SES18.03

BIPOLAR PERSONALITY DIMENSIONS AND THE CHOICE OF MOOD STABILIZERS IN LONG-TERM TREATMENT

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That bipolar temperamental dimensions could predict response to mood stabilizers is a provocative possibility about which there is little solid data from control trials. In this presentation I will summarize clinical considerations which make this approach attractive. The most consistent associations between temperament and bipolar types or course patterns are: 1) cyclothymic and bipolar II and rapid-cycling course; 2) depressive temperament and dysphoric mania; 3) hyperthymic temperament and recurrent or chronic mania. The first and the second have clinical evidence for better response to divalproex; the third one is notorious for mood stabilizer compliance and is often treated with depot neuroleptics. Carbamazepine seems to work best in the absence of bipolar family history. Lithium, by contrast, seems to work best in bipolar family positive euphoric manic states without inter-episode dysfunction, i.e., presumably without temperamental disturbance. Lithium augmentation of antidepressants tends to work in individuals with pseudo-unipolar depressions arising, according to our clinical observations, from the substrate of sunny or hyperthymic temperament. Extremely dysphoric irritable, hostile patients with depressive dips (considered "borderline") tend to respond thus to carbamazepine, divalproex, and lamotrigine; however, there is some data that hostility per se in these patients might respond to lithium. In brief, these clinical ideas need to be tested empirically.

SES18.04

PERSONALITY DIMENSIONS AS PREDICTORS OF TREATMENT OUTCOME IN AFFECTIVE DISORDERS

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Background: Previous evidence from many quarters has indicated that people with both anxiety and depressive disorders who also have personality disturbance have a worse outcome than those with no personality abnormality. This was investigated more closely in a 12 year prospective study of 210 patients with DSM-III panic disorder, generalised anxiety disorder and dysthymic disorder.

Design: Randomised controlled trial of drug treatment, cognitive and behaviour therapy and self-help for 10 weeks followed by treatment in similar 'mode' wherever possible for next two years. Follow-up of as many as possible of original cohort after 12 years. Premorbid personality status recorded using the Personality Assessment Schedule (PAS)(Tyrer and Alexander, 1979) at baseline, with classification by personality severity as well as type (Tyrer and Johnson, 1996).

Results: 203 (97%) of original sample followed up. 17 had died. There was no difference between the proportions of those who had died with regard to initial personality status. Significantly worse outcome was shown in those with baseline personality disturbance and this was greater for those with more severe personality disorders.

(1) Tyrer, P. & Alexander, J. (1979) Classification of personality disorder. *British Journal of Psychiatry,* **135,** 163–167.
(2) Tyrer, P. & Johnson, T. (1996) Establishing the severity of personality disorder. *American Journal of Psychiatry,* **153,** 1593–1597.

SES18.05

TREATMENT OF SOCIAL PHOBIA: THE ASSOCIATION OF PERSONALITY AND AFFECTIVE SYMPTOMS

P. Bech

No abstract was available at the time of printing.

S54. Functional brain imaging: the future for psychiatry

Chairs: R.M. Murray (UK), P.K. McGuire (UK)

S54.01

THE PATHOPYSIOLOGY OF FORMAL THOUGHT DISORDER

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Formal thought disorder (FTD) is one of the core features of schizophrenia. However, little is known about its functional-anatomical correlates. In a series of experiments with functional Magnetic Resonance Imaging (FMRI), schizophrenic patients with and without FTD and healthy controls were investigated, using language perception and production paradigms. In a first set of experiments, subjects read sentence stems out aloud and had either to complete it in a meaningful way or choose between two words that made sense. A reading condition served as a baseline. In a second set, Rorschach inkblots were presented and subjects asked to speak about them, while echoplanar images were acquired. The utterances were recorded, the phenomenology of FTD was analysed and related to the BOLD effect. The neural correlates of the rate of articulation, positive and negative TD, usage of peculiar words and sentences were analysed using event related and correlational analysis. Our data showed, that schizophrenic patients with FTD differ fundamentally in the differential activation of the right and left superior temporal gyrus. The pathophysiological correlates of single symptoms, such as neologisms could be isolated for the first time and phenomena, such as 'conctretism' explained. The results are in line with findings in brain lesioned patients and neuropsychological experiments in controls as well as structural imaging studies in schizophrenia that linked FTD to abnormalities in the superior temporal gyrus. A theory that links these and other findings will be outlined.

S54.02

USING PET TO STUDY DOPAMINE RELEASE IN VIVO

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Theoretically, PET has the potential to detect neurotransmitter release in vivo associated with behavioural and pharmacological challenges if sufficient endogenous neurotransmitter is released to cause appreciable change (via receptor occupancy) in the number of 'available' receptors targeted by a radioligand. Increasing evidence suggests radioligand displacement by pharmacological manipulation of endogenous neurotransmitter release can be detected in vivo. For example, dosing human subjects with d-amphetamine, which

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releases dopamine, results in decreased 11C-Raclopride or 123I IBZM binding to striatal dopamine D2 receptors. This pharmacologic challenge methodology has recently been applied by research groups to patients with schizophrenia, depression and Parkinson's disease. The detection of dopamine release by behavioural manipulation, however, is relatively unexplored. In vivo techniques in animals suggest dopamine release may occur during behavioural paradigms involving motor learning, novelty, stress and reward. Our recent studies have attempted to index dopamine release as a result of behavioural manipulations in man. For example, using a dual scan approach with 11C-Raclopride subjects (n = 8) were studied playing a video game involving motor learning, novelty and reward. Compared to a baseline condition, the striatal binding potential of 11C-Raclopride was significantly reduced (mean change ventral striatum −13%) during the video game condition (ANOVA F7.72, P < 0.01) suggesting that dopamine had been released. Furthermore, there was a significant positive correlation between performance on the game and 11C-Raclopride displacement which was greatest in the ventral striatum (r = 0.86, P = 0.017). These results suggest this cognitive challenge methodology may enable the neurotransmitter correlates of specific cognitive processes to be described.

S54.03

FUNCTIONAL ANATOMY OF AUDITORY HALLUCINATIONS

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We used functional MRI to examine the neural correlates of 1) cognitive processes putatively relevant to auditory hallucinations, and 2) auditory hallucinations themselves. Images were acquired on a 1.5T system and analysed using nonparametric methods. In study 1, patients with schizophrenia who had a history of frequent hallucinations were compared with volunteers. Images were acquired while subjects imagined another person's speech, which entails the implicit generation and monitoring of inner speech. Volunteers engaged a network of areas including the inferior frontal and temporal cortex bilaterally, the SMA, cingulate cortex, and the cerebellar cortex. Patients prone to hallucinations differed from controls in showing attenuated activation in the lateral temporal cortex and fusiform gyrus/cerebellum. Study 2 employed a within-subject event-related design, comparing activity in patients with schizophrenia when they were and were not experiencing auditory hallucinations. Hallucinations were associated with activation in a network that resembled that engaged during imagining speech, except that there was an absence of activation in the SMA and cerebellum, but additional activation in the left parahippocampal cortex, and in the right thalamus and inferior colliculus. These data suggest there is a close relationship between auditory hallucinations and inner speech, and are consistent with the notion that hallucinations represent inner speech which has been misidentified as 'alien' due to defective verbal self-monitoring.

S54.04

A SYSTEM MODEL OF ALTERED CONSCIOUSNESS: INTEGRATING NATURAL AND DRUG-INDUCED PSYCHOSES

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Introduction: Hallucinogenic 5-HT2A agonists (e.g. psilocybin) and dissociative NMDA antagonists (e.g. ketamine) produce psychotic symptoms, cognitive and behavioural deficits associated with schizophrenic psychoses. Hence, exploring the biological mechanisms of psychotomimetic drug actions may provide new insights into the pathophysiology of schizophrenias.

Method: The effects of racemic, S- and R-ketamine and psilocybin on brain activity was investigated in healthy human volunteers using FDGPET and psychometric measures (n = 51). In addition, the effects of the atypical antipsychotic clozapine and the 5-HT2A antagonist ketanserin on S-ketamine- and psilocybin-induced metabolic alterations and behavioural changes were investigated (n = 2 × 10).

Results: Both ketamine and psilocybin produced a marked prefrontal activation and metabolic changes in associated limbic, temporal and parietal regions, and in the basal ganglia and thalamus, pretreatments with clozapine significantly reduced ketamine-induced fronto-limbic hyperactivity and behavioural effects, while ketanserin completely blocked psilocybin-induced metabolic and behavioural changes. A pixel-by-pixel covariance analysis (SPM96) revealed that different psychotic syndromes relate to different neural networks including fronto-parietal, temporal, striatal and thalamic structures.

Conclusion: The results indicate that limbic cortico-striato-thalamic pathways may be a common neural substrate of psychotomimetic drugs and that disturbances within these pathways may result in a deficit thalamic gating which in turn may lead to a sensory overload and psychosis.

S55. Depressive disorders in women

Chair: D. Moussaoui (MA)

S55.01

DEPRESSION IN TUNISIA: ANOTHER GENDER INEQUALITY?

S. Douki. *Tunisia*

No abstract was available at the time of printing.

S55.02

POST-PARTUM DEPRESSION: A PROSPECTIVE STUDY

D. Moussaoui. *Morocco*

No abstract was available at the time of printing.

S55.03

PMS/PMDD: DIAGNOSIS AND TREATMENT

M. Steiner. *Canada*

No abstract was available at the time of printing.

S55.04

PREMENSTRUAL IN THE GENERAL POPULATION: AN EPIDEMIOLOGICAL STUDY

N. Kadiri. *Morocco*

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