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Recent Memory Impairment in Unilateral Temporal Lesions

Four cases of temporal lobectomy are presented to illustrate the type of memory defect which may occasionally follow such lesions.

The amnesia is characterized by severe impairment of recent and little involvement of remote memory.

The explanation of the rarity of this complication is discussed.

The anatomical basis would seem to be local cortical, possibly hippocampal, damage rather than interruption of afferent or efferent tracts from the medial temporal structures.

(Author's Abstr.)

Studies on Effect of the Injection of Alumina (Aluminum Oxide) Cream into the Basal Ganglia

A standardized preparation of alumina (aluminum oxide) cream was injected into various subcortical nuclei in 16 monkeys, in amounts known consistently to produce seizures when placed on the motor cortex.

The animals were observed and serial electroencephalograms recorded, employing pentylenetetrazol U.S.P. (Metrazol) activation over a period of from 5 weeks to 14 months (average 7 months).

There were no spontaneous seizures. Eight animals developed spontaneous electroencephalographic alterations, and four demonstrated some increased sensitivity to pentylenetetrazol-induced seizures.

On histological study the lesions were found to lie in most of the principal basal ganglia and thalamus.

(Authors' Abstr.)

Depressive Affect and Endocrine Functions

The mean hydrocortisone levels of depressed patients are elevated as compared with levels for normal controls. Protein-bound iodine levels are also elevated, but not significantly.

In general, the more emotional distress the patient is undergoing, the higher the hydrocortisone level. There is a significant relationship between those patients who are suffering intensely, are retarded, and unable to cry, and those who are less depressed, agitated, and crying. The hydrocortisone levels parallel this relationship, the most intensely depressed and retarded group having distinctly higher levels than the less depressed group.

A correlation matrix of the first occasion is presented to demonstrate existing relationships among subgroups of the study.

The multiple correlation indicates that (*a*) the variable of psychomotor retardation, or inhibition of crying, may be used for the prediction of elevated hydrocortisone levels, and (*b*) when protein-bound iodine levels are predicted, multiple factors should be used for weighting the prediction.

On the subsequent occasions of testing the ratings of depression, hydrocortisone and PBI levels fall. However, this was not true of the EST group, and an explanation is suggested for the relationship of function of the adrenal cortex and the thyroid in depression.

(Authors' Abstr.)

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Effects of Induced Hyperthermia on Some Neurological Diseases

A series of 100 subjects, 16 normal persons and 84 patients with neurological diseases, were immersed in water at 104 to 110°F. and observed for neurological changes.

There were 2 instances of tetany, manifested by carpopedal spasm, hyperactive reflexes, and a positive Chvostek sign, and 1 instance of decreased grip strength in the 16 normal subjects who were immersed.

Each of the 12 patients who had multiple sclerosis developed neurological changes, which occurred more frequently and, in general, at a lower elevation of body temperature than in patients with other diseases of the nervous system.

The appearance and disappearance of neurological signs often paralleled the rise and fall of body temperature in patients with multiple sclerosis, but changes occasionally occurred without any elevation in body temperature.

Because patients with multiple sclerosis can develop serious neurological dysfunction on exposure to heat, they should avoid excessive heat, especially hot baths.

Of a group of 72 patients with diseases of the nervous system other than multiple sclerosis, 40 showed significant neurological changes. These were the development of, or intensification of, nystagmus, in 24 patients; appearance of visual field changes, in 4 patients; change in the ankle jerk, in 10 patients; decrease in grip strength, in 10 patients; appearance of seizures, in 3 patients; change in the plantar response, in 3 patients, and decrease in visual acuity, in 2 patients.

Mental changes were observed in both the intact and the patient groups, but more frequently in the latter, and especially so in patients with multiple sclerosis.

Nine of twelve patients with multiple sclerosis developed the syndrome of dysfunction of the medial longitudinal fasiculus. Six of these had predominance of nystagmus in the abducting eye prior to the appearance of other parts of the syndrome. Such changes were not seen in the 72 patients with other diseases of the nervous system.

Nine patients with multiple sclerosis developed nystagmus or showed an intensification of pre-existing nystagmus; five showed a decrease in visual acuity; one showed a decrease in grip strength, and one developed a change in the plantar response. Such changes were also seen in 40 of a group of 72 patients with other diseases of the nervous system.

(Authors' Abstr.)

Narrowed Attention

A psychiatric, psychological, and social study of 45 randomly selected and representative surgical patients 65 years and over is reported.

1. Deterioration of mental capacity progressed in 11 cases during their hospital surgical treatment. The following aetiologic factors were significant:

(*a*) Patients of 70 and over were more liable to progression of mental deterioration.
(*b*) The acute brain syndrome or delirium preceded chronic deterioration in seven cases.
(*c*) Antecedent anxiety, depression, and severe emotional disturbances were associated with later deterioration in nine patients.
(*d*) Patients who had lost an accepting and comfortable home environment were more liable to deterioration.

2. Depression of a disabling kind appeared in 22 of the total 45 cases. This affect was forced by a complex combination of psychodynamic factors, including perception of lack of capacity to resist everyday stress, hostility and guilt, perception of defect in body image, loss of self-esteem, impairment of ability to remain active, and threat to self-preservation.

3. Projection and paranoid ideation were significant psychopathologic phenomena in nine cases. Principally, this reaction occurred in response to the real or imagined indifference of those persons significant to the elderly patient.

4. Two over-all responses of the aged to surgery are described, the reactions of "renewal" and "depletion". Renewal is intended to characterize a self-concept of repair, hope, and freedom to continue activity and a capacity to invest affect outside the individual. Depletion is intended to characterize an awareness or half-awareness of a sense of personal deterioration, with lessened capacity to meet stress and a need to draw resources inward, to withdraw, and to mobilize for self-preservation. It is theorized that the psychodynamic effect of the reaction of depletion has pathophysiologic consequences.

(Authors' Abstr.)

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Lysergic Acid Diethylamide (LSD-25) Antagonists

The effect of 1-methyl-d-lysergic acid diethylamide (MLD-41) has been studied in the Siamese fighting fish and in man.

MLD-41 affects both the Siamese fighting fish and man similarly to LSD-25 (d-lysergic acid diethylamide). However, there are important differences; in the fish it is about one-tenth as effective as LSD-25, and in man the threshold of response is two to three times as high. In the non-psychotic test group studied, the threshold was approximately 70 μg when taken orally.

Tolerance development to LSD-25 was achieved by administering MLD-41 for five to six days before administering LSD-25. The experiments reported indicate that approximately 100 μg. of MLD-41, administered with increasing doses to 350 μg. on the last day, protects against 100 μg. of LSD-25 taken orally.

BOL-148 (2-bromo-d-lysergic acid diethylamide) produces tolerance to LSD-25, but the effect for equal weights is much less, approximately one-third that of MLD-41.

The implication of the rapid and effective development of tolerance to LSD-25 by MLD-41 is considered in relationship to a chemical theory of the schizophrenias and the possibility of therapy if the chemical theory is validated.

(Authors' Abstr.)

MARCH

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Studies with Ceruloplasmin and a New Hallucinogen

A recently synthesized atropine-like compound, N-ethyl-3-piperidyl benzilate, induced altered feeling states, visual and auditory hallucinations, and increased serum ceruloplasmin in seven of nine patients.

Infusion of four pyrocatechol amines—epinephrine, levarterenol, isoproterenol, and serotonin—appeared to have no effect *per se* on serum ceruloplasmin. Iproniazid, an amine-oxidase inhibitor, was likewise ineffective.

Serum ceruloplasmin undergoes small, but significant, increases during psychiatric disturbances of neurotic type and proportions, and decreases by a similar amount during periods of tranquility.

(Authors' Abstr.)

Urinary Excretion of Some Products of Tryptophan Metabolism in Schizophrenic Patients

A chromatographic method for the qualitative determination of hydroxylated products of indole metabolism is described. The method is applied as a pilot study of the urinary excretion of hydroxylated indoles in schizophrenic and non-schizophrenic subjects. Results

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indicate that a hydroxylated indole or tryptophan derivative which does not appear to be either 5-HIAA or 5-HTA is deficient or in low concentration in the urine of schizophrenics. Additional control measures and quantitative techniques must still be employed before the observed differences can be properly evaluated.

(Authors' Abstr.)

APRIL

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Relation of Emotional Responses and Changes in Plasma Hydrocortisone Level after Stressful Interview

The present report has attempted to investigate the relationship between emotional response and the plasma level of hydrocortisone under the impact of a stressful interview. Two major areas of psychological-endocrine interaction were examined: (1) the effect of emotional response and (2) the effect of the psychological stimulus on the change in the hormone level. The degrees of increase in anxiety, anger, depression, and a combined affect rating were found to be significantly and linearly related to the change in the plasma hydrocortisone level. This relationship was maintained even though the affect change was rated for only a short time period. It would appear that the plasma level of hydrocortisone is increased by any type of emotional arousal. However, data were presented which indicated a particularly striking effect when anxiety of a disintegrative nature was developed in the course of the stress interview. Stimulus-hormone relationships were also found to occur, but these relations were generally less striking than response-hormone relations. The stresser's attitude and his total stimulus intensity rating tended to parallel the change in plasma hormone level. A significant stimulus-hormone relationship occurred when the stimulus produced a relatively intense emotional response in the subject. The findings presented are of special interest because this experiment included only a moderate range of emotional responses. The limited data available on more extreme responses suggest that an even greater degree of adrenocortical activation occurs.

(Authors' Abstr.)

MAY

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Memory Deficit Produced by Bilateral Lesions in the Hippocampal Zone

Bilateral removal of the hippocampus and hippocampal gyrus in man produces loss of recent memory. As soon as he has turned his attention to something else, the patient is unable to remember what was happening a moment earlier. It is as though he had made no record of present experiences. He also had a retrograde memory loss that covers a considerable period before operation.

This is a confirmation of the suggestion of Glees and Griffith, based on the evidence of autopsy study of a patient with bilateral brain lesions. "The suggestion is made", they wrote,

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"that the hippocampal formation of the adult seems to be essential for recent memory". In their case, as well as in the authors' cases, the hippocampal gyrus was destroyed along with the hippocampus.

Psychological study of the authors' patients shows that, in spite of the above-noted deficiencies, memory for the distant past is not lost, nor is there corresponding loss of attention, concentration, reasoning ability, or previously acquired skills. The intelligence quotient shows no drop when compared with pre-operative testing. There is no interference with speech, and the memory of words is unimpaired.

It may be concluded that an essential part of the recording mechanism is contained in the hippocampal zone. Certainly, also, another part of the mechanism lies in the central integrating circuits of the brain stem, circuits that have duplicate connections with the two hippocampal areas.

These conclusions are based largely on the post-operative study of four patients in whom this distressing complication appeared. Two of the patients were found to have this defect after unilateral excisions had been carried out in the treatment of temporal lobe epilepsy, the contralateral hippocampal zone apparently having been injured by incisural herniation at birth. Two patients were added, for the authors to study, in whom bilateral hippocampectomy had been carried out by Dr. William Scoville, in his search for a better operation to replace frontal lobotomy, as a treatment for hopeless psychotics. The symptom complex was identical in all four.

This case analysis was undertaken originally because of remorse that two of the patients should have suffered a complication. It is a severe handicap to them, although both continue to earn their living, which had been threatened by the frequency of their pre-operative cerebral seizures. But the study, which was intended primarily to serve as a warning so that others, as well as the authors, might avoid this pitfall, has opened up new and exciting evidence.

Neurosurgeons who hope to cure temporal-lobe seizures by removal of one anterior temporal lobe and all of the hippocampal zone should bear in mind that the squeezing of the baby's head at the time of birth, which produces temporal herniation and incisural sclerosis, may occasionally destroy the hippocampal zone on one side and injure that zone on the other. Thus the major epileptogenic discharge may be on the side of the less severe injury. Removal of the zone on that side might then be expected to result in this loss of recent memory. Such a loss is what occurred in the two cases that have been reported.

The authors have carried out careful psychological study of more than 90 other patients before and after the same unilateral operation, and they showed no evidence of general memory loss. Under normal conditions one hippocampal area duplicates the work of the other and carries on when one is removed.

For the time being, in order to guard against such memory losses, we have adopted the policy that when the initial electroencephalographic study points to independent abnormality in both inferior temporal regions, no removal should be made of either hippocampal zone.

The analysis of this complication of recent memory loss, undertaken as a neurosurgical project, has thrown welcome light on the location of some portion at least of the ganglionic record of current experience. It has demonstrated that this record is anatomically separate from the neurological mechanisms that are related to words, skills, and concepts that have been previously acquired.

(Authors' Abstr.)

Effect of Hypothalamic Lesions on the Amygdala Syndrome in the Cat

In the cat the "amygdala syndrome" does not appear after bilateral ablation of the amygdaloid complex if there has been previous destruction of the ventromedial hypothalamic nuclei or the mammillary bodies; and the amygdala syndrome, once produced by the amygdala ablation can be abolished by the hypothalamic lesions. Examples of lesions and theoretical considerations are included.

(Authors' Abstr.)

Studies in the Effect of Lysergic Acid Diethylamide (LSD-25)

Under the influence of lysergic acid diethylamide (LSD-25), for both normals and schizophrenics, there is a significant increase in the perceived size of one's own body and its parts, and no significant change in the perceived size of external objects. These findings are interpreted in terms of the assumption that LSD operates as a primitivizing agent, which is assumed to lessen the definiteness of the boundary of the body in relation to the surroundings.

(Authors' Abstr.)

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Parkinsonism, Schizophrenia and Ataractic Drugs

The appearance of the neurological symptoms of parkinsonism in ataraxic patients is usually regarded as an undesirable "side-effect". The true significance of parkinsonism, however, becomes evident when its psychological symptoms are also taken into account. While these characteristic mental signs—bradyphrenia and emotional indifference—are probably closely related to the therapeutic effect of the ataractic drugs it is believed that the neurological symptoms of parkinsonism are not undesirable in themselves. They may require specific, additional medication, but their appearance indicates that a therapeutic dosage has been reached.

In using the parkinsonian effect of ataraxics as a basis, an attempt is made to illustrate the close relationship between schizophrenia and extrapyramidal system.

(Author's Abstr.)

Phrenotropic Action of Methylphenidylacetate (Ritalin)

Improvement following Ritalin therapy ranged from better self-care to restoration to active and substantially normal life outside the hospital. Verbalization was restored and/or normalized, and many patients reported feeling more "alive", "interested" or "normal" than for a long time. Delusional and hallucinatory trends were greatly reduced. Physical and mental lethargy caused by necessarily large doses of various ataraxic or anticonvulsant drugs responded well to Ritalin, as previously reported by Ferguson and Carter and further confirmed by Lazarte and Petersen. The writer has commented on several of these points previously, and feels that the findings in the series now being reported reinforce the earlier impressions. Carter also reported no deleterious effect of Ritalin in patients with pre-existing convulsive disease. In cases of chronic brain syndrome associated with senile disease confusion was lessened and alertness increased. In those with chronic brain syndrome associated with cerebral arteriosclerosis, orientation and clarity of thinking improved.

While Ritalin may produce hyperactivity requiring reduction of dosage or discontinuation, usually this can be controlled by reserpine, chlorpromazine or meprobamate, and there is no evidence thus far that it will aggravate pre-existing convulsive disease. This drug rarely produces a significant increase in normotensive or already hypertensive blood pressure, but in an occasional case such as the arteriosclerotic patient cited it may be contra-indicated.

(Author's Abstr.)

Subcortical Functions of Tridione and Desoxyn in Mental Illness

Recent work in neurophysiology is reviewed, with reference to the Papez circuit and the "Visceral Brain" which is proposed as the anatomical substratum of the subconscious mind. Correlation of clinical syndromes with the effects obtained by stimulating centres along the Papez circuit in the hippocampal formation, fornix, hypothalamus, and cingular gyrus is offered.

Clinical work with Tridione and Desoxyn is reported in a series of 16 patients. Dramatic recoveries and improvements have occurred in 11 of these severely ill psychotic patients.

As a working hypothesis, it is assumed that all motor nerve impulses arising in the central nervous system must find some effector pathway. If the original intention is repressed, a pathway is found to make a muscle move, a gland secrete, or a control centre to function.

Anatomical divisions and physiological responses in the central nervous system suggest that man has two brains working antagonistically and synergistically; one the neocortex, the other the visceral brain, composed of limbic lobe with its cingular gyrus, Island of Reil, claustrum, basal ganglia, amygdala, hypothalamus, and hippocampal formation.

(Author's Abstr.)

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Frontal Leucotomy and Its Congeners

With the numerous operative procedures described by the author, it would seem that after maybe another twenty years the choice would narrow down. But since surgeons are by nature inventive, it seems more probable that additional measures for producing lesions in various areas will be described. The really remarkable thing, however, is that every described operation can be counted upon to produce exactly the proportion of responses that Moniz reported in his first monograph in 1936, one-third recovered, one-third improved and one-third unimproved. Results are better or worse depending more upon the choice of the patient and less upon the choice of operation.

(Author's Abstr.)

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A Comparative Study of Modified and Unmodified Electric Shock Treatment

The results and complications of modified and unmodified shock treatment, and patients' attitudes toward each, were compared in groups of subjects randomly selected for each treatment. The results of the two treatment methods were not significantly different. There were also few differences in patients' attitudes toward the two procedures. Complications, however, were more frequent among patients given the unmodified treatment than among those given the modified treatment. Restlessness just after treatment was also more common with the unmodified method. It was concluded that modified shock treatment is the method of choice.

(Author's Abstr.)

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Effect of Rauwolfia Alkaloids and Related Substances on Chromatophores

It is shown that those *Rauwolfia* alkaloids which are hypotensive and sedative to man in small dosage, namely, reserpine, raunormine and rescinnamine, and which have been shown to be releasers of serotonin, catechol amines and histamine in large dosage, are potent dilators of fish chromatophores in extreme dilution. This response of the fish melanophores is highly specific with respect to the drug causing the response, the cells which respond, and the class of vertebrates whose cells react. There is a local action in innervated cells. A general action is suggested, possibly via hypophyseal hormonal release.

(Author's Abstr.)

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Recovery from Insulin Coma and Hematoencephalic Exchange

In deep insulin hypoglycemia rabbit brain loses approximately fifty per cent. of its normal content of free glutamic acid. Glutamic acid administered either intravenously or subcutaneously will restore the level of free glutamic acid but the cortical electroencephalogram does not return to normal. Glucose alone given intravenously increases the free glutamic acid in the brain and the normal pattern of the cortical electroencephalogram returns. From this the authors draw the following working assumptions: (1) that the free glutamic acid used by the brain during deep insulin hypoglycemia does not yield sufficient energy to maintain the cortical electroencephalogram; (2) administered glutamic acid enters the brain more freely in the animal subjected to deep insulin hypoglycemia than in the normal rabbit but does not influence significantly the electrical activity of the cortex; (3) treatment with glucose restores the glutamic acid level and the electrical activity.

(Authors' Abstr.)

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Effects of Lobotomy in Childhood

Although lobotomy is an irrevocable and drastic procedure, the authors' twelve cases were such severe chronic problems that the only alternative to attempted relief of symptoms was custodial institutional care. The follow-up would seem to have justified the operative procedure. It could have been argued that growth may have accounted for the improvement. However, two or three facts argue against this. (1) Most cases of chronic childhood schizophrenia have not shown improvement. (2) The post-encephalitic cases have not improved. (3) The experience with hemispherectomy has shown that severing of brain connections has brought about marked satisfactory reduction or disappearance of behaviour disorders even of severe abnormalities of behaviour.

(Authors' Abstr.)

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A Method for Differential Diagnosis of Brain Damage in Adolescents

On the basis of age and sex differences, nine of the thirteen ratios originally presented by Hewson were modified and successfully used to differentiate organic and non-organic adolescent subjects.

Among the 160 control subjects (40 of each sex in a young and in a late adolescent age range), 92 per cent. had non-organic summary diagnoses according to the adolescent ratios. Hewson's original ratios yielded only 73 per cent. non-organic diagnoses for this group. Of the 40 experimental subjects, 100 per cent. of those who had positive neurological diagnoses had organic diagnoses according to the adolescent ratios. Only 80 per cent. of these subjects had organic diagnoses when Hewson's original ratios were used. In the group who showed no residual neurological impairment, 38 per cent. of those suspected of organicity had organic diagnoses according to both Hewson's and the adolescent ratios. In the remaining subjects who showed no residual neurological impairment but who had convulsive disorders, 67 per cent. had organic diagnoses according to the adolescent ratios while only 16 per cent. were classified as organic by Hewson's original ratios. Relationships between the present I.Q. and the age of the subject at the time of injury indicated that early injured subjects had lower I.Q.s than did later injured subjects.

(Authors' Abstr.)

Seizures with Promazine

1. Twenty-one chronic psychotic patients were given promazine over an average period of 68 days, with maximum doses ranging from 100 mg. to 1,800 mg. a day.

2. Of this group, six patients experienced a total of 11 grand mal seizures during promazine therapy. All these patients were receiving 900 mg. daily or more at the time of the convulsions.

3. Five patients also administered 900 to 1,500 mg. a day did not have seizures during therapy.

4. No patient of the 10 receiving less than 900 mg. daily had fits.

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5. In three patients with clinical fits with promazine, serial EEG tracings showed paroxysmal records during drug use only; in two others with seizures, a normal record was found with and without the drug.

6. It is concluded that in this series the administration of high doses of promazine was associated with the occurrence of grand mal convulsions.

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Experience with "BGE", A Naturally Occurring Indole Compound

"BGE" occurs during the intermediate metabolism of tryptophane in microbes. It can be isolated from mycelium of the mould *neurospora crassa*. It also occurs in pathological human urine. A substance apparently identical with "BGE" is formed by the action of hydrogen peroxide, cortisone or ascorbic acid on tryptophane, and is probably tryptophane with a hydroxyl group at the beta position and indole double-bonded shifted to the indolenine position. The compound is easily oxidized to beta-OH-oxindole-alanine. Oxindole-alanine is a component of the toxin of the fungus *amanita phalloides*. BGE is present in high amounts in all fast-growing cells, i.e. in human carcinoma tissue and also occurs in the urine of persons suffering from bacterial infections. The ingestion of cortisone markedly decreases the urinary secretion of indole-acetic acid, while BGE appears in high amounts. The author found that the ataraxic drugs, reserpine, Frenquel and chlorpromazine, all interfere with tryptophane metabolism, and are to be regarded as metabolic poisons. The author found that chemical manipulation of BGE gave rise to fumes which produced in him psychotic symptoms much resembling those from mescaline and LSD-25. These symptoms were relieved within half-an-hour by a 100 mg. tablet of Frenquel.

G. W. T. H. Fleming.

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Lactic Dehydrogenase of Cerebrospinal Fluid in the Differential Diagnosis of Cerebrovascular Disease and Brain Tumor

The concentration of the enzyme, lactic dehydrogenase, has been examined in spinal fluids from a series of patients with a variety of disorders. Significantly higher enzyme levels have been found in the cerebrospinal fluid of patients with cerebrovascular accidents as compared with normal individuals and patients with neurological disease including brain tumor. The test is suggested as useful in the differentiation of cerebrovascular accident from other disease with similar clinical picture.

(Authors' Abstr.)

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Symposium on Head Injuries: Physiological Basis of Concussion

1. Since the effects of mechanical alterations at the moment of impact in head injury must ultimately be reflected by alterations of the properties of neuronal membranes, this has been studied by recording the electrical activity at various levels of the nervous system.

2. Whereas there may be surprisingly little change in the spontaneous electrical activity of the cerebral cortex and many subcortical structures, there is consistent reduction of activity in the reticular formation of the mid-brain following a concussive blow.

3. Whereas there is no alteration of conduction of sensory impulses over the classical sensory pathways to thalamus and cortex, evoked sensory responses in the reticular formation are blocked or markedly attentuated by concussion.

4. Since it is known that such sensory driving of the reticular activating system is necessary to maintain consciousness, the genesis of coma following head injury would seem to be on this basis.

5. These alterations of properties of neuronal membranes following concussion may be related to biochemical alterations, including the metabolism of acetylcholine, which are known to follow concussion.

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The Spiral After-effect and Reversible Figures as Measures of Brain Damage and Memory

A group of 32 brain-damaged adolescent boys (CBS) and a group of 35 emotionally disturbed non-psychotic boys (ED) of equated age were administered the spiral visual after-effect (SVA), two reversible figures, and a memory paragraph for immediate and delayed recall.

A significantly greater percentage of the brain-damaged group did not perceive SVA, and the duration of SVA for this group was significantly longer than for group ED. Rate of reversals for both reversible figures was significantly lower for group CBS, and a significantly smaller percentage of group CBS reported reversals spontaneously. No relationship was obtained between SVO and reversible figures.

For both immediate and delayed recall, group ED was significantly superior. There was no significant difference in memory loss over time. The duration of SVA showed a significant negative relationship to the measure of immediate recall, and the rate of Necker Cube reversals was significantly related to the measure of memory loss over time. No other correlation between memory, SVA, reversible figures, and groups was significant. The possibility that the two significant findings might be spurious is discussed.

The data are viewed in relation to diagnostic problems, recent theorizing about cortical functioning, and the possibility of further refinement of the SVA procedure.

(Authors' Abstr.)

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Distribution of Carbon-14 Labeled Isoniazid in Brain

1. The distribution pattern of carbon-14 labeled isoniazid in the central nervous system of cats was determined by radio-assay of dissected tissue samples and auto-radiography at several time-points following injection of the drug. A well defined and consistent pattern of distribution from animal to animal was revealed.

2. Attempts to relate the local concentration of carbon-14 label to local vascularity in the central nervous system disclosed general agreement for some areas, but gross inconsistencies in others. The labelled drug was present in high concentration in hippocampus despite relatively lower vascularity, while the opposite was true in the geniculate bodies and inferior colliculi which are regions of high vascularity in the cat.

3. Hippocampus was unusual in another respect in that the relative concentration remained high throughout 12 hours, while the relative concentration in other areas of brain was falling.

4. It is concluded that factors other than local vascularity condition the distribution of this drug in the central nervous system of cats. These factors are not understood at present.

(Authors' Abstr.)

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Celontin in Patients with Refractory Epilepsy

Sixty-two epileptic patients with various types of seizures previously partially or totally refractory to former anticonvulsant therapy were treated with Celontin (N-methyl-a, a methylphenylsuccinimide) in doses up to tolerance. In nearly all instances, the new drug was added to or replaced part of the previous maintenance medication. Of the 54 patients who received Celontin long enough for adequate evaluation, six patients achieved complete seizure control, six were distinctly improved, and five patients experienced an increase in seizure frequency on the drug. The remainder noted little or no improvement. Age, clinical seizure type, and electroencephalograph pattern bore little relation to the level of improvement. Principal side effects were sedation and ataxia, usually related to over-medication with Celontin or additive effect of Celontin with other anticonvulsant agents. Two patients demonstrated evidence suggestive of liver damage. Six patients noted undesirable psychic reaction, in two instances requiring hospitalization. Periorbital oedema occurred in three patients, albuminuria in one, and skin rash in two individuals. Other side reactions were minor and transient.

It is felt that this drug is a useful addition to the therapeutic armamentarium against the epilepsies, particularly in patients with residual abortive or minor seizures subsequent to fair control of major attacks.

(Authors' Abstr.)

A Study of Cholinesterase and Ali-esterase in Various Neurologic Diseases

1. The true-cholinesterase, pseudo-cholinesterase, and ali-esterase activities of cerebrospinal fluid in 159 patients with various neuropathologic conditions were determined. The two cholinesterases were estimated by their activity on the same substrate, acetylcholine, and differentiated by the use of Mytelase, a specific true-cholinesterase inhibitor.

2. In the studies in multiple sclerosis, hemiplegia after cerebrovascular accident, epilepsy, myasthenia gravis, and Guillain-Barré syndrome, a wide range of activity was evident for the three enzymes studied. Cerebrospinal fluid was found to contain an active ali-esterase, using phenyl acetate as a substrate.

3. A high true-cholinesterase activity was found in seven cases of myasthenia gravis, one of cortical atrophy, and one of porphyrinuria.

4. No evidence of any deviation in pseudo-cholinesterase or ali-esterase activity was evident in the spinal fluid in multiple sclerosis.

5. A difference in ali-esterase activity in cases of epilepsy from organic causes as compared to the idiopathic form was observed.

6. A high ali-esterase activity was found in the Guillain-Barré syndrome, which was correlated with the high albumin fraction in cerebrospinal fluid.

(Authors' Abstr.)

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The Action of Autonomic Drugs on Normal Persons and Neuropsychiatric Patients: The Role of Age

In experimental studies on cats it has been shown in the authors' laboratory that simple autonomic tests reveal the state of excitability of the hypothalamus. The degree of the hypotensive action of Mecholyl indicates the state of sympathetic hypothalamic excitability, whereas the pulse-slowing reflex induced by the rise of the systolic blood pressure upon intravenous injection of norepinephrine indicates the state of parasympathetic hypothalamic excitability. The application of these tests in normal persons and neuropsychiatric patients shows:

1. The sympathetic excitability declines progressively with increasing age in normal individuals and mental patients. This decline is independent of changes in the blood pressure level since it occurs in groups of persons whose mean blood pressure is practically the same in the three age groups studied.

2. In view of the considerable influence exerted by the age factor on the sympathetic excitability indicated by the Mecholyl test, a comparison between normal persons and groups of patients is valid only when similar age groups are compared. Significant differences exist between the control and the mental group under these conditions. At all ages the sympathetic hyper-reactors and hypo-reactors are in the majority in the group of mental patients, whereas they are in a minority in the control group. Sympathetic hypo-reactors are present in schizophrenics at the age of 25 and less but are absent in the control group.

3. Somatic therapy is recommended in functional mental disorders with the view to restoring physiological autonomic excitability at the hypothalamic level. This recommendation

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is based on four groups of data showing that (*a*) the Mecholyl test indicates sympathetic reactivity at the hypothalamic level; (*b*) autonomic changes indicated by the reaction to Mecholyl are paralleled by changes in behaviour (Funkenstein *et al.*); (*c*) procedures such as electroshock, which according to the physiological analysis increase central sympathetic reactivity, benefit patients who are sympathetic hypo-reactors but not sympathetic hyper-reactors; (*d*) procedures such as the inhalation of high concentrations of carbon dioxide, which has been shown to diminish the reactivity of the sympathetic division of the hypothalamus and the intensity of the hypothalamic-cortical discharge, are beneficial in the treatment of sympathetic hyper-reactors but are contraindicated in the case of sympathetic hypo-reactors.

Statements (*c*) and (*d*) refer to the clinical work of Funkenstein *et al.*, and Moriarty respectively, and the physiological work elucidating the nature of the Mecholyl test. The therapeutic effect of carbon dioxide therapy was predicted in 1953.

4. The quotient:

$$\frac{\text{Maximal rise of the systolic blood pressure}}{\text{Maximal diminution of the heart rate}}$$

following the intravenous injection of 0·005 mg. norepinephrine has been used as an indicator of parasympathetic hypothalamic excitability, since physiological work showed the dependence of this quotient on the excitability of the anterior hypothalamus. This quotient showed variations too great to permit the recognition of any difference between the control group and the neuropsychiatric group. However, the work showed that the parasympathetic reactivity declines in the normal and abnormal groups with increasing age.

Increasing age is, therefore, associated with a decrease in sympathetic and parasympathetic central reactivity. Whether the state of autonomic balance changes with increasing age cannot yet be said.

(Authors' Abstr.)

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The Effect of Oral Ethanol on Glutamic Pyruvic and Glutamic Oxalacetic Transaminase Activity in the Rat Liver

1. The effect of the ingestion of a 20 per cent. alcohol solution as the sole source of fluid on glutamic pyruvic and glutamic oxalacetic transaminase activity in rat livers has been compared with pair-fed, isocaloric and pair-fed, and ad lib-fed controls, under conditions of varying food intake, in two experiments. All animals received adequate amounts of lipotropic factors and vitamins throughout.

2. At 24 weeks the hepatic GOT/GPT ratio was significantly higher in the alcohol-fed group, as compared with the pair-fed water-fed controls.

3. In both experiments there was a diminution in hepatic GPT activity in the alcohol-fed group at 8 weeks as compared with any of the controls, a change which was independent of calorie intake. This change was not observed in brain.

4. Upon starvation there was a significant increase in hepatic GPT activity in the alcohol-fed group and the pair-fed controls only.

5. These changes are interpreted as indicating a direct effect of alcohol on the liver of rats.

(Authors' Abstr.)

Treatment of the Acute Alcohol-Withdrawal Syndrome

An outline of medical therapy for the acute alcohol-withdrawal syndrome has been presented. It is based on the clinical impression, supported to some extent by laboratory observations, that the alcoholic, during withdrawal, suffers from acute dehydration and acute starvation, and is in need of sedation. Intravenous glucose, salt and water are given, and sedation is achieved primarily with chlorpromazine. By immediately attending to these three primary factors—dehydration, starvation, and need for sedation—the withdrawal period is shortened, complications are minimized, the need for prolonged sedation is eliminated, and nursing care is made easy. The average physician, without extensive experience with alcoholism, is given a safe method of handling the acute withdrawal syndrome in a general hospital.

(Author's Abstr.)

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