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The Amygdalae and Behaviour

The individual and social behaviour of 15 cats and 18 rhesus monkeys was recorded and analysed during a control period of from 3 to 15 months, during which the animals were also trained to solve increasingly complicated problems. Adaptational conflicts were used to induce persistent experimental neuroses in 3 kittens, 2 cats, 3 young monkeys and 8 adult ones. The amygdalae were then totally ablated, with some injury to the surrounding areas, in 6 of the cats and all of the monkeys; in the remaining 9 cats only the lateral or the medial amygdalae were removed.

Post-operatively, the cats exhibited: (1) no general amnesia for previous learning; (2) only mild amelioration of neurotic behaviour; (3) moderate motor restlessness; (4) variable sexual drive including a phase of hypererotism; (5) markedly altered interactions with other cats and humans; (6) slowed re-learning due to low motivation and erratic or perseverative performance on both simple and complex tasks; and (7) severe disorganization of adaptive behaviour after short periods of isolation and inactivity. The adult neurotic animals were; (8) markedly amenable to therapy although the kittens' very low resistance to the re-induction of neuroses were only mildly so; whereas (9) all showed neuroses.

In comparison, the monkeys showed (1) an initial increase in oral activity; (2) extensive amnesia for previous learning, coupled with (3) limited diminution of neurotic symptoms in the young animals as contrasted with almost complete amelioration in the adults; (4) the ability to regain pre-operative performance levels on learned problems, although the re-training period was lengthened by altered motivation, restlessness in the testing apparatus, and precipitate or inflexible responses; (5) tolerance of the proximity of or handling by a single human, contrasted with (6) fear responses to other animals or when more than one human was present; (7) increased inter-animal aggression, possibly related to (8) hyper-sexuality; and (9) diminished resistance to the re-induction of neuroses.

The theoretical implications of these findings were briefly considered.

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Mental Symptoms in Cases of Tumour of Temporal Lobe

In the series of 61 temporal lobe tumors there were mental symptoms in 50 cases. As initial symptoms there were mental manifestations in 37 cases before any neurological signs appeared. The symptoms were as follows: (1) fits (hallucinations, visual illusions, dreamy state, automatism, psychomotor equivalent, temporal epilepsy), (2) changes in personality, (3) disorders of mood, (4) schizoform psychosis, (5) parietal mental symptoms, (6) psycho-organic syndrome.

A definite mental syndrome of tumor of temporal lobe is not assumed. The author would only emphasize, that the psychic syndromes are never manifestations only of damage of a circumscribed part of the brain, but always as a damage of the function of the brain as a whole. From the clinical symptoms and their connections with the local lesions, one can only conclude that certain neuron groups play a greater part in some or in specific brain activities. On the basis of literary data, of the author's material and observations with electric stimulations of the cortex by Penfield and co-workers, it is assumed that some type of hallucinations, *déjà vu* experiences, dreamy states, automatism, psychomotor equivalence, temporal epilepsy

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can be—with great probability—significant of temporal lobe lesions. Paying more attention to these symptoms and making greater use of the results of other examinations it will be possible to make an earlier and more accurate diagnosis to establish the temporal lobe tumor.

(Author's Abstr.)

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Studies on Mescaline, VIII: Psychodynamic Observations

Psychodynamic observations made during the mescaline-induced state in 124 patients are reviewed. Mescaline produces a "state of being" in which the clinical spectrum can range from sleep to rage and from normalcy to thoroughly disorganized mental states. Anxiety is considered the background upon which the mescaline experience evolves. One may consider the mescaline-induced state under three headings: (1) hostility-aggression, (2) sexuality and (3) the transference. Various recurring symbolic gestures were noted, and many were frequently of a sexual nature.

The primary role of anxiety is reviewed and some theoretical concepts presented. Much further work remains to be done.

(Author's Abstr.)

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Phenyltoloxamine, a new phrenotropic agent with limited clinical experience in psychiatry, was evaluated by combined psychiatric, physiologic, and psychometric methods. A double-blind method was used comparing the drug with reserpine and placebo.

The results showed that phenyltoloxamine, at a dose of 400 mg., produced sedative and moderate hypnotic effect, reaching a peak in 4–5 hours. At peak of action it produced drowsiness and slowing of psychomotor and mental performance. This was followed by a state of relaxation, increased learning, and improved performance.

In contrast to reserpine, autonomic and visceral side effects were not observed. Muscle tension was reduced.

The findings indicated a cortical rather than sub-cortical site of action.

Its clinical uses are indicated.

The importance of multidimensional evaluation and proper methodologic control was discussed.

(Authors' Abstr.)

Atropine-Like Poisoning Due to Tranquilizing Agents

A case of atropine-like poisoning manifested by absence of sweating, hyperthermia, pupillary paralysis, dry mucous membranes, and delirium, is reported. These findings are ascribed to the anti-cholinergic properties of the tranquilizing agents of the phenothiazine group of drugs.

(Authors' Abstr.)

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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.)

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

Psychological study of our 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 our own 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 us 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 our 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 ourselves, 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 the other side. 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.

A careful psychological study of more than 90 other patients was carried out 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, the authors 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 preciously 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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Ceruloplasmin, Transferrin, and Tryptophan in Schizophrenia

Thorough investigation of copper and ceruloplasmin levels in normal and schizophrenic subjects gave no indication that these substances are altered quantitatively in schizophrenia. It remains to be shown whether or not qualitative differences exist in this disease. The same study of iron and transferrin levels shows that, while schizophrenic subjects have lowered quantities of these substances, the levels in the other patients studied were lowered as much or more. Investigation of tryptophan excretion of normal and schizophrenic subjects on normal-, high-, and low-tryptophan diets gave no indication that increased tryptophan excretion was associated with schizophrenia. The findings give clear evidence that diet must be rigidly controlled before metabolic investigations can be considered to be of significance.

(Authors' Abstr.)

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Urinary Excretion of 5-Hydroxyindoleacetic Acid in Psychotic and Normal Subjects

The daily excretion of 5-hydroxyindoleacetic acid (5-HIAA) in schizophrenics does not differ significantly from that of non-schizophrenic subjects. If in schizophrenia there is a basic alteration of the metabolism of 5-hydroxytryptamine, it is not reflected in the amount of its endmetabolite, 5-HIAA, excreted in the urine.

Parenterally injected 5-hydroxytryptamine may appear in the urine as 5-HIAA. In non-schizophrenic subjects the recovery rate averages 25 per cent., while in schizophrenic patients it averages 42 per cent., with individual values higher than 90 per cent. in some acute schizophrenics.

Chromatographic study has revealed the presence of indole metabolites different from 5-HIAA in the urines of catatonic patients and of acute schizophrenics in general. Such metabolites are perhaps responsible for the high incidence of positive results in the qualitative colour reaction, although the urinary concentrations of this substance are not increased. The results do not support the hypothetical existence of a primary disturbance of systemic serotonin metabolism in schizophrenia. The abnormalities found in some acute schizophrenics,

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especially the catatonics, are regarded as added evidence for an enzymatic disorder affecting the general metabolism of biological amines in the early stages of schizophrenia.

(Authors' Abstr.)

Observations on Schizophrenic Patients After Iproniazid and Tryptophan

Seven schizophrenic patients were given iproniazid and L-tryptophan for a period of six weeks.

During the experimental period, the patients exhibited an increase in energy level and motor activity and improvements in the ability to accept interpersonal relationships, and displayed more affect. In addition, their voluntary intake of protein and tryptophan increased. These changes became apparent about two weeks after the initiation of the experimental period.

During the course of the experiment the 5-hydroxyindoleacetic acid excretion per 24 hours diminished. This low excretion was rapidly reversible after the cessation of drug administration.

In a tryptophan-load test 26 schizophrenic patients did not exhibit any increase in 5-hydroxyindoleacetic acid excretion over the basal level after tryptophan administration, while 17 controls showed an 100 per cent. increase in the excretion of this compound. No difference between the two groups at the basal level was observed.

Some implications of the results obtained in relation to serotonin metabolism are discussed.

(Authors' Abstr.)

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Cerebrospinal Fluid Neuraminic Acid Deficiency in Schizophrenia

1. The mean neuraminic acid content of cerebrospinal fluid in schizophrenic patients is shown to be considerably below that of non-schizophrenic adults, and comparable only to values found in some children under 7 years of age.

2. The method employed for the preparation of crystalline neuraminic acid from purified bovine brain ganglioside for use as standard is detailed.

3. The method employed for determination of neuraminic acid in cerebrospinal fluid, together with the precautions to be observed, is described.

4. The concept of a barrier-antibody system and its possible relationship to the psychoses is presented. The susceptibility of this hypothesis to experimental validation or negation is stressed.

5. It is concluded that an important new area for further investigation has been indicated.

(Authors' Abstr.)

SEPTEMBER

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Cerebrospinal Fluid Free Cholesterol as Index of Activity of Multiple Sclerosis and Allied Diseases

Free and esterified cholesterol was determined in the CSF, using a turbidimetric method for the estimation of digitonin-precipitable sterols.

Esterified cholesterol, but no free cholesterol, was found in the spinal fluid of normal controls.

In infections and neoplasms of the nervous system, the elevation of total- and free-cholesterol fractions was found to correlate with the elevation of the spinal fluid protein.

In amyotrophic lateral sclerosis, multiple sclerosis, and other similar demyelinizing diseases, the CSF cholesterol is independent of the level of CSF protein. The correlation between free CSF cholesterol and the clinical evaluation of activity of the disease would seem to indicate that the presence of free cholesterol may be useful as an objective index of activity of the demyelinizing process.

(Authors' Abstr.)

Azacyclonol (Frenquel) in Chronic Schizophrenia

Nineteen chronic schizophrenic men, divided randomly into two groups, were intensively studied by a double-blind crossover design for a total of five months to evaluate the effectiveness of azacyclonol (Frenquel). A daily dose of 120 mg. of azacyclonol had no significant effect on the thinking or behaviour of these chronic schizophrenic patients. Extravagant claims for this drug made by some previous investigators were not supported by this study.

(Authors' Abstr.)

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Effect of Blood Plasma from Psychotic Patients upon Performance of Trained Rats

Intraperitoneal injection of blood plasma from the majority of schizophrenic and other severely psychotic patients into rats produced a syndrome resembling, but not identical with, that produced by injection of LSD. In rats trained to climb a rope, the injection of 1 ml. of plasma produced a deficiency in performance which could be objectively and quantitatively measured. Comparisons of the effects of plasma from 80 psychotic patients and 82 non-psychotic subjects, including both general hospital patients and normal subjects, showed a marked and highly significant difference between the two groups. Cerebrospinal fluid had much less effect than plasma.

(Authors' Abstr.)

Effects of Lysergic Acid Diethylamide (LSD-25) on Intellectual Functions
I. Memory

LSD-25 in doses of 72 μg. significantly impaired memory for only certain kinds of material, as measured by the Wechsler Memory Scale. On the one hand, the ability to draw geometric

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figures from memory, the ability to reproduce brief prose passages, and the ability to count backward, say the alphabet, and perform serial addition were all affected by the drug. On the other hand, the ability to learn paired associates, the ability to repeat series of digits, orientation for time and place, and memory for personal and current information appeared to be unaffected by the drug at the dose level employed.

II. Abstract Thinking

LSD-25 in doses of 72 μg. significantly impaired abstract thinking, as measured by the Gorham Proverbs Test. The difference in scores under control and under drug conditions resembled the difference reported in the scores of normal subjects and chronic schizophrenics. Contrary to expectations incorrect abstractions were commoner than concrete responses not only under control conditions, but also in the drug state.

(Authors' Abstr.)

Thiopropazate Hydrochloride (Dartal) Chemotherapy for Emotional Disorders

Thiopropazate hydrochloride (Dartal) chemotherapy has been employed in the treatment of 104 psychiatric patients, the majority of whom were schizophrenics. The drug has a definite ataractic effect for both acute and chronic disturbances, and 77 patients (74 per cent. of the total group) showed some overall improvement on the drug. The drug is particularly useful in treating patients with association defect, depersonalization, and anxiety; and, although the statistical significance of the drug effect is not as definitive, it also appears to be helpful in treating patients manifesting delusions, withdrawn sociability, flattened affect, and anorexia. Patients with mood depression do not respond to thiopropazate therapy and demonstrate greater improvement when taking placebo.

No serious side-effects were encountered, but the development of excitation and Parkinsonism-like symptoms in some patients produces considerable secondary anxiety, necessitating discontinuation of the medicine. No evidence of myeloid depression has been found. On a milligram basis, thiopropazate hydrochloride is about five times as potent as chlorpromazine (Thorazine), and the recommended dosage is 5 to 10 mg. four times a day.

(Authors' Abstr.)

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Thyroid Therapy of Schizophrenia

Thyroid extract or thyroxine with vitamins, given to 120 schizophrenic patients, none of whom was recognized to have periodic catatonia, resulted in the recovery of 54. The recovery percentage in 80 patients given thyroid therapy for at least 100 days, which is considered to be the shortest time which can be called adequate, was 67·5. Of these 80 adequately treated patients, 60 received some form of conventional therapy (usually shock) in addition to thyroid extract or thyroxine. The immediate results are superior to those attained with adequate shock therapy in a public hospital or with various conventional methods in a private hospital.

Of 23 patients given thyroid therapy for 100 days or more after an illness of less than six months, all recovered. Of 43 patients treated for 100 days or more after an illness of less than two years, 39 (90·7 per cent.) recovered. Fifteen of the 80 patients (or 19 per cent.) recovered without requiring any shock therapy, and two of these 15 had been ill for five years or more. Those thyroid patients who received shock therapy required much less of it than had to be given to control patients who received no thyroid medications.

Relapses are known to have occurred after 24 of the 54 recoveries, but each relapse was preceded by a period of time in which the patient failed to follow directions given him as to necessary medications and laboratory tests. The incidence of relapse among those who follow directions after discharge is believed to be very small.

(Author's Abstr.)

A New Antiphobic Agent, Benactyzine

In conformity with suggestions in the American literature, and contrary to that reported by the European literature, benactyzine has been found to be an antiphobic and mild anti-depressant drug but without any skeletal-muscle-relaxing effect. There are reports of slight sedative action and of slight muscle relaxation qualities (relief of night cramps).

Some physiological by-effects have been reviewed and found to be mild and relatively infrequent.

Toxicity, in the dose indicated, has not been a serious factor in clinical use.

(Authors' Abstr.)

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Correlation of Rhinencephalic Electrograms with Behaviour

Six patients with chronically implanted intracranial electrodes were studied under the influence of d-LSD-25, l-LSD-25, mescaline, and correlations attempted between the electrograms and behavioural observations.

An increase in beta activity and a disappearance of alpha characterized in both cortical and subcortical recordings seemed to be associated with anxiety or its derivatives.

Paroxysmal activity induced in the hippocampal, amygdaloid, and septal regions seemed to be associated with overt expressions of disturbed psychotic behaviour.

Spread of such paroxysmal activity until it became generalized in the cortex seemed to interfere with the full expression of the psychotic behaviour.

Chlorpromazine not only proved an effective blocking agent as far as the behaviour was concerned, but also abolished or minimized the appearance of the low amplitude fast activity

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as well as the paroxysmal subcortical activity. The possible sites of action of LSD-25, mescaline, and chlorpromazine are discussed with reference to the problems of psychomotor epilepsy, episodic psychotic reactions, and schizophrenia.

(Authors' Abstr.)

EEG Frequency-Pattern Variation and Intelligence

An experiment was performed to test a hypothesis, suggested by Walter's work, that there is a relationship between test intelligence and EEG frequency-pattern variability. This involved the application of the coefficient of concordance (Kendall's W) to frequency analyser data to yield a single summary measure of frequency-pattern variability. The hypothesis was not confirmed.

(Authors' Abstr.)

Cyclic Variations in EEG During Sleep and Their Relation to Eye Movements, Body Motility, and Dreaming

In 33 adults, discrete periods of rapid eye movement potentials were recorded without exception during each of 126 nights of undisturbed sleep. These periods were invariably concomitant with a characteristic EEG pattern, stage 1.

Composite histograms revealed that the mean EEG, eye movement incidence, and body movement incidence underwent regular cyclic variations throughout the night with the peaks of eye and body movement coinciding with the lightest phase of the EEG cycles. A further analysis indicated that body movement, after rising to a peak, dropped sharply at the onset of rapid eye movements and rebounded abruptly as the eye movements ceased.

Records from a large number of nights in single individuals indicated that some could maintain a very striking regularity in their sleep pattern from night to night.

The stage 1 EEG at the onset of sleep was never associated with rapid eye movements and was also characterized by a lower auditory threshold than the later periods of stage 1. No dreams were recalled after awakenings during the sleep onset stage 1, only hypnagogic reveries.

(Authors' Abstr.)

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*Electroencephalograms of Normal, Full-term Newborns Immediately After Birth with Observations on Arousal and Visual Evoked Responses. *Ellingson, R. J.* .. 31

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Electroencephalograms of Normal, Full-term Newborns Immediately After Birth with Observations on Arousal and Visual Evoked Responses

1. EEGs of 277 normal, full-term babies, ages 22 minutes to 125 hours, were recorded. Loud auditory stimuli were presented during sleep in 52 cases; single and repetitive light flashes 65 cases.

2. In general, previous descriptions of EEG patterns during wakefulness and sleep in newborns were confirmed. No relationship was observed in these data between EEG patterns and (*a*) type of maternal analgesia during labour, (*b*) type of maternal anaesthesia during delivery, or (*c*) length of 2nd stage of labour.

3. Loud auditory stimuli during sleep may elicit the following generalized responses with or without movement: (*a*) flattening of tracings, (*b*) K-type response (rare), or (*c*) K-type response followed by flattening of tracings. Spontaneous movement during sleep may also be followed by flattening of tracings.

4. Single light flashes to the eyes often elicit evoked potentials in the occipital area. These responses tend to differ from those observed in adults in the following ways:

(*a*) They are of more variable wave-form.
(*b*) They are of more variable amplitude.
(*c*) They show greater "fatiguability".
(*d*) They are of much longer latency (160–220 m/sec.).

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5. Trains of light flashes at 2 f/sec. or faster tend to elicit responses at the beginning (ON responses) and end (OFF responses) of stimulation. "Driving" effects were observed in only 2 cases, at 2·5–3·5 f/sec.

6. The evoked response data are interpreted as reflecting the physiological immaturity of the newborn's nervous system associated with its anatomical immaturity. The major factor accounting for the long latencies of evoked responses is felt to be slow conduction in the afferent fiber tracts, but retinal and synaptic events may also be contributory. The peculiarities of wave-form and amplitude are felt to be functions of the immature visual cortex.

(Author's Abstr.)

Electroencephalographic Changes and Hyperammonemia

Seven patients suffering from a variety of clinical diseases and in stages of consciousness varying from normal alertness to deep coma were found to exhibit "triphasic" waves in their electroencephalographic tracings. All 7 had in common elevation of their blood ammonia levels.

The literature on blood ammonia and triphasic electroencephalographic waves is reviewed and the following conclusions are drawn: Elevation of the blood ammonia level may be accompanied by the presence of triphasic waves in the electroencephalographic tracing. However, the presence of triphasic waves more consistently indicates an elevation of the blood ammonia level. Since elevation of the blood ammonia level represents only one variable finding in a generalized metabolic disturbance, the presence of triphasic waves and their relative frequency in a single tracing do not correlate with the absolute level of the blood ammonia. The triphasic waves appear to bear no direct relation to the state of consciousness nor to the presence or absence of detectable hepatic disease or electrolyte disturbance.

It is suggested that the triphasic waves in these patients' electroencephalograms, together with their elevation blood ammonia levels, indicate an as yet unknown metabolic disturbance which may affect the reticular activating system and its diencephalocortical connections.

(Author's Abstr.)

Electroencephalographic Findings in Acute Carbon Monoxide Poisoning

1. EEGs were obtained on 33 patients from the first to the ninetieth day after acute carbon monoxide poisoning.

2. The EEGs were abnormal in 18 patients, the abnormality consisting of extreme slowing in 10, marked slowing in 3, slight in 1 and in 4 the slowing was confined to the temporal leads. The slowing was asymmetrical in 14 patients, the abnormality being equally frequent on left and right.

3. The incidence of EEG abnormality was highly correlated with the patients' age, duration of unconsciousness and state of consciousness. Eight per cent. of patients over 50 had an abnormal EEG; 33 per cent. of patients under 49. Ninety-five per cent. of patients unconscious in the hospital more than 7 hours had an abnormal EEG; 7 per cent. of patients unconscious less than 6 hours. All comatose or semi-comatose patients had an abnormal EEG; 25 per cent. of those with consciousness unimpaired. The incidence of EEG abnormality in the first week was considerably higher than when more than a week had elapsed between poisoning and EEG examination.

4. Of 20 patients with no or slight EEG abnormalities, 12 recovered fully and none died. Of 13 patients with markedly abnormal EEGs, 2 recovered fully and 5 died.

(Authors' Abstr.)

The Effect of Drugs on Arousal Responses Produced by Electrical Stimulation of the Reticular Formation of the Brain

Thresholds for behavioural and EEG arousal produced both by electrical stimulation of the reticular formation and by afferent (auditory) stimulation have been determined in *encéphale isolé* cat preparations. The effect of graded doses of pentobarbitone, chlorpromazine, atropine, hyoscine, physostigmine, amphetamine and *d*-lysergic acid diethylamide (LSD-25) on these thresholds were studied.

Pentobarbitone, in doses considerably smaller than the anaesthetic dose, blocked arousal responses completely, but chlorpromazine, even in large doses, caused only a slight rise in the thresholds for direct stimulation of the reticular formation. It blocked arousal produced by afferent stimulation.

Atropine, hyoscine and physostigmine produced a marked divergence between behavioural and EEG thresholds; atropine caused a rise in the EEG threshold and physostigmine a fall, whilst the behavioural threshold remained unchanged. The effects of hyoscine were similar to those of atropine except that it caused a slight rise in the threshold for behavioural arousal, consistent with a slight sedative effect.

Amphetamine caused the thresholds to fall until a dose was reached at which the preparation was fully alert, both behaviourally and in terms of the EEG activity. LSD-25 had no effect on the arousal threshold for stimulation of the reticular formation but produced a marked lowering of the threshold for arousal to afferent (auditory) stimulation.

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The relation between these findings and the results of previous investigations is discussed, together with the possible sites of action of the drugs studied. Three different sites of action are postulated: (*a*) a direct action on the reticular activating system (pentobarbitone and amphetamine); (*b*) an action at the brain stem level but related to afferent collaterals entering the reticular formation (chlorpromazine and LSD-25); and (*c*) an action not directly related to the reticular formation of the brain stem but possibly to diffuse thalamocortical projections (atropine and physostigmine).

(Authors' Abstr.)

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Studies on the Cortical Pacemaker: Synchrony and Asynchrony of Bilateral Recorded Alpha and Beta Activity

1. By measuring and charting the times elapsed between peaks of normal alpha and beta waves recorded simultaneously from right and left homologous areas in 52 human subjects, an attempt has been made to deduce the probable source for rhythmic control of these normal frequencies.

2. Bilateral alpha and beta rhythms are probably under the control of a subcortical pacemaker or system of pacemakers. The possibility of transcallosal influences are not entirely ruled out, but seem unlikely under the circumstances discussed.

3. Shifting bilateral synchrony-asynchrony of these normal rhythms may be accounted for by one of two possible mechanisms:

(*a*) the cortical rhythm may partially escape from the deep control, then be forced to return to synchrony by the influence from below, or

(*b*) the primary source of the rhythm oscillates physiologically from side to side.

4. The progression of latencies in the occipito-frontal direction suggests transmission delays within the pacemaker itself, or in its deep subcortical connections.

5. It seems very likely that the reticular formation of the brain stem and the diffuse thalamic projection system, operating in series, provide the anatomical substratum for the physiological observations of the present study.

(Authors' Abstr.)

Viscero-sensory and Somato-sensory Representation in the Rhincephalon

1. A viscero-sensory and somato-sensory representation in the hippocampus of the marsupial phalanger is shown.

2. Stimulation of the stomach, electrically, mechanically and chemically modifies the hippocampal activity, with electrical stimulation eliciting the most striking results.

3. A slow wave is evoked in the hippocampus 500 m/sec. after stimulation. Where a primary response with short latency occurred, no slow wave ensued, and evidence is presented that the primary response may have resulted from stimulation of adjacent somatic structures.

4. A somato-sensory representation in the amygdala is demonstrated, with no viscero-sensory representation evident.

(Author's Abstr.)

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Rhinencephalic Lesions and Behaviour in Cats. An Analysis of the Klüver-Bucy Syndrome with Particular Reference to Normal and Abnormal Sexual Behaviour

1. In a series of 122 cats, lesions were placed in the amygdala-pyriform cortex and in other rhinencephalic areas in 82. Forty animals were used as controls.

2. Observed variations in normal sex behaviour and sex behaviour following hormone administration are described.

3. Sex hormones have behavioural effects on prepubertal animals specific to the type of hormone.

4. Sex hormones have behavioural effects in adults depending on the sex of the animal or previous conditioning, although their effects on target organs depend on the hormone.

5. Male hypersexual behaviour may be induced by lesions restricted to the pyriform cortex.

6. This effect (5) is not due simply to a raised testosterone titre.

7. Hyperphagia has been produced by lesions restricted to the basal and lateral part of the amygdala.

8. Seizures observed in some animals were closely correlated with fear-like behaviour and damage to the hippocampus.

9. Cataleptic changes were associated with lesions involving the rostral amygdala and basal ganglia.

10. Other phenomena observed were: hyperthermia, emotional changes and oral behaviour. These are discussed.

11. It is suggested that many of the phenomena associated with stimulation or destruction of the pyriform cortex may be secondary to the hallucinations and fugues of psychomotor epilepsy, though other changes are difficult to explain on this basis.

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Isolated Lesions of the Fastigial Nuclei in the Cat

Attempts were made to produce localized lesions of the fastigial nuclei in a series of 30 cats in order to study the resulting physiologic deficits and the associated fiber degeneration. Lesions of the fastigial nuclei were produced unilaterally in 15 cats and bilaterally in 5 others.

The following conclusions were drawn:

1. Unilateral lesions of the fastigial nucleus produce bilateral degeneration in the uncinate fasciculus, which is quantitatively more abundant on the side opposite the lesion.

2. Unilateral lesions of the fastigial nucleus produce ipsilateral fiber degeneration in the justarestiform body which terminates in the vestibular nuclei, particularly Deiters' nucleus.

3. Fibers of the descending limb of the uncinate fasciculus project to all vestibular nuclei, though the greatest number of fibers pass to the lateral and spinal vestibular nuclei, and to the dorsal paramedian area of the reticular formation of the pons and medulla.

4. Fibers of the ascending limb of the uncinate fasciculus pass rostrally dorsal to the brachium conjunctivum and at the level of the inferior colliculus the fibers begin to disperse.

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Fibers are projected to the nuclei of the posterior commissure, the posterior commissure, the nuclei of the lateral lemniscus and at thalamic levels enter the parafascicular and centromedian nuclei.

5. Fibers originating from the fastigial nuclei do not ascend in the brachium conjunctivum and do not enter or terminate in the red nuclei, the motor nuclei of any of the cranial nerves, the medial longitudinal fasciculus or any of the so-called cerebellar relay nuclei.

6. Unilateral lesions of the fastigial nucleus in the cat produce disturbances of equilibrium and ataxia involving axial and appendicular musculature; these disturbances undergo relatively rapid attenuation according to a specific pattern.

7. Physiologic disturbances resulting from complete and incomplete unilateral destruction of the fastigial nuclei could not be distinguished by the nature or severity of the deficits.

8. Bilateral lesions of the fastigial nuclei in the cat provoke quantitatively more severe and enduring ataxia and disturbances of equilibrium than unilateral lesions, and the attenuation is prolonged.

Hypotheses presented are:

1. Physiologic phenomena resulting from localized destruction of the fastigial nuclei are probably due to the removal of inhibitory influences of this structure upon the vestibular nuclei.

2. The ascending limb of the uncinate fasciculus may relay vestibular impulses to thalamic and other supra segmental levels.

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Exceptional Memory for Dates and Weather in a Schizoid Psychopath

The patient was a laboratory technician aged 27. The chief of the unusual skills he possessed was that given any date in the preceding 16 years he could rapidly say on what day of the week it fell and what the weather was. He had lost a succession of jobs and repeatedly failed examinations. Therefore he had consulted an occupational psychologist who found that in most abilities he was above the 90th percentile of the professional class. Because of the oddities in his behaviour he was advised to seek neuropsychiatric help. The neuropsychiatrist to whom he went was particularly interested in his memory ability and after his admission as an in-patient referred him to the psychological department for elucidation of this. The principal abnormal features of the patient's behaviour were numerous stereotyped mannerisms in gestures and movements, exaggeratedly deliberate enunciation of speech, and a tendency to express himself in cliches wherever possible. There was no evidence of thought disorder, delusions, or hallucinations.

In the psychological session the patient was asked the weekday of 80 dates presented in randomized order but systematically covering the 16-year period. He was right in 74 and the other six were wrong by a day only. He showed strong self-involvement with his skill which made searching consideration of his method of working difficult. It emerged, however, that he operated by a number of anchor dates of which he knew the weekday and related all other dates to these by invariant calendar relations. From further investigation it was possible to identify 118 anchor dates. These all related to either personal events or unusual weather. The total number at his disposal was estimated as more than 500. His memory for weather was more troublesome to check precisely but in 12 presented instances his statement corresponded to the contemporary newspaper account. In connection with each anchor date he recollected the sequence of weather conditions up to the next anchor date. In fact dates, weather, and personal events were linked in an intricate system of cross-association.

He had certain other memory skills. He knew all squares up to that of 1,000 and all cubes up to that of 100. He could multiply four-place by four-place numbers in his head. His account indicated that he worked by factorization with auditory-motor imagery. He also experienced synesthesia, associating a constant colour image with each number from 0 to 9, but this was not utilized in his calculations. In all tests of abilities applied to him his scores were very high except in the Hanfmann-Kasanin where he showed marked concreteness of thinking. While answering questions in the various parts of the examination but particularly in calculations his muscles became very tense and he exhibited the mannerisms of rapidly twirling and untwirling a handkerchief. Biographical inquiry indicated that he had been fond of studying calendars and almanacs from an early age. The development of his special skills, however, began at the age of 11 after hearing a lightning calculator on the radio. It was then that he started a diary, recording important personal events and the weather and committing special dates to memory. He disclaimed all knowledge of the lives and methods of the classic arithmetical prodigies.

The various tests and enquiries suggested that his skills could be analysed as dependent on the following factors: (*a*) a capacity to remember discrete details much above average, (*b*) high numerical ability, (*c*) a special interest in numbers, regular sequences, and recurrences, and weather, (*d*) a narrow range of general interests, (*e*) unusual concern with the minor events of his own life, (*f*) fondness for reviewing his life with or without the aid of diaries, (*g*) a habit of relating each event as it occurred to its date, weekday, and weather, (*h*) increasing self-involvement with his skills and deliberate cultivation of a large reserve of anchor dates, and (*i*) incessant practice.

The patient was treated with insulin and left the hospital after a few months. He has remained without neuropsychiatric care for over eight years now, showing neither improvement nor deterioration of symptoms, as a recent follow-up revealed. The pattern of losing jobs and failing examinations continued, his mannerisms have remained unchanged. His parents, who are quite well-off, are tolerant of his peculiarities. His memory skill continues as the chief interest of his life. Not only has he maintained it but he has tried to make it cover an earlier period than his diaries, taking national events as anchor dates and learning the weather from past records.

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Aromatic Metabolism in Schizophrenia. I. Statistical Evidence for Aromaturia

1. The work of 20 authors who have reported on aromatemia or aromaturia in schizophrenia has been briefly reviewed.

2. The overnight urine of 109 schizophrenics, 315 non-schizophrenic mental patients and 223 normals has been studied chromatographically. The schizophrenics appeared to excrete a higher than normal concentration of aromatic compounds. Based on an arbitrary scale which takes into account the number of coloured areas and the intensity of these areas on an unidimensional chromatogram, the schizophrenics have a rating of $8 \cdot 1 \pm 0 \cdot 3$, the non-schizophrenics $5 \cdot 0 \pm 0 \cdot 2$, and the normals $5 \cdot 0 \pm 0 \cdot 1$.

3. The chromatographic rating has been found to vary from day to day for both schizophrenic and normal individuals.

4. The distribution curves of the normal, non-schizophrenic and schizophrenic groups show considerable overlap: this overlap is attributed to: (*a*) daily variation in the aromatic excretion, (*b*) diagnostic error, (*c*) error in measurement, and (*d*) unknown factors.

5. Diet and emotional stress are not considered to play a dominant role in this aromaturia.

(Authors' Abstr.)

Aromatic Metabolism in Schizophrenia. II. Bidimensional Urinary Chromatograms

The significance of the comparative studies reported is that they serve to confirm previous quantitative reports of excessive aromatic excretion by schizophrenics. They indicate the possibility that a qualitative difference may exist as well.

(Authors' Abstr.)

Impairment of Abstracting Ability in Multiple Sclerosis

In view of experimental and clinical findings it is predicted that patients with multiple sclerosis will manifest a loss in the ability to function at the abstract level. Seventeen M.S. patients, 14 males and 3 females, are closely matched with 17 control patients having no C.N.S. disorder on age, sex, education, intelligence, and race. Both groups are given the Wechsler-Bellevue Intelligence Scale, Form I, and the Grassi Block Substitution Test, the latter requiring different levels of functioning on the abstract-concrete continuum. The results confirm the prediction: the M.S. patients perform significantly poorer on the G.B.S.T., especially on the abstract levels. Additional analysis controlling for the possible interfering effects of visual-motor difficulty in M.S. gives rise to the same results. It is concluded that a

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moderate loss of the ability to abstract in patients with multiple sclerosis is demonstrated and that such a loss roughly parallels extent of neurological disturbance.

(Authors' Abstr.)

A Comparison of Monoureide and Diureide Sedatives. With Respect to Drug Habituation, Untoward Effects and Mortality Rates

1. Three separate clinical investigations, including a total of 371 case studies and a comprehensive survey of medical literature, failed to show a single case or manifestation of drug habituation following continued use of acetylcarbromal or bromisovalum (bromural), singly or in combination.

2. The absence of untoward effects attributed to acetylcarbromal or bromisovalum is in sharp contrast to the frequent and serious neurological and psychiatric manifestations reported and the common occurrence of drug habituation following use of the barbiturates.

3. Due to the fact that the monoureide sedatives are non-habit-forming, have no side effects, no hangover and no contraindications, the authors believe that the acetylcarbromal bromisovalum combination is much preferable for continued use as a sedative or somnifacient to the dangerous and habit-forming barbiturates.

(Authors' Abstr.)

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On the Participation of Adaptive Hormones in Disease Susceptibility. *Selye, H.* .. 97

The Nature of Apraxia

It is concluded that in its highest elaboration mimetic and propositional behaviour is related to conceptual organization of space, objects and persons, in the dominant hemisphere. Such behaviour is more highly vulnerable to pathologic changes than is direct physiologic reaction to external events. The resulting disorder is ideational apraxia. Perseveration of identification is a mild form of the same defect. Acquired specialized motor function that requires a leading hand for its performance is closely related to cortical dominance but can be affected independently of symbolic function. The relationship is probably through the conceptual defect underlying constructional apraxia. Related symbolism and dexterity may be separately managed by different hemispheres, independently vulnerable to unilateral lesion, and independently controlling the subcortical motor apparatus for the two sides.

Apraxia that is independent of conceptual function (kinetic apraxia) can be traced to the abnormal operation of released sensory factors that direct the physiological aspects of behaviour.

There are two general types of disturbance, exemplified by frontal and parietal kinetic apraxia, both of which show perseveration of sensory effects. Bilateral kinetic apraxia first and most seriously affects gait and other bilateral motor performance. When the normal equilibrium of cortical praxis is already disturbed, it is possible to induce tremor by concurrent stimuli with conflicting effect. Subcortical extra-pyramidal lesions release the same apractic reactions in persistent (dystonic) form. There are more commonly mixed forms where conflicting reflex effects lead to instability of posture, athetosis and tremor. The static (tonic) aspects of such disorders of movement can be identified with the prolonged operation (perseveration) of sensory factors.

(Authors' Abstr.)

Visceral Brain, its Component Parts and Their Connections

The olfactory, visceral, hippocampal and hypothalamic neural mechanisms are described. Their interconnections receive special attention. Together they form the visceral brain or limbic lobe. Working together these several parts subserve the basic biologic needs of the individual. Olfaction takes part in primitive search for food, feeding and identification of odorous objects in the environment. A primitive olfactory "motor" pathway from the nucleus basalis to the habenula, thence to interpeduncular nucleus, to tegmental and reticular formation is illustrated. The visceral cortex, claustrum, uncinate bundle and amygdala are described with some interpretation. Their relations to the original olfactory mechanisms, internal capsule, and basal ganglia are indicated. The hippocampal formation, as a cortical dependency, and its mechanism for integration of emotional states, arousal to action, hypothalamic and cortical responses are considered. Hippocampal, neuronal mechanism is illustrated. The hypothalamic nuclei, their amygdalar, forebrain, hippocampal, autonomic and hypophysial connections are illustrated and defined. It is pointed out that large-celled nuclei conduct nerve impulses; whereas the granule cell nuclei may possibly have a cholinergic function. Most of the reactions of the visceral brain are biologically grounded, close to the reflex-like level of

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innate activities. They are designed to preserve, maintain and protect the individual, and control his vegetative needs, an important segment of inner life. From this point of view each mechanism appears to have an appropriate structural design.

(Author's Abstr.)

Effects of Septal and Amygdaloid Lesions on Emotional Behaviour and Conditioned Avoidance Responses in the Rat

A study was conducted with rats to investigate the effects of septal and amygdaloid lesions upon avoidance conditioning, and overt emotional behaviour. The latter was measured on a six-component rating scale. Conditioning was carried out in a shuttle box, so arranged that the rat could move through a door from one compartment to another to avoid a shock signalled by a buzzer. Results were as follows:

1. Septal lesions produced a dramatic increase in overt emotionality, whereas unoperated controls and operated controls with neocortical and cingulate lesions showed no such damage.
2. Septal lesions decreased the number of trials required to learn the avoidance response.
3. Lesions in the amygdaloid nuclei of normal animals did not significantly alter overt emotionality.
4. There were no differences in rate of acquisition of conditioned responses between normal rats and rats with amygdaloid damage. However, the response latencies of the amygdaloid preparations were significantly lengthened. Throughout the experiment, no other group differed from normals in response latency.

(Author's Abstr.)

FEBRUARY

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The Cingulates and Behaviour

Nine cats and 11 monkeys were studied for from 3 to 12 months preoperatively for (*a*) spontaneous behaviour, (*b*) learning capacity, and (*c*) the neurotogenic effects of motivational conflicts. Ablation of cingulate areas 23 and 24 then produced the following results:

1. Minimal amnesia for previous learning, but increased incidence of error and impaired precision of acquiring new skills.
2. A tendency to diffuse and precipitate activity.
3. Diminished motivation, especially for initiating or completing goal directed tasks, with the exception of area 24 monkeys.
4. Moderately increased aggressivity toward other animals and man.
5. Lowered thresholds of startle and fear, except in three cynamologos monkeys.
6. An accentuation of the effects of isolation in exacerbating the above reactions.
7. In one instance, maternal pre-emption of food at the expense of a nursing baby.
8. Minimal or no relief of phobic, regressive, socially maladaptive, and other aberrant behaviour in the neurotic animals, but with greater amenability to retraining and other therapy.
9. Generally increased susceptibility to the reinduction of experimental neuroses, again with the exception that two area 24 monkeys showed an increased tolerance to conflictual experiences and in one of these the authors were unable to induce a neurosis even after 6 months of effort.

The theoretical and clinical significance of these findings is briefly discussed.

(Authors' Abstr.)

Glutamic Oxalacetic Transaminase in Cerebrospinal Fluid

1. The control value of glutamic oxalacetic transaminase of the spinal fluid among 30 subjects was $16 \cdot 8 \pm 7 \cdot 6$ units.
2. A significant elevation of spinal fluid GOT in acute cerebrovascular accidents was noted in 9 out of 32 tested patients, comprising 28 per cent. of the total.
3. In patients with acute cerebrovascular accidents high spinal fluid GOT levels tend to indicate poor prognosis and low GOT levels a favourable prognosis.
4. The spinal fluid GOT in patients with brain tumours was normal except in those with obstructive hydrocephalus. In one case of congenital internal hydrocephalus there was marked elevation.
5. The convulsive disorders showed elevated spinal fluid GOT only when the specimens were taken during or soon after the end of the convulsion.

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6. The spinal fluid GOT was found to be normal in the other neurologic diseases included in this series.

7. Transaminase levels in one human brain was highest in the cerebellum, followed by the pons, cerebral cortex and white matter, hypothalamus and thalamus, in that order.

(Author's Abstr.)

Clinical and Laboratory Observations on LSD-25

1. LSD-25 can be used to demonstrate the integration of basic neurophysiology with well-known concepts of psychopathology.

2. LSD-25 has the astonishing quality of bringing into focus the patient's repressed emotional attitudes, conflicts, etc., and permits their reactivation. The hallucinatory experiences are not always symbolic, but in the majority of the patients these were not difficult to interpret with knowledge of the patient's developmental history, defences, etc.

3. The intense transference develops and may be capitalized on with direct, interpretive, Rosen type psychotherapy centering on the re-experiences as well as for reconditioning of "breaking up" of obsessiveness circuits in favour of more appropriate thinking circuits. Improvement was also produced by psychocatharsis.

4. LSD-25 effects are mediated through the reticular activating substance and hypothalamic-pituitary-adrenal axis, as demonstrated physiologically.

5. In the number of cases presented, most had placebos for control and all except the chronic brain syndromes demonstrated some degree of improvement in the sense that they were able to return to society and their families in a more productive capacity.

(Authors' Abstr.)

Some Pharmacologic Correlations of the Chemotherapy of Mental Disease

In concluding the review of the dynamically active field of the pharmacotherapy of mental disease one is tempted to point out three generalizations of drug action which appear to be crystallizing.

1. Mental depression may be related to either a neurohumoral deficiency of cerebral serotonin or some sympathomimetic amine or to some enzyme disorder such as a monoamine oxidase over-activity in the adrenergic excitatory mechanisms of the brain which might produce such a deficiency.

2. Drugs which are most effective in curbing the acute mania, motor excitement and hallucinations of the schizophrenic reaction are those which interfere in some manner with the adrenergic excitatory centres for emotional responses in the brain as exemplified by reserpine and chlorpromazine.

3. Psychoneurotic symptoms respond most favourably to drugs which have a minimum of side effects and produce a relaxation of neuromuscular tension and anxiety with a minimum of drowsiness and other symptoms of central nervous system depression.

(Author's Abstr.)

MARCH

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The Effects of Two Antiserotonin Substances (BAS and BAB) and of Bufotenin on the Spontaneous Electric Activity of the Brain

1. BAS (benzyldimethylserotonin) induces convulsive-like non-spreading electric discharges in the hippocampus of the rabbit.

2. BAB (benzyldimethylbufotenin) produces continuous fast activity localized to the lenticular nucleus, chiefly in the putamen. The amplitude is three to four times larger than that of waves of comparable frequency normally present in the lenticular nucleus and in other parts of the rabbit brain.

3. Bufotenin (N,N-dimethylserotonin) causes the disappearance of slow wave high voltage activity and introduces an enduring "alert" desynchronized pattern.

4. The electroencephalogram in 12 to 15 chronic psychotic patients did not show significant changes under treatment with BAS. In three subjects only, however, a decrease of the amplitude and slowing of the fundamental alpha activity were observed.

(Author's Abstr.)

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Clinical Evaluation of BAS (Benzyl Analog of Serotonin): A Tranquilizing Drug

The effects of BAS, the benzyl analog of serotonin, were studied on 24 chronic, moderately disturbed female psychotic patients. The most prominent beneficial action, that of tranquilization, was noted in 22 of these patients. Tranquilization was attained at dosage levels varying between 50 to 200 mg. per day. The maximum tolerated dose was 300 mg. per day. Among the paranoid patients who improved, the delusions became less important. The intensity and frequency of the hallucinatory experiences diminished. In hebephrenic patients, speech became less dissociated. These salutary psychiatric effects, however, were marred by untoward reactions involving the general health of some patients who lost weight chiefly because of a profound feeling of weakness and fatigue. Another disturbing side reaction deserving comment is ataxia which was extensive in some patients. The effects of BAS are compared with those of reserpine which they resemble in many ways, but are not seen to the same extent with both drugs. The clinical similarities of BAS and reserpine are ascribed to the indole group, which their chemical structures have in common. Their different non-indolic moieties are regarded as being the causes for the clinical dissimilarities exhibited by these two drugs.

(Authors' Abstr.)

Studies on the 5-Hydroxytryptamine (Serotonin) Content in Human Brain

The presence of serotonin in human brain structures has been demonstrated. The areas of the allocortex had higher serotonin concentrations than the isocortex. The highest concentration of serotonin per unit weight of tissue is in the mesencephalic structures (mainly substantia nigra and probably red nucleus); the diencephalic structures (hypothalamus) contain also relatively large amounts of this neurohormone. The cerebellum as well as the isocortex have the lowest concentrations of serotonin.

(Authors' Abstr.)

APRIL

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Psychologic Changes Induced by Reserpine Therapy on a Group of Severely Disturbed Psychotics

Eighty-eight psychiatric patients, nearly all schizophrenic and all considered to be among the most severely disturbed, were divided into matched pairs to form an experimental (reserpine) and a control group (placebo). A preliminary evaluation was made using Lorr's Multidimensional Scale for Rating Psychiatric Patients, an abbreviated Wechsler Bellevue Intelligence Scale, and individual Rorschach. The experimental group then received reserpine and the control group placebo for a period of 7 weeks. Then a second evaluation was made. The medications were reversed and a third measure was made 7 weeks after the switch in medications.

Results show that the average patient of this study becomes more compliant, submissive, communicative, and outgoing, but perhaps somewhat more dysphoric after reserpine therapy. Intellectual functioning as shown by Wechsler-Bellevue performance is improved, but there seems to be no significant improvement in potential ego strength as shown by the application of Klopfer's Prognostic Rating Scale to the Rorschach.

A decrease in pathology was suggested by the three measures which were employed. The beneficial effects of reserpine were more pronounced for the group which had received reserpine initially than for the group which had received reserpine after a period of placebo treatment. It was further suggested by these measures that patients changed from reserpine to placebo do not maintain the gains made on the drug.

The relatively greater gains for the reserpine group during the first 7-week period suggest the importance of non-drug factors which must be taken into account in any subsequent research.

(Author's Abstr.)

MAY

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Skin Histamine Reaction in Schizophrenic and Non-Schizophrenic Mental Patients

Schizophrenics can be differentiated by skin histamine reaction from other patients only as a group. There are some individual schizophrenics who have a strong histamine skin reaction and some individual non-schizophrenic patients who have a weak histamine skin reaction. The hope that it would be possible to develop a specific skin histamine test for schizophrenia appears to have been too sanguine. All tests, either physiological or psychological, for schizophrenia so far attempted, managed to differentiate schizophrenics as a group, but failed to diagnose the individual patients. One can refer to these tests as being peripheral, because they measure, usually indirectly, only secondary (dependent) variables. The real diagnostic test for schizophrenia is yet to come. It will probably coincide with the discovery of the key metabolic disorder responsible for schizophrenic illness.

(Authors' Abstr.)

The Phenomenon of Auditory Hallucinations in Chronic Alcoholism

1. The phenomenon of auditory hallucinations in chronic alcoholism has been studied. Clinical observations of 76 instances of this illness are recorded and illustrative case histories are presented.

2. Although the occurrence of auditory hallucinations was the outstanding feature in all the cases, several clinical forms could be distinguished: (*a*) in 68 instances the hallucinations were benign and transient and were frequently associated with other signs of prolonged inebriation and abstinence; (*b*) in 8 cases the hallucinations persisted for several weeks or months; (*c*) in 4 of these the illness was indistinguishable from the first type at its outset, but later the characteristic symptoms of schizophrenia developed.

3. Our observations indicate that a syndrome may emerge in relationship to excessive drinking which is clinically indistinguishable from schizophrenia. The patients with this syndrome, prior to its appearance, could not be considered schizophrenics and the age of onset was later than that usually encountered in schizophrenia. The concept, that the schizophrenic-like illness is simply "latent schizophrenia made manifest by alcohol" is neither logical nor consistent with the observed facts.

4. The current theories concerning the aetiology of auditory hallucinosis are critically evaluated. Data are presented to show that the development of auditory hallucinations depends not only on the effect of prolonged inebriation, but ultimately on the effect of withdrawal of alcohol. The factor or factors responsible for the prolongation of the illness and for the occasional transition to a schizophrenic-like form, are unknown.

(Authors' Abstr.)

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Hexafluorodiethyl Ether (Indoklon): Its Use as a Convulsant in Psychiatric Treatment

Hexafluorodiethyl ether was administered to 60 of 120 patients randomly selected for convulsive therapy. In the 720 treatments administered to these 60 patients there was no failure in bringing about a *grand mal* convulsion. Also, there was no evidence of any change in sensitivity or tolerance to the standard convulsive dose with progressive treatment. The convulsive seizure was similar to that produced by electric stimulation, except for a more gradual onset. There appeared to be less immediate post-convulsive anoxia, and immediate post-convulsive psychomotor activity appeared diminished in comparison with E.C.T. Subjectively, a majority of those patients who had been exposed to both types of treatment

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felt less apprehensive with the inhalation procedure. From these results it appears that Indoklon is an effective and safe convulsive agent that can be administered safely and conveniently on a large scale basis.

(Authors' Abstr.)

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The Limbic System with Respect to Self-Preservation and the Preservation of the Species

The greater part of the phylogenetically old cortex is contained in the great limbic lobe of Broca. This lobe is found as a common denominator in the brains of all mammals. Together with its subcortical cell stations it comprises a functionally integrated system, which, in keeping with Broca's terminology, may be referred to as the *limbic system*. Evidence is cited which indicates that the frontotemporal portion of the limbic system is largely concerned with mechanisms that are involved in obtaining and assimilating food and are thereby essential to *self-preservation*. Attention is then turned to recent findings that are beginning to suggest that another portion of the limbic system, involving parts of the septum, hippocampus and cingulate gyrus, is concerned with expressive and feeling states that are conducive to the *preservation of the species*. Some of the implications of these new findings in regard to a number of provocative neurological questions are discussed.

(Author's Abstr.)

Circulating Epinephrine and Norepinephrine in Changing Emotional States

In a study of 60 hospitalized psychiatric patients, it was found that circulating levels of epinephrine and norepinephrine tend to change in accordance with changes in an individual's emotional state. The presence or absence of certain descriptive and personality features indicates the frequency with which this parallel relationship will occur. Through an analysis of these factors, it seems possible to distinguish subgroups of the population in whom changes in epinephrine or norepinephrine, or both, tend to be reliable indicators of similar changes in the patient's emotional status.

(Authors' Abstr.)

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Preliminary Study of a New Anti-Depressant Drug

1. In this controlled study thirty-two schizophrenic patients were given various doses of SKF #5 without significant improvement.

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2. Twenty-five seriously depressed patients were treated with this drug and improvement was noted in 76 per cent. of the group.

3. The development of high levels of alkaline phosphates in twelve patients suggests that further appraisal of these findings should be done in a longer range study.

4. The observable side effects were not of a serious nature.

5. The effective dose appears to be between 60 and 300 mg. per day. Initial doses should be as low as 25 to 30 mg. per day.

(Authors' Abstr.)

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Studies on Multiple Sclerosis. I. Multiple Sclerosis Viewed as a "Chronic Disseminated Encephalomyelitis". II. Etio-Pathogenesis of Multiple Sclerosis (Infectious Allergic or Toxic Allergic)

No appreciable clinical differences seem to exist in support of a differential diagnosis between acute multiple sclerosis, the early stages of multiple sclerosis, and the acute or sub-acute varieties of post-exanthematic, post-vaccinal, or post-infectious encephalomyelitides.

The value of relapses and remissions which in the past was considered an important differential feature favouring multiple sclerosis, has lost its importance in the face of relapses and remissions occurring also in various types of acute disseminated encephalomyelitides.

From a pathological standpoint no appreciable differences exist between the lesions of acute disseminated encephalomyelitides, the post-vaccinal ones, acute multiple sclerosis and the acute foci related to relapses in chronic multiple sclerosis.

It is therefore proposed to label multiple sclerosis as a "chronic variety of disseminated encephalomyelitis". Multiple sclerosis may then represent the chronic stage of any acute disseminated encephalomyelitis and not a transformation of a disease into another one.

The general biological factors which determine in some cases a simple acute and reversible encephalomyelitic process and in others a chronic progressive process leading to irreversible glia scars are the expression of the immuno-biological constitution which governs reactions of individuals or groups of individuals, to various noxi. The organization of individual immuno-biological defenses is the result of constitutional hereditary factors, modified by age, environment and adaptation.

Acute disseminated encephalomyelitides and multiple sclerosis have a common aetio-pathogenesis. This the author would like to label "Infectious-allergic" or "Toxic-allergic".

The toxic etiologic component of the combination, as well as of the infectious one, may be different in various groups of cases, just as it is different in measles, scarlet fever, variola, varicella or influenza. The toxic or infectious etiologic components must combine with a partial antigen in order to create a complete "demyelinating encephalitogenic antigen". This complete antigen will trigger off an allergic reaction. The ultimate pathogenic mechanism responsible for the clinico-pathologic changes will thus remain an allergic one.

This concept of "infectious-allergic", or "toxic-allergic" etio-pathogenesis of "acute and chronic disseminated encephalomyelitis" is an elaboration of the author's earlier general concept (1944) that the pathology of multiple sclerosis could be viewed in the light of an "allergic reaction of the central nervous system".

We do not know under what biochemical or immuno-biological circumstances the combination of an infectious or toxic agent and partial antigens occurs. Factors of our individual immuno-biological organization and related protective mechanism must play an important role toward that combination, as well as toward the type of pathological reaction leading to an acute transitory or to a chronic type of disseminated encephalomyelitis. Very little is also known about possible mutations of viruses or bacilli which, particularly in the case of atypical tuberculosis, may play an important role in the type of pathologic reaction of the nervous tissue related to "toxic-allergic" or "infectious-allergic" etio-pathogenesis of multiple sclerosis.

(Author's Abstr.)

The Histologic Structure of the "Inclusion Bodies" of the Neurons in Pick's Disease. A Study with Silver Carbonate

The complex histopathologic picture of degeneration of neurons is broken down into its component parts by the silver carbonate technic, so that various degenerative types can be recognized. The outstanding histopathologic phenomenon is the transformation of the intracellular fibers into amorphous material called "inclusion bodies" which fully confirms the conclusion of Alzheimer (2). However, the degeneration of the intracellular structures is not confined to the fibers, does not run a uniform course and does not always culminate in the

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formation of amorphous inclusions. The latter phenomenon is least conspicuous in Type I in which the entire system of fibers is transformed into a coarse network.

Type II on the contrary, is characterized by one or more sharply outlined "inclusion" bodies in the cytoplasm, some of which are surrounded by a ring of fragments or a halo.

In Type III the neurons are greatly enlarged, contain numerous vacuoles filled with a substance which stains reddish brown with oil red "O"; it probably is a lipoid. In more advanced stages the cells become homogeneously stained brown red or blue black, the vacuoles disappear and no histologic details can be recognized.

Type IV represents the final stage of destruction of nerve cells which are reduced to amorphous fragments and have lost all semblance of normal structure.

Disintegration of the nuclei of the neurons is less conspicuous than that of the cytoplasm because the former are frequently destroyed early in the course of degeneration; those which survive are swollen and blurred, and are partly extruded from the cell. In spite of advanced degeneration, numerous dendrites are preserved.

The degeneration of the neurons overshadows other histopathologic changes to such an extent that it cannot be doubted that Pick's disease is a primary disease of the parenchyma. The effects of destruction of neurons on the myelo- and glia-architecture are profound, but cannot be discussed here beyond stating that there are also "inclusion bodies" in the astroglia and that various degenerative changes occur in the oligodendroglia. There are usually numerous microglia elements in the form of gitter cells, many of them are laden with fat.

(Authors' Abstr.)

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Diffuse Traumatic Degeneration of the Cerebral Gray Matter

A diffuse degeneration of the cerebral gray matter is described in a 14-year-old boy who died 10 months after closed traumatic injury to the skull. Extensive cortical devastation and gliosis with selective involvement of the central gray matter and without evidence of crude traumatic destruction of hemorrhage were the outstanding features. The parenchymal lesions appeared to be related closely to the concussive force; a constellation of factors which included edema, thixotropy, and vasal disturbances were undoubtedly important in the pathogenesis.

(Authors' Abstr.)

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Some Aspects of the Relation of Ceruloplasmin to Wilson's Disease

The results of determinations of the concentration of the plasma protein, ceruloplasmin, in various clinical conditions are presented. These show that Wilson's disease is characterized by a marked deficiency or absence of the protein, but that neither liver disease nor neurologic disease of various other kinds is associated with diminished concentrations of ceruloplasmin. In fact, in both of these latter groups the mean value for plasma ceruloplasmin was significantly ($P<0{\cdot}01$) greater than the mean of the normal group. Although the mean concentration of plasma ceruloplasmin in a group of schizophrenic patients was slightly higher than the mean of the normal group, determination of the concentration of ceruloplasmin seems to be of no value in differentiating schizophrenic from normal individuals. Studies performed in patients with Wilson's disease indicate that their deficiency of ceruloplasmin is a consequence of impaired synthesis of the protein.

(Authors' Abstr.)

Effect of Prolonged Treatment with Tranquilizing Drugs upon Two Enzymes of the Central Nervous System

Superimposed upon a fluid state of carbonic anhydrase content of the central nervous system in the controls, the data presented would seem to clearly indicate that the tranquilizing drugs produce an increase in carbonic anhydrase in areas of the brain, which appears to culminate in the hippocampus and brainstem. In growing animals the effect is more diffuse than in adult animals. There has been shown an optimum point in the course of injections after which the carbonic anhydrase content deteriorates.

(Author's Abstr.)

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Uncinate Fits

1. The history of the concept of uncinate seizures is reviewed. Observations on 55 patients form the basis of this report.

2. Olfactory phenomena occurred most frequently, usually in the form of hallucinations. The hallucinations ranged from crude, unrecognizable sensations of smell to complex multisensorial elaborations. In rare instances olfactory "reminiscences" and illusions are reported.

3. The uncus appears to be the cortical centre for smell. In one patient necropsy revealed focal gliosis in the uncus.

4. Gustatory phenomena were limited to undifferentiated hallucinations of taste.

5. Twelve patients reported rhinostomal sensations consisting of burning, tingling, or crawling sensations in the nose, mouth, or throat. In the majority they were associated with olfactory or gustatory hallucinations.

6. Interictal or postictal illusions of smell or taste or, less commonly, hallucinations, are described by some patients.

7. The relationship of these phenomena to "dreamy states", ictal affect, and vegetative disturbances during seizures was analysed. An attempt was made to extend the concept of the functions of this area to explain the association of these events.

(Author's Abstr.)

MAY

*The Use of Anticoagulants in Cerebral Thrombosis. *Fisher, C. M.* 311
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The Use of Anticoagulants in Cerebral Thrombosis

Anticoagulant drugs have been administered to 58 patients with symptoms and signs of the various stages of cerebral thrombosis due to atherosclerosis. The data suggest that anticoagulant therapy abolishes transient ischemic attacks and prevents or postpones the arrival of a threatening stroke. When used in the early stage of a progressively evolving stroke due to cerebral thrombosis, the downhill course appears to be satisfactorily arrested and reversed. Patients observed for periods both on and off anticoagulants fared better while receiving anticoagulants. A group of 37 cases rather comparable to the anticoagulant group were observed without anticoagulant therapy and ran a far less satisfactory course than the treated patients. From this preliminary clinical exploration, anticoagulant therapy may be regarded as a promising therapy in cases of cerebral thrombosis encountered in the earlier stages; certainly in the author's experience it seems more beneficial than any other mode of therapy used at present and it is relatively safe. The increasing frequency with which stroke patients are seen in the clinic, at a point in their illness when anticoagulants might be effective, indicates that this therapy may be of great significance in medical practice. The present data do not provide incontrovertible evidence of the therapeutic efficacy of anticoagulants because satisfactory control patients have not been studied.

The tentative indications for anticoagulant therapy in transient cerebral ischemic attacks and cerebral thrombosis have been discussed at some length.

The clinical picture of transient ischemic attacks has been described and their differential diagnosis discussed.

(Author's Abstr.)

JUNE

Focal Seizures Due to Chronic Localized Encephalitis. *Rasmussen, T., et al.* 435
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*Subcutaneous Hemorrhages in Multiple Sclerosis. *Swank, R. L.* 497

Localization Within the Amygdaloid Complex of Anesthetized Animals

1. The corticomedial division of the amygdaloid complex appears to be the area concerned with regulation of autonomic responses from this region.

2. The blood pressure responses from the amygdaloid area appear to be mediated through the region of the ventromedial nucleus of the hypothalamus. Respiratory responses from the amygdaloid complex also appear to be associated with this structure.

3. The basolateral division appears to be concerned with the somatic responses reported from this area, especially with movements of the face and jaw. Sustained jaw opening was obtained at lowest threshold from the basal medial nucleus, and the lowest threshold for jaw closure was found to be in the lateral nucleus.

4. The reactions elicited by stimulation of the amygdaloid complex appear to be a function of this area and not due to spread of stimulation current to adjacent structures.

(Authors' Abstr.)

The Narcolepsy Syndrome

A series of 158 cases with narcolepsy has been reviewed.

Evidence is strongly suggestive that the narcolepsy syndrome is a nonepileptic disturbance of subcortical origin. It appears to be a state of depression of the arousal system, possibly from a neurohumoral deficiency.

(Author's Abstr.)

Subcutaneous Hemorrhages in Multiple Sclerosis

Frequent and periodic occurrence of small spontaneous subcutaneous hemorrhages in multiple sclerosis is reported.

(Author's Abstr.)

JULY

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Investigation of the Primate Amygdala: Movements of the Face and Jaws Afterdischarge and the Anterior Commissure

Gloor has summarized the evidence regarding the known corticopedal pathways of the amygdaloid complex. Such pathways go to the homologues of the temporal polar and insular cortex. In this investigation an after-discharge was recorded from the parietal cortex of the monkey following repetitive stimulation of the homolateral amygdaloid complex. The latency of this response was not measured, but such an after-discharge may indicate a polysynaptic pathway between the amygdaloid complex and the homolateral parietal cortex.

Bucy and Kluver, Lauer, and others have found that a part of the anterior commissure provides an anatomic connection between the amygdaloid complexes. It has been demonstrated here that a repetitive electrical stimulus in one amygdaloid complex can be followed by an afterdischarge in the other amygdaloid complex and this can be recorded from the region of the anterior commissure. When the afterdischarge was recorded from the amygdaloid complex, the

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facial movements which had been ipsilateral to the side of the stimulation became bilateral. After the anterior commissure was severed, it was no longer possible to record the after-discharge in the amygdaloid nucleus contralateral to the one stimulated, and the facial movements pursuant to stimulation of one amygdaloid complex remained ipsilateral to the side stimulated.

These experiments have demonstrated that epileptiform discharges may arise in the amygdaloid complex of one temporal lobe and spread to the amygdaloid area of the other temporal lobe by way of the anterior commissure, and that such spread can be prevented by interrupting the anterior commissure.

(Authors' Abstr.)

Somatic and Visceral Responses from the Cingulate Gyrus

1. An account is presented of the results of stimulation and destruction of portions of the cingulate region of 15 Macaca mulatta monkeys. A pattern of somatic movements was found on the anterior portion of the cingulate gyrus which repeated itself in reverse order on the posterior portion of this gyrus. In this pattern, movements characteristic of emotional expression, involving the musculature of the face, the head, and the neck were present upon stimulation of all points on the gyrus. They were either homolateral or bilateral. The movements involving clonic flexion, extension, and internal rotation of the upper and lower extremities were either contralateral or bilateral.

2. Increased strength of stimulation (7 to 10 volts) produced convulsive movements comparable to those seen in certain forms of epilepsy.

3. Autonomic phenomena included respiratory, cardiovascular, sudoriferous and pupillary changes, and piloerection. These resulted both from stimulation and from destruction of the rostral and the caudal parts of the cingulate gyrus.

(Authors' Abstr.)

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Epileptic Cephalea

Five cases of paroxysmal headaches in children are described.

The nature of the headaches was clarified by electroencephalograms, which revealed epileptic activity in all cases, especially during photic stimulation.

With the exception of one who had convulsions in the first week of her life, none of these children had experienced frank seizures.

Epileptic cephalea seems to appear as the sole manifestation of a latent epileptic tendency and deserves a special place among the various forms of headaches.

(Authors' Abstr.)

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Implications of a Five-Year Study of 700 Basal Ganglia Operations

A five-year follow-up study of more than 700 operations of anterior choroidal occlusion, chemopallidectomy, and chemothalamectomy leads to the following conclusions:

1. This investigation has resulted in a roentgen-anatomic-physiologic method of basal ganglia surgery which can relieve tremor and rigidity of Parkinsonism in 80 per cent. of properly selected cases, with a risk of mortality of 2·4 per cent. and a risk of hemiparesis of 3 per cent.
2. Tremor, rigidity, deformity, and incapacitation of parkinsonism can be relieved without the infliction of any neurologic or psychologic deficit.
3. Five-year cures of the symptoms of tremor, rigidity, deformity, and incapacitation can now be documented in this series of cases.
4. On the basis of this study, parkinsonism can no longer be considered a hopeless, progressive, incurable disease. Inasmuch as the incapacitating symptoms of tremor, rigidity, and deformity have been alleviated by surgery of the globus pallidus and thalamus for as long as five years without recurrence, a more hopeful and realistically optimistic viewpoint can be adopted concerning this disease. The therapeutic implications of this statement apply not only to surgical therapies but to the future development of medical treatment as well. Moreover, the symptoms of dystonia musculorum deformans have been alleviated during the course of this study for periods up to three years without recurrence. Thus, this disease can no longer be considered as necessarily incurable or irreversibly progressive.
5. The treatment of choice of many cases of parkinsonism and of all cases of dystonia musculorum deformans is surgery of the globus pallidus and thalamus.
6. Lesions confined to the globus pallidus and/or ventrolateral region of the thalamus on one side of the brain do not result in any motor, sensory, intellectual, or psychologic deficit. The extent to which such lesions can be inflicted on both sides of the brain requires further elucidation.
7. Clinical studies leading to a more physiologic classification of the subdivisions of the overall parkinsonism syndrome are required if therapy and further basic investigations are to be conducted intelligently and fruitfully.
8. Many of the older concepts of basal ganglia function, pathogenesis of tremor and rigidity, and therapy of hyperkinetic diseases have been rendered suspect and some completely disproved by this and other investigations. There is a further need for evaluation of many concepts of extrapyramidal disease which have been allowed to become dogmatic and which do not occur with existing facts. However, not only must we be willing to re-evaluate former concepts, but we must also be on guard against replacing them with new dogmas too soon. Our entire understanding of the role of basal ganglia and the extra-pyramidal system must be viewed in the context of the contributions of these structures to overall brain function. Our present state of knowledge does not permit more than working hypotheses. These should not be misinterpreted as facts until they are proved beyond any doubt.

(Authors' Abstr.)

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Long-range Effects of Electropallidoansotomy in Extrapyramidal and Convulsive Disorders

Follow-up studies of stereotaxic operations on the basal ganglia performed from 1948 to 1958 are presented.

Fractionated electropallidoansotomy was applied to (1) paralysis agitans and parkinsonism, (2) other involuntary movements of extrapyramidal origin, and (3) certain types of spasticity, including a case of tonic perseveration of voluntary innervation. In a

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fourth group—convulsive disorders refractory to anticonvulsive medication and showing seizure discharges in the forebrain ganglia—pallidoansotomy was used alone or combined with amygdalotomy.

(Authors' Abstr.)

A New Drug for Petit Mal Epilepsy

This article reports upon the effect of PM 671 in controlling or reducing petit mal attacks in 109 patients, many of whom were considered intractable cases.

The present drug, PM 671, on the basis of effectiveness against petit mal attacks, mildness of side effects, and holding ability, offers more promise than other succinimide compounds and medications tested in the past ten years.

Quick and dramatic reduction of attacks occurred in most of 109 patients studied, and side effects were mild and infrequent. Side reactions were occasional drowsiness and dizziness, with some nausea and gastric distress—usually on high doses. Nausea and gastric distress are basic side effects to all succinimide compounds, but, fortunately, they are rare and not particularly disturbing. No deleterious changes in the blood picture have been noted to date, and urinary findings are within normal limits. No skin rashes have been noted.

Studies revealed that PM 671 is also outstanding in the lack of "slippage"—that property in a drug of slowly losing its holding power. Quite a few patients, never before helped by any drug, have been completely controlled for several years on PM 671.

For the group as a whole, an overall 85 per cent. reduction in attacks was obtained in the treatment of petit mal epilepsy. Complete control of petit mal attacks was secured in 42 per cent. of patients treated; practical control with an 80 to 99 per cent. reduction in attacks in 24 per cent.; and partial control, 5 to 79 per cent. reduction, in 26 per cent.

Experience to date indicates that PM 671 is essentially a petit mal drug. Much more effectiveness was noted in the treatment of pure petit mal cases—where pure petit mal existed alone or was combined with other types of seizures—than when a "mixed" petit mal element was present. Results showed that 83 per cent. of all pure petit mal cases had a reduction in attacks of at least 80 per cent. after therapy; only 29·5 per cent. of the mixed petit mal cases reached this high level of control. The individual frequency of attacks likewise did not appear to have any relation to the effectiveness of medication.

(Authors' Abstr.)

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Partial Equivalence of Chronic Alcohol and Barbiturate Intoxications

1. Ten morphine addicts in good physical health, eight of whom were addicted to barbiturates, volunteered for an experimental study which involved withdrawal of opiates, continuous intoxication with pentobarbital or secobarbital for 22 to 44 days, substitution of alcohol for barbiturates for 14 days and, finally, abrupt withdrawal of alcohol.

2. The clinical symptoms of the intoxications induced by barbiturates and by alcohol were similar, but after substitution of alcohol the EEG pattern changed from that characteristic of barbiturates to that characteristic of alcohol.

3. The "major" symptoms of abstinence due to abrupt withdrawal of barbiturates are convulsions and delirium. The anticipated frequency and severity of these symptoms were reduced significantly by the substitution of alcohol. The incidence and severity of "minor"

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symptoms of barbiturate abstinence (anxiety, insomnia, tremor, anorexia, vomiting and weight loss) were reduced.

4. When alcohol was discontinued abruptly after 14 days of substitution, convulsions or delirium or both appeared in three of nine patients who completed the experiment.

5. It is concluded that alcohol is not a complete substitute for barbiturates in patients chronically intoxicated by pentobarbital or secobarbital, but that it is a partial substitute.

(Authors' Abstr.)

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