suffering from early Alzheimer's disease (AD), it is often difficult to find any typical findings in electroencephalography (EEG) or magnetoencephalography (MEG) such as a slowing of the dominant posterior rhythm or an increase in diffuse slow activity. In the present study, we evaluated the attenuation of basic rhythm in early AD patients whose MEG did not show the aforementioned findings. Seven patients with probable AD were selected according to NINCDS-ADRDA criteria (age; 75.3 ± 5.5, Mini-Mental State Examination; 22.6 ± 2.7). We also selected seven age-matched normal control subjects (NC) (age; 74.1 ± 5.0, Mini-Mental State Examination; 28.3 ± 1.6). MEG activities were recorded with a 64-channel whole head magnetometer in a magnetically shielded room. MEG signals during eye-open and eye-closing states were digitized at 625 Hz and filtered using a combined 60 Hz notch filter and 200 Hz low pass filter. For data analysis, BESA (brain electrical source analysis) software was used. At first, the event-related synchronization (ERS), ranging from 8 to 15 Hz, was calculated and its current source density was superimposed on the individual MRI image. After that, each image was converted to be standardized by using Brain Voyager QX and compared the 3D-maps of AD with that of NC. As a result, we could not find any significant difference of the peak frequency between these two groups (AD; 10.4 ± 1.7 Hz, NC; 10.5 ± 0.4 Hz). However, the ERS after eye-closing was not clearly defined in AD compared to NC. The current source density of the ERS in AD was increased significantly in frontal lobe compared to NC. These findings suggest that the analysis of the attenuation of basic rhythm might be useful for the identification of early AD.

P1-186

Correlation of LORETA sources of cortical activities and cognitive function in elderly epilepsy patients

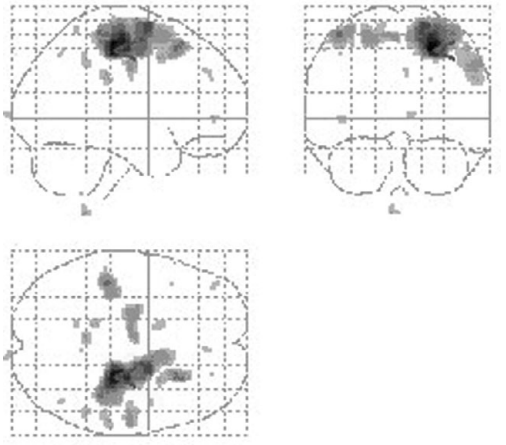
Leonides Canuet[1]; Ryouhei Ishii[1]; Masao Iwase[1]; Michiyo Azechi[1]; Ryu Kurimoto[1]; Koji Ikezawa[1]; Takayuki Nakahachi[1]; Hidetoshi Takahashi[1]; Masatoshi Takeda[1]

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Physiological aging is known to be closely related to cognitive decline. Likewise, long-term epilepsy has been reported in association with cognitive changes. The effects of frequent seizures and the chronic use of antiepileptic drugs have been proposed to play a role in this association. In the present study we evaluated the correlation between sources of cortical activities and cognitive function in elderly epilepsy patients. All patients were ascertained from an outpatient clinic of Psychiatry at Osaka University Hospital. Of 79 epilepsy patients, 15 elderly patients with localization-related epilepsy were enrolled in this study (mean age 63.8 years ± 4.4 SD, range 60–73 years; 9 men, 6 women; mean epilepsy duration 20.8 years ± 10.9 SD). Patients with brain organic lesions (tumor, infarction), primary dementia or comorbid psychiatric disease, and taking benzodiazepines, barbiturates or antidepressant medications were excluded. Mini-Mental State Examination (MMSE) was performed on all patients (mean MMSE score 25.5 ± 8.4). Digital EEG was recorded using a 19-channel EEG (International 10–20 System). Thirty-second artifact-free EEG epochs during eye-closing states were selected and subjected to frequency domain analyses by means of standardized Low-Resolution Electromagnetic Tomography (sLORETA). Functional brain images in the conventional frequency bands (delta, theta,

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alpha 1, alpha 2, beta 1, beta 2, beta 3) were obtained. The sources of cortical activities detected by sLORETA were correlated with the cognitive function, as measured by the MMSE scores. As a result, there was a trend towards a positive correlation of activation in alpha 2 frequency band (10–13 Hz) in the left inferior temporal and posterior cingulate cortex (PCC) with the MMSE scores ($r = 0.71$; $p = 0.064$). These preliminary findings suggest a possible association of activation in temporal and limbic structures in the left hemisphere and better cognitive function in elderly patients with long-term epilepsy. A larger sample may help clarify this association.



P1-187

P1-187

Correlation between neuroimaging and treatment response in late-life depression

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Treatment-resistant depression is relatively common in the elderly, but its neurobiological basis is poorly understood. Magnetic resonance imaging (MRI) is a tool extensively used for studying depression in the elderly. Several voxel-based-morphometry (VBM) studies have detected a lot of gray and white matter abnormalities in late life depression.

Objective: The objective of this study was to investigate the correlation between neuroimaging and treatment response in late-life depression.

Methods: Eighteen elderly patients with depression (mean age = 71.7 SD = 7.2) and eleven group-matched comparison subjects (mean age = 71.45, SD = 7.4) were included. Brain MRI scans were obtained on all these subjects. Before the MRI acquisition, a psychiatrist administered the following psychiatry tests: Mini-mental State Examination (MMSE), Cognitive Test of the Cambridge Mental Disorders of the Elderly Examination (CAMCOG), Bayer Activities of Daily Living scale (B-ADL), Montgomery-Asberg Depression Rating Scale (MADRS), and Hamilton Rating Scale for Depression (HAM-D). All the elderly depressed patients were submitted to a treatment algorithm for depression. The group of patients was divided in two groups, one including 77% that have showed remission, based on the criteria of scores 7 on the MADRS scale and 8 on the HAMD, and another group including 23% that have not showed remission. Response to antidepressant treatment was assessed prospectively. Treatment resistance or non-remission was defined as non-responsiveness to at least 24 weeks including scores bigger than 7 and 8 on the MADRS and HAMD, respectively. MRI scans were processed by SPM2. Differences between groups were assessed controlling for age, total brain volume, and education.

Results: There was a significantly white matter reduction in the Sub-Gyral, parietal lobe ($p = 0{,}016$) in the response group of patients compared with the control group. There was a trend for smaller fronto-temporal volumes of gray matter in the treatment-resistant patients in the both hemispheres when a correlation with the control group were made and the same structures were found when we correlated the treatment-resistant patients with the remitted group.

Conclusions: The reduction showed in the white matter is related in the literature, and it is one of the possible pathways of depression in the elderly. However, further studies are necessary to better understand this question.

P1-188

Experience and perception of group home staff regarding end-of-life care for the elderly persons with dementia in Japan

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A "group home" (GH, hereafter) is a small nursing unit for fewer than 9 elderly residents with dementia. Group homes have come to play key roles in end-of-life care for elderly persons. The purpose of this study is to clarify experience and perception of GH staff who provide end-of-life care for the elderly persons with dementia and to identify their specific needs for the development of training program.

The self-administered surveys were mailed to 1,062 GHs in the Kinki area, Japan, in February 2007 after obtaining the Aino University Ethics Committee approval. Managers and staff at GHs were invited to answer the following questions about end-of-life care at GH, including: their experience (Experience); their perception (Perception); types of needed nursing activities (Activities); and needed training programs (Program).

Completed surveys from 484 manager- and 1,792 staff-respondents (374 facilities, 35.1%) were returned. The respondents' median age and years of experience at GH were 43 years (range = 18–86) and 2.0 years (range = 0.1 −13 years). About 60% of respondents had a care-worker license; 28% of the facilities have had at least one opportunity to provide end-of-life care; and 65% of the facilities had a future plan to provide end-of-life care.

Over 30% of respondents experienced providing care to support activities of daily living, talking to the residents, and observing symptoms. About 60% of the respondents reported observing symptoms, alleviating pain, and providing palliative family support are needed to their training program. About 40% of the respondents recognized the importance of inter-professional coordination. Over 90% of managers and staff hoped to acquire more knowledge through training programs to be able to provide better care.

The number of end-of-life care experiences showed a high correlation with the number of items selected from "Experience" (r = 0.81) and "Perception" (r = 0.77), but a low correlation with "Activities" (r = 0.29) and "Program" (r = 0.14). The GH staff wished to participate to end-of-life care after gaining knowledge and skills in observing symptoms, understanding patient and family needs, and coordinating care with medical organizations. The level of end-of-life care experience was not a predictor for GH staff to formulate concrete images for "Activities" or "Program." The development of a new training program incorporating training skills in inter-professional coordination and collaboration is highly recommended.

P1-189

Development of the Japanese-DOLOPLUS2: A Pain Assessment Scale for the Elderly with Alzheimer-Type Dementia

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Analgesics are less frequently prescribed for patients with advanced dementia where pain assessment is difficult than for cognitively intact patients. The DOLOPLUS 2 is a behavioral pain assessment scale for elderly patients with verbal communications disorders. It rates five somatic items, two psychomotor items, and three psychosocial items as indicators of pain; a score greater than or equal to 5 out of 30 indicates the presence of pain. The aim of this study was to translate The DOLOPLUS2 from French into Japanese and then assess its reliability and feasibility in clinical practice.

The translated instrument was evaluated with reference to Japanese patients with Alzheimer-type dementia experiencing pain during rehabilitation post-surgery for hip fracture and unable to use any self-report pain measures. After translation and back-translation, "Version 1" was tested with three patients by 21 registered nurses. Ratios of ratings by the nurses and researcher were matched. Semi-structured interviews were conducted with some of the nurses to assess instrument reliability and feasibility issues. And, patient case studies were recorded. Results provided the basis for "Version 2" which was then tested with six patients and 31 nurses using the same procedures as the test for "Version 1."

The ratio of matching scores for "Version 2" (77.5%) was significantly higher than for "Version 1" (59.8%). The matching ratios for "Version 2" for the breakpoint pain/no pain were 80.6%. Nurses' comments in the interviews were summarized: for "version 1", difficult to use and some Japanese expressions need improvement; for "Version 2", in addition to the same comments as for "version 1", nurses' comments included no changes needed and feasibility of this measure. Analysis of patient case studies and patterns of scores with "Version 2" indicated that both scores and matching ratios were

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high only when patients had special events such as beginning full weight bearing.

On the basis of these results we have written The Japanese-DOLOPLUS2. Our experience suggests that this instrument may be reliable and feasible for use in clinical practice. We recommend testing to formally establish its psychometric properties in Japan.

P1-191

Horticultural therapy and music therapy for the elderly living in a nursing home

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Horticulture and music are popular among the elderly. These interventions are incorporated in many elderly care institutions these days. The purpose of this study was to investigate the psychological effects of horticultural therapy (HT) and Music Therapy (MT) for the elderly living in a nursing home and to compare the results. We conducted HT for 16 subjects and MT included 14 similarly matched subjects. We assessed the psychological functions before and after once-a-week therapy during a three month period with The Philadelphia Geriatric Center Morale Scale (PGC) and the General Health Questionnaire 28 (GHQ-28). All scores were analyzed using a two-sample Wilcoxon test in SPSS13.0J. A P-value of < 0.05 was considered statistically significant. All subjects were well informed of the study and consented to take part in the study before the interventions. The post PGC scores of HT subjects were significantly better than the initial scores. The scores of GHQ-28 were significantly increased among each group. Then we analyzed the detail of the GHQ-28 scores. The results of Social dysfunction and Severe depression were significant in the HT group, while those of Anxiety and insomnia were significantly reduced in the MT group. It is easy to enjoy gardening and music for many elderly people because they are very familiar with these activities. In this study, we made a comparison between HT and MT. After 3 months of participation in HT, there were remarkable effects in psychological functions in comparison with MT. In HT, although subjects worked individually, they shared the growing of plants in common, and the plants and vegetables which they cultivated became a topic of conversation. Moreover, after subjects went back to their nursing home, they were concerned about the plants and looked forward to the next session. This suggests that HT has an effect on their quality of life. On the other hand, it is difficult for the elderly to sing loudly without reserve in a nursing home, so singing familiar songs caused mitigation of their stress in MT. Although many of them remarked that MT was very enjoyable, difficulty in using bells did not lead to other effects. In the future, a long term study is needed to examine the effects of MT.

P1-192

Development of a comprehensive environmental questionnaire for the homebound elderly: An examination of the reliability and validity among Japanese people

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Objectives: In our previous study, a comprehensive environmental questionnaire for the homebound elderly (CEQ) was developed and tested for face and content validity. The questionnaire consists of 15 environmental items in 5 domains (social, physical, institutional, informational, and religious), which affect life satisfaction in homebound, Japanese elderly. The aim of this study was to examine the reliability and criterion-related validity of the CEQ.
Methods: Participants were 360 elderly persons in east, west and capital of Japan (185 male, 175 female, mean age of 74.5 years). One hundred eighty-two of the 360 elderly participants were healthy, while 178 required day care services or home-visit rehabilitative services. They were asked to complete the CEQ and WHOQOL-BREF (Japanese version), and after one month they were asked to complete the CEQ again. The reliability of the CEQ was measured by Cronbach's alpha analysis and the test-retest method. The criterion-related validity was measured by the correlation coefficient between total score of the CEQ and environment domain score of the WHOQOL-BREF. All of the statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) ver. 14.0J for Windows.

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Results: Cronbach's alpha coefficient was .841, and the intraclass correlation coefficients (ICC) by the test-retest method ranged from .604 to .814 ($p < .001$). The maximum ICC was for "To have a company to live with" of social domain. The correlation coefficient between total score of the CEQ and environment domain score of the WHOQOL-BREF was .655 ($p < .01$).

Conclusion: The Cronbach's alpha analysis showed the high reliability of the CEQ. Generally, the test-retest reliability was high, but was somewhat lower in a few environmental factors. Thus, these environmental factors require further examination. The CEQ showed high criterion-related validity when compared to the environment domain of WHOQOL-BREF, meaning the CEQ is a useful tool for understanding the environments surrounding homebound elderly. Future studies will examine the construct validity of the CEQ by factor analysis.

P1-193

The effect of art therapy for aged patient with dementia; a study throught the practice by aged health facilities

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Japan is now aging society because14% of it population are senior citizens. Aging population is a worldwide demographic transition phenomenon but in Japan the population seems to senesce at the alarming rate if compared with other developed countries.

The Ministry of Health Lavor and warefare reported 160,0000 senior citizens are suffering from dementia and the number is estimated to exceed 300,0000 by the year 2025.

Despite the gloomy prediction nothing much was done either to identify the cause of dementia among senior citizen's or to search for a remedy or cue for this problem.

We started our experiment by utilizing art as therapy for group of dementia senior citizens who frequent one of the Health result suggests that the art therapy could change the behavior property and that the change might differ according to the personality of the patient.

We are proposing the art therapy as the series of pilot experiments.

In the preparing the research report we have asked the consent of the patients and his family and changed some details to kept the privacy and as a respect to human right.

P1-194

Learning about dementia care using WEB learning

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Objective: Educational activities are an important component of dementia care. These activities take the form of communicating knowledge about dementia. The objectives of this study were to create Web learning content regarding knowledge about dementia for use in dementia education and to verify the usefulness of this content.

Methods: Web learning content for learning of knowledge about dementia was created. The topic of the content was "What is dementia?" Steps for content creation were to create original copy and then create storyboards and voiceover copy based on the original copy. Animation was created from storyboards and then the voiceover was included. Next, 2 studies were conducted to verify the usefulness of the content created. Study 1 covered care staff. The study period was February 2006. Subjects were 21 caregivers at a special nursing home for the elderly and a health care facility for the elderly who require long-term care. These individuals were new staff members with less than 2 years of experience. First, subjects were given a test asking about knowledge of dementia based on content specifics. Next, subjects viewed and heard the content. Finally, subjects were again given the same test as they took initially. Then, test results for the 2 rounds of testing were compared. Study 2 was conducted to determine responses of content users to a Web-based survey after content was posted on the Website (the Dementia Care information Network, or DCnet).

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The study period was March 2006. The survey contained items on assessment of content specifics and understanding of what was learned.
Results: In Study 1, results of comparing test results for the 2 rounds of testing revealed a significant difference (according to a Wilcoxon signed-ranks test) in mean scores on the first and second round of the test. In Study 2, responses to the survey were obtained from 29 users of the Web content. Results indicated that 72% of respondents assessed content specifics as easy to understand. With regard to understanding of what was learned, 76% of respondents answered that their understanding improved.
Discussion: The fact that a significant difference in the 2 rounds of test results was noted suggested that specifics of the Web learning content conveyed knowledge as gauged by the test. Results of the Web-based survey indicated the usefulness of content specifics. Thus, the content created has specifics that communicate knowledge about dementia for educational purposes.

P1-195

Treatment of Japanese restless legs syndrome patients with dopamine agonists

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Objective: To determine the effective dose of dopamine agonists in Japanese patients with restless legs syndrome (RLS).
Methods: Eight cases of idiopathic RLS, three of RLS with Parkinson disease (PD), and one of RLS with iron deficient anemia participated in this study. All cases were diagnosed based on the clinical criteria of the International RLS Study Group. RLS severity was evaluated with International RLS Study Group (IRLSSG) Rating Scale Version 2.2.
Results: For 8 idiopathic RLS patients, the IRLSSG questionnaire scores improved with 1mg of daily cabergoline or 0.25mg of pramipexole at the endpoint. For 3 RLS cases with PD, the score was 21.7 ± 3.7 before the treatment, and RLS symptoms completely disappeared with 1mg of cabergoline. Two of RLS cases with PD required additional dopamine agonists later because of parkinsonism. Dopamine agonist was less effective for RLS symptoms due to iron deficient anemia than idiopathic RLS. No adverse event with dopamine agonists was reported in this study.
Conclusion: One mg of daily cabergoline or 0.25 mg of pamipexole is effective in some Japanese patients of RLS.

P1-196

Correlation between dementia onset and daily living functions in Japanese elderly: A 5-year cohort study

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Background and purpose: Studies report that a higher level of instrumental activities of daily living (IADL), intellectual activities (IA), and psychosocial activities lower the risk of dementia onset. However, it is still not clear which are the main contributing factors. This cohort study analyzes the correlations between the risk of dementia onset and various psychosocial factors.
Methods: The study used data of 2,725 elderly aged 65 years or over in Aichi Prefecture as of 2000, collected through the Aichi Gerontological Evaluation Study (AGES) Project. End point of the study was the onset of dementia, determined by whether a participant required long-term care according to the criterion used in Japan's Public Long-Term Care Insurance System (Level II or higher: observation of symptoms and behaviors that cause the daily life impediment and degradation in intellectual functions that causes communication difficulty), based on face-to-face interviews and physician diagnosis. Out of 2,725 participants, 2,204 were subject to analysis 5 years later, which included 210 who developed dementia and 1,994 who retained a healthy life (i.e. no mental or physical needs for care).The Kaplan-Meier Survival Analysis was used to determine the survival rate for retaining healthy life, and the Cox Proportional Hazards Regression Analysis was used to calculate the hazard ratio (HR) for dementia onset. The Tokyo Metropolitan Institute Gerontology Index was used as the psychosocial index. This index consists of 13 items with three

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domains: IADL (5 items), IA (4 items), and social role (SR) (4 items). Relative hazard ratios of each item in these three domains were calculated adjusted for age, sex, years of education, and self-rated health.

Results: Only 59–85% of those who responded "no" to each item in the IADL, IA, and SR domains retained healthy life, while 90% of participants who responded "yes" did so ($p < 0.001$).The HR for dementia onset in 5 years were significantly low for those responded "yes" in cooking (HR: 0.43, $p < 0.001$), visiting someone in hospital (HR: 0.48, $p < 0.001$), writing documents (HR: 0.51, $p < 0.001$), providing advice to someone (HR: 0.54, $p < 0.001$), using public transportation (HR: 0.58, $p < 0.01$), and reading newspapers(HR: 0.58, $p < 0.01$).

Conclusions: Our results indicated that daily living functions such as IADL, IA, and SR lowered the risk of dementia onset among community-living elderly.

P1-197

Increased publication of dementia studies

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Recently the population of the elderly increased rapidly and in addition of physical problems related to aging, importance of mental issues in the elderly has seemed to be increased. To confirm the increased importance of mental issues in the elderly, we surveyed the numbers of publication of the issues on psychogeriatrics. The term, "ementia", "dementia care", and "Alzheimer", were surveyed employing PubMed, and numbers of publications including "dementia", "dementia care", and "Alzheimer", are increased from 2804 (1990) to 5754 (2006), from 227 (1990) to 809 (2006), and from 1397 (1990) to 4770 (2006), respectively. Our study suggests that the numbers of publication related to dementia increased and that the publication on "dementia care" increased at the most highest ratio.

P1-198

Memory and physical mobility in physically and cognitively independent elderly

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Close relationships between cognitive function and physical mobility in the elderly have recently been reported. In this study, we examined the relationship between memory and physical mobility in aging in the physically and cognitively independent elderly.

We recruited 183 elderly people aged 60 years or older. From these participants, as subjects for this study, we selected those who (1) had MMSE scores of over 23, (2) could walk one kilometer without any assistive device, (3) had reliable informants and (4) had the full scores on the Physical Self-Maintenance Scale (PSMS) and the Instrumental Activities of Daily Living Scale (IADL) rated by their informants. We excluded any subjects that (1) had a neurological or psychiatric disease in the past or in their current medical history, (2) had a head injury with unconsciousness for more than one hour, (3) were under active therapy for life-threatening cancers and were in poor condition due to a chronic disease. Memory was assessed by using the Rivermead Behavioral Memory Test (RBMT) and a total standardized Profile score was used as an index of overall memory status. Additionally, we made a "score independent of walking ability" to exclude the effect of physical mobility on the RBMT score and a "score independent of prospective memory" to exclude the effect of executive function on the RBMT score. Basic physical mobility was assessed by using the Timed Up & Go test (TUG). The score was expressed as the time in seconds to perform the sequence of the action required in TUG.

The subjects were 51 men and 96 women, having a mean age of 72.6 ± 5.7 years (range, 60 to 90 years), and a mean educational attainment of 12.0 ± 2.8 years (range, 6 to 20 years). The TUG score significantly correlated with the total standardized Profile score ($rs = -0.21$, $p < 0.05$) and the scores independent of walking ability ($rs = -0.23$, $p < 0.01$) and prospective memory ($rs = -0.23$, $p < 0.01$). Controlling for age, sex, education, and the presence of risk factors of cerebrovascular disease did not change the results.

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Memory is associated with basic physical mobility in independent elderly people. Because the TUG score significantly correlated with the scores independent of walking ability and prospective memory, the correlation was not a superficial one due to physical mobility or executive function. Our findings suggest that maintaining basic physical mobility can slow memory decline during aging.

P1-199

Musical hallucinations in the normal and the deaf

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Musical hallucinations are experiences of hearing music with all the qualities of hearing real music but without any sound being made. This a descriptive report of twenty four cases of people with acquired deafness and 6 people with pre-lingual deafness that experienced musical hallucinations.

The author will describe musical hallucinations in 19 normal children and adults' non-psychiatric population. Five people reported the onset of hallucination prior to adulthood. In this presentation the author demonstrates that musical hallucinations are not necessary pathological and can occur as a normal experience in people (children and adults) who have no contact with mental health services and no concurrent mental disorder. The presentation will recognize that children can experience musical hallucinations.

The concept of musical imagery, memory and hallucination will be discussed in terms of psychopathology, prevalence and aetiological mechanisms.

The author will conclude that musical hallucinations are commoner than previously thought off but people don't report it; that the neural network involved in music listening interacts with perception and memory to produce musical experiences whether imagery, memory or hallucination (This is coloured by the characteristic of the individual personality and background in a dynamic way); and that musical hallucination should be thought as a continuum with normal experiences and clinical syndromes.

P1-200

The effects of fall prevention on depressive symptoms among the aged: A randomised controlled trial

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Population-based studies have shown depression to be associated with falls. Despite its relatively high prevalence among the aged, depression has often been neglected in fall prevention. The aim of this study was to determine the effects of fall prevention on depressive symptoms among the aged. This study is part of a multifactorial fall prevention programme implemented in the town of Pori, in western Finland among 65-year-olds and older home-dwelling aged who had fallen at least once during the year previous to randomisation. Persons willing to participate and fulfilling the inclusion criteria (N = 591) were randomly assigned to an intensive preventive programme (intervention group) or to a counselling group (controls) separately in two age groups (65–74 and 75-year-olds or older). Depressive symptoms were measured by the 30-item Geriatric Depression Scale (GDS) consisting of 30 questions with a dichotomic response format (yes-no). The changes within the groups from baseline to 12-month follow-up were analysed by the Wilcoxon Signed Rank test. The Mann Whitney U-test was used to analyse the differences between the groups in sum score of GDS at baseline and to analyse the differences in the change of GDS sum scores between the groups from baseline to follow-up. All statistical analyses were performed with the SAS System for Windows, version 9.1 (SAS Institute Inc., Cary; NC, US). P-values less than 0.05 were considered statistically significant. The full GDS data with no missing items were available for 464 persons. There were no significant differences between the intervention and control group in background variables. A significant decrease in depressive symptoms during the 12-month intervention was found in the intervention and the control groups. In subgroup analyses, persons with a high amount of depressive symptoms at baseline benefited most in absolute terms. A significant difference in the change of depressive symptoms between the intervention and control groups was found among men and older subjects. Multifactorial fall prevention had beneficial effects on depressive symptoms especially among men and older participants. Depressive symptoms may, thus, be reduced by non-drug methods, which is especially important among the fall prone aged.

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P1-201

The clinical use of P300 event-related potentials for the evaluation of donepezil treatment for Alzheimer's disease

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Objective: To evaluate the effect of donopezil (5mg/day) treatment upon auditory P300 event-related potentials (ERPs) and cognitive change amongst patients afflicted with Alzheimer's disease (AD).

Methods: Thirty-four patients suffering from AD, according to DSM-IV and NINCD-ADRDA criteria, underwent evaluation of their cognitive function (defined by Cognitive Ability Screening Instrument, CASI and Mini-Mental State Examination, MMSE) and P300 ERPs at the commencement of, and during, a 20-to-22-week study period. During this period study participants were administered donepezil at 5mg/day. Paired Student's t-testing and application of Pearson's correlation were used for statistical analysis of study data.

Results: All patients completed the study in full. Reduction of P300 latency ($p = 0.007$) over time, associated with a parallel improvement as regards cognitive performances (CASI scores, $p = 0.045$; MMSE scores, $p = 0.011$) were observed for the study-group patients being administered donepezil. The P300 latency for these individuals was significantly positively correlated with the mean CSAI score but not with the mean MMSE score at baseline ($p = 0.045$, $p = 0.060$) and at end-point ($p = 0.009$, $p = 0.086$).

Conclusion: Donepezil treatment revealed both a cognitive improvement for study participants, and also a P300-latency reduction subsequent to the drug's administration for a period of 20–22 weeks. P300 latency would appear to be a reliable objective instrument for the assessment of cognitive response to donepezil for patients afflicted with AD.

P1-202

Environmental factors affecting the life satisfaction of healthy Japanese elderly: A questionnaire survey

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Objectives: We developed a comprehensive environmental questionnaire for the homebound elderly (CEQ). The CEQ consists of 15 environmental items in 5 domains (social, physical, institutional, informational, and religious), and has been tested for validity and reliability. The aim of this study was to identify environmental factors that affect the life satisfaction of healthy Japanese elderly.

Methods: Participants consisted of 182 elderly living in east, west and capital of Japan (107 male, 75 female, mean age of 69.7 years) who answered the CEQ and the Visual Analogue Scale (VAS) to measure life satisfaction. To identify the environmental factors that affect life satisfaction, we performed a multiple regression predicting CEQ scores with VAS scores. Prior to testing regression models, we used a stepwise backward selection procedure to reduce the number of independent variables to a smaller number of predictors. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) ver. 14.0J for Windows.

Results: A multiple regression analysis with stepwise backward selection was used to determine a VAS score (dependent variables) from 15 CEQ scores (independent variables). We found 4 predictors of high life satisfaction (Table 1). These were, "To have safe dwelling (No.10)," "To have good relationships with friends and acquaintances (No.6)," "To be able to adequately use medical and welfare services (No.12)" and "To have good family relationships (No.4)."

Conclusion: The factor that most positively contributed to life satisfaction was, "To have safe dwelling." Although participants of this study were healthy, it is inevitable that their health will eventually deteriorate with age, and safe living place will be become an increasingly important factor for life satisfaction. While this study focused on healthy elderly people living in 3 areas of Japan, further research is needed to evaluate the environmental factors that contribute to the life satisfaction of elderly in need of care, and who live in other areas.

P1-203

Pain perception, anxiety and attachment style in the elderly population

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Table1 Summary of Multiple Regression Predicting CEQ scores with VAS scores

Independent variable		SE	β	t	p
No.10	"To have safe dwelling"	2.002	.216**	3.095	.002
No. 6	"To have good relationships with friends and acquaintances"	1.955	.230**	3.432	.001
No.12	"To be able to adequately use medical and welfare services"	1.964	.204**	3.008	.003
No. 4	"To have good family relationships"	1.772	.163*	2.423	.016
multiple correlation coefficient(R)= .544		R^2=.296		adjusted R^2=.280	

** p<.01 * p<.05

P1-202

Kevin Woo[1]; Joel Sadavoy[2]

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Pain is a multidimensional construct. Despite experiencing the same noxious stimulus, individuals experience and report pain in different ways. A constellation of factors may be involved in the mediation of pain perception and adjustment to pain. Anxiety is related to the pain experience in various clinical populations. Although the exact mechanism is not clear, anxiety may lower pain threshold and heighten the feeling of pain. According to the attachment theory, It is contended that cognitive model of self and other may influence the perception of pain. These cognitive models, represent cognitive-affective schemas, are developed over time based on recurring attachment experiences. Four attachment patterns or styles have been identified in terms of the intersection of two underlying dimensions: the positivity of a personal model of the self and the positivity of a personal model of hypothetical others. The patterns emerged are classified as secure (positive self and positive other), and three insecure attachment styles: preoccupied-ambivalent (negative self and positive other), fearful-avoidant (negative self and negative other), and dismissing (positive self and negative other). Attachment style differences have been found in systematic patterns of expectations, emotional reactivity, strategies for distress management and social behaviour based on an individual belief about the self and others. As such, attachment may provide a framework on which pain experience can be constructed. Accumulated evidence has demonstrated that attachment relationship continue to play an important role throughout the life span into old age. The purpose of this presentation is summarizing the literature that explores the relationship of attachment style and the experience of pain. It is hypothesised that secure subjects will report less pain and anxiety than other attachment styles. Individuals characterized by insecure attachment particularly, fearful avoidant and ambivalent styles of attachment, are associated with anxiety that may exacerbate the pain. Second, insecure individuals may experience more intense pain since they are more likely to maintain hypervigilant and catastrophize their symptomology than secure individuals. Third, insecure individuals may incline to report more somatic symptoms than those who are securely attached.

P1-204

Dementia in the elderly at an acute hosptalization setting: a case-control study in Taiwan

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Purpose: This project is to investigate the characteristics and outcomes of dementia patients during their hospitalization in the acute wards other than Neurology and Psychiatry.

Methods: A matched case-control study of dementia vs nondementia subjects among the elderly patients aged 65 years or older. Dementia was defined as Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) = 3.4 or greater or those

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who had been diagnosed so before hospitalization. Nondementia was selected by matching with same gender and age within five years in a 1:1 fashion with dementia subjects.

Findings: We consecutively surveyed a total of 3680 newly admitted patients in Orthopedics, Urology, Chest, Metabolism and Cardiology wards in a period of 6 months. Among them, 1753 were aged 65 years or older. The prevalence of dementia varied greatly among the departments, ranging from 8.1% to 19.6%. Only 27.8% of Dementia Group had a previous diagnosis of dementia. A total of 90 matched pairs were selected. The proportions of stroke and hypertension and the number of categories of comorbid disease was significantly higher in dementia group than in nondementia group. In Urology, Chest and Cardiology, total scores of CIRS were significantly higher in dementia group. The length of stay was 11.9 ± 8.82 days and 8.5 ± 5.00 days in Dementia and non-dementia groups, respectively ($p = .005$). The 5 most common events encountered were difficulty in communication, urine/stool incontinence, and refusal of nursing care, verbal aggression and agitation. The number of person-days of events was significantly associated with .37 day longer of hospital stay. The cost of hospitalization was not significant between cases and controls or among departments; however, it was associated with events, accounting NT$1860 per one person-day of events. Three-month mortality rates were 10.6% vs 3.4% (odds ratio 3.35, $p = .0632$).

Conclusions and suggestions: The prevalence and acute care problems of demenia were different among departments. Events of problems were significantly associated with hospitalization length and cost, indicating early recognition of dementia and training of care givers (family members or clinicians) may reduce the cost and increase the quality of care. This provides principles for designing the care guidelines for dementia.

P1-205

A study of the validity and reliability of the Chinese version of the hierarchic dementia scale (CV-HDS)

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With the rapid growing of the older adult population, heavier demands on the health care system across the globe are inevitable. Dementia, a common disorder among the elderly, is characterized by progressive decline in cognitive abilities, which in turn, lead to decline in functional performance. As a result, early detection and treatment of cognitive deficits is crucial in slowing down the functional deterioration, thus, enhancing the quality of life of the elderly persons.

The present study aims to develop a Chinese version of the Hierarchic Dementia Scale (CV-HDS) for the use in geriatric and psychogeriatric population in Hong Kong and to examine the validity and reliability of the CV-HDS.

The HDS was translated into Chinese by a qualified translator. The content validity and cultural relevance were evaluated by six expert panel members. Sixty two elderly people with a diagnosis of dementia were recruited in North District Hospital and Home for the Elderly by purposive sampling method. Internal consistency, test-retest reliability, inter-rater reliability and construct validity were evaluated.

The CV-HDS demonstrated satisfactory psychometric properties. Test-retest reliability and inter-rater reliability were high ($\alpha = 0.94$ and $\alpha = 0.89$ respectively). High value of Cronbach's alpha ($\alpha = 0.94$) demonstrated excellent internal consistency. The concurrent validity of CV-HDS, through correlation with its scores with that of the Chinese version of Mini Mental Status Examination was well established (ranged from $r = 0.58$ to $r = 0.78$, $p < 0.01$).

The CV-HDS is a reliable and valid instrument for assessing cognitive deficits in people with dementia. It can provide a more detailed assessment of cognitive functions, which in turn, can facilitate treatment planning and contribute to the betterment of patient services, and to the professional development of the geriatric and psychogeriatric rehabilitation.

P1-206

Parcellar spread myoclonus in Alzheimer's disease: Our experience

Bruno Brancasi[1]; Vania Durante[1]; Antonio Superti[1]; Salvatore Ottaviano[1]; Maria Troito[1]; Antonella Cusanno[1]; Roberta della Porta[1]; Paolo Lamberti[1]

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P1-206

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Alzheimer's disease (AD) is a neurodegenerative illness initially affecting short-term memory, then attentive and executive functions, language, space-time orientation and superior cortical functions. As seizure are relatively frequent in the advanced phase, myoclonus is not described frequently. It can involve the limbs, face and trunk and is defined as a sudden, brief, rapid and shock-like unintentional muscular contraction. This typical manifestation of some neurological pathologies, rarely is described in AD. Four patients observed in our Alzheimer's Evaluation Unit, respectively of 63, 60, 78 and 85 years affected by severe AD lasting six years, showed diffused parcellar myoclonus, chiefly at the limbs, at rest and during movements. Myoclonus severity has been evaluated in quantity, amplitude and frequency by the UMRS (Unified Myoclonus Rating Scale) at rest, during movement and sensorial stimulation; moreover they were submitted to electrophysiological evaluation by video-polygraphic recording with EEG and surface EMG from dorsal and palmar muscles of the forearms, in rest conditions, during simple actions and multiple sensorial stimulation. The four patients respectively achieved a score of 15, 21, 8 and 0 on UMRS at rest and respectively a score of 13, 8, 10 and 9 after sensorial stimulation. Myoclonus during movement was not evaluated because of scarce collaboration. The EEG showed irritative cortical activity not localized on a specific derivation, to which sometimes corresponded bursts of rapid electromyographic activity of the muscles, with myoclonus showed by the video. In scientific literature, cortical myoclonus affecting AD patients is rarely described and not well defined. In our daily clinical activity with AD patients we met this symptom and observed its negative interference on normal rest activity, especially in these subjects not able to understand, control and correct adequately their action. The probable cortical origin

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leaded us to interpret this manifestation as the output of an irritation that could invalidate the residual cortical activity. Therefore we judge important to establish the incidence of this phenomenon and its relationship with disease severity and to monitor it in terms of quantity, spatial and temporal distribution and interference with motor performances and daily living ability.

P1-207

The risk of post-stroke epilepsy

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Introduction: Stroke is the most common cause of seizures in the elderly, and seizures are among the most common neurological sequel of stroke. We studied clinical features of post-stroke epilepsy.
Methods: We included 124 patients with stroke, 55 pts (mean age 67 ± 6.7 y) with post-stroke epilepsy (PS) and 69 pts age matched (mean age 65 ± 7.1 y) without seizures (S) which were included randomly. All of them had CT scan. The National Institut of Health Stroke Scale (NIHSS) were compared between the two groups. To test differences between the groups Student-t test in Chi-square were used.
Results: The mean interval from stroke onset to seizure presentation in PS group was 8.7 ± 7.1 months (range from 4 months – 1.5 years). Partial seizures with or without secondary generalization were the commonest type of late post stroke epileptic seizures. We found significantly higher NIHSS score in PS group compared to S groups (7.2 ± 5.1 vs. 9.4 ± 5.9; $p = 0.029$). We found more hemorrhagic strokes in PS group (34.5% vs. 17.4%; $p = 0.037$). Cortical involvement was found in 44.9% of S pts and 63.6% of PS pts. The difference was significant ($p = 0.047$).
Conclusion: The risk of post-stroke epilepsy is higher in patients with cortical involvement, hemorrhagic stroke and lower NIHSS score.

P1-208

Parcellar spread myoclonus in Alzheimer's disease: Incidence and therapeutic response to levetiracetam

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Alzheimer's disease (AD) is a neurodegenerative cerebral illness that evolves in three phases: light, moderate and severe. During severe phase myoclonus can appear, which is a sudden, brief, rapid and shock-like unintentional movement. Cortical myoclonus is a typical manifestation of some neurological pathologies and levetiracetam has proven therapeutic effectiveness in its reduction. Levetiracetam is a new antiepileptic drug which seems to inhibit of the N-type Calcium channel, the reduction of intraneuronal calcium release and the partial inversion of the reduction of the calcium tide induced by GABA and glycin. We tried to verify the effectiveness of this drug in the treatment of myoclonus affecting four severe AD patients followed in our Alzheimer Evaluation Unit. Myoclonus severity has been evaluated in quantity, amplitude and frequency by the UMRS (Unified Myoclonus Rating Scale) at rest, during movement and sensorial stimulation; moreover they were submitted to electrophysiological evaluation by video-polygraphic recording with EEG and surface EMG from dorsal and palmar muscles of the forearms, in rest conditions, during simple actions and in the course of multiple sensorial stimulation. The patients were submitted under therapy with levetiracetam (Keppra) 500 mg/die for one month and then the protocol of the study was repeated. The data obtained by the UMRS after therapy show that in the four patients the myoclonus at rest improved to 5, 0, 2 and 0 in comparison with 15, 21, 8 and 0 respectively at time zero. The myoclonus after sensorial stimulation changed from 8, 13, 10 and 9 before the treatment to 3, 10, 2 and 4 after the drug. Before treatment the EEG showed a mildly slow basal activity and frequent irritative cortical figures, such as isolated spikes, not localized on a specific derivation and inconstantly followed by electromyographic bursts of the recorded muscles, also showed by the video-recording. After therapy also the neurophisiological data drastically change coherently with the objective findings, confirming the origin of the abnormalities and the efficacy of the treatment. The four cases we studied and treated show that levetiracetam was able to significantly reduce the AD cortical myoclonus, in spatial distribution, frequency and amplitude. This reduction appears to improve the ability of the patients to behave some elementary action and consequently ameliorate their quality of life.

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P1-208

P1-209

The relationship between depression and androgen deficiency in middle-aged and older non-castrated men in psychiatric outpatient visit

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Objectives: The objectives of the study were to find the relation between major depressive disorder (MDD) and partial androgen deficiency of the aging male (PADAM), and to determine whether symptoms on Aging Male Symptoms Rating Scale (AMS) differed between patients with/without MDD, and differed between patients with/without PADAM.

Methods: 176 consecutive non-castrated psychiatric male outpatients aged 50 to 79 who were, non-psychotic, bipolar disorder, cognitive disorder, and psychoactive substance abuse were enrolled to complete Androgen Deficiency in Aging Male Questionnaire (ADAM), AMS (psychological, somatic, and sexual dimensions) and Hospital Anxiety and Depression Scale (HADS). All patients had been treating with psychotropic medications. The Structured Clinical Interview for DSM-IV (SCID-P) was administered to establish a diagnosis of MDD. Statistical analyses were carried out using SPSS 11.0.

Results: There were significant correlations between HADS and AMS subscales. The prevalence of PADAM had no difference between populations with and without MDD; while the total AMS score, the AMS psychological, somatic and sexual subscales were higher in patients with MDD. In addition, AMS scores were higher in patients with MDD for all except three symptoms, and were also higher in patients with PADAM for all except four symptoms. Analysis of variance (ANOVA) revealed simple main effect of MDD on those patients with PADAM.

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Table 1
The prevalence of PADAM in patients with and without major depressive disorder

	Patients without major depressive disorder ($N=129$)		Patients with major depressive disorder ($N=47$)	
ADAM	Frequency	Percent	Frequency	Percent
YES	118	91.5%	46	97.9%
NO	11	8.5%	1	2.1%
TOTAL	129	100%	47	100%

Not significant percent difference between patients with and without depressive disorder.(Pearson Chi-square, $p > 0.1$)

Table 2
The HADS and AMS scores in patients with and without major depressive disorder

	Patients without major depressive disorder ($N=129$)	Patients with major depressive disorder ($N=47$)
HADS total score	12.5 ± 5.56	25.7 ± 5.76**
Depression score	5.39 ± 2.68	14.2 ± 2.72**
Anxiety score	7.10 ± 3.93	11.5 ± 4.69**
AMS total score	36.4 ± 9.31	49.4 ± 10.6**
Psychological score	10.5 ± 3.68	15.4 ± 4.62**
Somatic score	15.2 ± 4.13	19.9 ± 4.65**
Sexual score	10.8 ± 3.59	14.1 ± 4.12**
17 Items		
Well-being, impaired	2.31 ± 0.80	2.96 ± 0.95**
Joint complaints, more	1.98 ± 1.00	2.49 ± 1.06*
Sweating, increased	1.53 ± 0.81	1.68 ± 0.86
Sleep disturbance, more	2.82 ± 1.23	3.51 ± 1.14*
Sleep, need for more	2.22 ± 1.04	2.98 ± 1.15**
Irritability, increased	2.01 ± 1.00	2.70 ± 1.37*
Nervousness, more	2.42 ± 0.94	3.34 ± 1.18**
Anxiety, more	2.17 ± 0.94	2.96 ± 1.28**
Physical exhaustion	2.36 ± 0.79	3.28 ± 0.99**
Muscular weakness	2.03 ± 0.82	2.96 ± 1.00**
Depressive, more	2.09 ± 0.92	3.51 ± 1.12**
Passed peak	2.06 ± 0.99	3.19 ± 1.14**
Burned out	1.75 ± 0.88	2.94 ± 1.15**
Decrease of bread growth	1.18 ± 0.48	1.43 ± 0.77
Sexual potency, impaired	2.66 ± 1.17	3.15 ± 1.16
Morning erections, less	2.57 ± 1.05	3.28 ± 1.12**
Libido, disturbed	2.29 ± 1.11	3.11 ± 1.24**

All values are shown as mean ± SD.

* $p < 0.01$, significant difference between patients with and without depressive disorder.

** $p < 0.001$, significant difference between patients with and without depressive disorder.

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Conclusions: Aging symptoms are prevalent in population of psychiatric male outpatients aged over 50. Symptoms of PADAM were often overlapping with those of MDD. MDD did not increase the prevalence, but worsen the severity of PADAM. By AMS item comparison alternately grouped with MDD and ADAM, "excessive sweating" and "decrease in beard growth" did not differ in each comparison. "Joint pain and muscular ache" and "irritability" were easily affected by MDD and were less relevant when making diagnosis of PADAM. "Decrease in sexual desire/libido" can be regarded as the core symptom of PADAM. In evaluating depression and anxiety in aging men, psychiatrist should be aware of the interaction between MDD and PADAM and request laboratory analysis of testosterone when indicated.

P1-210

Examination of care team formation aiming for person-centered approach (PCA) by jointly utilizing the center method to support persons with dementia and the results of care

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Objective: Examine the relation between qualitative changes of care teams by utilizing the Center Method to Support Persons with Dementia (CM) developed as a tool common in multiple dementia care professions and results of care related to dementia cases.
Method: Analyze data of the follow-up survey (questionnaire survey, single case study) targeting 388 care teams which jointly utilized the Center Method for four months.
Results: 59.5% teams came to practice collaboration in PCA, while 40.5% did not (PCAT vs N-PCAT). As the result of care after four months, 90% of PCAT group replied in the affirmative, significantly higher than N-PCAT group (75.8%). ($p < 0.01$) Regarding specific results, identified in the PCAT group were palliation of BPSD and increase in act like oneself, self-directing scenes and independent behavior. ($p < 0.01 \sim 0.05$).

It was recognized as one of the useful tools to utilize the Center Method continuously and formulate PCA-oriented teams in order to improve results of care for persons with dementia.

P1-211

The assessment tools for the Korean long-term care system in the elderly with dementia

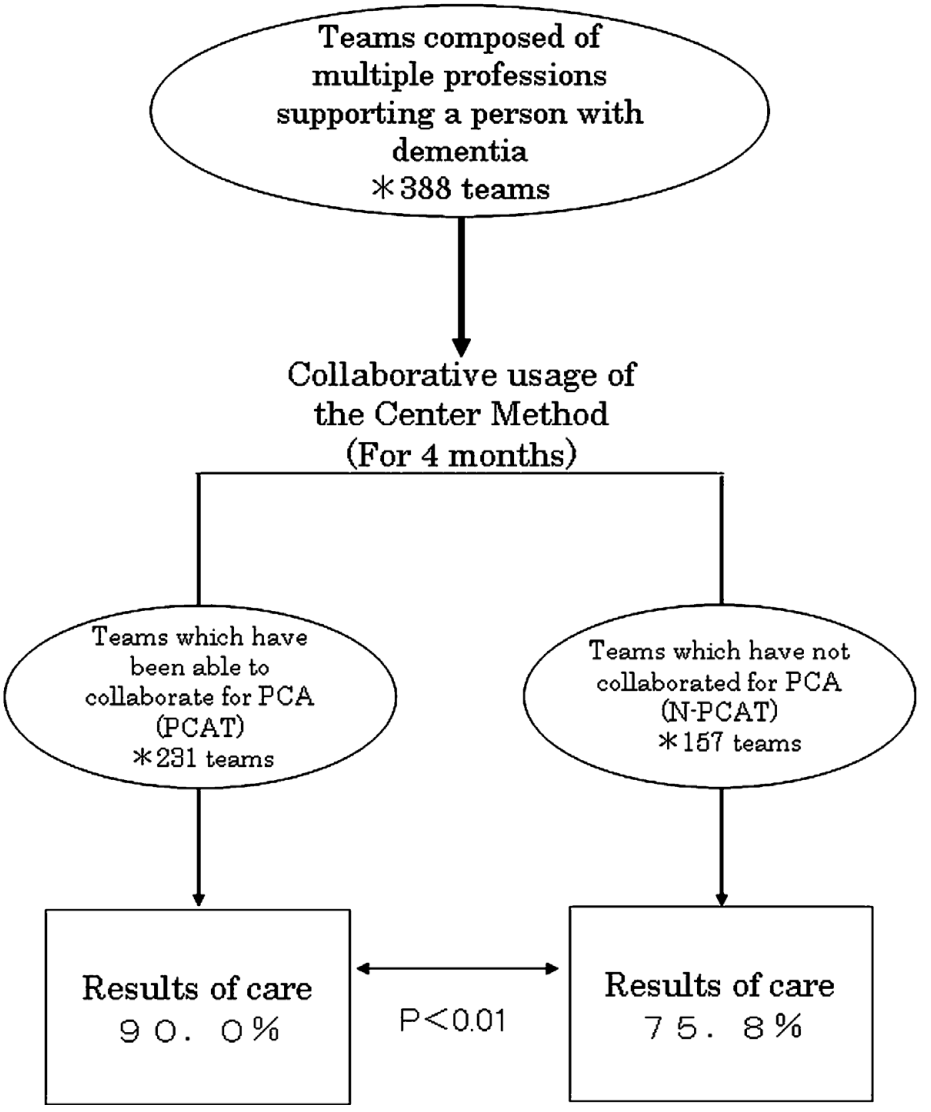
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Purpose: The rapid increase of elderly population was raised as an important social issue in Korea. In line with it, the development of the Korean Long-Term Care System has been activated. In quick development of the System, there was insufficient time to make valid assessment tools for grade the elderly for an offer of the service. Also there are no specific concerns for the elderly with dementia in the assessment tools, although they need different care compared with the elderly without dementia. For the further development of the Korean Long-Term Care System, we reviewed the results of the pilot enforcement carried out by government.
Methods: We reviewed the first 4000 elderly people out of 23,899 subjects who were enrolled by the second pilot enforcement of the Korean Long-Term Care System. We compared 534 subjects who had been diagnosed as dementia by clinicians and 284 subjects who were not remarked specifically in diagnosis and medical treatment. We analyzed the data with SPSS 12.0.
Results: 47.4% of the elderly with dementia were graded as grade 1 (the mildest grade) and 48.9% of the elderly without any remarks were not graded in the Korean Long-Term System. 76.4% of the elderly with dementia wants to receive facility services, but the subjects with grade 1 cannot receive the services. The elderly with dementia had higher scores in sub-items of ADL, cognitive functions and behavioral problems than the elderly without any remarks ($p < 0.001$). The mean grade of the subjects who had all impairment in cognitive function and the subjects with no impairment in this subitem were not different statistically ($p = 0.067$). The

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Research Outline



P1-210

behavioral problems had same problems as cognitive function ($p = 0.328$). In multiple regression, ADL, cognitive function and behavioral problems affect a little portion to the grade (adjusted $R^2 = 0.043$). Among these, behavioral problems had largest effect on the grade (ADL; $t = 5.691$, cognitive function; $t = -3.431$, behavioral problems; $t = 11.044$).

Conclusion: The cognitive function and behavioral problems had a little effect on the grade in the Korean Long-Term Care System. Although we could assume that the elderly with dementia in our study had more severe dementia than the elderly in the community by definition, we concluded that they were not graded enough. The assessment tools

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for the Korean Long-Term Care System need more sophisticated concerns to the elderly with dementia.

P1-212

Influence of emotional life on HRQOL

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Province Vojvodina with 2 million inhabitants, average age of 38 years, and with life expectance for females 75 and for males 70 years, is demographically old population. The aim of Health policy of Serbia is to make people to live longer but also to improve the Quality of life (QOL) of people, so it is very important to measure QOL and the factors that influence on it. The objective of this paper is to define the influence of emotional health to the global Health related Quality of life (HRQOL). In previous survey we defined QOL-OLD index as overall numerical value of health related quality of life in elderly population, which showed high validity and reliability. Our hypothesis was that the influence of emotional health to the global score of QOL-OLD index is less then 20%.This study included representative sample of people aged 60 and above (n = 373) using special questionnaire with 36 items grouped in six domains. This investigation was conducted through postal poll. One domain/scale is emotions about life, transformed score (range 0–100) was calculated for total health related quality of life index and for emotional scale. Emotional life scale is about individual emotions in personal life, attitude towards close family, self-esteem, emotions about past, present and future life and feelings of self appreciation in present life. The mean value of transformed score of emotional life scale is 56.6 (95% CI confidence interval 54.4–50.7). There is significant difference between gender and level of education, but no significant difference by age and marital status. Females and persons with lower levels of education have significant lower mean value of transformed score. Analysis showed that emotional health influence on total QOL-OLD index with 16.3% and thereby lowering total value of QOL-OLD index of 71.8. Average values of total QOL-OLD index are significantly lower for females, persons with lower levels of education but also for older elderly and old persons living alone. Emotional life scale has the lowest mean value among other scales influencing the total QOL-OLD index. Emotional life is important part of total QOL-OLD index and as such, it should be differed from depression, however, often decreasing or loosing of emotional relations with others can be beginning of depression. That is the reason why it is important to monitor and assess emotional scale as a part of total HRQOL.

Keywords: emotional life, quality of life, elderly.

P1-213

Health education for active ageing

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Health education process lasts during the whole life span. Health education of the elderly people needs to be specific according to major health problems and specific educational needs. One of the major health problems among elderly are injuries caused by falls. It is well known that elderly people after injuries and subsequent decreased mobility and social contacts, often suffer from mental disorders mostly depression. Aim of the paper is to present 3 year Health Education Project, in the first year directed to health education of elderly about most frequent mechanisms and prevention of injuries caused by falls. The next two years topics will be directed to mental health and physical activity. Local community as well as local authorities (on municipality level) was partners in this Project. The first phase (in year 2007) of the Project is creation of health educational brochure calendar, illustrated with the most usual situations in which old people fall at home and street. Those situations are: wet floors at home, floor clutter, loose carpets, climbing on chairs, in shower, smudged glasses, standing up from chair, tripping on flexes, situations on the street (curbs, icy pavement), lights off when going to the bathroom at night, worn-out slippers, untied laces. Calendar was distributed to geriatric and retirement homes, primary health care professionals, retirement associations etc. Educational instructions were given to professionals working with elderly. Also, raising interest of the population was carried out through media. Monitoring and process evaluation give us feed-back information about design, usefulness and acceptation of this kind of approach. Health educational needs of the elderly people can be addressed according to their major health problems, using special programs and specific educational methods, and taking in account settings, interests of local

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community, in order to improve health and to accomplish active ageing.

Keywords: health education, elderly, injuries

P1-214

Assessment of distress and pain in patients impaired by psychotic phenomena

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Background: Few existing studies suggest that psychosis blunts an individual capacity for suffering. Implication of this finding is that in patients who are impaired due to psychosis, the presence of such an impairment somehow renders an increased tolerance to pain and distress. However, pain and distress is not only sensory experience but also affective, cognitive and evaluative experience. Measures of multidimensional domains of distress measurements have been largely lacking in this population.

Study Design/Measurements: Subjects were recruited from a cohort who had schizophrenia spectrum disorders at Veteran Administration System (n = 57). The McGill Pain Questionnaire-SF was used to assess multidimensional pain experience while associated psychotic symptoms were measured using PANSS scales. And depressive symptoms were measured using HAMD scales. The data was analyzed by Mann Whitney U test.

Results: 57 subjects rated distress using the McGill Pain Questionnaire. The subjects were divided into low and high pain groups to compare their degree of psychosis and pain perceptions. The Mean Affective and Cognitive Pain Rating Index scores were 6.52 in low pain group and 12.1 in high (p 0.001). The mean PANSS rating scores were 60.8 for low pain group and 71.2 for the high group(p 0.01). The presence of psychotic symptoms did not necessarily indicate an impairment in overall measures of suffering. And depressive scores on both groups were not large enough to serve as a significant confounder.

Discussion: The affective and cognitive capacities to perceive distress did not have an inverse relationship with degree of psychosis as previously suggested. In contrast to existing data, the presence of psychotic symptoms did not necessarily indicate an impairment in patient's capacity for suffering distress. These findings suggest a need for multidimensional assessment tool to adequately measure pain and distress in patients who are impaired by presence of psychosis, and may have implications for development of a valid and reliable multidimensional assessment tool to measure distress in patients who are impaired by psychosis or cognitive impairments.

P1-215

Poor participation in stroke patients undergoing inpatient rehabilitation: Incidence and clinical correlates

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One of the important factors traditionally viewed by rehabilitation professionals in determining functional outcome is patient motivation and participation in rehabilitation. It is believed that 'unmotivated' patients are likely to participate less in rehabilitation and have poorer functional outcome. Some of these patients may even risk early termination of, or exclusion from rehabilitation services. The objectives of this study are a) to evaluate the incidence of poor participation in stroke patients undergoing inpatient rehabilitation programme, b) to correlate level of participation with age, sex, stroke severity, functional status, depression, fatigue, social support and health attitudes and beliefs. This is a cohort study of stroke patients admitted to a tertiary rehabilitation centre for inpatient rehabilitation over one year. The following instruments are used: Pittsburgh Rehabilitation Participation Scale (PRPS) to assess level of participation in occupational and physical therapy, National Institute of Health Stroke Scale (NIHSS) to measure neurological impairment, Elderly Assessment of Cognition Questionnaire (EACQ) to assess cognition, Functional Independence Measure (FIM) to assess independence in activities of daily living, Center for Epidemiologic Studies, Depression (CESD) to screen for depression, Fatigue Severity Scale (FSS) to evaluate fatigue and the Lubben Social Network Scale (LSNS) to evaluate premorbid social support. Except for the LSNS, these instruments were administered on admission and discharge. To date, 26 patients (mean age 60.1 years, 14 males, 12 females) were recruited. The mean length of stay in rehabilitation was 23.6 days. 7 patients (26%) were found to have poor participation during rehabilitation on admission. Poor participation was not related to age, sex, length of stay in rehabilitation, NIHSS, cognition, depression, fatigue and level of social support. Patients who were poor participators were

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functionally more dependent on admission as evidenced by significantly lower admission FIM scores compared to those who were good participators (59.9 versus 78.1 respectively, $p = 0.015$). Preliminary results of this study revealed that poor participation is not uncommon in stroke patients undergoing inpatient rehabilitation and is associated with greater dependence in activities of daily living.

P1-216

Poststroke depression in Chinese patients: prevalence, clinical correlates and impact on activities of daily living and quality of life

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The aims of this study is to assess the prevalence of depression, clinical correlates, and impact of depression on activities of daily living and health-related quality of life in Chinese patients who had survived 1 year or more after a stroke. This is a cross-sectional survey of Chinese patients attending the outpatient clinic of a tertiary rehabilitation centre in Singapore. Patients were interviewed on depression, activities of daily living and Health-related quality of life by using Beck Depression Inventory, Modified Barthel Index and Medical Outcomes Study 36-Item Short-Form Health Survey, respectively. Ninety-two Chinese patients, 58 men, 35 women with mean age of 60.7 years were interviewed. Poststroke depression was present in 28 patients, and this was mild in most patients. Only 4.3% of depressed patients were on anti-depressants. Poststroke depression was not significantly related to age, sex, marital status, location of stroke and Modified Barthel Index score. Depressed patients however had significantly lower scores on all health-related outcome domains except for that of Physical Function and Bodily Pain. In conclusion, poststroke depression is common and clearly has negative impact on health-related quality of life in Chinese patients with a chronic stroke.

P1-217

Is unhealthy lifestyle predicts dementia onset among elderly 65 years and older in Japan?: A 5- year follow-up study

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Background and purpose: Dementia is a major cause of disability among aging populations. Unhealthy lifestyle, illnesses or depression are risk factors for dementia. In preventing or delaying dementia onset, finding modifiable risk factors will be beneficial. Our study purpose is investigating factors associated with dementia onset among non-institutionalized elderly in Japan.

Methods: We used data from the Aichi Gerontological Evaluation Study (AGES) which is an ongoing prospective cohort study that started in 1999 in Japan. Self-administered survey was conducted in 1999 and respondents (1463 men and 1797 women) were followed for 5 years for dementia onset from February 2000 to 2005. Dementia onset was determined according to the criterion (based on face to face interview and physician diagnosis) used in Japannese Public Long-Term Care Insurance System. Cox hazard model was employed to calculate the hazard ratios for dementia onset after adjusting for age in years and sex. Those died or moved out from the study site during the follow-up period was considered censored.

Results: Out of 3260 subjects, 222 persons (6.8%) developed dementia during the 5 year follow-up period. In Cox models, female gender had a higher odds for dementia (1.38, $p < 0.05$). However, gender difference in dementia onset became insignificant after adjustment for age, while older age remained a significant risk factor for dementia with an hazard ratio (HR) of 1.11, $p < 0.001$ for one year increment. Age-adjusted analyses indicated that higher depression score measured by Geriatric Depression Scale-15 (HR of 1.04 for one point increment, $p < 0.081$), poor/fair self-rated health (HR of 1.31, $p = 0.051$), smoking (HR of 1.60, $p < 0.05$), regular drinking (HR of 1.96, $p < 0.067$), no exercise (HR of 2.00, $p < 0.05$), having no psychological well-being (ikigai) or hobby (HR of 1.48, $p < 0.01$) were all significantly associated with higher risk of dementia.

Conclusions: Our results confirmed that lifestyles and poor mental health are associated with dementia onset among general population. Studies suggest healthy lifestyles are associated with better mental health. If changes in lifestyle can help prevent or delay onset of dementia, such knowledge will be beneficial not only for health providers, but also for elderly populations and their families as well.

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P1-218

HIV among the elderly: a sociodemographic survey at an HIV/AIDS clinic in Kampala, Uganda

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Introduction: The availability of HAART has improved the lives of many people living with HIV/AIDS including those in resource poor settings, thus enabling them to live longer lives. With the HIV/AIDS epidemic now in its third decade, many have reached old age. The elderly living with HIV/AIDS are more likely to be vulnerable to the multiple social, psychological and physical problems associated with HIV/AIDS. No studies in Uganda have addressed the unique social and other associated characteristics of the elderly population living with HIV/AIDS in Uganda.
Objective: This study aimed to describe the sociodemographic characteristics as well as the social and support needs of elderly patients attending an HIV/AIDS clinic in Kampala, Uganda. It will also attempt to make recommendations for age-appropriate social and other interventions.
Methods: The paper will present results of a retrospective survey of patient records who attended the Mild May centre, Kampala in Uganda between January 2001 and January 2007. Details of the socio-demographic and illness characteristics as well other social needs were collected on a standardized questionnaire.
Results: The Mild May centre has registered 122 patients of >60 years old of whom 51 are still active patients. Some of the patients are on different types of HAART regimen while others are not. Indeed some receive forms of traditional treatments. The unique socio- demographic characteristics as well as special needs of this HIV elderly population will be described.
Conclusion: HIV/AIDS is increasingly becoming a common problem among the elderly. The unique sociodemographic and special needs characteristics as well as social support needs of this population will be described. Specific interventions will be suggested. It is hoped that these recommendations will help policy makers in planning appropriate interventions for the elderly with HIV/AIDS in Uganda.

P1-219

Ultra-brief pulse electroconvulsive therapy for depression: does age predict response?

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Objective: The clinical and cognitive effects of bifrontal ultrabrief pulse (0.3 msec) electroconvulsive therapy (UBPECT) and right unilateral UBPECT were compared, in the treatment of patients with a depressive episode, in different age groups.
Method: Sixty four patients with a depressive episode that was highly medication refractory, and with a high degree of comorbidity were treated with a course of bifrontal UBPECT at 1.5 times seizure threshold (ST) or unilateral UBPECT at 6 times ST by random assignment. The Hamilton Rating Scale for Depression (HDRS) and the standardized MiniMental State (MMSE) were administered at baseline and repeated during and after the course of treatment, by a blinded rater. Outcomes were compared in different age groups ($\leq$55 versus >55, and $\leq$60 versus >60).
Results: 64 patients (22 male, 42 female) were included, with a mean age of 55.28 years (SD11.95, range 25.27 till 81.94). At the end of the treatment course 78.1% of the patients responded ($\geq$50% decrease HDRS-scores). 65.63% (N = 42) achieved the soft remission criteria, (HDRS score $\leq$10), whereas 39.06% (N = 25) met the strict remission criteria (HDRS score $\leq$7). Age did not predict outcome, nor did it predict the number of treatments needed to achieve response or remission criteria. MMSE scores registered one week after the final ECT treatment were higher than baseline MMSE scores.
Conclusions: Bifrontal UBPECT at 1.5 times ST was as efficacious as unilateral UBPECT at 6 times ST and neither of these treatment techniques resulted in cognitive impairment, as measured with the MMSE. Age did not predict response or speed of response.

P1-220

Care needs of Psychogeriatric patients

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Background: In the last two decades mainly related with previous conceptualization, remain aged people in the Psychiatric Hospitals. These patients were admitted time ago when began their psychopathology and due to several circumstances they are still living in the medical setting even thought in some cases they probably do not need. At present professionals working in this field know the various care needs in this population mostly distant from the cause of admittance because of the low psychopathological level frequent comorbidity social withdrawn functional loss and others. In Catalonia Spain since the Autonomous Government developed the sociosanitary model some of these patients were included in other kind of resources even so remains aged population living in Psychiatric Hospitals with needs care totally different from the classical Psychiatric Services and that implies a considerable change in the care model and in the professional's specialization.

Objectives: Describe the profile of patients in the Psychogeriatric Department describe the various group between them and according to the results propose the best resource for them.

Methods: In a sample of 104 patients actually living in the Psychogeriatric Department the authors analyzed clinical sociodemographical traits functional level psychopathological level treatments comorbidity and social state by means of chart review Barthel scale BPRS and Charlson index. The statistic analysis by means of Statistical Software.

Conclusions: They were 77.8% females and 22.1% males with a mean age of 75.2 years old (range 44–95y) mean length hospitalization 28.9 years (range 0–73y) diagnostic distribution as: Schizophrenia (78.8%) Dementia syndrome (5.76%) and a mixed various diagnostic group (14.4%). Analyzing the schizophrenic patients and according from the psychopathological level the authors described two first groups starting from that and considering the comorbidity and the functional autonomy they described a total of nine subgroups as Geriatric patients N 21 dependent or autonomous Psychiatric patients N 58 with comorbidity or not and dependent or autonomous Social patients N 6. In view of that facts they proposed to adapt the different patients groups to the sanitary and social resources possibilities The Psychiatric group should be remain at Monographic Hospital Geriatric group would be better in a sociosanitary service and the Social group do not need any specific sanitary resource.

P1-221

Prevalence of orthostatic hypotension and blood pressure levels among home-dwelling elderly aged 75 years or more with and without dementia

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Orthostatic hypotension (OH) is a common clinical finding among the elderly: the prevalence has been reported to be between 6%–30%. OH and postural hypotension can be caused by a variety of factors in the elderly. OH is a risk factor for falls, dizziness and behavioural symptoms in elderly persons with dementia.

The aim of this study was to determine the prevalence of orthostatic hypotension in elderly persons with and without dementia and to examine the relation between blood pressure and dementia.

This study is a part of population-based GeMS-study (Geriatric Multidisciplinary Strategy for the Good Care of the Elderly) consisted of all persons aged 75 years or more living in Kuopio, eastern Finland in 2004. From this population a random sample of 1000 persons was taken. These results are based on the information from 653 home-dwelling elderly with orthostatic test. The use of medicines and physical and mental health was collected in geriatric assessment done by a geriatrician and trained nurse. Medical registers were also available. OH was defined by the drop of patient's systolic blood pressure $\geq$20 mmHg or by the drop of patient's diastolic blood pressure $\geq$10 mmHg or both after one or three minutes from supine to standing position. Dementia was defined according DSM IV criteria.

Among these home-dwelling elderly the prevalence of dementia was 12% (n = 75). Blood pressures in sitting position were lower in the elderly with dementia than elderly without dementia (SBP: 140 mmHg vs. 146 mmHg; DBP: 77 mmHg vs. 80 mmHg). Of all the elderly with dementia 7% (n = 5) SBP in sitting position was lower than 110 mmHg. Despite the lower blood pressures in sitting positions, orthostatic hypotension occurred more frequently in elderly with dementia than in elderly without dementia (43%, n = 32 vs. 33%, n = 188). However, the difference was not

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statistically significant ($p = 0.080$). Of all the elderly with dementia for 13% ($n = 10$) the drop of systolic blood pressure after 1 minute standing was 30 mmHg or more and after 3 minutes standing 5% ($n = 4$) the drop was 30 mmHg or more.

Orthostatic hypotension is a common clinical finding among the elderly persons with dementia. Moreover, the prevalence numbers in this study demonstrate that OH and low blood pressure are more common than has been reported in elderly persons without dementia. Clinicians should exclude OH in persons with dementia to diminish risks for falling and behavioural symptoms.

P1-222

ECT to older people at Shinshu University hospital

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Objective: Electroconvulsive therapy (ECT) has been more useful in treating patients with various psychiatric diseases. This report is to investigate the backgrounds of the cases, that were 70 years or older and medicated with ECT at Shinshu University Hospital (SUH) from January, 2004 to December, 2006.

Methods: At first, we investigated the operation records of SUH concerning the data of patients who had experienced ECT during the above-mentioned period. Thereafter, we selected 70-year-or-older patients out of all the ECT's cases, and examined their age, sex and clinical diagnosis, the number of the treatment, and their outcomes and complications

Results: A total of 84 patients were treated with ECT during three years. Eight cases were 70 years old or more, including a male and 7 females. The highest age out of the cases was 77. Three times up to 15 times of ECT were done repeatedly in one clinical course. Six cases underwent one course, and 2 cases did 2 courses within three years. Concerning psychiatric diagnoses, there were 2 schizophrenic patients, 2 patients with depression, a case with persistent somatoform pain disorder, and the others. Regarding psychiatric conditions, depressive, catatonic, and delusional states were prominent in these cases. All the cases showed the complications such as delirium, amnesia, transient hypotension after intravenous Thiopental and arrhythmia. The symptoms were seen more apparently than those of young patients. Almost the cases were well improved with ECT, except for a case that had discontinued the treatment in the second course because of arrhythmia. However, even the case had a good recovery before the second courses. Conclusions: This examination suggested that ECT was certainly effective also for the old psychiatric patients. However, they were easily afflicted with side effects of ECT. So that, it should be more careful to take ECT for the old, and we must evaluate physical conditions to know them exactly before the procedure.

P1-223

Cognitive impairment in patients with idiopathic normal pressure hydrocephalus

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Cognitive impairment in patients with idiopathic normal pressure hydrocephalous (iNPH) has not been clearly documented. We performed standardized neuropsychological assessments of 21 patients with iNPH and of 42 patients with Alzheimer's disease (AD) matched to the patients with iNPH 2:1 by age, sex, and Mini-Mental State Examination score. Compared with the AD group, theiNPH group scored significantly higher on the orientation subtest of the Alzheimer's Disease Assessment Scale and on the general memory and delayed recall subtests of the Wechsler Memory Scale-Revised (WMSR), and significantly lower on the attention/concentration subtest of the WMS-R and on the digit span, arithmetic, block design and digit symbol substitution subtests of the Wechsler Adult Intelligence Scale-Revised. The impairment of frontal lobe functions is disproportionately severe and memory impairment is disproportionately mild in patients with iNPH compared with AD. To identify the neuropsychological tests that most likely distinguish

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Table Neuropsychological test scores of patients with iNPH and AD

Test/subtest	iNPH	AD	p
ADAS			
orientation (correct response)	6.3 ± 1.8	4.8 ± 2.1	0.009
construction (correct response)	4.2 ± 0.77	4.5 ± 0.97	0.38
WMS-R			
general memory	48.7 ± 27.8	34.9 ± 16.4	0.02
attention/concentration	40.0 ± 10.5	48.6 ± 12.4	0.008
delayed recall	16.0 ± 15.1	4.8 ± 5.4	<0.001
WAIS-R (scaled score)			
information	7.8 ± 2.0	7.4 ± 2.1	0.47
digit span	7.3 ± 2.5	9.6 ± 2.8	0.003
vocabulary	7.6 ± 2.0	7.9 ± 2.4	0.62
arithmetic	6.6 ± 1.5	8.0 ± 1.9	0.007
comprehension	7.0 ± 2.7	7.4 ± 3.1	0.57
similarities	7.8 ± 3.1	7.1 ± 2.3	0.29
picture completion	7.8 ± 2.9	8.0 ± 3.4	0.78
picture arrangement	6.0 ± 2.0	7.0 ± 2.4	0.09
block design	6.1 ± 3.0	8.1 ± 3.1	0.019
object assembly	6.0 ± 3.2	7.7 ± 3.2	0.052
digit symbol substitution	5.3 ± 2.2	7.6 ± 3.1	0.003

Results are given as means ± SD

P1-223

patients with iNPH from those with AD, a stepwise discriminant function analysis was used. The statistical significance of a stepwise discriminant function analysis was set at $p < 0.15$, because of the exploratory nature of the study. Four variables retained significant F values: the WMS-R general memory (partial $r^2 = 0.26$, $F_{1,58} = 20.1$; $p < 0.0001$), the WAIS-R digit span (partial $r^2 = 0.19$, $F_{1,58} = 13.47$; $p < 0.0001$), the WAIS-R digit symbol substitution (partial $r^2 = 0.29$, $F_{1,58} = 24.2$; $p < 0.0001$) and the WAIS-R similarities (partial $r^2 = 0.07$, $F_{1,58} = 4.3$; $p = 0.0429$). The discriminant analysis was performed as follows: classification score for iNPH = 0.0147 × general memory + 0.5183 × digit span − 0.2159 × digit symbol substitution + 0.9194 × similarities − 5.274, and the classification score for AD = −0.1071 × general memory + 1.186 × digit span + 0.6872 × digit symbol substitution + 0.4070 × similarities −7.876. This model correctly predicted 85.7% of the cases of iNPH and 85.7% of the cases of AD. Recognition of these cognitive features of iNPH contributes to an early diagnosis, which can lead to a better prognosis.

P1-224

Frequency and clinical features of corticobasal degeneration and progressive supranuclear palsy in the memory clinic of Yokohama Comprehensive Care Continuum

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Corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) are two rare but devastating neurological disorders. The clinical features of PSP and CBD have been neurologically oriented, whereas the psychiatric symptoms including dementia have not been well examined. In this study, we surveyed the frequency and clinical features of the patients diagnosed with CBD or PSP in the memory clinic of Yokohama Comprehensive Care Continuum. CBD was diagnosed according to the criteria proposed by Boeve et al. 1). PSP was defined by the criteria established by the National Institute of Neurological Disorders and Stroke (NINDS) and the Society for PSP (NINDS-SPSP) 2). From the 4,630 patients we received from October 1992 to September 2006, we diagnosed eight CBD patients (3 men, 5 women) and 16 PSP patients (10 men, 6 women). The mean age of consultation was 78.8 ± 7.9 in CBD patients and 73.8 ± 8.2 in PSP patients. As for clinical features, patients with CBD commonly exhibited dementia and personality changes, whereas patients with PSP commonly displayed personality changes and affective disorders. The frequency of each clinical feature differed between the two disorders. Patients (CBD, PSP) exhibited dementia (87.5%, 56.2%), personality changes (87.5%, 75.0%), psychosis (32.8%, 18.8%), and affective disorders (50.0%, 81.3%) at the indicated frequencies for each disorder. Despite the infrequent diagnoses, we should always remember to seek the clinical features of these disorders when we treat patients at memory clinics.

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P1-225

A case suffering from Creutzfeldt-Jakob disease with a rapid course

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Background: We have described a Japanese patient (male, right-handed, age 68 at onset) diagnosed with the sporadic Creutzfeldt-Jakob Disease (CJD), characterized clinically by rapidly aphasia and frontal lobe impairment prior to the development of myoclonus and other symptoms of CJD. CASE REPORT The neuroradiological picture (MRI) showed non-specific features of cerebral atrophy (including both cortical and subcortical). Diffusion weighted image revealed high signal area along the cortex of the frontal, temporal and occipital lobes predominantly in left side. An EEG revealed periodic synchronous discharges. Myoclonus occurred predominantly on the right upper and lower limbs. Rapidly progressive aphasia and frontal lobe impairment were clearly present in the initial course of dementia. In this patient, it took only 11 weeks period from first symptom of psychological features of dementia to death.

Conclusion: We (including psychiatrists and family physicians) should take account of the possibility of CJD in any patients over age 60 presenting with rapid aphasia and frontal lobe impairment even when other symptoms of dementia may not be immediately noticeable.

P1-226

Distribution of neurofibrillary tangles in diffuse neurofibrillary tangles with calcification (DNTC)

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The clinical symptoms of diffuse neurofibrillary tangles with calcification (DNTC) are: early disturbance of memory, disorientation, apraxia, agnosia, amnestic aphasia and perseveration suggestive of Alzheimer's disease (AD) as well as personality change, irritability, early signs of disinhibition, bizarre or antisocial behaviors, "Denkfaulheit", and an oral tendency suggestive of Pick's disease(PD). The neuropathological findings of this disease are: temporal lobar atrophy, widespread neurofibrillary tangles (NFT) without senile plaques, and pronounced calcareous deposition in the brain. In this study, the appearance and distribution of NFT in DNTC were investigated neuropathologically using Gallyas-Braak silver stain in order to elucidate the disease entity and the neuropathological characteristics of this disease. Six cases neuropathologically

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diagnosed as DNTC were studied (two males and four females). The age at death ranged from 56 to 73, with an average of 63.5 ± 7.5 years. Neurofibrillary changes in each area were rated as follows: seldom if ever detected; slight; mild; moderate; severe. In each case, NFT were seen throughout the cerebral cortex, especially in the temporal and limbic lobes. The distribution pattern of NFT in the limbic lobe was similar to that in AD. In the temporal lobe, NFT were distributed more numerously in the anterior than in the posterior area. The temporal pole showed the highest density of NFT including numerous "ghost tangles", compared to those of AD. The severity of neurofibrillary changes in the temporal pole was found to be a neuropathological characteristic of DNTC. The prominent neuropathological finding of DNTC in the temporal pole may contribute to the clinical features of this disease, such as personality change, irritability, early signs of disinhibition, bizarre and antisocial behaviors. These clinical symptoms are similar to PD whose neuropathological findings include circumscribed atrophy of bilateral temporal lobes in spite of absence of NFT. Meanwhile, the hippocampus of the present study exhibited severe atrophy resembling AD. This feature and the analogous NFT distribution between AD and DNTC are compatible with the clinical analogies between both, such as early disturbance of memory, disorientation, apraxia, and agnosia. The neuropathological findings of DNTC may explain the clinical features of this disease as a partial mixture of AD and PD syndromes.

P1-227

Validation of grading scale for evaluating symptoms of idiopathic normal pressure hydrocephalus

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Idiopathic normal pressure hydrocephalus (iNPH) is characterized by a triad of disorders (cognitive impairment, gait disturbance and urinary incontinence). We developed an iNPH grading scale (iNPHGS) to rate the severity of the triad and to classify symptoms with a wide range of severity. In this study, we confirmed the reliability and validity of this scale in 38 patients with iNPH. Inter rater reliability of this scale was high. The iNPHGS cognitive domain score significantly correlated with the Mini Mental State Examination (MMSE), Frontal Assessment Battery and Trail Making Test scores, the gait domain score with the Up and Go test and Gait Status Scale (GSS) scores, and the urinary domain score with the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) score. The MMSE, GSS, and ICIQ-SF scores significantly improved after CSF removal in responders but not in non responders who were judged CSF tap test based on changes of iNPHGS. It is expected that this scale will help to determine the best procedure for predicting the outcome of a shunt operation in patients with iNPH.

P1-228

Immunohistochemical study of TDP-43 in brains of patients with limbic neurofibrillary tangle dementia

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Recently, TDP-43 was identified as the major component of the ubiquitin-positive inclusions in frontotemporal lobar degeneration (FTLD) with or without symptoms of motor neuron disease and in amyotrophic lateral sclerosis (ALS). However, the relationships between the deposition of tau and the accumulation of TDP-43 have not been examined well. Although some studies have indicated that neurofibrillary tangles (NFTs) in Alzheimer's disease (AD) are negative for TDP-43, other studies have shown that a small number of NFTs in AD and Guam parkinsonism-dementia complex have

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TDP-43 immunoreactivity[1,2]. Limbic neurofibrillary tangle dementia (LNTD), which is one of tauopathies, is a dementia disorder characterized by the presence of numerous NFTs in the limbic area with the lack of amyloid depositions. The hippocampal region of LNTD shows higher NFTs density than that of AD. In this study we have studied the presence of TDP-43 immunoreactivity in NFTs, neuropil threads and other tau positive structures in eight LNTD cases. The presence of TDP-43 pathology was assessed by screening sections of hippocampus, basal forebrain (including amygdala and basal nucleuses of Meynert), midbrain, pons and medulla with immunohistochemistry, which was performed according to previously published procedures 1). Both the polyclonal and monoclonal antibodies to TDP-43 were used. We found that any other tau positive structures were negative for TDP-43 in LNTD. Based upon these results, the interaction between tau and TDP-43 is thought to be irrelevant.

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P1-229

The utility of expressed emotion (EE) in the standard database structure of dementia

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Aims: We aimed to evaluated the utility of expressed emotion(EE) in the standard database structure of dementia.
Methods: We evaluated clinical items and medical treatment/non-medical treatment and an effect and affect display (EE) of a family burden degree and a family in outpatients clinic of the Kochi Medical School hospital and related hospitals.
Results: MMSE and NPI, ZBI, GHQ, correlation of FAS continued being low, and CDR and NPI, ZBI, GHQ, FAS showed high correlation, and even AD group was similar. In addition, as for ZBI and GHQ and the correlation between FAS, it is thought that ZBI,GHQ, FAS are useful for an index to watch effect of treatment of the AD patient very highly. It is thought that ZBI, GHQ, FAS can be superior for an index of AD effect of treatment from the above.
Conclusions: Therefore family care burden degree evaluation and evaluation of family affect display (EE) were thought to be important for treatment standardization of Alzheimer's disease as a data accumulation item.

P1-230

The differential influence of pain and fatigue on physical performance and health status of patients with cancer

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Physical dysfunction is a frequent consequence of cancer and its treatments. The problem contributes to psychosocial distress, compromises quality of life, and adds to the disease burden for patients. Improvement of physical function therefore should be a primary goal of treatment; the use of appropriate assessment and outcome measures is fundamental to that process.

The purposes of this study were to investigate the psychometric properties of a Japanese language version of Physical Performance Test (PPT) Battery and characterize physical function in patients with cancer referred for rehabilitation.

A total of 105 patients with cancer participated in this study. All patients had a diagnosis of cancer. Individuals who had symptomatic cardiovascular disease or who were unable to walk were excluded. The subjects completed the Japanese language version of the PPT Battery: the time taken to complete various tasks (a 15 m walk at fastest speed, a 15 m walk at preferred speed, repeated standing from sitting, tying a belt, putting on a sock, repeated reaching up, picking up coins), the distance walked in 6 minutes, and the distance reached forward while standing were measured. Two self-report questionnaires, one on sensory evaluation of pain and the other on affective evaluation of pain; the Functional Independence Measure (FIM), which evaluates activities of daily living; and Brief Fatigue Inventory (BFI) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) were simultaneously administered to the subjects. This study was approved by the ethical committee of our institution, and informed consent was obtained from all participants.

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The results for reliability showed that the ICC values for inter-rater reliability and intra-rater reliability were 0.89 or more for every item. The results for validity showed significant associations between the scores for all of the items in the Japanese language version of the PPT Battery and total scores for the FIM and BFI.

Significant associations were found between scores for the Japanese language version of the PPT Battery and pain. Pain has a substantial impact of physical performance of patients with cancer. Fatigue also impacts physical performance. Compromised ability to perform certain physical tasks affects quality of life. Further investigation of the roles of these relevant variables is needed.

P1-231

Assessment of quality of life (QoL) as outcome in dementia and MCI intervention trials: A systematic review

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QoL scales for use in dementia patients are available, though seem rarely used in clinical trials. In a previous study we found no QoL instrument that was valid for the entire course of dementia. Four instruments best represented domains of QoL important to patients and domains professional caregivers focus on. Two were self-rating instruments: SEIQoL, applicable in mild to moderately severe dementia patients and their proxies, and QOL-AD, applicable even in more severe dementia, and applicable by proxies both for rating their own QoL and for rating patient QoL. If self-report is no longer possible also the observational instruments Qualidem and DSDAT can be used.

The aim of the study was to review how often QoL measures are used as endpoints in Mild Cognitive Impairment (MCI) or dementia intervention trials, in patients as well as proxies. We also aimed at reporting responsiveness and minimal important difference (MID) in QoL, the latter representing the smallest change that patients or proxies perceive as an advantage, or that could lead patient or clinician to consider a change in treatment.

We conducted a systematic review (SR) of the use of QoL measures as outcome measure in pharmacological and non-pharmacological intervention trials. Furthermore the selected scales were placed in the context of the currently available QoL measures. Randomized controlled trials (RCTs) were identified by searching the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group in April 2006. This register contains records from major healthcare databases like CENTRAL, MEDLINE, EMBASE, CINAHL and PsycINFO. We also checked references and systematic reviews, covering the period until September 2006.

117 pharmacological and 108 non-pharmacological RCTs were identified. One of the pharmacological and four of the non-pharmacological studies used QoL as primary outcome. Two of the pharmacological and three of the non-pharmacological studies used QoL as secondary endpoint. Altogether QoL was assessed in only 4,4% of the RCTs. Two RCTs reported on responsiveness of the applied QoL instrument.

We showed that QoL is seldom used as effectiveness endpoint in clinical dementia trials. A major limitation is that many studies do not provide clear information on effect sizes, responsiveness and most important: MID. QoL measures should be applied more often in clinical trials as currently no disease modifying drugs are available.

P1-232

Tai Chi for physical and mental health of patients with Parkinson's disease

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Background and objective: Exercise is recommended for the every patient with Parkinson's disease (PD) regardless of clinical severity or any other form of management. Tai Chi exercise, which improves flexibility, equilibrium as well as mental health, can be successfully applied for PD patients suffering from rigidity and gait disturbance. The authors studied the effects of Tai Chi on functional fitness and quality of life (QoL) in PD patients. Sixteen mild PD patients (Hohen and Yahr stage 2–3) were recruited and they were divided into Tai Chi (9 females,

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age 67.7 ± 7.98) and control group (7 females, age 60.1 ± 7.90). Patients with Tai Chi group performed modified program from Tai Chi for Arthritis developed by Dr. Paul Lam, scheduled at 3 times/week and 45–65 minutes/time for 8 weeks. All the medications were fixed during the program and we assessed parkinsonian symptom, functional fitness, depression, activity of daily living (ADL) and quality of life.

Results: Demographic and clinical characteristics were not different between both groups. Tai Chi group showed significant improvement in physical strength, flexibility and equilibrium ($p < 0.05$). Functional fitness of control group was not changed and their parkinsonian symptoms, depression, ADL and QoL were significantly deteriorated ($p < 0.05$). Parkinsonian symptoms and depressions showed no change or some improvements but QoL improved especially in the domain of emotion in the Tai Chi group ($p < 0.05$).

Conclusion: The authors could find that Tai Chi improved physical and mental health and suggest it could be successfully applied for the patients with Parkinson's disease.

P1-233

Outcome measures in clinical trials: Reliability and validity of the camberwell assessment of need for the elderly in Portugal

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Introduction: The *Camberwell Assessment of Need for the Elderly*/CANE is a fundamental tool for multidimensional evaluation in neuropsychiatric diagnoses.

Aim: To study CANE reliability and validity, in Portuguese population.

Method: The development of the Portuguese version followed transcultural validation rules. The resulting version (2004) was defined concerning acceptability in routine clinical settings, with several multidisciplinary group discussions, providing opinion on face and content validity. A cross-sectional multicentre study included teams from Northern and Southern Portugal with a convenience sample. Easycare (Philp, 2000), GHQ-12 (Goldberg, 1978), MMSE (Folstein, 1975), Barthel Index (Mahoney and Barthel, 1965), GDS-15 (Yesavage, 1983) were used for validity criterion.

Results: In this study 79 elderly patients (75,9% female) were considered, mean age (sd) was 73,82(6,64) years. Most patients lived at home, were married/widowed, living with a family caregiver female. Only 31,6% had no carer. Psychiatric diagnoses were mostly dementia syndromes (60,8%) and somatic comorbidity (84,8%). Raters identified significant needs: memory, food, household skills, physical health, daytime activities, money, psychological distress, company and self care (sometimes, unmet needs). As expected, users, carers, staff and raters did not state coincident views regarding users needs. Interrater reliability was assessed calculating percentage of complete agreement and K coefficients for the first section of the CANE (level of need present) for each item. The values of K ranged 0,76–1,00 (mean values: 0,96patient, 0,93carer, 0,95staff, 0,90rater). For a subsample of 46 respondents, test-retest reliability was assessed. The mean value of K was: 0,80patient, 0,77carer, 0,87staff, 0,81rater. The ICC score ranged 0.816–0.937 (95% CI) in total (met/unmet needs). Criterion validity was explored considering CANE and measures: EasyCare (r_s 0,654; $p \leq 0{,}001$); GDS (r_s 0,613; $p \leq 0{,}01$); GHQ (r_s 0,573; $p \leq 0{,}01$) and Barthel Index (r_s – 0,560; $p \leq 0{,}001$).

Discussion and conclusion: Unmet needs were associated with depression, but not with severity of dementia or level of dependency. In this validation study, interrater and test-retest reliability were globally encouraging. The same applies to criterion and construct validity issues. This version of the CANE seems a promising tool for research and practical use in Portuguese old age psychiatry and mental health teams.

P1-234

Efficacy of donepezil in the reduction of ECT-induced cognitive impairment

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Background: Acute cognitive impairment is commonly found in individuals receive electroconvulsive therapy (ECT), but the prevention or treatment of the condition is still largely unknown. Donepezil, an acetylcholinesterase inhibitor, is effectively used for enhancing cognitive function in dementia disease. However, relatively few studies have been conducted on donepezil effect in the reduction of ECT-induced cognitive deficit.

Methods: Twenty subjects with an acute episode of schizophrenia participated in a randomized, open-labeled, placebo-controlled study of donepezil (5 mg/day) on cognitive impairment-inducing ECT (modified bilateral multiple-ECT; 6 sessions). Quetiapine was used in all subjects for co-treatment of psychotic symptoms. The Mini Mental State Examination (MMSE), the Alzheimer's Disease Assessment Scale (ADAS), the Wechsler Memory Scale (WMS), the Train the Brain computer program (Sermion), and the Trail making A and B were used to examine cognitive functions of the subjects at baseline and one-hour after ECT session-3 and -6 respectively. Subjects with severe cognitive impairment (MMSE score <24 for two consecutive days) were terminated from the study for subject safety. The time to dropped-out effect between the two groups was analyzed using Kaplan-Meier survival curve (Tarone Ware statistics). Intention-to-treat analysis was performed for treating the missing data points.

Results: Compared to baseline, subjects from both groups (donepezil; $n = 10$, or placebo; $n = 10$) had significantly lower scores on MMSE, ADAS-delayed recall, and WMS-logical memory II after ECT sessions-3 and -6 ($p < 0.05$). Impaired digit backward after ECT was observed within the placebo group ($p < 0.05$), but not in the donepezil group. Subjects with donepezil treatment had significantly higher total MMSE score at the end of ECT course than placebo group ($p = 0.002$). A rate of survival (i.e., no severe cognitive impairment) over time in subjects received donepezil was significantly higher than controls (90% vs 50%, respectively; $p = 0.05$). There was no difference between groups with respect to demographics, baseline cognitive function scores, and baseline severity of psychotic symptoms.

Conclusion: Results showed that donepezil had the efficacy in the reduction of acute cognitive impairment-inducing ECT. Donepezil may have clinical implication for the treatment of ECT-induced cognitive deficit.

P1-235

The sensitivity and specificity of the gerontological personality disorders scale in flemish institutionalised elderly

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Introduction: Little is known about the course of personality disorders across the life span. A major problem is that the current DSM nosology does not account for age-associated changes in behavior and interpersonal functioning. Consequently, existing instruments to assess the presence of personality disorders, which are often based upon the axis II of the DSM, are insufficient to use among an older population. However, recently, in the Netherlands, the Gerontological Personality disorders Scale (GPS), adjusted to the use in older adults, has been developed as an instrument to diagnose personality disorders.

Objective: This study was performed to evaluate reliability and validity in terms of sensitivity and specificity scores of the GPS in institutionalized elderly in Flanders (Belgium).

Methods: The GPS (16 items), consisting of 2 subscales, i.e. habitual behavior (HAB; 7 items) and biographical information (BIO; 9 items)was administered to 61 elderly (19 were patients of a psychiatric hospital, while 42 were residents of a residential care facility). The presence of personality disorders, based on DSM-IV criteria was determined by a psychiatrist.

Results: A binary logistic regression analysis showed that the GPS was not able to predict whether a subject had a personality disorder or not according to the diagnosis of the psychiatrist (95% C.I. 0.356–5.381, $p = .639$).Concerning reliability, internal consistence of HAB items and BIO items were respectively moderate and fair, while test retest reliability of the HAB and BIO items were respectively fair and good. However, in our Belgian population, sensitivity (S) of the GPS was very low ($S = 33.3\%$); specificity (Sp) was higher ($Sp = 73.5\%$).

Conclusion: Despite good psychometric properties of the GPS in the Netherlands and despite fair reliability in our study, the sensitivity of the GPS, in its original form, is still too low to use this instrument in

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clinical practice in Belgium. Probably Dutch people have linguistic usage different from that of Belgian people. Moreover, the fact that most of the subjects were institutionalized may have accounted for poor predictive validity of the GPS. Nowadays, the items of the GPS are being rephrased and validation research of this new version of the GPS is ongoing. Future research should be done to ascertain whether this new GPS will also be usable in a Belgian population.

P1-236

10 year anti-Alzheimer medication (anti-AD) utilization review at the VA Palo Alto Regional Health Care System

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In the last 10 years, a number of new anti-Alzheimer's (anti-AD) medications have been introduced into clinical practice. Our study objectives were to assess the changing patterns of anti-AD medication use in the VA Palo Alto Health Care System (VAPAHCS) over that time and associated clinical events including mortality. This study was a retrospective database study. All patients who received a prescription for donepezil, rivastigmine, galantamine, or memantine between March 11, 1997 and March 31, 2007 were included. The VAPAHCS serves a population of approximately 370,000 veterans in a 10 county area in Northern California. Primary, secondary and tertiary care is provided in 3 hospitals and 6 community-based clinics with the Palo Alto VA serving as the hub. Over 100,000 veterans have medical and pharmacy records in the system. To identify patients who received anti-AD medications, drug prescription data were retrieved from the VAPAHCS electronic database. These and other objective patient data (i.e. diagnoses, demographics, clinic visits, deaths, etc.) are stored in a Microsoft Sequel Server 2000 warehouse. Data reaches this warehouse upon retrieval of information electronically entered by healthcare providers into the VistA Computerized Patient Record System (CPRS), and is updated monthly. After the target patients were identified, records were matched by patient identification numbers with their demographic and diagnosis data. Microsoft Access 2003 was used to categorize drug prescription patterns and perform basic analyses. A total of 1673 patients received anti-AD medication during the study period. The use of both cholinesterase inhibitors and memantine has increased over time in all age groups, especially patients over the age of 80. There was also increased use of anti-AD medication combinations and increased mortality over time. Table One depicts the basic mortality data on all patients between 80 to 90 years of age taking anti-AD medication combinations. More detailed analyses indicate complex interactions among these anti-AD combinations, age, other medical problems, and death.

Anti-AD Medication Profiles for Patients 80–90 Years of age.

	Total Population.	Total Living	Total Deceased
Donepezil	739	469	270
Galantamine	10	8	2
Rivastigmine	3	1	2
Memantine	32	23	9
Donepezil + Memantine	151	105	46
Donepezil + Galantamine	16	12	4
Donepezil + Rivastigmine	4	3	1
Memantine + Galantamine	9	5	4
Memantine + Rivastigmine	3	1	2
Total	967	627	340

P1-236

P1-237

Incidence of second hip fractures and medication use among patients with sequential hip fractures

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Over 90% of hip fractures result from a simple fall, and a history of an osteoporotic fracture is known to be a significant risk factor for future fractures. The etiology of falls is multifactorial but a few risk factors for falls are as easily modifiable as medication use. The objectives of this study were: 1) to determine incidence of second hip fractures in 60+ population; 2) to describe changes in pharmacotherapy between first and second hip fractures, especially the use of those psychotropics which increase the risk of falling and pharmacotherapy for osteoporosis. This study was performed in Central Finland. In 2002–2003, the mean population of the study area was 239 000, and 20.8% of the residents were aged ≥60 years. Identification of cases and acquisition of clinical data were based on hospital registers and medical records. The patients who had sustained a hip fracture in 2002–2003 were followed up for subsequent hip fractures until 2006. Data on deaths were obtained from Statistics Finland. A total of 501 persons aged ≥ 60 years sustained their first hip fracture in 2002–2003. During the follow-up of 936 person-years, 34 of them suffered a second hip fracture. The cumulative incidence of second hip fractures was 5.08% (95% CI: 3.30 to 7.78) at one year, and 8.11% (95% CI: 5.73 to 11.43) at two years after the first fracture. The second part of this study investigated 75 patients with two non-contemporaneous hip fractures. The number of psychotropic drug users rose from 27 (36%) to 44 (59%) between the first and second hip fractures. Twenty five (33%) patients used benzodiazepines and 23 (31%) took two or more psychotropics concomitantly at the time of second hip fracture. Osteoporosis had been diagnosed in 17 (23%) patients only, 12 (16%) patients used bisphosphonates or calcitonin, 15 (20%) used calcium and 9 (12%) vitamin D supplements at the time of latter fracture. In conclusion, the recurrence rate of hip fractures is rather high; one in 12 patients sustains a second hip fracture within two years after the first one. Surprisingly, diagnosis and adequate treatment of osteoporosis are often overlooked. Even though psychotropic drugs are known to impair gait and increase the risk of falling and fall-related fractures, they are widely used by patients who have suffered a hip fracture.

P1-238

Psychotropics, opioids, antiepileptics and anticholinergic medications and the risk of fractures in old age: A longitudinal population based study

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The aim was to describe and analyse relationships between the use of benzodiazepines and related drugs, antipsychotics, antidepressants, opioids, antiepileptics, anticholinergic medications and the risk of fractures in a population aged 65 years or over.

This study was part of a larger longitudinal, epidemiological population based study carried out in the municipality of Lieto, South-Western Finland. The population consisted of residents in the municipality of Lieto who were born in 1926 or earlier (N = 1283). Of these residents, 1196 (93%), 488 men and 708 women, participated. Data about the use of medications was collected during interviews of the participants and from the medical records. Information about fractures was collected from medical records. Fractures were confirmed with radiology reports. Totally, data on fractures were obtained for 1177 (98%) of the baseline participants. Pathological fractures were not included. Only the first fracture was included into the analyses. For analyzing the prevalence of fractures, two follow-up periods, viz. three and six years were used. During the follow-up period of three years (1.1.1991–31.12.1993) 113 participants (9.6% of the baseline population) sustained 121 fractures. In the follow-up period of six years (1.1.1991–31.12.1996) 178 participants (15.1% of the baseline population) sustained 221 fractures.

In age adjusted regression analysis the concomitant use of two or more benzodiazepines, that of two or more antipsychotics, concomitant use of opioid and benzodiazepine, concomitant use of opioid and antipsychotic and the use of opioid and any other medication included in the analyses associated with the risk for fractures in men. Women who used concomitantly antiepileptic and antipsychotic or antiepileptic and benzodiazepine had an increased risk for fractures. In multivariate analysis, where other risk factors for fractures were standardized, the concomitant use of two or more antipsychotics and that of two or more benzodiazepines were associated with the risk for fractures in men, but the risk of fractures was not related to the use of drugs in women.

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The study has shown that concomitant use of certain medications is associated with fractures in older men.

P1-239

The use of psychotropics and the risk of cognitive decline in the aged: a longitudinal, population based study in Finland

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Aims: To analyze the relationships between the use of benzodiazepines or benzodiazepine related drugs (BZD/RD), antipsychotics or antidepressants or their concomitant usages either with each other or with opioids, anticholinergics or antiepileptics and the risk of cognitive decline in a population 65 years or over.

Materials and methods: The material was based on the longitudinal population study carried out in two phases (1990–1991 and 1997–1998) in Lieto, South Western Finland. The number of the population surviving was 617. Cognitive abilities during both phases were measured by the Mini Mental State Examination (MMSE). The data on the use of medications was based on interviews and medical records. Analyses were performed separately for sexes among all participants and among those with normal cognitive abilities (MMSE 24–30) at baseline by comparing participants using the medication or group of medication concerned 1. with participants not using this medication or group of medication or 2. with those using no central nervous system (CNS) affecting medications mentioned. Mann-Whitney U test was used to test the differences at baseline and the differences of changes in MMSE sum points during the follow-up. Age and atrial fibrillation or flutter, were used as covariates in multivariate analyses.

Results: The mean age at baseline was 71.0 ± 5.6 years. After adjustments, the use of an opioid was associated with greater cognitive decline in those with MMSE 24–30, and the use of an anticholinergic medication predicted cognitive decline in men. After adjustments, the higher decline in MMSE sumpoints was associated with the concomitant use of BZD/RD and opioid in both sexes with MMSE 24–30 and in women with MMSE 24–30; with the concomitant use of BZD/RD and any CNS affecting medication in both sexes aged 75 or over and in men aged 75 and with the concomitant use of an opioid and any CNS affecting medication in those with MMSE 24–30. The use of antipsychotics, antidepressants or antiepileptics was not associated with greater cognitive decline.

Conclusions: The use of opioids or anticholinergics may be independent risk factors for cognitive decline in the aged. The concomitant use of BZD/RD and some other CNS affecting medication and the concomitant use of an opioids and some other CNS affecting medication are associated with higher risk of cognitive decline. The use of two or more CNS affecting medications in the aged should be based on critical assessments.

P1-240

The purchase of psychotropics in community-dwelling patients with Alzheimer's disease

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The aims of this study were to describe how patients with Alzheimer's disease (AD) purchased psychotropics during the year 2005, and how their purchases differed from those of people without AD.

The National Prescription Register, managed by the Social Insurance Institution (SII), records all purchases of reimbursable prescribed drugs made by permanent non-institutionalised residents in Finland. Before getting reimbursements for antidementia drugs, the patient with AD must send a medical certificate from his neurologist or geriatrician to SII to verify the diagnosis.

At the end of the year 2005, there were 28093 registered patients with AD in Finland. A control pair for each one was extracted from the database of the Finnish Population Register. The controls were matched in terms of age, sex and the place of residence. In the study and the control group there were 32% male and 68% female persons. Their age varied from 42 to101 years and the mean age was 79.7 years.

Psychotropics were widely used. During one year 55.1% of patients with AD and 31.4% of the

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control persons purchased psychotropics. The number was even bigger (57.4%) within patients using anti-dementia drugs. Antipsychotics were purchased by 22% of the patients with AD and 4.4% of the controls. The numbers were 30.6% and 24.9% to anxiolytics-sedatives and 30.0% and 10.7% to antidepressants. Patients with AD used more atypical (18.8%) than traditional antipsychotics (4.5%). Tricyclic antidepressants were rarely in use, 1.2% of patients with AD purchased them. More patients with AD purchased medium-acting benzodiatsepines (17.8%) than controls (11.0%). The use of benzodiazepine-like sleeping pills was similar (nearly 14%) in both groups. Drug purchases from all psychotropic drug classes (antipsychotics, anxiolytics-sedatives and antidepressants) were more common in patients with AD (4.6%) than control persons (1.2%). The same kind of situation was found with combinations of two different groups of psychotropics.

The purchasing of psychotropics was substantial in the group of patients with AD, and the use of anti-dementia drugs did not lower it. Although the patterns of prescribing neuroleptics were better than in earlier studies, still more careful consideration is needed before prescribing psychotropics to the elderly patients, especially to those with AD.

P1-241

Comparing profiles of atypical antipsychotic usage in older and younger adults with bipolar disorder

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Atypical antipsychotics are approved for use in bipolar disorder in the US for the management of acute mania, mood stabilizers or, more recently, depression in bipolar disorder. In older patients with bipolar disorder, polypharmacy is often present, yet little is known about medication profiles. Because of their expense, atypical antipsychotics account for a significant portion of mental health care budgets. In this study, we compared the medication profiles of younger and older bipolar patients who had been prescribed atypical antipsychotics. This retrospective study included 2,148 veterans with primary or secondary diagnoses of bipolar disorder in the Veterans Affairs Health Care System (Service Network 21) during the 2004 and 2005 fiscal years. We established profiles by using age, gender, psychiatric inpatient service usage, and psychotropic prescriptions (mood stabilizers, antidepressants, typical antipsychotics, acetylcholinesterase inhibitors, and an NMDA antagonist). A Receiver-Operating-Characteristic Program was used to develop profiles. Overall, prescriptions for an atypical antipsychotic (olanzapine, risperidone, ziprasidone, quetiapine, clozapine, or aripiprazole) were associated with prescriptions for anticonvulsants and any psychiatric hospitalizations. Of the 739 veterans aged 60 years and older, 29% were prescribed an atypical antipsychotic, whereas 38% of the 1,409 veterans aged 59 years and younger were prescribed an atypical antipsychotic. Older patients who were prescribed an anticonvulsant and had at least one psychiatric hospitalization had an 89% chance of also being prescribed an atypical antipsychotic, compared to a 75% chance in younger adults. Younger patients, on the other hand, were most likely to be prescribed an atypical antipsychotic if they were receiving an anticonvulsant and a typical antipsychotic (77%). The use of anticonvulsants and inpatient hospitalization appear to be the strongest correlates of use of atypical antipsychotics use in older patients with bipolar disorder. This could reflect illness severity or the lack of tolerance of typical antipsychotics in older adults. Overall, rates of all antipsychotic use were higher than previously reported in a similar population with bipolar disorder.

P1-242

Switching elderly mentally disabled persons to perospirone and prolactin level

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Background: Awareness of secondary osteoporosis caused by major tranquilizer-induced hyperprolactinemia is still lacking in the field of psychiatry. We herein report our experience switching elderly mentally disabled patients on long-term major tranquilizers to perospirone while monitoring prolactin level and bone density.

Methods: We switched 17 patients in the ward for elderly mentally disabled persons who we examined directly to perospirone, a serotonin dopamine antagonist, between Jul 2004 and Jan 2007. We were not able to switch patients all at once since the

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study was conducted while clinically treating patients. Changes over time in bone density as determined by X-ray, blood prolactin concentration, NTx were recorded. Patients who met the diagnostic criteria for osteoporosis were given treatment for it. **Results:** A total of 12 (average age 71), completed the study. Ten suffered from schizophrenia, one from organic psychosis, and one from general paresis. Before switching, they were given a typical antipsychotic and risperidone. Some of the patients in the schizophrenia group undergoing long-term hospitalization were also given another drug in addition to perospirone after switching. The average prolactin level showed a downward tendency. It was 57.4 ng/ml at the first measurement, 49.7 at the second, 40.2 at the third, and 36.0 at the fourth. The average bone density at the first measurement was 0.346 g/cm^2, which was 97.5% of the same-age mean and 66.6% of YAM. The average bone density at the second measurement was 0.360, which was 97.6 of the same-age mean and 68.4 of YAM. **Conclusion:** 1) A high rate of hyperprolactinemia was seen with use of a typical antipsychotic and risperidone, and the prolactin level decreased in many patients after switching to perospirone. Bone density improved or the status quo was maintained, but a clear conclusion cannot be drawn because some of the patients were taking medication for osteoporosis. 2) The fact that the prolactin level is high for a prolonged period of time indicates that this has an adverse effect on the body even if subjective symptoms are absent. This suggests that prolactin must be measured and the major tranquilizer switched early when it is found to be elevated in the case of treatment of schizophrenia during the acute phase, and that typical antipsychotics are suitable as the drug of choice in certain cases only. 3) A drug like perospirone is believed to be suitable for elderly mentally disabled persons.

P1-243

Motor and Processing Skills after Functional Enhancement Program (FEP) for Chinese elders with dementia

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Functional deterioration is integral to the dementia syndrome. Significant impairment in everyday functioning has been considered as an essential criterion for the diagnosis. The loss of independence greatly affects mood state, quality of life and caregiver burden. However, little attention has been paid to the development of a structured approach to enhance the everyday functioning ability of elders with dementia. In a recent study, we evaluated the change in functional skills in demented elders after completion of a functional enhancement program (FEP) developed with a standard and structured approach.

61 Chinese subjects (50 women, 11 men) with DSM-IV diagnosis of Alzheimer's disease or vascular dementia were recruited for participation of a randomized controlled trial. Subjects were randomly assigned into 2 groups. Participants in test group (T) were trained with daily tasks appropriate to the level of impairment, and considered to be more significant by the participants. The participants of control groups (C) were trained with a set of arbitrarily chosen daily tasks appropriate to the level of disability. Fundamental principles of the FEP include the comprehensive pre-intervention evaluation of components of functional deficits, tailor made selection of training tasks, encouragement of success with errorless approach and positive reinforcement. To evaluate the effectiveness of the FEP, Assessment of Motor and Process skills (AMPS) was conducted before and after the FEP.

The mean age of the participants was 83.98 ($SD = 6.5$) years. There were no differences in baseline severity of dementia, age, Mini-mental state and AMPS scores before the FEP ($p > 0.05$). After the FEP, significant improvement in AMPS process skills was found (Wilcoxon signed ranks test, $z = 3.9$, $p < 0.001$). Statistically non-significant modest improvement was found in AMPS motor skills ($z = 1.6$, $p = 0.11$). No significant difference in the change of AMPS scores between the test and control groups (Mann-Whitney U test, $p > 0.05$).

The results suggested specific functional components of everyday activities could be enhanced in people with dementia. The training schedule should be appropriate to the level of impairment and adapt to the deficits of subjects. It appeared that the processing skills of both T and C subjects were improved. Although the personal significance of specific daily tasks did not affect the enhancement of function, its influence of mood state should be further explored.

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P1-244

Cognition and depressive symptoms in a community sample of elderly subjects from São Paulo, Brazil

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Introduction: Depression is a serious health problem in elderly, and perhaps is the most frequent cause of emotional suffering and impairment in quality of life. Studies of prevalence in elderly disclosed average rates of 1.8% for major depression, 9.8% for minor depression, and 13.5% for clinically significant depressive symptoms, evidencing the clinical importance of episodes with lesser severity and intensity. Moreover, depression in clinical samples reaches about 5% to 10% of the outpatients and 9% to 16% of the inpatients, generating increase of mortality and costs of treatment. A recent meta-analysis showed that persons with a history of depression were more likely to be diagnosed as having Alzheimer's disease later in life. Objective: To determine the frequency of depressive symptoms in a population sample of elderly Brazilians and its association with social-demographic factors, cognitive deficits and other clinical and psychiatric conditions.
Methods: A randomized population sample of 1,563 individuals was evaluated through a screening scale of depression for the elderly with 10 items (GDS-5 + 5 items), Mini-Mental State Examination (MMSE), Bayer Activities of Daily Living scale (B-ADL) and a social-economic questionnaire.
Results: The frequency of depressive symptoms varied from 16.1% to 61.6%. After multivariate analysis, there was association of these symptoms with B-ADL ($B = 0.173$; $p < 0.001$), previous history of depression ($B = 0.152$; $p < 0.001$), schooling ($B = -0.124$; $p < 0.001$), psychotropic using ($B = 0.130$; $p < 0.001$), physical exercises ($B = -0.122$; $p < 0.001$), hypertension ($B = 0.095$; $p < 0.001$), alcoholism ($B = 0.098$; $p < 0.001$), diabetes ($B = 0.068$; $p < 0.007$), female gender ($B = 0.080$; $p < 0.003$) and marital status ($B = -0.052$; $p < 0.045$).
Conclusion: There was a high frequency of depressive symptoms and significant association with the activities of daily living, and other clinical conditions, as diabetes and hypertension. In this cross-sectional survey, we did not observe association of the depressive symptoms with lower MMSE scores.

P1-245

Spirituality, religion and aged persons mental health

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Background: There has been a need to include the spiritual and religious dimension of patients into their psychiatric care.
Objective: To review the evidence for this need and to suggest the parameters which this dimension might be applied.
Methods: The phenomenology of spirituality and its relevance to psychiatry is considered. The concept of the psychiatrist and the clinician as a healer is visited. The evidence that exists for the need of spirituality and religiosity for the patients is examined.
Results: There is a need to address patients spiritual needs at different levels. Using data and experience the authors suggest what psychiatrists might do and what they might not do. Thus this need of the patient might be attended to in an ethical and sensitive manner.
Conclusion: In considering the spiritual dimension of the patient the psychiatrist can send an important message that he or she is concerned with the whole person – a message that enhances patient physician relationship, which is likely to increase the therapeutic impact of their interventions.

P1-246

The effects of group-based counseling, guidance and adjustment education on depressive symptoms among coronary artery disease patients after a coronary bypass graft surgery

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Depressive symptoms are common among coronary artery disease patients undergoing bypass surgery. They may lead to increased risk of mortality and worsened quality of life. Traditionally, rehabilitation of cardiac patients has focused on reduction of physical symptoms and improvement of health behaviours, while psychosocial factors have gained less attention. The aim of the present study was to determine the effects of a group-based counseling and guidance programme on depressive symptoms compared to usual care among patients undergoing non-acute CABG surgery. This study is part of a randomised controlled intervention trial with 3-, 6- and 12-month follow-ups, conducted among the patients living in the District of the Heart Association of Uusimaa, Southern Finland, and undergoing coronary artery bypass graft surgery (CABG) between May 1998 and December 2001. An invitation to the study was sent to 449 patients and 365 (81%) accepted to participate. Of 314 having a non-acute operation, 153 patients were randomised into intervention and 161 into control group. Population of the present study consisted of all non-acute patients with a full data of depressive symptoms (Zung Self Rating Depression Scale, ZSDS, n = 190 or Beck Depression Inventory, BDI, n = 203) in all four measurement points. Intervention consisted of individual and group-based guidance, counseling and adjustment education, in addition to usual care. A total of five nurse-led group meetings were organised; one before and four after the surgery. The control group only received usual care. Depressive symptoms were measured with two structured self-rating measures (BDI, ZSDS). Changes between baseline and follow-ups (3-, 6- and 12-months) were analysed with a two-way analysis of variance (repeated measures ANOVA) with a 4-level within-subject time factor (baseline, 3, 6 and 12 months) and a 2-level between-subjects factor (intervention, control group). The amount of depressive symptoms decreased in both groups during the intervention, decrease being highest during the first three postoperative months, measured by both ZSDS and BDI. No significant between-group interactions were detected. The amount of depressive symptoms decreased after the CABG surgery. Group-based counseling and guidance did not produce additional benefits among cardiac surgery patients. Since similar changes were detected in both groups, most of the effect may be accounted for the spontaneous recovery after the surgery.

P1-247

With the courage of a discoverer: a professionally-led support group for people with non-reversible memory deficits

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Persons who got recently confronted with the diagnosis of dementia go through a very difficult phase in their life: next to the bewildering diagnosis, there are the repeated, hurtful confrontations with one's own deficits, the fear of further deterioration and loss of identity, the confrontation with an environment that equally got upset by the diagnosis and with a society that often considers dementia as a taboo.

The support group is an initiative of FOTON, the Bruges Expert Centre on Dementia. The local memory clinics gave their full support. The initiative wants to bring together people with a diagnosis of dementia and, at least, some awareness of their illness. The primary goal is to offer them a context of safety and comprehension where rather painful experiences as well as 'new discoveries' can be discussed. Each session is started with some psychomotor exercises that give people the occasion to carefully discover the boundaries of their body. The imitative started in September 2005 and definitely grow over the past two years. It happens to be a real 'piece of luck' for the participants and a wonderful experience for all of the coaches. In this presentation the way of action, primary goals as well as first results and shared experiences will be presented.

P1-248

Attitude, conditions and TV-violence in elderly people

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Introduction: elderly people often have aggressive and fearful attitudes towards the environment. Social stress negatively influences the quality of their life. Frequent news and images of violence can injure stability, facilitating anguish and alienation.

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Methods: the research examines: a) attitudes, conditions, culture of elderly people; b) emotions and opinions about images of television violence.
Hypotheses: 1) aged people are sensitive to worries and violence; 2) women have better emotional control.
Materials: a) Questionnaires presented in semistructured interviews; b) televised presentation of sixteen violent image sequences (eight of direct and eight of indirect violence and four scenes of environmental violence); c) Questionnaire I-R on aggressiveness; d) IPAT (ASQ) scale; e) Geriatric Depression Scale (GDS).
Participants: 302 elderly people (156 F. 146 M.), living in cities and suburbs,170 at home and 132 in nursing home, were interviewed.
Results: women have greater autonomy than men. Elderly people, living at home, wish for better health and love, (particularly women); whilst men want to see their sons' realisation in life and their grandchildren growing up; they have a positive attitude towards the future: hope (50,00%) but they fear institutionalization (39,41%) and illness (39,41%). Elderly people, living in nursing home, wish for a good death (34,09%), a clear mind (33,33%), have more worries (52,27%), fear pain (39,39%). Aged people are afraid of disability (57,28%) and the occurrence of cognitive deficits (40,73%). Women living in cities are afraid of aggression (74,36%), because they feel defenceless (37,18%). The scenes of direct violence stimulated: pain, anguish, fear, blame, moral harmfulness; those of indirect violence: shame, anguish, pain, sadness, inhumanity; those of environmental violence: sadness, fear, moral harmfulness, uselessness, anguish. Women are more sensitive, but also had better control of their emotions. Self images are prevalently positive in elderly people. Indigence and lower levels of instruction are regretted. GDS shows a greater change in mood in elderly institutionalized people and in women. IPAT: low levels of anxiety.
Conclusion: elderly people are satisfied about their health and life, especially men; those living in cities are more sensitive to worries and to social conflicts. Women seem more vulnerable, but are better at controlling their emotions. News and scenes of television violence are deprecated.

P1-249

Waiting to become grandparents

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Introduction: the birth of a child represents a change and grandparents can be of substantial help to young parents. What do grandparents think, remember, feel whilst waiting for the positive event to occur? How do they live the period prior to the new event? Methods: the research examines attitudes, emotions, self images, perceived body image and future image, of people who await their first grandchild.
Hypotheses: 1) the birth of a first grandchild stimulates positive emotions; 2) women and men wait for the first grandchild in different ways.
Materials: 1) Questionnaire presented in semistructured interviews; 2) Zung-Self-Rating Anxiety (SAS). We interviewed 60 grandparents (30 F., 30 M.) in two hospitals in North Italy.
Results: every interviewed person is satisfied with the idea of becoming a grandparent. To become grandparents is perceived as a further engagement (46,67%); a natural experience (46,67%), a new role (43,27%), and especially by men; as a form of self-realization (43,33%); a change of life (41,94%) and by women; as a moment of reflection (25,81%) and a sign of progressive aging (20,69%). Grandfathers express satisfaction (60,00%), serenity (38,33%), whilst grandmothers express happiness (87,10%), excitement (72,58%), serenity (33,87%); they both feel younger (43,33%). Interviewed people trust their relatives new roles. Affective relationships seem positive; grandfathers are more satisfied about their married life than grandmothers. About the future, grandparents are worried, serene, trusting. Interviewed people hope to preserve good health (81,67%), to see the growth of their grandchildren (74,17%), (especially women), to follow the realization of their own children (63,33%), (especially men), to meet friends (48,25%), to travel (43,33%), to learn new things (36,67%), to improve their culture (31,67%) (especially women). Interviewed people have a positive image of themselves and their body; they desire to undertake more activities, to live a long time. Some grandparents desire to be more creative (31,67%), to have more patience (33,33%), to be more engaged (21,67%); others desire to be more efficient, quiet, clear minded. SAS: more anxiety in men than in women.
Conclusion: the birth of the first grandchild is perceived positively. Waiting for the first grandchild stimulates thinking, emotions, changes, prospects. Women have developed a greater aptitude for

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becoming grandmothers and they express their experiences and emotions better.

P1-250

A psychosocial model of care in a psychogeriatric tertiary care facility: The Sandringham experience

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In an innovative private-public partnership, Sandringham Care Centre (SCC) was designed as a stand-alone facility to provide care to 46 older adults with tertiary level psychogeriatric needs. Since little literature to guide program design at the tertiary care level, SCC chose to implement a model of care based on a psychosocial rehabilitation approach. The model of care for SCC was developed using the principles identified in the Guidelines for Elderly Mental Health Care Planning for Best Practice for Health Authorities (BC Ministry of Health, 2002), developed by the BC Psychogeriatric Association through a broad provincial consultation with serviced providers, older adults, seniors organizations, policy makers, program planners, educators and researchers in the field of psychogeriatrics. Researchers at the Centre on Aging, University of Victoria were engaged to: 1) evaluate the implementation of this model of care and 2) describe changes in the population receiving care at SCC over 12 months. To evaluate the implementation of the model of care, data were collected through semi-structured interviews with Central Care Corporation (CCC) and SCC administrative staff and external key informants. For describing changes in the people receiving care at SCC, a single group pre-test post-test design to examine individuals at admission and after 12 months was used. The Resident Assessment Instrument Mental Health Version 2.0 for Inpatient Adult Psychiatry (interRAI-MH 2.0), an instrument made up of 28 quality indicators for mental health, was administered at admission and after 12 months. In addition, an Administrative Data Collection Instrument (ADCI) was used to document staffs perceptions of: 1) changes in specific psychiatric symptoms between inter-RAI MH 2.0 assessments, and 2) the reasons for the changes. Having a philosophy of care and a planned approach for implementing it appeared to have had positive benefits. On the interRAI-MH 2.0, more improvement than deterioration was seen over the year following admission. On the ADCI, improvements were reported in areas such as sleep, appetite, mood, social functioning, and overall quality of life. To our knowledge, this is the first longitudinal examination of residents receiving care in a specially-designed psychogeriatric tertiary care facility. It is anticipated that future research will further our understanding of those clients that benefit most and least from specific models of care.

P1-251

Respecting the aging clientele: A training program for commercial service providers

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Given the increasingly aging population, there is a pressing need to improve the understanding and attitudes of commercial and health service providers to older persons. To address this need, the University of Melbourne Academic Unit for Psychiatry of Old Age, the Inner East Community Health Service, in collaboration with older people from the community, conducted a pilot Community Based Interactive Educational program in the municipal of Boroondara in Melbourne, Australia. A program of 4 educational and discussion seminars was designed to assist local businesses and organisations to further understand the issues facing elderly people and utilise this information in their delivery of services. Key focus areas included the promotion of practices and behaviours that contribute to safe and healthy environments, improvements of the health, well-being and inclusion of socially isolated residents, raising community awareness of disability and promoting access and inclusion, and identifying effective responses to new and emerging community needs. Program objectives included education about the physical, social and psychological changes of ageing, discussion of attitudes towards older people, and development of practical strategies for improving service provision to older clients. The program was attended by 28 representatives from various community and commercial organisations providing services to older people, including local government, community associations, banks, hospitals, and ambulance and taxi services. The sessions provided an

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opportunity for these service providers to further their knowledge and understanding of key issues and attitudes towards older people through presentations given by experienced healthcare professionals and older people themselves. Group discussions also provided opportunities for service providers to share experiences and ideas about service provision to the elderly. The program directly resulted in several initiatives taken within the organisations to improve responses to elderly stakeholders and in the development of an innovative charter, applicable to any business or service: The Boroondara Charter for Quality Customer Service for the Elderly as Key Stakeholders. Delivery of this interactive educational program and the widespread application of the principles of the charter will hopefully engender a more caring community attitude and response to older people, not only in the municipal of Boroondara, but throughout wider society.

P1-252

Social connection and health in older people

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Lack of social contact and social isolation have been linked to poor quality of life, depression, poor physical health and increased mortality in older people. The aim of this study was to examine the relationship between support network and physical and mental health measures in a large sample of community dwelling elderly. 1337 individuals over the age of 65 were recruited from 5 local GP practices and interviewed at home using GMS AGECAT. Social network was measured using Wengers Network Typology. Cognition was measured using the MMSE. Physical health was based on self-report. A restricted social network was associated with never being married, with self- rated physical disability and the level of cognitive impairment. A poorly integrated social network was associated with lower self-rated quality of life, increased risk of depression but not anxiety in this population. Network type is an important predictor of quality of life and a range of physical and mental health outcomes in older people. Interventions that improve social connection are likely to impact positively on quality of life and health outcomes in community dwelling elderly.

P1-253

Practice of mind body exercise is associated with better cognitive function in Chinese older persons in Hong Kong?

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Background: Physical activity (PE), especially aerobic exercise (AE), was associated with better cognitive function in late life. However, implementation of exercise program as a health promotion strategy is limited by different personal and cultural factors. In a recent population survey, the association between modality of PE and cognitive function was explored.
Methods: The population survey was conducted in 2005 and 2006, 6100 subjects were screened at Phase 1. All subjects were assessed with Chinese Mini-Mental State Examination (MMSE) and a Memory Inventory (MIC). PE was measured by a questionnaire (No exercise, NE; Toning and stretching, SE; Strenuous aerobic exercise, AE; mind-body exercise, MB). 914 subjects completed Phase 2 cognitive assessments with ADAS-Cog, and Category Verbal Fluency Test (CVFT).
Results: Regular practice of AE and MB was associated with higher MMSE scores (one way ANOVA, $p < 0.001$). Subjects with NE or SE only were more likely to be suffering from clinical dementia (chi square $= 74.5$, $p < 0.001$). MMSE scores were negatively correlated with age in NE, SE and AE groups (partial correlations controlled for educational attainment and sex, $p < 0.001$). No significant age effect on MMSE scores was found in the MB group ($r = -0.081$, $p = 0.064$). The SA and MB groups with longer exercise habits had higher scores in the episodic memory and CVFT (Mann-Whitney U, $p < 0.01$).
Conclusions: MB was likely to offer benefits on cognitive function in older adults. As MB is a safe and cost-economical intervention, its potential in early intervention for Mild Cognitive Impairment and early dementia should be further explored.

P1-254

Kinsei (Venus) band: Experience of a person with Alzheimer's disease co-creating rock music

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In 2006 a day-care service program started in response to the needs of dementia patients and their family members in Tokyo. It is a grass-roots service with all-volunteer staff, including health-care professionals. Using Kitwood's approach to person-centered care, a rock band was formed to fulfill one participant's dream. Mr. A, 52 years old, was diagnosed with early-onset Alzheimer's disease (AD) three years before. By knowing his disease he felt his life was over. Gradually he has been experiencing difficulties in memory, language, and performing daily activities. One day he expressed his hope for playing rock music, which he had enjoyed greatly in his high-school years but had not played since then. The band consisted of Mr. A (drum), his wife, 2 health-care professionals (one a jazz musician), and 4 musicians. After three months of intensive practice, a successful concert was held. The purpose of this study was to describe the experience of being a part of the band members and to explore the meaning of the experience. The ethnographic method was employed in this study. Data were collected by participant observation, semi-structured interviews, field notes, and documentary film over a 7-month period. All interviews were tape-recorded and transcribed. Qualitative data analysis revealed six themes: commitment, sense of interrelatedness, co-creating music (communication via music, etc.), joy, self-actualization (start of new life, enjoying life together, reflecting meaning of music, satisfaction from the work), and empowerment. This culture, especially co-creation, of band music seemed to enhance psychological well-being and empower the people involved. For the person with AD, empowerment included increased self-confidence and pride, feeling getting better, determination to live life as much enjoyable as possible, etc. Commitment included playing rock music to start a new life despite of having AD, a will to play his music somehow in the band. In addition, vividness, energy, and enjoyment of live rock music seemed to have healing power in it. Although the primary purpose of the band did not have a therapeutic component, the band music apparently provided healing to the person with AD. This new musical approach for supporting strength and hope/dream of persons with AD suggests how health-care professionals can identify and encourage the afflicted person to use their remaining abilities and enjoy life together.

P1-255

First session of dementia care mapping in Mirandola special care unit

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Introduction: The present paper describes the very first map to be conducted in Italy, using Dementia Care Mapping at CISA, a nursing home for older adults, which includes a special care unit for dementia.

Materials and methods: The method adopted was the application of all of the steps involved in a mapping session, by a mapper having acquired the basic and advanced steps of training (MVG, Mapper A) with a Receptive Mapping Partner Mapper B: a) briefing was given due importance, and carried out with special care, b) the mapping itself was performed over a 6 hour period in a communal area, observing 5 residents, each of whom represents a variety of the characteristics which make each person unique, c) at the feedback session the Staff were impressed by all the data processing possibilities: how clearly the Behaviour Category and WIB profiles yield a picture of what had gone on during the mapping session.

Discussion: In Italy the prevailing approach to dementia is still the standard paradigm, that implies a very medicalised view of dementia simply as an irreversible disease destroying the brain, often ignoring both the subjective experiences of the sufferers, and their place within the social world. Although there is no official recommendation in Italy for a person-centred approach to dementia care, in this facility it is enacted spontaneously by the staff, whose training, according to person-centred principles, is considered a priority by their manager.

Results: The first DCM session suggested the possibility for greater Staff awareness, lead to the identification and avoidance of instances of Malignant Social Psychology, and to the discovery of creative examples of Positive Person Work; special attention will be devoted in future sessions to cultural differences which emerged in the first Italian application of the instrument and which will have to be faced and overcome.

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$$① \quad X_{ij} = P_{ij}/(T_j - P_{ij}) \qquad ② \quad X_i = 100 \times (\sum_{j=1}^{N} X_{ij})/N$$

P1-256

P1-256

Analysis of interaction of patients at "Ball Passing" in a ward for dementia

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Objective: To examine the behavior of patients (pts.) who received more balls at the "Ball Passing" game in the recreation programs in a psychiatric ward for dementia.
Methods: At Ball Passing, the data was collected during 7 min. in a sponge ball session with 4 balls (within about 50 min.) once/week. Pts. Sat freely in a multipurpose space in the ward, and they were told to give the ball to anyone to whom he/she liked to give it. Number of balls were calculated by Index {< Number of balls received at a session/sum of balls received, (1) > sum of days attended} sum/no. of attendance x 100 <(2)>. And the Index was analysed by categories.
Results: The game was played 12 times x 2 times. There was no statistical difference between male-female, the degree of accessibility, etc. But, the higher MMSE group got more balls then lower MMSE group, statistically.
Conclusions: The cognitively higher group received more balls. But, there were some who hardly gave balls to anyone. And there was a problem in introducing statistical method for analyzing the activities of those people. But it is a good means for evaluation and treatment of severer cases of dementia.

P1-257

Improvement of quality of life (QOL) in the demented elderly by the Fukuyama Yuai-Outdoor Activity Care Program (FY-OACP): influence of self-determination capacity and vitality levels on QOL outcome after intervention

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The Japanese Quality of Life Inventory for the Elderly with Dementia (QOL-D) was developed consisting of 3 categories (the 1st, vivid communication with surroundings; the 2nd, self-expression; the 3rd, control of behavioral disturbances) and 24 items (Kamata K, et al., 2001). We also developed the Fukuyama Yuai-Outdoor Activity Care Program (FY-OACP) and demonstrated that it relieved demented elderly inmates of indoor stressors, normalized pituitary-adrenal hyperactivity, increased immune activity, markedly reduced BPSD and improved QOL in the demented elderly (Suemaru S, et al., 1997; 1998; 2003). The aim of this study was to investigate the influence of self-determination capacity and vitality on QOL after the FY-OACP intervention. The subjects were 20 inmates (3 males and 17 females; the mean age, 78.0 years). According to the Mini-Mental State Examination (MMSE) scores assessed by a clinical psychologist, based on the standard generally adopted, the subjects were divided into two groups: the self-determination capacity group (MMSE score $\geq$12; the mean, 16.8; n = 11) and the self-determination incapacity group (MMSE score < 12; the mean, 5.0; n = 9). Moreover, vitality in these groups was examined using Vitality Index (VI) (Toba K, 1998). The former was defined as a high vitality group while the latter was as a low vitality group (the mean VI scores, 7.6 and 4.9, respectively). The FY-OACP was performed in the green-grass ground of the hospital for one hour everyday for one month and a half. Before and after 1.5-month intervention, the QOL-D 1st, 2nd, 3rd category and total scores were assessed using the QOL-D, and their changes after the intervention were statistically analyzed. A significant correlation was found between MMSE and VI. In the self-determination capacity, high vitality group, the QOL-D 1st, 2nd, 3rd category and total scores were all significantly improved after the intervention. On the other hand, no significant changes in these QOL-D scores were observed in the

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self-determination incapacity, low vitality group. In conclusion, the improvement of QOL levels after the FY-OACP intervention was found in the demented elderly with self-determination capacity and high vitality but not with self-determination incapacity and low vitality. These findings indicate that the self-determination capacity and vitality levels influence the outcome of QOL after the intervention.

P1-258

Effects of one-year formative art therapy for patients with Alzheimer's disease

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Objective: Art therapy is often employed as a treatment activity for individuals with dementia, however, empirical evidence regarding its effect on cognitive improvement is insufficient. We evaluated the effects of a one-year formative art therapy program on cognitive functions of individuals with Alzheimer's disease (AD).

Methods: The subjects were 36 patients, who were recruited from an outpatient geriatric clinic in Tokyo. Based on results of a clinical interview and brain imaging investigations, all were diagnosed with AD. Informed consent was obtained from all subjects and their caregivers prior to participation in the study. The subjects were assigned to either the intervention group ($n = 17$) or control group ($n = 19$) according to their intent to participate in a one-year formative art therapy program. Cognitive status was evaluated in both groups using a Mini-Mental State Examination (MMSE) and Wechsler Adult Intelligence Scale-Revised (WAIS-R) examination at the time of entrance to the study (baseline) and 1 year later. Subjects in the intervention group participated in a formative art therapy program 3 times per month for 3 hours each during the one-year period of study. In that program, artists specialized in such therapy taught and directed various art activities, including drawing, painting, and forming. The subjects in the control group received typical outpatient treatment. To evaluate the effects of the one-year formative art therapy, a two-way (time and intervention) analysis of variance (ANOVA) with repeated measures was conducted.

Results: The mean ages of the subjects in the intervention and control groups were 74.6 ($SD = 6.6$) and 73.0 ($SD = 7.3$) years old, respectively. Age at baseline, age at onset, years of education, and sex distribution did not differ significantly between the 2 groups. By using repeated measures of ANOVA, significant interaction effects with respect to group and time were observed in the results of the following WAIS-R subtests; 'digit span' [$F\ (df = 1,34) = 5.3$, $p < 0.05$], 'object assembly' [$F\ (df = 1,34) = 4.1$, $p = 0.05$], and 'digit symbol' [$F\ (df = 1,34) = 4.4$, $p < 0.05$].

Conclusion: These results suggest that the one-year formative art therapy program was effective for individuals with AD in regard to improved attention function and visual information processing.

P1-259

The effect of stress-coping in late-life mental health

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Background: Depression and Anxiety in elderly are highly prevalent, yet there is little evidence to guide targeted prevention strategies. To support healthy and enjoyable life of the elderly, stress-related problems should be psychologically improved, and the profitable prevention approach for Japanese elderly is needed. We examine the relations between stress coping styles and mental health of elderly.

Objectives: This study was addressed to investigating psychological factors and stress-coping strategy of both elderly and young people.

Methods: The questionnaire packet contained an informed consent, General Health Questionnaire (GHQ), Ways of Coping Checklist (WOC), State-Trait Anxiety Inventory (STAI), the Medical Outcomes Survey Short-Form 36 (SF-36), and health related checklists. Statistics included Student t test, correlation analyses and multiple regression analysis.

Results: All participants who had no symptoms were included, and gave consent to participate in this study, had no missing data and their data were analyzed. Compared with 114 Young subject (57 males, 57 females, age: 20.33 ± 1.0 years), 211 elderly people (149 males, 68 females, age: 64.18 ± 10.4

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years), showed lower GHQ score (2.22 ± 2.59 vs. 5.04 ± 3.12, $p < 0.05$), and lower score of Confrontive Coping (5.12 ± 3.33 vs. 6.93 ± 3.54, $p < 0.05$), Seeking Social Support (6.14 ± 3.10 vs. 8.48 ± 4.23, $p < 0.001$), Accepting Responsibility (4.80 ± 2.51 vs 6.07 ± 2.51, $p < 0.001$), Escape Avoidance (6.68 ± 3.93 vs. 10.73 ± 4.26, $p < 0.001$) in WOC. Meanwhile, A multivariate logistic regression model evidenced that a coping skills of Confrontive Coping (OR = 1.4; 95% CI = 1.1–1.7; $p < 0.01$) and Accepting Responsibility; OR = 1.2; 95% CI = 0.98–1.41; $p < 0.001$) were the only predictors of mental health in elderly, which was not found in young.

Conclusion: These results suggest that the ways of coping with the stressors differs in generation; and may be important points for the intervention of mental health.

P1-260

The development of a simple reminiscence observational rating scale (RORS)

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Purpose: Observational rating scales are suitable to assess the effect of reminiscence therapy on elderly patients with dementia. We attempted to develop a simple Reminiscence Observational Rating Scale (RORS). This study aims to examine the interrater reliability and the criterion-related validity of RORS.

Methods: The subjects for this study were 68 elderly inpatients with dementia (average age 79.7 ± 10.6 years). RORS is composed of eight subscales designed to rate four domains and eight items, such as cognition (memory, attention of the scene), verbal (verbal fluency, verbal clarity), emotion (participation desire, enjoyment, and expression), and interpersonal relations (cooperation). After the sessions, we examined the interrater reliability between clinical psychologists and occupational therapists. Moreover, clinical psychologists rated the subjects' activities by using RORS and the Todai-Shiki Observational Rating Scale (TORS). The criterion-related validity between RORS and TORS was examined by the calculation of the correlation coefficient and the good-poor analysis using SPSS.

Ethical considerations: All subjects and their family members were informed about the purpose and method of this research before obtaining their written consent.

Results: Statistical analyses revealed that the κ coefficients between the clinical psychologists and the occupational therapists were as follows: cooperation 0.72, memory 0.71, participation desire 0.66, enjoyment 0.65, attention of the scene 0.64, expression 0.64, verbal fluency 0.62, and verbal clarity 0.62. Moreover, the analyses also revealed that the Spearman rank correlation coefficient between the total scores of both RORS and TORS was 0.77 ($p < 0.01$), and the χ square value by the good-poor analysis based on the total scores of RORS and TORS was 12.44 ($p < 0.01$).

Discussion: In this study, we attempted to develop a simple RORS and examined the interrater reliability and the criterion-related validity of RORS. As a result, the interrater reliability between the clinical psychologists and the occupational therapists indicated a substantial consistency. Moreover, a strong correlation was observed between the total scores of RORS and TORS, and a statistically significant difference appeared in this correlation. Therefore, it was believed that RORS showed interrater reliability and criterion-related validity with TORS. Thus, RORS was useful as a rating scale for reminiscence therapy.

P1-261

A psychological approach for people with early Alzheimer's disease

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Introduction: The importance of early detection and treatment for people with dementia is clear. When patients are diagnosed in the early stages of Alzheimer's disease or some other age-related illness, their family members feel helpless and uneasy about their future. Therefore, it is extremely important for health care professionals to provide their patients with psychological support. This led us to launch a psychotherapeutic program called "Yurinoki-kai" seven years ago. Its main goal is to provide psychological support to Alzheimer's patients. We will discuss our program in detail, including its accomplishments and remaining issues.

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<Overview of the Program> Our program is different from other programs for the elderly in that most staff members are certified clinical psychologists, and we mainly offer psychological treatment. We started the aforementioned psychotherapeutic group program in July 2000 as a membership-based program. People diagnosed with dementia and their family members were the principal subjects of our program. We usually met twice a week for two hours. The program had three goals: easing stress, facilitating positive social interactions, and enhancing creative abilities and skills. Staff members also included music therapists, recreational therapists, artists, physical and occupational therapists, and peer volunteers. Cumulatively, 42 people participated in the program. They suffered from different types of dementia, but most suffered from Alzheimer's. Our program explored many different methods such as the following: reminiscence/life review, music therapy, recreational therapy, and art therapy. We occasionally used other methods such as music concerts, poetry reading, gatherings and parties, so both patients and family members could both participate in and enjoy them. We also organized meetings for family members so that they could discuss issues and difficulties they faced. We tried to provide program contents suitable for adults. This would enhance the participants' ability to express themselves and be sensitive to the participants' needs.

Discussion: The program allowed patients to enjoy themselves without focusing on their lost ability. This was made possible by our specialized support system and flexible program contents which focused on personal interactions and included their inner world.

P1-262

Psychotherapeutic relaxation of Schultz autogenic training type in neurosis in elderly

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After having briefly presented the Progressive Autogenic Training (TAP), technique of Psychotherapeutic Relaxation resulting from the method of Schultz enriched by psychoanalytical concepts, the authors report the label clinical of a 70 year old woman suffering from neurosis and treated by TAP during three years. The analysis of this observation makes it possible to approach adaptation of the framework of the TAP specific to the elderly, the elements of psychology of ageing and the psychotherapy processes concerned in the change of this patient. She realized through this somato-psychic therapy, a true Face lift of Self.

Keywords: Progressive Autogenic Training (TAP), elderly, neurosis, psychotherapy, body.

P1-263

APCATS- the first community psychogeriatric team in Singapore: The first year and beyond

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Although psychogeriatric services have been developed in Singapore since 1993, the lack of community-based mental health services remains a major service gap. Aged Psychiatry Community Assessment and Treatment Service (APCATS) was launched in Jan 2006 based on well-tested model of aged psychiatry community mental health services in various other countries. APCATS is delivered through a multidisciplinary team of mental health professionals. It provides assessment and treatment for frail elderly with mental problems in their homes and selected nursing homes. The key outcome measures include hospital admission, length of hospitalization, caregiver burden (Zarit Burden Interview and NPI-CDS) and satisfaction. Rating scales used to assess response to intervention include the Mini-Mental State Examination (MMSE), Montgomery-Asberg Depression Rating Scale (MADRS), Neuropsychiatric Inventory (NPI), Clinical Global Impressions (CGI-I). Modified Barthel Index (MBI) is used to quantify the functional status of the patients. At the end of year-one, it received 160 referrals and accepted 87. Of the 87 patients, 62 were visited by end 2006. The mean age was 76.2 (SD 8.7), 56.5% were male, 51.6% were diagnosed with dementia, 21.0% depressive disorder and 19.4% schizophrenia. Referrals were mostly from the Institute of Mental Health (75.8%) and community hospitals (14.5%). 64.5% of the patients were residing in their own home. 46.4% have a MMSE of 11–19, while 28.6 3% have a MMSE of 0–10. 45.2% have a MBI below 60

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(severe or total dependence). Caregiver burden was rated to be fairly low at baseline: mean score of 20.8 (SD 16.3) for ZBI and 6.1 (SD 6.6) for NPI-CDS. At 3 months, 64.9% and 50% had a 20% or more improvement on the MADRS (N = 37) and NPI (N = 20) respectively. Based on the CGI-I, 51% were rated to have improved while 39.2% remained unchanged at 3 months. All the caregivers rated a high level of satisfaction with the service. Comparing the 6 months pre- and post-APCATS enrolment, the total number of hospitalization of patients (N = 51) was reduced from 33 to 4, and total length of hospitalization reduced from 790 to 131 days. Thus preliminary data validates the clinical utility and effectiveness of APCATS in reducing hospitalization. It was also well received by caregivers. Going forward, APCATS will serve as the template to implement the Area-based Community Psychogeriatric Service Framework under the National Mental Health Blueprint from 2007 to 2012.

P1-264

Palliative care for the elderly: First steps in Nizhny Novgorod, Russia

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Nizhny Novgorod is one of the ancient and largest cities in Russia. The population of the city is about 1070000. The demographic aging is amongst the highest in the country. In 2006 the rate of 60 years and over people was 22.4%. The mortality among the elderly is as much as 8.5 among the adults mortality rate. It was Nizhny Novgorod where the first Geriatrics Center in Russia was founded in 1989. Since then the Geriatrics Service has been established in the region. Today it comprises a Regional Geriatrics Center, a Glaucoma Center, geriatrics consulting rooms in district and city polyclinics, nursing and geriatrics departments in hospitals, psychogeriatric departments. A network of municipal centers including daytime departments is being developed in different districts. Nizhny Novgorod was and remains amongst a few areas in Russia where a network of nursing departments and hospitals was established where the elderly could have palliative care services for the first time. Along with provision of comfort it is important for the elderly if their death is respected when their life can no longer be maintained. Nowadays patients with dementia need palliative care as this disease is very prevalent, it has a decade-long course, it causes a progressive loss of function, personhood and identity, and it requires special communication skills and attitude to patients. What is more, traditional geriatrics does not always give optimal relief to terminally ill patients with dementia, and palliative care units still do not manage patients with cognitive and behavioral problems. For this reasons special nursing hospitals and homes for the elderly with dementia have been establishes in the region. Now we urgently need to improve quality of end-of-life care for the elderly living in geriatric facilities and of course for those with cognitive and behavioral problems. To fulfill this goal we have to provide good education in end-of-life care for specialists, raise public and policy makers awareness about state of the art and need in end-of-life care for older population improvement. We have developed some proposals for the Geriatrics Service reorganization taking in consideration the need for end-of-life care so we could bring palliative care approach into all geriatrics settings and into dementia units as well.

P1-265

Audit on consultation-liaison psychiatric services for older persons at West Middlesex University Hospital

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Objective: to assess effectiveness of nurse led psychiatric liaison services and suggest how the service can be developed.

Methods: Audit on Liaison nurse's activity record, collateral information, referral forms and patients records for 10 months.

Results: 141 patients referred for general mental health assessment (89), capacity/placement (12), medication review (9) and other assessments (31). In all patients no record of consent for assessment has been found and in 21 no primary referral reason identified. 56 patients have been not medically fit for assessment when referred and 11 died before fully assessment was made. In 91 cases family details were known but only in 58 cases family has been involve. Patients have been assessed and manage in 51 cases soly by Liaison nurse, SHO or Consultant (21) and jointly in 69 cases. 6 patients have been

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admitted to the psychiatric ward under Mental Health Act. Liaison nurse made face to face 599 consultation where 21 patients had one consultation, but 77 more than 3 consultations. From them, 2 have had more than 12 consultations. Standard psychiatric interview, MMSE and GDS were use for assessments. Data from 104 patients were eligible for individual diagnoses. Depression and dementia were most frequent diagnoses (53), but delirium or confusion only in 11 cases. 88 patients needed follow up by CMHT after discharge. 20 patients had no any psychiatric needs.

Conclusions: Psychiatric Liaison nurse led services provided high standard of care regarding effectiveness. However some legal and ethical issues have to be address. Patients consent or lack of capacity has to be recorded as well their medical condition and fitness, reason for referral and contact details of the families and carers. Most common reason for referral was general mental health assessment. More than one third of all patients were not medically fit for assessments. 1/7 did not have reason for referral and 20 no any psychiatric needs Liaison nurse alone managed 51 cases but needed assistance from doctors in others. Majority of patients needed follow up on the medical word or after the discharge. Only few patient were diagnosed with delirium.

Recomendations: A new referral forms and standardised assessment tolls to be designed with the established rating scales. Use of ISD-10 classification to be part of standard practice. Present services are unable to meet current level of demand. Liaison team Consultant and nurse could be provided if founding is found to create that team.

P1-266

Outreaching service for elderly dwellers with mental health needs residing in Hong Kong Island

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Purpose of the study: Many elderly people with mental health needs are under diagnosed and neglected by the society. The project was therefore aimed to visit more than 15 districts within Hong Kong Island to identify the group of elderly people in need of mental health intervention. The project was lasted for one year.

Objectives: 1. To promote mental health education for the elderly in local districts within Hong Kong Island 2. To identify the elderly dwellers living with mental health needs 3. To assess the health and social needs of the elderly dwellers residing in 15 districts 4. To arrange follow up services for them

Methods: A group of volunteers with nursing and social work background was recruited for the project. A briefing was given about the whole project. An assessment pack including personal particulars, living condition, finance and health status; appetite, sleep pattern, pain and bowel habit etc in the past two weeks as well as level of social activities and contacts with family and or with friends in the past few months. Lastly, their cognitive functioning was assessed by way of Chinese version Abbreviated Mental Test (AMT).

Result: 15 districts were visited within 12 months and over 2,000 elderly dwellers attended the public mental health education seminar. 1236 participants were successfully interviewed. Verbal consent was obtained prior to the interview. Almost 50% belonged to the old group (age 71–80) followed by the very old (aged 81 or over). Over 60% have at least one chronic illness. The frequency of going out was low with less than 50%; the choice of outdoor activities was confined to visiting local shopping mall. The contact with family members was low compared with friends. Less than 10% received retirement pension and two third were heavily depended on old age allowances and support from children.

Conclusion: In Hong Kong, elderly people are living longer but become socially isolated as the age increases. The present findings indicate that their insights into their mental health needs were poor. A small number of participants needed urgent attention from social worker after the interview with emotional problems. Some were successfully referred to appropriate agents for intervention. The project has indeed succeeded to reach to those who have never been come in contact with local social services.

P1-267

An alternative care milieu for older persons with behavioural challenges

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There are over 15,000 long-term care beds in Toronto (Canada) with over 3200 people on waiting lists for these beds. Many of these individuals have behavioural issues that challenge their

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eligibility for placement in a LTC Home. According to the Onatrio Ministry of Health and LTC (2005), over 718 individuals on the waiting list for a LTC Home in Toronto have been assessed as aggressive, resistive, disruptive, alcoholic or exit-seeking. The authors of this paper have proposed a concept design which would see service enhancements in the provision of psychogeriatric services in Toronto, Canada. The concept, which has been put forward to the provincial government of Ontario, involves addressing the need of older persons with dementia and other mental disorders who are currently hospitalized on psychiatric units and do not need the level of care provided in these units, but who are considered too agitated or aggressive to be admitted in existing long term care homes, even when these homes offer specialized programs for patients with agitation or aggression. The authors estimate that there are 10–20 such patients at any time in the Toronto region. They (and their team) propose to organize a 12-bed long term care program that could provide care to these older persons. The creation of a 12-bed unit as described above would fit into provincial government policy directions both with respect to mental health and long-term care (LTC). A recent high-profile inquest into the death of 2 residents at the hands of a demented elderly resident within a LTC Home in Toronto in 2004, also identified a number of challenges related to gaps in services for seniors with mental health and behavioral disturbances in the long-term care setting. The unit being proposed would be one step towards addressing some of the identified system service gaps.

P1-268

Using routine patient outcome measurements to improve clinical care and service delivery

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Australia made a decision to introduce a system in which all consumers of public mental health services should have a standard set of clinical outcome measures during care. The Health of the National Outcome Scales suite of measures is at the core of the system. This has been accompanied by the introduction of a national minimum data set, and an agreed performance framework for mental health services. This is intended to allow an improved understanding of the question: What services are provided to whom, with what effect and at what cost. Focusing upon mental health services for older people, this paper aims to give an overview of the system introduced in Australia, highlight some lessons that can be learnt from its implementation, and illustrate how this system can be utilized to improve clinical care and service delivery. This will be achieved through a review of relevant policy documents, reflection upon participation in relevant national committees, and a description of implementation of the outcome measures within an Aged Care Psychiatry service. Although not without controversy, it has been possible to introduce a system of routine outcome measurement in Australia. Ongoing challenges include in maximising compliance with collection of data, the accuracy of this data, and in linking relevant data management systems. However, it has been possible in the service described in this paper; through identifying opportunities to use data to inform practice, and adapting collection and reporting practices to assist this; to achieve high rates of completion of measures. These measures have provided insights into the service and its consumers that were not available previously. These have been used to guide clinical care and service improvement. The collection of routine outcome measurements within psychogeriatric services has can improve the understanding, and performance, of services. With appropriate implementation, this strategy has significant potential to improve the mental health care of older people.

P1-269

Is the Long-term care Insurance System appropriate for Alzheimer's disease in Japan?

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Background: The Long-term care Insurance System started in 2000 in Japan. We conducted a dementia survey and researched what kind of social resources were used. Then we compared the care levels between Alzheimer's disease (AD) and vascular dementia (VaD).

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Methods: We initiated a dementia survey in Itoigawa city, a rural area of Japan in 1997. There were 33,120 inhabitants and 7,847 of them were aged 65 years and older. The first phase of the survey included medical history, activity of daily living (ADL), psychiatric and behavioral symptoms, and Mini-Mental State Examination. We had 6,394 valid answers and screened 914 subjects who were suspected of dementia. In addition, two hundred samples were selected randomly out of 5,480 people who were not suspected of dementia. The second phase of the survey was put in practice for a total of 1,114 subjects. Pairs of psychiatrists and nurses made house-to-house visits and examined them in detail. Clinical diagnoses were based on the Consortium to establish a registry for Alzheimer's disease and Diagnostic and Statistical Manual of Mental Disorders, Fourth edition. We had 829 valid answers and found 271 demented people. The prevalence rate of dementia was 6.2%, AD was 4.0% and VaD was 1.2%. In the survey, we found 252 elderly with Clinical Dementia Rating (CDR) 0.5. In 2004, we investigated these CDR 0.5 people using the same process as the previous survey in 1997. At the same time, we researched what kind of social resources they used.
Results: Of 252 CDR 0.5 people, 79 were dead. We investigated 111 subjects, 64.2% of the 173 survivors. Of the 111 people, 78 subjects developed dementia (70.3%), 43 were AD (55.1%), 23 were VaD (29.5%) and 12 were unknown and other types of dementia (15.4%). In comparison, 30 subjects remained CDR0.5 (27.0%) and 3 recovered CDR 0 (2.7%). Of the 78 demented people, 60 were using the Long-term care Insurance System, 28 were AD, 21 were VaD, and 11 were unknown and other types of dementia. In detail, support required, care level 1, 2, 3, 4, 5 were 7.1%, 17.9%, 17.9%, 21.4%, 21.4%, 14.3% in AD and 4.8%, 9.5%, 4.8%, 23.8%, 14.3%, 42.9% in VaD respectively.
Discussion: As for the subjects with VaD, ADL were lower because of their physical difficulties and the judgments of care level were serious. On the other hand, although the cognitive dysfunctions were severe, the subjects with AD kept high level of ADL and they could not use enough social resources.

P1-270

Assessment of cognitive deficits in elderly subjects living in a local community using Voxel-based specific regional analysis for Alzheimer's disease (VSRAD)

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Background: The use of voxel-based morphometry (VBM) has recently become a popular tool for the early diagnosis of Alzheimer's disease. The Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD) would be a clinically useful VBM that employs MRI.
Objective: To assess VSRAD as a tool for the detection of cognitive deficits in elderly subjects living in a local community.
Methods: Cranial MRI, the mini mental state examination (MMSE), frontal assessment battery (FAB) and Beck depression inventory (BDI) were performed on 112 non-demented elderly subjects (male, $n = 36$, aged 73.9 ± 5.0; female, $n = 56$, aged 74.9 ± 5.2) living in a local community. Regression analysis was performed between a Z-score in the bilateral medial temporal areas including the entorhinal cortex and the scores of MMSE, FAB or BDI.
Results: There was a statistically significant correlation between the Z-score and the score of MMSE ($r = -0.243$, $P < 0.01$), FAB ($r = -0.241$, $P < 0.01$) or BDI ($r = 0.223$, $P < 0.05$). The atrophy (%) in the interest region showed the highest correlation with the scores of MMSE ($r = -0.38$, $P < 0.001$) or FAB ($r = -0.381$, $P < 0.001$). The atrophy of whole brain gray matter had no correlation with MMSE ($r = -0.07$), FAB ($r = -0.072$) nor BDI ($r = 0.160$). When the subjects were divided into 2 groups by 2.0 of Z-score, the specificity and sensitivity of dementia (MMSE less than 23) was 47.6% and 50%, respectively (Chi square 13.2, $P = 0.0003$). To exclude a vascular dementia, the elimination of subjects with severe lacunar lesions attained the sensitivity to 71.4%.
Conclusion: VSRAD could be a useful tool for the detection of cognitive deficits in elderly subjects living in a local community.

P1-271

Sexual and marital satisfaction: Related factors in 45–65 years old women in south of Tehran, year 2006

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Sexual Functioning is an important aspect of health likely to influence by medical conditions and health care interventions and marriage confers health benefits. Management of Sexual satisfaction and marital satisfaction in middle and elder age improve the quality of life.

Aim: To determine the relationship between sexual satisfaction, its changes, and marital satisfaction according to personal characteristics.

Methods: This is a Cross sectional study (Year 2006). The valid and reliable questioner had two main parts: 1) Personal characteristics (age, couples; age difference, education level, job, No. of children, and No. of children who lives with their parents), 2) Sexual satisfaction, its change and marital satisfaction. (Visual scale was used) The samples used in this study consisted of 161 volunteer healthy women with healthy couples, who were chosen from the public centres of low socioeconomic district in south of Tehran. We exclude the women with University degree. Descriptive and interferential statistical method (ANOVA, Scheffe, Pearson correlation) were used.

Results: 41.71% of samples were in 45–49,31.05% was in 50–54,14.28% was in 55–60, and 13.04% was in 60–65 of age group. Due to difference of samples age with their husbands' age, 28.75% was in 0–4, 50% was in 5–9, and 21.25% was in 10–25 years age difference. Average of children's No. were 4.62 ± 2.01 and average of children's No., who lives with their parents were 1.98 ± 1.37. The highest average of marital satisfaction was in 60–65, sexual satisfaction was in 45–49, and sexual satisfaction change (decrease) was in 55–60 age groups. There was only difference between marital satisfactions according to average of age group. (ANOVA, $P = 0.03$) By using Scheffe test we found this difference between 45–49 and 50–54 years age group. Also we found correlation between marital satisfaction and sexual satisfaction (pearson correlation, $r = +0.728$) and between sexual satisfaction and its change. ($r = -0.215$)

Conclusion: According to personal characteristics, we only found difference between age groups. We found during early years of post menopause, there was more marital and sexual unsatisfied group, which may be because of not still coping with the menopause situation. We suggest having more education and consultation program for this group. Also we suggest having the same study with the same goals on other socio economical group and men too, for comprising the results.

P1-272

The psychosomatic tendency of suicide among the elderly in Mie Prefecture, Japan between 1989 and 2002

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Background: The aim of the present study is to show the causative factors of suicide among the elderly (over 65) in Mie Prefecture, Japan, and we discuss the prevention of the suicidal factors among elderly group.

Methods: We investigated all records during the fourteen-year period 1989–2002 in cooperation with Mie Prefectural Police Headquarters. From all cases classified as suicides, we extracted data on age, sex, and background, and we focused suicide among the elderly group.

Results: During the test period, the number of total suicides was 5048 (3276 male and 1772 female suicides) in which that of the elderly was 1513 (691 male and 822 female suicides). The rate of suicides in the elderly group was approximately 30% of the total in all age groups. Especially, the rate of suicides in the elderly group among the women was approximately 46.3%.

In causative factors and medical history as backgrounds among elderly group, the major causative factors of suicide were suffering from physical illness and psychiatric disorders. Physical diseases were not negligible backgrounds in elderly group. Notably, cardiovascular disease and orthopedic disease were most frequent causative factors of suicide other than malignant neoplasm.

Conclusion: The improvement of home nursing and health care systems should be involved in the

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prevention of suicide among the elderly who suffering from physical illness. The patients who suffer from physical illness should be given physical and mental support. In order to prevent suicide, not only psychiatrists but also general practitioners as well as co-medical and general public staffs should be provided for the education of co-morbid depression of physical diseases and psychiatric disorders.

P1-273

Identifying suicide tendency amongst community-dwelling elderly individuals resident in Taiwan

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Objective: The purpose of this cross-sectional study was to identify the clinical and demographic characteristics of a group of elderly Taiwanese individuals who featured a tendency toward suicide.
Methods: The study population consisted of 178 community-dwelling individuals aged 65 years or over, living in one neighborhood of Ku-Shan District, Kaohsiung city, Taiwan. A variety of study measures including demographic factors, stressful life events arising during the six-month period prior to study, level of social network, the Taiwanese brief version of the World Health Organization Quality-of-Life Instrument (QOL), Geriatric Depression Scale (GDS), Mini-Mental State Examination (MMSE), Activities of Daily Living, the suicide tendency component of the Mini-International Neuropsychiatric Interview assessment and the Pittsburgh Sleep Quality Index (PSQI) were applied to study participants. We compared these variables between those who featured a tendency toward suicide and those who did not. Logistic regression analysis was applied to identify possible risk factors for suicide tendency amongst such an elderly population.
Results: Forty-three of the study subjects did not live in the study locale on a permanent basis, 11 passed away over the study duration and 25 suffered from physical disease (eg. hearing loss, severe neurological disease) and did not complete the full suite of measures. In total, 99 subjects (52 males) completed the evaluation, they featuring a mean age of 73.5 ± 5.4 years. Seventeen of the study subjects who featured a suicide tendency also revealed a tendency toward 1) experiencing financial stressors ($p = 0.021$), 2) a less-than-average social network ($p = 0.004$), 3) poor activities of daily living ($p = 0.022$), 4) poor scoring for the four domains of the QOL test (Physical, $p = 0.003$; Psychological, $p = 0.000$; Social relationships, $p = 0.000$; Environmental, $p = 0.001$), 5) poor perceptions of sleep quality ($p = 0.000$) and 6) a worse-than-average degree of depression ($p = 0.000$). The logistic regression model for study data revealed that the possible risk factor for suicide tendency was degree of depression.
Conclusion: Depression is the most-important risk factor for suicide tendency amongst later-life individuals.

P1-274

Living in aging community associated with lower suicidal ideation: a multilevel analysis from Taiwan Psychiatric Morbidity Survey (TPMS)

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This study examined the compositional factor of urbanization associated with suicidal ideation. The data was taken from the Taiwan Psychiatric Morbidity Survey, a face-to-face household survey on stratified multistage random adult sample ($N = 10135$), conducted from 2003 to 2005. All respondents clustered in 90 districts were interviewed by using of World Health Organization Composite International Diagnostic Interview (WMH-CIDI) to measure psychiatric morbidities and their risk factors. Urbanization related compositional variables of each district were obtained from another official household census carried out in 2000, which included population density, population ratio of people with college or above educational levels, population ratio of elder people over 65 years old, population ratio of people of agriculture workers and the number of physicians per 100,000 people. MLwiN version 2.02 with Markov chain Monte Carlo method was applied for multilevel logistic regression modeling. The prevalence of suicidal

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ideation were 7.5% for lifetime and 1.8% for last 12-month. In single-level multivariate logistic regression analysis, the younger generation, women, ever married, lifetime psychiatric morbidity and self-reported chronic physical conditions were significantly associated with higher prevalence of the lifetime and last 12-month suicidal ideation. Among the urbanization indexes, population ratio of elder people over 65 years old was the only one to have ecological correlation with the prevalence of suicidal ideations. This association was unchanged after adjustment of the birth cohort effect. Our study revealed that living in aging community is independently associated with lower risk of lifetime and past 12-month suicidal ideations.

P1-275

Studies on the females' death attitude and their sense of a life worth-living in Japan

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Purpose: The number of suicide cases in Japan has increased since 1990 and accounts for more than 30,000 deaths annually from 1998 through 2006. We therefore evaluated the difference of the death attitude between elder and young females.
Methods: We analyzed the responses of 60 high school teachers in Japan as to three questionnaires, i.e. the DAP (Death Attitude Profile), sense of a life worth-living and views of life and death.
Results: The results of questionnaires indicated that the elder group(40–59 years, 25 females) had significantly higher tendency in the neutral acceptance of death, the escape acceptance of death, the death as release of the soul and the view of lifetime; on the other hand lower tendency in the willingness than the young group(22–39 years, 35 females).
Conclusions: We concluded that elder high school teachers in Japan are different from young ones in an attitude toward death and the will. In order to promote mental health and to prevent suicide, it is necessary to take the age into consideration when the effective strategy is planed. Our analyses of three questionnaires suggest new insights into suicide prevention.

P1-276

Suicide prevention for the elderly

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Yuri-Town (merged into Yuri-Honjo City since 2005) had ca. 6000 population and the proportion of the elderly was 25%. In the year 1994 there were 11 suicides and 8 of them were the elderly. From 1997 we started to provide suicide prevention measures for the public nurses and inhabitants. At first we performed a Quality of Life survey of the elderly and proposed a model named ring of promoting psychological health based on the survey results. Namely the characteristics of those who feel minor stresses and are less depressive were as follows: having any hobbies, having someone to consult with, coping with their physical and/or economical problems, keeping a good sleep and rest, and having characteristically flexibility. And those who have these characteristics would less tend towards suicide. We made pamphlets with this model and distributed them to Town-dwellers. Also, we made a picture-story show to provide information about depression and suicide. Nowadays, a self-help group of senior citizens have been undertaken enlightenment activities with this picture story show. Moreover, we proposed gymnastic activities for the elderly in order to enjoy life. It was difficult to talk about suicide early on the prevention activities. So what we did was to talk with the elderly about how to enrich their lives for decrease of suicide.

P1-277

A study of the relation between the suicide attempt and the melatonin secretion rhythm in elderly patients with major depressive disorder

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Background: Aging is often associated with circadian rhythm disturbances expressed in the sleep-wake rhythm. Previous studies of sleep disturbances in elderly have disclosed that they often show disrupted

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sleep-wake pattern and nighttime sleep fragmentation, sever sleep disturbances may lead to depression and cognitive impairments. The sleep-wake rhythm is mediated by melatonin and the daily fluctuations in melatonin concentrations change in aging. Aim: We investigated the relation between the suicide attempt and the melatonin secretion rhythm in elderly patients with major depressive disorder.

Methods: Elderly patients with major depressive disorder (MDD, n = 24, M/F = 10/14; average age = 75.2, range = 65–85) and elderly patients with major depressive disorder who did suicide attempt within a week (MDD-SA, n = 20, M/F = 11/9; average age = 74.5, rang = 65–83) were recruited. In every participant, five days actigraphy measurements were calculated for a quantitative description of the sleep-wake rhythm and the daily rhythm of serum melatonin secretion level were measured. The MMSE and the HRS-D-17 were also measured for every participant. These data were compared with each group and normal control elderly participants group (Control, n = 20, M/F = 5/15; average age = 74.7, range = 65–84).

Results: There were significant differences between MDD and MSD-SA in the sleep-wake rhythm including Number of awakenings, Sleep percent and Wake time after sleep onset (in-bed-period), Duration of sleep episodes and Wake percent (out-of-bed period). MDD-SA was more disrupted quantity and quality of the sleep-waking cycle than MDD. In melatonin secretion level, in comparison with Control, MDD was more significant attenuated AUC for area under the curve of serum melatonin secretion for 24 hours and Peak time for the corresponding to the highest mean melatonin level. MDD-SA was found more significant deteriorated in AUC, Peak time, Nocturnal-AUC for melatonin secretion in the nighttime from 00:00 to 04:00 and Daytime level for melatonin secretion from noon to 16:00 than Control and moreover AUC than MDD. The MMSE and the HRS-D-17 scores in MDD-SA were significant lower than those in MDD.

Conclusion: These findings suggest that poor quality of sleep-wake rhythm and cognitive impairments in MDD will relate to attenuation of melatonin fluctuations. And these more changes in MDD will be associated with their suicide attempt.

P1-278

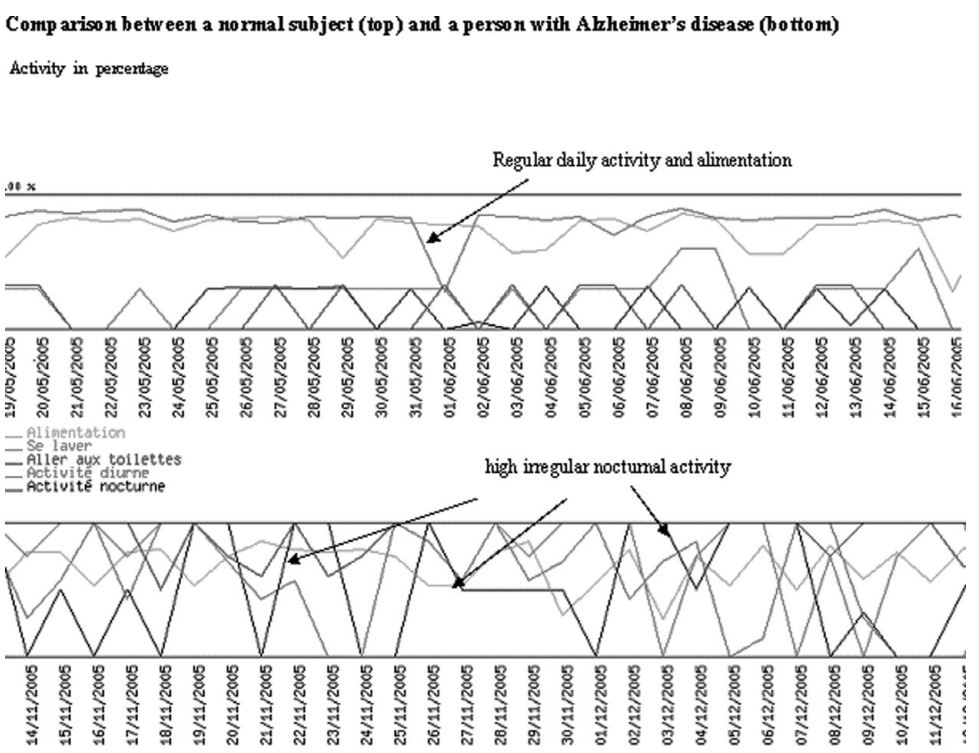
A study of reality orientation with the intervention of a humanoid robot named QRIO

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An increase in the number of elderly dementia patients requiring medical and nursing care and a serious decrease in the number of staff required for this care are anticipated in Japan. Robots are presently used for assisting in physical labor in care settings, but they have seldom been used in psychiatric-related approaches. Therefore, we decided to attempt Reality Orientation (RO) with the assistance of a humanoid robot QRIO for elderly dementia patients, and we assessed its clinical effectiveness by using various scales. To determine the effectiveness of QRIO-assisted RO, 31 elderly dementia patients with a FAST level of around 5 were selected and were divided into three groups: Group A, in which QRIO-assisted RO was implemented; Group B, in which conventional RO using only humans was implemented; and Group C, in which recreational therapy and group training were implemented with no RO. For subjects in groups A and B, a total of ten RO sessions of < 1 hr each were held on a weekly basis. For the assessments, a specially created survey on the patients' impressions of the robot, Holden Communication Scale, NM Scale, N-ADL Scale, HDS-R, and Tokyo University Observation Assessment Scale were conducted. As results, subjects in Group A got to perceive QRIO as a creature and were more active during RO in relation to those in other groups, and their high levels of interest, attention and concentration during RO contributed to the maintenance of communication ability and cognitive function. After 2 and a half-month interval, however, subjects in Group A lost their positive affection for the robot, and they returned to their original level before starting the RO program. Thus, it is very important to continue the RO program for such elderly patients with dementia. In order to clarify whether such positive affection could be exclusively attributed to the humanoid robot or not, we will further conduct the RO with the assistance of a pet robot AIBO for elderly dementia patients. This examination should provide us the mechanistic insight into the positive affection. Furthermore, if other type of robot is also effective, a continuous RO program will be much more easily performed with the assistance of various types of robots.

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P1-279

P1-279

A new approach of home surveillance for autonomous in home patients with mild dementia

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Background: In France from people over 75, only 5% have bad health and at 80 still 73% are living at home,1 4% with the family and only 13% in institutions. Around 700 000 are dependent and by 2020 this number will increase until 25%. The number of people at home with dementia in its early states is around 90.3%. There is an important interest in detecting autonomy loss in this vulnerable group in order to implement opportune aid, as a key solution to keep them at home in good conditions. We propose an innovative method that detects electrical activity from the most common used home tools and from room lights and then translates the information into the probability of having done the main activities of daily living (ADL).

Objective: We did a pilot study on a new surveillance method of activity at home for people living alone and we wanted to see if the system was able to differentiate between normal subjects and a person with moderate Alzheimer's disease (MMSE 20).

Method: 13 volunteers over 75 years participated. They had to live alone and be independent for ADLs, have a reference person and a physician. The exclusion criteria were: having severe cognitive impairment (MMSE < 16), being out of home very often and being to ill or susceptible of being hospitalised at short term. ADLs are represented in percentage, resulting from using an electric tool at a specific hour according to the person's habits. The system was installed and after a week it was verified by an interview, if the registered activity corresponded to the real ADL done.

Results: Mean study period was 3.4 months. Activity is shown as: daily, nocturnal, using WC, eating and bathing. All subjects have a personal regular pattern, but the AD patient activity with an impact on her alimentation. In her medical records this information absent, because she always referred being fine. The patient lost weight, fell and broke her hip a few months after the study.

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Conclusion: This non invasive method can be a solution to home surveillance for this population at risk and is cost effective.

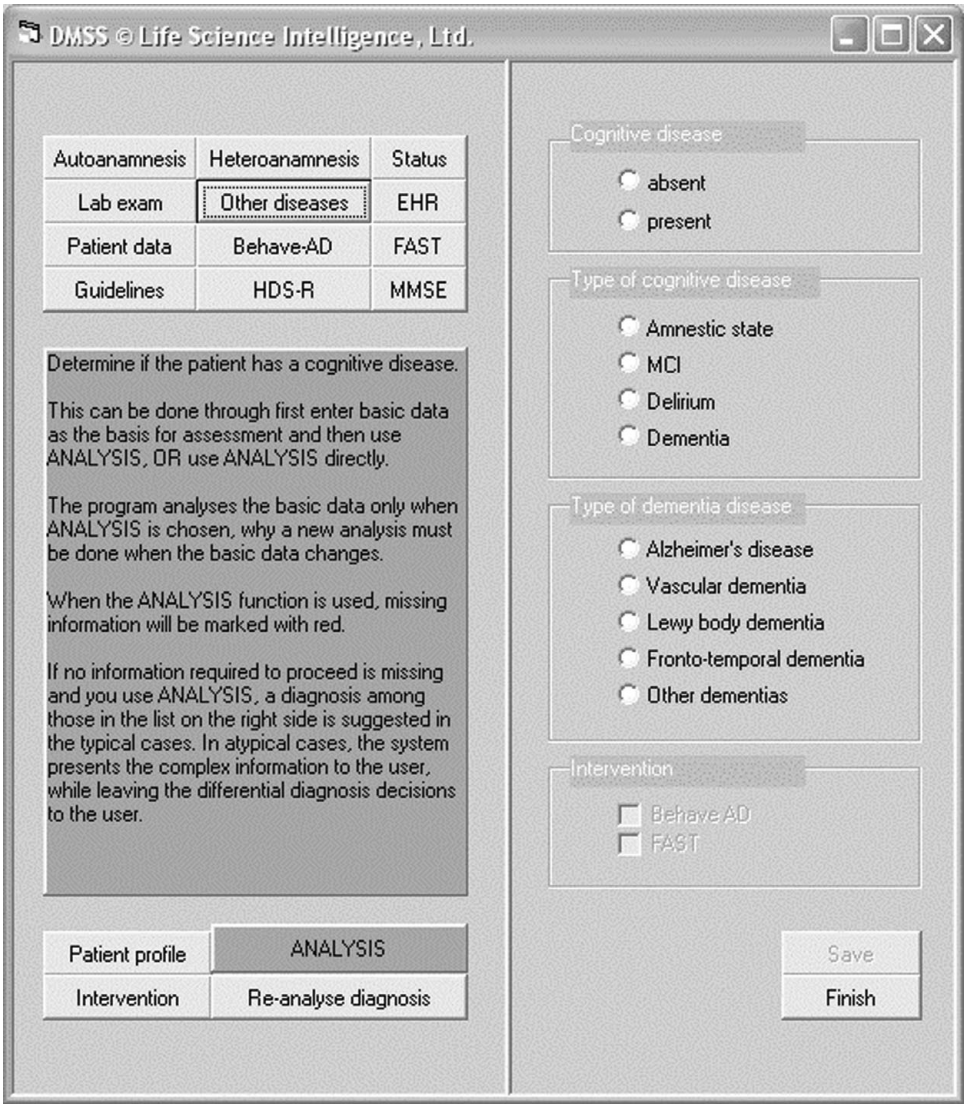
P1-280

DMSS – Dementia management and support system for interactive reasoning and decision-making

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An evaluation is currently being made of the initial Japanese prototype version of a dementia management support system (DMSS-SJ) based on a Swedish decision-support system under development (DMSS). The purpose of the DMSS-systems is to support clinical diagnostic reasoning in the investigation process by providing guidance to what evidence is needed, which clinical guidelines and cognitive screening tools to use and to analyse evidence in different perspectives, i.e., sets of clinical



P1-280

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guidelines, using artificial intelligence techniques based on logic. Support is provided to both experienced physicians and less experienced, in both typical and atypical cases of cognitive disorders. The purpose of the current evaluations is partly to investigate the need for adjustments of the system to the Japanese society. In the initial pilot study, the system's compliance with clinical practice in Japan, compliance with clinical guidelines and compliance with decisions made by experts were investigated. The study design was qualitative, in order to capture as many aspects as possible related to the use of the system, with interviews and observations of the system in use. Eight experienced physicians with expertise in different fields related to cognitive disorders participated and a total of 26 patient's cases. The patients' clinical diagnoses included a range of both common and rare diagnoses. The results of the pilot study indicate important aspects and amendments which need to be addressed and handled before proceeding further with more extensive evaluations with the system integrated in clinical practice in Japan. The results include differences in terminology, usage of clinical guidelines and screening-tools, and a difference in how they perceive the interactive reasoning compared to the results from Swedish evaluations. The results indicate also similarities, primarily in reasoning procedure, the logistics of the investigation of dementia and the major purposes of a decision-support and management system for dementia care. To primary care physicians, support for diagnosis is desirable, however, the major need for support lies in support for assessment of how to care for the patient, interventions, primarily other than drug treatment and determine the level of aid the patient need in relation to the care provided by Japanese health care system. DMSS is being adjusted and developed based on the results.

P1-281

Effect of cultural factors on mental health of aging South Asians in Canada

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Despite the fact that South Asians are the second largest visible minority group in Canada, little research exists on their mental health, especially on the aging adults. This research is aimed at studying the impact of cultural factors on mental health of aging South Asian immigrants in Canada. Data were collected from a telephone survey with a random sample of 220 aging South Asians aged 55 years and over. Hierarchical multiple regression analysis was used for examining the effects of sociodemographic, physical health, and cultural factors on mental health. A second set of multiple regression analysis was used to determine the predictors of mental health on four mental health subscales (Vitality, Social Functioning, Role-Emotional, Mental Health). The findings showed that a higher level of social support, better physical health, and greater English competency were associated with better mental health, however religious affiliation was found to have negative effect on mental health. Religion was the only cultural variable significant in all four mental health subscales regression analysis. A multitude of factors influence the mental health of the aging South Asians, which should be addressed when developing intervention to address their mental health needs.

P1-282

Efficacy of donepezil for memory and cognition dysfunction associated with Alzheimer's disease and factors related to its efficacy

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Objective: We valuated the efficacy of the treatment for Alzheimer's disease (AD) donepezil (DPZ) and factors related to its efficacy.
Subjects: Enrolled in the study were 175 patients diagnosed with AD by DSM-IV, including 137 treated with DPZ and 38 who visited the outpatients' clinic of this hospital before the launching of DPZ.
Methods: St. Marianna University's Computerized Memory Test consisting of five tasks (IVR, DVR, DVRG, MST, and MFT) were conducted before and about 48 weeks after starting treatment. Patients were divided into two groups, one with improvement and the other without improvement, with respect to tasks which showed significant improvements. Binomial logistic regression analysis was conducted to determine factors related to the efficacy of DPZ.

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Results: Changes in MST, which reflects the power of attention and concentration, showed significant differences between the treated and non-treated groups. Patients with improved MST and those with aggravated MST showed significant differences in ages and HDS-R scores.
Conclusion: DPZ failed to inhibit the progression of word memory dysfunction but did inhibit impairment of the power of attention and concentration. The drug's efficacy was related to the start of treatment at relatively low ages and high HDS-R scores.

P1-283

Cholinergic pathways involvement and deteriorated attention: Are 'asymptomatic' white matter changes or infarctions really asymptomatic?: The Osaki-Tajiri Project

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Background and purpose: Many findings on the relationship between white matter hyperintensities (WMHs) as shown by MRI and cognitive functions varied due to different methodology. In previous studies, periventricular (PVH) or deep white matter hyperintensity (DWMH) has been used for assessing WMHs independent of specific neuronal pathways. The Cholinergic Pathways Hyperintensies Scale (CHIPS) (Bocti et al), a semiquantitative MRI visual rating scale to assess WMH regarding cortical cholinergic pathways, was firstly applied to assess WMH with Alzheimer's disease. Since the lesions involving the cholinergic pathways may deteriorate attention and the function was easily affected by sampling method, we studied the relationship between damage on the cholinergic pathways and attention using a less-biased community database.
Methods: We performed community-based study for all older residents in 1998 and 625 subjects were randomly selected for MRI. After excluding those with brain tumors, mood disorders and Alzheimer's disease etc, 507 subjects were included in this study. Mini-Mental State Examination (MMSE) was performed to assess global cognitive function, and Digit Symbol (WAIS-R), digit span, word fluency were examined as attention tasks. The subjects were divided into two groups according to the presence of cerebrovascular disease (CVD). The CVD(-) group ($n = 358$, non-demented) was divided into three subgroups according to age and education. We scored CHIPS, PVH and DWMH and examined the correlations between MRI measures and cognitive functions. The CVD(+) group ($n = 150$) was divided into two subgroups according to involvement of the cholinergic pathways. Among the subgroups and CVD(-) group, differences of cognitive functions were examined.
Results: For the CVD(-) group, there was a correlation between CHIPS and Digit Symbol only in the 80 y + group ($\tau = -0.243$, $p = 0.009$), while PVH and DWMH showed no significant correlations. For the CVD(+) group, the cholinergic involvement subgroup showed significantly lower scores on Digit Symbol and word fluency compared with other subgroups regardless of no MMSE differences. This difference remained significant on word fluency when subjects with strategic lesions such as thalamus, caudate head and internal capsule were excluded.
Discussion: CHIPS may be relevant to attention in older old non-demented subjects. Cholinergic pathways involvement by CVD may specifically deteriorate attention regardless of global cognitive function.

P2-1

Alzheimer's disease: Perceptions of family interaction and burden by primary caregivers

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With the increasing life span of the elderly population the world over, Alzheimer's disease has become an issue of global concern. While research in this area has mostly focused on its neuro-biological aspects, the families of these persons and the implications of having such a person as its member has not been a much investigated domain particularly in the Indian context. Understanding the intra familial dynamics in such families besides the burden faced by them in several aspects of their life would promote better psycho-social management of these patients, thereby ultimately promoting their quality of life. This study was hence planned to investigate the nature of interaction pattern and the burden of caring experienced by the families of persons with Alzheimer's disease. It uses a descriptive

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cum diagnostic design and was carried out with the families of all 64 persons registered with the Urban Community Dementia Service at Kalamaserry, India. The instruments administered were the FAST (Functional Assessment Staging Test, Reisberg et al., 1984), the FIPS (Family Interaction Pattern Scale, Bhatti et al., 1982) and the Family Burden Scale (Pai and Kapur, 1981). Data analysis reveals that the interaction pattern in the majority of these families was categorized as being < low < particularly with regard to leadership, role, cohesion and communication. Family burden experienced was < high < in terms of disruption of family interaction, leisure and routine family activities. The association among various dimensions was tested using various statistical procedures and these findings will be elaborately presented in the conference. The implications for better psychosocial management of families with such persons have also been discussed in the paper.

P2-2

The efficacy of galantamine on the attention and the frontal function of the patients with dementia of Alzheimer type

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Objective: To prove effect of galantamine on attention criteria in Alzheimer's disease and Vascular dementia patients.

Method: Ninety-nine AD patients (mean age: 73.4 ± 8.4yrs) who show attention deficit were recruited. AD patients and VaD patients were screened by NINCDS-ADRDA and NINDS-AIREN respectively. All subjects were not hospitalized. The subjects underwent clinical tests of MMSE, S-IADL, NPI-Q, GDS, Visual CPT, Visual Span, Color-trail making test, and Stroop test. Statistical methods were t-test and Wilcoxon test.

Results: In MMSE, both groups showed improvement in attention among 5 criteria.($p < 0.05$) In S-IADL and NPI, patients show improvement, but non-significantly. Changes in SCNT score of VaD patients showed that commission error, and reaction time improved significantly ($P < 0.01$). Subgroup analysis showed that moderate group in VaD showed more improvement in NPI and reaction time.

Conclusion: This study showed that Galantamine has potential benefit to AD patient in attention domain because it showed the efficacy in choice and simple reaction time. For VaD patients who have attention deficit, Galantamine also might have potential benefit to reduce reaction time. And I think that all this efficacy is coming from the mechanism of galantamine which stimulates nicotinic receptor of AD and VaD patients.

P2-3

Food diet with nucleic acids

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It is well know that malnutrition is an important cause of death. The purpose of this study is to demonstrate that a balanced diet with carbohydrates, proteins and very little fat provides more brightness and energy to the brain cells of sick people. I have been interested in studies of Dr. Arthur Kornberg and Benjamin Frank about the production of nucleic acids to preserve health and restore it rhinitis damaged. At the Alzheimer's nursing home in Monterrey Mexico, we have worked for a year whit two groups of 35 patients of both sexes, aged between 60 and 90 years old, all of which had Alzheimer's disease and serious mental and physical problems. Group A were treated in their homes with an restricted diet. As a result, the sickness rapidly progressed and there was no hope for improvement. Group B were treated at our nursing home with a balanced diet and the result was a surprising improvement in their mental and physical aspects. Their skin became hydrated and healthy and thus their body temperature was controlled, and they were also more resistant to infections. Additionally, they slept better and the constipation disappeared. Our study shows that eating healthy food is very important to getting more energy to the cells, as well as the need to restore the damaged nucleic acids to create their own, better quality DNA and RNA.

P2-4

Validation of ASHA FACS – functional assessment of communication skills for Alzheimer's disease population

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Since the beginning of Alzheimer's disease (AD), language problems interfere in engagement, social life and individual's protection and have impact on one's independence. Information about such alterations, obtained from a natural context, contribute for diagnosing AD. Limitation on the ability to communicate functionally, that is, to utter and understand a message independently and efficiently in response to everyday demand is one of the most important complaints of AD relatives and caregivers. Therefore, there is a need for providing an instrument in Portuguese that assess communication in a natural context for diagnosing and following patients with AD and their relatives/caregivers. This study aimed to validate the Functional Assessment of Communication Skills – ASHA FACS for a Brazilian population. The ASHA FACS is composed of four domains: Social Communication, Communication of Basic Needs, Reading, Writing and Number Concepts and Daily Planning. The scale was translated and adapted into Portuguese. Then, 32 mild AD patients, 25 moderate AD patients and 51 elderly without dementia were examined. The AD patients and the control group answered the Mini-mental State Examination (MMSE), the Geriatric Depression Scale (GDS) and Alzheimer's disease Assessment Scale (ADAS-cog). The ASHA FACS assessment was answered by their relative/caregiver. The scale internal consistency, its inter and intra-examiners reproducibility and scale's criterion validity were researched by correlation with Adas-cog. The sensitivity and specificity were also researched. Statistical analyses indicated that the ASHA FACS has excellent internal consistency (Cronbach's Alpha = 0.955), test-retest reliability (interclass correlation coefficient [ICC] = 0.995; $p < 0.001$) and inter-examiners (ICC = 0.998; $p < 0.001$). Besides, it showed excellent criterion validity when correlated with Adas-cog. The ASHA FACS scale showed good sensitivity (81.4%) and specificity (84.3%) values once it is an ecological and broad evaluation. The ASHA FACS Portuguese version is a valid and reliable instrument to verify communication alterations in DA patients. This scale fills an important gap of efficiency indicators for speech language therapy in our country.

P2-5

The neuroprotective effect of apoliporotein E on the oxidative stress in Alzheimer's disease

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Objectives: The aim of this study was to know whether apolipoprotein E (apo E) had neuroprotective effect against oxidative stress in Korean patients with dementia.

Methods: The subjects were consisted with 38 patients with dementia of the Alzheimer's type and 41 normal aged controls with age over 60. The clinical data were obtained by structured interview and medical records, plasma apo E level and total antioxidant capacity (TAC) were measured, and the severity of dementia (MMSE, CDR, GDS), activities of daily living(ADL, IADL) and depression(Geriatric Depression Scale) were evaluated using various rating scales.

Results: 1) The mean(± S.D.) plasma level of apo E in dementia was 4.71 ± 1.96 mg/dl,and that of TAC was 2.87 ± 0.16 mmol/L. 2) The only factor influencing on the plasma apo E level in dementia was scores of the Geriatric Depression Scale ($p < 0.05$). However, variables such as age, severity of dementia, activities of daily living, and plasma TAC level did not correlate with apo E. 3) There were no statistically significant differences between variables with normal apo E and those with elevated apo E.

Conclusion: This study could not support that apo E had neuroprotective effect against oxidative stress in dementia.

Keywords: Dementia, Apolipoprotein E, Total antioxidant capacity, Geriatric Depression Scale.

P2-6

Longitudinal study on dementia in an urban community of Beijing City in two decades

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Objective: To investigate prevalence of dementia and related factors among people aged 65 and over in an urban of Beijing City based on two surveys carried out in the same area both in 1986 and 1997, and to

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analyze the dynamic change of dementia prevalence in two decades.

Method: Using cluster sampling, 1562 elderly aged 65 and over were interviewed by a set of fully structured assessments in a one-stage process developed by the 10/66 group for dementia in an urban district of Beijing City. Dementia patients were diagnosed in accordance with ICD-10.

Results: The prevalence rate of dementia among the elderly people in 2004 was 4.1%, which was similar to 1997's result (3.2%). There were no statistical differences among the three surveys on prevalence of moderate and severe dementia (2.8%,1.9% and 1.8%). The prevalence rates of dementia were increased with age. In 2004, the patients with AD were much more than those with VD, which was similar to the 1997's result and dissimilar to the 1986's result.

Conclusion: The three surveys in the same district during two decades show that the level of dementia prevalence is rather stable. The prevalence of dementia increase with age, In the recent 10 year, AD has been the most common subtype of dementia in urban Beijing.

Keywords: Dementia Prevalence Alzheimer's disease Vascular dementia.

P2-7

Domain-specific cognitive functions associated with social engagement: Takashima study in Japan

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Early detection of Alzheimer's disease is very important since the currently available pharmacological treatments work most effectively if used early in the course of disease. However, because of the gradual onset of this disease, early symptoms are often ignored or missed. It would be useful if we could 1) know the normative levels of social engagement (i.e., physical and non-physical hobbies and social activities) especially among the oldest old for whom this type of data is still sparse compared with those among the younger old, and 2) identify commonly conducted activities among the elderly which are strongly associated with either overall or domain-specific cognitive functions. This would help family members be aware of any changes associated with potential cognitive decline through the changes in the frequency of engagement in specific activities. We conducted face-to-face interviews with age stratified randomly sampled non-institutionalized elderly aged 65 and over living in Takashima County in Shiga prefecture in Japan, with over-sampling those aged 85 and older. We defined normative subjects as those who 1) are free from any disabilities in Activities of Daily Living (ADL), 2) had Mini-Mental State Examination Scores $\geq$21, and 3) had $\leq$2 disabilities in Instrumental ADL (IADL). Among the 303 normative subjects with the above inclusion criteria out of 391 subjects who completed the interview, we examined the frequencies of engagement in various activities and compared them by age group. We created three index scores indicating the total levels of engagement in physical hobbies, non-physical hobbies and social activities separately. The association between these index scores and the cognitive domains, which include working memory and attention, learning, memory, psychomotor speed, executive functions, language, and visuo-spatial abilities, were examined using Generalized Linear Models. Even after controlling for various confounders including age, sex, years of education, depressive symptoms, number of prescription medications, and number of IADL disabilities, higher engagement in social activities was found to be associated with memory and executive functions, but not other domains, and higher engagement in non-physical hobbies were associated with all domain-specific cognitive functions. Providing the information on specific activities associated with cognitive functions could aid in early detection of AD in the community.

P2-8

Grip strength and incidence of dementia in a Japanese population: RERF's adult health study

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We studied association of mid- to late-life handgrip strength to dementia, specifically Alzheimer's disease (AD) and vascular dementia (VaD). Data are from the Radiation Effects Research Foundation's Adult Health Study, a prospective study based on biennial health examinations. A total of 2286 non-demented subjects, aged 60 years or older at baseline examination, were screened for dementia between 1992 and 2003. Diagnosis of dementia was made based on the DSM IV criteria. A total of 206 new cases of dementia (AD: 107, VaD: 54, Mixed: 25) were diagnosed during the average six years of follow-up. For 2020 subjects, grip strength at baseline examination of the dementia incidence study was measured, and 1207 subjects had their grip strength measured in 1970–1972. Comparison of age-specific mean grip strength between subjects who did and did not develop dementia showed mean grip strength at late life was lower among subjects who developed dementia, but the difference of grip strength between these two groups at mid life was smaller than that at late life. We analyzed risk factors of dementia and its subtypes at baseline examination, including sex, age, education, blood pressure, history of DM, and stroke. All dementia showed significant association with sex, age, education, and stroke history. Age and education were related to AD, and sex, age, blood pressure, and stroke were related to VaD. After adjusting for these confounding factors, we analyzed the effects of grip strength change through mid to late life. Incidence of dementia was significantly associated with loss of former grip strength, independent of potential confounding factors. Association with loss of grip strength was similar in AD and VaD. These results support the notion of regular exercise for improvement of physical and musculoskeletal fitness to prevent onset of dementia.

P2-9

Biochemical analysis of amyloid beta in M-CSF deficiency (op/op) mice brain and serum

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Alzheimer's disease is characterized by excessive deposition of amyloid beta peptide (Aβ peptide) in the brain. AD brain shows increased neuronal expression of M-CSF in proximity to Amyloid deposition. M-CSF in cerebrospinal fluid from AD patients was elevated. Phagocytosis of Aβ on microglia was accelerated by M-CSF stimulation. M-CSF plays a role in the differentiation, proliferation and survival of monocyte-macrophage cell lineage as well as microglia. The precise roles of M-CSF involved in amyloid beta deposition and accumulation are unknown. Osteopetrotic (op/op) mice are absence of macrophage colony-stimulating factor (M-CSF) due to an autosomal recessive inactivation mutation of the M-CSF gene. Previously, an immunohistochemical study was reported that amyloid beta deposition was found at one month old op/op mice brain, and M-CSF injection alleviated the amyloid deposition accompany with microglia partially recovered the numbers at the brain. Here, we evaluate brain and serum amyloid beta in the op/op mice at one month age. In contrast, we could not found amyloid deposition of the op/op mice at one month age by immunohistochemistry. We failed to detect Aβ in the SDS and formic acid brain extract of op/op mice with immunoblotting. The level of brain CHAPS soluble Aβ in op/op mice analyzed by ELISA is similar that of normal litermate. Interestingly, we found significant decline of Aβ40 in the serum of op/op mice, though the level of soluble Aβ was not changed in the brain. In conclusion, we could not found endogenous amyloid deposition or accumulation of soluble/insoluble Aβ of the brain, but the serum Aβ was decreased in the M-CSF deficiency (op/op) mice.

P2-10

Activities of daily living: Outcome during three years in donepezil treated Alzheimer's patients

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The Swedish Alzheimer Treatment Study (SATS) is an open, 3-year, multicentre study in a routine clinical setting. The objective of this poster is to analyse and present the outcome of longitudinal change and possible subgroups with respect to Activities of daily living (ADL) function measured by different scales (PSMS, FAST and IADL) in patients treated with donepezil for three years (n = 435).

The patients were assessed with several rating scales including ADL at baseline and every 6 months for a total period of three years. IADL scores were compared to the expected change in untreated patients based on a mathematical model by Green et al. A two-step cluster analysis was performed to reveal any natural groupings (clusters) of the patients based on the ADL scores at baseline.

After three years of donepezil treatment the total mean change in PSMS score was 3,2 ± 3,6 and in FAST 1,8 ± 2,1 points. The three-year change in IADL-score was 6,1 ± 5,4 points whereas the expected change using the mathematical model was 15,8 ± 5,6 points.

The different ADL scales were linearly correlated with each other and with cognition measured by MMSE and ADAS-cog at all assessment points. However, the strength of the relationship increased over time with p-values < 0,000 from 18 months and onwards. The three scales showed no significant difference between gender at baseline but after three years the IADL mean decline from baseline was significantly worse among women.

A cluster analysis showed two subgroups that significantly differed in age ($p < 0{,}000$), duration ($p < 0{,}05$) and cognition ($p < 0{,}000$) at baseline. No significant difference in gender, apoE4-carriers or mean dose of donepezil was observed. The two subgroups also deviated significantly in the long-term outcome of ADL score particularly measured by the PSMS scale ($0{,}000 < p < 0{,}05$).

Increasing strength in the linear correlation between the three ADL scales as well as cognition was observed during the three years of the study. The IADL scale showed a decline of function less than expected compared with untreated patients in a mathematic model. Long term IADL scores deteriorated significantly more in the female gender than in the male.

Cluster analysis based on ADL scores at baseline, identified two subgroups: with different mean age and cognitive ability and dissimilar rate of change in functional decline predominantly shown by the PSMS scale.

P2-11

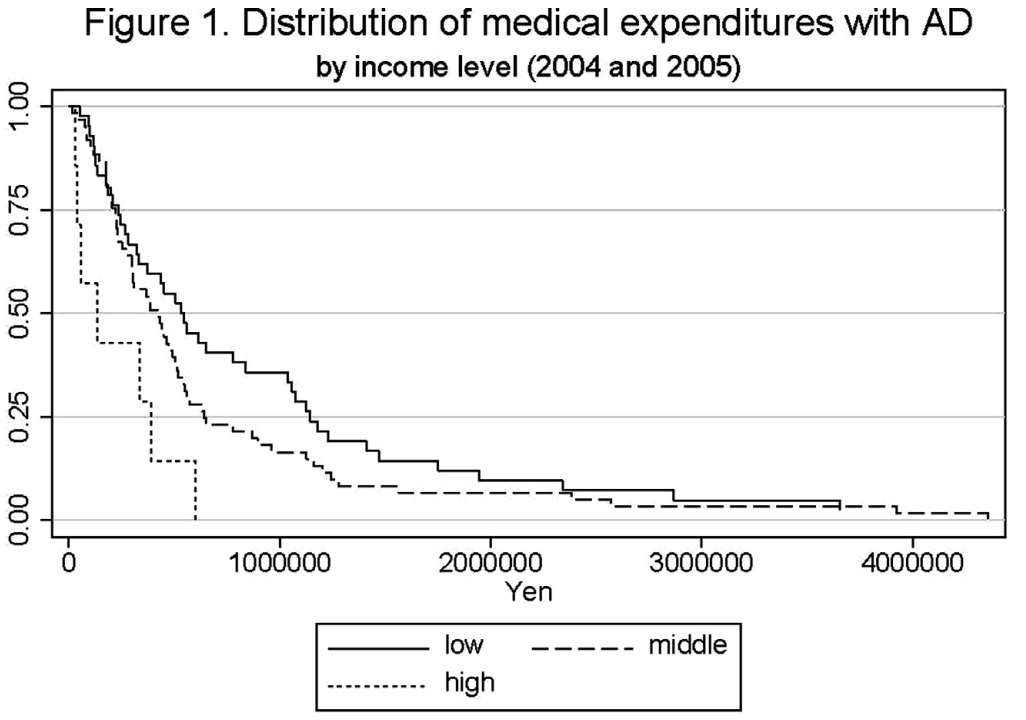
Medical expenditure of patients with Alzheimer's disease: Do the rich spend more?

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The purpose of this study was to investigate the relationship between medical expenditure of older people with Alzheimer's disease (AD) and income in Japan. Data were derived from past two-year medical claims and master data of the National Health Insurance (NHI) in a medium-sized city in Aichi prefecture. Medical claims contained medical expenditure, copayments, and monthly hospital visits; master data consisted of basic information, such as sex, year of birth, and income. Moreover, the NHI medical claims reported ICD 10 codes only in May. From these data, we extracted 55 patients with AD who visited the doctor in May 2004 or 2005, and we totaled the patient's medical expenditure for 1 year. Total annual medical expenditure was on average 711,502 yen, ranging from 15,480 to 4,651,330 yen. The average age was 82.3 years, ranging from 66 to 93 years. 27.3% of patients were male, 28.2% had at least one hospital stay, 98.2% visited an outpatient department at least 1 day per year, and 45.5% visited a pharmacy. 38.2% of patients were members of a local resident tax-exempt household (low income), 6.4% had taxable income of >1.45 million yen (high income), and 55.4% were considered middle income. Figure 1 shows the estimated hazard function of medical expenditure according to income. The median medical expenditure was 530,920 yen in the low-income group, 421,100 yen in the middle-income group, and 133,160 yen in the high-income group. We analyzed the difference in medical expenditure [an explanatory variable was log(expenditure)] using a panel data method, because this data contained fifty five patients with two periods. Since the F test was 2.32 ($P = 0.0024$), the Breusch-Pagan test was 7.74 ($P = 0.0054$), and the Hausman test was 9.01 ($P = 0.6206$), we chose the results of the random effects model. The result showed that if patients had inpatient visits, or were aged 60–70 years, medical expenditure increased by 70 or 50%, respectively. Moreover, in the high-income patients, medical expenditure decreased by

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P2-11

46%. This means that the low-income patients were not prevented from visiting hospital, and they were treated by a doctor.

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P2-12

Validity of a 15-minute multi-domain computerized cognitive battery for moderate to severe impairment

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While several paper-based screening tools exist for assessment of moderate to severe dementia, there is a need for more brief but comprehensive assessment of cognitive function in these individuals for purposes of longitudinal tracking and monitoring of treatment effects. The objective of this study was to evaluate the validity of a 15-minute computerized battery for cognitive assessment of moderate to severe cognitive impairment in the elderly. 97 older adults (age: 76.6 ± 11.0; education: 10.4 ± 4.6 years; 13% computer users) completed the 15-minute technician-administered computerized Moderate-Severe Impairment Battery (MODS; NeuroTrax Corp., NJ) assessing orientation, memory, executive function, visual spatial processing, and verbal function. Participants received an expert clinical diagnosis of cognitively healthy ($n = 4$), MCI ($n = 24$), or dementia ($n = 55$) and were staged according to the Clinical Dementia Rating (CDR) scale. Overall MODS score was compared across CDR stages by between-groups ANOVA. The Pearson correlation between MODS score and CDR sum of the boxes (CDR-SB) was computed. Effect sizes (Cohen's *d*) were computed for differences in MODS score as a function of caregiver-reported cognitive symptoms and activities of daily living (ADLs). MODS performance was significantly poorer with increasing CDR stage ($p < 0.0001$), and all pairwise comparisons were significant ($p < 0.004$); there were no differences in

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age ($p = 0.47$) or education ($p = 0.36$). A correlation of 0.71 ($p < 0.0001$) was found between MODS score and CDR-SB. Large effect sizes were obtained for caregiver-reported difficulty managing finances ($d = 1.25$) and medications ($d = 1.03$); there were medium effect sizes for decline over 6 months ($d = 0.67$) and difficulty remembering ($d = 0.54$) or finding the right words ($d = 0.46$). In conclusion, a 15-minute computerized battery demonstrates good discriminant validity across CDR severity stages, high construct validity, and meaningful relationship with ADLs. Thus the Moderate-Severe Impairment Battery is valid and practical for tracking change in patients with impaired function.

P2-13

Validation of the 7 minute screen for the detection of early-stage Alzheimer's disease

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Objective: The 7 Minute Screen (7MS) is a screening battery for use in the primary care setting to identify individuals with a high probability of Alzheimer's disease (AD). This test is consisted of four pre-existing cognitive tests (temporal orientation, enhanced cued recall, clock drawing, and verbal fluency), each measuring a different aspect of cognition. The present study is designed to examine the predictive validity of the 7MS to distinguish between patients with early-stage AD and healthy control subjects.

Methods: Sixty-three patients who were diagnosed as having probable or possible AD (NINCDS-ADRDA criteria) and 91 community-dwelling elderly individuals of comparable age, sex distribution, and education were administered the 7MS and other cognitive screening batteries. All patients were rated Clinical Dementia Rating (CDR) 0.5 to 1, categorized into early-stage AD and all participants obtained a score of less than 6 for Geriatric Depression Scale (15-item version).

Results: Mean scores for patients and control subjects on all four tests were significantly different. Exploratory factor analysis showed a strong unidimensional structure. Correlation analysis indicated high concurrent validity between the 7MS and existing standard cognitive screening batteries (e.g., MMSE). The sensitivity for the early-stage AD was 90.5% with a specificity of 92.3%. When administered to population base rates with high (20%) and low (5%) prevalence, the positive predictive value (PPV) was 91.1% and 68.4% with a negative predictive value (NPV) of 97.6% and 99.5%, respectively. In correlation analysis and multiple regression analysis, demographic effects (age, sex, and education) were not significantly associated with the total score of the 7MS in control subjects.

Conclusions: The results showed that the 7MS had a high level of sensitivity, specificity, PPV, and NPV. We also found that the 7MS was not affected by demographic characteristics. These findings demonstrated that the 7MS was useful screening tool for discriminating patients with early-stage of AD from intact individuals.

P2-14

Systemic cytokines; BPSD and the progression of Alzheimer's disease

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There is increasing evidence to suggest that centrally acting cytokines have an important role to play in the development or progression of Alzheimers disease (AD). However, there is also evidence to show that the production of systemic cytokines by tissue macrophages can induce cytokine synthesis within the brain. Under normal circumstances the systemic production of cytokines leads to sickness behaviour such as apathy, fatigue and appetite suppression. However, we hypothesise that problems may arise in AD where microglia are already in a primed state and in this situation the presence of a second stimulus, such as a systemic inflammatory event leads to an exacerbation of the neurodegenerative process and cognitive decline in AD subjects. We have completed a number of studies that lend support to this hypothesis. Animal studies have shown the activation of primed microglia by peripheral endotoxin challenge, intended to mimic a peripheral infection, leads to an increased secretion of central cytokines and, in addition, there is evidence of neuronal loss following this challenge. In a previous clinical pilot study we have shown that AD patients experiencing systemic inflammatory events show a markedly greater rate of cognitive decline compared to subjects with no intervening

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systemic inflammatory events. We have now completed a larger 6 month study examining the longer term consequences of peripheral pro-inflammatory cytokines on cognitive decline and the appearance of BPSD in 300 AD subjects. Patients were examined on 4 occasions 2 months apart over a 6 month period. At each visit a history was taken of the number and nature of systemic inflammatory events over the preceding 2 months; the presence of neuropsychiatric features using the Neuropsychiatric Inventory and cognitive function using the ADAS-Cog. At each time point a blood sample was taken for peripheral cytokine production and markers of inflammatory disease. We present data showing evidence that a number of BPSD are related to the peripheral production of pro-inflammatory cytokines and that these symptoms are identifiable as sickness behaviour. Furthermore, the production of peripheral pro-inflammatory cytokines is associated with a greater rate of cognitive decline in AD subjects supporting the hypothesis that systemic inflammatory events, principally infections, are a driving force in the neurodegeneration of AD.

P2-15

Enumeration in Alzheimer's disease and other late life syndromes

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In typical visual enumeration tasks, people have to determine the number of objects present in their visual field. For normal subjects, response times increase little for enumerating up to 3 or 4 items (known as subitization) whereas they increase substantially and linearly beyond this range (known as counting). This pattern does not change with normal ageing. In Alzheimer's disease (AD), subitization span has been reported to be decreased and counting rate appears to be slowed. If confirmed, this would be a rare qualitative difference between AD and normal ageing. Our objectives were to test enumeration deficits in early AD and compare these with normal older people, those with depressive disorder and vascular dementia. We hypothesised that: 1. Subitization span and counting rate would differ between AD and normal older people 2. These differences would be specific to AD. Four groups were recruited; those with AD, major depression, vascular dementia, and normal older people free from cognitive impairment. Cognition, mood, processing speed and visual attention were assessed and each participant completed 2–3 blocks of 45 enumeration trials requiring decisions on how many items from 1 to 9 were present in a visual display. Groups were well matched for age and years of education. AD patients (n = 19) were significantly slower overall than both normal controls (n = 21) and those with depression (n = 15), while those with vascular dementia (n = 6) were numerically slower than controls but faster than AD patients. Counting rate for larger numerosities was slower in both dementia groups than in controls and in those with depression. Calculation of subitization spans was complicated by a surprising but consistent tendency to take longer to enumerate a single item compared with two items, especially for participants in the AD group. In a subgroup of those with AD, repeating the task confirmed this finding and showed that it was specific to a single item appearing in an otherwise blank field. In people with mild to moderate AD, response times on enumeration tasks are marginally slower than for normal controls but not reliably different to those with Vascular dementia. This test is therefore unlikely to help differentiate early AD from some other pathological conditions of late life. However, a consistent pattern of slow speed in evaluating single objects that was particularly evident in AD patients seems worthy of further investigation.

P2-16

A responder analysis of tarenflurbil (Flurizan), a selective Aβ42-lowering agent, in mild Alzheimer's disease: Analysis from a phase 2 study of up to 24 months

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Background: Tarenflurbil is a Selective Aβ42-Lowering Agent (SALA) that lowers brain levels of Aβ42 in a mouse model of AD and chronic dosing in this model prevents defects in learning and memory suggesting the potential for tarenflurbil to have disease-modifying properties. In subjects with mild AD (MMSE 20–26) randomized to 800 mg BID, statistically significant benefit was observed at 12 and 24 months in activities of daily living and global function with positive trends observed in cognition.

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Methods: This was a placebo-controlled trial evaluating tarenflurbil treatment in 207 patients with mild-to-moderate AD for up to 24 months. At randomization, 94% of subjects were on stable acetylcholinesterase inhibitor therapy. Primary outcomes were ADAS-cog, ADCS-ADL, and CDR-sb. A post-hoc responder analysis was performed in subjects with mild AD (MMSE 20–26) in which a responder was defined as a subject who shows improvement or zero decline from baseline over 12 or 24 months.
Results: 60% of subjects randomized to 800 mg BID showed improvement or no decline on at least one primary outcome at month 12 compared to 39% of subjects on placebo ($p = 0.063$). At 24 months, 42% of subjects randomized to 800 mg BID were showed improvement or no decline on at least one outcome, compared to only 10% of subjects randomized to placebo ($p = 0.02$). These and additional analyses suggest that subjects treated with tarenflurbil show an increasing response rate over time on primary outcomes in a dose dependent manner.
Conclusion: These analyses further justify the ongoing Phase 3 clinical trials of tarenflurbil as an amyloid-based treatment strategy for mild AD.

P2-17

Modification of the randomized withdrawal and staggered start clinical trial designs: Toward a practical demonstration of disease modification in Alzheimer's disease (AD)

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Background: Demonstration of Disease Modification in AD is a complicated methodological and regulatory issue that has been approached in several ways. Among the strategies proposed are those based on measuring clinical outcomes in modified cross-over type studies: 1. the randomized withdrawal design and 2. the staggered start design. These two designs are complicated by long study duration, leading to unbalanced dropout rates introducing bias. A suggested alternative is a parallel groups design comparing slopes and severity of disease at baseline.
Methods: The staggered start design can be mathematically proven to be equivalent to the randomized withdrawal design. A proposed natural history staggered start design based on parallel groups is compared to the staggered start and randomized withdrawal designs to see whether it is capable of distinguishing between a disease modifying and a symptomatic treatment.
Results: A natural history staggered start design is described in which an analysis of slope divergence is combined with an analysis assessing differences in treatment effect depending on severity of disease at baseline. This design is shown to be mathematically equivalent to a staggered start or randomized withdrawal design.
Conclusion: The staggered start and randomized withdrawal designs are impractical because of the long duration of treatment required, the bias and loss of power introduced by the associated high dropout rates, and ethical concerns. A novel and practical parallel groups design allows measurement of the same underlying patterns of drug effect, with differentiation of symptomatic and disease modification drug effects, without the drawbacks of these cross-over approaches.

P2-18

Sensitive Notch signaling assay aimed at Aβ production inhibitor screening

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Background: γ-Secretase inhibitors, which reduce Aβ production, were studied as therapeutic drugs for Alzheimer's disease. But γ-secretase activate other functional proteins such as Notch1, so γ-secretase inhibitors may cause serious side effects for human. Therefore, development of γ-secretase inhibitors that inhibit Aβ production without affecting the Notch signaling is expected. Sensitive screening methods for Aβ production inhibitors have been established, e.g. ELISA, but Notch signaling activity is not observed sensitively so far.
Objectives: We made several luciferase reporter constructs to measure Notch signaling sensitively.
Methods: Four to eight copies of RBP-J binding site derived from Hes-1 promoter were inserted into Hes-1-luc reporter construct, which contains Hes1

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promoter and luciferase gene. These constructs were co-transfected with active Notch1 constructs (NEXT or CC>SS) or control vector into HeLa cells, and various concentrations of γ-secretase inhibitors were added. Notch signaling was measured by dual-luciferase reporter assay.

Results: As the number of RBP-J binding site of reporter constructs increase, luciferase activity was raised in Notch1 transfected cells. Hes-YP, which containing eight RBP-J binding site and PEST domain, increased luciferase expression levels about 1000 fold higher than Hes-1-luc. Inhibitory effects of γ-secretase inhibitors were observed in Hes-YP transfected HeLa cells with or without transfection of active Notch1 construct. This result indicates endogenous notch signaling could detect in Has-YP transfected cells.

Conclusions: Sensitive reporter assay method of Notch signaling activity is established.

P2-19

Exploring factors associated with wandering in Alzheimer's disease patients using integrated circuit tag monitoring system

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Introduction: Patient with Alzheimer's disease (AD) often displays wandering behavior. Although various devices were used to monitor movement patterns of AD patients, continuous monitoring of multiple patients remains difficult. The purpose of this study was to objectively describe movement patterns and to examine factors associated with ambulation in AD patients using the integrated circuit (IC) tag monitoring system (Matrix Co, Japan).

Materials and methods: Edibility criteria: 1) patients hospitalized in the dementia care unit at A Hospital, Osaka, Japan; 2) diagnosed as AD, 3) being able to walk independently, and 4) informed consent obtained from the authorized proxy. The research was approved by the Osaka University and the hospital. Demographic data and medical information were obtained from the medical record. The IC tag monitoring system was used to measure the distance moved per hour and per day.

Results: 18 AD patients were monitored up to 4 months. 10 were hospitalized before the monitoring started, and 8 were monitored after being admitted to the unit. Patient characteristics: the mean age 69.7 $\pm$ 9.9 years; sex ratio: 8/10(M/F); duration of AD: 4.5 $\pm$ 3.1 years; mean years of education: 10.4 $\pm$ 2.7 years; the mean Mini-Mental State Examination (MMSE) score: 10.3 $\pm$ 7.9. Regarding Neuropsychiatric Inventory (NPI), 61.1% of residents had agitation/aggression; 50.0% had irritability/lability; 38.9% had motor disturbance; and less than 30% had other behavior symptoms (delusions, hallucinations, depression/dysphoria, etc.). The median distance walked per day was 1042 m. The subjects' age was strongly associated with the mean distance walked per day ($r = -0.71$, $P < 0.01$) but not the median distance walked during study period. However, no correlation was found between the distance walked and the other variables collected. In order to examine the stability of the distance walked per day, the subjects were stratified by the duration of hospitalization (1st period: being hospitalized < 30 days; 2nd period: being hospitalized ≥ 30 days). However, two groups did not differ significantly in any of the variables examined.

Discussion/conclusion: Previous research reported the association between wandering behavior and cognitive impairment. In our study, age was the only factor associated with the distance walked in AD patients with low MMSE scores.

P2-20

Plasma dehydroepiandrosterone sulfate in dementia patients

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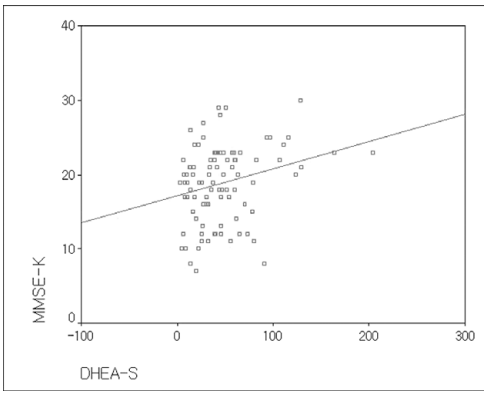
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Background: The purpose of this study was to compare serum DHEA-S levels of Korean normal subjects with that of Korean dementia patients, thus comparing the difference among different types of dementia.

Methods: Subjects were 98 patients diagnosed with dementia. Controls were 31 patients who had visited a family medicine outpatient clinic for a general physical examination.

Results: The mean serum DHEAS levels were lowest in the Alzheimer's dementia group with a level

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P2-20

of 39.52 ug/mL. Mean serum DHEAS levels were highest in the control group, with 93.55 ug/mL. Serum DHEAS levels tended to decrease more with vascular dementia compared to Alzheimer's disease, but this failed to be statistically significant. We compared the correlation of serum DHEAS levels with MMSE-K, S-SDQ scores, and age. Serum DHEAS levels decreased with aging, showing a negative correlation, but did not show any correlation with S-SDQ scores. Serum DHEAS levels showed a statistically significant positive correlation with MMSE-K scores.

Conclusions: The finding of this study supports the role of DHEAS as a risk factor for Alzheimer's disease.

P2-21

A transdermal rivastigmine patch for the treatment of Alzheimer's disease

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Transdermal patches offer many advantages over oral formulations. The new rivastigmine patch is the first transdermal treatment developed for Alzheimer's disease. It offers smooth and continuous drug delivery, and sustained inhibition of both acetylcholinesterase and butyrylcholinesterase. Pharmacokinetic studies showed that the 10 cm^2 rivastigmine patch delivers similar exposure to 12mg/day capsules.

The objectives of the IDEAL study were to evaluate the efficacy, safety and tolerability of rivastigmine patch and conventional capsules *versus* placebo, and assess caregiver preference for patch over capsules.

IDEAL consisted of a 24-week, randomized, double-blind, double-dummy, placebo- and active-controlled study of rivastigmine patches (10 cm^2 and 20 cm^2) and capsule (12mg/day) *versus* placebo, followed by a 28-week open-label extension (OLE). In the double-blind phase (DBP), patients were titrated to target doses at 4-week intervals, starting with 5 cm^2 patch. Upon entering the OLE, all patients were switched directly to 10 cm^2 rivastigmine patch and titrated to 20 cm^2. Primary DBP evaluations included assessments of cognition and global functioning. Primary OLE evaluations included adverse events and serious adverse events.

1195 patients were randomized to the DBP, and 870 (72.8%) entered the OLE. During the DBP, the rivastigmine patch 10 cm^2 demonstrated equivalent efficacy to higher doses of capsules, with three times fewer reports of nausea or vomiting. This is reflected in the higher percentage of patients reaching target doses (96.2% *versus* 63.3%). At Week 24 over 70% of caregivers preferred the patch to the capsule. During Weeks 1–4 of the OLE, the 10 cm^2 patch was well-tolerated by patients formerly randomized to rivastigmine capsule or patch; $\leq$ 2.5% reported nausea, $\leq$ 1.9% reported vomiting. In both phases, no unexpected safety issues arose, and skin tolerability was good.

The target dose rivastigmine patch 10 cm^2 provides equivalent efficacy to higher doses of capsules with a dramatically improved tolerability profile. A transdermal patch may be the optimal way to deliver rivastigmine, allowing patients to reach target therapeutic doses and achieve maximum benefits from treatment. Preference for the patch may have the potential to improve compliance, enabling patients to stay on and benefit from treatment for longer.

P2-22

Study of the preservation of visuoperceptual capacities in Alzheimer's disease patients

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Introduction: The slow and yet constant evolution of the Alzheimer type (ATD) into dementia has become the major problem of our society and the memory is always affected al an early stage of the ATD.
Objective: The disorder or decline of these functions may have a profound impact on daily life activities. However, the visuoperceptual functions and inconscious recall are well preserved in ATD patients. Therefore, this study aims to evaluate these processes experienced by ATD patients.
Methodology: My research aims to exam this disease by submitting 20 ATD patients, at an early stage of the illness, to cognitive tests, along with a longitudinal study (11months after) of the control group with matched subjects. In order to test the visuoperceptual function nomination in two different series, matched picture and oral word and dictation were used. In order to evaluate the unconscious recall word completion test and semantic index recall were used. In order to evaluate these exams, two levels of analysis were considered: a traditional approach (on the group) and an analysis on the interindividual differences. For the statistical treatment, we used the 10 version SPSS software; correlation, test X2, ANOVAs were calculated.
Results: The statistical analysis made possible to categorize three types of patient groups showing a great heterogeneity among them. The tests using pictorial, audio stimuli and word-lists showed better results. The performance of ATD was also better in the tests with facilitation strategies. Finally, the results showed that memory declines in the ATD are not only quantitative but also qualitative (paraphasia).
Conclusion: The study of the results showed that the ATD performances improve somewhat by providing facilitatory strategies (semantic index recall), pictorial and /or audio stimuli. But this performance level did not reach the level of the control persons. Therefore, the memory decline does not depend only on the person but also on the type of task, contexts and aids (oral or visual). The memory declines show difficulty to access the lexical semantic stock which turns into an Anomia affecting spontaneous expression on the ATD patients.

P2-23

Cognitive effects of memantine in moderate to severe Alzheimer's disease: A responder analysis

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Memantine is a moderate-affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist approved in the US and Europe for the treatment of moderate to severe Alzheimer's disease (AD). In a 28-week, double-blind, placebo-controlled trial in moderate to severe AD (Reisberg et al., 2003), the memantine-treated group (n = 126; 20 mg/day) demonstrated significantly better cognitive performance on the Severe Impairment Battery (SIB) at endpoint compared to the placebo-treated group (n = 126). In this post hoc analysis, the percentages of patients demonstrating a response on the SIB total score and three SIB subscales (Memory, Language, and Praxis) were compared by treatment group across the trial and at endpoint. Response on the SIB was defined in three ways, with increasing stringency: 1) no decline/improvement (score change $\geq$0, compared to baseline), 2) strong improvement (score change $\geq$4), and 3) very strong improvement (score change $\geq$8). Comparisons of responder percentages were performed using a generalized estimating equations model with treatment group, visit, and treatment group-by-visit interaction as fixed effects and baseline value as covariate. On the SIB total score, the proportion of no decline/improvement responders in the memantine group was significantly higher compared to the placebo group at study endpoint (37.5% vs. 22.9%; P = .048) and across the entire trial (P = .005). Similarly, the proportion of strong responders was significantly higher in the memantine group at study endpoint (19.8% vs. 6.0%; P = .015) and across the trial (P < .001), while the proportion of very strong responders was significantly higher in the memantine group across the entire trial (P = .014), and supported memantine treatment at study endpoint (10.4% vs. 2.4%; P = .06). At study endpoint, significant memantine response was demonstrated for no decline/improvement responders on the subscales of Language and Praxis. Across the entire trial, the memantine group had a significantly higher proportion of no decline/improvement responders on the subscale of Praxis and a significantly higher proportion of strong responders on all three subscales. In patients with moderate to severe AD, a significantly greater percentage of memantine-treated patients demonstrated cognitive improvement or no

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cognitive decline, relative to untreated patients. Similar results were seen when cognitive domains of Memory, Language, and Praxis were examined.

P2-24

P300 event-related potentials in late-onset depression and cognitively impaired elderly

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Background: The Event related potentials (ERPs) of P300 component can be used as a measure of cognitive deficits. Some studies reported the findings of ERPs in Alzheimer's disease (AD) as reduced P300 amplitude and prolonged P300 latency, while only a few studies report a prolonged P300 latency in depressive disorder. In clinical setting, cognitive decline in late-onset depression should be differentiated from cognitive impairment of early AD or mild cognitive impairment (MCI).
Objectives: We aimed to investigate whether the findings of ERPs shows any differences between older patients with depression, mild AD and MCI.
Methods: 23 patients with depression, 25 patients with mild AD patients who fulfilled NINCDS-ADRDA criteria and 19 MCI patients were included in this study. 17 age matched control subjects were also included as well. All subjects underwent clinical interview, comprehensive neuropsychological tests, and ERP recordings. Other medical conditions known to cause dementia and depression were excluded by following neurological, serological and imagery test including Computed tomographic imaging scan (CT-scan) and Magnetic resonance imaging (MRI).
Results and conclusion: Compared with patients with depression and normal controls, AD and MCI patients showed significantly reduced P300 amplitude and prolonged P300 latency. However, there were no differences between mild AD and MCI group. Our results shows that reduced P300 amplitude and prolonged P300 latency in ERPs might be a characteristic finding in MCI and AD patients, but not in patients with depression. We concluded that depression can be differentiated from cognitively impaired patients, such as AD or MCI by P300 ERP findings and MCI may represent a dementia prodrome rater than benign aging process according to the result of this neurophysiologic study.

P2-25

The association between severity of Alzheimer's disease and comorbid depressive symptoms in community-dwelling Korean elderly

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Background: Some studies have revealed quite a number of patients with Alzheimer's disease (AD) suffer from depressive symptom during their illness. Depressive symptoms in patients with AD have been known to be related to poor quality of life, increased health care utilization and costs, greater need for institutionalization, and even higher mortality rates. Objectives: We aimed to investigate the association between the severity of AD and presence of comorbid depressive symptoms and putative risk factors for depression in AD.
Methods: We screened 2,421 community-dwelling elderly with MMSE-KC (Korean version of MMSE in CERAD-K). 237 elders with score below −1.5 SD in MMSE-KC according to the normative data adjusted by age, sex and education were assessed by comprehensive neuropsychological test and clinical interview in the use of CERAD-K packet. 83 elderly were diagnosed as AD. The severity of dementia was assessed by Clinical Dementia Rating (CDR). Patients with severe medical illness,

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cancer, and other conditions that cause dementia and with other psychiatric illness except for depression were excluded. Depressive symptoms were evaluated by Korean version of Geriatric Depression Scale (GDS-K) and clinical assessment of depressive symptoms in CERAD-K packet. Other behavioral and psychological symptoms of dementia were assessed by Neuropsychiatric Inventory (NPI).

Results and conclusion: The prevalence of all depression including minor depression was 46%. There was no significant association between depressive symptoms and the severity of AD. Among other neuropsychiatric symptoms, apathy was correlated with the severity of AD, which consisted with previous similar studies. Our results show that depressive symptoms are common in patients with AD. However, depressive symptoms are independent to the severity of illness. As a result, regardless of the severity of AD, discrete assessment of depression with other behavioral symptoms of AD must be taken, even in very early stage of illness. Although it is difficult to discriminate apathy and depression, these results also show that these symptoms can be differentiated in terms of the progression of illness.

P2-26

White matter lesions on magnetic resonance imaging of the brain in Alzheimer's disease patients

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Brain images of patients with Alzheimer's disease (AD) on magnetic resonance imaging (MRI) show an atrophy of cerebral tissue and pathological white matter lesions (WML). The presence of these lesions is one of the factors supporting the diagnosis of probable Alzheimer's disease, however their clinical usefulness requires further studies.

The aim of the study was to assess the frequency of the WML appearance in the brain of patients with AD on the FLAIR and T2 sequences of MRI and search for correlations between the size and location of WML and the stage of clinical progression of the disease and factors which can determine their increase.

The studied group consisted of 48 ambulatory patients (28 women and 20 men) with the diagnosis of probable AD, according to DSM-IV and NINCDS-ADRDA criteria, in various stage of the disease (MMSE score: 3–24 points). The T2 and FLAIR MRI sequences of the brain of each patient were assessed using the White Matter Lesions Semiquantitive Rating Scale, taking into consideration the amount, size and distribution of WML.

WML of the brain were seen in all patients on T2 and FLAIR sequences. The positive correlation between the patients' age and the amount and size of WML, especially in frontal and parietal area (T2: $r = 0{,}33$, $p < 0{,}05$; FLAIR: $r = 0{,}37$, $p < 0{,}05$), as well as in periventricular region (T2: $r = 0{,}34$, $p < 0{,}05$; FLAIR: $r = 0{,}35$, $p < 0{,}05$) has been shown on both sequences. On T2 sequence, lesions in subcortical nuclei also correlated with age ($r = 0{,}37$, $p < 0{,}05$). There was no correlation between the size or distribution of lesions and either the stage of the disease or the gender. The amount of WML in subcortical nuclei and occipital region was larger in patients with hypertension ($p < 0{,}05$).

The significant factor correlating with the location of WML in patients with Alzheimer's disease is the age of a patient. Hypertension correlates with the amount of WML in subcortical nuclei and occipital region. The presence of WML does not depend on the stage of the disease.

P2-27

Associations between methylenetetrahydrofolate reductase gene and Alzheimer's disease in Korean elders

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Objective: The association between methylenetetrahydrofolate reductase (MTHFR) c.677C > T (A222V) polymorphism and Alzheimer's disease (AD) is controversial. The objectives of the study were to investigate the association between MTHFR c.677C > T polymorphism and AD in Korean elders and to the extent to which it is modified by the

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major components of one-carbon metabolism and apolipoprotein E (APOE) genotype.

Methods: 732 community residents aged 65 or over were clinically assessed for AD. Genotyping was performed for MTHFR c.677C > T and APOE; serum levels of folate, vitamin B12, and homocysteine were assayed. Age, gender and education were included as covariates.

Results: A trend of association between TT genotype of MTHFR c.677C>T and AD was found [adjusted OR (95% CI): 1.73 (0.80–3.74)]. The association was significant in the presence of below-median vitamin B12 level [3.66 (1.14–11.71)] and in APOE e4 non-carriers [2.97 (1.00–8.55)] with significant interaction terms, and bordered on significance in the presence of above-median homocysteine level [2.73 (0.94–7.90)].

Conclusions: These findings suggest gene-environment and gene-gene interactions on the risk of AD in Koreans.

P2-28

Disturbances in everyday life activities are based on apraxia for vascular dementia but not for Alzheimer's: The Osaki-Tajiri Project (4)

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Objective: To determine whether disturbance in the sequence of using tools affect activities on everyday life (such as self-care, preparing meals, doing the cleaning, and intellectual activities) in patients with Alzheimer's disease (AD) and vascular dementia (VaD).

Methods: Fifteen patients with probable AD (NINCDS-ADRDA) and 12 patients with probable VaD (NINDS-AIREN) were studied. MRI was used to evaluate their vascular lesions. All of them met the following excluding criteria; 1) MMSE scores <10, 2) severe aphasia or visual agnosia, 3) paralysis of the dominant hand, and 4) depression and severe psychotic manifestations. There were no significant differences between the patients with AD and VaD for age, educational level, gender, and MMSE. The vascular lesions in VaD patients included bilateral thalamus and white matter. Analysis 1: Everyday life activities were assessed using the Social Activities Questionnaire (SAQ). Analysis 2: Apraxia was evaluated using the single tool tasks (pantomiming the use of tools/using actual tools), and the sequence tasks of using tools. The sequence abilities were assessed with three processes for each task, and the number of sequence errors was counted.

Results: 1. The SAQ scores of both AD and VaD patients were significantly lower than normal value, supporting clinical observations. 2. AD and VaD patients could use actual tools correctly, however, they had some errors of pantomiming the use of tools. The scores of the sequence tasks in VaD patients were significantly lower than that of AD. When we instructed AD patients to pay attention to the sequence tasks by using cues such as photos, they could correctly perform it, however, these cues were not useful for VaD patients.

Comment: AD patients can use tools and perform the sequence tasks although they cannot pantomime some tools. It suggests that disturbances in everyday life activities for AD patients may be affected by attention or memory impairment but not apraxia. On the contrary, some VaD patients' disabilities may be based on apraxia.

P2-29

ALSOVA, a prospective intervention follow-up study on recently diagnosed patients with mild Alzheimer's disease and their caregivers – the study population at the baseline

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Alzheimer's disease (AD) imposes a heavy and rapidly increasing economic burden on the social and healthcare systems in different countries. The largest increase in dementia costs is related to institutional care. While dementia has devastating impact on quality of life of the family caregivers, the families play important roles in the patient care and decision making.

Our objective was to examine and compare the factors that are related to the quality of life, coping and life control of both patients and caregivers. Effects of a psychoeducational and rehabilitation intervention program on quality of life of the patients and caregivers and caregivers' burden will also be studied.

The study is a prospective follow-up study that includes 241 recently diagnosed AD patient-caregiver pairs who entered the study between 2002 and 2006. Data collected includes age, sex, education, physical health, medication, household composition, living arrangements, general well-being, caregiver strain, depression, quality of life and resource utilization. The AD patient-caregiver pairs will be randomized to two study groups: (1) Traditional care + intensive psychoeducational courses for patient and caregiver during first two years after a diagnosis, and (2) traditional care.

At the baseline the caregiver was most frequently a spouse, in 70% of cases, and in 23% of the cases the caregiver was a child. A total of 73% of the patient-caregiver pairs were living together. The mean MMSE score of the patients was 21.5 ± 3.4 and mean ADCS-ADL score was 65.4 ± 9.3. Only 18% of the patients had no neuropsychiatric symptoms, and 37% of the patients had symptoms in at least three different NPI domains. As many as 33% of patients could be diagnosed as having at least mild depression. Up to 43% of the AD patients had another medical condition besides AD, and 60% used at least three different medications. Almost all (96%) used AD medication, most often acetylcholinesterase inhibitors.

Although the patients were at the early stage of AD at the baseline, the neuropsychiatric symptoms were surprisingly frequent in these patients. Patient's depression was associated with quality of life of the patients at the baseline.

P2-30

Apathy and white matter anisotropy in Alzheimer's disease: A Diffusion Tensor Imaging study

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Apathy is a syndrome of decreased initiation and motivation, and is a common and disabling symptom in Alzheimer's disease. However, white matter changes have not been investigated in Alzheimer's disease with apathy. This study included twenty patients with Alzheimer's disease with apathy and nineteen patients without apathy. They were received clinical evaluation, the CERAD-K battery, MRI and DTI imaging. Fractional Anisotropy (FA) was measured in eight region-of-interests (ROI) which consisted of left and right frontal, temporal, parietal white matter and genu and splenium of corpus callosum. They were transformed with spatial normalization and analyzed with SPM5. The mean MMSE scores showed no significant difference between groups ($p = 0.52$). The FA value decreased significantly in right frontal lobe sub-gyral white matter (p value $= 0.001$) and splenum of corpus callosum (p value $= 0.004$) in Alzheimer's disease with apathy, compared those without apathy. On the contrary, the FA values showed no significant difference in sub-gyral white matter of left frontal lobe and genu of corpus callosum, and those of right and left temporal and parietal lobes. In conclusion, this study showed that the disconnection of right frontal lobe plays an important role to appear apathy in Alzheimer's disease.

P2-31

A functional magnetic resonance imaging study of working memory abnormalities in Alzheimer's disease

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Background: Impaired processing of working memory information is one of the broad ranges of cognitive deficits seen in patients with Alzheimer's disease (AD).
Objective: We aimed to elucidate the differences in brain activities involved in the process of working memory between AD patients and healthy comparison subjects.
Methods: Six patients with AD were recruited along with eight healthy volunteers as a comparison group. Functional magnetic resonance imaging (fMRI) was employed to assess cortical activities during the performance of a 1-back working memory paradigm using the Korean alphabet as mnemonic content. Subsequently, the difference in neural activities between the two groups was analyzed.
Results: The AD group performed the tasks with reduced accuracy. Group comparison analysis revealed that the AD group showed decreased brain activity in the left frontal pole (BA10), the left ventrolateral prefrontal cortex (BA 47), the left insula (BA13), and the right premotor cortex (BA6) compared to the control group. The AD group showed increased activation in the left precuneus (BA7) compared to the control group.
Conclusions: A decreased level of activation in the prefrontal cortex and an increased level of activation in the parietal neural networks from the patient group may document altered verbal working memory process in the patients with AD.

P2-32

Functional interaction of serum Tumor Necrosis Factor-alpha and Insulin Growth Factor-I in Alzheimer's disease

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Recent experimental data suggest that the signaling pathways of tumor necrosis factor-alpha (TNF-alpha) and insulin-like growth factor I (IGF-I) are functionally interrelated and contribute to the pathogenesis of Alzheimer's disease (AD). It has been demonstrated that TNF-alpha counteracts the capacity of IGF-I to promote neuronal survival and antagonizes brain amyloid-beta clearance induced by serum IGF-I, whereas IGF-I reverses neuronal apoptosis mediated by TNF-alpha. Interactions between peripheral IGF-I and TNF-alpha systems, as well as the effects of the treatment with a neurotrophic compound (Cere) on these factors were investigated in AD patients. Serum TNF-alpha levels were significantly higher in AD and mild cognitive impairment (MCI) patients ($p < 0.01$ and $p < 0.05$, respectively) than in control subjects when the effects of age were controlled. A significant reduction ($p < 0.05$) of age-adjusted total IGF-I, but not dissociable-free IGF-I levels was observed in AD as compared with controls. TNF-alpha correlated negatively with total IGF-I in AD, MCI and control groups, as well as with dissociable-free IGF-I in AD ($p < 0.01$), but not in MCI and control subjects. Serum levels of soluble TNF Receptor I (sTNF-RI) and IGF binding protein 3, both having pro-apoptotic activity, were also found to be increased in AD patients as compared with controls ($p < 0.01$ and $p < 0.05$, respectively). However, sTNF- RII and IGFBP-1 showed no changes in AD sera. In mild to moderate AD patients enrolled in a 24-week, double blind, placebo-controlled trial with three dosages of Cere, we found that Cere increased free IGF-I levels significantly at 10 ml ($p < 0.05$) and 60 ml doses ($p < 0.01$), and reduced serum TNF-alpha and sTNF-RI values in a dose-dependent manner with respect to placebo. No significant changes were detected in total IGF-1, IGFBP-1, IGFBP-3 and sTNF-RII after treatment with Cere. These results showing a negative interaction between serum TNF-alpha and dissociable-free IGF-I suggest that the opposite influence of inflammatory and growth factors on AD pathology have a peripheral representation, which can be modified with neurotrophic drugs like Cere.

P2-33

Clinical risk factors for Dementia of Alzheimer type in Japanese memory clinic

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Background and objectives: Several risk factors of Dementia of Alzheimer type (DAT) and mild cognitive impairment (MCI) have been reported in epidemiological studies and some of these risk factors are important in a point of treatable factor. However, these risk factors have not been fully evaluated in Japanese memory clinic. We compared clinical information and laboratory tests of the patients with DAT and MCI in our memory clinic with those of normal control to determine clinical factors for intervention in DAT and MCI.
Methods: Data from all the consecutive patients with DAT and MCI, who consulted our memory clinic, were compared with data from normal controls. In all the patients, 129 patients were diagnosed as DAT (97 women and 32 men, 76.6 ± 7.4 years old, MMSE 19.2 ± 5.3), 42 patients were diagnosed as MCI (24 women and 18 men, 72.2 ± 7.9 years old, MMSE 26.6 ± 2.3). Diagnosis of DAT was based on the criteria of NINCDS-ADRDA, diagnosis of MCI was based on the criteria of Petersen (Arch Neurol, 1999; 56:303). From interviews, MMSE (28.3 ± 1.5), and brain MRI, 30 subjects (15 women and 15 men, 74.3 ± 5.2 years old) were identified as normal controls. Hypertension, diabetes mellitus, hyperlipidemia, heart disease (ischemic heart disease or arrhythmia), cerebral vascular disease, alcohol intake, and smoking were taken from medical record. HbA1c, glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, hypersensitive CRP, vitamin B12, folic acid were examined in the plasma or serum. Statistic analysis was evaluated with chi-square test and Mann-Whitney U test, significance was established at the $p < 0.05$ level.
Results: Less alcohol current drinker ($p = 0.0145$), higher HbA1c level ($p = 0.0003$), higher glucose level ($p < 0.0001$), lower HDL level ($p = 0.0347$), higher LDL level ($p = 0.0157$), lower vitamin B12 level ($p = 0.0003$), and lower folic acid level ($p < 0.0001$) were found in DAT patients, compared with normal control. Higher HbA1c level ($p = 0.0137$), higher glucose level ($p = 0.0019$) and lower folic acid level ($p = 0.0012$) were found in MCI patients, compared with normal control. Normal controls had more often arrhythmia than DAT patients ($p = 0.0247$). The results of MCI patients was similar to those of DAT patients except more smoking in MCI ($p = 0.0371$).
Conclusions: Glucose intolerance, cholesterol metabolism and metabolism related to folic acid could be candidates for intervention in DAT and MCI.

P2-34

Amyloid β protein induce macroautophagy

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Macroautophagy is known as bulk degradation system in cytoplasm. Many recent studies showed that this mechanism contribute with many neurodegenerative diseases. Previous data suggest that macroautophagy could relate to Alzheimer's disease (AD) pathology. Accumulation of abnormal proteins, especially β-amyloid (Aβ) is a major pathology of AD. And according to the amyloid cascade hypothesis, the accumulation of Aβ is a critical step of AD pathology. Our results shows Aβ exposure induce macroautophagy.

P2-35

Anti-Alzheimer drug NSAID has no trade-off effects among anti-inflammation, microglial activation and suppression of amyloid pathology

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Inflammation is one pathological change in Alzheimer's (AD) brain and closely related to activation of microglia which can clear amyloid beta protein (Aβ) and/or cause neurodegeneration. Our group demonstrated that NSAID (ibuprofen) suppresses amyloid pathology in Alzheimer model mice that is confirmed by more than 11 in vivo studies. We previously showed that ibuprofen suppressed levels of IL-1β and α1-antichymotrypsin, factors that are not only inflammation-related but also pro-amyloidogenic. On the other hand, amyloid pathology in APP Tg mice is also reduced by Aβ

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vaccination. Vaccination which caused brain inflammation in a clinical trial is pro-inflammatory and activates microglia, one potential anti- AD mechanism of vaccination. Both NSAID and Ab vaccination suppress amyloid pathology, but have contrasting effects on inflammation. This possible conflict between NSAID and Aβ vaccine was addressed in this study. Ibuprofen levels in APP Tg mice (TG2576) fed with 375 ppm ibuprofen in diet, which has been shown to suppress amyloid burden (-55.9%) were measured. Ibuprofen levels in plasma, liver and brain were $47.04 \pm 5.17\,\mu$M which was close to the therapeutic window of rheumatoid patients, $14.36 \pm 1.80\,\mu$M and $4.07 \pm 2.03\,\mu$M which is above the COX inhibition IC50 in whole blood assays. These results suggested that ibuprofen in this dose have anti-inflammatory effects. Multiple microglial markers were evaluated. CD11b and CD11c immunoreactivity per amyloid plaque in APP Tg mice were not suppressed by ibuprofen. Though amyloid burden which can stimulate microglia was suppressed, global mRNA levels of CD11b, CD11c, CD68 (macrosialin) nor iNOS in cortex were not suppressed by ibuprofen. In primary cultured microglia cells, 5~50 μM ibuprofen inhibited COX activity, but did not suppress mRNA levels of CD11b, CD11c and CD68. At extremely high level of ibuprofen (500 μM) suppressed the expression levels of CD11c and CD11b mRNA. These data suggested that middle or high doses of ibuprofen suppress inflammation without disturbance of microglia activation. In vivo and *in vitro* data suggested that 375 ppm in diet ibuprofen suppresses amyloid pathology but does not disturb microglia activation which can clear Aβ. There is no evidence to show a real conflict between ibuprofen and Ab vaccine.

P2-36

Falls in inpatients with dementia

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Background and objective: Falls are major health problem among the elderly, especially in patients with dementia. The aim of this study was to identify characteristics associated with falls in patients with dementia in a dementia word.

Methods: This prospective study comprised 94 consecutive inpatients with dementia (49 men and 45 women, mean age of 81.5 ± 7.3 years). Minimental State Examination (MMSE), Clinical Dementia Rating Scale (CDR), Neuropsychiatric Inventory (NPI), Barthel Index (BI), and other clinical features were investigated.

Results: Fall events were confirmed in 42.6% (40/94). Fallers did not differ from non-fallers on any parameter except history of falling (fallers: non-fallers = 80.0%: 57.4%, $p = 0.02$), isolation on admission (fallers: non-fallers = 85.0%: 1.9%, $p < 0.01$), delusion on admission (fallers: non-fallers = 4.0: 1.9, $p < 0.03$).

Conclusions: Falls in a dementia word can be predicted using history of falling, need of isolation on admission, and existence of delusion on admission.

P2-37

Il-1β, Il–6 and TNF-α inflammatory cytokines and lymphocyte subset markers in patients with Alzheimer's disease (AD)

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Objective: Inflammatory and immunological processes have been shown to be part of the pathogenetic events underlying AD. In this study investigated whether immunologic abnormalities could be found in a randomly chosen group of patients with AD compared with well-matched controls.

Methods: 88 patients (46 male and 42 female; age range, 64 to 78 years) with AD and 24 age- and sex-matched healthy subjects (HS) were included in the study. Flow cytometry was carried out by using monoclonal antibodies. Lymphocyte proliferation was calculated as a stimulation index (SI), and IL-1β, IL-6 and TNF-α were measured in supernatants of peripheral blood activated with LPS and cultured for 72 hours at 37°C.

Results: The mean percentage of CD3 and CD4 T cells in the lymphocyte population was significantly higher in AD patients than in the healthy group. However, the percentage of CD45RO was significantly reduced ($p < 0.05$) in the AD group (33.8 ± 3.6) with respect to the HS group (45.6 ± 2.9). Blastogenic responses to Con A, PHA and PWM and NK cytotoxicity revealed a diminished proliferation response to Con A (SI: 19.8),

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PWM (SI: 20.8) and PHA (SI:23.0) mitogen stimulation as compared to controls (Con A: 22.8; PWM: 25.5; PHA: 26.3). The LPS-induced increase in all cytokines was greater in the AD group (IL-1β, 128 pg/ mL, $p < 0.05$; IL-6, 88 pg/mL, $p < 0.01$; TNF-α, 95 pg/mL, $p < 0.01$) with respect to the HS group (IL-1β, 77 pg/mL; IL-6, 55 pg/mL; TNF-α, 62 pg/mL).

Conclusions: The results presented in this study show that immunological abnormalities can be detected in a randomly selected group of patients with AD compared with a matched control group and that peripheral immune cells may participate in cytokine up-regulation, and possibly contribute to both brain tissue inflammation and neuronal damage.

P2-38

Inflammatory and immune responses in patients with Alzheimer's disease (AD)

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Reactive microglia appear in almost every type of central nervous system (CNS) disorder, including infection, trauma, stroke, degeneration, and demyelination. These inflammatory cells are the major source of CNS-derived cytokines, help to regulate wound healing in neuronal tissues, and serve as an important link between systemic immune responses and the CNS. Understanding the pathophysiology of AD is critical for the possibilities to improve the treatment of this disorder; and although the activation of microglia is thought to be a central event in the pathogenesis of AD, the primarily activating agent is unknown so far. In order to better understand the disease-specific mechanism of microglial activation, we examined patients peripheral blood for both a related macrophage/lymphocyte activation and an accelerated apoptosis. Blood samples of 10 ml were drawn from 60 patients clinically diagnosed for probable AD, 20 control individuals and 20 patients with vascular dementia (VD). The mononuclear cells were separated by standard centrifugation and studied for their phagocytosing capacity in a cell adhesion assay, for CD26, CD69, CD72 expressions and for their apoptotic activity by flow cytometry. In the majority of AD cases, both accumulation of apoptotic cells and correlated macrophage and lymphocyte activation were found dependent on the clinical severity. In the mild and moderate stages of dementia, the fraction of macrophages was increased and only a weak accumulation of apoptotic cells was seen. In the severe stages, the number of macrophages declined and the removal of circulating apoptotic cells was impaired. Short-term cultures of unstimulated PBMC made these processes more evident. This study provide information on the expression of activation markers in peripheral immune cells. In the late-onset sporadic form of AD the peripheral blood macrophage system is chronically activated in response to an excess of apoptotic cells.

P2-39

Cholesteryl ester transfer protein (CETP) gene and cholesterol in Alzheimer's disease

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CETP is primarily involved in the redistribution of lipids in reverse lipid transport pathways, transferring cholesteryl esters from HDL cholesterol to TG-rich lipoproteins in exchange for triglycerides. This reverse cholesterol transport is considered an antiatherogenic phenomenon. Genotypic variation in the CETP gene has been associated with CETP mass and activity, and higher plasma HDL-C and apolipoprotein A1 levels. Dementia is becoming a major concern, especially in western countries, and Alzheimer's disease (AD) is the most common form of dementia. High plasma cholesterol levels (T-CHOL) are believed to be a risk factor for dementia, and comparisons of plasma T-CHOL levels between healthy control subjects and AD patients have shown conflicting results. We have investigated the genotype and allele distribution of the CETP Taq1B polymorphism in Control subjects and in AD patients, as well as its influence on the levels of blood lipid parameters. A total of 347 subjects were included in the study, 174 controls and 173 patients with AD. Our results showed no significant differences in allele and genotype frequencies between control subjects and AD patients. We found genotype-related variations in T-CHOL and LDL-C levels in controls and in AD patients, being the B2B2

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genotype the lowest lipid levels. There is a clear interaction between CETP Taq1B polymorphism and diagnosis that affects T-CHOL and LDL-C levels. Thus, AD patients with B1B1 genotype, present higher levels of T-CHOL and LDL-C than controls with the same genotype, suggesting the interaction of other factors, either genomic or environmental, with CETP in the regulation of lipid metabolism.

P2-40

CYP2D6 in the Spanish population with dementia

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Introduction: The CYP2D6 gene codes for an enzyme involved in the biotransformation of commonly prescribed drugs. The CYP2D6 gene is highly polymorphic, with a series of alleles that encode enzymes with null or minimum catalytic activity. The frequently used drugs for dementia treatment are substrates of the CYP2D6 isoenzyme. In addition, allelic variation of the CYP2D6 gene has been suggested to be associated with CNS disorders.
Objective: a) To determine the prevalence of CYP2D6.3, 4, 5, 6, 7, 8 and 10 alleles and the multiplication of the CYP2D6 gene in healthy subjects and in patients with dementia in the Spanish population. b) to assess a potential relationship between CYP2D6 polymorphisms and dementia.
Materials and methods: Genotyping was performed by long-PCRs, minisequentiation and real-time PCRs in 110 and 88 DNA samples obtained from patients with dementia and healthy subjects, respectively, in the Spanish population.
Results: Results show that between 5,6 to 9% of total subjects were poor metabolizers and approximately 6% were ultrarapid metabolizers. The Hardy-Weinberg equilibrium was confirmed for genotype frequencies of both groups. The distributions of alleles, genotypes and phenotypes of the CYP2D6 among dementia patients and controls were not significantly different.
Conclusions: These data suggest that the treatment of patients with dementia can be improved via the phamacogenetic assessment of drug metabolic pathways. The similar genotype frequencies found in patients with dementia and control subjects indicate that the CYP2D6 is unlikely to represent a risk factor for dementia susceptibility in the Spanish population.

P2-41

Similar pharmacogenetic patterns of CYP2C19 in Spanish and Colombian populations

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Introduction: The CYP2C19 isoenzyme is responsible for the formation of active or inactive metabolites of important drugs. The CYP2C19 gene is polymorphic, with a series of alleles that encode enzymes with null or minimum catalytic activity. Moreover genotypic or phenotypic studies of this gene do not exist in the South American Mestizo and Spanish Caucasian populations.
Objective: The objective of this investigation was: a) to determine the prevalence of alleles CYP2C19*1, CYP2C19*2, CYP2C19*3, CYP2C19*4, CYP2C19*5, CYP2C19*6 and CYP2C19*8 in DNA samples of Spanish and Colombian populations; b) to compare the genotypes and allelic frequencies found in these ethnic groups.
Materials and methods: Genotyping was performed using minisequentiation and real-time PCRs in 189 and 183 DNA samples obtained from Spanish Caucasian and Colombian Mestizo individuals, respectively.
Results: Within the Colombian subjects we found 83.6% of carriers of the two wild-type alleles (extensive metabolizer, EM), 15.3% of heterozygous of one nonfunctional allele (intermediate metabolizer, IM) and 1.1% of carriers of two nonfunctional alleles (poor metabolizer, PM). Within the Spanish subjects we found 77% of carriers of both native alleles (EM), 21.8% were heterozygous of one nonfunctional allele (IM), and 1.1% were homozygous *2/*2 (PM). The Hardy-Weinberg equilibrium was

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confirmed for the genotype frequencies of both populations.

Conclusions: Both allelic and genotypic prevalence of the CYP2C19 gene are statistically similar among the two ethnic groups. This data suggest that there are no differences in pharmacogenetic responses among Colombian Mestizos and Spanish Caucasians, in relation to drugs metabolized by the CYP2C19 enzyme.

P2-42

Genetic polymorphisms of cytochromes P450: CYP2D6, CYP2C19 and CYP2C9 in Spanish population

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Introduction: Cytochrome P450 (CYP) enzymes are involved in the biotransformation of large number of xenobiotic compounds. The major polymorphic human CYP enzymes, CYP2D6, CYP2C19 and CYP2C9 metabolize about 50% of commonly prescribed drugs. The activity of these enzymes is characterized by a broad inter-individual and inter-ethnic variability. The mutations in CYPs genes can encode enzyme products with abolished (poor metabolizer, PM), reduced (intermediate metabolizer, IM), normal (extensive metabolizer, EM) or increased (ultrarapid metabolizer, UM) enzyme activity.

Objective: To determine the prevalence of most common allelic variants of the Cytochrome P450 enzymes CYP2D6 (*1, *3, *4, *5, *6 and *1xN), CYP2C19 (*1, *2, *5) and CYP2C9 (*1, *2, *3) and to predict genotype and phenotype frequency in the Spanish population. Materials and methods: Genotyping was performed by a combination of long-PCRs, and allele-specific real-time PCRs in a total of 393, 360, and 293 Spanish individuals for CYP2D6, CYP2C19 and CYP2C9 studies, respectively.

Results: The frequency distribution for CYPs polymorphic alleles, genotypes and phenotypes corresponded to the frequencies of other European populations. Genotyping for polymorphic CYP2D6 revealed that 5.6% of total subjects were poor metabolizers and 5.1% were ultrarapid metabolizers. The most common inactive allele in this population was CYP2D6*4 (frequency 0.18). Within the CYP2C19 study only the CYP2C19*2 mutant allele (frequency 0.13) was detected. The phenotype frequencies of CYP2C19 were 2% of poor metabolizers and 23% of intermediate metabolizers. The phenotype frequencies of CYP2C9 were 5.11% of poor metabolizers and 32.4% of intermediate metabolizers. The Hardy-Weinberg equilibrium was confirmed for all genotype frequencies.

Conclusions: The CYP2D6, CYP2C19 and CYP2C9 genotype frequencies found in the Spanish population were similar to those found in other European studies. The data suggests that the treatment of Spanish patients can be improved via the clinical use of CYP2D6, CYP2C19 and CYP2C9 genotyping and the phamacogenetic assessment of drug metabolic pathways.

P2-43

Detecting subtle language impairment in patients with mild cognitive impairment with picture description task

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We studied language function in subjects with mild cognitive impairment (MCI, n = 20) and mild Alzheimer's disease (AD, n = 27), and compared their performance with that of cognitively normal elderly individuals (NC, n = 20). Language testing in this study included a normative communicative test (Communicative Abilities in Daily Living: CADL), confrontation naming test (Test of Lexical processing in Aphasia: TLPA), one-minute verbal fluency task (semantic category: animal, phonetic category: initial syllable /hu/, /a/, and /ni/), and picture description task (The Boston Cookie-Theft picture description task). The analysis of the picture description task is divided into two aspects, syntactic and semantic. We expected that language deficits of MCI and mild AD patients would be more readily identified in the picture description task and verbal fluency task rather than in aphasic tests such

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as CADL and confrontation naming test. The results were following: 1) the MCI group showed the comparable to those without cognitive impairment on CADL and confrontation naming test, 2) as expected, performances of the NC group were better than those of the MCI and mild AD groups, but no significant differences were shown between MCI and mild AD group in verbal fluency task. 3) in the Cookie-Theft picture description task, performances of the MCI patients were noninformative, inefficient, and empty on semantic aspects compared to the NC group. However, no differences were observed among the three groups including the mild AD group on syntactic aspects. These findings suggest that the picture description task is useful in detecting the subtle language deficits in subjects with MCI. In conclusion, this study demonstrates that the picture description task can sensitively detect complex integrated communication abilities, although it is very quick and simple.

P2-44

Treatment benefits of memantine in moderately severe to severe Alzheimer's disease patients with behavioural symptoms

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Recent study results show that there are behavioural benefits of memantine in Alzheimer's disease (AD), and long standing evidence that behavioural disturbance is associated with an accelerated disease progression. Symptoms of agitation and psychosis are frequently distressing for the patients who experience them and increase caregiver burden and related clinically significant depression. Furthermore these symptoms have been repeatedly highlighted as major determinants of institutionalization and increased direct costs of care. In the context of recent serious safety concerns about the use of atypcial antipsychotics in people with Alzheimer's disease, we examined the effects of memantine in patients with specific behavioural symptoms. A post-hoc subpopulation analysis was conducted on pooled data from three large 6-month studies of moderately severe to severe AD. Patients were included in the Behaviourally Disturbed Subpopulation (BDS) if they had baseline NPI sub-item scores above or equal to 1 on any of these: agitation/aggression, delusions or hallucinations. Of 983 patients, 593 (60%, 287 placebo, 306 memantine) met the BDS entry criterion. Compared to those without these symptoms at baseline, placebo-treated patients in the BDS showed greater decline across all outcomes (SIB, CIBIC-plus, ADCS-ADL_{19} and NPI). However, relative to placebo, there were statistically significant benefits for memantine for all outcomes in the BDS (SIB, CIBIC-plus, ADCS-ADL_{19} and NPI) at all visits (LOCF, OC). Compared to placebo, memantine-treated BDS patients were statistically significantly less likely to withdraw, withdraw due to adverse events, and withdraw due to agitation, aggression or psychosis. While these analyses were post-hoc, the results provide further support for the efficacy of memantine across all domains, in moderately severe to severe AD. Furthermore, they highlight the utility of memantine in the treatment and prevention of key behavioural symptoms, with potential safety advantages compared to other pharmacological treatments currently prescribed.

P2-45

10/66 Population-based studies: Preliminary results on the prevalence and impact of dementia

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Well-designed epidemiological research is lacking in many world regions, particularly in low and middle income countries where two thirds of the world estimated 24 million people with dementia live. Earlier studies have suggested that the prevalence of dementia may be considerably lower in developing than in developed parts of the world. Descriptive research can clarify the extent of the problem in those regions, and identify its social, societal and public health impact. One phase cross-sectional surveys of all over 65 year old residents in catchment areas in ten LMICs (China, India, Nigeria, Cuba, Brazil, Dominican Republic, Venezuela, Mexico, Argentina and Peru). Sample size is generally 2000 per country. Comprehensive assessment of sociodemographics, SES, cognition, functioning, care arrangements, physical and mental health. Diagnosis of dementia according to (more restrictive) DSM-IV

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criteria and (less restrictive) 10/66 algorithm. "Needing much" care was coded by interviewers on the basis of observation and all available information. Prevalence of 10/66 dementia is generally double that of DSMIV dementia. DSMIV dementia is particularly rare in India, attributable to the small proportion of family informants confirming cognitive decline and social impairment, even in the presence of objective evidence of memory impairment. In other centres 10/66 dementia is more prevalent and DSM IV dementia slightly less prevalent than DSM IV dementia in Europe. 10/66 dementia is overwhelmingly the most important contributor to "needing much care" in all centres. Earlier studies may have underestimated the prevalence of dementia in regions with very low awareness of this emerging public health problem.

P2-46

Alzheimer's disease-associated peripheral markers are interrelated to lipid metabolism

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AD pathology is associated with many processes such as vascular dysfunction, oxidative stress, lipid metabolism, vitamins defect and beta-amyloid deposition. We analysed the levels of total cholesterol (TC), HDL-cholesterol (HDL), LDL-cholesterol (LDL), VLDL-cholesterol (VLDL), triglycerides (TG), apolipoprotein E (ApoE), total nitric oxide (NO), B12 vitamin (B12), angiotensin-converting enzyme (ACE) and beta-amyloid 1–42 (Aβ) from serum of AD patients and non-demented control subjects. Atherogenic indexes were calculated: TC/HDL and LDL/HDL. The aim of this study was to correlate some of the main AD-associated markers in order to observe their possible involvement in AD pathology. A positive correlation NO/HDL and a negative correlation between NO and atherogenic indexes were observed in the two groups. ApoE levels were also positively correlated with TG, TC and VLDL in AD and controls. However, in AD, we observed that ACE were positively associated with TC, VLDL and TG. Aβ exhibited a positive association with HDL and a negative correlation with atherogenic indexes and LDL. It seems that ApoE and ACE are directly associated with vascular risk lipid markers while NO and Aβ show a positive interaction with an atheroprotective effect and a negative influence on atherogenic markers in AD patients. In conclusion, all of the studied AD-associated parameters showed significant correlations with cholesterol and triglyceride metabolism. These data might suggest the existence of a common final pathway associated with lipid metabolism and vascular function which migh contribute to AD pathogenesis.

P2-47

Endothelial NOS3 polymorphism influence on peripheral vascular markers in Alzheimer's disease

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Oxidative and vascular factors are implicated in Alzheimer's disease pathology. In the vascular system, nitric oxide is generated by endothelial nitric oxide synthase 3 (eNOS3) and has an important role in vascular tone. Recently, a significant association between G894T and e4a/b polymorphisms in eNOS3 gene and Alzheimer's disease (AD) was found. The presence of the T allele and the 4a variant is associated with vascular risk, and the GG genotype increases the risk of developing late-onset AD. We analysed Total-cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, triglycerides, apolipoprotein E, nitric oxide (NO) and 1–42 beta-amyloid levels according to eNOS3 polymorphisms in the serum of 39 patients with AD and 28 control subjects. We have not found any association between the genetic variants of eNOS3 gene and serum nitric oxide levels. However, we found a strong positive correlation between HDL-cholesterol and NO in AD patients with the T allele of the G894T polymorphism and in AD patients without the "a" allele of e4a/b NOS3 polymorphism that did not appear in AD patients with GG polymorphism and AD group with presence of allele "a". The same HDL-cholesterol/NO correlation was observed in all eNOS3 polymorphism groups in healthy subjects. Adding the two vascular risk polymorphism eNOS3 (T and "a" allele) we found an inverse negative NO/HDL-cholesterol correlation in healthy subjects carrying vascular risk alleles with respect to those without T or "a" allele. We did not find any change between the Alzheimer group with or without vascular risk polymorphisms.

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The addition of the two vascular risk eNOS3 alleles seems to have a different effects on NO/HDL-cholesterol correlation in AD. HDL-cholesterol and NO are suggested to have atheroprotective effect. The different pattern found in both AD and control subjects carrying vascular eNOS3 polymorphisms might be related to the vascular pathology potentially involved in AD.

P2-48

Brain optical topography in Alzheimer's disease and vascular dementia

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Alzheimer's disease and dementia with vascular component (DVC = VD + MXD) are the most prevalent forms of dementia in developed countries. Both pathologies have many similarities that in certain cases are difficult to diagnose and treat. Some studies have demonstrated that there are significant differences in 25% of more than 100 parameters such as anthropometry, cardiovascular function, aortic arteriosclerosis, brain atrophy, blood pressure, blood biochemistry, hematology, and other parametric variables between AD and DVC (Cacabelos et al., Neurol Res. 2004 Jul; 26(5):459–80). We have investigated brain hemodynamics in both forms of dementia and found differences between both clinical entities. We have assessed brain oxygenation patterns by using Optical Topography (OT), which is a special type of spectrometry with near infrared light developed by Hitachi. This technique can measure relative variations of hemoglobin (Oxy-, Deoxy- and Total-Hb) concentrations in the brain cortex, in response to activation by different stimuli. We have measured cortical activation after photic stimulation with white light for one minute. OT recordings have been performed in the occipital cortex of 31 patients with dementia (age: 72.34 ± 10.50 years; range: 43–88 years): 14 AD (age: 74.52 ± 7.21 years; range:65–88 years) and 17 DVC (age: 69.92 ± 11.8 years; range:43–82 years), and 21 Control subjects (age: 52.30 ± 14.92 years; range: 18–72 years). The parametric variation in the concentrations of Oxy-Hemoglobin, Deoxy-Hemoglobin, and Total-Hemoglobin indicates that AD and DVC have a different pattern of activation in response to photic stimulation. Both types of dementia also differ from controls in their pattern of brain oxygenation. According to our results, brain Optical Topography is a valuable technique to establish diagnostic criteria for the early identification of senile dementia.

P2-49

Profile of the caregivers of Alzheimer's disease patients attended in a Reference Center for Cognitive Disorders

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Objective: To evaluate the profile and the caregiver burden of patients with Alzheimer's disease attended in a Reference Center for Cognitive Disorders
Methods: We evaluated caregivers of AD patients collecting demographic data and information on the relationship with the patient, if he/she lives with the patient, time as caregiver and measured the burden with the Zarit scale. The patients had been evaluated with the scales and tests to investigate the cognition (Cambridge Cognitive Test – CAMCOG; Mini-examination of the Mental State), the presence of psychotic alterations and behavior (Inventory Neuropsychiatry – NPI) and the intensity of the functional impairment (Questionnaire of Functional Activities – QPF, of Pfeffer et al.).
Results: Regarding the 31 caregivers with Alzheimer's disease, 77.4 were female, daughters, the mean age was 58.6 years, the educational level was 8.1 years, 68% of the caregivers lived with the patient, 71% did not work. The time mean as a caregiver was 3 years. Twenty-seven percent of the caregivers presented mild to severe burden. In the analysis with linear regression the only variable that presented significant association with the caregiver of the burden had been prop up them of the NPI and the CAMCOG.
Conclusion: The social demographic characteristics of the sample are similar to those of studies performed in other countries. However, the average time as a caregiver and the frequency of caregivers with mild to intense burden, were smaller than the ones reported in international studies More studies are necessary to verify if the caregiver of the

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burden is less intense in our way. The intensity of the neuropsyquiatrics disorders and the gravity of the cognitive decline had been the main factors associates to the overload in this study.

P2-50

Regional atrophy in Alzheimer's disease measured by optimized voxel based morphometry and comparison of hippocampal atrophy with manual ROI volumetry

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Purpose: Optimized voxel based morphometry (VBM) has been increasingly applied to investigate differences in brain morphology between a group of patients and control subjects. Optimized VBM permits comparison of gray matter (GM) volume at voxel-level from the entire brain. The purpose of this study was to assess the regional GM volume loss measured by optimized VBM in AD compared to controls, and to measure hippocampus volume using manually delineated volumetry and compare the results to optimized VBM findings.

Materials and methods: Twenty-three AD (70 ± 8 y; m/f = 7/16, Mini-Mental State Exam [MMSE] = 22.2) and 20 cognitively normal elderly control subjects (69 ± 4 y; m/f = 10/10) were included in this study. Optimized VBM was performed with statistical parametric mapping (SPM2).The ROI-based hippocampus volumetry was manual traced using an in-house program.

Results: The AD group had a lower whole brain GM% compared to controls ($45.0 \pm 2.1\%$ vs. $48.4 \pm 1.6\%$, $p = 0.00001$). VBM analysis reveals many regions exhibiting GM loss, including hippocampus, amygdala, anterior cingulate, posterior cingulate, insula, frontal lobe and middle temporal complex. The hippocampal volume of AD patients measured by manual ROI volumetry was significantly lower than that of controls (1.5 ± 0.3 ml, 0.12% vs. 2.5 ± 0.3 ml, 0.19%, $P < 0.001$), consistent with optimized VBM findings.

Conclusions: The hippocampal volume in AD patients was significantly smaller than in controls using both optimized VBM and manual delineated ROI analysis. Optimized VBM analysis is a quick and objective method for evaluating regional atrophy from the whole brain.

P2-51

A 67-year-old patient with Down syndrome and Alzheimer pathology

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Down syndrome is a congenital malformation syndrome that can be caused by various chromosome abnormalities, especially by trissomy 21. Patients usually develop early signs of neurological senility, manifesting clinical dementia usually initiating on the fourth decade of life. The underlying brain pathology exhibit varying degrees of neuritic plaques and neurofibrillary tangles identical to those observed in typical cases of Alzheimer's disease (AD). We report an autopsied case of a Down syndrome patient whose clinical mental deterioration was diagnosed after the age of 60. A 67-year-old woman with Down syndrome gradually developed memory disturbance and functional dependence beginning at age 61. CT findings suggested diffuse cortical atrophy, confirmed by the neuropathological examinations carried out on the autopsy. Macroscopically, the brain showed a severe weight reduction (760 g) due to global cortical atrophy and enlargement of ventricular spaces. Microscopically, numerous senile plaques (SP) with high predominance of neuritic plaques and core plaques as well as neurofibrillary tangles (NFT) were found on parietal, frontal, temporal and occipital cortexes on a symmetrically bilateral distribution, as well on the hyppocampus, subcortical nuclei and brainstem. Immunohistochemestry techniques against hyperfosforilated-tau (PHF-1, gift of Dr. P. Davies) amyloid (4G8 – signet) and α-synuclein (EQV-1, gift of Dr. K. Ueda) were used. Most of the pathologic findings developed on the layers III and V of cerebral cortex, as the typical distribution found in AD. The case was classified as Braak stage VI and CERAD stage 3. No changes related to α-synuclein were found.

Conclusions: Advances in health care in the last decades allowed important increase in life expectancy of patients with Down syndrome, as is reported

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in this case. However, the prevalence of dementia in these patients increases with age progressively in each decade. This process occurs 30–40 years earlier than in the general population with the same typical pathological findings of AD.

P2-52

Impact of the traditional Chinese medicine, Yi-Gan San, on neuronal survival and neurogenesis following insults associated with aging and Alzheimer's disease

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Herbal medicine products have been used in the treatment of behavioral and psychological symptoms of Dementia especially in elderly patients. They have also reported useful for cognitive impairment of Alzheimer's disease (AD) as well as choline esterase inhibitors and NMDA-receptor antagonist. However, cellular mechanism of these herbal drugs for understanding their clinical efficacies have not yet almost unknown. In the present study, we investigated the effect of traditional Chinese medicine, Yi-Gan San, which has been shown to have therapeutic efficacy for cognitive impairment and agitation in AD and Dementia with Lewy bodies (DLB), on neuronal survival and neuronal differentiation change induced by the injuries models for aging and AD, using cultured neural cells from rat embryos. For analysis of survival function change, we evaluated the neuroprotective effect of Yi-Gan San against beta amyloid-, hydrogen peroxide- and glutamate-induced injuries in cortical neurons using MTT and LDH method, compared to the effects of donepezil and atypical antipsychotic olanzapine. To analyze cellular mechanism, we focused on the protein expression change of alpha-synuclein and phosphorylated alpha-synuclein, which reported to be aggregated in Lewy bodies in DLB patients, in injured neurons. For analysis of neurogenesis, we evaluated the neuronal differentiation change of neural stem cells (NSCs) by using a method based on cell counting and ELISA. The results revealed that Yi-Gan San could directly modulate neuronal survival and neurogenesis function in aging and AD conditions. The different potential of Yi-Gan San, donepezil and olanzapine on neuroprotection and neurogenesis possibly relate to the therapeutic efficacy profiles of these drugs. The alteration of alpha-synuclein expression will be discussed in detail.

P2-53

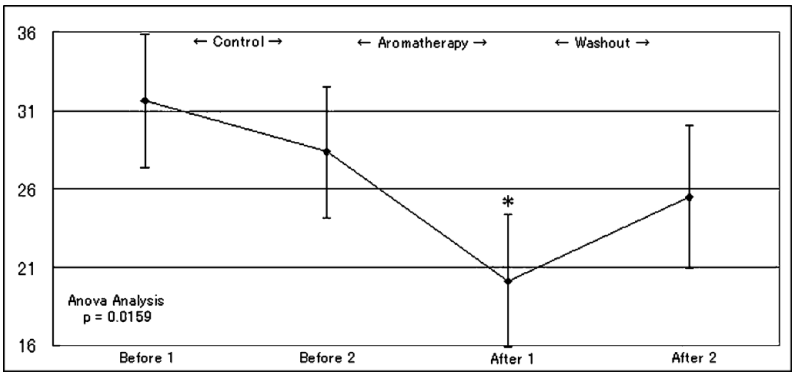
Use of serum insulin-like growth factor-I levels to predict psychiatric nonresponse to donepezil in patients with Alzheimer's disease

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Objective: Insulin-like growth factor-I (IGF-I) deficiency may be involved in cognitive deficits seen with aging and in neurodegenerative diseases such as Alzheimer's disease (AD). This study was aimed at investigating whether non-responder to donepezil could be predicted using decreased serum levels of IGF-I in AD patients.
Design: This study involved 106 elderly subjects: 50 patients with AD and 56 age-matched controls without dementia. In patients with AD, donepezil was given orally 3 mg/day for 4weeks and 5 mg/day for another 12 weeks. AD patients were divided into responders and non-responders based on the changes in Mini-Mental State Examination (MMSE) scores before and 16 weeks after treatment with donepezil. Serum levels of IGF-I and atherogenic lipoproteins were determined.
Results: Before treatment with donepezil, there was a significant inverse correlation between serum IGF-I levels and the MMSE scores in all subjects. Serum IGF-I levels and the MMSE scores were significantly lower in AD patients than in non-demented controls and were the lowest in non-responders to donepezil. On multiple logistic regression, non-responders to donepezil showed decreased serum IGF-I levels < 110 ng/ml and MMSE scores < 15 points before treatment.
Conclusion: These findings suggest that decreased levels of serum IGF-I combined with MMSE scores before treatment could predict non-responders to

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P2-54

donepezil among AD patients, which may be a simple and practical method for selecting patients expected to show a response to treatment.

P2-54

Effect of donepezil on individual behaviors in patients with severe Alzheimer's disease

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Problem behaviors are an important clinical manifestation of Alzheimer's disease (AD) and are associated with greater caregiver burden, greater cost of care, and are a major reason for nursing home placement. In randomized clinical trials of donepezil, behavioral benefits have been demonstrated, but significant drug-placebo differences in total Neuropsychiatric Inventory (NPI) scores are not always apparent. Analysis of individual behaviors may be more meaningful than the total score of a behavioral measure. The objective of these analyses was to examine behavioral benefits in donepezil-treated patients whose cognition and global/function/behavior stabilized or improved. Patient data were pooled from two 6-month randomized, placebo-controlled studies of donepezil in severe AD (MMSE $\leq$12, FAST 5–7d). Cognition was assessed by the Severe Impairment Battery (SIB), global function by the Clinician's Interview-Based Impression of Change-Plus caregiver input or the Clinical Global Impression of Improvement, Activities of Daily Living (ADL) by the AD Cooperative Study ADL-severe, and behavior by the 12-item NPI. At month 6, changes on individual NPI items were analyzed for ITT-LOCF donepezil patients showing multi-domain responses. Neither study showed significant between-group differences in total NPI for the all donepezil patient group, although both donepezil and placebo groups showed improvement from baseline. Among a subgroup of donepezil-treated patients showing combined domain response A-stabilized/improved cognition and improved global function or ADL or behavior-significant improvements vs. a pooled placebo group were seen for apathy/indifference, anxiety, and agitation (Table). For combined response B-stabilized/improved cognition and global function and ADL-significant improvements were seen for apathy/indifference and anxiety, with agitation and eating disorders showing borderline significance; for combined response C-improved cognition ($\geq$4 SIB points) and stabilized/improved global function and ADL-significant improvements were seen for apathy/indifference, with anxiety, agitation, aberrant motor behavior and eating disorders showing borderline significance. Notable differences between donepezil responders and the placebo group were not seen for other NPI items. In conclusion, AD patients showing multi-domain responses to donepezil may demonstrate distinct patterns of behavioral improvement despite varying and inconclusive results on the total NPI.

P2-55

Patients' versus caregivers' reports of quality of life in Alzheimer's disease

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Objectives: This study investigated the differences between patient and caregiver reported Quality of Life (QOL) in Alzheimer's disease (AD) and assessed the relationship of patient QOL and cognitive function, activities of daily living (ADL) and behavioral and psychological symptoms of dementia (BPSD).
Methods: Fifty-one patients with AD and their caregivers participated. Patient QOL was assessed using by the Korean version of Quality of Life-Alzheimer's Disease (KQOL-AD) scale. Each patient and caregiver rated the patient QOL. Korean version of mini-mental state examination (K-MMSE), ADL and neuropsychiatric inventory (NPI) were also assessed.
Results: There were significant correlations between patients and caregiver reports of patient on mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores around the house, ability to do things for fun, money, and life as a whole, and total KQOL-AD scores. Patient ratings of patient QOL-AD were higher than caregiver ratings on most patient QOL measures. However, there were no significant differences between patient and caregiver ratings on any QOL item. QOL Scores of patient QOL were significant correlated with NPI scores, but were no significant correlated with K-MMSE and ADL scores.
Conclusions: Caregiver and patient reported QOL did not differ. Patients seem to be able to assess their own QOL properly although they have impairment in cognitive function or activities of daily living. BPSD of AD patients adversely affect patient QOL.

P2-56

Quality of life in Korean Alzheimer's dementia patients

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Objectives: The aim of this study was to analyze factors affecting quality of life (QOL) among Korean dementia patients.
Methods: The subjects were consisted with 54 patients with dementia of the Alzheimer's type and 54 normal aged controls with age over 60. The QOLs were assessed with the Korean Version of the Quality of Life in Alzheimer's Disease: Patient and Caregiver Report (KQOL-AD). For analyzing factors affecting QOL in dementia, the clinical data were obtained by structured interview and medical records, serum homocysteine levels were measured, and the severity of dementia (Mini-Mental State Examination, Clinical Dementia Rating, Global Deterioration Scale), functional activities (Activities of Daily Living, Instrumental Activities of Daily Living) and depression (Geriatric Depression Scale) were evaluated using various rating scales.
Results: 1) The mean ($\pm$ S.D.) score of KQOL-AD in patients with dementia of the Alzheimer's type (24.30 ± 5.06) was significantly ($p < 0.005$) lower than those in normal aged controls (26.56 ± 3.25). 2) The factors influencing on KQOL-AD in patients with dementia of the Alzheimer's type were age ($p < 0.01$), cognitive function ($p < 0.01$), severity of dementia ($p < 0.01$), activities of daily living ($p < 0.01$), depression ($p < 0.01$) and serum homocysteine levels ($p < 0.05$).
Conclusions: In conclusion, multiple factors including problems originated from dementia itself as well as causes fundamentally related with pathophysiology of demenita might influence on the quality of life in patients with the Alzheimer's dementia.
Educational objectives: At the conclusion of this presentation, the participant should be able to recognize the factors affecting quality of life among Korean dementia patients.

P2-57

Use of psychoactive drugs among older people living in a Brazilian community

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It is estimated that the older Brazilian population (65+) will grow from 2.7% in 1960 to 14.0% before 2050. The rising prevalence of neurodegenerative diseases and affective disorders has already been verified in studies performed in large Brazilian cities. The purpose of this retrospective study is

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to evaluate psychoactive medication use in older residents of a Brazilian community. All residents aged 65+ (n = 161) of one neighborhood of Campo Belo, Brazil (population 48,000) were evaluated regarding the use of psychoactive drugs. Among the 161 older people, 21 (13.0%) regularly used prescribed anxiolytics, antidepressants and/or anticonvulsants. All anxiolytics (except buspirone in one case) were intermediate- or long-acting benzodiazepines (BZDs) and were used regularly by 15 (9.3%) individuals. Antidepressants (exclusively tricyclics and tetracyclics) were used regularly by four (2.5%), and anticonvulsants by five (3.1%). No subject or caregiver reported use of neuroleptics or drugs to treat Alzheimer's or Parkinson's diseases (except one case of biperiden). Cinnarizin, flunarizin and codergocrine were used by 13 (8%). The data suggest improper prescription practices. All except one anxiolytics users were being prescribed long-acting BZDs. Antidepressants were apparently underutilized and belonged to classes that represent second-line options for older individuals. Drugs of disputed therapeutic efficacy (cinnarizin, flunarizin and codergocrine), were widely prescribed. The only drug used to treat Parkinson disease is not appropriate for older patients. Since no antipsychotic drugs or drugs to treat Alzheimer's disease were being used by this population, it is important to ask whether the psychiatric manifestations of these common conditions were being treated with BZDs or even barbiturates. The population of the Arnaldos neighborhood must be considered a young population since older residents account for less than 4% of the total. However, it seems that some of the public health problems characteristic of aged populations are already present in this community. The increasing prevalence of neuropsychiatric problems related to the ageing process, coupled with difficulties in accurately diagnosing and correctly treating these conditions may be causing the high level of inappropriate psychoactive drug use.

P2-58

Activity of superoxide dismutase in Alzheimer's disease

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Background: The reactive oxygen species are natural metabolic products and they are in each cell in the body. But sometimes they can injure cells by reacting with cell component e.g. lipids, nucleic acid. Under normal conditions, antioxidant defenses detoxify most reactive oxygen species and limiting damage to repairable level. These defenses include enzymes superoxide dismutase, catalase, gluthatione peroxidase and reductase. A growing body of data suggests that free radicals are involved in the pathogenesis of Alzheimer's disease. The level of free radicals is growing and the activity of enzymes is decreased in the same time. There is not efficiency. Several studies have confirmed these findings, but there is conflicting information regarding the activity of some of the enzymes. We need to check it. And reducing oxidative damage may be beneficial in the treatment and prevention of Alzheimer's. The aim of the present work superoxide dismutase activity was evaluated in the following stages of disease, age and gender.

Instruments and methods: We examined 49 patients, 49 controls. Alzheimer's disease was diagnosed according to ICD-10 criteria. The intensity of cognitive decline was assessed by: The Mini Mental State Examination Scale, Clock test, Global Deterioration Scale by Reisberg, Clinical Global Impression. Hachinski Scale was made. Psychiatric and somatic examination, CT or NMR, laboratory exam were preformed Enzymes activity was evaluated by means of spectrophotometric method by using BIOTECH method.

Results: Significant increase was noted in the activity of superoxide dismutase in the early stage of the disease. There was not correlation between enzymes activity and age. Significant decrease was noted in the activity of superoxide dismutase in ill men.

Conclusions: The results may suggest the ineffective function of anti-oxidative enzymatic marker's barrier play role in Alzheimer's disease and lack of correlation between age and activity SOD-1 can confirm that this process in not normal aging.

P2-59

Complexity analysis of Gamma band EEG correlated with severity of Alzheimer's disease

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Objectives: The Gamma band power is an index of cognitive functions. A characteristic finding of

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EEG abnormality obtained from nonlinear dynamical methods in Alzheimer's disease (AD) patients is a decreased complexity. Non-linear EEG analysis can provide information about the functioning of neural networks that cannot be obtained with linear analysis. In this study, we attempted to explore the relationship between gamma band complexity and AD.

Methods: The AD group consisted of 22 patients who fulfilled the DSM-IV criteria of AD with no space occupying lesions confirmed by brain CT or MRI. The normal control (NC) group consisted of 22 subjects with no personal history of psychiatric or neurological abnormalities. The band pass filtering was used for gamma frequency band (30–50 Hz) before nonlinear analysis. The Grassberger-Procaccia algorithm was used to calculate correlation dimension (D2) from the EEG. We explored the D2 value of gamma band, MMSE score, and duration of illness.

Results: The D2 value of gamma band was most significantly lower on T3, T5 ($P < 0.01$) and Fp1, O1 ($P < 0.05$) electrodes in the AD patients compared to NC group. And the D2 value of whole band complexity was significantly lower on O1, O2 electrodes ($P < 0.01$, $P < 0.05$) in the AD patients compared to NC group. But the D2 value of whole band complexity was significantly higher on Fp2 electrode ($P < 0.05$) in the AD patients compared to NC group. The MMSE score had a significant positive correlation with the D2 value of gamma band complexity in the AD patients. There was a negative correlation between the duration of illness and the D2 value of whole band complexity in the AD patients.

Conclusions: Our results showed that AD patients had decreased gamma band complexity on left temporal area. And gamma band complexity was well correlated with the MMSE score. We suggest the decreased gamma band complexity in the EEG can be a hallmark of decreased complexity of Alzheimer's patients.

P2-60

Involvement of the prostaglandin E_2 receptors, EP2 and EP4, in the production of amyloid-β peptides both *in vitro* and *in vivo*

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Amyloid-β peptides (Aβ), generated by proteolysis of the β-amyloid precursor protein (APP) by β- and γ-secretases, play an important role in the pathogenesis of Alzheimer's disease (AD). Inflammation is also believed to be integral to the pathogenesis of AD. Here we show that prostaglandin E_2 (PGE_2) stimulates the production of Aβ in cultured human embryonic kidney (HEK) 293 or human neuroblastoma (SH-SY5Y) cells, both of which express a mutant type of APP (APPsw). We have demonstrated using subtype-specific agonists that, of the four main subtypes of PGE_2 receptors (EP1–4), EP4 receptors alone or EP2 and EP4 receptors together are responsible for this PGE_2-stimulated production of Aβ in HEK293 or SH-SY5Y cells, respectively. An EP4 receptor antagonist suppressed the PGE_2-stimulated production of Aβ in HEK293 cells. This stimulation was accompanied by an increase in cellular cAMP levels and an analogue of cAMP stimulated the production of Aβ, demonstrating that EP2 and EP4 receptor-coupled increases in the cellular level of cAMP are responsible for the PGE_2-stimulated production of Aβ. Immunoblotting experiments and direct measurement of γ-secretase activity suggested that PGE_2-stimulated production of Aβ is mediated by activation of γ-secretase but not of β-secretase. Transgenic mice expressing APPsw showed lower levels of Aβ in the brain, when they were crossed with mice lacking either EP2 or EP4 receptors, suggesting that PGE_2-mediated activation of EP2 and EP4 receptors is involved in the production of Aβ *in vivo* and in the pathogenesis of AD.

P2-61

Angiotensin-converting enzyme converts Aβ1–42 to Aβ1–40 and its inhibition enhances brain Aβ deposition

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The abnormal deposition of the amyloid β-protein (Aβ) in the brain appears crucial to the pathogenesis of Alzheimer's disease (AD). Recent studies suggested that highly amyloidogenic Aβ1–42 is a cause of neuronal damage leading to AD pathogenesis and that monomeric Aβ1–40 has less neurotoxicity than Aβ1–42. We found that mouse and human brain homogenates exhibit an enzyme activity converting Aβ1–42 to Aβ1–40, and that the major part of this converting activity is mediated by the angiotensin-converting enzyme (ACE). Purified human ACE converts Aβ1–42 to Aβ1–40 as well as decreases Aβ1–42/Aβ1–40 ratio and degrades Aβ1–42 and Aβ1–40. Importantly, the treatment of Tg2576 mice with an ACE inhibitor, captopril, promotes predominant Aβ1–42 deposition in the brain, suggesting that ACE regulates Aβ1–42/Aβ1–40 ratio in vivo by converting secreted Aβ1–42 to Aβ1–40 and degrading Aβs. The up-regulation of ACE activity can be a novel therapeutic strategy for AD.

P2-62

ATP-binding cassette transporter G4 is highly expressed in Alzheimer brain

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It is well known that apolipoprotein E (apoE) ϵ4 is the risk for Alzheimer's disease (AD). Since high-density lipoprotein (HDL) particle has the apoE as its core protein, a cholesterol metabolism is affected by the function of apoE in brain. ABCG4, membrane cholesterol transporter has been implicated to mediate cholesterol efflux from cells in the presence of HDL. Previous report shows HDL-mediated cholesterol efflux is significantly high in overexpression of ABCG4 *in vitro*. ABCG4 is found to be expressed in the brain and eyes by Northern blotting. So far, precise localization of ABCG4 in the brain has not been shown. The specificity of the anti-ABCG4 antibody was tested by western immunoblot analysis using AD brain tissue, and single band was detected as ABCG4 protein which was corresponding to approximately 97 kDa. In AD brain tissues, immnunohistochemistry using the anti-ABCG4 antibody gave staining of some cells with microglia-like morphology. They were also positive with the antibody to LCA, a marker of microglia. Microglial cells located in the senile plaques were also positive to ABCG4. In non-neurological cases, no positive staining to ABCG4 was seen in the cortical and nigral tissues. In situ hybridization histochemistory revealed that ABCG4 mRNA was located in some cells in AD. The microglial cells closely related to senile plaques expressed mRNA signals of ABCG4. It is first report to show that ABCG4 transporter is highly expressed in AD brain. The expression could be linked to a lipid metabolism in the brain, and the development or progression of AD.

P2-63

Suppression of APP metabolism by DHHC family proteins

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Objective: We have isolated a novel membrane protein AID, which strongly suppressed production of metabolites of the amyloid precursor protein (APP). The AID contained the DHHC cysteine-rich domain (DHHC-CRD) with four putative transmembrane segments, and identified as one of the 23 mammalian DHHC family proteins, some of which were reported as protein palmitoyltransferases and implicated in membrane trafficking and subcellular targeting of proteins. Therefore, we analyzed regulatory mechanism of APP metabolism by DHHC proteins containing AID from the viewpoint how DHHC proteins modify the intracellular localozation of APP.

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Methods: First, we examined whether all DHHC family proteins can suppress the APP catabolism. FLAG- or Myc-tagged DHHC proteins were prepared and coexpressed with APP in cells. Production of Aβ in medium was examined with sELISA. Next, we examined whether DHHC family proteins including AID that showed the suppressive effect in Aβ generation could alter the intracellular localization of APP. Localization of APP were observed with confocal laser scanning microscope.
Results: We found that several DHHC family proteins including AID altered maturation of APP and suppressed production of metabolite of APP including Aβ generation by altering the subcellular localization of APP.
Conclusion: Several DHHC family proteins containing AID may regulate APP metabolism through the control of the intracellular localization of APP.

P2-64

Tissue analysis of growth hormone (GH) and α-melanocyte-stimulating hormone (α-MSH) in pituitaries of Alzheimer's patients (AD)

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The two major neuropathological findings of AD are senile plaques and neurofibrillary tangles. According to the amyloid hypothesis, the deposition of Aβ is important as a causative factor of this disease. Neprilysin degrades Aβ under the control of somatostatin, which inhibits growth hormone as well. On the other hand, α-MSH is suggested to be downregulated under conditions of chronic fatigue. When AD patients are under mental stress, α-MSH production may be somehow influenced. We carried out immunohistochemical analysis of 10 samples including 3 from patients with AD, 3 from patients with cerebrovascular problems, 1 Lewy body disease patient and 1 normal subject. On GH staining, the majority of samples showed a mild decrease in GH-positive cells. However, the numbers of surviving α-MSH positive cells were drastically reduced in all cases examined except for two non-AD cases. Examination of only ten samples did not allow for confirmation of this tendency. More samples should be included in future in order to examine changes in GH and α-MSH in AD.

P2-65

Specific binding of Aβ42 mimic peptides to prefibrillar soluble oligomer resulting in the inhibition of Aβ42-fibrillation

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Recently we established several human single chain Fvs (scFv) which bound to the Aβ42 fibril, not to soluble form (PD/AD 2007, Salzburg, 2007). As these scFvs inhibited the Aβ42 fibril formation *in vitro*, these antibodies may be of value for diagnosis and therapeutics of AD. However, smaller molecules like peptide which prevent Aβ fibrillation, have more preferable characteristics for the development of therapeutic agents. Previously we demonstrated that peptide phage library clones selected by a conformational epitope-recognizing and inhibitory monoclonal antibody (mAb) might display moieties that mimic a receptor/ligand-like three-dimensional structure (Nat. Biotech., 16, 267–270, 1998). These mimic peptides also had functional activity on receptor/ligand interaction. In this study, we attempted to isolate the peptide motifs which were recognized with anti-fibril Aβ42 scFv, B6. The B6 scFv binds to the Aβ42 fibril and inhibits Aβ42 fibril formation. We isolated phage clones from peptide phage display libraries and identified several different peptide motifs (B6-L1, B6-L10 and B7-C15). These phage clones significantly inhibited Aβ42 fibrillation. According to this result, synthetic peptides based on these phage motifs (B6-L1, B7-C15) had inhibitory effect on Aβ42 fibrillation by binding to prefibrillar soluble oligomers. Taken sequence homology analysis of these motifs to Aβ42 together, it is suggested that B6-L1 and B7-C15 might be mimics of Aβ42 fibril.

P2-66

Amyloid β N-terminal-end specific monoclonal antibody 82E1 reduced β-amyloid toxicity in culture cells and cerebral amyloidosis in an Alzheimer mouse model

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Introduction: We have developed a monoclonal antibody named 82E1, which is highly specific and sensitive against amyloid β (Aβ) N-terminal-end. Since the 82E1 antibody does not cross-react with full-length Aβ precursor protein (APP), it is strongly proposed that this antibody can be applicable for an antibody drug therapy. Here, we examined the effect of 82E1 antibody in terms of Aβ toxicity in culture cells and cerebral amyloidosis in Alzheimer mouse model brains.

Materials and methods: In *in vitro* study, rat pheochromocytoma PC-12 cells were cultured and Aβ42 and antibody, 82E1 or control IgG, was added to the each well. After 1 day culture, Aβ toxicity was assessed by MTS or LDH assay. In *in vivo* study, the 82E1 antibody was administered to 16-month-old Tg2576 mice (Alzheimer mouse model) with once a week by intraperitoneal injection at a dose of 10 mg/kg, while PBS was administered for control group. After 12 times administrations, animals were euthanized and brain Aβ levels and cerebral amyloidosis were examined by ELISA and immunohistochemical image analyses, respectively.

Result: The 82E1 antibody ameliorated the Aβ toxicity in PC-12 cells compared to control IgG. Moreover, the administration of 82E1 reduced brain Aβ levels/cerebral amyloidosis in Tg2576 mice.

Conclusion: These findings provide evidence that the administration of 82E1 antibody might be valuable therapeutic strategy for reducing Alzheimer pathology.

P2-67

Expression of reticulon 3 in Alzheimer's disease brain

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β-secretase BACE1 is a membrane-associated aspartyl protease necessary for the generation of β-amyloid protein (Aβ). Recently, we identified reticulon 3 (RTN3) and RTN4-B/C as BACE1-associated membrane proteins that can inhibit BACE1 function. RTN3 is known to be expressed highly in the brain. In this study, we studied the expression pattern of RTN3 in the human brain and also examined whether RTN3 is involved in the pathology of Alzheimer's disease (AD). Immunohistochemical staining using a specific antibody against RTN3 revealed that RTN3 immunoreactivity is mainly present in pyramidal neurons in the human cerebral cortex. Double immunofluorescence for RTN3 and Aβ indicated that RTN3 does not localize in senile plaques. Western blot analysis of brain homogenates detected no significant difference in expression levels of RTN3 between control and AD brains. Biochemical subcellular fractionation showed that RTN3 co-localize with BACE1 in various fractions including endoplasmic reticulum (ER) and trans-Golgi network (TGN) fractions. Interestingly, the relative abundance of RTN3 appeared to be increased in ER fractions and decreased in part of TGN fractions in AD samples, compared to control samples. Our results demonstrate that RTN3 is abundantly expressed in pyramidal neurons in the human brain and suggest that RTN3 may be involved in the pathological mechanisms of AD.

P2-68

4 cases of clinically diagnosed as Alzheimer's disease without accumulation of amyloid in the brain revealed by PIB-PET

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Background: Recently, amyloid deposition in the brain can be evaluated by ^{11}C PIB-PET in patients with Alzheimer's disease (AD). However, there has been few reports about the relationship between the

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degree of the amyloid deposition and the disease by using the technique.

Objective: We investigated the association on between the level of amyloid accumulation in the brain and the AD.

Methods: We performed PIB-PET to 12 AD cases and 5 normal controls. All AD patients met NINCDS-ADRDA criteria. PIB binding was calculated using the Logan graphical analysis method to yield regional distribution volume ratio (DVR) with cerebellar as reference. We used the mean cortical DVR (MCDVR) value as an index of amyloid accumulation. Cerebrospinal fluid (CSF) Aβ40, 42, tau, p-tau, and plasma Aβ40, 42 levels were measured in AD subjects. All studies were approved by the Ethics Committee of Osaka City University Graduate School of Medicine, and informed consent was obtained from all the subjects.

Results: MCDVR value was significantly increased in AD as compared with the normal controls. However, 4 patients clinically diagnosed as AD showed no PIB accumulation. In addition, PIB negative AD subjects showed normal CSF Aβ42, tau, p-tau levels in the CSF.

Conclusions: It is useful to diagnosis AD in PIB-PET combined with biomarker, as there was a significant relationship between them. These PIB negative cases suggest they are not AD type dementia.

P2-69

Familial Danish dementia: Co-existence of Danish and Alzheimer amyloid subunits (ADan and Aβ) in the absence of compact plaques

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Familial Danish dementia is an early onset autosomal dominant neurodegenerative disorder linked to a genetic defect in the BRI2 gene and clinically characterized by dementia and ataxia. Cerebral amyloid and preamyloid deposits of two unrelated molecules (ADan and Aβ), the absence of compact plaques (CPs), and neurofibrillary tangles (NFTs) indistinguishable from those observed in Alzheimer's disease are the main neuropathological features of the disease. Biochemical analysis of extracted amyloid and preamyloid species indicates that as the solubility of the deposits decreases, the heterogeneity and complexity of the extracted peptides exponentially increase. Nonfibrillar deposits were mainly composed of intact ADan-(1–34) and its N-terminally modified (pyroGlu) counterpart together with Aβ-(1–42) and Aβ-(4–42) in around 1:1 mixture. The post-translational modification, glutamate to pyroglutamate, was not present in soluble circulating ADan. In the amyloid fractions, ADan was heavily oligomerized and highly heterogeneous at the N- and C-terminus. Its intact N-terminus was post-translationally modified (pyroGlu). Major ADan specie was ADan-(1–33) in neocortex whereas ADan-(1–34) in the hippocampus. Aβ was mainly Aβ-(4–42) and the presence of Aβ-(X-40) was negligible in all the regions tested. A specific interaction between ADan and Aβ molecules was demonstrated *in vitro* by ligand blot analysis using synthetic peptides. The absence of CPs in the presence of extensive NFTs suggests that CPs are not essential for the mechanism of dementia.

P2-70

Application of brief-neuropsychological scale to patients with Alzheimer's disease in early stage

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Objective: The Mini-Mental State Examination (MMSE) is the most widely used among the screening tools for detecting dementia in clinical practice. However, the MMSE is less effective in separating mildly demented patients from controls. The Mini-Dementia Scale (MDS) was developed to distinguish Alzheimer's disease (AD) patients from healthy elderlies. The Brief-Neuropsychological Scale (BNPS) is an extended version of the MDS and consists of the original MDS subtests and additional subtests including tasks for sentence memory (immediate and delayed) and executive function. The aim of this study was to investigate whether the BNPS would be useful to determine AD at a very mild stage.

Method: Participants in this study consisted of 35 patients with AD and age-matched 68 normal

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subjects. The patients were all mildly demented with the Clinical Dementia Rating (CDR) score being 0.5 (11 individuals), 1.0 (23 individuals), or 2.0 (1 individual), and fulfilled the DSM-IV criteria for AD at intake or after follow-up. The MMSE and BNPS were administered to all participants. All participants gave written informed consent.

Results: On each test, the mean score of the control group was significantly higher than that of patient group. The discriminant function analyses revealed that the correct classification rates for the controls and patients were 96.7% and 82.8% by the MMSE, 97.1% and 70.2% by the original MDS, and 100% and 100% by the additional subtests of the BNPS, respectively.

Conclusion: These results indicate that the BNPS is useful to screen AD patients in early stage.

P2-71

Peripheral ethanolamine plasmalogen deficiency in SDAT: Cause or effect?

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Compelling evidence of a biochemical mechanism that is causal to decreased cognitive function in senile dementia of the Alzheimer's type (SDAT) has remained elusive. We report here the first direct evidence that the severity of dementia is the result of a peripheral deficiency in ethanolamine plasmalogens (EtnPls's) in the majority of SDAT subjects. Serum analyses of 429 females and 323 males aged 40–95 of various degrees of dementia have shown that EtnPls's are decreased at all stages of SDAT and that they continue to decrease with increasing severity of dementia. EtnPls's are a major constituent of synaptosomal, neuronal, and glial membranes and are decreased in post-mortem SDAT brain tissue. These data support a hypothesis that the dementia observed in SDAT is due to a deficiency in EtnPls's.

P2-72

How does the people with severe dementia engage objects in daily life ? – Pilot study –

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Purpose: To know the better intervention as occupational therapist, it is important to assess how the people with severe dementia engage with objects and how to communicate to the world. Allen's Leather Lacing Assessment is the test battery, which has provided how the person with dementia engages with objects and tasks. In this study, we want to know how they engage with objects in daily life.

Method: Five such clients whose HDS-R scores were 0 point, and who were living in a geriatric health care facility for the elderly, were observed by the first author from 9 am to 5 pm on one usual day. The environment, events, stimuli from staffs and other clients, and clients' behavior, words, voice and facial expression were recorded. Then, we analyze data in qualitative way. We consider ethics enough.

Result: There are the 4 categories that (handle the objects on purpose), (touch the objects, which we can't understand the reason), (touch their body on purpose) and (touch their body, which is not on purpose). The more severe the dementia, the less the ability of communication, and the more difficult it is to do something on purpose. There is the relation between the ability of communication and the ability of engaging with objects.

Consideration: The more severe the dementia, the more difficult it is to engage with objects on purpose, and to communicate with others. If it is getting the world smaller for them, we should know that they can't handle or touch the objects voluntary, so we should give them chance to engage in occupation and stimulate them in comfortable way.

P2-73

Nutritional support for the patient of frontotemporal dementia(FTD): A case report

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Background: FTD is increasingly recognized as an important type of degenerative dementia but satisfactory pharmacological treatment has not yet been established. On the other hand, there is evidence

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that dietary lipids, oxidative stress and related antioxidant vitamins, and homocysteine-related vitamins can affect the risk of dementia. In this report, we examined the possibility of Nutritional support for the patient of FTD. Case: 78 years old man. Onset of the illness was on 74 years old. He had chest pain and depressive mood, and was diagnosed as depression. He had drug therapy (Fluvoxamine, Paroxetine, Milnacipran, Risperidone, Olanzapine, Aripiprazole, carbamazepine) and modified electroconvulsive therapy, but he did not become well. He had markedly anxiety and went hospital every day and said the same thing. His personality had changed. On 78 years old, he came our hospital. At that time his memory was slight deteriorates and examined the head CT. We found he suffered from FTD. We announced the name of disease to himself and his wife, and strengthened a social support system. Then I treated him using Paroxetine and Aripiprazole and did the nutritional support. After 6 month, he had no chest pain, and his anxiety reduced.

Conclusion: Cognitive impairment can be influenced by a number of factors and the effect of nutrition on cognitive function has become a topic. Although this is a one case report, we found the probability of nutritional support for the patient of FTD.

P2-74

Enhanced accumulation of phosphorylated α-synuclein in double transgenic mice expressing mutant βAPP and presenilin-1

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Purpose: A recent report showed that the accumulation of α-synuclein (α-syn) was detected in one third of Alzheimer's disease patients. However, the relationship between amyloid β protein (Aβ) and α-syn remains unclear. We analyzed the relation between the mutation of presenilin-1 (PS-1) and the pathological features of β-amyloidosis and α-synucleinopathy.

Methods: We generated doubly transgenic mice with over expressing mutant β-amyloid protein precursor (APP)(Tg 2576) and mutant PS-1 (PS1L286Vtg; line 198), and analyzed 19 double Tg APP+/PS+ mice at 5–23 months (young to old), 23 age-matched single Tg APP+/PS- mice and 11 non-Tg littermates. Immunohistochemical comparison was performed in these 3 groups by counting the area and the number of α-syn or phosphorylated α-syn (pα-syn)-positive dystrophic neurites per plaque (ASPDN, pASPDN).

Results: The acceleration of Aβ pathology was found with earlier onset and exaggerated numbers in double Tg APP+/PS+ than in single Tg APP+/PS-mouse brains. The accumulation of ASPDN and pASPDN was also accelerated in double Tg APP+/PS+ than in single Tg APP+/PS- mouse brains, especially in pASPDN. The number and area of α-syn and pα-syn, and the ratio of pα-syn positive neurites were significantly higher in double Tg APP+/PS+ than single Tg APP+/PS- mouse brains.

Discussion: Additional overexpression of mutant PS-1 accelerated Aβ-induced α-synucleinopathy and further facilitated the phosphorylation of α-syn, suggesting a direct association between mutant PS-1 and phosphorylation of α-syn.

P2-75

Understanding functional proteins of γ-42cleavage by proteomics analysis

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Purpose: Oligomerization of 42 amino-acid version of Amyloid-β peptide (Aβ42) is a key event in Alzheimer's disease (AD) pathology. γ-secretase cleavage of βAPP produces Aβ. This study focuses

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on function of γ-42 cleavage and demonstrates a new perspective on functional relationship between γ-secretase complex.

Method: We used two-dimensional difference gel electrophoresis (2D-DIGE), a fluorescence-based method that is highly effective in screening for differences of protein expression. Wild-type or FAD-linked PS1 L166P mutant were overexpressed in HEK293 cells and cells were treated with or without drug that effects on γ-secretase activity such. Cells were homogenized and separated into soluble, membrane and nuclear fractions by centrifuge and used as 2D-DIGE sample.

Results: By using 2D-DIGE technology, we demonstrated that more than 1000 spots/gel were separated from purified fraction. In addition, protein expression level was changed in several protein spots.

Discussion: It has been thought that the γ-secretase complex was composed of four major component, PSEN1, APH-1, PEN2, and nicastrin. It was recently reported that other γ-secretase modulator influence βAPP cleavage and AD pathology. Our data suggests that various protein not only already-known component modulate function of γ-secretase through transient or stably association.

P2-76

Alteration of concanavalin A binding glycoproteins in cerebrospinal fluid and serum of Alzheimer's disease patients

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Alzheimer's disease (AD), the leading cause of senile dementia, is characterized by the formation of senile plaques and neurofibrillary tangles in the brain. Today, diagnostic markers for detecting certain earlier stages of AD are needed. We measured concanavalin A (Con A) binding glycoprotein in the cerebrospinal fluid (CSF) and serum to clarify the modification of core mannose since we expected that aberrant glycosylation of glycoprotein might be usable as a new biomarker in AD. We used CSF samples from i) an AD group, ii) a non-AD dementia group including dementia with Lewy bodies (DLB) and normal pressure hydrocephalus (NPH) and iii) a non-dementia control group. Serum samples were then collected from the AD patients and the non-dementia controls. Glycoproteins in CSF and serum were detected by lectin blotting using Con A. In Alzheimer CSF, two Con A binding glycoproteins were significantly higher compared with non-dementia controls. Furthermore, using analysis of variance, four Con A binding glycoproteins detected from CSF of ADs showed significant differences among three groups. The levels of two Con A binding glycoproteins were significantly lower than non-dementia controls. These altered Con A binding activities did not depend on the amount of the proteins. Therefore, the data suggest that the aberrance of protein glycosylation relates to Alzheimer pathology and has some promise as a new biomarker for the diagnosis of AD.

P2-77

Serum glycoprotein as a new diagnostic marker for Alzheimer's disease

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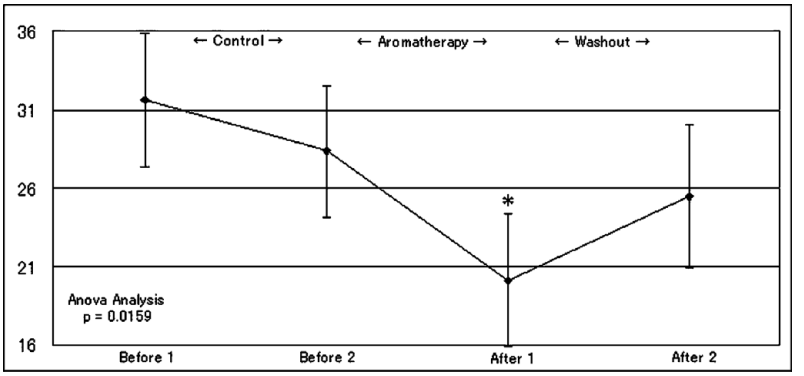
Objectives: We recently discovered that a few glycoproteins in the cerebrospinal fluid of Alzheimer's disease patients (AD) decreased lectin-binding. Consequently, we examined serum glycoprotein to find out if it could be used as a new diagnostic marker for AD.

Methods: We examined serum samples obtained from 34 AD patients and 33 non-dementia controls (NDC). The AD subjects were diagnosed according to NINCDS-ADRDA and DSM-IV criteria. We examined the serum glycoprotein using lectin blot analysis and enzyme-linked immunosorbent assay (ELISA). Statistical analysis was carried out with the Mann-Whitney U-test.

The study was approved by the Tottori University Ethical Committee and informed consent was obtained from each patient or their relatives prior to inclusion in the study. The study was performed in accordance with the Declaration of Helsinki.

Results: We identified a glycoprotein, an assumed glycoprotein χ, that showed a significant difference between the AD and NDC groups using lectin blot analysis. The content of glycoprotein χ was significantly reduced in the AD subjects compared with

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P2-78

NDC ($p < 0.005$). Furthermore, lectin-binding glycoprotein χ was significantly increased in the AD groups compared with NDC.

Discussion: These results suggest that the determination of glycoprotein χ may be useful as a new diagnostic marker for AD.

P2-78

Continued report of cognitive improvement on patients with Alzheimer's disease by aromatherapy

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In Japan, a remarkable increase in dementia patients in recent years has become a big social issue as this country develops into a super-aging society. Mainly, dementia caused by vascular disease and degenerative diseases such as Alzheimer's disease (AD), and the number of dementia patients is greatly on the increase. Drug therapy became possible for AD. However, curable treatments are still being researched. Treatment through sense stimulation is one of the ways to care for people with dementia. We studied the effects of cognitive function by aromatherapy in patients with AD. The subjects in our study were 35 elderly people, 20 with AD. (The subjects in the supplementary study were 42 elderly people, 29 of them with AD.) After a control period of 28 days, aromatherapy was performed during the following 28 days. After that, there was a wash out period of 28 days. For aromatic treatment, we used rosemary and lemon essential oils in the morning, and lavender and orange in the evening. We performed the following tests: the Japanese version of the Gottfries, Brane, Steen, Functional Assessment Staging of AD (GBS), a revised version of Hasegawa's Dementia Scale, Touch-panel Type Dementia Assessment Scale (TDAS), four times. The result of TDAS and GBS showed significant cognitive improvements. And with severely dementia, the result of TDAS showed significant improvement, too. These results suggest that aromatherapy may be useful as a type of complementary alternative medicine for AD patients.

P2-79

Beta cleavage by BACE1: New processing mechanism and BACE1 structure

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Sequential processing of amyloid precursor protein (APP) by membrane-bound proteases, BACE1 and gamma-secretase, plays a crucial role in the pathogenesis of Alzheimer's disease. Much has been discovered on the properties of these proteases; however, regulatory mechanisms of enzyme-substrate interaction in neurons and their involvement in pathological changes are still not fully understood. In addition, neuronal activity has an impact on β-cleavage of APP by BACE1

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to generate amyloid-β peptide (Aβ), however, the molecular mechanism remains to be elucidated. Cholesterol dependency of β-cleavage prompted us to perform analysis of immunoisolated, APP-containing, detergent-resistant membranes from rodent brain, which implicated syntaxin 1 as a key molecule for activity-dependent regulation of APP processing in cholesterol-dependent microdomains. In living cells, APP associates with syntaxin 1-containing microdomains through X11-Munc18, which mediates inhibitory effects on APP-BACE1 interaction and β-cleavage via microdomain segregation. Phosphorylation of Munc18 by cdk5 as well as Munc13-syntaxin interaction causes a shift of APP to BACE1-containing microdomains through dissociation of Munc18 from syntaxin 1. Neuronal hyperactivity, implicated in overproduction of Aβ, promotes the switching of microdomain association of APP as well as β-cleavage in a cdk5-dependent manner. We propose microdomain switching as a novel and general regulatory mechanism of membrane protein processing. Furthermore, we have recently found the structural change of BACE1 depending on pH, elucidating pH-dependent enzyme activity.

P2–80

Additional factors alter ϵ-cleavage precision of Amyloid precursor protein in *in vitro* γ-secretase assay

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γ-secretase cleaves the transmembrane domain of Amyloid precursor protein (APP) into Amyloidβ peptide (Aβ) and βAPP intracellular domain (AICD) by its γ- and ϵ- dual cleavage activity. These cleavages have important diversity. Aβ42 production, as a result of γ-cleavage diversity, initiate the pathology of Alzheimer's disease. ϵ-cleavage also has some diversity on the relative production of longer AICDϵ49 and shorter AICDϵ51 depending on its subcelluar location and environmental pH condition. To elucidate the precise molecular mechanism of the diversity is important for novel drug development. Although the mechanism is largely unknown, there are two hypotheses. One is that pH dependent conformational change of the same complex alter cleavage precision, and the other is that additional factors interacting with the active γ-secretase complex change the precision. In this study, we developed a convenient method to regulate the precision of APP ϵ-cleavage *in vitro*. A mixture of membrane fraction of cells and membrane wash solution was ultracentrifuged and the precipitate and the supernatant were served for experiments. *in vitro* γ-secretase assay and immunoprecipitation-MALDI-TOF Mass Spectrometry analysis revealed that this membrane wash procedure decrease the relative production of AICDϵ51 compared to that of AICDϵ49 on same pH condition, and the supernatant have potency to up-regulate relative AICDϵ51 production. These result suggest that there should be additional factors that interact with the active γ-secretase complex and increase relative AICDϵ51 production. This convenient method enables us to approach to the novel molecular target that regulate the precision of ϵ-cleavage of the γ-secretase.

P2–81

An autopsy case of familial Alzheimer's disasea with a novel mutation (D678N) in the APP gene

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Objective: To clarify genetic and neuropathological correlation in an autopsy case with familial Alzheimer's disease (AD) with a novel mutation (D678N) in the amyloid precursor protein (APP) gene. Patient: The patient showed amnesia at age 60. She was unable to recognize her family at age 65. During the next 10 years, her symptoms gradually progressed without stroke-like episodes and she was bed-ridden at age 75, when oral dyskinesia was noted. MRI at age 80 showed severe cerebral atrophy with moderate periventricular hyperintensity lesions on T2-weighted images but without focal

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ischemic or hemorrhagic lesions. She died of pneumonia at age 82. The patient has two demented (1 male, 1 female) and nine non-demented (5 males, 4 females) siblings. Her younger sister, the proband of this pedigree, was demented at age 60 and bedridden since the age of 75.

Results: Genetic analysis using the peripheral blood from the patient and the proband revealed a GAC to AAC nucleotide substitution in codon 678 of the APP gene exon 16, a novel missense mutation causing an amino acid substitution of Asp to Asn (D678N), confirmed by the PCR-SSCP followed by sequence analysis of genomic DNA. Neuropathological examination of the autopsy brain, weighting 900 grams, revealed fronto-temporo-parietal atrophy, more pronounced in the medial temporal structures. Microscopically neurofibrillary tangles were assigned as Braak and Braak stage VI, senile plaques as CERAD definite or Braak stage C. There were numerous Abeta1–40- and Abeta1–42-positive senile plaques in the cerebral and cerebellar cortices. Severe cerebral amyloid angiopathy (CAA) and CAA-associated microangiopathy were also evident in the subarachnoid space and parenchyma of the whole brain, resulting in multiple minute foci of old cortical infarcts and hemorrhages both in the cerebrum and cerebellum. There were, however, no lacunar infarcts in the basal ganglia and white matter. Deep white matter degeneration, arterio- and arteriolosclerosis, and marked widening of perivascular spaces were also noted.

Conclusions: We reported an autopsy case of familial AD with a novel mutation in the APP gene (D678N). The clinical manifestations of this patient were those of typical AD, characterized by progressive dementia without cerebrovascular complications in the clinical history. Advanced stage of Alzheimer-type pathology and severe CAA were characteristic findings in this patient.

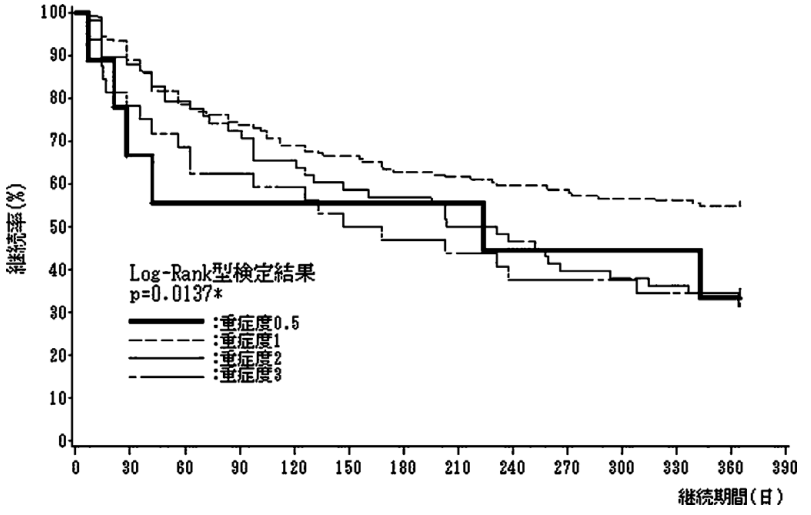
P2-82

Discontinuation of donepezil in geriatric clinic

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We investigated the rate and the reasons for discontinuation of donepezil prescribed in dementia patients in out-patient clinic of the Nagoya University Hospital July 1st 2003 to June 30, 2005.. A total of 264 patients were prescribed donepezil during the study period. The mean age of the patients was 79.6 ± 6.5 with 50.8% (90/177) with 50.8% (90/177) being female. The numbers of the patients categorized by clinical dementia rating (CDR) were as follows; CDR: 0.5 (n = 9), 1 (n = 164), 2 (n = 58), 3 (n = 32). Hundred forty-one out of 264 patients discontinued taking donepezil during the observation period. The mean age of the continued group and the discontinued group did not differ significantly (79.5 ± 6.7, 79.8 ± 6.4, respectively). Also sex of the patients



P2-82

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did not affect the discontinuation. Meanwhile the severity of dementia (CDR) did affect the discontinuation significantly. Those who had severer dementia discontinued taking donepezil earlier. The reasons for discontinuation were death or changes of the doctors (n = 72), ineffectiveness (n = 16), gastrointestinal side effects (n = 11) and others. More than half of the prescription of donepezil was discontinued in the current survey. The leading cause of the discontinuation was death or changes of the doctors, followed by ineffectiveness and gastrointesitinal side effects. Similar survey regarding the discontinuation of rivastigmine prescription carried out in Netherlands (Frankfort et al., 2005) showed that primary reasons of discontinuation were adverse events and non-response, which were similar to the current results. The current survey was conducted in out-patient clinic of the university hospital, where the patients were referred from local GPs or were accompanied by their caregivers who usually visit the clinic with relatively higher expectation for the treatment. Similar survey must be done in other types of clinics. The age and sex of the patients were not different between the continued group and the discontinued group, while the severity indicated by CDR was significantly associated with the discontinuation. Severity of dementia may be related with observed improvement of symptoms by donepezil or compliance of medications therefore may have affected the continuation rate in this survey. Further investigations to reveal factors associated with discontinuation of donepezil in patients with advanced dementia are necessary.

P2-83

Living with early-stage Alzheimer's disease in Japan – perspectives from afflicted persons

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Little empirical research has been conducted on the subjective experiences of persons with dementia in Japan. The purpose of this qualitative study was to describe and then understand the impacts of early-stage Alzheimer's disease (AD) on a person's life quality and to explore specific needs for this population. The participants consisted of 5 persons with early-stage AD who resided in Japan and were informed of their diagnosis. There were 3 females and 2 males aged from 50 to 76 years. Data were collected by in-depth interviews in a quiet room using semi-structured and structured interview guides. Length of single interviews ranged from 60 to 180 minutes and there were 2 interviews with each participant. All interviews were tape-recorded and transcribed. Qualitative-data analysis (Miles and Huberman, 1994) found six areas of impacts of AD on their life: health/cognitive abilities (forgetfulness, disorientation, inability to carry on group conversation, awareness of decline, etc.), functioning (loss of roles, etc.), psychological well-being (anxiety, fear, frustration, emotional pain, embarrassment, etc.), work (change in assignment, isolation, loss), stigma (hurt from others' responses, fear of discrimination, decreased socialization), family (nagging, not understanding, etc.). The hardest aspects of having AD were: 1) having nobody to talk with about concerns regarding AD, 2) being treated as though no longer a person with emotions and thoughts, and 3) fear of losing oneself. It was noted that some participants expressed gains from AD, such as a lesson for having empathy with others' feelings and thoughts. Specific hopes/needs were identified: not having AD, maintaining current cognitive state as long as possible, using one's own mind, something to do that would be useful to others, social life, enjoying what of one's life remains, family's understanding of AD, public education, community service for persons with early-stage dementia, and others. The results suggest that there are needs for: 1) educational programs for health professionals, 2) support programs for persons with early-stage AD that provide opportunities to do meaningful activities, to enhance psychological well-being and socialization, and 3) a supportive environment in the community, which would encourage afflicted persons to use their remaining abilities and assist them only in what they need.

P2-84

Toll like receptor 3 mediated pathogenesis in Alzheimer's disease

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Toll like receptor 3 mediated pathogenesis in Alzheimer's disease. Alzheimer's disease is characterized by two hallmark lesions: senile plaques,

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which are predominantly composed of Amyloid beta peptide, and neurofibrillary tangles, composed of filamentous aggregates of hyperphosphorylated tau protein. In addition, immunological and inflammatory changes including microgliosis, atrogliosis, complement activation, cytokine elevation and acute phase protein changes are also common phenomena in AD. These changes are thought to represent, at least in part, a response to the early accumulation of Amyloid beta 1–42 in the brain. However the precise mechanism is still not known. In this study the relevance of mechanisms on Amyloid beta mediated innate immune activation was investigated in relation to Toll like receptor 3(TLR3). TLR3 is a receptor working in innate immune system, and its expression in brain was already reported. Activation of TLR3 can mediate hyperphosphorylation of tau in SH-SY5Y human neuroblastoma cells as reported by our previous experiment (Psychiatry and Clinical Neurosciences, Article in press). Thus we further aimed to focus on TLR3 as a potential innate immune molecule that might be activated by Amyloid beta in the pathogenesis of Alzheimer's disease.
Method and result: SH-SY5Y cells were treated with Amyloid beta (25–35, 35–25, 1–42) and RNA was isolated and converted to cDNA to perform RT-PCR to observe Amyloid beta induced over expression of TLR3. Further to obtain quantitative data of time dependant and dose dependant increase of TLR3 mRNA by Amyloid beta, Taqman quantitative Real time PCR were performed. Finally Amyloid beta induced over expression of TLR3 was confirmed at protein level by means of western blot analysis. Employing human samples, we observed significant increased amount of TLR3 expression in AD brain compared to control brain by Real time PCR and also by immunohistochemistry analysis. Double immunohistochemistry with TLR3 and Amyloid beta was done and TLR3 positive cells were visualized in and around the amyloid plaque in AD brain.
Conclusion: Amyloid beta up regulates TLR3 in human neuroblastoma SH-SY5Y cells and expression level of TLR3 is significantly higher in AD brain compared to control brain. Our study suggests that TLR3 is involved in the amyloid beta induced activation of innate immunity in the neurodegenerative process of AD.

P2-85

Effects of Yokukansan on BPSD and memory disturbance induced by thiamine deficiency in mice

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Behavioral and psychological symptoms of dementia (BPSD) such as aggressiveness, hallucination, prowl and insomnia, occur frequently in the patients with dementia. BPSD are a significant burden for caregivers. Recently, Yokukansan (TJ-54), a Japanese herbal medicine for remedy of neurosis, insomnia and irritability, has been reported to improve BPSD in patients with dementia. On the other hand, thiamine deficient (TD) mice have been demonstrated to induce not only memory disturbance but also BPSD such as depression, anxiety and aggressiveness, suggesting that TD mice are a valuable tool for developing new drugs for BPSD. In the present study, we investigated the effects of TJ-54 on TD-induced psychological symptoms and memory disturbance in mice; TD mice were prepared by giving TD diet to male ddY-mice for 21 days. TJ-54 (0.5 and 1.0 g/kg) was orally administered to the mice every day (once a day) during the feeding period. Memory disturbance, anxiety, obsessive-compulsive disorder and aggressiveness were evaluated by a step-through passive avoidance, an open-field, a marble burying and a social interaction tests, respectively. In TD mice, obsessive-compulsive disorder, anxiety, memory disturbance and aggressiveness were observed on Days 14, 20, 20 and 21, respectively. TJ-54 improved the TD-induced BPSD as well as memory disturbance in a dose-dependent manner. These results suggest that TJ-54 is a useful remedy for BPSD, and support partly clinical results. It is also suggested the possibility that TJ-54 inhibits the progress of memory disturbance.

P2-86

Effect of Yokukansan on thiamine deficient-induced encephalopathy in rats: Electron microscopic analysis

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Yokukansan (TJ-54), which is a Japanese herbal medicine (Kampo medicine) has been reported to improve behavioral and psychological symptoms of

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dementia (BPSD) in patients with dementia. However, the mechanism is still unclear. We have demonstrated that TJ-54 inhibits thiamine deficient (TD)-induced psychiatric disturbance (memory disturbance, anxiety and neurological symptoms) and the degeneration of cerebral neurocytes in rats. In order to further clarify the effect of TJ-54 on neuronal degeneration, ultrastructual changes in the cerebral cortex, hippocampus and brain stem of TD brain were examined by electron microscopy in the present study.

Slight vacuolated edematous degeneration in neurons, vacuolated degeneration of oligodendrocytes and disarrangement of myelin sheath with intralamellar edema were observed in all areas. Perivascular hemorrhages were found in the brain stem. Severe edematous degeneration was found in astrocytes; various sizes of vacuolations in the swollen cytoplasm and dendrites were found in all areas examined. In addition, mitochondrial disintegration was found in the degenerated astrocytes. These results suggest that vulnerable region to TD is brain stem. TJ-54 inhibited the TD-induced neuronal degenerations in a dose-dependent manner, suggesting that psychiatric disturbance observed in TD rats is closely related to the degeneration of astrocytes. Inhibitory effect by TJ-54 of TD-induced degeneration in astrocytes may be related to the amelioration of psychiatric disturbance in TD rats.

P2-87

Characteristics of Yokukansan-therapy on aggressiveness induced by intraventricular Aβ-injection in mice

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Yokukansan (TJ-54), which is a traditional herbal medicine referred to as a "Kampo medicine" in Japan has been approved by the Ministry of Health, Labor, and Welfare of Japan as a remedy for neurosis, insomnia, and irritability in children. Recently, TJ-54 has been reported to improve BPSD such as hallucinations, agitation/aggression in the patients with dementia. To date, atypical or conventional antipsychotics are used to treat BPSD. However, these pharmacotherapies are known to induce extrapyramidal symptoms.

In the present study, in order to clarify the characteristics of TJ-54 for BPSD, the effects of TJ-54 and other drugs (haloperidol, risperidone, donepezil) on aggressive behaviors and motor activities were compared in Aβ-treated mice. Significant increase in aggressive behaviors was observed on the 7th day after injection of Aβ (500pmol) into the lateral ventricle of mice, and it lasted until the 28th day. The 3-week administration of TJ-54 (7th-28th day) significantly improved the aggressiveness in a dose-dependent manner without inhibition of motor activity. In contrast, haloperidol and risperidone significantly improved aggressiveness on the 28th day by single administration in a dose-dependent manner. However, motor activities were significantly suppressed. Donepezil was unable to inhibit aggressiveness even by 3-weeks administration. Motor activities showed a tendency to increase in a dose-dependent manner.

These results suggest that TJ-54 improves the aggressiveness without suppressing physical activity.

P2-88

An Asian traditional medicinal herb, Uncaria rhynchophylla, protects neuronal cells through transcription factor regulation

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Introduction: In the Alzheimer's disease pathogenesis amyloid beta peptide (Abeta) is considered to play one of the most important roles. We previously reported that Uncaria rhynchophylla, an Asian traditional medicinal herb has a potent inhibitory effect on Abeta aggregation (Fujiwara et al. J Neurosci Res 84: 427–33, 2006). Here we investigated if/how this herb protects neuronal cells against Aβ toxicity and what is the cellular and molecular mechanism of the biological effects of Uncaria rhynchophylla.
Methods: We employed human neuroblastoma SH-SY5Y cells and N2a cells. MTT assay was performed for cell survival studies. Activities of transcription factors were assayed using transcription factor assay kits (Clontech).
Results: In cultured cells we found that Uncaria rhynchophylla has a potent neuroprotective effect against Aβ1–42 toxicity. In several transcription factors investigated, activation transcription factor-2 (ATF-2) was most significantly modulated by Uncaria rhynchophylla.
Conclusions: Uncaria rhynchophylla is considered to elicit neuroprotective functions against Abeta toxicity through inhibition of Abeta aggregation and/or some other mechanisms. Furthermore this effect

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could be mediated by modulation of some transcription factors including ATF-2. We are now investigating what kinds of molecules are positively or negatively expressed by Asian traditional medicinal herbs.

P2-89

Novel therapeutic strategies useful for Alzheimer's disease from medicinal herbs and traditional Chinese medical formula

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Objective: To find novel therapeutic agents useful for Alzheimer's disease from traditional Chinese medical formula, we examined the effects of several of medicinal herbs and traditional Chinese medical formula on the aggregation of amyloid β protein (Aβ) in the mice brain and Alzheimer's disease-like phenotypes including impaired cognition.
Methods: In order to determine whether these herbs and traditional Chinese medical formula have the inhibitory effects on Aβ amyloidosis, we examined memory disturbance using the passive-avoidance task, and measured Aβ burden in the brain of APPsw transgenic mice.
Results: Our study demonstrated that three herbs (*Uncaria rhynchophylla*: chotoko in Japanese, *Cinnamomum cassia*: keihi and *Paeonia suffruticosa*: botanpi) and two traditional Chinese medical formula (*Pulvis depressionis hepatis*: yokukansan (TJ-54) and *Pilulae octo-medicamentorum rehmanniae*: hachimijiogan (TJ-7)) had inhibitory effects on accumulation of Aβ burden in mice brain, and reduced the amount of Aβ in concentration-dependent manners. Moreover, these herbs and traditional Chinese medical formula improved the long-term memory impairment in transgenic mice.
Discussion: Our results suggest that *Uncaria rhynchophylla*, *Cinnamomum cassia* and *Paeonia suffruticosa*, *Pulvis depressionis hepatis*: yokukansan and *Pilulae octo-medicamentorum rehmanniae*: hachimijiogan suppress the accumulation of Aβ burden in mice brain leading to long-term memory deficits. We conclude that traditional Chinese medical formula could have potency to be novel therapeutic agents to prevent and/or cure AD.

P2-90

Effect of oxcarbazepine in the treatment of agitation and aggression in dementia

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Background: Behavioral and psychological symptoms of dementia are frequent in patients with dementia. Especially aggression and agitation put a heavy strain on relatives and caregivers in nursing homes. This may lead to excessive use and misuse of psychotropic drugs, including the typical and atypical antipsychotics. According to systematic reviews of controlled trials and meta-analyses antipsychotics may cause serious and irreversible side effects. New psychopharmacological approaches are urgently needed.
Objective and hypotheses: The aim of the study is to evaluate whether oxcarbazepine is effective in the treatment of agitation and aggression in institutionalized patients with Alzheimer's disease and/or vascular dementia.
Methods: This 35-site, double-blind, placebo-controlled trial was carried out independently from pharmaceutical industry. In all, 103 institutionalized patients with Alzheimer's disease and/or vascular dementia with significant agitation and aggression were randomly assigned to receive oxcarbazepine (n = 52) or placebo (n = 51). Doses were adjusted as tolerated and trial medication given for 8 weeks. The main outcome was the agitation/aggression score of the Neuropsychiatric Inventory – Nursing Home Version (NPI-NH). Secondary outcomes were the Brief Agitation Rating Scale (BARS) total score, the use of rescue medication (Haloperidol) and the change in caregiver's burden total score as measured by NPI-NH.
Results: No statistically significant difference was found between the two groups for the main and secondary outcomes for the Intention to treat population (ITT). It should be noted, that for all primary

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and secondary outcome variables the subjects in the oxcarbazepine group generally perform better than those in the placebo group. According to the scores on BARS there is a tendency that oxcarbazepine may be efficacious compared to placebo, $p = 0.07$.

Conclusions: Although we could not find a statistical difference between oxcarbazepine and placebo in the treatment of agitation and aggression, a clear tendency was found in favor of oxcarpazepine as measured by BARS. One reason for the negative outcome may be explained by a low estimated placebo effect (20%) when calculating the sample size. The placebo effect was in fact 39.6%. Therefore, the number of patients needed to show statistically significant effect is too low.

P2-91

Changes in behavioural and psychological symptoms in patients with dementia during their treatment at the old age psychiatric hospital when measured by Neuropsychiatric Inventory and Cornell scale

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Background: Behavioural and psychological symptoms (BPSD) are a part of dementia which also includes delusions, hallucinations, aggression, anxiety, depression, apathy, irritability and sleep disturbances. These symptoms are often a source of distress for family and professional caregivers and are the main reasons for admission into old age psychiatry hospital.

Objective: To investigate the changes in behavioural and psychological symptoms of dementia in patients and distress for professional caregivers under the treatment of demented patients at old age psychiatry hospital.

Methods: The study is based on assessment of BPSD as observed by nursing staff. A sample of 39 patients, admitted into old age psychiatry hospital during 2006 were assessed for BPSD by the means of Neuropsychiatry Inventory (NPI) and Cornell scale for depression in dementia, at two points: one week after admission and near discharge. Relationship between sex, living environment and BPSD were studied.

Results: Prevalence of anxiety and depressive symptoms were significantly higher among women as compared to men with moderate to severe dementia. More than half (61.5%) of the patients had clinical significant depressive symptoms when measured by Cornell scale (total score 8 and more) on admission. There was a significant reduction in seven out of 12 variables, total NPI and Cornell score for all the patients as one group during the hospitalization. Women had a significant improvement on anxiety and depressive symptoms. Patients admitted from their homes had a significant improvement on irritability, and those who were admitted from institutions had a significant improvement on their depressive symptoms during the hospitalization. The changes in BPSD resulted in significant reduction in distress for professional caregivers.

Conclusions: By systematic assessment and management of BPSD, it is possible to reduce the intensity of BPSD, which is of concern for the patient and their caregivers. Such systematic assessment can also be of importance for professional staff in primary health services to provide better care to the patients with behavioural and psychological symptoms of dementia.

P2-92

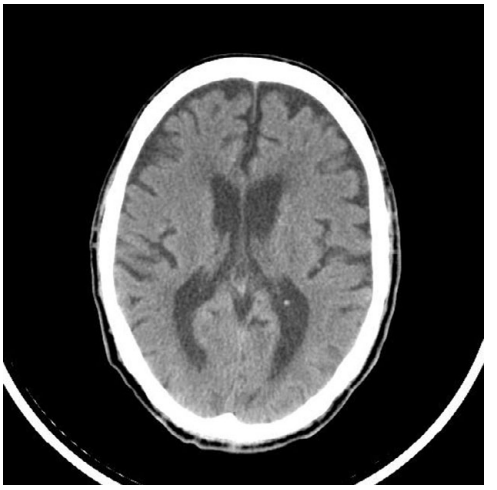
Kluver-Bucy syndrome in dementia: Literatures review and the report of two cases

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The Kluver-Bucy syndrome (KBS) is a cluster of symptoms including visual agnosia, strong oral tendencies with hyperphagia, hypermetamorphosis, increased sexual behavior, and emotional changes. This was originally produced in monkeys by ablating both temporal lobes. It can also appear in herpes encephalitis, brain trauma, epilepsy, tumor, Pick's disease, and Alzheimer's disease. The purpose of this article is to study the clinical manifestations and psychopathology of the Kluver-Bucy syndrome in patients with dementia. Case 1. This 90 year-old man is a patient with Alzheimer's disease. He exhibited hyperphagia and strong oral tendency. Inappropriate sexual advances towards the nurses were observed. His affect and behavior were usually blunted and withdrawal. However, sudden agitation was also noted when begging for food. Brain CT (figure) showed dilatation of cortical sulci, lateral and third ventricles. Atrophic changes were marked in the bilaterally anterior frontal and temporal

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P2-92

regions. MMSE score was 15. CDR was 2. Functional Assessment Staging of Alzheimer's Disease showed stage 5. Hachinski ischemia score was 3. Case 2. This 66 year-old male is a patient with vascular dementia. He was easily agitated for brief periods and had outbursts of anger. Increased sexual desire and inappropriate sexual behavior towards the neighbor were observed. MMSE score was 17. CDR was 2. Hachinski ischemia score was 8. Routine laboratory studies were insignificant. Brain CT showed dilated ventricles and atrophic change. Lacunar infarctions over bilateral basal ganglia and decreased density in periventricular deep white matter were noted. In summary, KBS is not only presented on those patients with temporal lobe lesions, but also on the patients with dementia. It is regarded as a part of behavioral and psychological symptoms of dementia. The clinical symptoms include binge-eating, hyperorality, sexual disinhibition, misrecognition of nurses/relatives, going into rages, hypermetamorphosis, and withdrawal/ apathy. Most patients expressed partial features of this syndrome. The occurrence of KBS in a patient with dementia should bring attention to the clinician the presence of bitemporal degenerative process.

P2-93

Psychiatric consultation in Dutch nursing homes. Association with neuropsychiatric symptoms in dementia

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Objective: To study psychiatric referrals of nursing home patients with dementia and to compare reasons for psychiatric consultation with prevalence estimates of neuropsychiatric symptoms.
Methods: This is part of a cross-sectional naturalistic study of 787 patients residing in 14 nursing homes in the Netherlands. Eligible patients were those that had dementia. Nursing homes physicians (NHP) noted the primary reasons for psychiatric consultation according the Neuropsychiatric Inventory items and two extra domains. Patients were subsequently assessed by an old-age psychiatrist. Reasons for referral were compared with recent prevalence data on neuropsychiatric symptoms in dementia.
Results: A total of 325/787 (41.3%) patients had dementia. Agitation, disinhibition and aberrant motor behavior were frequent reasons for referral (>25%). Psychotic symptoms, apathy and eating behavior changes were infrequent reasons (<10%) for seeking consultation. Agitation and disinhibition were more often primary reasons for consultation compared with prevalence estimates of these symptoms in dementia. Delusions, euphoria, apathy, irritability and eating behavior changes were less often reasons for referral compared with prevalence estimates.
Conclusions: This study is the first to examine psychiatric referrals in Dutch nursing home patients with dementia. Large differences exist between reasons for referral and actual symptom prevalence. Important psychiatric symptoms such as agitation and disinhibition are much more likely to be the primary reason for referral compared with other symptoms, particularly apathy. The apathetic, retarded and quietly (not causing any trouble) patient seems to be neglected.

P2-94

The behavioral and psychological syndromes among Korean elderly outpatients with Alzheimer's disease: A factor analysis of the neuropsychiatric inventory

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Background: Studying the behavioral and psychological symptoms of dementia (BPSD) across cultures and nations allows the identification of similarities and differences to determine the best approach to their management in a specific population. Although BPSD are also common in Korean elderly patients with Alzheimer's disease, few studies have been in the assessment of the behavioral and psychological syndromes in Korea.

Objectives: The aim of this study was to identify behavioral syndromes of the 12-item Korean version of Neuropsychiatric Inventory(K-NPI) in Korean elderly outpatients with Alzheimer's disease.

Methods: Two hundred and seventy-one patients fulfilling the criteria for diagnosis of probable Alzheimer's disease were recruited from psychiatry outpatients clinics of four university hospitals such as Seoul national university hospital, Boramae hospital, Kangwon national university hospital and Inje university SangGye Paik hospital between July 2004 and June 2005. BPSD were assessed using K-NPI. Principal component analysis with Varimax rotation was carried out on the composite scores of 12 symptom domains to identify behavioral syndromes (factors).

Results: Three factors were identified which accounted of 56.7% of the variance: mood/apathy factor – depression/dysphoria, anxiety, apathy; hyperactivity factor – delusion, agitation/aggression, disinhibition, irritability; aberrant behavior factor – hallucination, aberrant motor behavior, night-time behavior, appetite/eating disturbance. The syndrome mood/apathy and hyperactivity were more common, occurring in 76.1% and 70.3% of the patients respectively, than aberrant behavior, which occurred in 56.5%.

Conclusions: We found a distinctive factor structure of K-NPI in Korean elderly patients with Alzheimer's disease. The separation of delusion and hallucination into the different factors resulted in the extraction of a novel factor named as aberrant behavior. This finding might offer new insight of the BPSD as compared with other studies from western countries in the cross-cultural perspective.

P2-95

Symptoms of mental health and psychotropic drug use among old people in geriatric care, changes between 1982 and 2000

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Some major changes have occurred in the care of older people in institutions providing geriatric care from a few decades ago to today. How these changes regarding organization, diagnosis and pharmacological treatment, have affected the mental health of the population in general remains unclear.

The prevalence of symptoms of mental health in two comparable cross-sectional surveys from 1982 and 2000 were studied. The study population consisted of all the people living in geriatric care units in the county of Vasterbotten, in northern Sweden. Multivariate regression was used to correct for the effect of change in demographic structure.

Six out of fourteen symptoms showed a significant decrease. These were, expressed as descriptions of behaviours, Sad (OR 0.72), Crying (OR 0.67), Fearful (OR 0.73), Disturbed and restless (OR 0.84), Lacking initiative (OR 0.67) and Does not cooperate (OR 0.67).Two symptoms showed a significant increase, Overactive/manic (OR 1.44) and Hallucinates visually (OR 1.27). The use of antidepressants had increased from 6.5% 1982 to 39.9% 2000. The use of minor tranquillizers had increased from 13.2% to 39.2% and the prevalence of antipsychotic use had decreased from 25.1% to 20.5%.

This article clearly shows that the prevalence of several important symptoms and behaviours in a geriatric care population have decreased over the course of eighteen years, correcting for demographical changes. This might at least partly be accounted for by today's more widespread use of antidepressants and benzodiazepines.

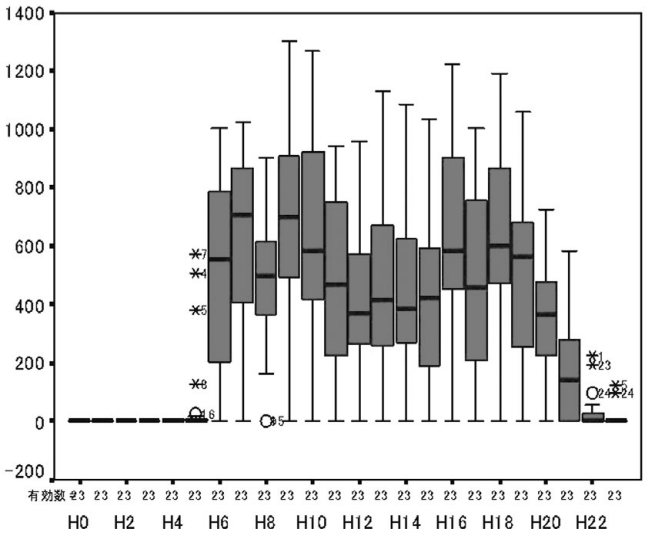
P2-96

Association between the mean distance walked and the type of dementia measured by the IC tag monitoring system

Nanae Segawa[1]; Miyae Yamakawa[1]; Kazue Shigenobu[2]; Kiyoko Makimoto[1]; Rumiko

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Figure : The mean distance walked per hour for R32 who was hospitalized >=30 days



P2-96

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Introduction: Demented elderly persons who wander are at a high risk for falls leading to severe morbidity. However, capturing wandering behavior objectively remains difficult. The purpose of the study was to examine the association between the mean distance walked and the type of dementia using the Integrated Circuit tag monitoring system (Matrix. co., Japan).

Participants and methods: Edibility criteria: 1) patients hospitalized in the dementia care unit at A Hospital, Osaka Japan; and 2) being able to walk independently. Demographic data and medical information were obtained from the medical record. The research was approved by Osaka University and the hospital, and the informed consent was obtained from the authorized proxy.

Results: 30 patients were monitored for up to 4 months in 2006. The mean age of the subjects was 69.8 ± 13.2 years. The mean duration of hospitalization was 214 ± 514.7 days, and the mean months since the diagnosis of dementia was 30.8 ± 34.8. The Mini Mental State Exam scores was 12 ± 7. Patients with Alzheimer's disease (AD) accounted for 63.3% (mean age = 69.2 ± 9.9 years) followed by Cerebrovascular dementia (VaD) (10%)(85.0 ± 5.3 years), and Frontotemporal dementia (FTD)(10%)(51.7 ± 19.7 years), dementia related to alcoholism (10%)(65.3 ± 8 years), and Dementia with Lewy bodies (DLB)(6.7%)(87.5 ± 0.7 years). Among patients with < 30 days of hospitalization, the median distance walked per day was 2026 m for AD, 667m for VaD, 246 m for DLB. Among those with ≥30 days of hospitalization, the median distance walked per day was 2003m for AD, 637 m for VaD, 355 m for DA, 1708 m for FTD, and 103 m for DLB. Although the number of subjects was small for some types of dementia, the mean distance walked by AD patients was longer than those with non-AD type dementia. In addition, the mean distance walked per hour for AD patients hospitalized ≥30 days showed two peaks, one in the morning and one in the evening.

Conclusion: The IC tag monitoring system illuminated the differences in the movement pattern among several types of dementia. The mean distance walked per day for AD patients was longer than that for patients with the other types of dementia. Unexpected finding was the bimodal distribution of the mean distance walked per hour, showing walking in the morning was as common as in the evening.

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P2-97

Association between activity level and the changes in bodyweight of people with dementia using the Integrated Circuit tag monitoring system

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Introduction: Wandering is reported to cause a severe care burden. Objective measurement of wandering behavior remains challenging until recently. The Integrated Circuit tag monitoring system (Matrix, co, Japan) became available for measuring movement patterns and activity levels for extended period. The objective of the study was to examine the association between the activity level and the changes in bodyweight in patients with dementia.
Materials and methods: Edibility criteria: 1) patients hospitalized in the dementia care unit at A Hospital, Osaka, Japan; and 2) being able to walk independently. Demographic data and medical information were obtained from the medical record. The research was approved by Osaka University and the hospital, and the informed consent was obtained from the authorized proxy.
Results: 34 subjects (15 men, 19 women) were monitored for up to 4 months in 2007. The mean days of monitoring per patient was 69 ± 30.1. The mean age was 69.4 ± 13.2 years with the mean Body Mass Index(BMI)of 20 ± 2.3 using the bodyweight measured at admission. The mean food intake was 95.8 ± 5.6% of the food served. The majority of the patients (n = 20) walked less than 1 km per day. The number of patients whose median distance walked per day exceeded 1 km was 14. The change in the mean bodyweight was −1.6 ± 4.36 kg. The food intake was 97.8 ± 2.9% of the food served. In contrast, the number of subjects whose median distance walked per day was less than 1 km was 20. Their bodyweight changed little, and their food intake was 94.4 ± 6.6%. After subjects were stratified by the amount of bodyweight change, 8 patients lost more than 1 kg between the admission and the end of the study with the mean decrease in body weight of 3.8 ± 4.4 kg. The median distance walked per day was 1523.3 m. The mean BMI decreased from 21 ± 2.4 to 19 ± 2.4, and their food intake was 94.5 ± 6.0%. In contrast, 6 subjects gained more than 1 kg with the mean increase of 2.9 ± 2.7 kg, and the mean BMI increased from 20 ± 1.7 to 21 ± 2.5 Their median distance walked per day was 399.7 m, and mean food intake of 95.6 ± 8.2%.
Conclusion: This study demonstrated the importance of measuring the amount of exercise in addition to body weight measurement and food intake. Assessment of proper amount of exercise is necessary for health management.

P2-98

Case studies on how cultural factors affect treatment-seeking behavior and case management of people with dementia in Singapore

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Singapore is a multi-racial society where Chinese compose the majority of the population. Recent statistics showed that individuals aged 65 and above compose 8.49% of our population1 with the prevalence of dementia at 6%. Recent clinical based study showed ethic variability in dementia where Alzheimer's disease (AD) more common in Indians and Eurasians, while vascular dementia (VAD) more common among Chinese and Malay. Not surprisingly, cultural beliefs and attitude towards health care utilization play an important role in treatment-seeking behavior. Often, carers seek treatment when patients exhibit memory difficulties which are often accompanied with behavioral and psychological problems. Behavioral and psychological problems of dementia (BPSD) cause severe distress in family members and carers, often leading to institutionalization. Our aim is to present 2 case studies on how cultural factors affect their treatment-seeking behavior and case management. We present 2 Chinese case studies for practical reasons that Chinese form the majority of the population. The cases were referred for an outpatient neuropsychological assessment. A is an 89 year old Chinese male. He has a 1–2 year history of gradual progressive memory decline. On neuropsychological testing, he is impaired in visual and verbal memory, processing speed and language. B is an 82 year old Chinese female. She has a 1 yr history of poor memory. On neuropsychological testing, she is impaired in verbal and visual memory, attention, executive functioning, language, visuoconstruction and processing speed. In both cases,

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carers report delusional beliefs that domestic helpers are stealing money from them. Studies found such reports to be common even among the Asian Americans. Chinese value money and such beliefs often result in dispute between the domestic helpers and the family members. Both carers also normalize cognitive decline. Consistent with studies on Asian Americans, such attitudes delay treatment-seeking behavior. To the author's knowledge, cultural factors have not been explored nor studied systematically in a Singaporean sample. This provides a taster that more systematic work needs to be done to for better psychosocial intervention and treatment plans.

P2-99

Depressive symptoms aggravate certain, but not all, cognitive functions in patients with moderate or severe dementia living in nursing homes

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Patients with dementia often exhibit concomitant depression. Yet, the neuropsychology of depressive symptoms in this population has been an underdeveloped research field. To date, the previous work yielded contradictory results. The need for research on this topic in nursing home settings is put forward by the fact that depression and severity of cognitive deficits in patients with dementia have important clinical implications. The present study examined the relationship between depressive and cognitive symptoms in patients with moderate or severe dementia living in nursing homes. The sample comprised 150 patients with a mean age of 86.2 years (SD = 6.8). The most prevalent causes of dementia were Alzheimer's disease (34%), vascular (17%), and mixed (15%) dementia. Two subgroups of patients were identified from the sample according to the participants' scores on the Cornell Scale for Depression in Dementia (CSDD): Group D- (n = 90) had less than 6 on the CSDD whereas Group D+ (n = 60) had a score of 6 and higher. A previous work has shown that a cut-off score of 6 and higher on the CSDD has a sensitivity of 93% and a specificity of 97% to detect geriatric depression (Korner et al., 2006). The cognitive functioning of the two subgroups was compared using the Hierarchical Dementia Scale (HDS). Statistical analyses were performed using non-parametric Kruskal-Wallis tests and one-way ANOVAs controlling for age, years of education, type and severity of dementia, and presence of probable delirium. Results indicated that the D+ group performed significantly worse than the D- group on the global HDS score. Importantly, the difference did not concern all cognitive domains. The D+ group performed worse than the D- group on the perception, attention/memory, and language subscales of the HDS only. Performance on calculation, purposeful movement, spatial constructional ability, and primitive reflex/motor function subscales were equivalent between subgroups. The functions more severely impaired in Group D+ are important for communication skills (language, attention, memory) and for contact with the reality (perception). Their disruption may thus influence the patients' functional impairment and the nursing home staff's burden. Treatment of depressive symptoms in moderate and severe dementia may ameliorate the cognitive impairment of the patients and this in turn may have important clinical repercussions in nursing home settings, both for residents and staff.

P2-100

Galantamine compared to Risperidone in BPSD symptoms: A one-center clinical trial in 100 patients

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Background: Studies have suggested that medication with Acetylcholineesterase inhibitors (AchEI) can be used to treat behavioural and psychological symptoms (BPSD) in dementia. In clinical practise, antipsychotics are often used, but side effects are common.
Objective: To compare treatment effects of head to head treatment between Galantamine (AchEI) and Risperidone in patients with BPSD and cognitive dysfunction.
Methods: Open randomized clinical trial where 100 patients mean 78.7 (±7.5) years, 67% females) with a NeuroPsychiatric Inventory score (NPI) > 10

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points and cognitive dysfunction were treated with either Galantamine (50 patients) or Risperidone (50 patients) for 12 weeks. Neuropsychiatric symptoms were assessed using NPI, CMAI, FAST, and caregivers stress using PGWB. Cognition was measured with Minimental state examination (MMSE). Clinical change was evaluated using CGI. In a subsample CIBIC was performed by an independent blinded rater. Patients were assessed at baseline, after 2 and 12 weeks.

Results: 91 patients completed the trial. Safety and tolerability were good. 58% were APOEϵ4 carriers. At baseline MMSE was (20.1 ± 4.6), NPI (51.0 ± 25.8), CMAI (46.5 ± 11.1) PGWB (76.6 ± 18.2).The majority of patients were on level FAST 4. In both groups there were statistically significant improvements after 12 weeks. In several of the NPI-domains Galantamine and Risperidone were equally effective, no statistically significant differences were shown. However, Risperidone showed a significant treatment advantage in the NPI-domains irritation ($p = 0.02$), agitation ($p = 0.02$) and a trend towards abberant motor behaviour ($p = 0.08$). Galantamine showed a trend to treatment advantage in the NPI domains apathy/indifference ($p = 0.09$) and sleep ($p = 0.07$). In total CMAI there was no significant difference however the domain verbal aggressive behaviour improved significantly more during Risperidone treatment ($p = 0.01$). Galantamine improved the total MMSE score with 2.8 p ($p < 0.001$) and Risperidone with 1 p ($p < 0.07$) over three months.

Conclusion: Treatment with Galantamine compared with Risperidone shows an equal treatment effect in BPSD assessed by NPI as primary endpoint except for treatment of aggressive behaviour, irritation, agitation and aberrant motor behaviour. Since the side effects of Galantamine are more benign than those of Risperidone, our data suggest that Galantamine could be used as first line treatment of BPSD unless aggressive symptoms are prominent.

P2-101

Developing best practice guidelines for prevention and management of aggressive behavior in nursing homes

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Older adults who are residents in nursing homes may become aggressive as a consequence of unmet need and communication difficulties. This is according to the need driven dementia compromised model. The occurrence of resident aggression in nursing homes has significant implications for both residents quality of life and for staff member's quality or work life. This presentation reports on a project conducted by a collaborative research team consisting of nursing managers, clinicians, researchers and educators with the objective to develop best practice guidelines for preventing and managing aggressive behaviour in nursing homes. The team systematically reviewed relevant studies published or reported prior to 2006, critically appraising the level of evidence and findings. Based on this review, a set of recommendations was developed and sent to external experts for validation prior to dissemination. The result is a concise set of best practice guidelines for dissemination. The project was funded by the Nursing Care Partnership Program, Canadian Nurses Foundation and the Collaborative Research Unit at Deer Lodge Centre.

P2-102

Neuropsychiatric symptoms and ApoE-4 in patients with cognitive deterioration: Impact on functioning

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Neuropsychiatric symptoms (NPS) are very frequent in patients with senile dementia (SD). It has been reported that NPS, especially psychosis and behavioural disturbances, impair functioning and cognitive performance, induce caregiver distress, enhance direct costs of care and lead to institutionalisation of SD patients. The frequency (NPIF), severity (NPIS) and total score (NPIT) of NPS, evaluated with the Neuropsychiatric Inventory (NPI), and their correlations with cognitive

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and functional performance were investigated in APOE-genotyped clinical populations of vascular dementia (VaD), Alzheimer's disease (AD) and mild cognitive impairment (MCI) patients. Patients with mild to moderate AD (N = 160), VaD (N = 46) and MCI (N = 45) were assessed with the NPI, the cognitive subpart of the Alzheimer's Disease Assessment Scale (ADAScog), the disability in AD scale (DAD), the Mini-Mental State Examination test (MMSE) and the Hamilton Depression Rating Scale (HDRS). ApoE genotype was determined in all patients. The results of our study indicate that: 1) in comparison with MCI, apathy and agitation were more frequent in AD and VaD patients, whereas aberrant motor behaviour was more prevalent only in AD cases; 2) irritability and sleep disorders appeared with a higher frequency in AD patients without the ApoE4 allele than in ApoE4 carriers; 3) NPIF, NPIS and NPIT scores were higher in AD and VaD than in MCI, even after adjustment for MMSE scores, and showed a significant increase in non-ApoE4 AD patients with respect to ApoE4 carriers; 4) NPIF and NPIS scores correlated negatively with functional performance (DAD scores), but not with cognitive measures in both AD and VaD; 5) apathy, agitation, delusions and aberrant motor activity were the best correlates for disability, whereas delusions and agitation correlated negatively with cognitive performance. According to the present results it seems that NPS can contribute to differentiate senile dementia (VAD and AD) from MCI and have an stronger impact on functional than on cognitive impairment in both VaD and AD; and that APOE genotype might influence the frequency of NPS in AD, other than those differentiating AD from MCI.

P2-103

Indicators of stability of ambulation among 8 residents in a dementia care unit, Seoul, Korea

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Background: Wandering in people with dementia is a significant safety issue world-wide. With the increased availability of technology, stability of nighttime ambulation over extended period can be measured with precision.

Methods: The integrated circuit (IC) tag monitoring system (Matrix, co., Japan) was set up to measure the distance moved per hour in a dementia care unit in Korea, 2006. This research was approved by the Ewha Womans University, and the informed consent was obtained from the authorized proxies. Microsoft Excel was used for data analysis. The following indicators of movements per hour were calculated: 1) mean distance moved per military hour, 2) mean distance moved per military moving hour (the hour when the movement was detected), and 3) the percentage of hours moved. The indicators of movement in the evening (21:00–24:00) and at night (00:00–6:00) were also calculated: 1)mean distance moved per evening, 2) mean distance moved per moved evening (evening when movement was detected), and 3) percentage of evenings moved.

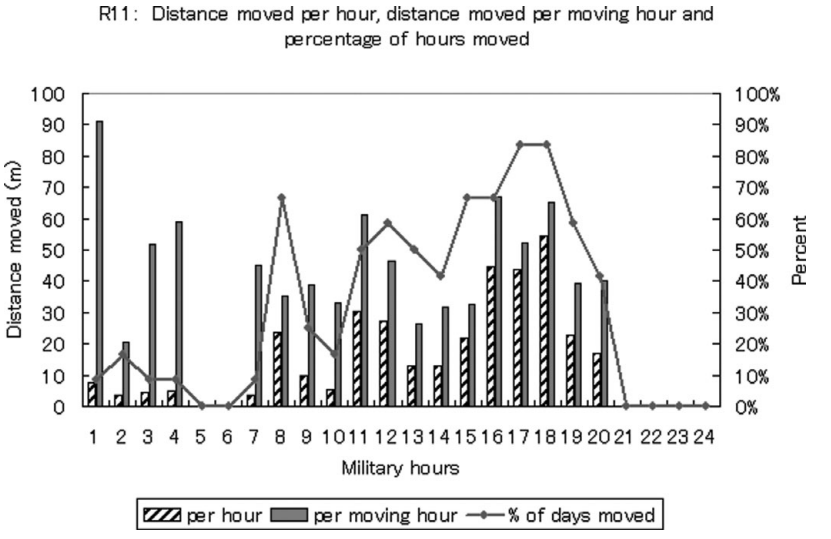
Results: 12 consecutive days of movement data were available for 8 patients. 5 had Alzheimer's disease, and 3 had vascular dementia. The mean age of the subjects was 76 years, and the mean Mini Mental State Exam was 16.8. The longest mean distance moved was 1334 m, and the shortest mean distance moved was 267 m. The case was presented in the attached figure to display the three indicators of movement per hour. The ratio of the mean distance moved per hour to the mean distance moved per moving hour indicates the stability of movement during the observation period, and considerable variations in this indicator were found among 8 subjects. When movements data were examined by day, 4 patterns of movements were found: 1) non-active in the evening and at night, 2) active in the evening but not at night, 3) non-active in the evening but active at night, and 4) active both in the evening and at night.

Discussion: The IC tag monitoring system enables to capture the detail movement of the dementia patients. It is easy to assess patterns of movement and contribute to examine factors influencing the distance traveled. Especially diurnal rhythm disturbances can be evaluated easily and the effects of intervention can be measured with precision.

P2-104

The effectiveness of antipsychotics for dementia by prescription database analysis from a large mental hospital in Taiwan

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P2-103

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Objective: The antipsychotics are widely used in the management of dementia. Comparing the effectiveness between antipsychotics is an important issue for clinicians. Recent literature showed "time to discontinuation" as a real-world indicator to compare the effectiveness of different antipsychotics. This study analyzed the prescription database of a large mental hospital by the practical marker.

Method: The pharmacy-prescription database from a large mental hospital in Taiwan was used and it was further limited to outpatients elder than 65 year-old and with diagnosis of dementia by ICD-9-CM. All patients receiving antipsychotics between 2002 and 2005 were defined as intend-to-treat populations and were followed for 180 days. Time to discontinuation was analyzed by survival analysis.

Result: Totally 617 treatment episodes were identified during the study period, 217 for risperidone, 216 for quetiapine, 102 for sulpiride, and 82 for the other antipsychotics. There were 299 males, 318 females and the mean age was 80.1 year-old (SD 6.88). No significant differences were noted between groups. The quetiapine group had more hospitalization history and prior use of second generation antipsychotics (compared with sulpiride group), and more prior use of first generation antipsychotics (compared with the other antipsychotics group). The risperidone group had more prior use of second generation antipsychotics when compared with sulpiride and the other antipsychotics. The continuation rates after 180 days follow-up were 35.3% for quetiapine, 23.5% for risperidone, 12.7% for sulpiride, and 17.1% for the other antipsychotics. The mean survival days by Kaplan-Meier survival analysis were 99.1 for quetiapine, 77.5 for risperidone, 65.6 for sulpiride, and 66.0 for the other antipsychotics. They were statistically different between groups by Log Rank test. Cox proportional hazard model revealed that only prior use of first generation antipsychotics and the antipsychotics used were major factors influencing the time to discontinuation.

Conclusion: Quetiapine and risperidone had fewer discontinuation rates and higher mean survival days when compared with sulpiride and the other antipsychotics.

P2-105

False recognition in auditory verbal memory as an indicator of dementia: relation to prospective memory

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Objective: False recognition (FR) is related to memory function and frontal lobe function. Prospective memory (PM) is related to memory, executive function including frontal lobe function. To investigate the relation between false memory and prospective memory, and the usefulness of an indicator of dementia, we assessed PM and FR in auditory verbal memory in amnestic patients.

Method: Seventy-three subjects who consulted our memory clinic were studied. The average age were 77.5 ± 5.8 years, and average education periods were 10.9 ± 1.9 years. They were diagnosed as 23 cases of Alzheimer's disease, 17 of vascular dementia, 4 of dementia with Lewy bodies, 7 of frontotemporal dementia, 14 of mild cognitive impairment (MCI), 8 of healthy subjects. Severity was assessed with Clinical Dementia Rating (CDR) and according to the diagnosis the subjects were divided into three groups: control subjects (CS), MCI and dementia (D) group. Rey Auditory Verbal Learning Test (RAVLT) was used as auditory verbal memory task (immediate recall: IR, delayed recall: DR, recognition: R and false recognition: FR), while "Appointment", "Belonging" and "Message" tasks in the Rivermead Behavioural Memory Test (immediate recall, delayed recall) were used as PM task. Mini-mental State Examination (MMSE) was used as a cognitive screening test.

Results: PM impaired groups in "Appointment", "Belonging" and "Message (immediate recall and delayed recall)" showed significantly higher scores in CDR. Although PM impaired groups in "Appointment", "Belonging" and "Message (immediate recall, delayed recall)" showed significantly lower scores in MMSE, RAVLT (IR and DR). While CS group showed significantly higher scores in MMSE, RAVLT (IR and DR) than MCI and D groups, RAVLT(R) showed no difference among three groups, and RAVLT (FR) is significantly higher scores in D group than in CS group. PM impaired group in "Appointment" and "Message" (immediate recall) in FR showed significantly higher scores than in non-impaired group. More frequent words in FR were "flower", "teacher" and "window", which had semantic familiarity with the correct words.

Discussion: We suggest false recognition is related to some PM of short time retrieval and of semantic familiarity with memory information. And false recognition can distinguish dementia from CS group, it is useful as an indicator of dementia.

P2-106

Valproic acid for behavioural and psychological symptoms in dementia: A case report

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Background: Behaviour and psychological symptoms in dementia (BPSD) are a very important problem for affected patients. BPSD affect more then 90% of patients with dementia and their management is difficult. The use of valproic acid has been reported for the treatment of some cases which do not respond to conventional drugs.

Case report: A 72-years male patient came to our observation for a progressive worsening of his cognitive functional status. The history revealed the presence of aggressive behaviour and emotional variability since young age. In 2003 it was confirmed the suspicion of multi-infarctual dementia. He had been treated with several different drugs and electroconvulsive therapy until the adolescence, without any real benefit. In 1990 treatment with lithium was started, with a partial remission of depressive and maniacal symptoms. This condition was maintained in the following years, adapting the treatment with barbexaclone and phenobarbital. At admission the patient complained of visual and auditory hallucinations, dysarthria, confused language, agitation, unsteadiness. Neuropsychometric assessment showed a score of 7/30 in MMSE (Mini Mental State Examination), 0/6 in ADL (Basal Activies of Daily Living), 0/8 in IADL (Instrumental Activies of Daily Living), while GDS (Geriatric Depression Scale) was not applicable. Although the serum levels of all drugs was in therapeutic range, we gradually discontinued lithium, phenobarbital and barbexaclone for the persistence of BPSD. After a week of wash-out, valproic acid therapy (500 mg day) was started. In the next five days the dose was increased to 1000 mg day, and after a month olanzapine (2,5 mg die) was started. This therapy induced a noticeable improvement in the state of health, with the reappearance of

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normal communication and understanding. After three months, a score of 13/30 in MMSE, 3/6 in ADL, 2/8 in IADL in GDS 7/15, NPI (Neuro-Psychiatric Inventory) with 28 of distress were observed. A further improvement in the general condition of the patient was observed, and an increase of his neuropsychological and social assessment was detected after 1-year. The last neuropsychometric assessment showed a score of 21/30 in MMSE, 4/6 in ADL, 3/8 in IADL in GDS 3/15, NPI with 3 of distress.

Conclusions: Our experience suggests that the administration of off-label valproic acid allowed a good control of BPSD, with a functional recovery; however other studies are obviously needed to confirm it.

P2-107

Quality of life and burden of spouses of Alzheimer's disease patients; individualized assessment with the schedule for the evaluation of individual quality of life (SEIQoL)

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Caring for persons with dementia is a multidimensional challenge, with progress of disease causing different types of problems, with different impacts on relationship and caregivers.

We assessed quality of life (QoL) of spouses of mild to moderately severe Alzheimer patients and explored its relationship with caregiver burden and patient cognition in a cross-sectional study.

QoL was measured with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL), which acknowledges the relevant individual QoL domains. Three burden indicators were applied: visual analogue scale (VAS), perceived stress scale (EDIZ) and Zarit Burden Interview (ZBI), with low scores for low and high scores for high burden. Patient cognition was assessed with the Mini-Mental State Examination (MMSE).

Of 112 spouses 97 could complete the SEIQoL. 87 spouses (53% male, mean age 72 years) fulfilled the SEIQoL internal reliability criteria, and had a mean SEIQoL score (0–100) of 68.6 (SD: 14.8). Most important QoL domains were: condition of patient (31%) and marriage (26%). Caregiver burden scores on VAS (0–100), EDIZ (0–9) and ZBI (0–48) were 44.1 (SD 23.5), 4.9 (SD 2.2), and 13.1 (SD 6.2) respectively. Mean patient MMSE score (0–30) was 20.3 (SD 4.2). In 46 participants the complete battery of tests was administered. Their mean scores were: SEIQoL 69,2 (SD 15,2); ZBI 12,6 (SD 6,3); EDIZ 4,7 (SD 2,3) and VAS burden 45,6 (SD 25). Mean patient MMSE for this subgroup was 19,5 (SD 4,8). A significant negative association was found between SEIQoL and ZBI, if MMSE score was >20. For the subgroup with MMSE score <20, MMSE was the only significant predictor of SEIQoL. In cognitively less impaired patients (MMSE >20), caregiver QoL is better and caregiver burden is lower. If MMSE was <20, better caregiver QoL was associated with better patient cognition. Thus, patient cognition is a predictor of caregiver QoL, and burden. QoL of spousal caregivers is lower than the QoL of mild stage AD patients and healthy contemporaries (own former research, data not shown).

Our data showed that caregiver QoL and burden is influenced most by the altered relationship with the demented person. Quality of life is already negatively affected, while the level of burden is still relatively modest. Evidence on the impact of caregiver burden, and the large number of caregivers involved, warrants that new interventions are evaluated on their impact on caregiver QoL and burden.

P2-108

Status quo for determining driving cessation of older adults with dementia in Japan

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Introduction: It is estimated that there are approximately 350,000 people with dementia who continue to drive in Japan (Y Arai 2005). With the amendment to *Section 103* of the Road Traffic Act in 2002, dementia is for the first time included as a reason for license revocation. However, it is argued that the implementation of the Act leaves much to be desired. In particular, it still remains to be defined

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who is ultimately in charge of the decision on driving cessation of older adults with dementia.

Objectives: The present study investigated: (1) who played a major role in driving cessation of older adults with dementia (hereinafter "the patients"); (2) what were the current practices regarding attempts for driving cessation of the patients by their family caregivers; and (3) what were the necessary requirements for enabling the cessation of driving.

Methods: The study subjects were 79 pairs of family caregivers and consecutive outpatients satisfying the diagnostic criteria for dementia at Ehime University Hospital from June 2004 to March 2006. The patients were assessed according to cognitive function, neuropsychiatric disturbances, and severity of dementia. The family caregivers were asked by a self-administered questionnaire including patients' driving habits and plans for driving cessation.

Results: (1) Whereas 54% of the family caregivers (sample size n = 37; multiple answer) answered that the patients themselves should determine whether to cease driving, 48% of the family caregivers actually made the decisions (sample size n = 21).

(2) Out of those family caregivers who doubted the driving ability of the patients (n = 18), only half attempted to encourage the patients to cease their driving.

(3) Availability of family members who can drive instead of the patients and encouragement from health professionals were raised as essential for enabling the cessation of driving.

Discussion: The findings regarding the necessary requirements for enabling the cessation of driving clearly indicated that whether the decisions would be made in practice were highly situation-dependent. It should therefore be a matter of policy, such as institutionalising the availability of transportation alternatives.

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P2-109

Caring of the end of life for Alzeimer's disease patients: Some theoretical and practical issues

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End-of-life care for patients with Alzheimer's disease has implications for patients, caregivers and society. End-of-life care for patients with dementia is extremely demanding of family caregivers. During the severe stage of the illness, patients lose the ability to communicate their needs and require significant assistance in activities of daily living. Physical consequences of the progression of dementia predispose persons with advanced Alzheimer's disease to infection and fever, especially aspiration pneumonia and urinary tract infections. Families of patients at this stage of dementia must determine of they can provide care at home or if the patients should be cared for in an institution. Quality of care in patients with end-stage dementia is an important factor when deciding where these patients should receive care. According to some authors, a major obstacle to quality home care is a lack of adequate training for caregivers. Caregivers who take advantage of programs such as support groups keep their Alzheimer's patient at home longer than those who do not. Patients who receive hospice care and pain control stay at home longer and are more likely to die at home. Patients who die at home have fewer symptoms and less discomfort than those who received care in other settings. If satisfactory care cannot be provided at home, patients with progressive dementia should receive end-of-life care in an institution. Deaths of demented patients raise a lot of ethical considerations. It is always difficult to know demented patients' awareness of the end of life. It is really difficult to accompany these patients, with whom communication is essentially nonverbal. During this delicate phase of the end of life, how can formal health professionals help the family members who are afraid of both death and dementia? A majority of authors conclude that end-of-life care for Alzheimer's patients can be provided at their home. This care can be facilitated by hospice programs, effective pain control and psychiatric care. Very important is the improvement of our communication skills with the patient and the facilitation of interdisciplinary exchanges with the caregiver's team and with the family members to allow acceptance of the death.

P2-110

Comparison of proxy-patient assessment and self-reported evaluation of depressive symptoms in the elderly

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Objectives: To determine the extent about whether proxy assessment can substitute for or add to patient with geriatric depression for self-assessment of somatic complaints, physical activity of daily living, and instrumental activity of daily living.
Design: A cross-section study design.
Methods: All subjects were outpatients to geriatric psychiatric clinics in a medical center and assessed with the Geriatric Depression Scale (GDS; long form) and the Short Portable Mental Status Questionnaire (SPMSQ). When the patient's self-assessed GDS score was >13 and a normal SPMSQ score was obtained, patients were interviewed to establish diagnosis according to DSM-IV and HAM-D was then applied to determine the severity of psychopathology. Meanwhile, their caregivers were given a GDS evaluation analogous to the original patient-version but written in the third-person. Activity of daily living (ADL) scale and psychosomatic symptoms were also allied to patients and caregivers separately during testing. The consistencies for these three aspects were also explored by diagnostic subtypes of depression.
Results: Totally, 102 eligible patient-caregiver dyads, with a mean age of 72.38 (SD = 5.69) among the subjects, were enrolled for the assessments. Sixty-five of the subjects were female (63.73%). Most of them (85.30%) were poorly educated (less than 7 years of education). For number of somatic complaints, physical activity of daily living, and instrumental activity of daily living, the intraclass correlation coefficients (ICC) between proxy and patient were all statistical significant (all p values < 0.01). The exploration of proxy-patient response consistency by subtypes of geriatric depression also identified positive for most subtypes, except for independent activities of daily life (ICC: −12.44, 95% CI: −523.33, 0.66) among the ones with major depressive disorder, recurrent, although insignificant.
Conclusions: Proxy reports for number of somatic complaints, physical activity of daily living, and instrumental activity of daily living may be a valid supplement to traditional retrospective self-reports used for clinical decision-making in geriatric depression management.

P2-111

Measuring the "senior friendliness" of geriatric mental health websites

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The Internet offers a rich, if disorganized, array of patient education and consumer health materials on the topic of late life mood disorders. Old age psychiatrists and geriatric mental health specialists need to know how to locate reliable websites that they can recommend with confidence to patients and family caregivers. In 2002, the US National Institute on Aging and the US National Library of Medicine issued guidelines for creating a "senior-friendly" website. The objective of this study is to measure how well the patient education and consumer health websites from major mental health organizations that are designed for use by older individuals meet these guidelines. A metric was constructed from the NIA/NLM guidelines, and the nine websites listed in the article entitled "Internet Resources: Late-Life Depression Resources for Patients and their Caregivers," published by the US Medical Library Association in 2003 were checked against the metric. In addition, eight additional websites identified in the workshop on "The Geriatric Professional's Guide to the Internet-I: Websites for Patients and their Families," presented at the American Association for Geriatric Psychiatry meeting in 2007 were similarly analyzed. The results indicate that the majority of these websites do not meet the guidelines, suggesting that specific website revisions are needed to make these sites conform to the senior-friendly recommendations. The poster presents these findings, as well as examples of both good and bad websites for consumer- and patient-oriented geriatric psychiatric content. *NOTE: an effort to replicate this study with Japanese websites on geriatric topics is underway, and may have results which can be discussed in Osaka.*

P2-112

Caregiver Activity Survey (CAS) in caregivers of community dwelling elderly with dementia

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Objective: Caregiver Activity Survey (CAS) has been designed to collect information about the time caregivers spend providing care during a typical 24-hour period. This study aimed to develop the Korean version of CAS (CAS-K) in caregivers of community dwelling elderly with dementia.
Methods: Study sample consisted of 61 dementia elderly and their caregivers. For the dementia elderly, data on demographic characteristics, cognitive function, activities of daily living, global severity of dementia, depressive symptoms, and physical illness were investigated. For the caregivers, CAS-K was administered, and data on demographic characteristics, care burden, and general psychopathology were assessed. Using the data above, analyses on reliabilities and validities of CAS-K were carried out.
Results: In the dementia elderly, global severity was classified into mild (N = 44; 72%), moderate (N = 12; 20%), and severe (N = 5; 8%). Mean caregiving time per day measured by the CAS-K was seven hours across all dementia elders. However, the time was increased according to the global severity of dementia. Test-retest reliability of the CAS-K was good. Times on the CAS-K was significantly correlated with scores on cognitive function, activities of daily living, and global severity of the dementia elderly; and with care burden and general psychopathology of the caregivers.
Conclusions: Our results suggest that the CAS-K may be a reliable and valid instrument for investigating caregiving time required by Korean caregivers. It could be used as an outcome measure of drug trials or an indirect index of costs in the management of dementia patients.

P2-113

Family and personal psychodynamic of care-givers immediate family members of patients with dementia: An inside story

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In Serbia more than 90% of patients with dementia are on home treatment and care. Most of them are under care of their immediate family members (spouse, children). Affiliation to the same family gives the care giver role an especially stressful impact. Previous relationship within the family as well as personal psychodynamic of the care-givers may predict their adaptability to the new role. Adaptation difficulties and family rigidity towards change especially when hierarchy is violated disturb the family homeostasis. Feelings of powerlessness, fear, pity, self-pity, anger, guilt, etc. arise out of chronic long-lasting frustration a care-giver family member is subjected to. Too much to elaborate and too much to suppress may amount to a decompensation of a somatic, psychosomatic, anxious and/or depressive nature. A care giver becoming a patient establishes a new dis-functional family homeostasis. This paper is a case-report illustrating the family and personal dynamic of care-givers (spouse and daughter) of a dementia patient previously an authoritative family, as well as professional figure. The course of eight years care through maladaptive towards adaptive family functioning, from personal crisis to partial resolution of crisis is presented from a both professional and intimate point of view. The importance of adequate treatment of the dementia patient, care-giver support network and introduction of an additional professional care-giver (nurse) is emphasized.

P2-114

Geriatric caregiver's burden

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There is limited studies about the role and burden of geriatric caregivers in Indonesia. However, the role of caregiver is very important in assisting the elderly to undergo their everyday life. This study examine the burden of caregivers and several aspects of the role of caregivers such as caring activities they provided, amount of time they spent to take care the elderly, etc. We also compared the role and burden between geriatric caregivers in a general hospital, geriatric community and elderly-home. The results of this study are expected to give information about the role and burden of caregivers in taking care the elderly, and inputs in educating and training for the caregivers in the future.

P2-115

Stress response symptoms in carers of home dwelling patients suffering from dementia; A longitudinal follow-up

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This study is part of the Norwegian Dementia in the Family Study (Nor-DIF) where one of the objectives was to investigate the stress response symptoms like intrusion and avoidance in the carers. Background characteristics of 84 carers and their home dwelling family member with dementia were recorded at baseline. The Impact of Event Scale, Geriatric Depression Scale (GDS), State Trait Anxiety Inventory (STAI-X1) and the distress scale of the neuropsychiatric Inventory (NPI-D) were filled in by the carers at baseline, after 4.5 and 12 month. The mental capacity of the patients, ADL-impairment and BPSD was assessed by means of the Mini Mental State Examination (MMSE), Disability Assessment for Dementia (DAD) and Neuropsychiatric Inventory (NPI), respectively. 61% of the carers were females, 74% spouses, mean age were 66.0 years (SD 12.75), 56% of the patients were females, and the mean patient age was 75.4 years (SD 7.37). Mean Intrusion was 13.2 (SD 7.98), mean Avoidance 10.4 (7.33), mean STAI 21.4 (7.29), mean GDS 8.5 (SD 6.51) and mean NPI-D 13.2 (SD 8.63). Mean MMSE was 20.9 (SD 4.87), mean DAD% 60.2 (SD 22.87), median NPI (frequency × severity) 19.5 (IQR 10.0, 32.0). Using ANOVA we compared the baseline scores with the scores 4.5 and 12 month after baseline and found no significant changes in Intrusion, Avoidance, GHQ, GDS, STAI and NPI-D or NPI. There was a significant decrease in the DAD-scores (mean difference 16.5 (95% CI 8.86 −24.12) and MMSE-scores (mean difference 2.5 (95% CI 0.70 −4.23) from baseline to the 12 month. At baseline a high level of Intrusion was explained by STAI, NPI-D and longer duration of dementia (R^2 44%), whereas GDS, STAI, younger carer and increased ADL-impairment contributed to Intrusion at 12 month (R^2 49%). At baseline Avoidance was explained by GDS and the carer being a spouse (R^2 12%), whereas GDS and STAI contributed to Avoidance at 12 month (R^2 32%). In contrast to the expected decrease in Intrusion, Avoidance that we se in people exposed to traumatic life events, we found a stabilisation of the reported scores, probably due to the chronic exposure to the stressors represented by the symptoms of dementia. However, over a year of observation the factors contributing to the stress responses change, reflecting a possible adaptation to some of the dementia symptoms. Long-lasting high levels of intrusion and avoidance seems to be associated with depressive feelings and anxiety in the carers.

P2-116

Aged psychiatric residential care: A reflective model

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NorthWestern Aged Persons Mental Health is the largest provider of Aged Mental Health services in Australia offering a comprehensive range of services to Northern and Western Melbourne, servicing about 200000 persons over 65. Service includes 5 residential facilities (120 high care beds 32 low care beds). Beds are governed by Aged Care Accreditation Agency assessing rigorous standards incorporating management systems, health and personal care, resident lifestyles and physical environments. Workforce within facilities is predominantly nursing with significant proportions being Enrolled Nurses (RN Div2s). This paper details a process of investigation and evaluation of nurses attitudes and beliefs in and to core business of the facilities as governed by Aged Care Accreditation Agency and Mental Health Act. Clinical Nurse Educators conducted a series of focus groups within facilities over a period of 6weeks. Focus groups were semi-structured and asked staff to discuss views and core purpose of facilities, what facilities do well and what improvements could be made. Aim of focus groups was to explore staff perspectives, experiences and identify opportunities for growth and development. Form was developed to capture views of staff unable to attend focus groups. Data from focus groups was themed and suggestions for range of educational activities, practice development and quality planning proposed and discussed with staff. Significant driver for development was staffs perceived lack of opportunity for peer review of residents management and lack of opportunity to contribute to development and implementation of care plans. Importance of relationship between professional nursing and operational management within facilities was recognised as important factor to success of project and regular meetings between nurse educators and managers were scheduled to ensure agreement about process and expected outcomes. Formal expectations of professional competencies of staff

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were negotiated and list of educational priorities agreed. Significant outcomes of investigation into staff opinions are 1. Implementation of structured case presentations using formal format to compare actual care delivery to residents documented care-plan enabling peer review and reflective practice 2. Establishment of reflective practice groups addressing areas for discussion as raised by staff 3. Development of training planned by nurse educators to address identified needs. This project will be fully evaluated in September 2007.

P2-117

The relationship between stress reaction and the attitudes towards dementia-related aggression among Japanese formal caregivers

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Objective: To study the relationship between caregivers' stress reaction and the attitudes towards dementia-related aggression.

Subjects and methods: The request to participate into the study, information sheets and the questionnaires were sent to the aged care facilities of San-in and Kinki Areas in Japan. The caregivers working in these facilities were asked to fill in the questionnaires consists of Maslach Burnout Inventory Japanese version (MBI) (Harada, 2000) and Japanese version (Nakahira et al., 2005) of Attitudes Toward Aggression Scale (ATAS) (Jansen et al., 2005).

Results and discussions: Fifteen hundreds caregivers (male; 16.5%, female; 83.5%) in the aged care facilities were included in the study. The average age of the caregivers was 37.8 years old, average length of professional care experience was 12.2 years. Of the respondents, 80% stated they had experienced an act of aggression from patient with dementia. The caregivers with negative attitudes towards the aggressive behavior of patients tended to show the burn-out in caregiving works. It was especially noted that the caregivers who perceived the aggressive behavior of the patients as unpleasant, tended to show the depersonalization attitude which treat the patients as non-human beings, and they were the most fragile caregivers who easily burn-out in their work.

P2-118

Effect to professional caregivers of reminiscence group therapy for the elderly with dementia

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It is said that the quality of health and medical services becomes higher in the case of health professionals have affirmative image to the elderly than negative image. In this study, we examined the effect of the reminiscence group therapy to the professional caregivers. It is well known that reminiscence group therapy is effective to the elderly with dementia. But the effect of this therapy to the caregivers is unknown. We examined the change of image to the elderly with dementia by joining in reminiscence group therapy for the demented elderly people. The image was measured by before and after when caregivers join in reminiscence group with nine items of image, such as "high motivation", "richness of affective expression" and "calmness". Factor analysis was done about nine items, and they were divided into two factors, "activeness" and "maturity". A change of an image was compared with these two factors. At the same time, another two control groups of caregivers were set to compare the change of image; group of the caregivers which join in daily speech session and which does not join in both verbal session. As a result, only in the caregivers of reminiscence group, a score rose about both factors significantly. These results suggest that caregivers that join in the reminiscence group may have new notice by watching the lively expression which is not seen in nursing home daily life and hearing the valuable life history of the elderly. So, the reminiscence group therapy is effective to cultivate the ability of the caregivers to understand the state of the elderly.

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P2-119

MR tracking of microglia transplanted in Alzheimer model rats

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The therapeutic use of microglia has recently received some attention for the treatment of Alzheimer's disease (AD), but few noninvasive techniques exist for monitoring the cells after administration. Here we present a magnetic resonance imaging (MRI) technology to track micrgolia injected into the lateral ventricle of Alzheimer model rats and the effect of the transplantation on the Aβ clearance.
Methods: We injected Aβ42 and saline into the left and right hippocampus of rats, respectively. Just after the injection, we transplanted primary-cultured rat microglia into the lateral ventricle. The transplanted microglia labeled with Resovist were traced by T2*-weighted MRI at a magnetic field of 7T. After MRI monitoring, we compared the MR images and the histochemical localization of exogenous microglia. We also measured amounts of Aβ42 injected into rat hippocampi.
Results and discussion: MRI revealed transplanted microglia along with the left lateral ventricle as the injection site at 1 day after the transplantation. At 8 days after, transplanted microglia were detected in Aβ-injected left hippocampus. Histochemically, CD68-positive microglia were accumulated around the Aβ deposit, and parts of them contained with Resovist. Although amounts of Aβ42 were gradually reduced even in the control rats, the reductions were significantly enhanced by the microglial transplantation. This study suggests the usefulness of MRI for *in vivo* monitoring of exogenous microglia. Exogenous microglia may migrate from the lateral ventricle to the Aβ-injected site and retain its phagocytic function.

P2-120

LGI3 accumulates in endocytic pathway of aged monkey brains; LGI3 colocalizes with Aβ *in vivo*

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Purpose: Leucine-rich glioma inactivated (LGI)3 is a member of the LGI family, and we have previously shown that Aβ up regulated LGI3 and that Aβ and LGI3 co localized on plasma membranes of cultured rat astrocytes. The function of LGI3 in brain, however, remains unknown. In the present study, we investigated LGI3 localization and the relationship between LGI3 and Aβ by using various aged monkey brains.
Methods: Sixteen cynomolgus monkey brains were used in this study. To investigate LGI3 localization in brain, we examined immunohistochemical analyses by using an antibody for LGI3, and several subcellular marker antibodies. To investigate the correlation of LGI3 with Aβ in brain, we also examined double-immunohistochemistry. Finally, we investigated age-related changes of LGI3 in brain by Western blot analyses. All animals were maintained according to the guidelines for experimental animal welfare.
Result and discussion: Immunohistochemistry showed that LGI3 was present in almost all neural cells, and mainly localized to plasma membranes and nuclei. In aged monkey brains, we found that LGI3 accumulated on/near plasma membranes of neurons, and they colocalized with endocytosis-associated proteins and lipid raft markers. Moreover, we found that LGI3 colocalized with Aβ in astrocytes. From western blot analyses, we found that LGI3 levels increased in monkey brain with aging. These findings indicate that aging causes accumulation of LGI3 in endocytic pathway, suggesting that LGI3 would correlate with endocytosis system in brain and Aβ metabolism in astrocytes *in vivo.*

P2-121

Effects of chronic exposure to aluminum in drinking water on an animal model of tauopathies

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We have reported that transgenic (Tg) mice overexpressing human tau protein develop filamentous tau aggregates in the CNS. We over expressed the smallest human tau isoform (T44) in the mouse CNS to model tauopathies. These tau Tg (PrP T44 Tg) mice acquire age-dependent CNS pathologies including insoluble, hyperphosphorylated tau and argyrophilic intraneuronal inclusions composed of tau-immunoreactive filaments. Therefore, these Tg mice are a model that can be exploited to elucidate mechanisms of tau pathology in various neurodegenerative tauopathies including Alzheimer's disease (AD). Aluminum (Al) has been implicated as a potential risk factor for AD in reports from various fields, including epidemiology, cell culture, and animal studies. In the present study, the effects of chronic exposure to Al on PrP T44 Tg mice, which can be considered vulnerable to tau-related pathology, were investigated in order to confirm whether or not Al has any effect on tau lesions. As previously reported animal studies, chronic Al exposure had certain deleterious effects on histology and behavior even on wild type mice, but they were significantly exacerbated in Tg mice. For example, the number of tau-positive inclusions in the spinal cord of Tg mice was decreased, and vacuolar degeneration was prominent, suggesting that cell viability was attenuated and the cells underwent a degenerative cascade rather than containing tau inclusions "safely". These results suggest that chronic Al exposure has a promotive effect on tau-related neurodegeneration.

P2-122

Aβ accumulation causes postsynaptic damage in Tg2576 mice

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In Alzheimer's disease (AD), it is believed that accumulation of amyloid β protein (Aβ) causes neuronal damage resulting memory disturbance, however, the mechanism of neurotoxicity of Aβ has not been solved yet. Recently synaptic damage by Aβ was shown *in vitro*. We have also shown that postsynaptic marker, drebrin, disappears from hippocampal synapses in AD. We analyzed the synaptic damage caused by Aβ accumulation in brain of Tg2576 mice, a model of AD. Tg2576 mice (n = 35, 8–32 month old) and their littermate nontransgenic mice (n = 10) were used. Paraffin sections of hemibrain were stained with antibodies against synaptic marker (synaptophysin, α-synuclein, drebrin). Amount of Aβ was measured in another hemibrain. In cerebral cortex and hippocampus of Tg2576 mice, staining of drebrin decreased with accumulation of Aβ. The staining of presynaptic marker was conserved. There was no change of synaptic markers in nontransgenic mice. Accumulation of Aβ may exert neurotoxicity by damage of postsynaptic membrane.

P2-123

Tau protein phosphorylation by oxidative stress via c-jun N-terminal kinase (JNK) activation

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Object: In order to make clear a hyperphosphorylation mechanism of tau proteins under oxidative stress conditions, we have investigated quantitative changes of phosphorylated tau proteins in culture cells after addition of oxidative chemical compounds, and also checked phosphatase activation, such as JNK and glycogen synthase kinase-3β (GSK-3β).
Methods: Nickel chloride was added to culture media of HEK293 cells to make oxidative stress condition, and then those cells were harvested at regular time intervals. Those samples were analyzed by western blotting, and checked the quantitative changes of phosphorylated tau proteins, activated JNK and GSK-3β.
Results: Twenty-four after addition of nickel chloride, there was an increased activation of JNK in the lysate of HEK293 cells, and at the same time, we detected an increased amount of phosphorylated tau proteins which was detected by AT8 antibodies.
Discussion and conclusion: It is known that tau proteins are hyperphosphorylated by phosphatases

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which are activated under a deficiency of neurotrophic factors or an accumulation of amyloid proteins. Our results indicate the possibility that an activation of phosphatases under oxidative stress conditions causes hyperphosphorylation of tau proteins.

P2-124

Aging attenuates dynactin-dynein interaction: down-regulation of dynein causes accumulation of enodogenous tau and APP in human neuroblastoma cells

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Background and aim: Impaired axonal transport may promote pathogenesis in neurodegenerative disorders, such as Alzheimer's disease (AD). We previously showed that tau, amyloid precursor protein (APP), and intracellular amyloid β-protein (Aβ) accumulate in the nerve-ending fraction of aged monkey brains, perhaps due to impaired axonal transport. In the present study, we assessed age-related changes of axonal transport motor proteins in aged monkey brains.

Methods: We examined westernblot and co-immunoprecipitation by using young and aged monkey brains to investigate age-related changes of axonal transport motor proteins. We also examined RNAi studies to investigate whether RNAi-induced down-regulation of motor protein causes intracellular accumulation of disease proteins in human neuroblastoma cells.

Results and discussion: Western blotting showed that kinesin, dynein, and dynactin (DYN) localizations dramatically changed with aging, and dynein level in nerve-ending fractions increased significantly. Co-immunoprecipitation analyses showed that DYN-dynein intermediate chain (DIC) interactions decreased, suggesting that age-related attenuation of this interaction may cause the impairment of dynein function. Moreover, RNAi-induced down-regulation of DIC in human neuroblastoma cells caused endogenous tau and APP to accumulate, and their subcellular localizations were also affected. Our findings suggest that aging attenuates DYN-DIC interaction, representing one of the risk factors for age-related impaired dynein function, and even for accumulation of disease proteins.

P2-125

Immunohistochemical study on TDP-43 protein in amyotrophic lateral sclerosis/parkinsonism-dementia complex of the Kii peninsula of Japan

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Background: Anti-TDP-43 antibody positive inclusion was reported in the brains and spinal cords of frontotemporal lobar degeneration with ubiquitin-positive, tau-negative inclusion (FTLD-U) and sporadic ALS in 2006. The purpose of this study is to reveal TDP-43 protein in Kii ALS/PDC brains and spinal cords immunohistochemically.

Objective and method: Formalin-fixed, paraffin-embedded sections of the medial temporal lobes and spinal cords derived from six patients with Kii ALS/PDC were submitted for the study. Anti-tau antibody (AT8, Inogenetics) and anti-TDP-43 antibody (TAR DNA-binding protein 43, Protein Tech Group) were used for immunohistochemical analysis. Results: Immunohistochemistry with anti-TDP-43 antibody revealed neuronal cytoplasmic, dot-like or threads structures in the hippocampus and spinal cord. Some of TDP-43 positive inclusions co-existed with tau positive inclusions in the double staining with anti-tau and anti-TDP-43 antibodies.

Conclusion: Recently TDP-43 was reported to deposite in the Gaum PDC brains. Accumulation of TDP-43 may be common process in Guam and Kii ALS/PDC.

P2-126

CRB2 binds to presenilin complexes resulting in inhibited secretion of amyloid-β peptides

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γ-Secretase mediates intramembrane cleavage of type I transmembrane proteins such as amyloid-β precursor protein (APP) and Notch receptor. Proteolytic processing of APP yields neurotoxic amyloid-β (Aβ) peptides in Alzheimer's brains, whereas γ-cleavage of Notch releases the intracellular domain that is critical for the signal transduction. Recently, Herranz et al. have reported that Drosophila transmembrane protein Crumbs negatively regulates Notch signaling. Mammalian homologues for Crumbs are known as scaffold proteins controlling the formation of adherens junctions. Among the homologues, CRB2 is expressed in the brain at a higher level. We investigated a modulatory role of CRB2 on γ-secretase cleavage of APP. When over expressed in APP-expressing HEK293 cells, CRB2 suppressed secretion of Aβ peptides. CRB2 knockdown using siRNA caused increased secretion of Aβ from SH-SY5Y neuroblastoma cells. CRB2 did not affect ratio of Aβ42 to total Aβ. Analysis using the truncation mutants indicated that the N-terminal extra cellular domain of CRB2 is dispensable for inhibition of γ-secretase cleavage. Co-immunoprecipitation study suggested that CRB2 binds with presenilin, APH-1 and nicastrin, but not with PEN-2. CRB2 immunoreactivity was detected in neurons in the cerebral cortices and hippocampi of human autopsy brains. Our results suggest that CRB2 binds with presenilin complexes to negatively regulate γ-secretase activity in mammalian cells.

P2-127

Characteristics of γ-secretase activities in I213T mutant PS1 knock-in mice brain

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Objective: Mutations in Presenilin (PS) genes account for the most cases of familial Alzheimer's disease (FAD), and alter γ-secretase activity to enhance the ratio of Aβ42 to Aβ40. However, it is still unclear how these mutations modify Aβ metabolisms and contribute to AD-related pathophysiology. We previously demonstrated that PS1 FAD mutations reduce γ-secretase cleavage on Aβ40 more dramatically than Aβ42 in cell culture models. To expand these findings into more physiological status, here we further investigated γ-secretase activity in brain lysate of I213T mutant PS1 knock-in mice.
Methods: CHAPSO solubilized brain lysate purified from wild-type, heterozygous, homozygous adult mutant mice were incubated with 500 nM recombinant APP-C99FLAG substrates. De novo generated Aβ levels were measured by western blot using anti-Aβ antibodies.
Results: When incubating each brain lysate with APP-C99FLAG, robust de novo Aβs generation were observed in each sample. These activities were almost completely abolished by the presence of γ-secretase inhibitors, so that we could exclude non-specific activity in these reactions. As well as previous our results using cell model, de novo generated levels of Aβ40 significantly reduced without changing levels of Aβ42. This reduction of Aβ40 generation was seen in PS1 mutant allele dose-dependent manner.
Discussion: These findings indicate that PS1 FAD mutations impair catalytic activity of γ-secretase enzyme only for Aβ40 but not for Aβ42 generation, which may be the cause of increase in the ratio of Aβ42/Aβ40 in brain with PS1 mutation.

P2-128

Different phenotypes of mouse expressing human wild and mutant P301L tau

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(Purpose) To understand the effects of mutant human tau over expression in mouse brain, we examined pathological and behavioral changes in

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transgenic (Tg) mice overexpressing wild-type and P301L mutant human tau.

Methods: Tg mice overexpressing 4R2N isoform of human tau with or without P301L mutation under control of alpha CaMKII promoter were generated, and selected mouse lines with the same expression level and distribution. The brains were transcardially perfused with 10% formaldehyde under anesthesia. Paraffin sections were immunostained with various antibodies against phosphorylated tau and glial markers, as well as Nissl staining for stereological counting of neuron numbers. This study was conducted following the Guidelines for Conducting Animal Experiment of RIKEN.

Results and discussion: Wild-type tau Tg mouse showed the accumulation of highly phosphorylated tau in parahippocampus without biochemical sign of NFT formation. On the other hand, P301L tau Tg mice did not exhibit the accumulation of highlyphosphorylated tau in the same region, but neuronal loss accompanying with astroglyosis was observed in parahippocampal region In Morris water maze, Wild type tau Tg was completely impaired an ability of learning and memory. P301L mouse was somewhat impaired learning ability compare to non-Tg mouse, but could retain an ability of memory. These results suggest that different forms of human tau affect neurons in the distinct manner, leading to learning disorders in these Tg mice.

P2-129

The JAK2/STAT3 signaling axis regulates memory in Alzheimer's disease

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Upregulation of toxic soluble amyloid beta (Aβ) is implicated in the pathogenesis of Alzheimer's disease (AD). Intracellular events in neurons related to memory impairment in AD, however, remain poorly understood. Here we report that p-STAT3 levels in hippocampal neurons decreased in both AD model mice and AD patients. Intracerebroventricular administration of Aβ1–42 downregulated p-STAT3 while passive immunization with anti-Aβ antibody conversely restored hippocampal p-STAT3 levels in Tg2576 mice, indicating that upregulation of Aβ1–42 causes p-STAT3 downregulation. Intranasal administration of Colivelin rapidly elevated p-STAT3 levels in the hippocampal neurons and completely restored cognitive function in Tg2576 that had already suffered memory impairment. In addition, chemical inhibition of the JAK2/STAT3 axis significantly impaired cognitive function, which correlated with the dysfunction of the basal forebrain cholinergic systems. Thus, the JAK2/STAT3 axis plays a critical role in cognitive function and provides a novel target in AD therapy.

P2-130

GABA-related acceleration of aging process in Alzheimer's model mouse

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AD can be considered as an acceleration of aging-associated memory loss. GABA modulates synaptic plasticity that is believed to be essential for memory formation. By lowering excitatory post-synaptic potential, GABA functions to suppress hippocampal LTP, a form of synaptic plasticity. To see if GABA may be involved in the acceleration of aging process in AD, we examined the effect of GABA on hippocampal LTP in brain slices of PSAPP transgenic mouse. The extent of GABA effect on LTP was estimated by subtracting the level of LTP measured in the absence of GABAA receptor antagonist, bicuculline, from the LTP level in the presence of bicuculline. Larger GABA effect was observed in 'middle aged' PSAPP than 'middle aged' nonTG. Large GABA effect resulted in low LTP level that was correlated with its low memory score of 'middle aged' PSAPP, as assessed by Morris water maze. In contrast, GABA effect was reciprocally diminished at 'old' age of PSAPP, resulting in higher LTP level than 'old' nonTG. Consistently, 'old' PSAPP appeared to remember about repeated experience even better than 'old' nonTG. But, 'old' PSAPP mouse simultaneously showed less accurate learning and lack of memory flexibility. 'Old' nonTG showed large GABA effect like 'middle aged' PSAPP. Large GABA effect in 'old' nonTG mouse is

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consistent with aging-associated increasing tone of GABAergic system in human brain. Large GABA effect in 'middle aged' PSAPP in comparison with such effect in 'old' nonTG indicates that acceleration of aging process in AD may be related to the accelerated increase of GABA effect.

P2-131

Evaluation of the dopaminergic system in the substantia nigra in aging-accelerated *klotho* mice

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Purpose: Aging is the most prominent risk factor for Parkinson's disease, and the number of dopaminergic neurons in the substantia nigra pars compacta is known to decreases with normal aging. However, consensus regarding how advancing age may predispose the dopamine system to Parkinson's disease is lacking. The *klotho* gene has been identified as an aging suppressor gene, and mutation causes multiple phenotypes resembling human aging in mice. This study investigated dopaminergic neurons in the substantia nigra in *klotho* mice.
Methods: Paraffin brain coronal sections 8 μm thick were made from *klotho* (*kl/kl*) and wild-type mice (8-week-old, male), and immunohistochemistry was performed using rabbit polyclonal anti-tyrosine hydroxylase (TH) antibody. To assay the number of dopaminergic neurons in the substantia nigra pars compacta, total numbers of TH-stained neurons in the substantia nigra pars compacta were counted in 4 mice from each group. TH-positive neurons were counted in right and left substantia nigra pars compacta of every fifth section throughout the entire substantia nigra pars compacta.
Results: Numbers of TH-positive neurons in substantia nigra compacta from *klotho* mice were significantly decreased compared to those from wild-type mice.
Conclusion: The *klotho* gene may act to preserve the dopaminergic system during aging.

P2-132

Analysis of transgenic mice overexpressing mutant tau and GSK-3β

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Background: Glycogen synthase kinase-3β(GSK-3β) plays important roles in neurofibrillary tangles (NFT) via accumulation of phosphorylated tau, Alzheimer's disease and tauopathies. It is important to elucidate the mechanism of GSK-3β involved in NFT and neuronal cell death, to develop novel therapy.
Objective: To elucidate immunocytochemical changes of cytoskeltal structures in GSK-3β transgenic mice (Tg), Thy-1 mutant Tau (P301L) Tg and GSK-3β/Tau double Tg.
Methods: To examine immunocytochemical study and Western blot of GSK-3β Tg brains and mutant Tau Tg brains at 3, 8 and 12 months.
Results: Immunocytochemical study of GSK-3β Tg showed that the immunostaining of GSK-3β increased in the cytoplasm and dendrites of neuronal cells in 3 to 12 months. Western blot showed that expression of human GSK-3β was same level in 3 and 12 months. The reduction of the level of the microtubule-associated protein 2 (MAP2) in brain, and immunoreactivity of neurofilament by antibodies SMI-31, NF-200 slightly decreased in the dendrites of neurons. Tau (P301L) Tg showed the cytoplasm of neuronal cells and dendrites were immunostained by GSK-3β, but less immunostained by MAP2. GSK-3β/Tau double Tg showed more immunostained by human tau and GSK-3β, while MAP2, SMI-31, NF-200 slightly decreased.
Conclusions: These findings suggested that over expression of GSK-3β *in vivo* led to decrease of phophorylated neurofilaments and MAP2 protein in neuronal cells, leading to aberrant change of cytoskeltal structures and neuronal dysfuction.

P2-133

Preclinical pharmacological property of lurasidone, a novel atypical antipsychotic

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agent: I. Antipsychotic and anxiolytic activities with minimum side effects

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Lurasidone is a novel atypical antipsychotic drug under clinical development. Lurasidone showed potent to moderate binding affinities for dopamine D2, serotonin (5-HT)2A, 5-HT1A, 5-HT7 and noradrenaline α2C receptors, but weaker affinities for noradrenaline α1, α2A and 5-HT2C receptors, whereas the affinities for histamine H1 and muscarinic acetylcholine receptors were only negligible. Lurasidone antagonized dopamine D2 receptor-mediated behaviors, such as methamphetamine-induced hyperactivity and apomorphine (APO)-induced stereotyped behavior and climbing behavior, and also inhibited conditioned avoidance response. Lurasidone potently inhibited 5-HT2 receptor-mediated behaviors, such as tryptamine-induced forepaw clonic seizure and *p*-chloroamphetamine-induced hyperthermia. Furthermore, lurasidone showed significant improvements in animal models of mood and anxiety disorders, such as a conditioned fear stress-induced freezing behavior test, the Vogel's conflict test, and a social interaction test. On the other hand, at doses up to 1000 mg/kg, acute lurasidone administration never induced sings of the extrapyramidal motor side effects such as catalepsy and bradykinesia. Anti-α1-noradrenergic, anti-cholinergic and central nervous system (CNS) depressant actions of lurasidone were also very weak, compared with the other antipsychotics including risperidone or olanzapine. Whereas olanzapine significantly increased c-fos expression in orexin-expressing hypothalamus neuron, lurasidone showed only comparable effects to the vehicle control. These results demonstrate that lurasidone possesses potential anti-dopamine D2 and anti-5-HT2 actions, and anxiolytic-like effects with extremely weak liabilities of extrapyramidal side effects and other CNS depressant side effects. These findings suggest that lurasidone would possess broad clinical efficacies and superior safety profiles to the existing atypical antipsychotic drugs. These safety characteristics of lurasidone seem to be suitable for not only psychosis in schizophrenic patients, but also delusion or BPSD in elderly patients.

P2-134

Preclinical pharmacological property of lurasidone, a novel atypical antipsychotic agent: II. Cognitive effects in animal models

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Lurasidone is a novel atypical antipsychotic drug under clinical development. Lurasidone has moderate to potent binding affinities for dopamine D2, serotonin (5-HT) 2A, 5-HT1A, 5-HT7, and noradrenaline α 2C receptors, but has very low binding affinity for acetylcholine muscarinic M1 and histamine H1 receptors (see accompanying poster). In order to compare the effect of lurasidone and the other antipsychotics on cognitive function, we investigated 1) the effect on the learning in the passive avoidance (PA) test in normal rats, 2) the effect on cognitive impairment induced by scopolamine in the rat PA test, and 3) the effect on cognitive impairment induced by MK-801 in the rat PA, Morris water maze (MWM), and radial-arm maze (RM) tests.

Lurasidone (1–30 mg/kg p.o.) did not impair the learning of normal rats, while other atypical antipsychotics (risperidone, clozapine, olanzapine, and aripiprazole) impaired the learning. In scopolamine-induced amnesia model, lurasidone (30 mg/kg p.o.) significantly reversed the learning impairments induced by scopolamine. In contrast, risperidone and olanzapine were inactive against scopolamine-induced learning impairment in this test. In MK-801-induced cognitive impairment models, lurasidone (1 and/or 3 mg/kg p.o.) potently reversed MK-801-induced impairments of learning and memory in the rat PA, MWM, and RM tests. Risperidone and clozapine partially attenuated MK-801-induced impairments of learning and memory in the PA test but not in MWM and RM tests. Aripiprazole and haloperidol did not reverse the impairments of learning and memory in any tests.

The present findings demonstrate that lurasidone has not only a less cognitive impairing activity, but also more pro-cognitive effects comparing with the other atypical antipsychotics tested in the present study. It is suggested that lurasidone would be more effective in treating cognitive impairments in clinic.

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P2-135

Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals in the nervous system

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Oxidative stress is a causative or at least ancillary factor in the pathogenesis of major neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis as well as in cases of stroke, trauma, and seizures. The high lipid content of nervous tissue, coupled with its high metabolic activity, makes it particularly susceptible to oxidant damage. Oxidative stress arises from the strong cellular oxidizing potential of excess reactive oxygen species (ROS), or free radicals. Most of the superoxide anion radical (O_2^-.) is generated in mitochondria by electron leakage from the electron transport chain and through the Krebs cycle. Excess O_2^-. reduces transition metal ions such as Fe_3^+ and Cu_2^+, the reduced form of which in turn react with H_2O_2 to produce hydroxyl radicals (·OH) by the Fenton reaction. ·OH is the strongest of the oxidant species and reacts indiscriminately with nucleic acids, lipids and proteins. There is no known detoxification system for ·OH; therefore, scavenging · OH is a critical antioxidant process. We show here that hydrogen (H_2) has potential as an antioxidant in preventive and therapeutic applications.

We induced acute oxidative stress in cultured cells by three independent methods. H_2 selectively reduced the hydroxyl radical, the most cytotoxic of ROS, and effectively protected cells; however, H_2 did not react with other ROS, which possess physiological roles. We used an acute rat model in which oxidative stress damage was induced in the brain by focal ischemia and reperfusion. The inhalation of 2% H_2 gas markedly suppressed brain injury by buffering the effects of oxidative stress. Thus H_2 can be used as an effective antioxidant therapy; owing to its ability to rapidly diffuse across membranes, it can reach and react with cytotoxic ROS and thus protect against oxidative damage.

Inhalation of H_2 has already been used in the prevention of decompression sickness in divers and has shown a good safety profile. Notably, H_2 has no risk of flammability or explosion at a concentration of less than 4.7% in air. We propose that H_2, one of the most well-known molecules, could be widely used in medical applications as a safe and effective antioxidant with minimal side effects. Further studies of revealing the precious mechanisms by which H_2 protects cells and tissues against oxidative stress are in progress.

P2-136

Design report: Randomized prospective learning therapy study on elderly Japanese in Osaka

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The randomized controlled single-masked trial is being performed to determine the effectiveness of non-pharmacological interventions. In Japan learning therapy and similar programs become popular. Day care houses where occupational therapy and/or recreation activities are commonly performed also become prevalent instantly after the long term care insurance started. Though the evidence of the effectiveness is still limited, many different kinds of non-pharmacological programs are running. The expectation to the non-pharmacological activities is seriously increasing. In this study, the effectiveness of learning therapy and occupational therapy will be estimated in the cross over trial. Because dementia and cognitive functions depend on bio-psycho-socio factors, social and biological factors also will be assessed. Our goal is establishment of the more effective non-pharmacological programs and to reveal the factors required for the successful program.150 elderly persons who can perform the activities were recruited from in the six day care houses in Osaka. Participants who received day care

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service in the long term care insurance facilities may be at risk of loss of independence. Their cognition is normal to moderately declined. Participants in each institute are randomized. MMSE score, age, the duration of education, sex are matched in the center. We developed two different intervention programs. One is learning therapy consist of reading and calculation. Calculation includes simulation of daily living shopping. The other is intensive occupational therapy. Each training session is 30 min, twice a week and continues six months. After six months intervention, the program will be switched and the second six month intervention will be performed (cross over trial). We addressed not only cognitive functions but also biological status such as genotype and biological markers related to dementia. At baseline, nonfasting patients have blood drawn for DNA and biochemical analysis. Primary outcome focus on cognitive function using ADAS, MMSE and FAB those are single masked. The preference of the activities is self reported at the baseline. GDS, MOSES, FIM and Zarit are assessed every 6 months. FIM, TORS and attitude on the program are assessed every session. Because of the potential carry-over effect, not only the pooled effects (cross over) but also the first six months effects will be analyzed.*The first three authors contributed equally.

P2-137

Classification of psychotic symptoms in dementia with Lewy bodies

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Objective: The aim of this study is to determine empirically a possible classification of psychotic symptoms, and identify the frequency of such symptoms in dementia with Lewy bodies (DLB).
Methods: We conducted a factor analysis of the psychotic symptoms in 100 patients with DLB.
Results: Four factors were obtained. Factor 1 was closely akin to misidentifications, including Capgras syndrome, phantom boarder, and reduplication of people and place. Factor 2 consisted of reduplication of people, the belief that deceased relatives are still alive, and the belief that absent relatives are in the house, which was classified as a type of misidentification or paramnesia. Factor 3 was akin to visual hallucinations of non-human objects, and factor 4 mirrored the hallucination of people and feeling of presence. Delusions were independent from these factors. Following the results of the factor analysis, the rates of each symptom group were identified. Hallucinations were the most frequent psychotic symptoms in DLB (78%), followed by misidentifications (56%) and delusions (25%).
Conclusions: This study suggested that hallucinations, misidentifications, and delusions should be separately considered in the understanding of underlying pathophysiology or psychopathology of DLB.

P2-138

Neurosin cleaves the NAC region of α-synuclein

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Background: α-Synuclein (α-syn) aggregation is the cardinal neuropathological feature in dementia with Lewy bodies and Parkinson disease. Several studies suggested a direct role for α-syn in the neurodegenerative process in these diseases. Neurosin is one of serine proteases predominantly expressed in a CNS to play an important role in metabolism of α-syn, because the previous report showed that neurosin exists in Lewy bodies and degrades α-syn *in vitro*. However the details of the processing of α-syn by neurosin have not been clarified.
Method: Cleavage sites of α-syn by neurosin were investigated by LC/MS/MS analyses of neurosin-digested fragments of recombinant α-syn. Furthermore, we evaluated the temporal course of neurosin-catalyzed degradation of wild-type and mutant α-syn by SDS-PAGE of resultant peptides sequentially derived from those α-syn proteins that were incubated with neurosin for varying time.
Findings: The dominant cleavage site of α-syn by neurosin was between Lys80 and Thr81. Neurosin digested A30P mutant α-syn less efficiently than the wild-type one.

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Interpretation: Neurosin cleaves α-syn dominantly at approximately the mid-portion of the NAC region, which is known to be responsible for the polymerization of α-syn. This result suggests that neurosin inhibits the polymerization of α-syn by cleaving it within the NAC region. Our result also suggests that the pathological process of A30P mutation may have some relevance to the relatively inefficient proteolysis of A30P mutant α-syn by neurosin compared with that of wild-type α-syn.

P2-139

Rivastigmine sustains cognitive and behavioural function for up to five-and-a-half years in patients with Lewy body dementia

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Objective: Lewy body dementia is a common but frequently under diagnosed form of dementia, characterised by fluctuating cognitive impairment, attention deficits, visual hallucinations, parkinsonism and other neuropathic features. Recent findings have confirmed that patients with Lewy body dementia have deficient cholinergic CNS pathways, and it has been proposed that acetylcholine-enhancing agents may have pharmacotherapeutic benefits. Several short term studies have demonstrated that the dual cholinesterase inhibitor, Rivastigmine, evokes clinically significant improvements in Lewy body symptoms, but long term data are sparse. This long-term study aims to discover whether rivastigmine can sustain cognitive and behavioural function in patients with Lewy body dementia.
Design: Open label, single centre study involving five patients with confirmed diagnoses of Lewy body dementia.
Materials and methods: Five patients all male, mean age at diagnosis; 76.8 ± 4.9 years(range 70–84 years)were diagnosed with Lewy body dementia between April 1999 and December 2001. Baseline cognitive and behavioural function were assessed using the Mini Mental State Examination(MMSE)and Behavioural Pathology in Alzheimer's Disease Rating Scale(BAD). Mean baseline values for MMSE and BAD were 23 ± 3.9 (range 17–27) and 8.3 ± 3.9 (range 3–12) respectively. All five patients received rivastigmine (1.5 mg b.d. initially, rising to 3–6 mg b.d). All concurrent medications were noted.
Results: Rivastigmine was administered for a mean duration of 41.4 ± 18.0 months(range 21–66 months). Over the treatment period, rivastigmine maintained mean MMSE and BAD scores at 18.8 ± 5.9 and 6.7 ± 2.0 respectively (changes from baseline minus 4.2 ± 9.0 and minus 1.7 ± 4.2 respectively). Two of the five patients reported improvements in MMSE, and one of three patients reported improvements in BAD. Rivastigmine treatment was well tolerated by all five patients. Despite a large number and range of concomitant medications, no drug to drug interactions were observed throughout the study duration.
Conclusion: Rivastigmine is well tolerated and can sustain cognitive and behavioural function for up to five and a half years in patients with Lewy body dementia.

P2-140

Cognitive function in early Parkinsonism; a population based study

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Objective: To determine the frequency and pattern of cognitive function in patients with Parkinsonism in a very early phase of the disease development.
Methods: Patients were identified in a longitudinal population based study of Parkinsons disease and Parkinsonism. Eighty three patients with idiopathic non-drug induced Parkinsonism were included during a three year period. The patients and 30 age- and sex-matched healthy control subjects underwent a comprehensive neuropsychological assessment of cognitive function.
Results: Patients with Parkinsonism demonstrated significantly poorer performance than healthy controls in tests of verbal and non-verbal episodic memory including both free and cued recall in immediate and delayed tasks, category fluency, attention, psychomotor function, visuospatial function and certain aspects of executive function. No differences were found in working memory, verbal fluency and in some aspects of executive function. Complex tasks were generally more difficult than simple tasks for the patient group.

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Conclusion: Cognitive dysfunction is present in patients in a very early phase of Parkinsonism. Neuropsychological evaluation may be important for early identification and prognosis.

P2-142

Value of CSF-Aβ42, total tau protein, phospholyrated tau protein in the differential diagnosis of DLB from AD: comparison with ^{131}I-MIBG radioactivity

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Objective: We elucidate the concentrations of CSF-Aβ42, total tau protein: CSF-Ttau, phospholyrated tau protein: CSF-Ptau in the patients with DLB and the patients with AD.
Methods: We studied 19 patients with DLB, 93 patients with AD and 42 control patients who had no disease in central nerves systems. We measured CSF-Aβ42, CSF-Ttau and CSF-Ptau in the patients with DLB, AD and control. In addition, we studied ^{123}I-MIBG radioactivity: MIBG in the patients with DLB and AD. We compared CSF marker with MIBG to discriminate DLB from AD. The study protocol was approved by the Institutional Ethics Committee.
Results: Aβ42: DLB 440.6 ± 209.4 pg/ml: mean SD, AD 341.1 ± 135.8, Control 699.8 ± 227.6: DLB vs Control: 0.0001; DLB vs AD $p < 0.05$; AD vs Control $p < 0.0001$. Ttau: DLB 228.9 ± 65.9 pg/ml, AD 536.8 ± 349.9, Control 134.1 ± 98.8: DLB vs AD $p < 0.0005$; AD vs Control < 0.0001. Ptau: DLB 44.2 ± 18.9 pg/ml, AD 61.7 ± 39.1, Control 33.9 ± 17.1. AD vs Control < 0.0001. MIBG early H/M ratio: DLB 1.43 ± 0.17, AD 2.05 ± 0.13; DLB vs AD $p < 0.0001$. MIBG delayed H/M ratio: DLB 1.25 ± 0.16, AD 2.05 ± 0.16; DLB vs AD $p < 0.0001$.
Conclusions: The concentrations of CSF-Aβ42 in DLB were significantly lower than that in control, and higher than that in AD. The concentrations of CSF-Ttau and CSF-Ptau did not differ significantly between DLB and Control. Our study showed many overlap in the levels of CSF-Aβ42, CSF-Ttau and CSF-Ptau between DLB and AD. MIBG is a useful tool for discriminating DLB form AD.

P2-143

Development of DNA microarray-based high-throughput gene analysis system and its application to the molecular diagnosis of familial Alzheimer's disease

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Background: A number of genes have been identified for familial Alzheimer's disease (AD) and for familial frontotemporal dementia (FTD), necessitating comprehensive analysis of causative genes. In addition, there is a possibility that the mutations of causative genes can be identified in sporadic patients. In order to fulfill these demands, we have established a high throughput mutational analysis system based on resequencing microarrays.
Materials and methods: The microarrays include the sequences of all the exons and flanking introns of *APP*, *PSEN1*, *PSEN2* and *MAPT*. Genomic DNAs were amplified with specific PCR, and the PCR products were labeled and hybridized to the microarray.
Results: We have identified a heterozygous point mutation of *PSEN1* substituting threonine for isoleucine at codon 143 in a patient with familial AD. The age at onset of the two patients in this family is characterized by very early onset (33 and 41). Neuroimaging examination revealed marked atrophy and hypoperfusion in the bilateral parietal and occipital lobes, which were quite similar among the patients. The mutation was originally described in a Belgian family. The age at onset in the Belgian family is also characterized by very early onset, suggesting a strong genotype-phenotype correlation in patients with the I143T mutation.
Conclusions: The DNA microarray-based high-throughput gene analysis system is capable of conducting comprehensive analysis of causative genes of familial AD, which should be highly useful for elucidation of the genotype-phenotype correlations of familial AD and FTD.

P2-144

A Novel ELISA system for endogenous mouse Amyloid-beta 1–40 in blood

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Introduction: Transgenic mouse models, which carry a transgene coding for the human amyloid precursor protein (APP), are widely used for Alzheimer's disease (AD) research, but substantial effort in colony maintenance as well as complex intellectual property issues limits flexibility with this approach. Alternatively, non-transgenic mice can be considered, but have not yet been widely used in the assessment of Aβ-lowering interventions: a primary reason is the limited sensitivity of mouse Aβ ELISAs. However, the study of Aβ reduction in non-transgenic mice using a sensitive and specific mouse Aβ ELISA provides a valuable tool in the development of therapeutic agents. Previously, we have developed a new mouse monoclonal antibody (MoAb) called 14F1 and new Aβ ELISA detecting mouse endogenous Aβ 1–40 and 1–42 at the sub nM range, but it was not sensitive enough to detect Aβ in blood samples.
Materials and methods: We newly developed a rabbit polyclonal antibody against the N-terminal end of mouse Aβ 1–16 and used it for the establishment of a novel ELISA system in combination with an anti-Aβ 40 specific monoclonal antibody (Clone 1A10).
Results: This ELISA system was very highly sensitive and specific to detect endogenous mouse Aβ 1–40 in blood samples and had a low cross-reactivity against human Aβ 1–40 (less than 1%).
Conclusion: We have developed a novel ELISA system which can measure Aβ 1–40 in blood samples of non-transgenic mouse/rat, and it is considered to be a useful in monitoring of mouse endogenous Aβ40.

P2-145

Stage Estimation of Dementia (SED): A proposal of a practical method for estimation of the stage in the course of dementia for the clinician

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Summary: We produced a useful estimation method which conveniently indicate the stage of the natural course of dementia.

Introduction and method: For us clinicians, what is most essential to diagnose the situation and prognosis of dementia patient is correct estimation of the stage. From this view-point, we tried to make a new SED (Stage Estimation of Dementia) assessment. First we supposed that every types of dementia (Alzheimer type, Mixed type, Vascular type and so on) goes on with almost similar symptoms and signs in each stage. Secondly, we also supposed that every types of dementia has different span of natural course. Based on these two principle hypotheses, eighteen symptoms and signs were weighed with different points–total points 1500. Plotting each dementia patient's point on the scale we could know the stage in the course of this disease simply and conveniently.
Conclusion: We produced SED test. To perform this test, only two minutes were enough asking family or care workers about eighteen symptoms and signs simply if presented or not ever since. How to perform this test and the availability of this test will be discussed.

P2-146

More attention to chemical restraints and abuse with medications

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Background: Chemical restraints are drugs administered for the purposes of discipline or convenience and not required for the treatment of the medical condition. The use of drugs as chemical restraints is documented, but there are few studies about the prevalence and types of this kind of mistreatment.
Aim: The aim is to encourage performance of studies about chemical restraints and abuse with medications by presenting 1.a case study about the concomitant use of psychotropics in long-term wards, and 2. case studies about the concomitant use of psychotropics, anticholinergic drugs, opioids and antiepileptic drugs; and positive effects of withdrawal of the majority of these drugs on cognitive and functional abilities of old patients.
Materials and methods: The first material consisted of patients born in 1939 or earlier in long-term wards in Pori City Hospital in Finland. Data were collected in 2005. The materials for individual case studies were derived from Finnish long term wards

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participating in the development of care between 2005 and 2007.

Results: The cognitive and functional abilities of the aged patients in the long term wards were poor: 95% were not able to walk independently and 82% scored 10 sum points or less in the MMSE. Three or more psychotropics were regularly given to 33%, and regularly or irregularly to 53% of the patients. The effects and side effects of drugs were not documented in medical or nursing records, and psychotropics were used to control the behaviour of the patients. The individual case studies about the effects of withdrawal of concomitant use of several psychotropics or several psychotropics, anticholinergic drugs, opioids and antiepileptic drugs will be presented.

Conclusions: The common concomitant use of psychotropics, the use of psychotropics to control the behaviour of the patients, and the lack of documentation of the effects and side effects of the drugs give rise to suggest that psychotropics were used as chemical restraints in these long-term wards. The individual case studies give evidence about positive effects of withdrawal of psychotropics, anticholinergic drugs and opioids in the aged using concomitantly several kinds of these drugs.

P2-147

Differences in expectations of baby-boomer to concepts of the homes for the elderly in the future, when they are suffering from dementia or not

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The ratio of elderly people at least 65 years old is over 20% in Japan and continually growing. Previously, most of elderly people have wanted to receive care by family at home when they were in need of care. Resent survey shows increasing of people who will choice to admit the homes for the elderly in their old age. Especially assuming that they are suffering from dementia, more people tend to choice the homes for the elderly. The purpose of present study was to clarify the differences in expectations to concepts of the homes for the elderly of baby-boomer in the future, when they are suffering from dementia or not. Subjects were all baby-boom generation born in 1947–1950 who lived in local city in Japan. Questionnaire was mailed to them and 781 were completed. "Scale of Orientation toward Homes for the Elderly" which was developed for the study was used to measure peoples' expectations to concepts of the homes for the elderly. This scale has 15 items and consisted of three domains and four subcategories; "Safety and Comfort (subcategory: amenity, life support)", "Autonomy (subcategory: choice, privacy)", "Function as Community". The type of dwelling in which they want to live in need of care was also asked. Each question ware answered both assuming they were in need of care for low functional capacity and for dementia. As results, assuming they need care for low functional capacity, nearly half people choice the homes for elderly as their dwellings, while assuming with dementia around two-thirds people choice the homes for elderly. Among three domains the score of "Safety and Comfort" is the highest and the second was "Function as Community", "Autonomy" was the lowest. Including subcategory all seven scores were lower assuming with dementia than low functional capacity, and showed significant differences ($p < 0.0001$). In "Autonomy", "Function as Community" and their subcategory, there ware big differences between the score of assuming two conditions, while "Safety and Comfort" and its subcategory showed comparatively small differences. This suggests that people consider that person with dementia needs livelihood support services at homes for the elderly, but the interaction between residents aren't important for their incompetent to take part in the human relationships and respecting their autonomy are not always necessary.

P2-148

Evaluating simple environmental control intervention for a fronto-temporal dementia patient with diurnal rhythm disturbance

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Introduction: Environmental control is recommended for caring Fronto-temporal dementia (FTD) patients. However, objective measurements for movement pattern were not available. The purpose

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of the study was to evaluate the effective interventions for reducing diurnal rhythm disturbances in the FTD patient using the Integrated Circuit (IC) tag monitoring system (Matrix co, Japan).

Methods:

Setting: 60-bed dementia care unit in A hospital, Osaka, Japan.

Participants: a male FTD (Pick type) with diurnal rhythm disturbance, 62 years of age, right-handed, 16 years of education, 8 years of FTD. Procedure: 1st intervention: For two-week period, all the doors to the patients' rooms in the unit were kept open as a part of environmental control, and in the following 2 weeks all the doors were kept closed without being locked. 2nd intervention: in order to increase the patient's activity, the staff tried to walk with the patient during the day for 2 weeks, while all the doors to the patients' rooms were closed. Then, in the following 2 weeks, no intervention except for door closing policy was attempted. The patient's movement patterns were monitored by the monitoring system. This research was approved by the ethics committees from Osaka University and the hospital. The informed consent was obtained from the authorized proxy.

Result: 1st intervention: The percentage of the days with nighttime ambulation (0:00–6:00) was reduced from 42% to 31%. The mean distance walked at night was decreased from 547 ± 780 m to 307 ± 235 m. 2nd intervention: The percentage of the days with nighttime ambulation increased to 92% during the 2nd intervention, and it was reduced to 50% in the non-walking period. The distance walked at night was 480 ± 359 m in the intervention period and was reduced to 328 ± 388 m in the non-walking period.

Discussion: This study demonstrated the effectiveness of environmental control to affect stimulus-bound behavior using the IC tag monitoring system. Active intervention by the staff nurse seems to disturb stereotypy, which may have contributed to diurnal rhythm disturbances. A simple environmental control of door-closing policy was most effective for keeping the FTD patient to enter the other patients' rooms and reducing the nighttime ambulation.

P2-149

Immunohistochemical investigation of Lewy pathology responsible for visual misidentification of patients with dementia with Lewy bodies

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Dementia with Lewy bodies (DLB) patients show visual misidentification symptoms including visual hallucinations. They are associated with hypoperfusion or hypometabolism in the occipital lobe using SPECT or PET study. We examined 20 autopsied cases of DLB using pathological and α-synuclein-immunohistochemical methods, and investigated Lewy pathology including Lewy bodies (LB) and LB-related neurites in the primary visual pathway (lateral geniculate body and Brodmanns area 17), secondary visual pathway (pulvinar, Brodmanns areas 18 and 19, and inferior temporal cortex), amygdala, claustrum, insular, precentral, postcentral, transverse temporal, transentorhinal and cingulate cortices, to clarify the relationship between visual misidentification and Lewy pathology in the visual pathway. The amygdala has reciprocal connections by relay of the inferior temporal cortex with the primary and secondary visual cortices (visuo-amygdaloid pathway) and modulate sensory processing according to cognition and emotion. The claustrum is known to have strong reciprocal connections with the visual areas (visuo-claustral pathway). Consequently, the insular, inferior temporal, transentorhinal, cingulate cortices, BA18, 19, amygdala and claustrum revealed strong Lewy pathology, while BA17, precentral, postcentral and transverse temporal cortices showed weaker Lewy pathology. The secondary visual pathway revealed significantly severer Lewy pathology than the primary visual pathway. When the correlation coefficient of Lewy pathology is compared between the claustrum and the other regions, BA 18, 19 as well as the insular and transentorhinal cortices demonstrated a higher correlation coefficient. These findings suggest that the degeneration of not the primary visual pathway but the secondary visual pathway induces the dysfunction of the visuo-amygdaloid pathway and participates in visual misidentification of DLB patients. In addition, Lewy pathology in the claustrum

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is more closely associated with that in the visual areas than that in the auditory, somatosensory and motor areas, and the insular and transentorhinal cortices may connect visual areas with the limbic areas by relay of the visuo-claustral or visuo-amygdaloid pathway.

P2-150

Language and semantic memory impairment of semantic dementia with motor neuron disease

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We report a case of right-handed 60-year-old Japanese man who showed semantic dementia with motor neuron disease (SD with MND). He noted difficulty in naming people and remembering characters of kanji when he was 58 years old. 6 months later, he was aware of word finding difficulty in common objects, and of muscle weakness of his right hand. Neurological examination revealed muscle atrophy and weakness in his all limbs with fasciculation, especially in his right upper limb. Bulbar signs were not seen. Snout reflex was shown without other pathological reflexes, and deep tendon reflexes were normal. Sensation, coordination, and gait were also normal. On needle electromyography, evidence of denervation was seen in muscles of brainstem, cervical, thoracic, and lumbosacral areas. He was diagnosed as clinically probable-laboratory-supported ALS by El Escorial criteria. On neuropsychological examination, his behavior was normal and his episodic memory was well preserved. Spontaneous speech was fluent, and its quantity was not reduced. He had severe word finding difficulty, and used pronouns excessively. Repetition of 20 syllables was spared. He had disturbance in comprehending some words. When he was asked "Which is your kikite (a Japanese word meaning dominant hand)?" he said "What is kikite?". His syntactic comprehension appeared to be preserved. Semantic paraphasia was sometimes seen, phonological one was not. He had difficulty in writing kanji, showing paragraphia phonologically equivalent but semantically inappropriate. Paragraphia was also seen in writing kana-characters, mistaking for morphologically-resemble ones. Performance of naming and pointing tests for 200 words was severely impaired. A two-way naming deficit was seen in some words, but the words differed from day to day. His anomia was not category-specific, seen even in pointing color words. His language profile was rated as word-meaning-aphasia, and he met the criteria for semantic dementia by Nearly et al. MRI showed atrophy of the bilateral frontal and left anterior temporal regions. SPECT disclosed hypoperfusion in the same regions. He was diagnosed as SD with MND. He had some atypical language features for SD. 1. A two-way naming deficit was seen only in a few words and it was fluctuating. 2. Anomia was seen even in color category. 3. Kana writing was impaired even at an early stage of course. We discuss the association between the specific features of language impairment and SD with MND.

P2-151

Difference in the functions of the right and left frontal lobe: Consideration of a Pick disease case with asymmetries of cortical atrophy and CBF

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Objective: We have treated a female patient of Pick disease (PD) who had a predominant pathology of the frontal lobe. We report the details of this case in order to discuss the difference in the functions of the right and left frontal lobes.

Case report: The patient was 58 years old when she was referred to our hospital (December of X year,) due to a marked loss of drive. She graduated from a university, had worked in an office, married at the age of 24 years and has been a housewife for 34 years. Since Spring of X-1 yr, she gradually became slow with her domestic duties, but took a walk with her dog regularly 2 times in the morning and evening, while she suddenly bought expensive furniture without a definite reason. There were neither difficulties in ADL nor complaints of forgetfulness, moreover no unusual behaviors. In the first medical examination, the score of HDS-R (almost equivalent to MMSE) was 29/30 points. The head MRI revealed a marked frontal lobe atrophy which was a little more intense in the right than in the left. In the 3D-SSP (e-ZIS) imaging from SPECT (99 mTc-ECD), a localized decrease of cerebral blood flow (CBF) was predominantly seen in the right

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prefrontal cortex containing an orbital area and it was distinctly severe compared to the left one. Based on these findings the patient was diagnosed as Pick type of frontotemporal dementia. On April of X + 1 yr, both MRI and SPECT showed more deteriorated findings, with HDS-R score being 16 points. The profile of BADS (Behavioral Assessment of the Dysexecutive Syndrome) was as follows: Total profile points: 5/24 (disabled level), Rule Shift Card Test; 1/4, Action Program Test; 0/4, Key Search Test; 3/4, Temporal Judgement Test; 2/4, Zoo Map Test; −1/4, Modified Six Elements Test; 0/4.As to the clinical frontal symptoms of this case, so far, apathy is the foreground symptom, while disinhibition such as unusual behavior and stereotype symptoms except for walking with her dog has been scarecely observed.

Discussion and conclusion: Summarizing this case, the patient who suffers from a apathetic form of PD has a predominant injury in the right prefrontal cortex containing dorsolateral, medial and orbital areas. There has hardly any discussion so far on the difference in the functions of the right and left frontal lobe. From the findings shown above, it seems that the right frontal lobe could not contribute at least to the production of disinhibition or mostly a stereotype symptom in PD.

P2-152

Signs of ALS in frontotemporal dementia – a retrospective clinical and neuropathological study

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Objective: To investigate clinical and neuropathological signs of motor neuron disease (MND)/amyotrophic lateral sclerosis (ALS) in deceased individuals with a clinical and neuropathological diagnosis of frontotemporal dementia (FTD).
Methods: The clinical records and the neuropathological material of 18 FTD cases, clinically followed at the Dept of Psychogeriatrics and examined postmortem at the Dept of Pathology, Lund University Hospital, between 1995 and 2004, were thoroughly evaluated. Six control cases, three without degenerative brain disease, two with Alzheimer's disease and one with Creutzfeldt-Jakob's disease were selected for comparison of the neuropathological findings. Demographic data, as well as clinical symptoms consistent with motor neuron disease were noted. A directed neuropathological examination/revision, focusing on motor neuron specific hallmarks was carried out. The number of neurons and the grade of degeneration in the anterior horns of the spinal cord, as well as the grade of degeneration of the hypoglossal nuclei, were assessed by two observers.
Results: Clinical symptoms consistent with MND, including swallowing problems, were noted in 16 out of 18 cases, mainly late during disease. One case was clinically diagnosed with FTD-ALS. In 12 out of 18 cases it was possible to assess the spinal cord and in 17 out of 18 cases the hypoglossal nuclei could be assessed. There was a moderate to severe degeneration of the anterior horns in all FTD cases with assessable spinal cord. In the six control cases the anterior horns were normal in all but one case, where it was mildly degenerated. The hypoglossal nuclei showed some degree of degeneration in 10 cases, three of which were severely degenerated. Four cases were tau-positive, 12 cases tau-negative and in two cases no tau-staining had been carried out. Anterior horn and hypoglossal degeneration was seen to a similar extent in the tau-positive as in the tau-negative cases.
Conclusions: These findings suggest that the association and overlap between FTD and ALS might be even more common than previously described. Perhaps, FTD and MND/ALS should be seen as a pathological spectrum rather than two distinct diseases.

P2-153

Insight in FTD and AD: Conceptual analysis and empirical evaluation of the consensus criterion

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Background: Loss of insight is a core criterion of FTD. However, according to clinical experience, FTD patients may be aware of their disease, and insight might be lost in AD.
Objective: To investigate the presence and absence of insight in the diseases, the relation between cognition and insight, and to suggest a new formulation of the diagnostic criterion.

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Methods: Eight FTD and ten AD patients diagnosed by medical and neuropsychological examination, CT and PET participated. Insight was defined as: State awareness: Insight into the own state, e.g. consciousness of the alteration of the condition. In its absence, one is unaware and in a state of denial of alterations and fails to see a problem. Illness awareness: Knowledge that the alterations are symptoms of illness. In its absence, the patient is aware of a problem, but does not interpret it as a sign of illness. Medical awareness: Insight into the fact that the altered condition is an illness caused by given factors. Cognition was assessed by neuropsychological tests and insight by semi-structured, quantified interviews. Data were analysed with non-parametric methods.

Conclusions: Insight were present in three FTD and six AD patients. Two types of insight emerged: emotional insight associated with frontotemporal functions, and cognitive insight, related to posterior cognitive functions. These results suggest that loss of insight should not serve as a core criterion of FTD, but serves well as a supportive criterion of the disease. The results also suggest that insight does not necessarily imply that inappropriate behaviour is controlled.

P2-154

Clinicopathological spectrum of amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) on TDP-43 immunohistochemistry in Japan

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TDP-43-positive inclusions have been identified as hallmark of ALS and FTLD. We reviewed TDP-43 immunohistochemistry in 5 cases of sporadic ALS, 26 ALS with dementia, 3 primary lateral sclerosis (PLS), 5 FTLD and 6 ALS of long survival with respirator assist (massive ALS). TDP-43 was positive in all inclusions including skein-like and hyaline inclusions in lower motor neurons, neuronal cytoplasmic inclusions (NCIs), dystrophic neurites, neuronal intranuclear inclusions (NIIs) in cerebral cortices and basal ganglia, and oligodendroglial inclusions. In ALS-D numerous NCIs were found particularly in superficial layers of limbic system with few neurites and no NNIs. In PLS NCIs and neurites were both in superficial and deeper layers, and basal ganglia. In FTLD numerous dystrophic neurites appeared predominantly in the frontotemporal cortices and striatum. One FTLD case showed mainly NIIs. Many TDP-43 immunoreactive inclusions were found in lower motor neurons of the spinal cord in ALS and ALS-D, and a few in FTLD. We conclude that ALS, ALS-D, PLS, FTLD and massive ALS are the spectrum of TDP-43 proteinopathy and clinical phenotypes were well correlated to the pathological pattern of TDP-43-positive inclusions.

P2-155

FTDP-17 mutation modify the intermediate formation of tau filament

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Background: Tau filament formation is a pathological hallmark of several neurodegenerative disorders, called tauopathy, including Alzheimer's disease (AD). We have identified granular tau oligomer as an intermediate for tau filament.

Objective: To reveal the involvement of the granular tau oligomer to the pathogenesis in familial tauopathy, frontotemporal dementia with Parkinsonism linked to chromosome-17 (FTDP-17), we evaluated the effect of FTDP-17 mutations on granular tau oligomer formation.

Methods: We examined the aggregation property in each recombinant tau construct (Wild type, P301L, V337M, R406W) by ThT assay, atomic force microscopy (AFM) and conformation dependent antibodies.

Result: While ThT assay showed the similar tendency of tau aggregation in mutants and wild type, AFM observation indicated the increase in the number of granular tau oligomer in mutants compare to wild tau. Tau oligomers of V337M and R406W have similar diameter distribution to wild type tau, but oligomers of P301L mutants was smaller diameter than the others. Conformation dependent antibodies commonly recognized those oligomers, suggesting that the mutant tau oligomers have the common structure with granular tau oligomer of wild type tau.

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Discussion: FTDP-17 mutant tau could form granular tau oligomer with the different size but the same structure as wild tau. This may suggest that formation of granular tau oligomer may play a key role of tau-induced neurodegeneration in FTDP 17.

P2-156

Pharmacogenetics of weight gain and obesity following clozapine treatment

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Introduction: Weight gain is a major problem associated with long-term antipsychotic drug treatment. Clozapine is known to induce particularly profound weight gain. Although the mechanism of it is not clearly understood, the 5-HT2C receptor and leptin are implicated in its development. The present study examined the effects of 5-HT2C and leptin gene polymorphisms on weight change and obesity in the patients on Clozapine.

Methods: 107 patients (mean age 39.5 ± 10.1 y.) meeting ICD-10 criteria for schizophrenia or schizoaffective disorder receiving Clozapine took part in this study. The patient assessment included an interview, measures of weight, height, waist-hip ratio, waist circumference, body mass index (BMI, kg/m2); blood samples were taken for random blood glucose and genetic testing for 5-HT2C and leptin gene.

Results: Central obesity was present in 102 (95.3%) defined by increased waist circumference (>8805; 94 cm males; >8805; 80 cm females) and obesity in 67 (62.6%) defined by BMI > 30; 96 (88%) patients were overweight (BMI > 8805; 25 kg/m2). Type II diabetes was present in 8 patients and type I diabetes in one. In 93 patients (62M, 31F) we assessed change in BMI and weight during treatment which was 2.6 ± 4.2 kg/m2 and 7.43 ± 12.35 kg, respectively. There was no association between 759C/T 5-HT2C receptor and -2548A/G leptin gene polymorphisms with BMI or weight. No association between 759C/T 5-HT2C receptor and -2548A/G leptin gene polymorphisms was found with change of BMI or waist circumference.

Conclusion: We found no significant association between 759C/T 5-HT2C receptor and -2548A/G leptin gene polymorphisms and changes in BMI or weight in the patients treated with Clozapine.

P2-157

Intron 7 polymorphism in amyloid precursor protein affects onset of Down syndrome dementia

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A tetranucleotide repeat is present in intron 7 of the amyloid precursor protein (APP). This gene is located on human chromosome 21 which is triplicated in Down syndrome (DS), also known as trisomy 21. Exon 7 of APP is alternatively spliced and different APP isoforms are differentially expressed, with respect to both tissue and dementia status. More specifically, the ratio of ubiquitously to neuronally expressed isoforms has been found to be increased in brain samples from patients with Alzheimer's disease (AD). Exon 7 contains a Kunitz inhibitor domain. People with DS develop Alzheimer's type dementia and pathology with an early age of onset. In a previous study the tetranucleotide repeat, attt5–8, in intron 7 was found to have an association with the age of onset of Alzheimer's type dementia in DS. First, a further 165 adults with DS were genotyped for this repeat, and the results were analysed with respect to the age of onset of dementia. APOE genotyping was also carried out. Second, a small cohort of participants of a clinical trial were genotyped and plasma β amyloid levels were measured. The presence of three copies of the allele which is six repeats-long resulted in an earlier age of onset, than when any other allele combination was present. In the clinical trial the presence of three six-repeat alleles was associated with lower plasma beta-amyloid 1–40 levels. This difference in the age of onset of dementia between the different genotypes may be due to an alteration in the levels of splice variants associated with AD. The polymorphism may also have a detrimental effect upon processing and clearance of beta-amyloid 1–40 in the brain resulting in the

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lower levels found in plasma. Further study will be required to elucidate the mechanism by which this polymorphism takes its effect.

P2-158

Impact of ApoE genotype on brain function as assessed by optical topography

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The APOE gene (19q13.2) encodes the apolipoprotein E that plays a role in lipid homeostasis. APOE has been identified as a major risk factor for dementia. Furthermore, it is involved in neurite outgrowth and differentiation, neural repair, and immunoregulation. This gene has 3 major alleles (e2, e3, and e4) associated with risk (APOE-4 allele) or protection (APOE-2 allele) for Alzheimer's disease and other CNS disorders. Functional genomic studies have revealed the association of APOE-related alleles with the phenotypic expression of biological traits (e.g. brain atrophy, cognitive decline rate, b-amyloid deposition, lipid metabolism dysfunction, immunologic dysregulation or therapeutic outcome). (Cacabelos, R.; Aging Health, 2005, 1(2): 303–348).We have investigated the influence of APOE on brain hemodynamics using Optical Topography (OT), which measures the hemodynamic response following brain activation and offers the spatial and temporal variability in the concentration and oxygenation of hemoglobin on the brain cortex. Brain optical topography patterns have been assessed in response to photic stimulation in 159 patients: 18 APOE 2/3 (11.25%), age: 51.61 ± 20.36 years (range: 18–79 years); 4 APOE 2/4 (2.5%), age: 66 ± 17.81 years (range: 44–83 years); 104 APOE 3/3 (65%), age: 54.95 ± 19.69 years (range: 7–89 years); 25 APOE 3/4 (15.625%), age: 61.35 ± 16.2 years (range: 25–83 years); and 8 APOE 4/4 (5%), age: 63.4 ± 10.39 years (range: 41–74 years).Statistic analysis shows significant differences in brain hemodynamics among different APOE genotypes: BDHb-2/3 vs BDHb-4/4 $p < 0.009$; SDHb-2/3 vs SDHb 4/4 $p < 0.02$; BTHb-2/3 vs BTHb 4/4 $p < 0.03$; STHb-2/3 vs STHb-4/4 $p < 0.03$; BOHb-2/3 vs BOHb-3/3 $p < 0.05$; SOHb-2/3 vs SOHb-4/4 $p < 0.03$; SDHb-3/3 vs SDHb-4/4 $p < 0.03$; BTHb-3/3 vs STHb-3/3 $p < 0.03$; STHb-3/3 vs STHb-4/4 $p < 0.001$; BOHb-3/3 vs SOHb-33 $p < 0.05$; SOHb-3/3 vs SOHb-4/4 $p < 0.007$; BDHb-3/4 vs BDHb-4/4 $p < 0.02$; STHb-3/4 vs STHb-4/4 $p < 0.02$; SOHb-3/4 vs SOHb-4/4 $p < 0.01$. According to our results, the presence of the APOE-4 allele has a deleterious effect on brain hemodynamics altering brain oxygenation which may contribute to poor cerebrovascular perfusion and chronic brain damage.

P2-159

Ace genotype-related changes in brain optical topography

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The ACE gene (17q23) encodes the angiotensin I-converting enzyme, which is a major component of the renin-angiotensin system. This system participates in the control of electrolytic balance and blood pressure and it may be associated with cerebrovascular and neurodegenerative pathologies, and with hypertension and arteriosclerosis, as well. This gene displays a polymorphism I/D expressed by insertion (I) or deletion (D) of Alu sequence of 287 base pairs in intron 16. There are 3 possible genotypes in the general population: D/D, I/D, and I/I. The allele D is associated with risk for heart attack, hypertension, diabetes mellitus, stroke, and cerebrovascular diseases. The ACE-I allele is associated with increased risk of developing late onset Alzheimer's disease, and associations between the ACE I/D and Alzheimer's disease have been reported by different studies in different populations. We have studied the impact of the ACE genotype on brain hemodynamics using a new technique called Optical Topography (Hitachi ETG-4000). This OT system utilizes absorption of near-infrared light by hemoglobin (Hb) to measure variation of blood volume in the vicinity of the cerebral surface. It measures variations in the concentration of oxygenated hemoglobin and deoxygenated hemoglobin in blood within the brain at multiple points simultaneously, and reconstructs an image and cinematically displays distribution of blood volume variation and the state of brain metabolism and cerebrovascular function. We have applied OT to 93 subjects: 41 ACE-D/D; age: 58.31 ± 15.83 years (range:24–84 years); 34 ACE-I/D; age: 60.97 ± 14.56 years (range: 27–86 years); and 18 ACE-I/I; age: 63.72 ± 13.27 years (range: 25–79 years). In the present study we assessed the relative variations in the concentration of Oxy-Hemoglobin, Deoxy-Hemoglobin, and Total-Hemoglobin in the occipital cortex during photic

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stimulation in the three ACE variants. Statistical analysis revealed differences in brain hemodynamics among the three ACE genotypes. ACE-D/D and ACE-I/I showed positive effects to stimulation. The ID carries had a more deficient response with the poorest topographic pattern of brain activation. This evidence suggests that the ACE genotype influences the phenotypic expression of brain oxygenation as well as genetic heterogeneity in brain function.

P2-160

Two cases of spinocerebellar ataxia that follows a psychotic disorder

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Spinocerebellar ataxia(SCA) is a group of progressive brain diseases characterized by in coordination of movement and degeneration of cerebellum or/and brain stem, or genetically by mode of inheritance and genetic abnormalities of each chromosomal loci. Causative genes have been identified in several hereditary SCA. In Japan, approximately 60% of SCA consist of sporadic disorders, and the rest mostly consists of a variety of late-onset autosomal dominant disorders. We have experienced rare two patients with psychotic disorder then followed by SCA, with family history of SCA. One case has been diagnosed as schizophrenia that has delusion and social withdrawal since twenties, another case was bipolar disorder that has several manic episodes such as flight of ideas and distractibility and depressive episodes such as depressed mood and apathy since late-teens. Both cases were diagnosed as SCA in their fifties. These patients met diagnostic criteria of schizophrenia or bipolar disorder from Diagnostic and Statistical Manual of Mental disorders, Fourth Edition (DSM-IV) and matched diagnostic criteria of SCA of Japanese Ministry of Health, Labor and Welfare. Major subtypes of SCA such as Machado-Joseph disease (MJD), SCA6, and dentatorubral-pallidoluysian atrophy(DRPLA) in Japan were excluded in the patient with bipolar disorder, whereas genetic analysis was not applied in the schizophrenic case. As long as we know, SCA that follows a psychotic disorder such as schizophrenia or bipolar disorder has never been reported. SCA patients sometimes show psychiatric symptoms such as depression in SCA2 or dementia in DRPLA after onset of SCA symptoms. One reason why patients with SCA are not diagnosed after they are diagnosed as mental disorder is the symptoms of ataxia might be similar to the side effects of psychotropic drugs such as antipsychotics and mood stabilizer, lithium. If these patients also have family history of psychiatric disorder cosegregated with SCA, it could be a clue to identify a new subtype of SCA and/or a new causative gene.

P2-161

Lithium inhibits βGSK3 transcription: evidences from *in vitro*, *in vivo* and human patient studies

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In patients with Alzheimer's disease (AD), there is evidence of increased systemic expression of active βGSK3, which apparently is associated with biological mechanisms that lead to the formation of senile plaques and neurofibrillary tangles. Due to its central role in the pathogenesis of AD, βGSK3 is currently one of the most promising targets in the development of pharmaceutical compounds. Whilst trials with specific GSK inhibitors in AD are under way, major attention has been focused on the neuroprotective effects of lithium. The direct and indirect inhibitory effects of lithium over GSK3 enzymatic activity have been documented by several groups. However, to the best of our knowledge, the effects of lithium on the mRNA transcription of GSK3 have not yet been addressed. To investigate this we used quantitative PCR to evaluate the transcriptional regulation of αGSK3 and βGSK3 in lithium-treated primary cultures of rat cortical and hippocampal neurons. We found a significant reduction in the expression of βGSK3 in hippocampal cells, which was

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then confirmed in vivo by measuring the regional intracerebral expression of GSK3 in lithium treated adult rats as well as in leukocytes of elderly patients undergoing chronic lithium therapy for bipolar disorder. In conclusion, our studies show that LiCl can modulate βGSK3 transcription *in vitro* and in vivo, in rat and human cells, under distinct therapeutic regimens. These observations offer a new and complementary explanation for the mechanisms of βGSK3 modulation by lithium reinforcing its therapeutic value for inhibiting key pathological pathways in Alzheimer's disease.

P2-162

Gender-related genetic loci associated with late-onset Alzheimer's disease on chromosome 10 q

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Objective: To reveal gender-related loci associated with late-onset Alzheimer's disease (LOAD) on chromosome 10q.

Methods: All subjects used here were collected by the Japanese Genetic Study Consortium for Alzheimer's Disease. We first prepared two sample sets for screening, *Exploratory* and *Validation*, comprising only *APOE-ϵ3*3* subjects. After being stratified by gender, these sets were used for a SNP-based association study. Subsequently, the samples were increased, and a total of 3192 subjects (1526 LOAD patients and 1666 controls) were used for further genetic studies. Logistic regression (LR) and multifactor dimensionality reduction analyses were performed to assess multifactor interaction in LOAD.

Results: We identified three gender-related loci associated with LOAD in an *APOE-ϵ4*-independent manner. As female-related loci, Locus A included in *CTNNA3* and Locus B containing five genes, *ENTPD7*, *COX15*, *CUTC*, *ABCC2* and *DNMBP* were discovered. As a male-related locus, Locus C included in an intergenic region between *LOXL4* and *C10orf33* was found out. LR analysis demonstrated that Loci A and B were directly interacted with female, while the Locus C showed no significant interaction with male.

Discussion: Recent epidemiological studies on AD revealed gender-related differences in its prevalence and incidence. Therefore, it is expected that gender-related genetic risk factors could exist. Our data suggest that these loci may affect LOAD onset through gender-specific mechanisms independent of the *APOE-ϵ4* allele, confirmed as a genetic risk factor beyond ethnicity.

P2-163

Association study of alpha-synuclein gene polymorphism in autopsy-confirmed degenerative dementia

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Introduction: Dementia with Lewy bodies (DLB) is characterized by alpha-synuclein (SNCA) immunoreactive protein deposition in both neurons and glial cells. However, there are no reports regarding the association of SNCA gene polymorphism with DLB and other related dementias.

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Materials and methods: Genomic DNA of the autopsied cases was extracted from dissected brain tissues. A total of 32 patients were diagnosed pathologically with DLB including Parkinson disease (PD). Additionally, 5 cases of limbic neurofibrillary tangle dementia (LNTD) and 4 cases of Pick disease were analyzed. We carried out PCR-RFLP method to genotype a common polymorphism (2-bp (CT) deletion (D) and insertion (I)) in intron 3 of SNCA gene. Moreover, we compared the allele and genotype frequencies among the subtypes of DLB (diffuse, transitional and brain stem type (PD)).
Results: The I allele was found in 56% of the DLB patients. The allele frequency was not different between DLB and control population (I(59%)D(41%)). Similar results were obtained in each subtypes. In LNTD, the allele frequency was similar: I(0.60)D(0.40). However, the prevalence of the II genotype was higher in Pick disease- II (4) ID (0) DD(0)($P = 0.02$ ($P = 0.054$: Yates' correction)).
Conclusions: No association was found between SNCA gene polymorphism and DLB in our preliminary study. However, the frequency was different in Pick disease.

P2-164

Two Japanese CADASIL families exhibiting R75P mutation of Notch3 not involving cysteine residue

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a familial multi-infarct dementia, which is characterised by recurrent ischaemic attacks leading to dementia. Most of the previously reported mutations resulted in an odd number of cysteine residues within the 34 epidermal growth factor-like repeats in the extracellular amino-terminal region of the Notch3 receptor. We report R75P mutation in two Japanese CADASIL families, not directly involving a cysteine residue located within the *Notch3* gene encoding the extracellular domain. Both families showed autosomal dominant inheritance. Probands of both families had repeated episodes of stroke and generalized convulsion. MRIs of these families showed T2 high signal lesions in basal ganglia and periventricular white matter, but less white matter lesions in temporal pole. Exons of the *Notch3* gene were amplified by PCR and subsequently analysed for Denaturing High Performance Liquid Chromatography. After heteroduplex changes were found, amplified DNA was sequenced. The patients in these families carried the missense mutation C to G at nucleotide 302 of the *Notch3* gene, which results in an arginine to proline amino acid change at codon 75. This mutation had not changed the number of cysteine residues, but coding the extracellular amino-terminal region of the Notch3 receptor. These families provide new issues for diagnosis and pathomechanism of CADASIL.

P2-165

Driving problems arising from dementia and various cognitive impairments

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Background: There is an urgent need to develop clinical methods for assessing the driving abilities of elderly people with cognitive decline as studies have suggested that a neuropsychological task and a diagnosis alone are not a robust predictor of driving skills in the elderly.
Objectives: To determine whether the problems that elderly people suffering from dementia have with driving can be attributed to one specific aspect of cognition, such as an aspect of visual attention or executive function.
Design: A case study that examined four cases in which driving cessation was recommended and prior written consent was obtained.
Setting: The cases were followed at the memory clinic of the geriatric outpatient unit, because of cognitive decline.

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Measurements: Medical histories were taken from the patients and their families, and the scores of various neuropsychological tests, brain imaging, and laboratory tests were used. We actively collected episodes concerning problematic driving as told by the patients' families.

Results: The cases showed that obvious driving problems follow various patterns and are caused by different cognitive impairments. A Case 1 (66-year-old man, VD after stroke) "ignores any car or pedestrian on his right side." This was attributed to his right homonymous hemianopia. Case 2 (71-year-old man, mild AD) had difficulty with quick on-the-spot judgments on the road, resulting from a decline in psychomotor- speed. Case 3 (66-year-old man, mild FTD) performed poorly on the Stroop Test and had a score discrepancy on the Digit Span Test, with good performance on the forward trial, but not on the backward trial. These results indicated that he could not carry out concurrent processing. Consequently, it was difficult for him to enter the flow of traffic. Case 4 (71-year-old man, moderate AD) was "He mistakes others" parking spaces for his own. This resulted from his memory impairment. In fact, he could not remember having taken tests 30 minutes earlier. In addition, he also had difficulty reversing his car, which was attributed to impaired visuospatial perception or organization.

Conclusion: These results suggest that driving ability cannot be attributed to a specific aspect of cognition, and that driving behavior can differ between dementia types. Therefore, we should judge the capacity of elderly people to drive in a comprehensive manner, and the nature and level of each cognitive aspect should be considered separately based on the diagnosis.

P2-166

A study of awareness of memory deficits in patients with dementias

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Purpose: In general, patients with dementia are often unaware of their cognitive or functional impairment. We investigated the level and frequency of awareness of memory deficits in 63 patients with Alzheimer's disease (AD), 17 patients with dementia with Lewy bodies (DLB), 14 patients with vascular dementia (VaD), and 56 patients with amnestic mild cognitive impairment (MCI).

Methods: The unawareness of memory impairment was evaluated with a standardized memory questionnaire system based on the Everyday Memory Checklist (EMC). The EMC scores for the patient's own rating, the caregivers' rating and the unawareness score, defined as the discrepancy between these (caregiver rating – patient rating), were analyzed.

Results: Although the EMC self-rating scores were comparable among the four groups, the EMC scores in caregivers were significantly higher in the AD group than in the DLB, VaD, and MCI groups. Therefore, the unawareness scores were significantly higher in the AD groups than in other groups. When an unawareness score of 9 or more was defined as significant, impaired awareness was found in 41 (65%) patients with AD, 1 (6%) patient with DLB, 5 (36%) patients with VaD, and in 19 (34%) patients with MCI.

Conclusions: We found that impaired awareness was found in two-thirds of patients with mild AD and even in one-third of patients with MCI. However, other dementias, in particular DLB, had less severe and less frequent unawareness of memory deficits than AD, suggesting the difference in the pathophysiology between them.

P2-167

Does fluoxetine have any effect on the cognition of patients with mild cognitive impairment A double blind, placebo control, clinical trial

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Mild cognitive impairment (MCI) may be a prodromal state for Alzheimer's disease. Recent researches suggest a role for other neuronal systems like monoaminergic hypofunction beside cholinergic dysfunction in age related cognitive decline. In several studies selective serotonin reuptake inhibitors demonstrated promotion in neurogenesis in the hippocampus. In this study, the effects of fluoxetine, a selective serotonin reuptake inhibitor, on memory and cognition of patients with mild cognitive impairment has been studied.

58 non-depressed patients with MCI were randomly assigned to take fluoxetine or placebo. The patients were administered the Structured

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Clinical Interview for DSM-IV (Diagnosis and Statistical Manual for Mental Disorders-fourth edition)Disorders, the Mini-Mental Status Examination (MMSE),, subtests from Persian standardized Wechsler Memory Scale (WMS) pre intervention. 44 patients completed the 8 weeks trial. Treatment response was defined as improvement in the scores of MMSE, subtests of WMS-III and Clinical Global Impression.

The patients in the fluoxetine group showed improvement in MMSE and immediate and delayed logical memory scores of WMS-III. The placebo group had not significant changes in the cognitive measurements.

Fluoxetine enhanced memory and cognition in the patients. This was consistent with pervious studies that emphasized the role of fluoxetine in improving memory and promoting neurogenrsis in the hippocampus. However; this is a preliminary study with small sample size and larger double blind placebo control studies are needed to confirm these findings.

P2-168

Conversion to dementia in mild cognitive impairment is associated with decline of N-acetyl aspartate and creatine as revealed by MR-spectroscopy

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Purpose of the present study was to longitudinally track changes of N-acetyl aspartate (NAA) and other relevant cerebral metabolites detectable by magnetic resonance spectroscopy (MRS) in subjects with mild cognitive impairment (MCI) and to analyse these changes with respect to the rate of cognitive decline and clinical disease progression. Fifteen subjects with MCI and 12 healthy elderly controls were investigated longitudinally (average follow-up period: 3.4 years) using absolute quantification of metabolites within the mid-parietal grey matter and the parietal white matter (NAA, myo-inositol, choline, creatine, glutamine). Our main findings include that a longitudinal decline in cognitive function (particularly in memory function) within the MCI group was predicted by a decline in absolute concentrations of the metabolic markers NAA and creatine. This effect was mainly explained by a significant decrease of NAA and creatine in those MCI subjects who converted to Alzheimer's dementia (AD) during the follow up period. Our findings support the use of MRS as a tool for objectively monitoring disease progression even during the earliest stages of AD.

P2-169

Prevalence and clinical correlates of Parkinsonian signs in community-dwelling Chinese older persons

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Mild parkinsonian signs (MPS) have been found to associate with cognitive decline, dementia and death in non-demented elderly. Although these signs are mild, they are not prognostically benign. This study reported the prevalence of MPS and examined the clinical correlates of parkinsonian signs including neuropsychiatric symptoms, cognitive impairment, functional impairment and medical illness burden in the community-dwelling non-demented Chinese older persons.

A random sample of 759 Chinese older persons from a thematic household survey was recruited. There were 389 normal elderly controls (Clinical Dementia Rating [CDR] 0) and 376 subjects with questionable dementia (CDR 0.5). The subjects with questionable dementia (CDR 0.5) were categorized into two groups: a MCI group (n = 291) and a very mild dementia (VMD) group (n = 85). The clinical correlates were investigated in each group.

MPS was defined as a score of two or more in the Unified Parkinson Disease Rating Scale (UPDRS) – motor scale. The prevalence of MPS was 16.5%, 33.0% and 49.4% in the normal control (NC), MCI and VMD groups respectively. Subjects with MPS had significantly lower functional scores than those without MPS after adjusting for the effect of age, sex and education in each diagnostic group. Abnormality in axial function, bradykinesia and rigidity were associated with lower scores in instrumental activities of daily living, and rigidity was associated with lower scores in basic activities of daily living in the whole sample after adjusting

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Table 1: Kruskal-Wallis test shows the comparisons of ADAS-cog scores between normal and MCI subjects

ADAS-cog	Normal (N=30) Mean±SD (median)	MCI (N=77) Mean±SD (median)	P value
Word recall	3.38±1.09 (3.5)	3.93±1.22 (4.0)	0.046
Word list recognition	1.41±1.17 (1.3)	1.83±1.57 (1.7)	0.304
Object/ finger naming	0 (0)	0 (0)	1.000
Verbal commands	0.2±0.48 (0)	0.51±0.75 (0)	0.035
Constructional praxis	0.60±0.50 (1.0)	0.78±0.53 (1)	0.127
Ideational praxis	0.10±0.31 (0)	0.55±1.12 (0)	0.049
Orientation	0.07±0.25 (0)	0.17±0.41 (0)	0.217
Remembering test instructions	0.57±0.50 (1.0)	1.00±0.81 (1.0)	0.010
Spoken language ability	0.07±0.25 (0)	0.21±0.59 (0)	0.323
Comprehension	0.23±0.50 (0)	0.73±0.79 (1.0)	0.001
Word finding difficulty	0.03±0.18 (0)	0.09±0.37 (0)	0.514
Total error scores	6.65±2.77 (5.8)	9.78±3.99 (9.3)	<0.0001
Delayed recall	3.17±2.04 (3.0)	4.29±2.20 (4.0)	0.015

P2-170

for age and education. UPDRS score was associated with age, medical illness burden and cerebrovascular accidents in the normal control and MCI groups. It was associated with cognitive impairment in the normal control group and neuropsychiatic symptom particularly apathy in the VMD group.

Parkinsonism features were common in the non-demented Chinese older persons. The prevalence of MPS increased with age and the severity of cognitive impairment. MPS were associated with functional impairment in the non-demented older persons. Different parkinsonian signs had different effects on basic and instrumental ADL. Neuropsychiatric symptoms, cognitive impairment and vascular risk factors had different patterns of associations with parkinsonism features in the older persons with different degree of cognitive impairment. The early identification of the high-risk groups for early intervention may help to reduce disability or delay the progression to dementia.

P2-170

The Alzheimer's disease assessment scale-cognitive subscale in community-based patients with mild cognitive impairment

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Background: The Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) is widely used to assess cognitive function of patients with Alzheimer's disease (AD). However, the data of the test in patients with mild cognitive impairment (MCI) is still limited and there is only few studies comparing ADAS-cog score between normal subjects and MCI patients. The data in Asian population is still in need.

Methods: There were 107 participants aged 50 and over diagnosed with MCI (n = 77) or normal (n = 30) recruited from a community-based setting in Bangkok. MCI was diagnosed according to Petersen's criteria. The neuropsychological battery including the ADAS-cog was used to assess the subjects' cognitive function.

Results: There was no difference in mean age of normal and MCI subjects 63.8 (7.3) vs. 66.3 (7.9) years, education 6.7 (3.2) vs. 6.1 (3.3) years, and male: female ratio 30% vs. 42%. The mean Thai mental state examination (TMSE) score in MCI patients was lower than normal subjects (26.5 ± 1.6 vs. 28.1 ± 1.8, $p < 0.0005$). Comparisons of ADAS-cog scores between normal and MCI subjects were tabulated in table 1. Correlation analysis showed statistical significance in inverse correlation between ADAS-cog scores and educational level ($r = -0.442$; $p = 0.015$ and $r = -0.303$; $p = 0.007$ in normal and MCI groups, respectively) and between ADAS-cog and TMSE ($r = -0.287$; $p = 0.125$ and $r = -0.382$; $p = 0.001$ in normal and MCI groups, respectively). There was no relationship between ADAS-cog scores and age and ADAS-cog scores and gender. The logistic regression analysis showed that the total error score of the ADAS-cog can predict the likelihood in predicting the MCI

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diagnosis with the odds ratio of 1.31 and 95% confident interval of 1.07–1.60 ($p < 0.008$) independent of educational level and TMSE score.

Conclusion: The ADAS-cog test is a useful tool in differentiating MCI from normal individuals. The total error scores is the most powerful variable in detecting patients with MCI among the ADAS-cog scores. Educational level may affect the ADAS-cog performance.

P2-171

Naturalistic experiment on relation between prospective memory and output monitoring in elderly adults

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Introduction: Daily life usually must accommodate various schedules involving, for example, work, house keeping, and commitments with friends and family, and people fulfill schedules at set times or in predetermined sequences. Keeping to schedules requires the use of prospective memory, that is, the ability to remember to do things at the right time. Additionally, to fulfill the schedule adequately without forgetting or repeating each plan, people must have the ability of output monitoring, which is the recognition that a plan was accomplished. The purpose of this study is to examine the influence of aging on prospective memory requiring output monitoring, and to examine the influences of retrospective memory (tested via the AVLT), external memory aids, and internal memory strategy on prospective memory performance.

Methods: Eighty-six healthy elderly adults (44 women and 42 men; mean age 68.56 years) were enrolled. We asked participants to use a cellular phone to call a number 21 times over a 1-week period under one of the following four conditions; time-based (TB), event-based (EB), day-based with output monitoring (DO), and week-based with output monitoring (WO). Under the TB, EB and DO conditions, participants were asked to call 3 times a day for 1 week: TB participants were to call at 8:00, 13:00, and 18:00; EB participants were to call after every meal (breakfast, lunch, and dinner); and DO participants were to call three times a day at any time but to leave an interval of 4 hours after the last call. WO participants were asked to call 21 times over the week at any time but to leave an interval of 4 hours after the last call.

Results and discussion: A 2 (age group; 60 s vs. 70 s) × 4 (condition) ANOVA for prospective memory performance did not yield any main effect or interaction, indicating that there were no differences in prospective memory performance among the conditions irrespective of age. For external memory aids and internal memory strategy, only external memory aids influenced prospective memory performance. Meanwhile for total recall and delay-recall on the AVLT, the main effect of age was significant, indicating a decline in retrospective memory performance among subjects in their 70 s compared to those in their 60 s. These results suggest that elderly adults can fulfill their schedule adequately by using the external memory aids that compensate for age-related retrospective memory decline.

P2-172

Restriction in complex activities of daily living in mild cognitive impairment

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The purpose of the present study was to examine whether patients with mild cognitive impairment (MCI) have impaired complex activities of daily living (ADL) as compared to cognitively normal controls, which areas of instrumental ADL are particularly involved. Sixty-seven patients with MCI (amnestic MCI = 49, nonamnestic MCI = 18) diagnosed according to research criteria and 34 cognitively normal controls were included. The Korean version-Mini Mental State Examination (K-MMSE), Seoul-Instrumental Activities of Daily Living (S-IADL), and Clinical Dementia Rating (CDR) were administered. The overall score on the S-IADL was significantly lower in the MCI group ($p = 0.000$). The patients with MCI were particularly impaired on the activities involving memory (e.g. taking medications, managing belongings, keeping appointment, and talking recent events) and executive or frontal related functions (e.g. using the telephone and preparing food/cooking). The S-IADL discriminated well between the patients with MCI and normal controls. The diagnostic accuracy of the S-IADL was high (AUC = 90.3%) in the

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differentiation of two groups. The sensitivity and specificity of the S-IADL were 82% and 88%, respectively, when the cut-off score was 2.5. The current findings suggest that impairment of complex ADL may be already present in MCI patients and the magnitude of these restrictions are greatest for those functional abilities that rely heavily on memory and frontal related function. Therefore the diagnosis of MCI should include rather than exclude observed or experienced minimal changes in complex everyday life activities.

P2-173

Brain functional asymmetry and memory in aged people

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Normal aging is characterized by the gradual decrease of the right-hemispheric ability to grasp at once numerous interrelations between objects and events and build a holistic polysemantic context based on multiple neuronal networks. It is a background of the episodic memory. The aged-determined deficiency of the episodic memory depends on the initial level of right-hemispheric skills. Due to multiple neuronal networks these skills are less sensitive to vascular brain disorders, and less dependent on the activation of the cortex from the brain-stem reticular formation, in comparison to the left-hemispheric skills responsible for the organization of the restricted monosemantic context as a basis of the logic semantic memory. Even when the incorporation of the new information in the net of episodic memory is partly loosened and less efficient due to the aging process, the access to the already created constructions of episodic memory are often available and in the absence of the competition with the new information the episodes from the past may became extremely vivid. In any case, at least the partial preservation of the right hemispheric skills is very helpful for the memory maintenance. However, if right hemispheric skills were initially poor developed and low and subject mostly relied on his left hemispheric skills and logic memory, based on few neuronal interlinks even a normal aging process related to the moderate brain vascular deficiency is usually accompanied by the prominent loss of memory. Clinical observations of aged people with different style of thinking in one family confirm our suggestion. Some recent data show that this mechanism may participate also in the development of Alzheimer's disease. In patients with the genetic predisposition towards this disease memory tasks cause more strong functional electrophysiological activation of the left hemispheric structures in comparison to the control age-matched group, and this activation correlated with the further negative dynamic of memory function (Bookheimer et al., 2000). We suggest that the control age-matched group not predisposed to Alzheimer's disease is characterized by the more strong right-hemispheric skills and has not to rely totally on the left hemispheric skills. Probably in order to prevent normal and pathological memory disturbance in aged people it is necessary to start training of the right hemispheric skills in early life periods.

P2-174

The quality analysis in attention tasks for mild cognitive impairment and health elderly – one year follow-up study

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Background: Mild cognitive impairment (MCI) is an operational definition for a cognitive decline in individuals that have a greater risk of developing dementia. There are few studies about the MCI patients with attention deficit.

Objective and hypotheses: We aim to investigate the difference of sensitivity and discrimination in the sustained and selected attention tasks between patients with mild cognitive impairment (MCI) and the normal controls over one year. The study was based on two hypotheses: (1) the sensitivity of MCI subjects was not well than control; (2) liberal trend would be applied in each task in MCI patients.

Methods: The patients with MCI (N = 6) and the normal controls (N = 6) were both examined at baseline and one year follow-up, respectively. Three tasks of a computerized battery for attentional performance were used, including the simple reaction time (SRT) task, the choice reaction time (CRT) task without warning signal, and the cued choice reaction time (CCRT) task.

Results: Using signal detection theory, compared baseline and follow-up on each task. Either at

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baseline or during follow-up (baseline phase: $F = 1.28$, $p = .009$; follow-up: $F = .282$, $p = .024$), the MCI group markedly decreased the sensitivity compared with the control group. At baseline of SRT task, MCI and control groups were not reached significant ($F = 2.622$, $p = .258$) on the sensitivity. Moreover, in follow-up phase, the sensitivity was significantly worse in MCI patients ($p = .040$). On the other hand, control subjects were higher sensitivity on CCRT task than MCI subjects ($p = .018$) at the beginning of study. However, one year later, the significant difference was not observed. For the aspect of discrimination, both groups did not statistically difference in each comparison within this year. However, in our finding showed that there is a conservatively tendency to apply SRT task in MCI subjects, comparing with the control subjects. Contrary to CRT task, the performance of MCI group is more liberal. However, in CCRT task, the conduction of the MCI patients revealed that more conservative at baseline and more liberal during follow-up.

Conclusions: As our result, MCI patients did have difference judgement standard on attention tasks. These difference could be another cure to differ MCI and normal.

P2-175

Combined brief neuropsychological tests of memory, orientation, and executive function can screen MCI subjects in a community: the Osaki-Tajiri Project (1)

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Background and purpose: Mild cognitive impairment (MCI) is a prodromal stage of dementia, and progress to dementia at a rate of 10% to 15% per year. One of the common clinical rating scales for the severity of dementia is the Clinical Dementia Rating (CDR). The CDR needs to obtain information from the collateral sources, therefore it is difficult to assess elderly people living alone. The purpose of this study is to develop a brief, sensitive and specific screening test for early detection of MCI and dementia.

Methods: As part of the Osaki-Tajiri Project 1), this study targeted 625 elderly subjects who were randomly selected from the community; 412 healthy subjects (CDR 0), 168 subjects with MCI (CDR 0.5) and 45 patients with dementia (CDR 1+). The concept of MCI herein approximates to that of CDR 0.5. Neuropsychological tests were administered to all subjects to assess memory, orientation, attention and executive function. We analyzed each of the neuropsychological tests retrospectively by receiver operating characteristic (ROC) curve and area under the curve (AUC).

Results: We found two sets of high AUC scores. The items of the first set (set-1) were orientation (time), memory (three words delayed recall and five objects recall) and executive function (word fluency, Trail-Making Test B, abstraction and judgment). The AUC was 0.819. The items of the second set (set-2) were orientation (time), memory (three words delayed recall and five objects recall), attention (digits backward and serial 3s subtraction) and executive function (word fluency, abstraction and judgment), and the AUC was 0.828. The set-2 was easier to be performed than the set-1. In contrast, the AUC of Mini-Mental State Examination test (MMSE) was 0.765. The set-1 and set-2 were more sensitive than MMSE in discriminating the subjects with MCI and dementia from healthy subjects.

Conclusions: We found that our two sets of orientation, memory and executive function could sensitively detect the subjects with MCI and dementia in a community than the MMSE. 1)Meguro K, et al. Arch Neurol 59: 1109–1114, 2002.

P2-176

Cognitive predictors for conversion to clinical dementia in Chinese older persons over a 20 month period

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Background: The significance of Mild Cognitive Impairment (MCI) as an at-risk state for progression of dementia has been well studied in the Caucasian populations. Due to diversities in cultural background, harmonization of cognitive test batteries for MCI have been limited in different

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communities. We reported the results of a recent prospective study of Chinese elders with MCI and very mild dementia(VMD). The aims of the study were 1) to evaluate if Clinical Dementia Rating (CDR) was useful in identifying at-risk subjects for further cognitive decline; 2) to determine if specific cognitive markers are useful in predicting short term decline.

Methods: Chinese volunteers (Aged ≥60 years) were follow up for 20 months. Subjects were categorized: Cognitively intact (NC) were subjects with CDR 0; MCI subjects were subjects with memory domain of 0.5 and/or no more than 2 non-memory domains rated as 0.5; VMD subjects were subjects with a global CDR of 0.5, having memory domains rated as 0.5 and 3 or more other non-memory CDR domains rated as 0.5 or 1. Cognitive assessments included the Chinese version of ADAS-Cog, 10-minute delayed recall, category verbal fluency test (CVFT).

Results: 243 subjects (80.31(8.01) years old) were followed for 20.4(4.24) months. 88 subjects were NC, 91 were MCI and 64 were VMD. At follow-up, 3(3.4%) of the NC group deteriorated to mild dementia (CDR 1); 16(17.6%) of the MCI group progressed to clinical dementia (CDR ≥ 1); 22(34.3%) of the VMD group satisfied clinical criteria for dementia (CDR ≥ 1)(Chi square = 25.38, $p < 0.001$). Logistic regression analysis was carried out to examine the baseline cognitive predictors for progression to clinical dementia in the MCI and VMD groups, significant predictors included a higher ADAS-Cog total score (indicating lower cognitive function) ($p = 0.028$, CI 1.01–1.21) and a lower CVFT ($p = 0.006$, CI 0.32–0.97). Delayed recall test score in the MCI and VMD groups was not a significant predictor for conversion to clinical dementia.

Conclusions: The results indicated that CDR can be used as a screening tool for detecting at risk group for cognitive deterioration. A concomitant poor CVFT will be predictive of cognitive decline. The findings offered information about testing characteristics for at-risk population in the Chinese older community.

P2-177

Early symptoms and signs of cognitive deficits might not always be detectable in persons who develop Alzheimer's disease

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Clinical syndromes such as Mild Cognitive Impairment are highly predictive of future development of Alzheimer's disease (AD), but how many of all individuals that will develop AD show detectable symptoms or clinical signs of dementia years before diagnosis? 152 incident AD cases were identified in a dementia-free cohort of 1417 persons aged 75–95, after three-year follow-up from a prospective population-based study, the Kungsholmen Project. Subjective memory complaints and objectively measured cognitive impairment were examined three years before AD diagnosis. The results showed that only half of future AD cases reported subjective memory problems three years before diagnosis. More than one third of incident AD cases did not exhibit detectable deficits in any of the investigated specific cognitive domains. Only 38.3% had both subjective complaints and domain-specific cognitive deficits. In conclusion, increasing the number of potentially identifiable and treatable preclinical AD cases is unfeasible unless more sensitive subjective and objective markers are identified.

P2-178

Dietary intakes of old age hostel residents with mild cognitive impairment

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Diets low in saturated fat but high in polyunsaturated fat from oily fish, high in antioxidants from fruit and vegetables, and low in sodium intake have been associated with reduced risk of dementia in older people. The potential association between dietary intakes and mild cognitive impairment (MCI) has not been adequately studied. The aim of this study is to examine the relationship between dietary intake and cognitive impairment in the elderly. Four hundred and thirty-five participants aged 75 years or over without dementia in 14 old age hostels were recruited. Cognitive function was assessed by the Clinical Dementia Rating (CDR). Participants with a CDR of 0 were classified as no dementia, and with a CDR of 0.5 were classified to have MCI. Dietary intakes of fruit, vegetable, fish and water over two days were recorded. For those who were cognitively normal, 24-hours dietary recall via face to face interview was used. For those who had MCI, their food intakes during the

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three main meals were recorded by direct observation. T-test was used to compare the dietary intakes of normal and MCI elders. Data of demographics, medical history, smoking, and SF-36 scores were also collected. There were 245 participants (222 female) with MCI group, and 190 participants (145 female) in normal group. The mean age of MCI group was significantly older than that of the normal group (84.3 ± SD 5.25 versus 82.1 ± SD 5.72, $p < 0.001$, student t-test). When compared with normal elders, the MCI participants also had lower educational level and were more likely to be current smokers ($P < 0.05$, < 0.001 respectively, Chi-square test). They had lower scores of physical functioning, vitality and mental health of SF-36 ($p < 0.05$, student t-tests). The comparison of dietary intakes between two groups showed that the MCI subjects had significantly lower daily intakes of vegetable (181.3 ± SD 83.8 versus 217.7 ± SD 97.5, g/day, $p < 0.001$, student t-test). This difference remained significant after adjustment for age. MCI subjects had lower intake of vegetables than cognitive normal older people. Dietetic interventions to promote healthy diets in this at risk group may reduce the risk of dementia.

P2-179

Do CSF biomarkers total Tau, Phospho-Tau and β-amyloid 42 help to predict progression of mild cognitive impairment to Alzheimer's disease: A systematic review of the literature and meta-analysis of the literature

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Background: The search for biomarkers as a diagnostic aid to the identification of patients in pre-dementia stages is a fast growing research area. In view of the low specificity attained with the clinically-based diagnostic criteria, including those for mild cognitive impairment (MCI), biomarker information will add precision to the diagnostic workout of incipient dementia, particularly Alzheimer's disease. The aim of this study is to systematically review and to meta-analyse relevant studies of the usefulness of CSF biomarkers, namely β-amyloid42 (Aβ42), Total Tau (T-Tau) and Phosphorilated Tau (P-Tau), in the prediction of conversion to Alzheimer's disease (AD).

Methods: Systematic review of the literature and meta-analysis.

Results: In accordance with most individual studies, the cumulative data support the notion that low CSF Aβ42 levels ($p < .001$), along with high T-Tau ($p < .001$) and high P-Tau ($p < .001$) levels help to predict conversion to AD given the diagnosis of MCI at baseline assessments.

Discussion: The results of this systematic review and meta-analysis of the literature support the idea that CSF Aβ42, T-Tau and P-Tau may be an important additional tool in the diagnosis and identification of MCI patients which have higher risk of progressing to AD. We further discuss some methodological issues that still need to be overcome to grant the determination of these CSF biomarkers with a wider applicability in clinical settings.

P2-180

Stability of mild cognitive impairment diagnosis in a clinical sample

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Background: The stability of a clinical diagnosis is an important step in the characterization of clinical syndromes. This study aims to assess the 1-year stability of the MCI diagnosis in a clinical sample.

Methods: Prospective study of a cohort of 54 older adults assessed at a university-based memory clinic in Sao Paulo, Brazil. Diagnoses of MCI and its subtypes were established according to Petersen criteria, according to clinical and neuropsychological data analyzed in multidisciplinary consensus meetings. Subjects were evaluated at baseline and reassessed after 12 months.

Results: Considering the whole group, 24% of the MCI subjects resumed normal cognitive function, and 4% converted to Alzheimer's disease (MCI-AD) on follow-up. MCI patients who resumed normal cognitive function were younger ($p = .007$) and had a better global cognitive performance according to the CAMCOG test ($p < .001$), as compared to patients who remained stable. Other clinical and demographic variables, including education level, were not different between these two outcome groups. Sixteen patients had pure amnestic MCI

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(aMCI), 6 of which (37.5%) resumed normal cognitive function after 12 months. Thirty-one patients had multiple domain MCI (mdMCI) and 7 had non-amnestic MCI (naMCI); only 4 (13%) and 1 (14%) of these patients (respectively) resumed normal cognitive function. All MCI-AD patients had a baseline diagnose of mdMCI.

Discussion: The single, cross-sectional diagnosis of MCI may have a limited prognostic relevance, in view of the lower 12-month conversion rate to AD as compared to the higher rates of recovery. The proportion of patients who resume normal cognitive functioning given the diagnosis of MCI in this study was similar than previously reported by Lowenstein et al. (2007).

P2-181

Lower fruits, vegetables and fluids intake are associated with very mild dementia (VMD) in Hong Kong Chinese: A cross-sectional study

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Nutrition plays a role in the ageing process of the brain. A healthy diet high in fruits and vegetables and low in fats have been recommended for brain health, while little has been said about the influence of fluid intake in cognitive function. We examine the association between dietary habits and the prevalence of VMD among a representative sample of community-dwelling older Chinese in Hong Kong. Cross-sectional survey. Community-living elderly men and women age 60 or over were interviewed as part of a large prevalence study of cognitive impairment in Hong Kong. Their dietary habits were recorded using the Mini-Nutritional Assessment (Chinese version) (MNA). VMD was diagnosed clinically by trained psychiatrists using the Clinical Dementia Rating scale (CDR) and defined as subjects with scores of 0.5 in memory plus 1 or more non memory domains rated as 0.5 or above, with global CDR being 0.5. Possible associated factors were examined using univariate then multivariate analyses. Among the 317 persons interviewed, 146 were diagnosed clinically to have MCI while 139 were normal. The mean age of these 285 elderly individuals was 70.6 $\pm$ 6.7 years, their mean body mass index was 23.2 $\pm$ 3.2, mean Mini-Mental State Examination score was 25.8 $\pm$ 2.8 and mean ADAS-cog score 12.0 $\pm$ 6.1, with 52% being women. The mean MNA scores of the VMD and normal subjects were significantly different (26.1 $\pm$ 1.9 versus 26.8 $\pm$ 1.7 respectively, $p = 0.002$). On univariate analysis of diet related items of the MNA, reduced intake and appetite, eating less vegetables and fruits, drinking less fluid, and feeling less healthy than others of the same age were associated with VMD (Table 1). After multivariate analyses using logistic regression and age and education as covariates, eating only 1–2 servings of vegetables and fruits per day (OR 3.831, $p = 0.039$) and taking $<$ or $= 5$ cups of fluids per day (OR 2.110, $p = 0.027$) remained significantly associated with VMD (Table 2). Older people with VMD have lower than normal intakes of vegetables, fruits and fluid, which may pose additional health risks, and increase their chance of progressing into dementia.

P2-182

High rate of conversion to Alzheimer's disease in a cohort of amnestic MCI patients

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A large proportion of patients with amnestic mild cognitive impairment (MCI) progress to Alzheimer's disease (AD). The rate of conversion is highly variable, depending on selection and inclusion criteria. Appropriate case selection criteria are paramount for drug trials aimed at slowing the course of MCI. In the present prospective study, a set of amnestic MCI criteria was applied that aimed to enrich the study population with prodromal AD patients. To assess memory, a composite z-score of three CERAD word list learning subscores was calculated (free recall, delayed recall, recognition). A mean score of minus 1 was applied as a cut-off criterion for inclusion into the study. Competing causes of memory impairment other than prodromal AD were actively excluded. A cohort of 88 amnestic MCI patients was included. 75 were available for follow-up. After a mean delay of 19 months, 44 percent were found to have converted to AD, corresponding to an annualised conversion rate of 28 percent. The rate of new diagnoses other than dementia or stable MCI was 6 percent. Statistical

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Table 1. Demographics and univariate analyses of dietary habits of VMD and normal older people

Factor	VMD (n=146)	Normal (n=139)	p value*
Age	72.4 (6.7)	68.6 (6.1)	0.000*
Female	81 (55.5)	68 (48.9)	0.268
Year of education	3.7(3.8)	7.0 (4.8)	0.000*
BMI (kg/m)	23.4 (3.3)	23.1 (3.1)	0.331
ADASCOG	15.5 (5.7)	8.3 (4.0)	0.000*
MMSE	24.4 (2.8)	27.2 (2.0)	0.000*
Decline in food intake and appetite			0.045
severe loss	3 (2.1)	1 (0.7)	
moderate loss	9 (6.2)	3 (2.2)	
no loss	133 (91.7)	135 (97.1)	
Weight loss in past 6 months			0.323
>3 kg	3 (2.1)	4 (2.9)	
1-3 kg	16 (11.0)	17 (12.2)	
none	105 (72.4)	107 (77.0)	
not certain	21 (14.5)	11 (7.9)	
Amount of rice, noodles, congee per day			0.642
< 1.5 bowls	6 (4.1)	1 (0.7)	
1.5 to 2.5 bowls	63 (43.2)	63 (45.3)	
2.5 or more bowls	77 (52.7)	75 (54.0)	
Servings of vegetables / fruits per day			0.001
< 1	13 (8.9)	4 (2.9)	
1 to 2	58 (39.7)	39 (28.1)	
2 or more	75 (51.4)	96 (69.1)	
Amount of fish, meat, chicken, egg or tofu per day			0.444
< 2 taels	6 (4.1)	3 (2.1)	
2 to 4 taels	57 (39.0)	48 (34.5)	
4 or more taels	83 (56.8)	88 (63.3)	
Amount of milk or milk supplement per day			0.444
< 1/2 cup	105 (71.9)	95 (68.3)	
1/2 to 3/4 cup	16 (11.0)	14 (10.1)	
3/4 cup or more	25 (17.1)	30 (21.6)	
Fluids consumed per day			0.000*
<3 cups	5 (3.4)	0 (0.0)	
3-5 cups	44 (30.1)	21 (15.1)	
>5 cups	97 (66.4)	118 (84.9)	
Is your intake adequate?			0.286
No	3 (2.1)	6 (4.3)	
Yes	142 (97.3)	133 (95.7)	
Uncertain	1 (0.7)	0 (0.0)	

*p<0.05

Student t test and Chi-square test for continuous and categorical data respectively, Mann-Witney U test for graded variables.

Table 2. Multivariate analyses of dietary factors associated with VMD *

Factor	N (%)	OR	95% confidence interval	p value
Servings of vegetables / fruits per day				
>2	169 (60.2)			
1 to 2	94 (33.9)	3.831	1.071, 13.704	0.039*
<1	17 (5.9)	1.347	0.748, 2.425	0.321
Fluids per day				
> 5 cups	213 (76.1)			
? 5 cups	67 (23.9)	2.110	1.090, 4.087	0.027*

* age, sex and education were significant covariates.

P2-181

analyses showed that neuropsychological test results at baseline were not instrumental to predict progression. This study has four main findings: a high annual rate of conversion from amnestic MCI to dementia of 30 percent, a diagnosis of AD in all but two patients who converted to dementia, a low rate of new diagnoses other than dementia at follow-up, and lack of predictive power of the neuropsychological tests that were performed at baseline. The high rate of conversion is likely to be explained by application of a composite and standardised measure of memory, by case selection from memory clinic patients and by active exclusion of competing causes of memory impairment. In summary, amnestic MCI patients as identified by the present set of criteria carry a high risk of median-term progression to AD.

P2-183

Cognitive functions of alcoholic patients in their forties

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Cognitive impairment is common to alcoholism. This report focused on investigating the relationship between alcoholism and cognitive functions in relatively young people through case-control study. We examined cognitive functions of patients with alcoholism compared to normal controls by means of MMSE (Mini-Mental State Examination), CDR(Clinical Dementia Rating), and GDS(Global Deterioration Scale). It was hypothesized that alcoholic patients would show greater cognitive impairment than normal controls. In the present study, cognitive functioning was examined after a minimum of 7days of abstinence in alcoholic patients aged between 40–49 years without comorbid psychiatric, neurologic, or systemic medical illness. The normal controls were selected from our healthy hospital staffs in their forties who were willing to participate in the study. The study is now in progress. So we don't have the test results yet. This research aimed at identifying cognitive impairment of alcoholic patients in their relatively young ages. Although instruments used in this study are the most widely used measures of cognitive impairment, they were designed as tools for global impairment and not specially adapted for use for alcoholic patients. This may be a limitation of the study.

P2-184

Combining cognitive tests in the screening for mild cognitive impairment

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Background: The identification of patients with Mild Cognitive Impairment at primary care settings is of great importance in the psychogeriatric practice. Because most brief cognitive tests, such as the Mini-Mental State Examination (MMSE), have been developed for the diagnostic screening of dementia, they are prone to false negative results due to ceiling effects when administered to patients with MCI. We hypothesize that this limitation may be in part overcome by combining different cognitive screening test.
Objective: To assess whether the combination of three commonly used cognitive tests, namely the Mini-Mental State Examination (MMSE), the Clock Drawing Test (CDT) and Verbal Fluency semantic category (VF) has a better sensitivity, specificity and accuracy profile as compared to either test alone.
Methods: One hundred and eighteen elderly subjects were consecutively assessed at an outpatient, university-based, psychogeriatric clinic. After comprehensive clinical and neuropsychological evaluation, 64 subjects were regarded as controls and 54 subjects were diagnosed as MCI. They were additionally tested with the Mini Mental State Examination (MMSE), the Verbal Fluency Test (VF) and the Clock Drawing Test (CDT). ROC analyses were performed to assess the sensitivity, specificity and the accuracy of each test and of the weighted sum of the three tests to discriminate MCI vs. controls.
Results: The outputs of the three tests, when considered separately, had a low accuracy to differentiate the MCI patients from controls (MMSE, AUC 0.702 ± 0.45 [0.607–0796], $p < .001$; VF, AUC 0.718 ± 0.47 [0.626–0.810], $p < .001$; CDT, AUC 0.677 ± 0.50 [0.579–0.776], $p = .001$). However, the association of the three tests yielded a considerably better accuracy (AUC 0.774 ± 0.45 [0.686–0.861], $p < .001$).
Conclusions: The association of brief cognitive instruments in routine evaluation of patients with cognitive complain is time-effective and adds accuracy to the identification of patients with MCI.

P2-185

Cognitive profiles, hormonal replacement therapy and related factors in Thai menopausal women

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Objective: The purposes of this descriptive study was to examine the characteristics of cognitions and related factors among menopausal women at menopausal clinic at king Chulalongkorn memorial hospital.
Methods: 210 subjects were systematically randomized. The instruments composed of self-reported questionnaires assessment for demographic data and related factors, CES-D, Thai-mini-mental state examination (TMSE) and neuropsychological battery in thai version including digit span (DS) test and visual memory span (VMS) test, verbal paired association I (VPA) test, and similarities (S) test, were used to evaluate for attention and concentration, verbal memory and learning and concept formation respectively. The data were statistically analyzed by using SPSS for windows version 11.5 for percentage, mean, standard deviation, Chi-square test, t-test, ANOVA, correlation, multivariate analysis.
Results: The results revealed that 99% of subjects had normal condition of TMSE score at least 24; with mean of 28.54 points. 96.2% of subjects had TMSE score more than 25 for possible cognitive impairment according to Petersen criteria. Others cognitive test scores were found to have normal distribution; DS (Mean = 14.47, S.D. = 2.81), VMS (Mean = 13.31, S.D. = 2.85), VPA (Mean = 4.58, S.D. = 1.27), and S (Mean = 14.59, S.D. = 4.36). Univariate analyses were performed and shown that subjects with TMSE score more than 26 were related with history of aerobic exercise. Subjects with TMSE score of possible cognitive impairment had lower S scores. Supplementary food using and HRT were not related with impairment of cognitive functions. Other factors including age, educational level, monthly income, and occupation were related with most cognitive score. Multivariate analyses revealed that low Educational level can predict low TMSE score. Low educational level and monthly income could predict low DS score. Low monthly income, older age and low educational level could predict low VMS score. Low VPA score could be predicted by low monthly income. And low S score could be predicted by educational level below diploma degree.

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Conclusion: The cognitive functions of most studied subjects were normal. Factors that could predict the cognitive function score were age and educational level. Subjects that had no aerobic exercise and low Concept formation score were related with low TMSE score. HRT was not significantly related with cognitive deficits in this study.

P2-186

Positive effect on emotional implicit memory in younger and older adults

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Background: Older adults tend to recall positive events over negative events (Mather and Knight, 2005). However, it is not clear whether this age-related positive effect occurs through intentional motivation for emotional memory or the implicit retrieval process for emotional memory. This study examined this positive effect on implicit memory using the word-stem completion task. If such an effect occurs without awareness, the performance of positive implicit memory would be higher than that of negative implicit memory.

Methods: Participants were young adults in their 20s (N = 24), and older adults in their 60s (N = 24) and 70s (N = 24). The stimuli were 90 non-emotional words, each with emotional picture associate. The pictures were selected from the International Affective Picture System (IAPS; Lang, Bradley, and Cuthbert, 1995). All stimuli were divided by the emotional valence of pictures into 30 positive, 30 negative, and 30 neutral conditions. The participants were presented 45 paired stimuli (15 positive, 15 negative, 15 neutral) as a learning task. After the learning task, subjects completed the free-recall task and word-stem completion task.

Results: A Condition (3; positive, neutral, and negative) × Age (3) ANOVA was conducted on implicit memory and explicit memory performance, respectively. *Implicit memory*. A significant main effect was found for Condition. In all age groups performance in the positive condition (M = 2.82) was higher than that in the negative condition (M = 2.15). *Explicit memory*. A significant main effect was found for Age and for interaction. Post hoc analysis revealed that the performance of young adults (M = 6.72) was significantly higher than that of older adults in their 60s (M = 3.60) and 70s (M = 3.63), and performance in the positive and negative conditions was higher than in the neutral condition in both older adult groups. However, in young adults, performance was significantly high in the order of negative (M = 8.33), positive (M = 6.88), and neutral (M = 4.96) conditions.

Conclusions: Implicit memory revealed that all age groups attended to positive material rather than negative material in the implicit retrieval process. Interestingly, explicit memory results in the young adults suggested that they attended to negative rather than positive material in the explicit retrieval process. Although neither older adult group showed an age-related positive effect on memory, they tended to recall positive material more than the young adults.

P2-187

Instrumental activities of daily living in mild cognitive impairment

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Background: Mild cognitive impairment (MCI) is separated from mild dementia by an absence of global intellectual deterioration and the preservation of activities of daily living (ADL). But, recent study report some MCI patients have impaired instrumental activities of daily living (IADL).

Objectives: To examine whether patients with amnestic and non-amnestic MCI (aMCI and naMCI) have impaired IADL as compared to healthy controls, and which items of IADL are particularly involved.

Methods: The sample consisted of 53 community-dwelling older adults in a welfare center of the aged, which was divided into three diagnostic categories: cognitively normal (N = 31), aMCI (N = 15, memory domains below −1.5 SD) and naMCI (N = 15, other cognitive domains below −1.5 SD, except memory domains). The 3 groups were compared on IADL and measures of cognitive function including Seoul Verbal Learning test (SVLT), Rey Complex Figure Test (RCFT), Korean-Boston Naming Test (K-BNT), Stroop test, and Korean-Mini Mental Status Examination (K-MMSE).

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Results: There were significant differences in four items of 15 areas on IADL and IADL total score between aMCI and cognitively normal, but not naMCI. Items of shopping [$F(2,50) = 4.20$, $p = 0.020$], transportation [$F(2,50) = 4.481$, $p = 0.016$], medicine [$F(2,50) = 3.99$, $p = 0.025$], keeping track of current events [$F(2,50) = 4.96$, $p = 0.011$] and IADL total score [$F(2,50) = 4.251$, $p = 0.020$] in aMCI were higher than cognitively normal.
Conclusion: aMCI may be restricted on IADL compared to healthy control group. Complex of ADL of naMCI was not significantly differed from aMCI and cognitively normal. It was suggested that naMCI would be distinguished from aMCI in characteristics and prognosis.

P2-188

The correlation between cognitive domains and instrumental activities of daily living items in mild cognitive impairment

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Background: IADL is used to quantitatively evaluate decline of social-occupational function of suspected dementia patients and has relation to cognitive functional change of dementia patients.
Objective: To estimate the effect of cognitive function on instrumental activities of daily living (IADL) items in mild cognitive impairment (MCI), compared with normal aged.
Methods: The sample consisted of 69 community-dwelling older adults in a welfare center of the aged, which was divided into three diagnostic categories: cognitively normal ($N = 31$), aMCI ($N = 19$, memory domains below -1.5 SD) and naMCI ($N = 19$, other cognitive domains below -1.5 SD, except memory domains). The 3 groups were compared on IADL, Geriatric Depression Scale, and measures of cognitive function including Seoul Verbal Learning test, Rey Complex Figure Test, Korean-Boston Naming Test, Stroop test and Korean-Mini Mental Status Examination.
Results: In aMCI, IADL items were significantly affected by each cognitive function: shopping (language: $\beta = -.66$, $p = .002$; executive function: $\beta = -.60$, $p = .004$), meal-preparation (executive function: $\beta = -.65$, $p = .017$), housework (executive function: $\beta = -.53$, $p = .029$; visuospatial: $\beta = -.45$, $p = .046$), transportation (verbal memory: $\beta = -.53$, $p = .035$; non-verbal memory: $\beta = -.43$, $p = .047$), transports (verbal memory: $\beta = -.56$, $p = .025$; non-verbal memory: $\beta = -.45$, $p = .032$), medication (executive function:$\beta = -.64$, $p = .016$), finances (executive function: $\beta = -.82$, $p < .001$; language: $\beta = -.47$, $p = .006$), dressing (non-verbal memory: $\beta = -.51$, $p = .032$), home appliances (verbal memory:$\beta = -.56$, $p = .025$; non-verbal memory: $\beta = -.45$, $p = .032$), locking doors (non-verbal memory: $\beta = -.64$, $p = .010$) and total score of IADL (executive function: $\beta = -.60$ $p < .010$; language: $\beta = -.46$, $p = .038$). 2 items of IADL were significantly affected by cognitive functions in naMCI: Keeping promises (visuospatial:$\beta = -.54$, $p = .044$) and hobbies (executive function: $\beta = -.56$, $p = .044$). In normal aged group, keeping promises was significantly affected by verbal memory ($\beta = -.44$, $p = .038$).
Conclusion: A number of IADL items were affected by cognitive functions in aMCI, particularly executive function. In a case of decline of social-occupational function of MCI patients, executive function would be focused.

P2-189

Mild cognitive disorder and depression: Treatment with association between galantamine and venlafaxine XR

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Objective: To evaluate the therapeutic response in patients with comorbility between Mild Cognitive Disorder and Depression in treatment with Galantamine, Venlafaxine XR and The two drugs associated.
Method: A group of 180 patients with symptoms of Mild Cognitive Disorder and Depression (DSM IV-R criteria) were separated in 3 groups of 60. Each group received different treatment in a 8 months period: Group 1: Galantamine 16 mg/day. Group 2: Venlafaxine XR 75 mg/day. Group 3: both drugs, same dose.
Results: The therapeutic response evaluated in Hamilton Scale for Depression(HAM-D), Montgomery and Asberg Depression Rating Scale

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(M.A.D.R.S.), Mini Mental State Examination (M.M.S.E.) and Global Clinical Impression (G.C.I.) scores during 8 months in the third group who received the two drugs associated, had much better response than the others.

Conclusion: The group who received the association of the nootropic agent Galantamine with antidepressant Venlafaxine XR had a relevant satisfactory therapeutic response (the best result), so there is a possible relation between the deficit in colinergic systems and depression. Could be cerebral colinergic systems deficit a generator of Depressive Disorder?

P2-190

Neural correlates of encoding and recognition in patients with mild cognitive impairment

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Although patients with Mild Cognitive Impairment (MCI) have significant memory impairment, their activities of daily living are not disturbed particularly. It is assumed that they compensate by using some strategies other than memory function, such as effort. At the neural level, this compensation might be associated with recruiting additional brain areas or increasing activation in the hippocampus and related structures within the medial temporal lobe. In this study, we investigated the neural correlates of compensation for memory impairment in patients with MCI using functional magnetic resonance imaging. Ten patients with MCI, aged between 64 and 78, participated this study. All patients have no clinical history of neurological diseases and their chief complaints were amnesia. They underwent neuropsychological assessment and were all diagnosed as MCI according to the criteria of Petersen. The mean (SD) scores of the Mini-mental State Examination and the Alzheimer's Disease Assessment Scale-Cognitive were 26.4 (3.0) and 8.4 (4.4), respectively. Their scores of the Clinical Dementia Rating were all 0.5. We conducted an activation study using functional magnetic resonance imaging and two memory tasks, that is *Encoding* and *Recognition* task. As materials to memorize, emotionally neutral photographs in International affective picture system were used. In *Encoding* task, they were required to look at the photographs presented sequentially and to memorize them. In control task for *Encoding*, meaningless pictures were presented but subjects needed not memorize them. In *Recognition* task, the photographs used in *Encoding* task intermingle with novel ones were presented and they were asked to distinct weather each presented picture was novel or recognizable. In control task for *Recognition*, they were required to reply weather they felt the presented meaningless pictures bright or dark. They responded to press a button. As a result, activations in the dorsolateral frontal cortex, medial frontal cortex and the cuneus as well as in the parahippocampal gyrus were revealed in *Encoding* task compared with the control task. In *Recognition* task an activation in the fusiform gyrus was shown. These activations might be involved in compensation for memory impairment in patients with MCI.

P2-191

Neuropsychological evaluation of amnestic mild cognitive impairment: Comparison of no cognitive impairment and early Alzheimer's disease

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Mild cognitive impairment (MCI) is a concept to fill the gap between cognitive changes associated with normal aging and those associated with dementia. MCI represents a high-risk stage for the development of AD, its heterogeneity requires subclassifications. Amnestic MCI (aMCI) has high likelihood of progression to AD at a rate of 10–15% per year. This study aims to determine whether the profile and severity of impairment in aMCI is intermediate between that seen in no cognitive impairment and AD and thus to identify neuropsychological prognostic markers able to predict evolution towards AD. We recruited 139 subjects between the age of 55 and 80-year-old people. 25 were cognitively intact, 21 were classified as having aMCI, 93 were classified as having early AD. Comparisons between individual groups were made using independent

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t-test, the Mann-Whitney U test. The mean age of the 139 subjects was 70.86 years, and mean years of educational level was 10.32. While naming functioning and complex figure copy deficits as well as memory impairments occur early in cognitive decline. And other areas of cognition measures including place orientation, concentration, calculation, verbal fluency deficits were not significantly impaired in aMCI than NCI. However, these were significantly impaired in AD than MCI. The current study provides a helpful clarification, suggesting that deficits were seen in patients with aMCI and worsen in mild AD. The early detection of subjects with MCI who are at high-risk of developing AD would help to optimize the potential benefits of intervention. And we believe that our results corroborate the predictive utility of neuropsychology, which is able to detect deficits before the clinical AD emerge and clinical course of patients diagnosed as having aMCI.

P2-192

A population-based investigation of neuropsychiatric symptoms in normal aging and mild cognitive impairment

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The population-based prevalence of neuropsychiatric symptoms in MCI was recently reported by Lyketsos and colleagues. These findings need to be replicated by a study of similar design that also utilized similar criteria to measure neuropsychiatric symptoms and MCI. To estimate the prevalence of neuropsychiatric symptoms in normal aging and MCI in a defined population. We also quantified the odds of having MCI given the presence or absence of a neuropsychiatric symptom. The Mayo Clinic Study of Aging is a population-based study designed to estimate the prevalence and incidence of MCI. A stratified random sample of elderly individuals of age 70 to 89 is being recruited from the target population of Olmsted County, Minnesota. All participants undergo neurological, neuropsychiatric, and psychometric evaluations. An expert consensus panel of physicians, psychologists and nurses determined the classification of normal cognitive aging, MCI, or dementia based on published criteria. The Neuropsychiatric Inventory Questionnaire (NPIQ) was administered to all study participants. The prevalence of neuropsychiatric symptoms were compared between each MCI case that was individually matched by age and sex with three cognitively normal controls. Consistent with the matched design, conditional logistic regression analysis was conducted by controlling for education. Odds ratio and 95% confidence interval were computed for each neuropsychiatric domain. Neuropsychiatric data were available on 314 participants with MCI and 941 cognitively normal individuals. There was a significant difference between MCI and cognitively normal individuals in the domains of apathy, depression, irritability, anxiety, agitation, appetite, delusions and disinhibitions. The prevalence of apathy was 18.5% in MCI ($n = 58/314$) vs 5.0% (47/941) in cognitively normal individuals, the OR and 95% CI were 4.30 (2.81, 6.57; $p < 0.0001$). Similarly, there were significant differences between the two groups in the domains of depression [OR (95% CI) = 2.70 (1.96, 3.71), $p < 0.0001$] and irritability [OR (95% CI) = 3.25 (2.20, 4.79), $p < 0.0001$]. The prevalence of neuropsychiatric symptoms in our study is comparable to the published report that used a similar design (population-based) and measurement instrument (NPI); however, we report a higher frequency of apathy and depression. Apathy may be the most distinguishing neuropsychiatric feature between MCI and normal cognitive aging.

P2-193

Social factors and psychiatric morbidity in elderly patients attending geriatric clinic

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Stressful life events and strains are usiqutous in nature and have been found to be associated with

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poor mental health and adversely affecting the psychological will being among the elderly.

Objectives: To study the social factor influencing on psychiatric morbidities in elderly patients.

Materials and methods: Patient aged > 60 yrs and attending in geriatric OPD were selected randomly. They were evaluated using specially designed proforma to find out social factors anxiety rating scale and Yesevage's geriatric depression scale were used to asses severity and anxiety and depression; presumptive stressful life events scale (PSLE) used to study the significance of recent life events in association with psychiatric morbidities.

Results: The sample size 400 patients aged > 60 yrs was included. There were 84% of male and 16% of female. Depression (30.7%), generalized anxiety disorder and recurrent depression (15.3% each) were major diagnosis given.

Depression patients were < 70 yrs (75%), male (75%), married (87%), belonged to joint families (62.5%) and small family size, had education upto graduation and income from 5000 to 15000. The majoring of patient had negative family, past psychiatric illness and substances abuse and positive cardiovascular system involvement (62.5%). On the other hand, anxiety patients were above 70 yrs, male and married and 50% involvement of cardiovascular system.

Recurrent depression was common in nuclear family (75%) with large family size (75%) and in patient with past history of psychiatric illness. Dysthymia disorder was seen in males (66.66%), married (83.33%), joint family with large family size and in patients with post history of psychiatric illness.

Stressful life events were common in psychiatric diagnosed patients.

Conclusion: Psychiatric morbidities are associated with physical illness (86%), cardiovascular disease in general and informed by social factor like education, family size and type, income, stressful life events.

P2-194

The impact of everyday life measures in MCI and AD

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Background: current MCI criteria rely mostly on cognitive measures; the extent to which ADL impairment should be accepted in MCI is not clear.

Objectives: To investigate the degree of functional impairment in MCI and AD and the relationship between ADLs and cognitive measures in both groups.

Methods: In this cross-sectional study, spouses/family members were interviewed with the Disability Assessment for Dementia (DAD) to assess patients performance in everyday activities. The DAD comprises basic activities of daily living (BADLs) and instrumental activities of daily living (IADLs). Patients were tested on cognitive measures (Addenbrookes Cognitive Examination) and the Clinical Dementia Rating Scale. Data were analysed using non-parametric tests, given their skewed distribution.

Results: 50 patients and respective spouses/family members participated, 25 MCI and 25 AD. Groups were well matched for age (MCI = 71.1, AD = 67.8) and education. The MCI group scored significantly better than the AD group on the ACE-R, DAD and CDR. As expected the AD group was significantly impaired on ADLs as judged by the DAD (100% patients presented with impairment, 50% marginal to mild, 50% moderate to severe). However, about 70% of MCI patients also showed deficits in ADLs, especially IADLs. In an attempt to explain this heterogeneity, we explored the relationship between ADLs and cognitive performance across the MCI-AD spectrum and found significant correlations between the ACE-R and DAD scores.

Conclusions: the prominent use of cognitive measures for the diagnosis of MCI might underestimate the degree of functional impairment a patient presents with. A better equilibrium between cognitive and ADL measures should be pursued in both clinical and research settings to produce more accurate diagnosis.

P2-195

Dementia and disabilities in Thai elderly project: Relationship among cognitive status, function, neuropsychiatric problems, income, and co-morbid diseases

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Objectives: We surveyed the elderly living in the catchment areas of Siriraj Hospital primary care unit in Bangkok during the year 2004. We determined the frequencies of mild cognitive impairment (MCI), dementia, activities of daily living (ADL) function, and neuropsychiatric (NP) problems in these elderly. We looked into the relationship among cognitive status, function, NP problems, levels of income, and co-morbid diseases.
Subjects and methods: We screened Thai elders age 60 and above in 2004 with a comprehensive geriatric assessment to determine possible disabilities, Thai Mental State Examination (TMSE), Thai ADL, Neuropsychiatric Inventory (NPI), and standard neuropsychological tests with cultural adjusted norms. History on co-morbid medical problems and levels of income were inquired. We diagnosed dementia by DSM IV criteria and MCI by modified Petersen criteria.
Results: 1998 community dwelling Thai elders were assessed. Only data from 1973 elders were analyzable. The prevalence of MCI was 21.54% and that of dementia was 4.15%. Mean numbers of NP symptoms in cognitively intact subjects, MCI, and dementia were 1.13(SD = 2.64), 1.70(2.10), and 2.62(2.44) respectively. Only 53.3%, 39.5%, and 15.2% of those with cognitive intact, MCI and dementia did not have NP symptoms. Mean Thai ADL scores were 0.38(1.22), 1.13(2.52), and 7.11(5.42) in normal subjects, MCI, and dementia accordingly. 55.8%, 48%, and 30.5% of Thai elders with cognitively intact, MCI, and dementia were currently working and earned some income. 53.5%, 42.5%, and 46.1% of elders with cognitive intact, MCI, and dementia had sufficient or good income with or without some savings. There were significant relationship between Thai ADL scores and levels of income ($r = -0.157$), numbers of co-morbid medical problems ($r = 0.179$), TMSE ($r = -0.334$), mean numbers of NP symptoms ($r = 0.248$), and age ($r = 0.280$). Significant relationship between numbers of NP symptoms and levels of income ($r = -0.300$) were found.
Conclusions: Our findings revealed that functional limitation in Thai elderly cohort is related to cognitive status, levels of income, NP problems, and increasing age. Majority of Thai elders were still working and actively earned some income. Majority Thai elders with MCI and dementia did not feel that they had sufficient returns.

P2-196

The new ecological assessment of visuospatial functions in patients with MCI using virtual radial arm maze

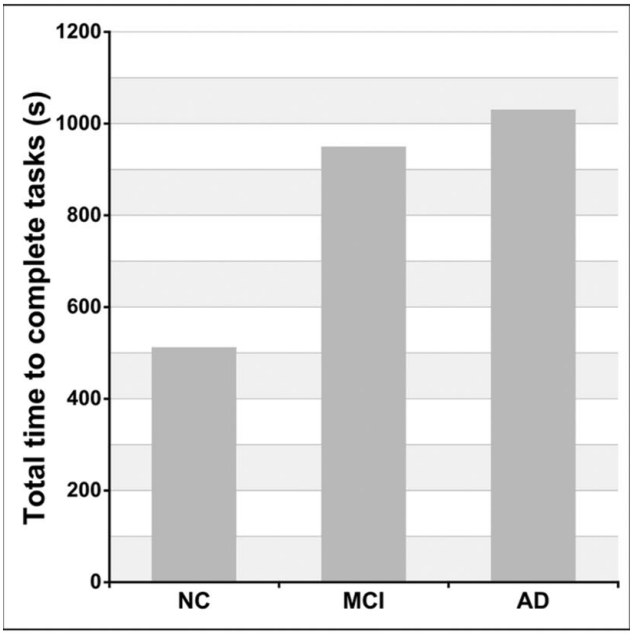
Kyung Ryeol Cha[1]; Jun-Young Lee[2]; Hee-Yeon Jung[2]; Chan-Hyung Kim[1]; Hong Shick Lee[1]; Byoung Hoon Oh[1]

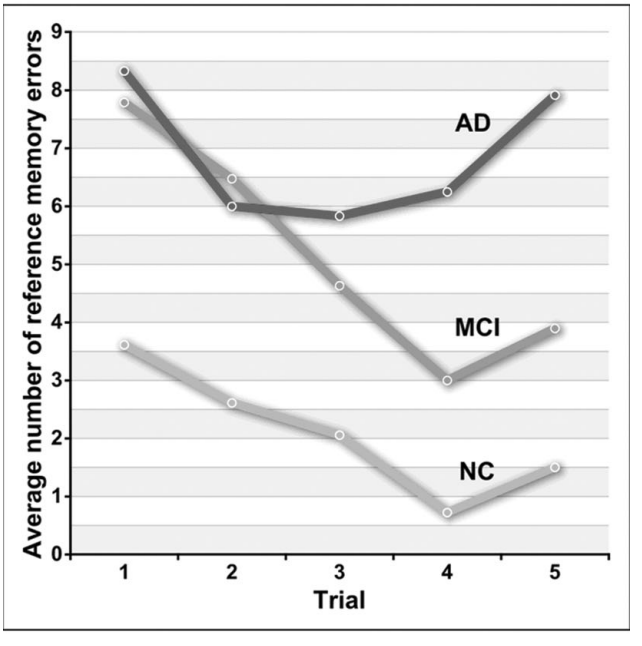
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Objective: Radial arm maze tasks are often used to assess spatial memory in nonhumans. Spatial memory has been known to be critically related to hippocampal size, but is difficult to test in humans in ecological environment. Through virtual radial arm maze (VRAM) test, we assessed the spatial memory in Normal control (NC), Mild Cognitive Impairment (MCI), and mild Alzheimer's disease (AD).
Methods: VRAM were administered to 18 NC, 19 MCI, 12 mild AD in an elderly outpatient clinic with A Korean version of the Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) scale, and Consortium to Establish A Registry for Alzheimer's disease (CERAD). And VRAM are administered to subjects five times. Mean scores of VRAM time (VT), working memory errors (VW), referential memory errors (VM) are compared between 3 groups using ANOVA. Correlations with visuospatial ability and verbal learning test in CERAD were evaluated using Spearman correlations.
Results: VT, VW, and VM were not correlated with visuospatial ability in CERAD (VM: $r = 0.19$, $p = 0.17$), but with verbal learning test (VM: $r = 0.63$, $p = 0.00$). VT, VW, and VM are significantly different between NC and MCI ($p = 0.02$), but not in MCI and AD (VM: $p = 0.25$). Learning effects of trials are not shown in only AD.
Conclusions: The results showed the spatial ability in humans using virtual reality. Spatial memory in MCI is impaired as AD, and spatial memory learning is not obtained in AD.
Keywords: VRAM; mild cognitive impairment; Alzheimer's disease; spatial memory.

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Results of virtual radial arm maze test





NC : Normal Control
MCI : Mild Cognitive Impairment
AD : Alzheimer's Disease

P2-196

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P2-197

Annual rate and predictions of conversion to dementia in subjects with mild cognitive or behavioral impairment. Predictors and rate of conversion

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Objectives: To investigate the population at risk for degenerative dementia and to determinate the predictors of conversion.
Methods: a cohort of 301 subjects (age: 72.2 + 8.1 years, 58% women, education: 12 years), who began with cognitive or behavioral impairment with no significant daily functional disability, was assessed and followed for five years (2000 to 2006). The risk of dementia was calculated with Kaplan-Meier statistics. Analyses were conducted in the entire sample and in subgroups of subjects (Mild Cognitive Impairment (MCI) (n = 239), Mild behavioral Impairment (MBI) (n = 45), and Late Onset Psychosis (N = 17).
Results: MCI had co-morbidities such as hypertension and dislipemia. In the neuropsychological performance memory impairments prevailed, and in the neuropsychiatry assessment behavioral symptoms were found. In the first year 13% converted towards dementia and 40% within three years (the majority transformed towards Alzheimer's dementia). Risk factors of the ones who transformed towards Alzheimer's dementia were education less than 12 years, MMSE less than 27, Boston naming test less than 51, IQ (Intelligence Quotient) less than 111, age more than 75 years, without labor activity at the present time, and presence of intrusions in memory recall (explain 69.2% of the variability of conversion). MBI had co-morbidities such as hypertension and familial history. In the neurological exam archaic and frontal reflex, neuropsychological performance executive dysfunctions prevailed, and in the neuropsychiatric assessment behavioral symptoms (disinhibition, apathy, and depression) were found. In the first year 8% converted towards dementia and 60% within three years (the majority transformed towards frontotemporal dementia). The risk factors of the ones who transformed towards frontotemporal dementia were education less than 12 years, presence of archaic reflex, TSH, previous delusions; depression and disinhibition explain 71% of the variability of conversion.
Conclusions: MCI and MBI are population in risk for degenerative dementia. MCI often represents the predementia stage of an Alzheimer's dementia and MBI of Frontotemporal dementia. The study of the risk factors can contribute an important evidence for the clinical activity and the decision making process of Public Health.

P2-198

Long-term efficacy and safety of galantamine in outpatients with mild cognitive disorder

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Objective: galantamine is a reversible, competitive cholinesterasa inhibitor that also allosterically modulates nicotine acetylcoline receptors. Inhibition of acetylcholinesterase, the enzyme responsible for hydrolisis of acetylcoline at the cholinergic cognitive impairment. To evaluate the efficacy, safety and tolerability of galantamine in long-term in Mild Cognitive Disorder.
Methods: a multicenter, open label, prospective, observational study enrolled 800 patients, more 50 years old with Mild Neurocognitive Disorder (DSM IV criteria), during 24 months of treatment with galantamine 16 mg./day. Assessments included the Mini Mental State Examination (MMSE), Clinical Dementia Rating (CDR), Alzheimer's Disease Assessment Scale (ADAS-GOG), Seven minutes test, Wiscosin card sorting test, Boston naming test, Token test, Raven Test, Brow-Peterson test. Trail making test, Functional Activities Questionnaire (FAQ), GO-NO-GO test, Global Deterioration Scale, Global Clinical Impression (GCI) and UKU scale of Adverse Effects.
Results: a total 800 outpatients were treated with 16 mg./day galantamine during 24 months, the therapeutic response evaluated with CDR, MMSE and the tests and scales of function cognitive measuring, GCI and UKU scale of adverse effects, comparing the baseline to final scores.
Conclusion: Mild Cognitive Disorder is being examined, so there are not enough treatment for this. A long-term treatment (24 months) galantamine improves cognition and global function, behavioral symptoms and the general state well being of patients with Mild cognitive Disorder. With incidence of adverse effects not significant and a very good profile of safety, the final results of the study suggest

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that galantamine may be particularly appropriate in the Mild Cognitive Disorder.

P2-199

Neuropsychological characteristics of individuals with mild cognitive impairment

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Objective: To determine the characteristics of cognitive function changes in mild cognitive impairment (MCI) by comparing the performance of neuropsychological tests between individuals with MCI and normal control.

Methods: Thirty-seven individuals with MCI and 40 healthy elderly controls were recruited in the study. The cognitive function was evaluated with a neuropsychological battery tests involved learning, memory, working memory, attention/concentration, processing speed, and executive function.

Results: Individuals with MCI performed poorer than normal control on most neuropsychological tests, such as all task of HVLT-R, delay racall and recognition of BVMT-R, WMS-R Logical Memory, Category Fluency and Word Fluency, WMS-III, Spatial Span, PASAT, time of Trail Making Test Part A and Color Trails Test, and WAIS-III, Digit Symbol. The difference between two groups is statistically significant ($p < 0.05$).

Conclusions: Memory impairment is the primary characteristics in individuals with MCI, which involves all kinds of processes in many types of memory. Verbal memory impairment is the most serious of all. Delay recall task is much worse in individuals with MCI than that in normal control. Moreover, individuals with MCI have some differences with healthy controls in executive function, attention/concentration and psychomotor speed.

P2-200

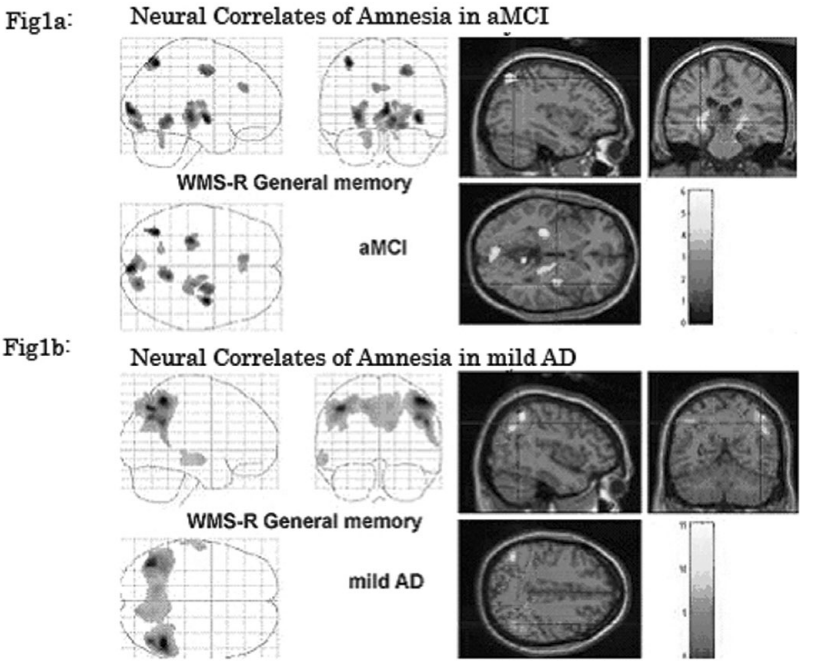
Neural correlates of amnesia in mild cognitive impairment and mild Alzheimer's disease: A brain perfusion SPECT study

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Amnesia is the hallmark clinical feature of Alzheimer's disease (AD) and the cardinal feature of amnestic mild cognitive impairment (aMCI). It was reported that aMCI patients converted to AD within 2–4 years from the baseline diagnosis at a rate that approximately 3.1 times higher than in subjects without cognitive impairment. Therefore, in various disciplines of neuroscience research aMCI has been paid attention as the group that includes very early stage of AD more than the number of normally aged subjects. However, to date, neural basis of amnesia in aMCI and mild AD are not well documented. A number of studies carried behavioral experiments as a primarily concern with little focus on the specific brain regions involved. Functional imaging studies although paid attention to detect regional cerebral involvement, neuroimaging and neuropsychological assessments have always been addressed separately. To elucidate neural correlates of amnesia, we examined rCBF distribution and its relation with recent memory function in aMCI and mild AD. 12 aMCI (Petersen's criteria), 11 mild AD (NINCDS-ADRDA for probable AD) patients and 15 normal subjects comparable for age, sex and years of education were consecutively recruited. Memory functions were evaluated by Wechsler Memory Scale-Revised (WMS-R) scores. Brain perfusion SPECT ^{123}I-IMP was assessed for each subject. We examined the pattern of hypoperfusion and the correlation between WMS-R General Memory and resting rCBF by SPM99 in aMCI and AD patients. SPM revealed a similar pattern of hypoperfusion observed in the left hippocampus, bilateral cingulate, precuneus, parietal and frontal cortices in aMCI and AD. However, the extent of hypoperfusion was greater in the AD group. WMS-R general memory scores correlated significantly to rCBF in the bilateral hippocampus, left superior parietal and right lingual gyrus in aMCI patients ($P < 0.01$). In mild AD, SPM showed significant correlations in the bilateral posterior cingulate, precuneus, and superior parietal and inferior parietal lobules ($P < 0.01$). These results suggest that medial temporal cortices play a central role solving

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P2-200

the recent memory tasks in aMCI patients whereas a greater neural network including the association cortices come into play an important role for the same task given to mild AD patients. Neural circuits implicated in recent memory function may differ between the patients of preclinical AD met clinical diagnostic criteria of aMCI and mild AD.

P2-201

N-cadherin enhances extracellular secretion of Aβ and modulates Aβ42/40 ratio

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In the present report, we evaluated whether N-cadherin-based contact modulates Aβ release. Here, we demonstrate that the inhibition of N-cadherin-mediated cell-cell contact in primary neurons reduces extracellular release of Aβ. Conversely, stable expression of N-cadherin into Chinese Hamster Ovary cells, expressing Swedish mutant of human amyloid precursor protein (APP) led to enhanced Aβ secretion. Moreover, N-cadherin expression decreased Aβ42/40 ratio in the media. The effect of N-cadherin expression on Aβ production was accompanied by the conformational change of PS1 into the more open state, which was demonstrated by fluorescence lifetime imaging technique (FLIM). These results indicate that N-cadherin-mediated synaptic contact modulates amyloid β secretion as well as Aβ42/40 ratio via PS1/N-cadherin interaction. Since N-cadherin is essential for synaptic function and plasticity, our current findings may provide potential link between synaptic activity and physiological secretory mechanisms of Aβ.

P2-202

Participation of Alcadein α and its proteolytic product in the axonal transport of APP and the generation of Aβ

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Aim: Alcadeinα (Alcα) is a type I membrane protein expressed in neuron. In the brain of Alzheimer's disease (AD) patients, Alcα accumulated in dystrophic neurites around disseminated senile plaques with APP, suggesting that both proteins were subjected to an aberrant vesicular transport in degenerative neurons. We found that Alcα directly associates with kinesin light chain (KLC) of kinesin-1, while APP indirectly associates with KLC *via* JIP1b. Understanding the molecular mechanisms of Alcα- and APP-cargos transport is important to reveal the cellular events prior to Aβ production in AD pathogenesis.
Method: Axonal transport of vesicles containing Alcα-EGFP and APP-EGFP in neuronal cells were observed with a TIRF microscopy system. Alcα and APP were expressed with or without JIP1b and KLC1 in HEK293 cells to perform coimmunoprecipitation analysis. The amount of secreted Aβ was quantified by sELISA.
Results: The interaction of APP to KLC1 through JIP1b was inhibited when excess amount of Alcα or AlcαICD presented. In such state, the transport of APP-cargos is suppressed and Aβ generation was increased.
Discussion: Predominant interaction of AlcαICD with kinesin-1 competes to the kinesin-1 association for APP. In contrast to AlcICD, AICD cannot inhibit the Alc association to kinesin-1, because it binds to JIP1b but not to KLC directly. Thus, cellular event prior to Aβ generation in AD may be unbalanced connection to kinesin-1 of APP cargos caused by competitive inhibition.

P2-203

Increased autophagic activity might not automatically induce amyloid β protein production

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Object: Accumulating evidence indicates that autophagy might be involved in pathogenesis of several neurodegenerative diseases. In Alzheimer's disease (AD), augmented LC3-II levels, the indicator of autophagic activity are reported and autophagic vacuoles are suggested to be a putative amyloid β protein (Aβ) production site. In this study we attempted to examine whether the increased LC3-II levels directly link to the overproduction of Aβ.
Methods: Using CHO cells stably expressing APP751, secreted and intracellular Aβ were detected either by immunoprecipitation or westernblotting, respectively. Autophagy and disturbance of intracellular cholesterol transport were induced by rapamycin or U18666A treatments, correspondingly. Using anti-LC3 antibody, authophagic activity was identified by westernblotting and autophagic vacuole formation was detected by immunocytochemistry.
Results: As previously reported, the rapamaycin treatment induced autophagy and over secretion of Aβ. Furthermore, increased intracellular Aβ levels were also detected, suggesting that autophagy might cause over production of Aβ. However, although the U18666A treatment augmented the LC3-II level and increased autophagic vacuole formation was confirmed by immunocytochemistry, both intracellular and secreted Aβ levels were reduced.
Discussion: Our findings show that increased autophagic activation might not automatically induce the overproduction of Aβ.

P2-204

Apo E isoform dependent cholesterol efflux is caused by intra-molecular domain interaction and inter-molecular dimerization

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Apolipoprotein E (apoE), a 34kDa protein, is a major cholesterol transporter in the brain and is produced mainly by astrocyte. The most common form is apoE3, which does not have domain interaction, whereas apoE4 has domain interaction. We previously reported that the level of cholesterol efflux induced by apoE4 is lower than that by apoE3 due to domain interaction. However, the domain interaction is partly responsible for the decreased cholesterol efflux induced by apoE4. Furthermore, we

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reported that the ability of N-terminal fragment to release cholesterol is greater than that of C-terminal fragment and it is ApoE isoform dependent. In this study, we investigated the involvement of dimerization of apoE3 in apoE isoform-dependent cholesterol efflux.

We used intact apoE3 dimers, intact apoE4 and carboxymethylated apoE3, which is a control of apoE3 monomers. The level of cholesterol efflux from cultured neurons induced by apoE3 dimers is the most highest of all. This is the case for N-terminal fragment of apoE3, that is, N-terminal fragment of apoE3 dimers induces greater cholesterol efflux than its monomers. Furthermore, ability of apoE to release cholesterol depends on ABCA1 proteins.

These results suggest that higher cholesterol efflux mediated by apoE3 than apoE4 is caused by dimerization of apoE3. In conclusion, there are two major factors, intra-molecular domain interaction and inter-molecular dimerization, that cause ApoE-isoform-dependent cholesterol efflux.

P2-205

Aβ amyloid accelerates accumulation of τ in neuronal processes

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In Alzheimer's disease, Aβ brain amyloidosis is believed to induce secondary tauopathy based on amyloid cascade theory. However, the relationship between Aβ amyloidosis and tauopathy has not been solved. We produced double transgenic mice by mating Tg2576 mice that exhibit amyloidosis and τTgP301L mice that show tauopathy, and analyzed the effect of Aβ accumulation on tauopathy in these mice. F1 littermates of Tg2576 mice $\times$ τTgP301Lmice (A$\beta+\tau+$mice (n = 22), A$\beta+\tau-$mice (n = 12), A$\beta-\tau+$mice (n = 55), and A$\beta-\tau-$mice (n = 21)) were analyzed from 8 to 23month old. Paraffin sections of brain were stained with antibodies against Aβ, τ, ubiquitin, and neurofilament. In A$\beta+\tau+$mice, start of τ accumulation was not accelerated compared with A$\beta-\tau+$mice. In A$\beta+\tau+$mice, phosphorylated τ accumulated in dystrophic neurites around senile plaque and in neuropil thread. Accumulation of phosphorylated τ was observed in neuronal processes in white matter only in A$\beta+\tau+$mice. From these findings Aβ amyloid may accelerate τ accumulation in neuronal processes.

P2-206

Quantitative change of APH-1 and presenilin in culture cells under various type of endoplasmic reticulum (ER) stress

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Aim: In order to investigate quantitative changes of APH-1 and Presenilin-1(PS1) and Presenilin-2 (PS2) under various type of ER stress, we have examined ER stress experiments using culture cells.
Methods: Chemical compounds (Brefeldin-A, Tunicamycin, Thapsigargin, Staurosporine) which cause various kinds of ER stress were added in culture media of human embryonic kidney cells (HEK293), human glial cells (KNS-42) and human neuronal cells (GOTO) with appropriate concentration, then those cells were harvested at regular time intervals. Those samples were analyzed by western blotting, and checked the quantitative changes of both full length and fragments of APH-1aL, PS1 and PS2.
Results: In HEK293 cells, the full length of both PS1 and PS2 proteins were increased 24 after addition of Tunicamycin, but there was no change in fragments of both proteins. In GOTO cells, the full length of PS1 and PS2 proteins were also increased 24 after addition of Tunicamycin, moreover, the full length of Aph-1aL proteins were decreased at the same time. There was no quantitative change of any proteins in KNS cells under ER stress conditions.
Conclusion and discussion: It has been known that Tunicamycin inhibits carbohydrate chain ornamentation and then normal folding of protein in ER. The results that only Tunicamycin caused quantitative change of PS1, PS2 and Aph-1 but not other chemical compounds, possibly indicate neuroprotective effects, including anti-apoptotic effects to inhibition

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of glycosylation, or pro-apoptotic changes of PS1 and Aph-1, which was previously reported in PS2.

P2-207

Dephosphorylation of Cdk5-phosphorylated FTDP-17 mutant τ

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Neurodegenerative tauopathies, including Alzeheimer desease, are characterized by abnormal hyperphosphorylation of microtubule-associated protein τ. One group of tauopathies known as FTDP-17 is directly linked to mutations of τ gene and these mutations may cause hyperphosphorylation of τ. However, it is not known why mutant τ is highly phosphorylated. The major τ kinases are Cdk5 and GSK3. Phosphorylation of FTDP-17 τ by these kinases has been studied and it is found that mutant taus are not phosphorylated more than WT *in vitro*. Phosphorylation is the balance between kinases and phosphatases. Therefore, we examined dephosphorylation of mutant taus, K257T, P301L, and R406W. τ was purified from E. coli extract, phosphorylated by Cdk5 *in vitro*, and dephosphorylated by protein phosphatases in the brain extract. R406W was dephosphorylated easier than WT, and P301L was dephosphorylated slowly. When we looked at site-specific dephosphorylation by 2D-phosphopeptide mapping, there was no difference in the dephosphorylation rate among phosphorylation sites. Then, we tested the effect of microtubule (MT)-association on τ dephosphorylation. Dephosphorylation of τ was remarkably decreased by association with MT. Association with MT may change the conformation of τ, in which dephosphorylation is unfavorable. These results remind us the report that PHF-τ is hardly dephosphorylated. To relate hyperphosphorylation to FTDP-17 mutation, we are now studying the effect of MT-association on dephosphorylation of τ in cells.

P2-208

Mutational analysis in early-onset familial Alzheimer's disease in Japanese population revealed *PSEN1* mutations, *MAPT* R406W mutation, and *APP* duplication

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Autosomal dominant early-onset familial Alzheimer's disease (EO-FAD) (OMIM 104300) with age at onset before 65 has been shown to be caused by mutations in amyloid precursor protein (*APP*) gene, presenilin 1 (*PSEN1*) gene, *PSEN2* gene, and microtubule-associated protein τ (*MAPT*) gene. To determine respective contribution of these genes to EO-FAD in Japanese population, we performed mutational analysis of the *APP*, *PSEN1*, *PSEN2*, and *MAPT* genes by sequencing genomic DNA from 11 probands of EO-FAD. We also determined gene dosage of *APP* by a real-time PCR analysis. In four probands, we identified four different *PSEN1* mutations including L286V, G378E, L381V, and L392V. The mean age at onset of patients with *PSEN1* mutations was 39 years (range, 30 to 47). In two probands, we found R406W mutation in the *MAPT* gene. Mean age at onset of the patients carrying *MAPT* R406W mutation was 52 years, and they showed slowly progressive AD-like phenotype. Furthermore, we identified *APP* duplication in two probands. No *PSEN2* mutation was found in this study. The four patients lacking a mutation in *APP*, *PSEN1*, *PSEN2*, or *MAPT* showed older age at onset (mean = 58 years old) than the patients with the mutations, and carry an ApoE ϵ4 allele. Collectively, this study demonstrates that mutations were found in approximately 70% of our EO-FAD pedigrees; *PSEN1* mutation is most frequent particularly in patients with age at onset before 50,

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followed by *APP* duplication and *MAPT* mutation. These results indicate the importance of examining *APP* gene dosage as well as *MAPT* sequencing in FAD patients.

P2-209

Assembly of two distinct dimers and higher-order oligomers from human full-length τ

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Abnormal accumulation of τ as filamentous structures is a neuropathological hallmark of neurodegenerative diseases referred to as tauopathies.

Objective and methods: To address whether (i) cysteine (Cys) or other residures are essential for full-length τ assembly and (ii) oligomeric full-length species is detectable in vivo, we analyzed both heparin-induced assembly of recombinant τ and assembly of τ from COS-7 cells transiently expressing different τ constructs.

Results: We demonstrated that τ assembly involves two distinct dimers (Cys-dependent and Cys-independent). During assembly, an increase of Cys-dependent τ oligomer was observed prior to detection of increased thioflavin T fluorescence signals. The latter event was accompanied by an increase of Cys-independent dimer. Fewer higher-order oligomers and aggregates were assembled from four repeat τ which has either the C291A/C322A mutation (cysless) or a hexapeptide deletion at residues 306–311 (ΔPHF6) compared to those assembled from wild-type τ. Assembly of distinct types of dimers was also observed in lysates from COS-7 cells expressing wild-type τ and brain extracts from mice expressing P301L mutant τ. In contrast, COS-7 cells expressing cysless or ΔPHF6 τ contained very little Cys-dependent dimer.

Discussion: The results indicate that intermolecular disulfide crosslinking along with PHF6 hexapeptide facilitates τ oligomerization, and that this event is accompanied by Cys-independent intermolecular bridging of microtubule-binding domain, leading to assembly of higher-order oligomers.

P2-210

Phosphatidylinositol 3-kinase/AKT pathway alters the ubiquitination of the γ-secretase complex and modulates its proteasomal degradation

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Background: Presenilin 1 is required for the activation of phosphatidylinositol 3-kinase(PI3K)/AKT pathway. Glycogen synthase kinase 3β(GSK3β), downstream of PI3K/AKT pathway, phosphorylates presenilin 1 and modulates its expression. Considering these two observations, the presenilin 1/γ-secretase complex may controls its own expression by a feedback loop.

Objective: To investigate the role and mechanism of PI3K/AKT pathway in controlling the expression level of the γ-secretase complex.

Methods: The expression levels of the components of the γ-secretase complex on PI3K, AKT or GSK3β inhibition were examined. The mRNA expression was examined meanwhile. The proteolytic system for γ-secretase complex was determined using the proteasome or autophagy inhibitors. The change in ubiquitination of the presenilin 1-containing immune complex on PI3K or AKT inhibition was studied by immunoprecipitation.

Results: Both PI3K and AKT inhibitors increased the expression of the γ-secretase complex components. GSK3β inhibitors cancelled such increase. The increase was caused by decreased degradation of the γ-secretase complex, not by mRNA upregulation. The γ-secretase complex was degraded by the ubiquitin proteasome system. PI3K/AKT pathway inhibition caused the presenilin 1-containing immune complexs more multi-monoubiquitinated than polyubiquitinated.

Conclusion: Inhibition of PI3K/AKT pathway made the γ-secretase complex more (multi-) monoubiquitinated and stable to proteasomal degradation.

P2-211

Non-astrocytic expression of apolipoprotein E in the brain

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Astrocyte is a major cell type that produces apolipoprotein E (ApoE) in the brain. We demonstrated that various cell types other than astrucytes harbor ApoE-like immunoreactivity (IR) in different conditions. Human autopsy samples with Alzheimer's disease (AD), cerebral infarction and Mongolian gerbils with induced ischemia were subjected to immunohistochemistry for ApoE and other cellular markers. In senile plaques (SPs) of AD, ApoE-like IR was concentrated in the microglia frequently accumulated in the center of SPs, while astrocytes around SPs are devoid of ApoE-like IR (Neurosci Lett 1995:195:5–8). In ischemic lesions (human or gerbil), ApoE-positive neurons and axons were sometimes observed in the area without ApoE-positive astrocytes (Stroke 2003:34:875–880). Neuronal localization of ApoE-like IR was confirmed by the colocalization of neuronal markers (NeuN) and the lack of colocalization with glial markers (GFAP for astrocytes and lectin for microglia) in experimental ischemia in gerbils. An increase in ApoE after ischemica was confirmed by an increase in ApoE-positive band in homogenate from ischemic focus relative to control. Furthermore, the homogenate from cultured cell line (GOTO) of neuronal origin exhibited an increased intensity of ApoE-positive band after exposure to hydrogen peroxide. Because ApoE is a molecule that is functional in neurons, precise identification of its in-vivo origin is necessary for understanding the role of ApoE. This is indispensable for construction of therapeutic strategy by modifying the expression of ApoE.

P2-212

Contribution of endogenous GRKs to phosphorylation of alpha-synuclein at Ser129 in cultured cells

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Objective: Alpha-Synuclein (aS) is a major protein component of Lewy bodies (LBs) in sporadic Parkinson's disease (sPD). Phosphorylation of aS at Ser129 has been identified as a major modification of aS in LBs. Furthermore, phosphorylation of aS Ser129 has been shown to enhance the toxicity of aS to dopaminergic neurons in a *Drosophila* model of PD. To clarify the protein kinase(s) involved in the pathogenesis of sPD, we investigated the contribution of endogenous GRKs to phosphorylation of aS Ser129 in cultured cells.
Method: We analyzed the level of phosphorylated aS Ser129 in SH-SY5Y cells transfected with wild-type or dominant negative mutant of G-protein-coupled receptor kinase (GRK) 2, GRK5 or GRK6 cDNAs. Also, we examined it in HEK293 cells transfected with siRNAs against GRKs.
Results: In HEK293 cells and SH-SY5Y cells, the expression of endogenous GRK2, GRK5 and GRK6 was observed. As well as GRK2 and GRK5, the level of phosphorylated aS Ser129 was increased by over expression of GRK6. In SH-SY5Y cells stably expressing aS, over expression of dominant negative mutant GRK6 significantly suppressed phosphorylation of aS Ser129. In HEK293 cells stably expressing aS, siRNA-mediated endogenous GRK6 knockdown significantly suppressed phosphorylation of aS Ser129.
Discussion: We demonstrated that GRK6 was one of the kinase associated with phosphorylation of aS Ser129 in cultured cells. Further study to determine the contribution of endogenous GRKs to phosphorylation of aS Ser129 in dopaminergic neurons would provide an insight for a potential therapeutic target in sPD.

P2-213

Effects of phosphoinisitides on gamma-secretase activity in detergent soluble/insoluble states

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Objective: We previously established a CHAPSO-solubilized γ-secretase assay system and found that the concentrations of detergents and phosphatidylcholine altered γ-secretase activity. This suggests that the composition of lipid bilayer has a significant impact on Aβ production. Recently, it has been reported that Aβ production in cultured cells is attenuated by phosphatidylinositol-4,5-diphosphate [PI(4,5)P2], one of phosophoinositides. However, it is not clear whether PI(4,5)P2 has a direct influence over γ-secretase activity. In this study, we have analyzed the effects of phosphoinositides on the γ-secretase.
Methods: CHAPSO-soluble and insoluble fractions of CHO membrane were incubated with C99-FLAG in the presence of phosphoinositides.
Results: Phosphoinositides attenuated the γ-secretase activity in the CHAPSO-solubilized membrane, in a dose-dependent manner. PI(4,5)P2 suppressed γ-secrertase activity even in CHAPSO-insoluble fraction of membrane. PI(4,5)P2 was found to inhibit association between γ-secretase and C99-FLAG in the soluble state. Kinetic analysis of Aβ production in the presence of PI(4,5)P2 suggested apparently competitive inhibition.
Discussion: Phosphoinositides are minor phospholipids in membrane. However, the presence of PI(4,5)P2-rich microdomains in membrane has been reported in a range of cell types. Further, γ-secretase was enriched in the microdomain of membrane. Here, we propose that phosphoinositides potentially regulate γ-secretase activity by suppressing its association with the substrate.

P2-214

The expression of mPGES-1 relevant to Alzheimer's disease pathology in mouse model of Alzheimer's disease

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The epidemiological studies have been indicated that long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) delays onset of Alzheimer's disease (AD) and reduces the risk of developing AD. NSAIDs inhibit the cyclooxyganase activities that catalyze the formation of prostaglandin H_2 from arachidonic acid, the precursor of prostanoids. Prostaglandin E_2 (PGE_2), which is main product of COX function as an inflammatory mediator. Actually, inflammatory pathologies have been observed in the brain with AD. Therefore we focused on PGE synthase (PGES) and considered whether there was expression difference between mPGES-1, mPGES-2 and cPGES in the brain of wild type mouse and amyloid precursor protein transgenic mouse (Tg2576). The isolated brains from both mice were fixed with formalin and brains were cut on fixed tissue. Immunohistochemical staining was carried out with anti-mPGES-1, mPGES-2, cPGES antibodies. Antibody against mPGES-1 showed strong immunostaining around neuritic plaques in Tg2576. There were no clearly differences between the two mice for mPGES-2 and cPGES. mPGES-1 is concerned with the synthesis of PGE_2 which is derived from COX-2. These results suggest that PGE_2 expression is increased in the vicinity of senile plaques. Although PGE_2 toxicity is unclear to date, mPGES-1 may have a potency to become a therapeutic target of AD.

P2-215

The understanding of prevention methods for dementia: A questionnaire survey for attendants at a dementia lecture

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Purpose: The purpose of this study is to know how citizens think about dementia and what kinds of methods they use for preventing dementia.
Methods: After attending at a dementia lecture, citizen who lived in the rural town answered the self-rating questionnaire for a view of dementia. 77 attendants (twenties to eighties, 63 women and 14 males) were involved in this study. All questions were anonymously answered.
Results: Almost half of the attendants had an experience either to care demented persons or to have close relatives and/or friends with dementia. It was clear that they have an anxiety for their onset of

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dementia for the future. They are doing several activities as prevention methods of dementia: working as volunteers, doing with planning as well as they can, watching TV quiz programs, reading books, exercising, making meals by themselves and so on.
Discussion: The more the percentages of the old people increase, the more do people have anxiety for having dementia and interests its preventing methods. It is concluded that we should educate them the exact prevention methods of dementia.

P2-216

Coping with dilemmas among female nurses caring for patients with dementia

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Objective: The health care needs of patients with dementia are various, and are influenced by aging and social situation. These factors complicate medical care. Moreover, society seeks higher quality and more efficient nursing than before, and nurses feel a dilemma when caring for patients with dementia. This study is aimed at clarifying the coping of nurses working in general wards who face this dilemma.
Methods: The participants were 84 nurses at 5 wards (excluding the emergency wards of psychiatry, pediatrics, obstetrics, outpatient, operating rooms, and intensive care units). Coping with dilemmas was measured by using a questionnaire consisting of 16 items previously developed by the author. A low participant score of 1–4 points suggested good coping strategies.
Ethical consideration: The questionnaire was designed to ensure privacy and anonymity while allowing participants to complete the form themselves. Participants inserted and sealed the completed questionnaire into an envelope that was provided in advance. The study was conducted with the approval of the ethics committee at Meiji University of Oriental medicine.
Results: The internal consistency of the 16 independently prepared items used to measure coping with dilemmas was tested to show a Cronbach's coefficient value of 0.7. To test the validity of item selection and dilemma factors the items were subjected to a factor analysis (maximum likelihood method: promax rotation). Of the 16 items, three had a factor loading of 0.4 or a difficulty in interpretation, and were deleted; 11 of the remaining items were used for analysis. Three items with a characteristic value of 1 were extracted and showed a Kaiser-Meyer-Olkin measure value of 0.7 and a cumulative contribution ratio of 62.9%. An explanatory factor analysis revealed three coping with dilemma factors among the 11 items investigated. These were factore1, dilemma regarding positive and cognitive action, factore2, dilemma regarding negative and cognitive action coping, and factore3, dilemma regarding keeping status quo and thoughtless coping.
Conclusions: Based on the psychometric properties, the coping with dilemma scale is a valid and reliable tool. The development of a program to support positive and cognitive action coping with dilemmas is suggested. Caring ethics are especially important to nurses in dementia care. Therefore, we would suggest the program support nurses caring for patients with dementia in general wards.

P2-217

Difficulties and possibilities in nursing care for people with frontal lobe dementia

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From a clinical perspective it is well known that nursing care for people with frontal-lobe dysfunction requires structure and clarity, while nursing care for people with other dementia diseases primarily has to be adjusted to their memory disturbances. In most studies concerning nursing care for patients with dementia the sample has been drawn from older people with varied dementia diagnoses, meaning that the specific nursing care for persons with frontal-lobe dementia has been difficult to identify. As there is a need for specific knowledge about nursing care for this group, the aim of the study was to describe nurses' experiences of difficulties and possibilities in the nursing care of people with dementia disease with predominantly frontal-lobe dysfunction. The study was carried out in southern Sweden as a descriptive qualitative study. Data was collected in interviews with 10 nursing staff (aged 40–53 years) working at a unit for care for persons with frontal lobe dementia. They had extensive experience of caring for people with dementia (in

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median, 22 years) and a majority had worked at the unit since it started, nine years earlier. The interviews were analysed with qualitative content analysis. The results showed that the difficulties experienced were related to the patients' lack of inhibition and judgement, anxiety, agitation, reduced ability to deal with physical needs, egocentricity, imbalance between rest and activity and depressed mood. The possibilities were seen in relation to the nursing staffs' professional encounters, characterised by being clear and consistent, a step ahead, flexible, calm and creating a positive atmosphere, close and trusting and being and doing things together. Continuous feedback and support were prerequisites for the engagement of the staff. In conclusion, this study highlights that nursing care in this context involves several ethical issues where the patients' integrity has to be balanced against a safe and secure environment. Nursing care is a sensitive but also demanding task, where nurses' actions can reduce the negative effects of the disease. It is therefore important to support staff in nursing care so they are able to manage their work and to reduce the risk of emotional exhaustion.

P2-218

Suffering from eating or lack of eating

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Suffering has been defined as a specific state of distress that occurs when the intactness or integrity of the person is threatened or disrupted. It lasts until the threat is gone or integrity is restored (Cassel, 1999). It is important to realise that suffering is a basic sensations, perceptions, emotions, or thoughts of any human being. Coping with suffering or fear of suffering at the end of life is an expectable and basic emotion, and part of everyone's life cycle. Aminoff et al. (2004) found a significant association between the level of suffering and malnutrition. According to Maslow theory, in order to survive, one has to fulfill the basic needs, and the first of them is nutrition. Namely, one has to identify the patients suffering from lack of proper nutrition and adjust, according to a constructed protocol, the appropriate nutrition, in order to improve their condition and prevent complications.

Aim: When examining issues related to treatment at the end of life, the question arises regarding the benefit of food to the patient. While feeding is necessary for living when the basic aim is to remain living, in situations where the patient suffers, he sometimes prefers to die rather than to keep on suffering. The aim of the study was to understand the differences between patients view and nurses regarding suffering from food or lack of food.

Methods: interviews with patients (n = 29) and nurses (n = 13), interviewed for their opinions regarding the suffering of the impaired communication patients relating to receiving or not receiving food. The opinions of the patients and the staff were then compared.

Results: The nurses felt obliged feed the patients at any cost, but in relation to themselves, the situation was reversed and they would not want to be fed at any cost. Finally, most of the patients and most of the nurses agree that a patient being fed through a feeding tube suffers less than a patient who does not receive food at all.

P2-219

Environmental sounds in nursing facilities: Subjective evaluation by elderly with dementia and elderly without dementia

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The purpose of this comparative descriptive study was to investigate differences between elderly with dementia and elderly without dementia in their subjective evaluation of environmental sounds in daily life in nursing facilities in Japan. Convenience samples of 12 elderly with dementia (mean MMSE = 16.7, SD = 5.1) in 3 nursing facilities and 30 elderly without dementia residing in the community participated in this study. Mean ages of the 2 groups were 84.1(SD = 8.2) years old and 72.0 (SD = 4.6) years, respectively. Six environmental sounds in nursing facilities were identified by the Sound Level Meter and were tape-recorded: the sound of shouting for joy in playing group games, the sound of a resident's yelling, the sound of multiple conversations at the same time, the sound of tableware hitting each other, the sound of a dragged wooden chair, and the sound of a cleaner. The environmental sounds were adjusted to the same loudness and were presented to each subject one at a time through headphones in a quiet room.

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Subjective evaluation (comfortableness, noisiness, annoyance, displeasure) was measured by 1) the use of a 5-Likert scale questionnaire ranging from 1 to 5 and 2) the subject's description of the perceived source of sounds.

Statistical analysis (Mann-Whitney test) revealed that there were significant differences between the 2 groups in the subjective evaluations of comfortableness and noisiness in the sounds from a resident's yelling and in the sound from a dragged wooden chair. Elderly without dementia evaluated these sounds as more uncomfortable ($p < 0.05$) and noisy ($p < 0.05$). In addition, there was a qualitative difference in the perceived source of the sounds. Elderly without dementia described the resident's yelling as "child's fretting" or "screaming from pain", whereas those with dementia perceived it as "song", "woman's voice" or "Bon-dancing (Japanese folk dance)". Regarding the sound from the dragged wooden chair, elderly without dementia described it as "sound of chair or something being dragged, "sound of poorly fitting doors", etc., whereas those with dementia described it as "not a good sound", "unrecognizable", etc. The results suggest that elderly with dementia perceive environmental sounds quite different from people without dementia, less uncomfortable and noisy but with the meaning of the sounds more vague. There is a need for health professionals to provide information on environmental sounds to persons with dementia.

P2-220

Cognitive response changes during adult day nursing care service for severe disabled elder with skilled nursing care needs

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Aims: In home care setting, adult day health care centers are less likely to admit severe disabled elder with skilled nursing care, even though elders might have nursing care needs or their caregivers have respite care needs during daytime. The aims of the present case-report study is to describe cognitive response changes during adult day nursing care for a severe disabled elderly person with skilled nursing care needs.

Methods: The participant was a woman aged 79 years old, in the severe stage of Parkinson disease, Chronic Obstructive Pulmonary Disease, and impaired cognition, with skilled nursing care needs including rehabilitation nursing, frequent sputum suctions, oxygen therapy, jejunostomy tube feeding, urethral catheter, bowel control, and complete locomotion or personal care assistance, and living at home with her husband aged 82 years old. Nurses who are also her primary visiting nurses, provided her day nursing care for approximate 8 hours per a day once a week for 3 months, with transportation care between her home and the nursing care facility. We have recorded the cognitive responses which included her expression level which scored from 1 to 6, conscious level which scored from 1 to 3, and the contents of verbal responses in detail, through the whole period of each day nursing care.

Results: Of all the day nursing care frequency, 25.0% was the specific nursing observation or vital sign check, 18.1% was sputum suction care, 14.8% was locomotion care assistance, 11.2% was transportation care, and 10.2% was personal hygiene care. Most of nursing care was provided by two nurses and some of those was provided by three nurses. Comparing to the first month of the intervention at the last month of that, the frequencies which have shown smiling expression, the awakening status without cognitive stimulation and the verbal responses which contents have certainly increased.

Conclusions: These results suggest the severe disabled elderly person with skilled nursing care needs have effects have improved their cognitive responses during the adult day nursing care service, while the nursing care was provided intensively. Although the effects of adult day nursing care should be investigated by conducting a well-designed research in future, we enhance and extend the adult day nursing care to improve their cognitive function or QOLs for the disabled elders with frequent skilled nursing care needs living at home.

P2-221

Natural activity: An explorative study of the interplay between cage-birds and older people in a Swedish hospital setting

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Older people are at risk of being affected by mental fatigue due to various age-related reductions and disease. Mental fatigue manifests itself through a reduced ability to concentrate. The method of alleviating mental fatigue with the use of stimulating natural settings or animal assisted activities is so far unexplored in Sweden, and subsequently it is important to study the method in a Swedish context in order to implement it as a recognized nursing intervention in the care of older people. The aim of this study was to describe the interaction between cage-birds and older people as it arises in spontaneous situations in a Swedish hospital ward setting. The study had an explorative observational design, and was conducted at a geriatric ward with a consecutive selection of participants. The observations were analysed using a constant comparative method influenced by Grounded Theory. The Attention restorative theory was used as the theoretical framework to guide the study. Our findings indicate that animal-assisted therapy has a positive effect on involuntary attention and mental restoration, as well as on enhanced social behaviour among older people. The result strengthens the assumption that animal companionship should be considered a beneficial nursing intervention for older people in order to prevent mental fatigue.

Keywords: Animal-Assisted Activities, Mental fatigue, Older people, Attention Restorative Theory (ART).

P2-222

Effects of a restraint-minimization programme in dementia care: A randomized controlled trial

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Physical restraints are commonly used in the care of older persons, especially among those suffering from dementia. However, the use of physical restraints has been challenged, partly from an ethical perspective and partly because it's preventive effects has not been proven. A range of negative effects and consequences of restraint use has also been described. There exists a great variation in the prevalence of physical restraints use between ward units, research has shown that knowledge about and attitudes towards physical restraints are factors discriminating high-use from low-use wards.

Aim: The aim of this study was to evaluate the effects of a staff education programme on the use of physical restraints.

Method: Forty group dwellings for persons suffering from dementia were randomized to a control or an intervention group. The intervention group consisted of 228 residents and the control group of 193 residents. The intervention consisted of an education program for nursing staff including one recorded seminar per month over six months, with themes such as complications to dementia, fall prevention and legislation about-, alternatives to- and side effects of- the use of physical restraints. Data on the use of physical restraints were collected during three weeks before and three weeks after, while information of fall incidences were collected during the whole study period and data on resident characteristics once before and after.

Results: There were no baseline differences between the groups, regarding the prevalence of physical restraints or fall accidents. At follow-up the intervention group showed a reduction in physical restraint use by 30.4% (from 24.7% to 17.2%) while the use had increased with 32.4% (from 25.0% to 33.1%) in the control group. Twenty-four percent of the residents subjected to physical restraints at baseline in the intervention group were in the follow-up restraint free, whereas only 6.9% were free from restraints in the control group. There were no significant differences in number of fallers or total number of falls between the two groups.

Conclusion: These results suggest that staff education can be one effective method for reducing the use of physical restraints in the care of elderly suffering from dementia, without increasing the incidence of fall accidents.

P2-223

Effects of a staff-education programme on violent behaviour among residents suffering from dementia: A randomized controlled trial

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Behavioural and psychological symptoms are common complications of dementia and affect a majority of persons with the disease. One behavioural

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symptom associated with dementia that is experienced by caring staff as difficult to handle is violent behaviour. Violence towards staff from patients has been described as physical violence, e.g. kicking, pinching, grabbing, scratching and biting and/or psychological violence, e.g. yelling, swearing, and threatening, and/or sexual violence, e.g. sexual harassment and obscene statements.

Aim: The aim of this study was to evaluate the effects of a staff education programme on the prevalence of violent behaviour in persons suffering from dementia.

Method: Forty group dwellings for persons suffering from dementia were randomized to a control or an intervention group. The intervention group consisted of 228 residents and the control group of 193 residents. The intervention consisted of an education program for nursing staff consisting of one recorded seminar per month over six months, including themes such as complications to dementia (BPSD), delirium and staff-resident interaction. Data on violent behaviour were collected once before and after the intervention by interviewing nursing staff.

Results: A statistical significant increase in mean score was found in the intervention group regarding self-rated knowledge how to care for persons with dementia while no change was found in the control group. There were no baseline differences between the two groups regarding the proportion of residents with violent behaviour. After six months the proportion of residents with violent behaviour had significantly decreased by 26.0% (41.3 to 30.6%, $p = 0.032$) in the intervention group and increased by 2.2% (35.2 to 36.0%, $p = 0.875$) in the control group. A within-subject comparison made pre- and post-intervention showed a significantly decrease of the proportion of residents with psychological violent behaviour in the intervention group compared to the control group (52.9% versus 31.6%, $p = 0.045$).

Conclusion: This study has shown that staff education can be one effective method for reducing the proportion of residents with violent behaviour in group-dwellings for persons with dementia.

P2-224

The development of Benchmarking in a Psycho-geriatric Ward at a Regional Hospital in Hong Kong

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Introduction: In psycho-geriatric setting, patients are usually frail; infections and injuries will compound their mental problems. Despite the improvement of mental state, falls, skin break-downs, poor oral intake, constipation and infections are problems that hinder their discharge. In 2003, there had been several patient falls within a month. This not only made patient suffer but the costing; manpower implications for patients and staff in long-term hospitalization was high and demanding as well. This stimulated author adopt risk identifications and evaluates out-come indicators to pivot strategies of nursing care in alliance with collaboration with others disciplines to promote positive changes, as well as facilitate a safe psycho-geriatric care.

Objectives: This article shares the development of Benchmarking in a Psycho-geriatric Ward at a Regional Hospital in Hong Kong since 2003 and proposes the future direction of psycho-geriatric nursing.

Methodology: Every patient is assigned to a Primary Nurse to assure optimal care via risk management. This will provide quality care in today's healthcare system where nursing care is often fragmented and discontinuous. Strategy of implementation A patient-centered risk identification strategy, focusing on collaboration with patients, family and all disciplines, is implemented. Manager designed the workflow and build up staff competence. Primary nurse understood her central role in managing a patient's condition. They were taught what to expect from the healthcare system prior to discharge. Home telephone-communication prevents risk of psychiatric emergency and facilitates family support during trail discharge in-security period. . A prepared and proactive strategy using evidence-based clinical information and a sophisticated patient-specific dataset guided the daily interventions and out-come management in patient care.

Results: In 2003, there were several falls happened in one month; Strategic management taken. In 2006, patient risks: fall, choking and medication error were minimized to zero and 59 patients were fruitful discharged without re-admission and risk happen.

Conclusions: Customers and health team members recognized the effective discharge and appreciated collaboration with us. Increased number and rate of discharge with care on discharge imply benefit to our patients back to community fulfill our mission. Health expenditure became more cost-effectiveness which had saved up money and manpower.

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P2-224

P2-225

The development of Primary Nursing at a Psycho-geriatric Ward in a Regional Hospital in Hong Kong

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Introduction: Healthcare systems are confronted with an accelerating epidemic of chronic diseases. In psychogeriatric setting, patients usually have one or more chronic diseases that compound their mental problems. The core functions of Primary Nursing are assessment of patients, planning of nursing care, collaborate with family and all disciplines, monitoring of changes to facilitate patient rejoin community.
Objectives: This article shares the experience of Primary Nursing implemented in a female psychogeriatric ward since 2003 in a Regional Hospital at Hong Kong and proposes the future direction of psycho-geriatric nursing.
Methodology: Every patient is assigned to a Primary Nurse to assure optimal care management functions as described above from admission and even after discharge. Strategy of implementation A patient-centered risk identification strategy, focusing on safe care and collaboration with other disciplines, is implemented. Primary Nurse was empowered in her designated roles to contribute to optimize patient experiences and outcomes. Her central role in managing a patients conditions and contributed her skills in collaborative care. Nurse Manager prepared a proactive strategy using evidence-based clinical information and a sophisticated patient-specific dataset guided this therapeutic relationship.
Results: Taking statistics of last years in which primary nursing system not yet implemented to comparison. In 2003–2006, 59 patients were discharged without readmission over the study period. The length of stay (LOS) was shorter comparing to identical study of last years.
Conclusions: Patient, relatives, health team members and nurses appreciated collaboration. The entire system of care was designed to enhance the continuous communication that also led to better outcomes and rewarding experiences. Primary Nurse built up their (Heart) in the patient care and develops nurse a mindset of safety subtlety. The way is ongoing with team collaboration.

P2-226

Visiting nursing care process of severe dementia elder with skilled nursing care utilizing adult day nursing care

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Aims: It is preferable to provide adult a day nursing care together with a visiting nursing care to a severe dementia elder. A day nursing care just started. The aims of the present case-report study are to describe the visiting nursing care process of the severe dementia elder with skilled nursing care utilizing the adult day nursing care.
Methods: The patient was a woman aged 79 years old, in the severe stage of Parkinson disease, Chronic Obstructive Pulmonary Disease, and dementia, with skilled nursing care needs including frequent sputum suctions, respiratory therapy, jejunostomy tube feeding, urethral catheter, bowel control, rehabilitation nursing, and complete locomotion or personal care assistance, and living at home with her husband aged 82 years old. We provided the adult day nursing care, which accompanied with the visiting nursing care, started for approximate 8 hours per a day once a week for 3 months to the patient. The primary nurses of the adult day nursing care were also assigned for the visiting nursing care. The data was collected from the adult day and visiting nursing care plans and the records written by the nurses in 3 months. We analyzed the data written by the nurses for the day and the visiting nursing care process qualitatively.
Results: According to the visiting nursing care records, mainly management of self-care deficit and the skilled nursing care were conducted, especially postural drainage and squeezing were conducted frequent. The descriptions which showed the patient' verbal responses and good expressions were increased at the visiting nursing care from the second months. Consequently the nurses added community difficulty as a problem at the visiting nursing care plans from the final month. On the other hand, at the day nursing care plans, the nurses reported the communication difficulty from the first month. The day nursing care problem showed high priority level for communication difficulty, while the visiting nursing care problem showed low priority level.
Conclusions: These results suggest the assessment from the day nursing care enhance the visiting nursing care regarding the communication difficulty. The importance of providing a day nursing care with a visiting nursing care together was confirmed.

P2-227

Basic behaviour among nursing home residents with severe cognitive impairment

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Background: It is important, that nursing home staff is able to identify functional capacity among resident with severe cognitive impairment. Only in this way, it is possible to deliver care in a way, that support remaining functions. All though nursing home resident's scores zero in different cognitive test, they always dispel basic behaviour (Zandi 1994). But the term basic behaviour has not been explored.
Objective: To describe basic behaviour among nursing home residents with severe cognitive impairment
Materials and methods: 16 residents in two special care units. Mean score at the Global Deterioration Scale: 5,8. Mean age: 85,5 years. The participants were observed for 24 days. Data was analysed according to directions by Spradley and Lofland. Data related to behaviour was organized into an ethogram.
Results: The analysis showed that all the participants had different types of behaviour that could be described as directed toward objects in the surroundings. The types of behaviour observed were vocal behaviour, eye movements, locomotion and movement with the hand. Differences in the basic behaviour among the residents were 1) diversity and 2) frequencies.
Conclusions: Behavioural observation of basis behaviour is a way to get information about the residents ability to perceive and act in the world around him. The information about basic behaviour can serve as a fundament for a more individual care and thereby promote a higher degree of quality of life.

P2-228

Back to basics: Building a healthy nursing workforce

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North Western Aged Persons Mental Health is largest provider in Australia delivering comprehensive range of specialist community, hospital and aged care residential facilities to Northern and Western metropolitan Melbourne, available to about 200000 persons over 65. Workforce is predominantly nursing with significant proportions being Enrolled Nurses (RN Division 2s).This details a process of education and development aimed at focusing education back to patient care, returning to basics reviewing delivery of education and training. Aged Persons is part of NorthWestern Mental Health and large network of health organisations. Internal review of education suggested education and training was not driven by client need but rather an adhoc process based on staff preferences and individual interests. Program initiated steps aimed at meeting needs of a complex service working in collaboration with five major hospitals and changing client profile including, complex medical needs associated with functional disorder, difficult behaviours associated with dementia, co-morbidity and increasing numbers of fitter clients with age related conditions. After reviewing client profile, core clinical skills were prioritised and development of workforce aligned to priorities. Senior Nurses and Clinical Educators within the service have taken leadership role in educational developments grounded in research based evidence and reflective practice. Initiatives have been undertaken and outcomes will be evaluated in August/Sept 2007. Review of undergraduate, graduate and postgraduate nurse training programs and professional relationships with educational providers with aim of raising profile of Aged Persons Mental Health early in nurses professional careers. Increased input into age related subjects after negotiation with providers, roles of preceptors and clinical educators have been extended Opportunities for Enrolled Nurses to undertake registered nurse training Opportunities for unregulated workers and ward clerks to undertake Enrolled Nurse training, Enrolled Nurse development programs to address co-morbidity such as diabetes, cardiac conditions and other age related conditions, Enrolled Nurse Medication Administration Endorsement (including IM and subcutaneous) Development of professional portfolios including aggression management, falls and back attack which attract a Senior Allowance. These initiatives are now being undertaken in a climate of reflective practice and a positive approach to access to conference and study leave.

P2-229

Improving the sound environment for comfortable living of demented elderly people (Results of investigations at group homes and nursing homes)

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Demented elderly people may fail to selectively distinguish environmental sounds and be confused. The revised edition of the Professional Environmental Assessment Protocol (PEAP) also recommends "incorporation of meaningful and pleasant sounds into life".

In this study, we measured noise at group homes (GH) and nursing homes (NH) to evaluate a sound environment in which elderly people can live comfortably.

Noise was recorded for 24 hours in the living rooms of GH and NH every second, and the progression of daily routines and responses of the elderly during the daytime were observed. Since the distribution of the measured noise levels was skewed, the most frequent, maximum, minimum, and median values were compared.

The most frequent, maximum, minimum, and median noise levels were 53.5, 92.6, 39.6, and 54.7 dB at GH and 60.0, 87.2, 32.5, and 58.7 dB, respectively, at NH. The noise level was higher at NH in both the daytime and nighttime, and noises of 60 dB occurred frequently even in the nighttime. At GH, the causes of the noises, which included the vacuum cleaner, were clear and were perceived by the elderly people. At NH, however, various noises including conversation mixed at NH, and the elderly people were not very responsive to abrupt noises of short durations. Demented elderly people began to drowse at an environmental noise level of about 50 dB, and the appearance of drowsing was not correlated with the severity of dementia. However, drowsing unrelated to the noise level was observed in severely demented and deaf elderly people.

This study clarified that environmental noise of about 50 dB induces drowsing in demented elderly people as well as confirmed the conventional knowledge that noises at 70 dB or above should be minimized and that interference of conversation by noise of daily living should be avoided at elderly care facilities. Further evaluation of sounds in the

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care environment is necessary with regard to both the sound intensity and quality.

P2-230

Aging and exercise effect on discrepancies between actual physical ability and its recognition in older adults

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Background: The age-related decline in metacognition in which older adults recognize their own physical ability as being at a higher level than it actually is has been cited as a factor in falling in some reports. And, some studies have reported that amount of daily exercise influences this discrepancy between actual physical ability and its recognition. However, empirical research has not addressed this issue to date.
Goal: To examine the hypothesis that an inability to recognize reduced physical ability and participate in a reasonable amount of daily exercise influences older adults" recognition of their own physical ability.
Method: Experiments used a two factorial design: Group (2: older adults, younger adults) × Condition (2: load, non-load). Subjects were 35 healthy older adults (21 males, 14 females) and 37 healthy younger adults (18 males, 19 females) who participated in a striding task under the following two conditions: in the load condition, the range of motion of both legs was restricted, and in the non-load condition, range of motion was unrestricted. Participants estimated their own striding distance under both conditions before we measured their actual stride. We compared both distances. We also recorded the amount of daily exercise participants undertook for one week.
Results: The two-factorial ANOVA showed a significant main effect of Group but no significant effect of Condition or interaction, suggesting that older adults recognize a decline in their physical ability more accurately than younger adults. Further, as compared to the older adults, the younger adults tended to recognize their physical ability as being at a higher level than it actually was. This suggests that older adults do not typically show a tendency to perceive their physical ability to be at a higher level than is actually the case. Correlation analysis between average activity time and discrepancy in load condition revealed a significant correlation ($r = -.402$), implying that older adults who exercised less were not able to recognize their reduced physical ability accurately. Moreover, correlation analysis between high-intensity activity time and discrepancy in the non-load condition showed a significant correlation ($r = .454$), suggesting that older adults who undertook high-intensity exercise for long periods estimated their own physical ability at a higher level than it actually is.
Discussion: Our data should prove useful in efforts to prevent falling in older adults.

P2-231

The effect of Lactobacillus helveticus fermented milk on sleep in elderly subjects

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Objective: To study the effect of *Lactobacillus helveticus* fermented milk on sleep in elderly healthy subjects.
Design: Prospective, randomized, double-blind and placebo-controlled, with a crossover design
Subjects: The study included 29 healthy elderly subjects aged 60–81 yr.
Methods: The study included two intervention periods of 3 wk each, separated by a 3-wk washout period. Subjects took 100 g of fermented milk drink or its placebo drink (artificially acidified milk) daily in the first supplementary period and the other supplement in the second supplementary period. For each period, we measured sleep quality by means of actigraphy and a sleep questionnaire.
Results: There was a significant improvement in sleep efficiency ($P = 0.03$) and number of wakening episodes ($P = 0.007$) in actigraph data after intake of fermented milk, while no significant changes were observed for the placebo. Although the difference

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between fermented milk and placebo was not statistically significant for any of the sleep parameters, fermented milk produced slightly greater mean values for many parameters.

Conclusion: This short-term intervention (3 wks) study indicates that *Lactobacillus helveticus* fermented milk may have more clear effects on improving sleep in healthy elderly people as compared with placebo.

P2-232

Clinical factors associated to quality of life ratings in elderly patients with epilepsy

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Epilepsy in old age is becoming increasingly common, and it is known to exert a potential psychosocial burden on the sufferers. Epilepsy etiology and the psychological and social problems in the elderly are different from those of younger subjects. The purpose of this work was to compare the clinical factors associated to quality of life (QoL) between young and elderly patients with epilepsy attending an outpatient clinic of Psychiatry at Osaka University Hospital. The Quality of Life in Epilepsy Inventory for Adults (QOLIE-31) was completed by 79 patients with symptomatic and cryptogenic localization-related epilepsy. In addition the Self-Reported Depression Scale (SDS) was used to evaluate the presence and level of depressive symptoms. Other measures consisted of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) in young patients, and the Mini-Mental State Examination (MMSE) in elderly patients, to evaluate intelligence and cognition, respectively. Patients with IQ < 70 and MMSE < 24 were excluded from the analyses. Other independent variables assessed were gender, comorbid medical or neuropsychiatric disease, age of seizure onset, presence of secondary generalized tonic-clonic seizures, epilepsy duration, antiepileptic drugs (AEDs) polytherapy, structural lesions (tumor, vascular), and seizure frequency. Linear regression analyses were performed to identify significant predictors of quality of life in epilepsy in both the young and the elderly patients group. The QOLIE mean scores were found to be similar in the young (62.0 ± 18.7 SD) and elderly (61.9 ± 16.4 SD) patients group. Similarly, the SDS Index mean scores indicated mild depression in both the young patients (52.0 ± 13.0 SD) and the elderly (51.25 ± 13.5 SD). Depression was found to be associated with impairment of QoL in the two groups, while comorbid disease showed association with impaired QoL only among the young patients. In the elderly patients, cognitive function as measured by the MMSE, showed a positive association with epilepsy-related QoL. Furthermore, AEDs polytherapy was associated with lower QoL scores only among the elderly. Our findings indicate that QoL in epilepsy is strongly influenced by depressive symptoms. In addition, clinical factors such as cognitive decline and AEDs polytherapy have a particular influence on QoL in elderly patients.

P2-233

Profile of patients attending a geriatric clinic in South India

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Background: Psychiatric disorders in the elderly are commonly associated with functional disability and increased medical costs. Though old persons have multiple diagnoses, the illnesses are treatable. Services concerned specially with elderly people who are mentally ill have formed in response to changing needs and expectations in society in developed countries. In comparison, specialty services for the geriatric population in India are only a handful. We report findings from one of the first geriatric clinics in India. The Geriatric Clinic at NIMHANS was first started in early 1990s and was revived in 1999, the Year of the Elderly.

Aim: To explore the socio demographic and clinical profile of patients attending the Geriatric Clinic and Services of NIMHANS.

Method: Retrospective Chart Review from the proforma used in the Geriatric Clinic. The Clinic functions as a weekly referral outpatient service with referrals from other psychiatry and neurology specialists.

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Results: Five hundred and twenty two such patients utilized the services in the six years from October 1999 to December 2005. Preliminary analysis of the data revealed that mean age of patients was 69.52 (7.91) years of age. Males formed 51% and females formed 49% of the population. Diagnosis made on the ICD10 by consultant psychiatrists shows a break up of all Dementias 44%, Depressive Disorders (F33, 34) 19%, Psychotic Disorders (F 20, 22,29) 19%. Bipolar Disorder 6%. It was found that about 50 percent of the sample had associated physical disorders commonest being hypertension, diabetes and cerebrovascular accidents. Almost half of patients (44%) lived with their families.

Discussion: Dementia accounted for almost half the attendees possibly related to the increased awareness and availability of drug treatments since 2000. Most of the elders had multiple diagnoses emphasizing the need to have comprehensive services and appropriately trained personnel to manage these clinics. There is a need to have more Old Age clinic all over the country and start specialized courses to manage neuropsychiatric problems in the elderly in India.

P2-234

Maintenance electroconvulsive therapy in the treatment of Parkinson's disease

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Parkinson's disease, a neurodegenerative disorder affects over 1% of the population over 60 years of age. Despite many new pharmacologic agents, Parkinson's disease remains a progressively deteriorating illness often complicated by psychiatric morbidity including depression, anxiety and dementia. Non-pharmacologic treatments have been employed in Parkinson's disease including pallidotomy and most recently deep brain stimulation. Electroconvulsive therapy (ECT) was noted to provide benefit for Parkinson's disease as early as 1947. There have been numerous reports on this subject published in the literature in the intervening years, predominantly regarding Parkinson's disease with co-morbid psychiatric illness, usually depression. There have been few reports of ECT specifically for the primary movement disorder symptoms of Parkinson's disease and still fewer articles reporting on the use of maintenance ECT in this condition. The author reported one such case, published in *Geriatrics* November 2003. We now present a review of the worldwide literature through a MEDLINE search on the use of maintenance ECT in Parkinson's disease. Parameters of study include whether the primary purpose of ECT was for the movement disorder of Parkinson's disease or for psychiatric comorbidity. Each case was examined for frequency and duration of treatment and for outcome. Secondary measures include an assessment of function, whether concommitant medications could be reduced, an assessment of side effects or untoward effects from ECT versus beneficial diminishing of medication side effects if there was a reduction of pharmacologic agents, and the global impression of each report's author on the effects of maintenance ECT in Parkinson's disease.

P2-235

Cholinesterase inhibitors in schizophrenia: a literature review

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To evaluate cognitive and clinical effects of the cholinesterase inhibitors administration for schizophrenic patients. Literature review on PubMed was conducted searching for articles which investigated cholinesterase inhibitors in patients with schizophrenia and cognitive deficit. Five open label and twelve double blind studies were found. In all open label studies there was an improvement in memory, attention and other executive functions. Only in two double blind studies there was an improvement of executive functions (sustained attention) and verbal memory. Improvement in psychopathology was seen only in two open label studies. Patients with schizophrenia and AD were included in only two open label studies where an improvement was noted. In the other three open label and in twelve double blind trials patients with cognitive deficits without dementia were included. Three studies evaluated effects of galantamine and positive results on sustained attention were seen in all of them. Cholinergic dysfunction underlying cognitive deficits in schizophrenic patients probably exists when they met criteria for comorbid dementia. When cognitive deficit is directly linked to schizophrenia results are poorer, except for galantamine.

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P2-236

Sleep-related injuries in the elderly: Community prevalence, socio-demographic and clinical correlates

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Background: Sleep-related injuries (SRIs) have been recognized to be a potential source of serious harm to the health of the elderly patients and their bed-partners. This study examines the community prevalence, nature and frequency of this under-researched public health problem and its socio-demographic and clinical correlates.

Methods: A prospective cohort of 2,941 non-institutionalized Chinese men and women aged over 65 were interviewed. The subjects were enquired on whether they had ever injured themselves and/or their bed partners during sleep; and if positive, the nature, frequency, and duration since the first onset of such injuries. The subjects were also examined on their sleep patterns and for features suggestive of sleep disorders using standardized instruments. Data on their demographic characteristics, physical health, drug history, consumption of alcohols or hypnotics were collected. Each subject was also examined with the Mini-Mental State Examination (MMSE), Geriatric Depression Scale (GDS), and the Self-Reporting Questionnaire (SRQ) on their mental health status.

Results: SRIs were identified in 128 subjects (4.4%); among them 116 had injured themselves, 11 had injured their bed-partners and 1 had injured both himself and his bed-partner. Most of the injuries (84%) occurred after the victims fell off from bed. The median time from first onset was 4 years (inter-quartile range = 2 to 10 years). In 52 cases (1.8%) SRIs occurred repeatedly. On multivariate logistic regression, factors that distinguished the recurrent sleep-related injurers from those who never had SRI in their life (n = 2,813) included male gender (OR = 2.9; 95% CI = 0.2–0.7); presence of nightmares more than once each week (OR = 3.4; 95% CI = 1.5–7.7); SRQ scored above cut-off (4/5; OR = 2.8; 95% CI = 1.6–5.2); having congestive heart failure (CHF; OR = 2.9; 95% CI = 1.1–7.2); chronic obstructive pulmonary diseases (COPD; OR = 2.2; 95% CI = 1.03–4.64); treatments with non-benzodiazepine anticonvulsants (OR = 30.5; 95% CI = 3.0–310.2) or β-blockers (OR = 2.0; 95% CI = 1.04–3.67).

Discussion: In this largest community study to-date, the prevalence of SRI is found to be relatively high. While further polysomnographic studies are instructive, a male predominance and frequency of nightmares in the cases could suggest of treatable causes like REM sleep behaviour disorder (RSBD). The formerly unreported link between SRI and CHF, COPD and the use of beta-blockers shall warrant further investigations.

P2-237

Schizophrenia-like psychosis after resection of recurrent parasagittal meningioma in an elderly epilepsy patient

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Chronic psychosis is an uncommon and serious complication of epilepsy. There are several reports on epilepsy psychosis associated to resection of some types of tumors, in particular ganglioglioma or dysembryoplastic neuroepithelioma involving mesial temporal lobe structures, such as the amygdala and hippocampus. In this study we report on an elderly patient (65 years old) with symptomatic localization-related epilepsy whom was diagnosed with a large, recurrent parasagittal fronto-parietal meningioma in the right hemisphere. Histological evaluation revealed atypical meningioma. After resection of the recurrent tumor, reduction in seizure frequency was greater than 90%. However, the patient developed a schizophrenia-like psychosis, which was characterized by paranoid delusions and persistent auditory hallucinations. Despite antipsychotic medications, the psychotic symptoms did not show improvement. Cyber knife treatment was also performed after a second recurrence occurred. The patient has good seizure-control on carbamazepine and phenytoin therapy. The fact that the psychotic symptoms were related to resection of a tumor in extratemporal regions is an interesting finding. Our finding is consistent with those of recent reports indicating involvement of the right parietal lobe, especially the inferior parietal gyrus with the development of a psychotic state in epilepsy patients. Since there was a good seizure-control and lack of epileptic discharges on the EEG, forced normalization phenomenon may underlie the

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mechanism for the development of chronic psychosis in this epilepsy patient.

P2-238

Cause of the death of institutionalized patients with psychiatric disorder at Kkottongnae sanatorium

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Purpose: Schizophrenia and other psychiatric disorder are associated with an increased risk of premature death.
Methods: We reviewed the death certificate and medical chart of the dead, who had had contact with medical service at Kkottongnae Ingok-Jae hospital between 1996 and 2004 (n = 2,381). ICD-9 was used to categorize the cause of death.
Results: The dead who had psychiatric diagnosis was 387(19.1% of All death). Cause of the death was respiratory 80(20.7), circulatory 65(16.8%), neurological 51(13.2%), infection 44(11.4%), Cancer 29(7.5%) And Accident 23(5.9%). the death from suicide was 5(1.3%). There were the differences between the dead with psychiatric diagnosis and the dead without psychiatric diagnosis. Compare to data from the dead without psychiatric diagnosis, mortality from gastrointestinal, infectious disease and accidents was high.
Conclusions: Compare to data from America and England homeless study that the death from accident was 8.7–26%(suicide 8.7–26%), Suicide cases in Kkottongnae sanatorium were very small. We should pay attention to early detection and prevention of gastrointestinal, infectious disease and accident in institutionalized patients with psychiatric disorder.

P2-239

Menopause consultation: Midwives' role in Iran

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Menopause is a natural phase of life, but transition into menopause is a major hormonal event and is associated in many women with both physical and psychosocial symptoms. A wide variety of changes are attributed to menopause and 75 percent of menopausal women experience some problems or discomfort such as: hot flashes, emotional changes and mood swings, irritability, nervousness, depression, impaired memory and concentration, fatigue, headache, insomnia, palpitations, decrease of olfactory ability, decreased libido, skin changes, dental changes, joint and muscle pain, vaginal and urinary tract changes, irregular uterine bleeding, osteoporosis, and cardiovascular disease, but only 10–20 percent seek medical help. Midwives are the first group who help women health in most societies and have an important role in the reproductive health of the community in Iran as basic coordinators between families and health centers. Their main duties are to take history, to offer care in different stages of life of a woman, and help the women in pre and postmenopausal stages. Consulting and educating women throughout life is another main duty of midwives in Iran.
Objective: To describe place of effective communication and consultation role of midwives for menopause women in Iran.
Results: Some women consider menopause as a normal life phase and a part of aging. Culture plays an important role in understanding menopause. Midwives dealing with such clients should allow them to express feelings, cry, get angry, and talk about their anxieties, mood changes. Communication and consultation role of midwives in different stages of menopause play an important role in reducing the complications of these normal phenomena. In Iran during B. Sc course, midwives learn about menopause and its complications and improve their consultation knowledge and skills during M. Sc course. Also clients enjoy entering a new phase of life.
Conclusions: Menopause is a new phase of life, which can be enjoyable by timely consulting with medical team such as an experienced midwife, which plays her role fully and properly trying to help her client in perimeopausal phase. In Iran, midwives in most governmental centers play an important role in consultation and preventing complication resulted. Change in Sex hormones in menopause may not cause major depression, but primary understanding of depression is very important in preventing it.

P2-240

Using electronic media before sleep can result in self-perceived insufficient sleep

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Introduction: Electronic media are widespread recently especially young generation. Surveys have conducted to find media caused perceived insufficient sleep in younger generation, while to our knowledge no study has revealed whether media causes sleep problems in elderly people. To screen insufficient sleeper, the difference of sleep duration between before workday and non-workday is simple but useful. Insufficient sleepers may sleep longer in non-working days to return sleep debit in free time, but counter cases were observed. We found heavier media users sleep shorter before non-workday. In this study we examine prevalence of perceived insufficient sleep in monitor members of an internet survey company. Also we examine which disparity between sleep duration they consider enough and that they actually had or disparity between that they consider enough and that they actually sleep are practical to screen insufficient sleep.
Method: We performed survey inquired sleep duration before workday, before non-workday and that they consider enough and also the survey asked the reasons they ascribed to their perceived insufficient sleep. These reasons were grouped into 5 categories.
Results: 14,121 members who received an email invitation to participate in the primary survey, 3,406 answered the questionnaire. 2,856 (82.5%) indicated that they had sleep problems. In senior subjects who are more than 60 years old, 554 of 969 (57.2%) had sleep problems. In senior subjects percentages of insufficient sleeper were increased with media use duration. We plotted receiver operating characteristic for each categories of reasons. The area under the curve (AUC) of the index of disparity between sleep duration they consider enough and that they actually had was higher than index of disparity of sleep duration between before workday and non-workday. Albeit those AUCs were not enough high.
Conclusions: In this study it was revealed long media use increase perceived insufficient sleep in not only young people but also elderly people. Because retired seniors will spend time to access media because some of them may be acquainted with computer on business, others may try to access internet for interest, it shall be important to see if they have insufficient sleep ascribed to media use.

P2-241

Relationship between nutrition and cognitive function in the elderly people

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Introduction: A meta-analysis of some studies has shown a significant relation between dementia and thin (BMI $<$ or $=$ 18) or dementia and obesity (BMI $>$ or $=$ 25) but not shown relation between dementia and overweight (BMI $=$ 23–25). However, in these study there have been very few reports. So we investigated whether how association the present nutrition status and cognitive function in the elderly people.
Methods: The subjects consisted of 100 elderly people living in Imari city Saga prefecture in Japan. Their ages ranged from 70 years at the youngest to 94 at the oldest with an average of 82 years. And this study was performed in Yamamoto Memorial Hospital and Kojima Hospital. Cognitive function was ascertained using Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR). The weight, Body Mass Index (BMI) measured by anthropometric of OMURON. Moreover 50 of the 100 subjects scaled the rate of body fat and muscle, too. Statistical analysis were performed using the statistical package Stat View. And Informed consent was obtained from all volunteers.
Results: Mean BMI was 23.4 ± 3.1 and mean MMSE score was $26.4 \pm 3.7$and mean CDR score was 0.09 ± 0.283. Mean rate of body fat was $29.9 \pm 8.9\%$. Mean rate of muscle was $26.0 \pm 3.6\%$. BMI was significantly correlated with MMSE ($r = 0.302$) and was negatively correlated with CDR ($r = -0.329$). The rate of muscle was negatively correlated with MMSE ($r = -0.337$) and was significantly correlated with CDR ($r = 0.408$). The rate of body fat was significantly correlated with MMSE ($r = 0.358$) and was negatively correlated with CDR ($r = -0.439$).
Discussion: It is suggested that overweight is associated between cognitive function in the present study.

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This fact shows that overweight maintain higher cognitive function than thin or obesity. Further detailed studies on elderly people with dementia must be made considering gender-related differences in body composition in a large number of people.

P2-242

Approach for prevention of dementia and support for people with dementia in a rural community

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Objectives: Elderly people with dementia increased remarkably, prevention of dementia is necessary. Recently it is reported that good care and circumstances for people with dementia reduced senile plaques in transgenic mice. It is very important for people with dementia to support good care and comfortable circumstances. And then, It is important for all the citizens to understand the Dementia, and to make the support network.

Therefore, we made picture book about people with dementia, and educated and communicated with school children using the picture book. We also made the SOS network with the children who had a picture book classroom.

Methods: We talked and discussed about people with dementia, with 1200 students in primary and junior high schools through group-work using the picture book. We examined understanding of students about people with dementia before and after classroom using the picture book. Moreover we followed to examine their understanding and activities of support for people with dementia to all students from the 1st grade to 3rd grade of Yoneo Junior high school.

Results: Children of 90% deepened the understanding of people with dementia, and were able to express the opinion about the supporting method. The effect to the family after the classroom was born, and moreover, the Yoneo-Junior high school especially worked on the theme of the dementia during year as a program, and held the dementia study association by the junior high school student for the family and the region. According to a follow-up survey, Students of 88% deepened the understanding still, and 70% of them performed to support in any way, for people with dementia Especially, they joined to SOS network for wondering of people with dementia.

Conclusion: In conclusion, the picture book might be useful to educate dementia and people with dementia for students. The project leads to understand dementia enough for not only children but also their family members and the citizen, and may contribute to early detection and prevention of dementia. And more we can expect the support network by children to be able to be done.

P2-243

Is ECT still useful treatment for older people with treatment resistant depression?

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Introduction: ECT remains controversial especially for older people. Critics of the treatment maintain that it is used mainly in older women who are too vulnerable to refuse and that ECT damages their brains. New Zealand has a very strong anti ECT lobby and the treatment may indeed be banned in the near future. If it is banned, will this be a major problem?

Method: This presentation is a naturalistic study of 78 older people who had ECT in Auckland, New Zealand. The patients had a variety of diagnosis and indications for ECT and a variety of modalities and techniques applied. The majority of patients had a depression rating scale (HRDS or MADRS) and a cognitive measure CAMCOG before ECT and on completion of ECT. Outcome was measured both clinically and by the patient achieving remission on the depression rating scales. In most cases, the clinical team was blind to the results of CAMCOG and the depression rating scales.

Results: Two thirds of the patients had a good outcome. For most patients, cognitive scores remained constant or increased following ECT. The presence of medical conditions did not adversely affect the results. Outcomes were worse for those patients having longer courses and use of double dose programmes.

Conclusion: ECT remains a viable and useful treatment for older people with little evidence that it is damaging to older people's vulnerable brains.

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P2-244

Cognitive assessment post elective surgery: The CAPES study. Identifying risk factors in post-operative cognitive decline

Pamela Melding[1]; Francois Stapelberg[1]; Snezana Mitrovic-Tosovic[1]; Richard Worrall[1]; Joanna Stewart[1]; Annabel Clarke[1]; Leesa Rowlands[1]; Jane Bryce[1]; Catherine Howie[1]

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Introduction: Every year, thousands of older people have major surgery. After the surgery, some notice that aspects of their memory or thinking (Cognition) deteriorate, an unexpected and unpredicted adverse event for them and their families. Cardiac surgery and acute surgery carries the highest risk; but elective surgery in otherwise well people may also have risk. Overseas studies indicate that post-operative cognitive decline (POCD) occurs in one or more cognitive aspects in 5–30% of people having elective surgery. However, these studies vary in quality and methodology. The most consistent data indicates a rate of at least 10%. This is significant, compared to the rate of overall decline in the general population, which is about 3% per year.

Risk Factors for POCD:

– Patient factors may include undetected mild cognitive impairment (MCI) or subclinical dementia. Other risk factors, may be pre-existing depression, particularly of vascular origin, or long-standing use of strong pain medications. Cerebrovascular insufficiency, diabetes, hypertension, hypotension, and cigarette smoking may also be risk factors because of their effect on cerebral circulation.

– Operative risk factors may include anaesthetic or surgical complications and post-operative delirium.

Health Significance: This study should identify patients most at risk with the aim of designing future studies to reduce the risk for POCD.

Design:

– A longitudinal, clinical study in patients over age 55, undergoing elective, joint replacement surgery.

– The patients are recruited on entry to the waiting list.

– 300 subjects recruited at two locations

– The patients are their own control.

– The assessment consists of a Depression Rating Scale (GDS), Anxiety Inventory (STAI), Cognitive Status (GP Cog), Health Status and Quality-of-Life scale,

– Cognitive Drug Research (CDR) Assessment Battery.

Progress: The study is currently about half way through. This poster explains the design of the study.

P2-245

Cognitive assessment post elective surgery: The CAPES study. Identifying risk factors in post-operative cognitive decline. Preliminary results

Pamela Melding[1]; Francois Stapelberg[1]; Snezana Mitrovic-Tosovic[1]; Richard Worrall[1]; Joanna Stewart[1]; Annabel Clarke[1]; Leesa Rowlands[1]; Jane Bryce[1]; Catherine Howie[1]

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Introduction: The CAPES study is a novel longitudinal clinical study that is currently assessing the risks for post-operative cognitive decline in older people following elective surgery. Risk factors for post- operative cognitive decline (POCD) may include undetected mild cognitive impairment (MCI) or subclinical dementia. Other risk factors, may be pre-existing depression, particularly of vascular origin, or long-standing use of strong pain medications. Cerebrovascular insufficiency, diabetes, hypertension, hypotension, and cigarette smoking may also be risk factors because of their effect on cerebral circulation. Other risk factors may include anaesthetic or surgical complications and post-operative delirium.

Design: 300 patients are recruited from the waiting list and have three pre-operative visits during the 3–6 month waiting period at which data concerning the patients medical surgical and psychiatric history is collected. The patient completes the cognitive tests on the Cognitive Drug Research battery at each visit, familiarizing them with the tests and diminishing practice effects. These control measures also gives information on the patients own natural rate of decline. After surgery the tests are repeated at 1 week post discharge, 3-months later and at one year. Perioperative data is also collected including delirium screening whilst the patient is in hospital recovering from the surgery.

Progress: The study is half-way through and preliminary data on the first 100 patients will be presented.

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P2-246

Research into mortality in the population of the patients of Municipal Institute of Gerontology, Belgrade

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Mortality in psychogeriatry has not drawn enough attention yet and in most research it is only part of a mosaic of different attitudes to the problem in this area, unfortunately not focused on properly.

Aim of the study is to estimate mortality of patients with mental disorders among the patients of Municipal Institute of Gerontology, Home Treatment and Care in Belgrade and interaction with evaluated demographic indicators (sex and age)

Design: Retrospective cross-sectional study.

The number of all deceased patients of the Institute, mortality each year and perceptual mortality of patients with severe psychological disorders (score 7+ Simon screening test) and with those ones without communication and interaction of analysed demographic factors (sex and age) were followed up in three-year period (1994–1996.) Screening test (Simon, 1968) for early detection of mental disorders, was used among newly admitted patients for assessing certain psychological functions. In our study with worsening of mental status of surveyed population (increased score achieved in Simon screening test) mortality is raised in three-year period (1994–1996.) as well as in each year. Perceptual mortality was higher in the group the old among patients with severe psychological disorders (7i+) or /and patients without communication in three-year period (1994.–1996.) as well as in each year. Opposite to the previous finding, mortality was more present in each year as well in three-year period (1994.–1996.) in the group the young old than in the group the old. Although mortality rate is doubled every 5 to 8 years, ie. it represent most obvious incidence curve dependent on ageing, our findings excludes age as the mortality risk factor from the previous finding which bring us back to the idea of increased mortality among the persons with severe psychological disorders.

Results of the research on mortality in the population of the patients of Municipal Institute of Gerontology in three-year period (1994–1996.) fit in the results of other world research; they identify a category of patients at higher mortality risk: persons with severe psychological disorders (7+) or/and ones without communication, males and older than 75.

P2-247

The brain bank for aging research project

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Background: The brain bank forms an essential infrastructure for neuroscience. However, in Japan, the institutional collection replaces the official open resource system.

Method: The Brain Bank for Aging Research (BBAR) is organized by a general geriatric hospital and an associated research institute, to store and utilize autopsy brain specimens of the hospital with the relatives' written informed consent, under the Japanese Cadaver Autopsy Act #18, in order to conquer age-associated motor and cognitive impairment. Principally half brain is frozen for biochemical and molecular studies and the other half is prepared for morphological studies. The BBAR committee reviews and approves each application for BBAR as a collaborative study, which should be supported by public funding and approved by the internal review board (IRB) of the applicant's institute. The BBAR Project includes prospective longitudinal clinical studies of dementia and parkinsonism, consisting of clinical work- ups with neuropsychiatric examinations, psychological test batteries, CSF biomarkerss, and structural (MRI) and functional (SPECT and PET: FDG, Dopamine and Amyloid) neuroimages. When these cases die, every effort is made to acquire autopsy consent to be registered to BBAR.

Results: The half frozen brains has been harvested since July 2001 and now sums up to 600 cases. All the resources are evaluated with Braak's staging system for neurofibrillary tangles and senile plaques, as well as our staging paradigm for Lewy bodies (JNEN 2003, 2004), argyrophilic grains (JNEN 2004), amyloid angiopathy, astrocytic tangles and ubiquitinated dots. All the vascular lesions were evaluated and compared with in- vivo images. Frozen small pieces of brains has been harvested since January 1995 and reach 1,700 cases. All the cases were evaluated with the stage paradigm described above and extraction of genomic DNA and apoE genotyping were completed. Glass slides and

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paraffin-embedded blocks have been accumulated since 1972 and reach 7,000 cases. All the clinical records and neuroimages are available for retrospective analysis. The BBAR now collaborates with more than 30 universities and research institutes in Japan.
Discussion and Conclusion: The resources of the BBAR, donated on the basis of a charitable spirit, belong to the public domain and are regarded as public resources to be utilized to contribute to advancing public welfare.

P2-248

Associations between agitation in patients with dementia and subjective health and job stress in care staff

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Background: Behavioral and psychological symptoms in dementia (BPSD) are important predictors of nursing home placement, and are associated with job stress, burnout and turnover in caregiver staff.
Objective: The objective of the current presentation was to study the associations between agitation in patients and job stress and subjective health complaints in care staff. Based on previous studies, theories in work, stress and health, and clinical experience we hypothesized that agitation is associated with job stress and subjective health complaint in care staff.
Methods: To measure agitation in patients we used the Cohen-Mansfield Agitation Inventory (CMAI). Severity of dementia was measured by Functional Assessment Staging (FAST). Job stress was measured with Perceived Stress Scale (PSS) and health complaints were measured with Subjective Health Complaint (SHC) Inventory.
Results: 211 patients (71% female) were included in the study: mean (SD) age 85.5, FAST 4.7 (2.1), CMAI sums core 39.9 (12.4). 197 care staff (95% female) was included in the study: Age 43.1 (12.9), and PSS sum score 22.21 (6.15). In the last four week prior to the data collection the three most frequent health complaints were back pain (62.4%), head ache (46.2%) and neck pain (45.1%). Perceived stress in care staff did not correlate with any of the CMAI items or sum score. These results remained after controlling for age, education, shift work and hours per week. However, there were significant correlations between several subjective health complaints on gastrointestinal problems ($p < 0.014$), and allergy ($p < 0.015$). These results remained after controlling for age, education, shift work and hours per week.
Conclusions: The hypothesis was only partly confirmed. There were no significant relations between experienced stress by the care staff and patient behavior. In contrast, the subjective health complaints in care staff and perceived control at work were associated with the frequency of agitation.
Keywords: Agitation, staff training, job stress, subjective health complaint, randomized controlled trial.

P2-249

CSF orexin levels in patients with neurodegenerative diseases

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Excessive daytime sleepiness has been widely accepted as a common problem not only in Parkinson's disease (PD) but also in other related disorders. Lowered excretion of orexin A (hypocretin 1) into the cerebrospinal fluid (CSF) is known to play a pathological role in narcolepsy and secondary hypersomnia due to hypothalamic dysfunction. We previously reported that CSF orexin levels in patients with PD, dementia with Lewy bodies (DLB), progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD). In this study, orexin was measured in CSF collected by lumbar puncture in 62 patients with PD, 13 patients with DLB, 19 patients with PSP, 10 patients with CBD and 60 patients with multiple system atrophy (MSA). Levels of CSF orexin (Mean $\pm$ SD pg/ml) were 302 ± 38 in PD, 297 ± 48 in DLB, 257 ± 35 in PSP, 252 ± 74 in CBD and 255 ± 30 in MSA. The occurrence of low orexin levels (< 110) was rare in all groups. However, PSP, CBD and MSA, which show wider distribution of neurodegeneration than PD, revealed significantly lower CSF orexin levels than PD. Orexin levels were inversely correlated with duration of morbidity in PSP but not in the other diseases studied. These findings suggest that

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loss of orexin neurons or impaired orexin neurotransmission might exist as a part of the neurodegeneration associated with these diseases.

P2-250

Leucine-rich α-2-glycoprotein is a potential biological marker for idiopathic normal pressure hydrocephalus

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Objectives: In the previous report, we worked on the proteome analysis of idiopathic normal pressure hydrocephalus (iNPH) patients' cerebrospinal fluid (CSF). From analysis results of proteins useful for the diagnosis of iNPH, we reported that leucine-rich α-2-glycoprotein (LRG) is markedly increased and so it is useful for the diagnosis. We are going to quantitate the LRG concentration and τ and TGF-β concentration in CSF, then comparatively review. Our objective is to establish the auxiliary diagnosis that makes the decision of the candidate for surgery for tap test negative cases and the prediction of the symptom improvement possible.
Methods: We studied 30 patients suspected clinically as iNPH according to the guidelines for diagnosis of iNPH and done tap test between June 2006 to April 2007. We comparatively reviewed the severity of iNPH, the MRI, the examination of higher cerebral functions, tap test, the existence or nonexistence of symptom improvement by shunt, LRG concentration in CSF. At the same time, we measured τ proteins in CSF as the chronic neuronal death marker by ELISA method.
Results: When LRG concentration is higher than 1000 pg/ml, it showed typical MRI features, and the tap test positive rate and the symptom improvement rate by shunt showed extremely high concentration.
Discussion: LRG showed high concentration in the cases which had typical MRI features of iNPH. By simultaneously measuring LRG and τ proteins in CSF, the prediction of the effect of surgery is possible and it makes the decision of the candidate for surgery useful.

P2-251

Prevalence of medical comorbidity in patients with dementia

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Purpose. Lifestyle diseases including hypertension, diabetes mellitus and lipid abnormality are recognized as risk factors for vascular dementia (VaD). It is recently noted that lifestyle diseases are also risk factors for Alzheimer's disease (AD) and have some effect on the progression of AD. We examined the prevalence of comorbid medical illnesses in patients with dementia.
Methods: We enrolled 64 consecutive outpatients referred to the Memory Clinic of the Department of Geriatric Medicine, Tokyo Medical University Hospital. All patients underwent general physical, neurologic and psychiatric examinations, extensive laboratory tests and computed tomography (CT) or Magnetic resonance imaging (MRI) and single photon emission CT (SPECT). The diagnosis of AD was based on the NINCDS-ADRDA criteria. The diagnosis of mild cognitive impairment (MCI) was based on the criteria by Petersen et al. We examined the prevalence of cormobid medical illnesses in patients with cognitive impairment.
Results: Of the 64patients, 15patients were excluded from this study because of depression, subdural hematoma, normal cognitive function. 49 patients with cognitive impairment consisted of 33 patients with AD, 16 patients with MCI, 10patients with other dementia. Across 49 patients with dementia or MCI, 41% had three or more comorbid medical illnesses, 47% had hypertension, 50% had lipid abnormality.
Conclusions: Since patients with dementia have a lot of medical comorbidity in our Memory Clinic, generalized management should be performed in the treatment and care of dementia.

P2-252

Pathological features of the Gallyas- and Tau-positive glia in the amyotrophic lateral sclerosis and parkinsonism-dementia complex of Kii peninsula of Japan

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Objectives: We report the widespread occurrence of Gallyas-positive and τ-immunopositive inclusion in the glial cells of central nervous system in patients with Kii ALS/PDC, in order to clarify whether or not Kii ALS/PDC is same spectral disease of Guam ALS/PDC.
Materials and methods: Seven autopsied brains and five spinal cords from seven Kii ALS/PDC patients (two PDC, three ALS, and two ALS/PDC) were submitted for the present study. The paraffin-embedded specimens were prepared for Gallyas-Braak staining and were stained with several anti-human τ antibodies, in sections of the frontal and temporal lobes, precentral gyrus, basal ganglia, thalamus, midbrain, medulla oblongata, and spinal cord.
Results: There were numerous argyrophilic threads and some grains, and various types of glial inclusions were observed by light microscopy. Particularly, we observed many granular hazy and crescent/coiled inclusions those had been reported by Oyanagi et al. in Guam ALS/PDC patients. In addition, there were a small number of tufted astrocytes or thorn-shaped astrocytes.
Conclusions: Glial inclusions of Kii ALS/PDC were almost similar to those of Guam ALS/PDC.

P2-253

Clinical database for dementia of the National Center for Geriatrics and Gerontology

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Purpose: The purpose of the present research is to produce a clinical database for dementia.
Introduction: As the population ages, it is very important to overcome this disorder. To follow up clinical courses, to evaluate treatment, and to perform clinical trials, it is essential to gather and follow up clinical data.
Results: 1. Database for dementia of the NCGG. This database consists of 11 items: a. basic patient information and history, b. physical examinations c. neurological examinations, d. psychiatric problems, e. comprehensive geriatric assessment f.. neuropsychological examinations g. neuroimaging, h. biochemical examinations. i. cerebrospinal fluid j. treatment k. support for discharge. It is important to control the quality of the database. If users do not have the same concepts for diagnosis and criteria, the database would not hold good. To avoid this crisis, it is necessary to hold conferences and meetings frequently. 2. Ethical aspects. Five problems exist in the construction of a database for dementia and osteoporosis: 1; restrictions on persons who can access the database 2; administration of safety of database, 3; restrictions on other researchers making offer of database 4; responding to open data system, correction, suspension of use 5; complaints. It is important that we progress with the study while giving special consideration from the standpoint of the subject.

P2-254

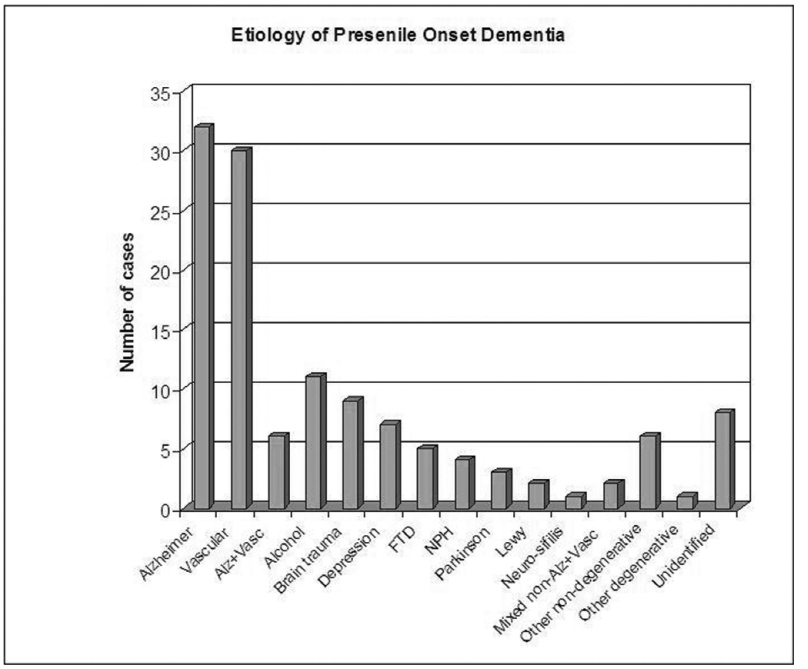
Proteomic analysis of microvessels of CADASIL brain

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CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is a familial vascular dementia that is linked to missense mutations in the Notch3 gene. One of the pathological hallmarks is the accumulation of GOM (granular osmiophilic material) between the degenerating vascular smooth muscle cells. However, the molecular mechanism of CADASIL doesn't understand at all. It is important to identify the accumulated molecule relating to the vascular degeneration. Then, we have attempted to analyze the protein in the microvessels of CADASIL brain. The CADASIL brain and the control brain were homogenated, and the microvessels were purified by the glass bead column. The microvessels were solubilized with RIPA buffer, Urea/Thiourea, and the formic acid. Each of the fractions was digested with the trypsin, and was analyzed with nanoLC/MS/MS. In the RIPA buffer and Urea/Thiourea soluble fractions of the CADASIL microvessels, we found that several heat shock proteins increased compared with that of the control microvessels. In case of the formic acid soluble fraction of the CADASIL, several collagens and spectrin beta increased compared with that of the

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P2-255

control, whereas alpha 1 actin decreased. These results correlate to the results of immunohistochemical approach well. It is possible that the microvessels of CADASIL brain is exposed to the stress such as protein misfolding.

P2-255

Presenile onset dementia in a tertiary care outpatient clinic

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Presenile onset dementia (PSOD) poses many challenges to physicians due to its diverse and complex etiological issues and to family members and caregivers due to changes in family dynamics. Researches on PSOD are encouraged since they may help diminish misdiagnosing and bring out strategies to meet this population's specific needs. The objective of this research was to study the occurrence and clinical features of PSOD in a specialized tertiary care outpatient clinic. The authors reviewed medical files of 125 patients with dementia syndromes with onset before the age of 65 years attended in the Behavioral Neurology Outpatient Clinic from 1996 to 2006. They represent 35.1% of all dementia cases in that 10-year period. The most frequent causes were Alzheimer's disease (AD) (25.6%), cerebrovascular disease (24.0%), alcoholism (8.8%), brain trauma (7.2%), and depression (5.6%). Potentially preventable and/or reversible (PREV) dementias accounted for 24.8% of cases. Age of onset ranged between 17 and 64 years and the number of cases increased as age advanced. There was a tendency for cases of vascular dementia (earliest onset case 31 years old) be younger than AD (earliest onset case 42 years old) at the onset of symptoms. All three cases of dementia with onset before the age of 30 were related to brain trauma. Two out of 32 pure AD cases were familial autossomal dominant not related cases. The time elapsed between symptoms onset and admission in the specialized service ranged from less than one a year to 11 years (mean of 2.5 $\pm$ 2.18 years). As for senile onset dementia, AD and vascular dementia were the

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most prevalent, although the proportion of AD cases was much lower in this sample of PSOD. PREV dementias accounted for almost a quarter of the total, a proportion which is higher than that for the overall dementias. Our data provide information on PSOD in a specialized outpatient clinic, which may be useful for the understanding of some peculiar aspects of dementia in a presenile population.

P2-256

Profile of dementia cases attending a city hospital in India

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Dementia patient's number in psychiatry o.p.d clinic in a Calcutta city mental hospital constitutes about 3.5% of total patients registered in one calendar year 2005. A total of 58 patients was clinically diagnosed as suffering from dementia as per ICD-10 diagnostic criteria. There were 28 female and 30 male. Age distribution was 62 to 84 years with a median average of 73 years. Only 40% patient could provide with a radio-imaging confirmation, mainly CT scan of brain and 2% MRI scan of brain due to paucity of funds and lack of facility in govt. mental hospital. Majority 52% was brought by spouse, 25% brought by their children (mainly sons).12% was brought by other family members. 5% pt's were referred by police or judiciary and the rest were brought by different agencies. Lack of memory and judgement, confusion and incontinance of urine and feaces were main presenting complaints. Etiological or type of dementia analysis shows over 65% are suffering from Alzheimer's disease, 22% were affected by vascular dementia, 10% from mixed vascular and Alzheimer's features, there was one case of Lewy body dementia in a 71 years female with fully developed Parkinson's disease and dementia with fluctuating cognitive function, visual hallucination and urinary incontinance. One case was an AIDS dementia with a positive +HIV (ellissa test) in a male who later developed acute confusinal state or delirium. Care giver profile was excellent as majority 88% were treated at their own houses. Only 10% received an institutional whole day caring. 2% only is being looked after in a NGO home. No dementia care home exists in any part of the city with a population of over 10 millions and an estimated number of dementia in elderly is no less than 250000. They were grouped into catagory 1) no external support 60% and 2) with minimum support 20% and 3) needing active support for less than 3 hours a day and4)very much supportive care needed for more than 3hours a day–only 5%. one year follow up and associated co-morbidity was also studied.

P2-257

Psychiatric symptoms, cognitive impairment and functional status in chronic schizophrenic and demented old patients

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Objectives: We try to assess the cognitive impairment, functional status and psychiatric symptoms in two groups of elderly patients with diagnosis of chronic schizophrenia and dementia and study the correlations between these variables.

Materials and methods: The sample we assessed included all inpatients of the units of our psycogeriatrics department. N total = 219; men 41 women 178 with mean age 77.8 ± 9.8 (41–96) years old, Dementia group: N = 82; men 26 women 56, mean age 78.3 ± 11.9 (41–96) Schizophrenia group: N = 137; men 15 women 122, mean age 77.6 ± 8.45 (51–96). We have analysed demographic, social and clinical data, reviewing all diagnosis and assessing psychiatric symptoms using BPRS for schizophrenia patients and NPI for dementia patients. All scales were administered by authors.

Results: Schizophrenia group N = 137; men 15 women 122, mean age 77.6 ± 8.45 (51–96), hospitalization years mean 35.3 ± 19.9. BPRS mean 35.4 ± 14.2 (2–68). MMSE mean 16.9 ± 7.7 (0–30). Barthel 73.1 ± 21.5 Dementia group: N = 82; men 26 women 56, mean age 78.3 ± 11.9 (41–96), hospitalization mean 4.4 ± 2.3 years. NPI mean 35.3 ± 25.7 (0–96). MMSE mean 8.48 ± 7.3. Cornell scale mean 9.7 ± 6.9 (1–29) Barthel 34.9 ± 29.7. Comparison between groups1- The MMSE scores are lower in dementia group comparing with schizophrenia group, although there is a big difference in hospitalization time between these groups (schizophrenia 35,5 years vs. dementia 4,4 years) 2 – Even though the median time of hospitalization of schizophrenia group is much longer than the dementia group, the functional status measured by Barthel index in schizophrenia group is quite good and much better that functional status of

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demented patients (schiz. 73.1 ± 21.5 vs dementia. 34.9 ± 29.7). The cognitive status of schizophrenia group (MMSE mean 16,9 ± 7,7) is much poorer than cognitive status of similar age healthy people. 3 – In our study group the cognitive impairment correlates with functional impairment. 4 – Even knowing that BPRS and NPI are different instruments, both measure psychiatric symptoms in our sample. The median score of both instruments are not very high, but there are very important individual differences [BPRS mean 35.4 ± 14.2 (2–68) and NPI mean 35.3 ± 25.7 (0–96)]. In our definitive study we analyze and discuss widely the correlations between the different variables studied.

P2-258

E-JUR-94013: a nutraceutical compound with immunomodulatory effects in the elderly

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E-JUR-94013 is a biotechnological product extracted from the marine species T. Trachurus. Its high lipoprotein content (70–85%) displays a modulatory activity on the human immune system. The aim of this study has been to determine the effects of E-JUR ingestion on several immunological parameters. In an elderly population (205 subjects, 68.41 years old as a mean value), the white cells of blood samples were analysed before and after the ingestion of 1500 mg per day of E-JUR for three months. The cell number and percentage of each white cell subpopulation were determined and classified into different subgroups. In subjects with leucocytosis (over $10.5 \times 10^2/\mu$), the number of leucocytes decreased by 26.09%. When leucocyte number was below $4.5 \times 10^3/\mu$, E-JUR-94013 increased leucocyte number by 19.75% ($p < 0.001$). Neutrophilia (over 70%) was corrected with a 35.47% of decreased ($p < 0.05$), and neutropenia ($p < 40\%$) was normalized with an increased of the neutrophil percentage by 25.74% ($p < 0.01$). E-JUR-94013 was also effective on lymphocytes, reducing lymphocytosis (over 40%) by 4.77% and improving lymphopenia ($< 20\%$) by 39.33% ($p < 0.05$). In cases of monocytosis (plus than 10%), the percentage of monocytes decreased by 4.67%, and when the percentage of monocytes that was lower than 4%, E-JUR-94013 induced a 90.97% increase ($p < 0.05$) on monocyte percentage. In eosinophilia (higher than 4.5%), eosinophils decreased by 32.16% ($p < 0.05$) and in eosinopenia (over 1.5%), eosinophil percentage increased by 55.96% ($p < 0.05$). Changes in basophil percentage was also significantly improved ($p < 0.05$). Ig E levels decreased a 8.54% and Ig M increased by 2.17%; Ig A and Ig G levels were significantly increased by 11.32% and 9.74% ($p < 0.05$), respectively. These results clearly show the powerful effects of E-JUR-94013 on BWC and Ig in elderly people with immunological faulty.

P2-259

Case study on a schizophrenic patient complicated with dementia-Focusing on the intervention by occupational therapist

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It is not unusual for schizophrenic patients who developed dementia to be treated in usual clinical settings for dementia, which results in problems with violent conducts. In some cases those patients with schizophrenia and dementia are forced to be cared in isolated rooms due to their violence. Violence, however, may be repeated by isolation. Further, dementia may be deteriorated with decrease in physical ability due to isolation. Since the patient with schizophrenia and dementia is equipped with higher physical ability than other dementia patients, we introduced ADL training to a patient with schizophrenia and dementia to prevent decline in physical ability and secondary impairment of ADL. The study of the clinical record of the patient reveals the relationship between the decrease in violence and the change in psychiatric evaluation in the group, which might be the characteristics of the schizophrenic patients complicated with dementia.

P2-260

Preventive measures and fact finding research on senile dementia and depression in the cold climate

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We live indoors for about six months in the snowy cold region. Moreover, the duration of sunshine is short, we must spend time indoors when it is cloudy, and there are snow storms. So the people with senile dementia and the ratio of sickness among the aged who experience seasonal depression in the evenings during winter is very high. On one hand, the group homes are increasing in recent years. On the other hand many people still live at home with their family or live alone. This is a part of the result of the investigation on the patients suffering from depression and the preventive measures for winter depression. The outline of the report is as follows: 1. The appearance of the ratio of depression, anxiety disorder, incidence of mental disease like paranoia, syndrome of twilight in the evenings, etc. 2. Correlation between problem behavior such as depression, and anxiety disorder with symptom of cataract. 3. The Chinese and the Japanese like bright red and vermillion colors compared to other races. How are people using these colors as preventive measures? Example: furniture, interior decoration goods, fabrics, table cloth and curtain, bedding and nightclothes, utensils, etc. 4. Attached to the traditional architectural design, why Japanese aged people like Japanese style interior corresponding to their age. Example: Natural soil, sand tatami mat, bamboo and wooden finishing materials, etc. 5. The spread of the aromatherapy using various fragrances to stabilize the mental condition. Could the effect of stabilizing the mental condition be expected at the nursing site and in daily life? 6. Has the wandering action been observed and an architectural space designed for rehabilitation made for winter? I grope for the possibility of preventive measures taken for the mental health and the brain before the medical treatment by a physician.

P2-261

Characterization of therapeutic antibody against Aβ bloomers for Alzheimer's disease

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Several lines of evidence may indicate that memory loss represents a synaptic failure caused by soluble amyloid β (Aβ) oligomers. The use of the antibody targeting to Aβ oligomers should be a straightforward immunoprotective therapy for Alzheimer's disease (AD). Thus we have generated monoclonal antibodies specific to Aβ oligomers. Among them, monoclonal 2C3 specifically recognizes more than 5-mer but not monomer as determined by Native-PAGE and size exclusion chromatography. With this 2C3, antitoxic activity was tested in differentiated PC12 cells, and antifibrillogenic activity was evaluated by thioflavin T assay and electron microscopy. The monoclonal not only neutralized Aβ42-induced toxicity, but also inhibited Aβ42 fibril formation. Both activities were observed at less than 1:25$\sim$50 molar ratio of 2C3-to-Aβ, indicating that oligomeric 2C3 conformer is present at lower concentrations. Importantly, the presence of 2C3 conformers, SDS-stable 4-, 5-, 8-, 12-mer, were confirmed in AD brain via 2C3 immunoprecipitation. In human entorhinal cortices at Braak NFT stages I-III, the accumulation of 12-mer precedes the appearance of cognitive impairment, and increased as Braak NFT stages progress, suggesting that 12-mer is conformational assembly responsible for *in vivo* neurotoxicity. We also found that oligomeric 2C3 conformer is present in CSF, and is increased in AD patients. Our results strongly suggest that the monoclonal 2C3 is a promising candidate for therapeutic antibody that is able to immunoneutralize neurotoxic Aβ oligomers.

P2-262

Quantitation of amyloid β protein in cerebrospinal fluid from patients taking various statins in comparison with control subjects

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Epidemiologic studies have reported that persons taking statins have decreased risk of Alzheimer's

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disease (AD). In addition, statins were reported to decrease amounts of amyloid β protein (Aβ) in vivo. To investigate effects of statins on Aβ in human brain, we quantified Aβ species in cerebrospinal fluid (CSF) from patients taking various statins in comparison with CSF from control subjects.

Subjects included 25 patients taking various statins who had hyperlipidemia as well as neurologic disease, and 26 neurologic patients without hyperlipidemia who did not take statins. Aβ 40 and Aβ 42 species in CSF specimens from these two groups were differentially assayed by sandwich enzyme-linked immunosorbent assay (ELISA). Prescribed statins included pravastatin in 14 patients, simvastatin in 3, and atorvastatin in 8.

Concentrations of Aβ 40 and Aβ 42 in CSF did not differ significantly between groups with and without statins. Some subjects in both groups also took corticosteroids, which did not appear to alter Aβ species concentrations in CSF. Statins have pleiotropic effects including cholesterol-lowering, anti-inflammatory, anti-oxidative, and antithrombotic actions. To clarify whether or not statins could suppress development and progression of AD, randomized controlled trials are necessary in addition to more basic studies concerning relationships between the pathogenesis of AD and the pleiotropic effects of statins.

P2-263

Snapshots of Amyloid-beta 1–42 conformers by human antibody-displaying phage library

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Active species of Aβ assemblies have been a discussion in AD. It has been reported that a specific Aβ protein assembly with around 56 kDa in the brain impairs memory (Nature, 440, 352–7, 2006) and that the globular Aβ42 oligomer is a homogenous and stable neuropathological protein in AD (J. Neurochem. 95, 834–47, 2005). Clearance of Aβ represents a potential therapeutic approach. Antibody-mediated clearance of Aβ by vaccination inhibited and cleared Aβ deposition in animals, however, inflammatory side effects caused by primed T cells were observed in humans. An alternative potentially noninflammatory approach to facilitate clearance is administration of human antibody against Aβ peptide (Nature Med., 8, 1263–9, 2002). In this study, we attempted to isolate the Aβ conformation-specific antibodies by direct reacting a human antibody-displaying phage library. We characterized the binding specificity of phage clones and scFvs by ELISA. In the result, these clones have three distinct specificities, i.e., 1) scFvs with predominant binding activity to fibrillar Aβ42, 2) scFvs with binding activity to both globulomer and monomeric Aβ42 and 3) phage clones with predominant binding activity to globulomer Aβ42. Particularly, B6 showed a fine specificity to a conformation of fibrillar Aβ42. Epitope analysis shows that the B6-binding site locates at the region of β2 sheet of C-terminus of Aβ42. B6 inhibited the Aβ fibril formation in a dose dependent manner, but they showed no inhibitory activity on globulomer formation, suggesting that fibrillation may be distinct from oligomelization.

P2-264

A new therapeutic agent for Alzheimer's disease: Modulation of reactive astrocytes by arundic acid (ONO-2506) reduces amyloidogenesis in Alzheimer transgenic mice

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Alzheimer's disease (AD) is the most common dementing illness and is pathologically characterized by the presence of intracellular neurofibrillary tangles and extracellular senile plaques primarily composed of β-amyloid (Aβ) peptides. We have shown that astrocyte-derived S100B was able to promote the amyloidogenic pathway as well as

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inflammatory responses in human astrocytoma U-373 MG cells, raising the hypothesis that S100B may be involved in the progression of AD. Moreover, we have shown that arundic acid (ONO-2506), which is known to negatively regulate astrocyte synthesis of S100B, inhibits the amyloidogenic pathway and inflammatory responses in U-373 MG cells. The above evidence raised the therapeutic possibility that ONO-2506 may attenuate AD pathology. Thus, we examined the prophylactic effects of ONO-2506 on brain Aβ and S100B levels in aged transgenic mice overproducing amyloid precursor protein (Tg APP_{sw} mice, line 2576). ONO-2506 was administered to Tg APP_{sw} mice for 6 months from 12 months of age and the effects of the agent on the above parameters were examined. ONO-2506 treated-Tg APP_{sw} mice showed significant reduction of both 0.15% SDS-soluble and 5M guanidine-soluble $A\beta_{1-40}/A\beta_{1-42}$ levels along with S100B levels in brain homogenates compared to vehicle treated-Tg APP_{sw} mice. Based on the above results, ONO-2506 deserves further exploration as a promising therapeutic agent for AD.

P2-265

A new therapeutic agent for Alzheimer's disease: Arundic acid (ONO-2506) attenuates cerebral amyloidosis and gliosis in Alzheimer transgenic mice

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Like microglia, reactive astrocytes produce a myriad of neurotoxic substances in various brain pathologies such as Alzheimer's disease (AD), trauma, and cerebral ischemia. Among the numerous products of reactive astrocytes, attention has recently been directed towards the possible detrimental role of S100B, because the protein has been shown to be highly expressed along with the progression of brain damage and to exert neurotoxic effects at high concentrations. The present study aimed to examine the possible role of astrocyte-derived S100B in the progression of cerebral amyloidosis and gliosis in transgenic mice overproducing amyloid precursor protein (Tg APP_{sw} mice, line 2576). For this purpose, arundic acid (ONO-2506), which is known to negatively regulate astrocyte synthesis of S100B, was perorally administered to Tg APP_{sw} mice for 6 months (from 12 months of age) and the effects of the agent on the above parameters were examined. Here, we report that β-amyloid deposits as well as β-amyloid plaque-associated reactive gliosis (astrocytosis and microgliosis) were significantly ameliorated in ONO-2506-treated relative to vehicle-treated Tg APP_{sw} mice at 19 months of age. These data thus bolster the view that pharmacological modulation of S100B-associated astrocytic activation by ONO-2506 may confer a novel therapeutic strategy against AD.

P2-266

Inhibition of amyloid beta fibrillation and formation of soluble amyloid oligomers by molecularchaperone

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Since the amyloid beta (Ab) aggregates are the cause of Alzheimer's disease, studies on its formation mechanism is important to develop the methods for prevention and treatment of Alzheimer's disease. In this report, we studied the effect of a molecular chaperone, prefolding (PFD) from Pyrococcus horikoshii OT3 on Ab aggregation. Lyophilized Ab peptide (2 mg/ml) was dissolved in HFIP. The solvent was then dried using a spin-vacuum system, and stored in −80 deg. The HFIP-treated peptide was dissolved in distilled water by vortex. After sonication, 1 mM peptide solution was diluted to 50 uM in PBS buffer with or without 50 uM PFD, and incubated at 50 deg. Transmission electron microscope (TEM) observation and Western blotting analysis showed that the soluble oligomeric (3–50 mer) Ab particles (typically about 10 nm in diameter) were produced by incubation with PFD, while fibrillar aggregates were produced in the absence of PFD. The cytotoxicity of Ab aggregates against PC12 cells (rat pheochromocytoma cells)

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was measured by MTT method and terminal deoxynucletidyl transferase-mediated biotin-dUTP nick end labeling (TUNEL) method. The Ab soluble oligomer formed by the incubation with PFD exhibited higher toxicity than the fibrillar aggregates without PFD. This finding is consistent with the recent results that soluble oligomers, the intermediates of amyloid fibrillation, have higher toxicity than amyloid fibril. We also confirmed that the Ab soluble oligomer induced apoptosis. Our data suggest that PFD recognizes these toxic soluble oligomers and prevents further fibrillation.

P2-267

Memantine monotherapy versus donepezil monotherapy for treatment of female patients with moderate to severe Alzheimer's disease

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Background: Cholinesterase inhibitor donepezil and N-methyl-aspartate (NMDA) antagonist, memantine are widely used for treatment of Alzheimer's disease.
Objective: This study compared the therapeutic effect of donepezil and memantine for treatment of female patients with moderate to severe Alzheimer's disease.
Methods: Thirty nine female patients with moderate to severe Alzheimer's disease were divided with two groups. Two groups were treated with donepezil (N = 11) monotherapy and memantine (N = 28) monotherapy for 12 weeks. They were assessed by Korean version of Mini-Mental State Examination (MMSE-K), Clinical Dementia Rating(CDR), and Global Deterioration Scale(GDS) before and after the treatment.
Results: There was no significant differences between two groups in pretreatment and posttreatment MMSE-K, CDR, and GDS scores.
Conclusions: Our results suggests that memantine monotherapy is effective as much as donepezil monotherapy for treatment of female patients with moderate to severe Alzheimer's disease.

P2-268

Omega-3 supplementation in mild to moderate Alzheimer's disease: Effects on neuropsychiatric symptoms

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Background: Epidemiological and animal studies have suggested that dietary fish or fish oil rich in omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), may have effects in psychiatric and behavioral symptoms in Alzheimer's disease (AD). An association with APOEϵ 4 carriers and neuropsychiatric symptoms in AD have also been suggested.
Objective: To determine effects of dietary omega 3 supplementation to AD patients with mild to moderate disease on psychiatric and behavioral symptoms, daily functions and a possible relation to APOEgenotype.
Methods: Randomized, double-blind, placebo-controlled clinical trial where 204 AD patients (74 ± 9 years) with acetylcholine esterase inhibitor treatment and a MMSE > 15 points were randomized to daily intake of 1.7 g DHA and 0.6 g EPA (omega 3 group) or placebo for 6 months. Then, all received the omega 3 supplementation for 6 more months. Neuropsychiatric symptoms were measured with Neuropsychiatric Inventory (NPI) and Montgomery Asberg Depression Scale (MADRS). Caregivers burden and activities of daily living (Disability Assessment for Dementia, DAD) were also assessed.
Results: 174 patients fulfilled the trial. 72% were APOEϵ 4 carriers. No significant overall treatment effects on neuropsychiatric symptoms, on activities of daily living or on caregivers burden were found. However, significant positive treatment effects on the scores in the NPI agitation domain in APOEϵ 4 carriers ($p = 0.006$) and in MADRS scores in non-APOϵ carriers ($p = 0.005$) were found.
Conclusions: Supplementation with omega 3 in patients with mild to moderate AD did not result in

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marked effects on neuropsychiatric symptoms except for positive effects on depressive symptoms (assessed by MADRS) in non-APOE ϵ 4 carriers and agitation symptoms (assessed by NPI) in APOϵ4 carriers.

P2-269

Evaluation of switching strategy with donepezil in the treatment of patients with mild-to-moderate Alzheimer's disease: Impact of previous exposure to acetylcholinesterase inhibitor on cognitive function

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The aim of this study is to evaluate the switching strategy with donepezil through the assessment of the impact of previous exposure to acetylcholinesterase inhibitor (AChEI) on cognitive function in the treatment of patients with Alzheimer's disease (AD).

Of seventy patients screened for this 26-week, single-blind comparison study, forty-five patients were recruited for intent-to-treat (ITT) population and then were classified into two groups, namely, Naive group (n = 33) and Switched group (n = 12), depending on the history of previous exposure to other AChEI. All ITT population satisfied the diagnostic criteria of probable AD according to the National Institute of Neurological and Communicative Disorders and Stroke – the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) and had to achieve a Korean version of Mini-Mental state Examination (K-MMSE) score of 10 to 26 points inclusive. Primary cognitive outcomes were measured by using Korean version of cognitive subscale of Alzheimer's Disease Assessment Scale (ADAS-cog-K) and K-MMSE. Secondary cognitive outcome measure was response rate at 26-week point of treatment. ITT-LOCF (Last observation carried forward) analysis method was adopted to compare therapeutic results between the two groups at baseline, 4 weeks, 13 weeks, and 26 weeks of treatment.

There were no significant between-group differences in the response rate of donepezil (63.6% for naive group vs. 33.3% for switched group; $\chi^2 = 3.27$, df = 1, p = 0.070) and also in adjusted change on ADAS-cog-K (Z = −1.67, p = 0.095) and K-MMSE (Z = −1.94, p = 0.051) at the point of 26 weeks of treatment. However, the results showed a modest tendency of unfavoring switching strategy with donepezil in the treatment of patients with AD.

This study showed that previous exposure to other AChEI does not have significant impact on cognitive function in the treatment, with donepezil, of patients with mild-to-moderate AD. However, further studies are necessary to replicate these findings and scrutinize switching strategy with donepezil.

P2-270

Therapeutic communication: Animal assisted therapy for elderly Japanese dementia patients

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Researchers theorize that Animal Assisted Therapy (AAT) may have a positive effect on people suffering from symptoms of dementia. Earlier work by this researcher found that elderly people showed improved emotional well-being after long term AAT sessions. This research, a work in progress, describes the effects of AAT on institutionalized dementia patients in Japan, adding to the little existing data describing detailed communication between people and dogs.

The purpose of this research was to describe the communication between dementia patients and a dog, in their initial AAT sessions.

The subjects consisted of four elderly residents of a special care unit for dementia at a private psychiatric hospital in a northern Japanese city. Three subjects were female, and one subject was male. The subjects were visited by volunteers who brought a small Toy Poodle dog. The activity studies were part of an Occupational Therapy program. The AAT session lasted 60 minutes, consisting of three components; about 10 minutes of discussion, about 40 minutes of communication with the dog, followed by about 10 minutes of discussion. The four subjects were seated around one table and two volunteers placed the dog on the table. The subjects were then

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able to freely feed, hold and play with the dog. Volunteers and staff helped and guided each subject in their interactions with the animal. In this research, only the first five minutes of each of the three component parts of the AAT session have been analyzed in minute detail. The University Ethics Committee of the researcher approved this project before initiation.

The communication of each subject was compared and broken down by video observation for; utterances, supplying a topic, expression and behavior. For the initial five minutes, subjects were unrelaxed. During the communication with the dog, subjects watched the dog and exhibited interest, according to the behavior observed. In the final five minutes, smiles were observed and subjects showed quick responses when talking about their communication with the dog.

Comparing the initial component with what followed, a positive effect was observed, as evidenced by the subjects natural, relaxed, vocal and physical response to the dog, as well as smoother interaction with volunteers by the subjects. The session was considered to have promoted dementia patients to respond spontaneously.

P2-271

Do cholinesterase inhibitors improve the subtle negative personality changes in Alzheimer's disease? A prospective study

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Personality changes negatively with the onset of Alzheimer's disease (AD), however research into the impact of anti-dementia drug treatments on personality change is limited and based on retrospective reports. This study aimed to extend current knowledge by prospectively examining the effect of cholinesterase inhibitors on personality in AD over 6 months. Carers of 33 newly diagnosed patients with AD who were starting cholinesterase inhibitor treatment completed Brooks McKinlay Personality Inventory reflecting four different time points: before diagnosis of AD; after diagnosis but prior to treatment; 3 months after initiating treatment; and 6 months after initiating treatment. Patients with AD [mean (sd): age = 79 (7.6) years; pre-treatment Mini Mental State Examination, MMSE = 21.0 (4.0)] were treated with therapeutic doses of donepezil (n = 18), galantamine (n = 13) or rivastigmine (n = 2). Personality scores became more negative after the onset of AD, as shown by a reduction in the total positive personality score ($p < 0.001$). After treatment, the total positive personality score significantly increased at both 3 months ($p < 0.001$) and 6 months ($p < 0.01$) reflecting an improvement for 87% of patients after 3 months, and 85% after 6 months of treatment. The majority of patients showed stability or improvement on all individual traits, with the greatest improvement in emotional stability. Other behavioural and psychological symptoms of dementia (Neuropsychiatric Inventory, NPI) and the severity of cognitive impairment (MMSE) were not predictive of the improvement on the personality inventory. These results suggest that cholinesterase inhibitors may have a beneficial effect on subtle negative personality changes in AD. The commonly used scales to assess behavioural and psychological symptoms may not capture these personality changes.

P2-272

Ginkgo biloba for mild to moderate dementia in a community setting: A pragmatic, randomised, parallel-group, double-blind, placebo-controlled trial

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There is a need for safe, cheap and effective treatments for dementia which can be used in the early stages of the disease. Ginkgo biloba is a herbal medicine which has generated much interest; however its benefits remain unclear.

We conducted within a UK population a community-based, pragmatic, randomised, double-blind, parallel-group trial where participants were

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given a standardised extract of Ginkgo biloba (120 mg daily) or a placebo control for six months. Our primary outcomes were cognitive functioning (ADAS-Cog) and participant and carer-rated quality of life (QOL-AD). The main analysis was Intention to Treat using multiple imputation techniques for the missing data.

We recruited 176 participants, mainly through general practices. In the ANCOVA model with baseline score as a co-variate (n = 176), Ginkgo did not have a significant effect on outcome at six months on either the ADAS-Cog score (p = 0.392), the participant-rated QOL-AD score (p = 0.787) nor the carer-rated QOL-AD score (p = 0.222). Analyses with evaluable data and per protocol showed similar results. A total of 63 adverse events were recorded (29 in the placebo group, 28 in the Ginkgo group).

We found no evidence that a standard dose of high purity Ginkgo biloba confers benefit in mild-moderate dementia over six months. The recruitment shortfall means a type II error is a possibility, although no trends were detected in the data. Based on our findings, Ginkgo is unlikely to confer benefit of any clinical significance and the implication of this is that we do not recommend its use in routine dementia care.

P2-273

Therapeutic activities significant to the Chinese elders with Dementia in Hong Kong

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Background: The loss of ability to perform the activities of daily living (ADL) and instrumental activities of daily living (IADL) in elders with dementia has been shown to be a manifestation of the decline in cognitive function. Participation in the activities which have once been enjoyable and meaningful to the elders will become more and more limited as the dementia progresses. While functional training has been suggested by some studies to be an appropriate rehabilitation strategy for the elders, identification of the activities significant to them or facilitative for their participation was rarely addressed. The purpose of this study is to identify the major ADL and IADL which are significant to the elders with dementia and are practicable for conduction in the homes for the aged in Hong Kong. The main objective is to develop a list of activities for use in the functional rehabilitation of the elders with dementia in Hong Kong.

Method: The list of activities was developed through three main stages. A panel of experts, who were occupational therapists experienced in working with elderly patients, was formed and a co-ordinator was identified to organize the whole course of work. The process was started with a focus group meeting among the panel of experts for soliciting a list of ADL and IADL that the Hong Kong elders commonly regarded as significant. In the second stage, questionnaires with this list of activities were sent out to the staff working in homes for the aged. The purpose was to invite their feedback on the significance of the activities on the list to the elders and the practicability of implementing the activities in the homes for the aged. Upon summarizing the feedback by the co-ordinator, a second focus group meeting among the panel of experts was held for consensus of opinions and finalization of the list of activities.

Result: 23 sets of feedback were collected from the 30 questionnaires sent out and interviews conducted. 21 ADL and IADL were identified as the activities significant to the elders with dementia and practicable for conduction in the homes for the aged in Hong Kong.

Conclusion: The list of activities developed can serve as an aid to workers if significance of the activities to the elders and practicability for conduction are the essential considerations in the rehabilitation process.

P2-274

Three-year outcome of Galantamine treatment in Alzheimer's disease in a routine clinical setting

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Background: Alzheimer's disease (AD) is the major cause of dementia in the elderly. AD is characterized by a progressive loss of cognitive and practical abilities. Multiple double blind, placebo controlled studies have shown beneficial effects of galantamine treatment on cognition and function in the short-term. What to expect in long-term treatment in a routine clinical setting has not been investigated.
Objectives: To describe and evaluate the three-year outcome on cognition (MMSE, ADAS-cog) and global rating (CIBIC) of galantamine treatment in Alzheimer's disease (AD) in a routine clinical setting.
Methods: The Swedish Alzheimer Treatment Study (SATS) is an ongoing open, longitudinal, multicenter study evaluating cholinesterase inhibitor (ChEI) treatment in AD. Patients are investigated at baseline, at 2 months and every 6 months for a total period of three years. Here we present the three-year outcome for the first 143 patients receiving galantamine in SATS.
Results: At baseline the mean (±SD) age of the patients was 72.5 (±8.1) years, the MMSE score 23.1 (±4.3) and the ADAS-cog score 17.2 (±9.0). The MMSE mean change was above the baseline level for more than a year. After three years of treatment the total mean decline from baseline in MMSE-score was 2.2 (±3.7) points. The ADAS-cog rise after three years was 4.5 (±8.4) points, significantly better ($p = 0.001$) than the score predicted by the Stern equation 7.3 (±4.6). After three years of treatment 42% of the patients were considered unchanged or better in the global rating (CIBIC). At this time 51% of the patients remained in the study.
Conclusions: Long-term galantamine treatment in a routine clinical setting resulted in a positive effect in cognitive tests compared to historical controls and mathematical models. After 3 years of treatment a positive global outcome was observed in more than 40% of the patients. Dropout was less than expected.

P2-275

Effects of donepezil on neuropsychiatric symptoms in patients with mild to moderate Alzheimer's disease: A 6 month open trial

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Object: The present study aimed to evaluate the effect of donepezil as an only treatment for AD patients with neuropsychiatric symptoms
Method: This study was a 26week prospective, open-labeled study with donepezil. patients with mild to moderate AD with neuropsychiatric symptoms at baseline (Neuropsychiatric Inventory [NPI] > 5 points) were treated with donepezil 5 mg daily for 4 weeks followed by 10 mg daily for a further 22 weeks. Treatment effects were evaluated on behaviour using the Neuropsychiatric Inventory (NPI); on cognition using the Korean version-Mini Mental State Examination (K-MMSE) and Alzheimer's Disease Assessment Scale-cognitive-preliminary Korean version (ADAS-cog-K); on function using the Seoul-Instrumental Activities of Daily Living Scale (S-IADL)Efficacy measurements were conducted at baseline and at weeks 26Results: The overall NPI improved significantly from 16.16 to 12.19 ($p = 0.014$) over the 26 weeks of therapy with donepezil, the particularly in subscales of agitation/aggression, depression/dysphoria. There was no significant change in the scores on K-MMSE, ADAS-cog-K, S-IADL.
Conclusions: The result of this study suggest that donepezil reduces behavioral symptoms, particularly agitation/aggression and depression/dysphoria, in patients with mild to moderate AD.

P2-276

The efficacy of memantine in moderate-to-severe dementia patients in Korea: The comparison of the efficacy in patients of Alzheimer's disease and mixed dementia

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The purpose of this study was to examine clinical efficacy of Memantine in moderate-to-severe dementia patients and to compare clinical efficacy in treating patients with Alzheimer's disease (AD) and Mixed dementia in Korea. This study included 32 patients (male = 13, female = 19) with the diagnosis of AD (N = 19) or Mixed dementia (N = 13). Only patients with scores of less than 15 on the Korean version-Mini Mental State Examination (K-MMSE) were participated. Primary efficacy

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measure was the Korean version-Severe Impairment Battery (K-SIB), and secondary measures included the K-MMSE, Seoul-Activities of Daily Living (S-ADL), Neuropsychiatric Inventory (NPI). All the patients were evaluated before the treatment and at the 12th, 24th week. The result showed that all the patients who were treated with Memantine did not show significant cognitive deterioration for 24 weeks. The total K-SIB score and the total K-MMSE score were maintained and were not significantly different from the baseline after 24-week treatment. Similarly, the total S-ADL score remained constant up to 24 weeks, and the total NPI score did not significantly increased for 24 weeks of the treatment, indicating no clinical functional impairment and behavioral problems. Also, there were no significant differences between patients with AD and patients with Mixed dementia in terms of cognitive deterioration, daily functional impairment, and behavioral problems; the total scores of K-SIB, K-MMSE, S-ADL, and NPI were not significantly different from the baseline after the treatment. Additionally, the result indicated that approximately 37% of the patients with AD and 46% of the patients with Mixed dementia were responding to Memantine. This study suggested that Memantine treatment had the efficacy of slowing clinical deterioration of cognitive functioning, daily functioning, and behavioral problems in patients with moderate-to-severe dementia, regardless of being subclassified as AD or Mixed dementia.

P2-277

Effectiveness of group cognitive treatment for the elderly with mild to moderate Alzheimer's disease in Taiwan

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Background and purpose: To prevent regression of the cognitive function in older people with Alzheimer's disease (AD), plenty studies with cognitive treatment or cognitive training have conspicuous outcomes. Ryuta Kaeasdhima (2006) indicates that utilizing simple materials, reading and arithmetic exercises could activate the function of prefrontal lobe. However, there are cultural differences in practical applications of these approaches. In this way, the authors adopted similar approaches according to our cultural background, trying to observe the effectiveness of group cognitive treatment with local social/cultural elements.

Methods: Subjects with mildly to moderately severe Alzheimer's disease participated the study. In experiment group, 12 subjects aged between 65 and 85 were enrolled, and 75% of them were illiterate. They received weekly group cognitive treatment for one year. Each session lasted for fifty minutes with utilization of simple materials, reading simple texts and arithmetic exercises matched with Chinese culture. Another 13 subjects at similar stages were selected as control group. All of patients are assessed with MMSE at baseline, middle and the end of the study. All data were computed with packed software SPSS for Windows.

Results: Average MMSE scores in the experiment group is maintained in the stable range (from 15.42 ± 4.77 to 15.58 ± 5.42, $F = 0.027$, $p > 0.05$); however, the other group is declined gradually (from 16.62 ± 4.89 to 15.38 ± 4.57, $F = 5.13$, $p < 0.05$). The result shows that group of the cognitive treatment is effective in the patient with mild to moderate stages of AD.

Conclusions: The study verifies that group cognitive treatment is effective and applicable to the patient with mild to moderate AD. It is accordance with the study of Kaeasdhima (2006) by utilizing simple materials could improve cognitive function. In conclusion, group cognitive treatment may have protective effect on the cognitive functions in the patients with mild to moderate AD.

P2-278

Association between metabolic syndrome and cognitive impairment in the elderly

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To determine the association between metabolic syndrome (MS) and cognitive impairment (CI) in the elderly.

Design: Cross-sectional study.

Methods: Two thousand four hundred and twenty-seven individuals were evaluated. CI was defined according to performance on the Mini-Mental State Examination, and MS was determined according to World Health Organization criteria. Multivariate

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logistic regression analysis examined the association between MS and CI, adjusting by potential confounders. Prevalence of MS was 22.7% (553) and of CI was 21.3% (518). In comparison with those without CI, those with cognitive impairment were older ($P < 0.001$), lees educated ($P < 0.001$), and had an elevated prevalence of MS ($P = 0.024$); in addition, this subgroup had more depressive symptoms ($P < 0.001$), more delirium ($P < 0.001$) and consumed more benzodiazepines ($P = 0.016$). Logistic regression analysis showed that MS is independently and significantly associated with CI even after adjustment for age, sex, depressive symptoms, and use of benzodiazepines (OR adjusted 1.45; 95% IC 1.046 to 2.035; $P < 0.025$). There were no interactions between MS and CI or with other variables. **Conclusions:** There is a significant and independent relationship between MS and CI. This result has potential implications for the development of evidence-based health promotion interventions. This provides preliminary evidence showing the interest of reinforcing the strategies towards risk factor modification in relationship with the MS this could have an impact on slowing down the serious consequences of cognitive impairment on elderly people's autonomy. Nevertheless, a longitudinal design is needed to verify the direction of the association between both entities. Longitudinal data is being obtained in the same cohort.

P2-279

Brain optical topography patterns in stroke, vascular encephalopathy and migraine

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Cerebrovascular disorders are characterized by a reduced blood flow in the brain which contributes to poor brain perfusion. The elderly have the highest risk to suffer these pathologies. With the increase of life expectancy, stroke and other age-related diseases are major problem of health in developed countries, and prevention will be essential to delay or avoid these pathologies. We have evaluated the difference among migraine, vascular encephalopathy and stroke in brain hemodynamics by using Optical Topography (OT). OT measures relative changes in tissue concentration of oxy-Haemoglobin, deoxy-Haemoglobin and Total-Haemoglobin in the surface of the cerebral cortex by beaming near-infrared light. We have investigated the activation of the occipital cortex in response to photic stimulation in controls subjects and in patients with, migraine, vascular encephalopathy or stroke. The stimulus used was a white light of 50 Hz placed at 130 cm from the patient.

Subjects: Controls: $N = 20$; age: 52.30 ± 14.92 years (range: 18–72 years); migraine: $N = 16$; age: 46.93 ± 11.84 (range: 25–73 years); vascular encephalopathy: $N = 28$; age: 67.33 ± 13.77 (range: 35–89 years); stroke: $N = 11$; age: 55.40 ± 13.96 (range: 35–75). According to our results, there are differences among subjects with cerebrovascular disorders and controls on brain hemodynamics as assessed by OT. Stroke and vascular encephalopathy exhibit a positive effect in response to stimulation with high individual variability; however, migraine shows a poorer response similar to the pattern observed in the general population. OT is becoming a novel diagnostic procedure to evaluate cerebrovascular disorders with direct or indirect impact on brain oxygenation.

P2-280

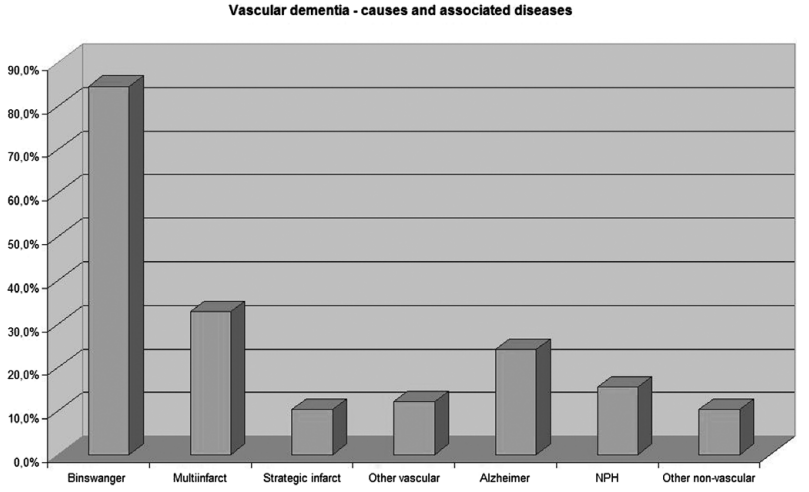
Vascular dementia in a tertiary care outpatient clinic

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Cerebrovascular disease is the second most prevalent cause of dementia both in populational and casuistry studies. Besides the high prevalence of vascular dementia (VaD), its importance lies on the fact that most cases have potentially treatable causes. This study aimed at describing clinical and imaginological features of patients with diagnosis of vascular dementia attended in the Behavioral Neurology Outpatient Clinic of a teaching hospital. We studied 58 patients (65.5% men), age range 40–90 years (mean age 68.9 ± 10.1). Of all cases, 51.7% were "pure" VaD, 24.1 VaD associated with Alzheimer's disease, 6.9% associated with

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P2-280

other degenerative diseases and 20.7% with non-degenerative diseases. In 65.5% of all cases, there was a single vascular cause even when other non-vascular diseases were associated with. Binswanger's disease (BD) was found in 84.5% of all the cases, multiinfarct in 32.8%, single strategically located infarct in 10.3% and other causes in 12.0%. In "pure" VaD, mean Fazekas' score was 4.2 ± 1.3 and mean Wahlund's score was 16.2 ± 5.5. When BD was the single cause (n = 12) of VaD, mean Fazekas' and Wahlund's scores were respectively 3.9 ± 1.2 and 14.9 ± 3.8. Vascular dementia is of common occurrence in specialized outpatient clinic both isolated and associated with other dementing diseases. BD was the most frequent cause in this casuistry, with relatively high severity of white matter changes.

P2-281

Discussion of dominant brain in vascular dementia of internal thalamic infarction – Comparison of two cases of various-side internal thalamic infarction –

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Background: If internal thalamic infarction occurred bilaterally or in dominant-brain side, it results in acute-onset dementia with cortical symptoms like motor aphasia and mutism. Damage of fornix and thalamo-mamillary tract as components of Papetz circuit located in anterior internal nucleus of thalamus produces amnesia. Hypersomnia in our case is due to internal-medullary lamina damage.
Methods: Neuro-psycholgical findings, HDS-R, MRI, EEG-power-spectral analysis were discussed. Case 1 was 62-year-old man. He admitted three days after delirium. Delirium disappeared at once, but mutism and disorientation of place continued permanently. HDS-R was 12. T2WI of MRI revealed left internal thalamic infarction. EEG power-spectral analysis gave us local-decreased frequency at left-middle frontal lobe. Case 2 was 32-yaer-old man. He could not wake up in the express train and had been sleeping for three days after admission. Memory of his three days was lost completely and movement of his left extremities was clumsy. HDS-R was 25. He got full recovery after a month. T2WI of MRI revealed right internal thalamic infarction. Result of EEG-power-spectral analysis was local-decreased frequency at right-middle frontal lobe.
Conclusions: Case 1 was dominant-brain internal thalamic infarction produced dementia. Case 2 was non-dominant-brain case resulted in full recovery. Damage of neural projection from internal-thalamic nucleus to frontal lobe introduced the local-decreased frequency of EEG-power-spectral analysis at same-side frontal lobe likely as the past study of SPECT.

P2-282

γ-Secretase inhibitors DAPT and L-685,458 perturb Wnt signaling

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To inhibit Aβ production is a major therapeutic target for Alzheimer's disease. γ-Secretase inhibitors suppress intramembrane proteolysis producing Aβ. However, γ-secretase blocking activity causes serious side-effects, since they usually inhibit sequential endoproteolysis of Notch receptors. Wnt, as well as Notch, is a crucial signaling pathway for differentiation. Both Notch and Wnt signaling cooperatively regulate differentiation of squamous cells in small intestine. In addition, γ-secretase inhibitor is known to affect the differentiation. Therefore, we asked direct effect of γ-secretase inhibitor on Wnt signaling.

First, we tested the effects of γ-secretase inhibitors DAPT and L-685,458 on Wnt signaling in cultured cells. Wnt signaling was assessed by modified luciferase reporter genes. The cells transiently transfected with reporter genes were treated with γ-secretase inhibitors and then measured luciferase activity of the cell lysate. Overexpression of Wnt1 or the presence of LiCl activated the reporter genes. Surprisingly, DAPT and L-685,458 significantly reduced both Wnt1- and LiCl-induced Wnt signaling. Next, to analyze whether γ-secretase activity involved in Wnt signaling, we used the cells expressing dominant negative form of presenilin which had no γ-secretase activity. However, dominant negative presenilin did not inhibit both Wnt1- and LiCl-induced Wnt signaling. These results suggest that the inhibitions of Wnt signaling were independent of γ-secretase activity of presenilin.

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