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Memory Disturbances after Electroconvulsive Therapy

It has been shown that electroconvulsive therapy has an adverse effect on the operationally defined variables "immediate reproduction", "delayed reproduction", "retention", and "forgetting" in three memory tests constructed for this study, called the 30 word pair test, the 20 figure test and the short story test. It may be concluded that electroconvulsive therapy has an adverse effect on the hypothetical variable "retention". It may also have an adverse effect on the hypothetical variables "learning" and "recall", but to a much smaller extent.

A study of the percentage of wrong answers among the failures three hours after learning in the word pair test does not lend support to *Janis'* hypothesis of a primary disturbance of "recall processes" after electroconvulsive therapy—the existence of such a disturbance of course not being disproved.

These conclusions are valid only for the time when the examination was done, i.e. six hours after the second treatment. The three memory tests mentioned may also, however, be useful in studying intellectual disturbances at a longer interval after treatment.

(Authors' Abstr.)

Personality Changes in Electroconvulsive Treatment

The present study was carried out in order to throw light on the following questions: (1) Are memory disturbances to be found in patients one week after three electroconvulsive treatments? (2) Are there any personality changes observable by the Rorschach test at the same interval after treatment? (3) Are there any differences in memory disturbances and other personality changes after three electroconvulsive treatments given twice a week or as a "block" on three successive days which could explain the clinically observed better effect of the block treatment?

The memory tests given to 37 patients revealed general improvement of results in the post-treatment investigation, the improvement being slightly better in the 16 patients treated with block E.C.T. The memory improvement is interpreted as due to the changes in emotional life brought about by E.C.T. This emotional improvement counterbalances the persisting psycho-organic symptoms which are evidenced in the post-treatment Rorschach tests. The Rorschach findings confirm the hypothesis (*von Baeyer and Grobe, 1947*) that the effect of E.C.T., even when given only three times, depends upon the psycho-organic syndrome which develops as a sequel of the treatment. However, it is not the psycho-organic syndrome as such which brings about the therapeutic remission, but this is produced by the reconstruction of the inner life, which takes place after each electroconvulsive treatment (*Delay, 1946; Alexander, 1954*) and it is this reconstruction that is profoundly affected by the psycho-organic syndrome. The hypothesis is put forward that the better effect of block E.C.T. is due to the slightly more pronounced organic injury and to the shorter intervals which obstruct a complete reconstruction of the later life during the intervals.

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Psychological Studies on a Patient Who Received 441 Electroconvulsive Treatments

The general impression obtained in the investigation of recall of dates and names was the same as in the psychological tests: A positive, cheerful attitude to the testing, serious attempts at solving the tasks, naïve delight at success, without knowledge of her mental deterioration. Although some improvement took place in the weeks following E.C.T., her psycho-organic symptoms were conspicuously more severe than those of the patients previously studied by the authors one week after three electroconvulsive treatments. Hence it seems justifiable to infer that a great number of electroconvulsive treatments cannot be given without producing psycho-organic changes in personality. Häfner (1951) came to the same conclusion regarding the effect of repeated blocks of E.C.T. Almost all the patients studied by Rabin (1948) showed personality changes of psycho-organic origin.

After a review of the literature on the effect of a great number of electroconvulsive treatments, a report is given on the results of psychological testing of a patient who had received 441 electroconvulsive treatments. Evidence is presented of psycho-organic changes of personality.

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Transorbital Leucotomy in Non-Institutional Cases

Results in 115 cases of transorbital leucotomy of non-institutional patients are reported. The author believes that this is an excellent technique for treatment of selected cases from private practice, as well as such institutional cases reported by others.

Studies of the psychoneurotic group are of particular interest and indicate another method of management of a very common and difficult problem.

Results in those patients operated for relief of intractable pain and suffering suggest that this procedure is effective and among the least drastic of surgical measures.

Several patients who had secondary dependency on narcotics, barbiturates, and alcoholic beverages obtained relief from these dependencies along with relief from the underlying disorders and none showed any withdrawal symptoms.

(Author's Abstr.)

Clinical Evaluation of Pacatal

1. Pacatal is capable of eliciting therapeutic responses in chronically psychotic patients.
2. It is most efficacious for those aspects of behaviour which are related to increased anxiety and least efficacious for judgment, insight, orientation, memory and affect.

3. The clinically significant side-effects are those related to the atropine-like action of Pacatal. Untreated eye complications, following prolonged administration of Pacatal, may lead to ulceration of the corneal epithelium.

4. It is recommended that any prolonged ocular disturbance as a result of Pacatal medication be treated with Neostigmine.

5. All the side-effects produced by Pacatal can be obliterated by symptomatic medication, lowering of daily dosage or discontinuation of the medication.

6. The results obtained with Pacatal are encouraging and warrant further investigation upon a prognostically better group of psychotic patients.

(Author's Abstr.)

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Some Interrelations of Social Factors and Clinical Diagnosis in Attempted Suicide: A Study of 109 Patients

1. A study has been reported of social factors in the suicide attempts of 109 patients brought to a general hospital immediately after having made a suicide attempt.

2. Patients with chronic alcoholism, conversion reaction, and sociopathic personality reported a much higher frequency of social difficulties, such as marital friction, divorce, job instability, and financial dependency, than did patients with manic-depressive psychosis and chronic brain syndromes. They not only were involved in more social difficulties at the time they made the suicide attempt, but also reported more such difficulties throughout their lives.

3. Just before the manic-depressive and chronic brain syndrome patients attempted suicide they were disturbed by feelings of depression, self-disgust, and worthlessness, but seldom by feelings of anger or spite towards other persons or by feelings of frustration or neglect caused by others, while the patients in the other 3 diagnostic groups showed the opposite pattern.

4. There were probably no psychiatrically well patients and probably no patients with an anxiety reaction (anxiety neurosis) in the entire group of 109 patients who had made a suicide attempt.

5. The interrelationships of social difficulties, diagnosis, and suicide attempt, based on the findings of this study, were discussed.

(Authors' Abstr.)

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Chemical and Electrical Stimulation of Hippocampus in Unrestrained Animals. I. Methods and Electroencephalographic Findings

This study represents one of a series of investigations on the functions of parts of the hippocampus and other structures of the limbic system. The present experiments were performed on cats and focused attention on an intermediate segment of the hippocampus lying between frontal planes A1.5 and A4.5 of Horsley-Clarke co-ordinates.

Reasons are given for employing "cholinergic" as well as electrical stimulation in this particular study. A method is described that allows one to stimulate electrically or chemically the same point in the brain and at the same time to record the electroencephalographic and behavioural changes in unrestrained animals.

Primary consideration is given to the electroencephalographic changes following the application of acetylcholine (with physostigmine), methacholine, and carbachol. Application of these agents in crystalline form militates against their escape from the region in which they are applied and thereby helps to circumvent a complication that occurs with the use of solutions. Such application also provides the most effective means of eliciting pronounced and enduring electroencephalographic changes. Evidence is presented that cerebral tissue greatly restricts the spread of soluble substances in the brain.

The most pronounced EEG changes are seen with carbachol. Two to four minutes after its application rhythmic potentials at about 20 per second appear and are frequently grouped in the form of spindles. Subsequently they increase in amplitude and may occur in long trains. Intermittently background slow rhythmic activity is seen, and at such times the fast potentials tend to group themselves near the peak and on the falling phase of the slow waves. Seven to fifteen minutes after the drug is deposited, high-voltage spikes begin to appear interspersed among the fast oscillatory potentials. Subsequently they may occur almost continuously for periods of 45 to 60 minutes, reaching amplitudes of 1,400 μ v to 1,600 μ v. After this prolonged discharge, the seizure gradually subsides during the next hour or two, dissipating in the same

patterns of activity that characterized its development. As it dies out, slow rhythmic activity becomes the conspicuous feature of the record.

The changes occurring with acetylcholine are in many ways similar to those seen with carbachol, but are much less intense and shorter in duration, seldom lasting more than an hour. Unless acetylcholine is used in conjunction with physostigmine, pronounced and enduring changes are not consistently obtained.

The application of methacholine is characteristically followed by the appearance of persisting slow rhythmic activity with super-imposed fast potentials. In the hippocampus this agent does not elicit the spike potentials seen with the former two drugs. A possible explanation of the difference in the respective seizure patterns is discussed.

When seizure activity is beginning to subside after the application of (1) acetylcholine and physostigmine or (2) carbachol alone, it shows a prolonged recrudescence following an after-discharge elicited by electrical stimulation at the point where the chemicals were applied. A recrudescence also occurs spontaneously when an animal is succumbing to an anesthetic dose of pentobarbital. Possible explanations for these phenomena are considered.

Attention is drawn to the similarity between the seizure activity induced by carbachol and that associated with injury discharges and electrically induced after-discharges. The possibility is suggested that injury and electrical stimulation result in a release of acetylcholine in an amount that temporarily exceeds the capacity of the local cholinesterase to bring about its destruction.

An investigation on the propagation of electrically and chemically induced hippocampal seizures to other cerebral structures is described.

The slow rhythmic activity that occurs in the hippocampus of waking animals under a variety of conditions is discussed in the light of the present experiments.

(Author's Abstr.)

Chemical and Electrical Stimulation of Hippocampus in Unrestrained Animals. II. Behavioural Findings

This paper deals with the behavioural findings following chemical and electrical stimulation of an intermediate segment of the hippocampus in the cat lying between frontal planes A1.5 and A4.5 of Horsley-Clarke co-ordinates. The preceding communication described a method that allows one to carry out such stimulations in unrestrained animals and at the same time record the electroencephalographic changes. In addition to the technical procedure, the electroencephalographic changes accompanying such stimulations were reported.

For reasons given in Part I, chemical stimulation was usually performed with "cholinergic" agents and involved the application of acetylcholine (and physostigmine), methacholine, and carbachol in crystalline form.

The behavioural manifestations following application of carbachol to the hippocampus correlate with three stages of the electroencephalographic changes: 1. During the stage of development there are few noteworthy findings. 2. When the seizure reaches its height (stage of culmination), pronounced changes occur and are characterized by the animal's lack of spontaneity of movement, pseudocatatonic manifestations, failure to respond appropriately to various manipulations, under-reactivity to noxious stimuli of moderate intensity, and sudden vacillation between violent activity and statuesque postures subsequent to intense noxious stimulation. Angry behaviour elicited by prolonged noxious stimulation is un-directed. Viscerosomatic, postural, and locomotor reflexes are retained. No significant spontaneously occurring autonomic manifestations are evident. 3. During the stage of subsidence the animal manifests enhanced pleasure and grooming reactions and is unusually receptive to genital stimulation. Sustained penile erection may be induced in male cats. If the high-voltage seizure activity associated with Stage 2 fails to develop, these are the only findings.

Except for an apparent enhancement of pleasure and grooming reactions, stimulation with acetylcholine and methacholine was followed by no significant behavioural manifestations that could be correlated with the bio-electrical changes induced by these drugs.

Enhanced pleasure and grooming reactions were observed following 14 of 26 chemical stimulations of the hippocampus. This compared with 2 such positive reactions following 28 stimulations elsewhere. They were not seen when empty needles were placed in the hippocampus. If the results of this exploratory study were subjected to statistical analysis, they would be highly significant.

The foregoing changes in dispositions are in marked contrast to the manifestations that occur if the drugs in question escape from the hippocampus into the overlying ventricle. In this event there results a syndrome characterized by contralateral circling, angry behaviour, and a number of autonomic manifestations.

The changes that can be demonstrated during hippocampal after-discharges elicited by electrical stimulation are in most respects similar to those described in regard to Stage 2 of carbachol-induced seizures. For several minutes following after-discharges a majority of animals showed enhanced pleasure and grooming reactions. In the male partial erections were sometimes noted during grooming in the genital region. A comparative study is presented to show that intensive post-after-discharge grooming is also a common finding in the rat. Here, too, one might note the presence of penile erection.

The foregoing experiments are discussed in the light of a number of problems pertaining to experimental psychology and clinical neurology. Continuing investigation is beginning to suggest that a neural system involving parts of the hippocampus, cingulate gyrus, and septum is implicated in the pleasure and grooming reactions and the sexual manifestations that have been described.

(Author's Abstr.)

Posterior Septal, Fornical, and Anterior Thalamic Lesions in the Cat

A variety of behavioural and vegetative changes were observed in 85 stock cats for periods ranging from 1 to 90 days following relatively small, bilateral, stereotaxically placed lesions in the septum, fornix, and anterior thalamus, which were histologically verified and analyzed. These alterations included impaired consciousness, hypokinesia, muscular plasticity, sustained grasping, the "jump" reflex, piloerection, marked hypothermia, and relatively persistent hyperglycemia, as well as a high incidence of early and late post-operative deaths. Rage reactions were conspicuously not in evidence. These results could not be anatomically correlated with discrete nuclear masses or their specific projections. The highest incidence of abnormality was associated with a combination of posterior septal, fornical and anterior thalamic destruction. Such lesions are so situated as to interrupt major rhinencephalic-hypothalamic and mesencephalic reticulothalamocortical projections, which are thought to account for the observed alterations. Serum sodium, potassium, and magnesium and blood urea nitrogen determinations, before and after the placement of lesions, showed no consistent changes.

(Authors' Abstr.)

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Adrenocortical Response and Phosphate Excretion in Schizophrenia

The variations in several indices of adrenocortical activity have been measured in 20 hospital orderlies, 18 catatonic schizophrenics, and 21 paranoid schizophrenics throughout a control morning (7.0 a.m.-12.15 p.m.) and other mornings before and after the administration at 9.0 a.m. of corticotropin (25 mg. i.m.) or of epinephrine (0.3 mg. s.c.).

During the control periods the catatonics excreted less ($P < 0.01$) phosphate than did the normals or the paranoids and more ($P < 0.05$) 17-ketosteroids than the normals. Both schizophrenic groups excreted more ($P < 0.05$) sodium than the normals; their urine volume also tended to be greater.

Both schizophrenic groups increased their excretion of phosphate as the morning progressed, but the normals maintained a relatively stable rate. After both corticotropin and epinephrine the excretion of phosphate was higher in the schizophrenics than in the normals, but when the spontaneous rate observed on the control day is subtracted from that observed after corticotropin the net effect of this agent appears to be a retention of phosphate.

As previously reported, the resting level of circulating eosinophils was lower and the response to corticotropin greater in the catatonics than in the normals or the paranoids.

These results support the suggestion that catatonic and paranoid schizophrenics differ as much from one another as they do from normals and suggest that the phosphate metabolism in this disease is worth intensive study.

(Authors' Abstr.)

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Galactose Treatment of Multiple Sclerosis

These initial observations are far from conclusive and the literature is replete with new treatments for multiple sclerosis which seemed promising only in the first report. As Schumacher (1950) has pointed out the validation of any treatment for this illness must be conducted over a period of several years. Such long term evaluation of galactose treatment is now planned, but it was hoped that a preliminary report of this work might stimulate other workers to make observations upon the method. With such reservations, however, we can state that the clinical findings suggest that a treatment regime involving administration of galactose is effective in reversing some of the symptoms of multiple sclerosis. One would suspect that only early or incomplete lesions would be most likely to reverse with such treatment. The sugar must be continually given to maintain the gains achieved. Failure to maintain improvement with oral administration, together with observation of blood galactose levels now in progress, would suggest that multiple sclerosis patients have a defect in galactose metabolism, and that such a defect may be concerned with the manner in which galactose is absorbed from the alimentary tract.

(Authors' Abstr.)

Evaluation of Transorbital Lobotomy with a Control Group

In terms of the measurements and indices used in this study, transorbital lobotomy was significantly more effective in relieving psychiatric disturbances and in enabling "backward" psychotic patients in a state hospital to be released from hospital than patients in a similar psychotic state receiving other somatic forms of treatment. In view of the poor prognosis of these patients and their long length of hospitalization, these results seem especially remarkable in favour of this mode of treatment for psychotic patients who are refractory to typical somatic therapies.

(Authors' Abstr.)

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Effect of Perphenazine (Trilafon) on Modification of Crude Consciousness

A double blind study has been carried out on 75 chronic male and female patients, divided into three equal groups of 25. The three groups received perphenazine 16 mg. t.i.d., placebo 16 mg. t.i.d., and chlorpromazine 25 mg. t.i.d. respectively for 30 days.

Patients were rated and tested before and after the trial. In addition, laboratory investigations were made at those times and preliminary, daily, and final clinical assessments were made.

Additional seven female patients were given either perphenazine or placebo in the same dosage for the same period. These seven were not tested but all had failed previously to respond to large doses of chlorpromazine.

Statistical procedures included analysis of variance and *t* tests of significance. The Rating Scale for anxiety and the Tapping and Dotting tests were found to be significant at the 1 per cent. and 5 per cent. levels respectively for the perphenazine group. Digit Symbol, Porteus Maze and Digit Span did not show significant differences. The significance of these differences was discussed.

Rating, testing, and clinical assessment all showed perphenazine to be similar in its actions to chlorpromazine, but with the advantage of greater efficacy and of a much more favourable therapeutic ratio. Side effects similar to chlorpromazine were found, but it is thought would be less likely to occur in smaller dosage. Hypotension was not encountered.

The preliminary findings concluded that perphenazine is likely to prove a more than useful weapon in psychiatric practice, with indications for use, and with side effects similar to those of chlorpromazine, but with greater potency and improved therapeutic ratio.

(Authors' Abstr.)

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Prochlorperazine (Compazine) in Emotional Disturbances

Prochlorperazine was used to complement supportive therapy in 52 psychoneurotic patients and found effective for relieving symptoms of anxiety, tension, and apprehension. On a dose of 5 mg., three to four times daily, 17 obtained an excellent clinical response; 22, good; 5, fair; and 8, poor. A single dose of the drug in sustained release (Spansule capsules) form provided an effect that lasted approximately twelve hours. Patients on the drug regained the ability to relax, sleep better, and adjust more efficiently to disturbing environmental factors. Four of 5 patients on the verge of hospitalization responded adequately, becoming amenable to supportive psychotherapy on an ambulatory basis. Three patients reported side effects, one each of drowsiness, dizziness and stomatitis. No jaundice, blood dyscrasias, or skin reactions occurred in the nine months the study required.

(Author's Abstr.)

Dimethylane in the Treatment of Anxiety Reactions

This study reports an investigation and evaluation of the usefulness of a comparatively new drug, Dimethylane (2,2-diisopropyl-4-hydroxymethyl-1, 3-dioxolane), in the control of anxiety and tension states. A rigidly controlled "double blind" method of investigation was used. Thirty patients with a primary diagnosis of "anxiety reaction" were carefully selected according to defined criteria. Half of the patients were given drug capsules for two weeks and then placebo capsules for two weeks, and for the other half the order was reversed. The capsules were identical and elaborate precautions were taken to make certain that neither the patient nor anyone in contact with him knew whether the patient was receiving drug or placebo. Evaluations on quantifiable scales of any change in frequency or severity of symptoms were made by both patients and examiners.

Patients generally demonstrated slight improvement, whether given Dimethylane or placebo. Contrary to the conclusions of some previous studies, most of which did not use control groups, no significant differences were found in the effects of the drug as compared to those of the placebo. In the authors' series there were no adverse side effects which could be clearly attributed to the drug.

The final impression was that Dimethylane is of little clinical value in providing symptomatic relief for patients suffering from generalized anxiety reactions, but that further investigation of this drug in the control of symptoms associated with such specific conditions as primary dysmenorrhoea and post-alcoholic psychomotor agitation seems warranted.

(Authors' Abstr.)

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Stress Conditioning in the Treatment of Schizophrenia and Neurotic Disorders

The authors have presented a report on the treatment of 98 patients diagnosed as schizophrenics and other disorders. Treatment consisted of stress conditioning or acclimatization to stress by a process similar to that operating in allergic desensitization.

Their procedure is to inject intramuscularly 3·0 c.c. of adrenal cortical extract for 12 days in order to rest the adrenal cortical gland which they assume to be overdriven even to the point of exhaustion in some cases. This is followed by a series of antigenic protein injections at weekly intervals beginning with a sub-reactive dose and progressively increasing it so that the patient becomes conditioned gradually to stresses.

(Authors' Abstr.)

Localized Electric Stimulation of the Diencephalon in the Treatment of Mental Disorders

Electric shock treatment is known to be of value in certain mental disorders, but has inherent physical hazards and adverse side effects, such as confusion, increased anxiety and memory loss. There are indications that diffuse stimulation of the entire brain with convulsion-producing currents is not always necessary for the attainment of results, and that therapeutic effects may be obtained by discrete stimulation of certain brain areas, particularly of the diencephalon. Conventional techniques make such discrete stimulation of specific brain areas difficult or impossible.

A method of non-convulsive electric stimulation is suggested in which comparatively high concentration of current in the diencephalon may be obtained, while stimulation of other brain areas, including the motor cortex, is kept at a minimum. In this procedure specially designed electrodes are used. One of these is placed centrally at the base of the skull. Treatment results so far have been most encouraging. No adverse side effects have been observed.

(Author's Abstr.)

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Figural After-Effects, "Brain Modifiability", and Schizophrenia

Using two separate samples, it was found that schizophrenic males, on the average, have a visual figural after-effect smaller than that of normals, a difference significant at the 1 per cent. level when one technique was used, significant at the 5 per cent. level when a second technique was used. Schizophrenics also show a smaller kinesthetic figural after-effect than normals, a difference which remains significant at the 1 per cent. level when time is strictly controlled. They show less increase in figure reversal from one test period to the next, at the 1 per cent. level. Finally, schizophrenics are, at the 1 per cent. level, significantly less affected by a temporary discoordination of the visual and kinesthetic images of the hand.

(Authors' Abstr.)

The Effect of Lesions in the Amygdaloid Area in Monkeys

The findings of this study need considerable amplification and extension, especially with respect to the matter of objective evaluation of behaviour changes. It nevertheless appears from the data which have been presented that there is some indication as to which specific neural structures are significantly related to the altered behaviour syndrome which has been described. As has been seen, one group of animals in which the amygdaloid nuclei were primarily involved showed no detectable behavioral alterations until the development of delayed necrosis, which presumably destroyed the circumferentially located tissues. On the other hand, all the monkeys that exhibited positive effects from the lesions suffered damage in the subpallidal region. Finally, the Group IV animals were subjected to the production of small lesions intended to involve primarily this subpallidal area. Three of this final group of four monkeys developed changes similar to, though less pronounced than, the changes seen in monkeys of Groups I and II.

It is suggested, as a preliminary attempt to reconcile the seemingly contradictory findings of earlier studies, that it is reasonable to suppose that the surgical approach used by the various investigators may have caused incidental damage to the subpallidal region in some cases and not in others. Schreiner and Kling state that the lentiform nucleus and lower portion of the claustrum were involved in the majority of their preparations. As judged from this statement, it would in all probability be true that the area immediately ventral to the globus pallidus was injured or destroyed in all their animals. In the cat subjects of their study there were pronounced changes in the direction of tameness, increased sexuality, etc. The surgical approach which was used, namely, retraction of the temporal lobe and visualization of the optic tracts in order to give access to the pyriform cortex and amygdala, would be expected to cause destruction of the subpallidal region. The changes brought about in cats as a result of this approach were very different from the effects produced in this species by Bard and Mountcastle, who approached the same area by a different route. The latter authors exposed the wall of the lateral ventricle to permit visualization of Ammon's formation. Using this precise landmark, which lies ventral and caudal to the amygdaloid nucleus, Bard and Mountcastle then removed the nucleus by suction. This latter approach, which would seem much less likely to cause damage to the subpallidal area than did the approach of Schreiner and Kling, resulted in production of "bad-tempered" animals in which the slightest stimulation provoked anger and attack.

Turning from the work on cats to that on monkeys, we may ask whether the surgical approach used by Bucy and Kluver (4, 7) would have been likely to cause destruction of the subpallidal region. The available descriptions of their lesions include no specific comment on this point, but it is stated that the entire amygdaloid nucleus and the adjacent portion of the tail of the caudate were removed. Complete removal of these two structures could hardly be accomplished without producing at least some injury to the directly overlying tissue of the subpallidal region. It is thus probable that comparable neural structures in the two species of animals, monkey and cat, are related to the tameness, hypersexuality, oral-activity, motor-hyperactivity forms of behaviour.

The main thesis of the foregoing paragraphs is that the subpallidal region in both monkeys and cats has an important relation to the behaviour changes which have been described. It is interesting to speculate, in terms of the fact that different elements of the tameness-hyperactivity-sexuality syndrome were more marked in one than in another of our animals, whether or not such differences may ultimately be correlated with slight variations in the location of the lesions. Different parts of the subpallidal region will be sampled by making small lesions with the radioactive needles in future studies, for the sake of determining whether or not the behavioural syndrome may be fractionated.

(Authors' Abstr.)

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5-Hydroxytryptamine (Serotonin, Enteramine) Content of Structures of the Limbic System

This report deals primarily with the results of a study of the 5-hydroxytryptamine (5-HT) content of cortical and subcortical structures of the limbic system. For the purpose of comparison and control, assays were performed on representative neocortical areas, as well as on a number of other non-limbic nervous structures.

All the cortical assays showing relatively high values of 5-HT were confined to limbic structures. These included the medial and lateral pyriform cortex, the entorhinal cortex, and hippocampus. All the remaining limbic cortical structures, as well as the neocortical areas that were sampled, had considerably smaller amounts of the amine. In the hippocampus (archicortex) the highest concentration of the amine was found to be in the gray matter immediately adjoining the white. Segments of the body of this structure showed no significant differences in assay values. In the limbic mesocortex there appeared to be a graded decline in values in a direction away from the olfactory trigone.

Assays of limbic nuclear structures were confined to the amygdala, septum, and hypothalamus. All had high values of 5-HT that were the same as, or exceeded, those of the caudate nucleus and of the tissue taken from the region of the putamen.

The region of the intercolumnar tubercle (located between the columns of the fornix which is the main conducting pathway of the hippocampus) had an average assay value which was more than three times that of the fimbrial fornix and was close to that previously reported for the area postrema. The tubercle and the area postrema are recognized to have anatomical similarities.

The parenteral administration of a monoamine oxidase inhibitor, iproniazid, resulted in an increase in 5-HT in some structures, but not in others. A number of determinations of 5-hydroxytryptophane decarboxylase activity provided further evidence that nervous structures which contain 5-HT are generally able to synthesize it.

(Authors' Abstr.)

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Rapidly Progressing Dementia in Disseminated Sclerosis

Two cases are described in which there was a rapid onset of global dementia associated with the clinical signs of multiple lesions in the brain and spinal cord, leading to the diagnosis of disseminated sclerosis.

Investigation in both cases showed abnormal EEG records, ventricular dilatation, and cortical atrophy.

Both patients had to be transferred to mental hospitals on account of their dementia, and the disease rapidly progressed to a fatal issue.

In one case the diagnosis of disseminated sclerosis was confirmed by post-mortem examination.

The rarity of dementia in disseminated sclerosis being of a degree requiring admission to a mental hospital is emphasized, and the significance of the air studies, EEG abnormalities and pathological lesions is discussed in relation to the mental disorder observed in these cases.

(Author's Abstr.)

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Effects of Cingulectomy on Social Behaviour in Monkeys

1. Bilateral cingular gyrus ablations were performed in five young *Macaca mulatta* monkeys, after systematic observations of their behaviour in response to man (individual-cage situation) and to other animals in social colony (group-cage situation).

2. Three of the five operated animals showed more aggressiveness (or fearlessness) in response to man immediately after operation and the group effect was significant. This change proved to be temporary, for the operated animals did not differ significantly from their pre-operative status in a post-operative comparison approximately two months later.

3. Only one of the operated animals showed any marked changes in the group-cage situation, and the interpretation of these changes is equivocal.

4. The differences among the effects in the several animals do not appear to be related to differences in the locus or extent of the lesions.

5. These findings were discussed in relation to previous studies: the effect on individual-cage behaviour appears to be a fairly consistent and repeatable effect of cingulectomy; the effects previously reported on group-cage behaviour may be a function of the inadequacy of the observational technique used in these studies.

(Authors' Abstr.)

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Drops of Protein in Brains of Hospital Patients

The paper described round pink drops of protein seen in brains of psychotic and mentally deficient patients who had some form of stupor prior to death. They were numerous in cases with clouded states, disorientation, stupor, catatonia, uremia, and "edema" of brain. The drops of protein came from dissolved lymphocytes. They were seen inside of small blood vessels and in the cerebral cortex in suspensions under phase contrast microscopes at 970 diameters. Lymphocytes filled with living, moving, mycotic spores were described. Many of them were dissolved by lysis and gave rise to round pink drops of protein. The drops were seen in spaces in gray matter and inside of the blood vessels. When lymphocytes died, they dissolved, including nucleus and spores, to form the drops of protein seen beside the vessels. The drops probably obstructed flow of cerebral fluid through glial spaces, and produced hypoxia or anoxia. In many schizophrenics cytolysis was a severe dissolution of nerve cells. At autopsy the brains gave the impression of edema, cloudy arachnoid and congested pial vessels. The origin of some of these drops was observed coming from dissolving lymphocytes. Most of them were formed prior to death. Their probable constitution was globulin which contained a lysin. They occurred at all ages when edema of the brain was seen. The whole process of their formation and nerve cell destruction gave a more complete picture of what took place in severe mental illness. The amyloid bodies of protein origin were the remains of a burned out disease of the brain. The authors have shown the sclerotic patches on blood vessels and indicated how they may restrict flow of blood and contribute to hypoxia as well as hypertension. Strains of mycotic spores in red blood corpuscles were presented as the probable source of those in nerve cells and sclerotic patches. Mycotic toxins including serotonin were discussed. Mycotic pigments were mentioned.

(Authors' Abstr.)

Doxylamine: A New Compound for the Symptomatic Treatment of Schizophrenia

Doxylamine is an antihistamine which has been used in small doses (as Decapryn) for many years in the treatment of allergic diseases. Recently large doses have been tried in psychotic patients. The drug appears to be safe in doses up to 1,600 mg. daily by mouth and encouragingly effective in many patients in daily dosage of 300 mg. to 900 mg. In a group of 108 female patients (mostly schizophrenic) it has been most useful in those who exhibit unpredictable, psychotic behaviour sometimes of an assaultive nature, in those who are moderately improved on other drugs but are making no further progress, and in those who suffer from hallucinations and delusions. It can be given concurrently with the other drugs commonly employed to modify psychotic symptoms.

(Authors' Abstr.)

Excretion of Urinary Corticoids in Mental Patients

Urinary corticoid excretion was studied in selected groups of 72 mental patients and a group of 37 normal controls; in a group of 19 mental patients before and after electroshock therapy; and in 12 patients during the course of electroshock therapy.

There was no significant association between age or sex and corticoid level.

The variability in corticoid excretion in the schizophrenic group of patients, both acute and chronic, was significantly greater than in the depressive and normal control groups.

The variability in corticoid excretion was significantly reduced following electroshock therapy.

(Author's Abstr.)

An Electrophysiological Analysis of the Actions of Some Drugs Useful in the Therapy of Psychotic Disorders

1. By the use of evoked electrocortical responses as an index of synaptic activity in the cat brain, the study of the action of drugs has been further examined in relation to its relevance to clinical data and to problems of mental disturbance.

2. The list of substances shown in this way to impair and disturb cerebral functions includes adrenaline and adrenaline derivatives, mescaline and lysergic acid diethylamide. To this have been added serotonin and bufotenine, both of which show very high cerebral synaptic inhibitory activity.

3. The serotonin naturally present in the brain can be caused to accumulate, by interfering with its destruction through the injection of iproniazid, until it produces cerebral synaptic inhibition.

4. The tranquilizers reputed to be of clinical use are correspondingly effective in preventing the impairment of cerebral synaptic function produced by mescaline in the cat.

5. The correspondence of the animal with the clinical data speaks for the pertinence of the animal technique developed.

6. This kind of study of function in units of the central nervous system offers promise of understanding the more complex patterns into which they can be built, the disturbances that may occur and the means of modifying them therapeutically.

(Authors' Abstr.)

Experimental Production in Rats of Abnormal Cycles in Behavior and Metabolism

The fact, that regular cycles can thus be produced experimentally by interference with the function of the thyroid gland surgically, chemically, or pharmacologically, should lead to a better understanding of the origin of cycles seen in psychiatric patients as well as in patients with periodic disease.

(Authors' Abstr.)

Toxicity of Blood Serum from Schizophrenic and Non-Schizophrenic Subjects

Blood serum from schizophrenic and surgical patients was highly toxic to strain L cells, whereas serum from healthy adults and from non-schizophrenic mental patients was in most cases less toxic. There was no significant difference in the toxicity of serum from healthy adults and from non-schizophrenic mental patients. There was good correlation between degree of serum toxicity, Lewis and Piotrowski score and the clinical diagnoses.

(Authors' Abstr.)

A Follow-up Study of Patients Treated by Thalamotomy and by Combined Frontal and Thalamic Lesions

Follow-up studies were carried out in 77 cases of thalamotomy. They show that the best long-range effects in cases refractory to non-operative procedures were obtained in severe anxiety neurosis and states of depression. Combinations of frontal lobe and thalamic operations were successful in about one-half of the cases in which either of these operations failed to improve the emotional disorder. Thalamotomy should be considered as a secondary operation in cases unrelieved by frontal leucotomy.

(Author's Abstr.)

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An Inquiry into the Mechanism of Action of Electric Shock Treatments

Pathologically, there may be temporary cellular changes following a fit. Physiologically, a convulsion appears to act as a non-specific stress situation. Biochemically, a contradiction exists. On the one hand, a fit seems to increase neuronal metabolism. On the other hand, a fit may depress neuronal metabolism or at least energy synthesis. The point is that none of these effects seems adequate to explain the mechanism of action of EST.

Richter has pointed out that the biochemical events occurring in a convulsion though dramatic are short lived. He postulates that perhaps a change in cell lipoproteins is important. It may be that the most fundamental process which occurs in a convulsion is some sort of change in structure at the intracellular level. Since energy is required not only for impulse transmission but also to maintain cell structure, shifts in energy synthesis or degradation could ultimately affect the organization of the neuron.

Manifestations of such a hypothetical cellular shake-up may be the shifts in ionic concentration, appearance of new substances outside the cell, change in the blood-brain barrier, restorative effect of pyrimidines, changes in cellular appearance, and so forth. Why a convulsion is necessary to produce this change and why it affects the course of the mental disease, are unanswerable questions at present. Indeed, at this level of study, the problem of the mechanism of action of electric shock treatment begins to merge with the problem of the causation of psychoses.

(Author's Abstr.)

Effects of Psychotomimetic Compounds on Certain Oxidative and Hydrolytic Enzymes in Mammalian Brain

In a study of mescaline and chemically related compounds, a series of nineteen phenethylamines and thirty closely related analogs were found to exert strikingly differential effects on alkaline phosphatase activity and on pyruvate utilization in brain tissue preparations. In addition, ten other compounds of neuropharmacological interest were tested for their influence on alkaline phosphatase and on lactic and malic dehydrogenase. Bufotenin and the tranquilizers significantly increased phosphatase activity. The lactic and malic dehydrogenase systems were relatively resistant to the compounds tested.

The influence of the mescaline analogs on enzyme activity has been analyzed in terms of the structural configurations of these compounds.

(Authors' Abstr.)

The Effects of Frenquel upon Chronic Disturbed Patients

1. Frenquel, given in divided doses totalling 60 mg. daily, did not significantly decrease delusions and hallucinations in this study.

2. Frenquel did not significantly improve ward adjustment in this experiment.

3. Frenquel appears to have no advantageous effect upon chronic female patients in this hospital, and there are suggestions that it may decrease inhibitory tendencies among some hallucinating patients. The question of whether the drug actually has a negative effect upon ward adjustment, as indicated by the earlier study, requires further investigation.

(Authors' Abstr.)

A Clinical Evaluation of Frenquel

Frenquel is an interesting drug. The results obtained with it in the treatment of acute psychotic states are variable and inconsistent. Nevertheless, the findings in this study suggest that it should be tried in acute schizophrenic reactions, particularly in those of recent origin in which the symptoms resemble those of mescaline and LSD-25 psychoses. It also may benefit senile confusional states, especially those originating after surgery. Although the results obtained in toxic psychoses are difficult to define, the use of Frenquel in such states is recommended. Finally, the combination of this drug with electroconvulsive therapy should be investigated further.

(Author's Abstr.)

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(Author's Abstr.)

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Electroencephalographic Effects of Intraventricular 5-HT and LSD in the Cat

An electroencephalographic study of the effects, in the brain of the immobilized conscious cat, of intraventricular injections of 5-HT and lysergic acid (LSD) reveals the following:

The cortical electroencephalographic effects, desynchrony with 5-HT and spindles with LSD, give little indication of more profound changes occurring in subcortical regions.

Both 5-HT and LSD characteristically depress the amplitude of activity in medial hypothalamic and thalamic nuclei and stimulate the bulbar reticular formation.

LSD evokes a high amplitude 50 per second rhythm in the pallidum, putamen, amygdala, and their projection systems, a change which roughly parallels in time the known duration of sham rage behaviour from a similar dosage of the drug.

5-HT retards the electroencephalographic activity of the same regions generally to an eight to 12 per second alpha rhythm, and again the temporal aspect of the changes correlates well with the known duration of lethargic behaviour evoked by the drug.

Doses of LSD which temporarily reverse the longer lasting behavioural lethargic effects of 5-HT similarly antagonize briefly the 5-HT effects on the electroencephalographic activity of pallidum, putamen, and amygdala.

It is suggested that "LSD-induced" high-amplitude burst of electroencephalographic activity in certain relay nuclei of the thalamus may contribute to aberrancies of sensation.

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Hypothalamic Seizures from Stimulation of Rhinencephalon and Isocortex in Cat

1. Hypothalamic seizure activity can be elicited by stimulation of amygdala, hippocampus, hippocampal gyrus, septum, and basal olfactory structures. The ventromedial nucleus is a prominent focal area of the hypothalamus for reception of "epileptic" impulses from the above structures. Stimulation at the same parameter of the ventral and of the dorsal portions of the hippocampus affected different parts of the hypothalamus. The hippocampal gyrus appears to by-pass the hippocampus in its projection to the hypothalamus. Stimulation of the posterior portion of the lateral amygdaloid nucleus produces longer seizure activity in the hypothalamus than do anterior portions of this nucleus. Results indicate that the amygdala affects the ventromedial hypothalamus directly and the mammillary body indirectly through the hippocampus. For reasons unaccounted for repeated constant stimulations of the same structure may result in seizures of varying character in the hypothalamus.

2. Stimulation of the dorsolateral isocortex at a constant, critical parameter showed that not all areas were epileptogenic for the hypothalamus. The most effective cortical epileptogenic areas were found in the temporal and occipital regions. Areas outside the temporal and occipital isocortex became epileptogenic with respect to the hypothalamus when stimulated at high voltage and long duration, and only after spread to temporal areas had occurred.

3. Some clinical implications relative to autonomic and psychomotor epilepsy and emotional states are discussed.

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Private Hospital Alcoholic Patients and the Changing Conception of the "Typical" Alcoholic
There has been a widespread misconception that alcoholics are usually characterized by a low degree of marital and occupational integration.

The support given to this misconception by most early systematic studies was a product of the kind of alcoholic populations available for study in mental hospitals, through police departments, relief agencies, and the like.

Malzberg's 1948 study of the New York State "alcoholics without psychosis" was the first to reveal a sizable population of alcoholics showing a high degree of marital and economic stability.

Straus and Bacon's study of over 2,000 male patients of the 9 pioneer clinics for alcoholics dealt the old stereotype a decisive blow. The typical clinic patient, they found, was still living at home keeping his marriage intact, and holding a steady job.

The present study has presented comparable data on the male patients of a large private hospital for alcoholics, the Shadel Hospital in Seattle, Washington. These patients were found to be characterized by an even greater—and substantially greater—degree of marital and occupational stability than was true of the clinic patients.

The differences indicate that the Shadel patients, as a group, had the highest degree of marital and occupational stability yet reported for any sizable alcoholic population.

This study, therefore, gives strong support to and broadens the base of the logic of the clinic study—that most alcoholics do not present a picture of considerable social and personal disorganization but rather of a fairly high degree of marital and occupational stability.

With some 4,500,000 alcoholics in the United States, and with only a fraction of them reaching Skid Rows or showing up for treatment, the vast majority must still be functioning in society in fairly normal fashion, hidden from general recognition. And to a large extent they are hidden by their failure to be as disorganized as the old stereotype would have the alcoholic be—hidden, in other words, by their surprisingly high degree of social and occupational stability.

The implications of this conclusion are far-reaching, suggesting a substantial refocusing of attention and effort on the part of rehabilitators, researchers and educators concerned with the problems of alcoholism.

(Authors' Abstr.)

Choice of Alcoholic Beverage among 531 Alcoholics in California

1. As part of a series of studies on the drinking habits of alcoholics, an investigation was conducted on 531 alcoholic subjects—491 men and 40 women—selected by the police for treatment at the Santa Rita Rehabilitation Center, Alameda County, California.

2. The group included 60 per cent. Protestants, 35 per cent. Catholics, and less than 1 per cent. Jews.

3. In comparison with major nationality groups in the surrounding area, the proportion of subjects with Irish and English backgrounds was relatively high, while the proportion of those with Italian, German and Canadian backgrounds was strikingly low, but the possibility of bias in the selection of the sample could not be ruled out.

4. The education of these alcoholics was limited, and their occupations were commensurate with their educational status. Nearly 20 per cent. were unemployed.

5. A generally unsatisfactory marital status was indicated by the finding that 18 per cent. of the subjects were single, 53 per cent. were either separated or divorced, and only 1 per cent. were living with their spouses. The marital status of 20 per cent. was not given.

6. Before their present commitment the majority of these alcoholics had received no treatment for their alcoholism, and inadequate treatment had been received by most of the others. Less than 40 per cent. of them had ever been exposed to the fellowship of Alcoholics Anonymous.

7. At the time of their earliest drinking experiences, distilled spirits represented the alcoholic beverage preferred and used by the majority of these alcoholics. Beer was ranked second and wine third, representing the beverage of choice for only about one-sixth of the group.

8. In their present drinking patterns, the majority of these subjects still express a preference for distilled spirits, but only 29 per cent. of the group are able to use spirits chiefly. On the other hand, although wine is still preferred by only one-sixth of the group, it is now the beverage of chief use of 49 per cent.

9. The drinking episodes of the alcoholics in this group appear to be rather lengthy, 45 per cent. of the subjects reported episodes lasting a week or more.

10. During a drinking episode, wine is used by 25 per cent. of the alcoholics at the onset, by 45 per cent. at the peak, and by 61 per cent. at the end.

11. An analysis of the data dealing with the so-called "winos"—those alcoholics who now use wine as their chief beverage—indicates that the majority of these individuals have always preferred alcoholic beverages other than wine since the time of their earliest drinking experiences. In the great majority of cases the present use of wine for their sprees seems to be determined almost exclusively by the circumstance that wine is the cheapest source of ethyl alcohol available to them.

12. The data do not support popular notions that "winos" or wine-using alcoholics are specifically addicted to wine, nor that alcoholism is related to the use of any particular type of alcoholic beverage.

(Authors' Abstr.)

Reserpine as an Adjunct in the Treatment of Alcoholism

A study of the effects of reserpine as an adjunct in the treatment of alcoholism was carried out in 71 patients in an outpatient clinic devoted solely to the treatment of alcoholism. The dose of reserpine used was 0.25 mg. 3 times a day. Of the 71 patients, the results in 30 cases could not be evaluated because of broken contact and must be presumed to be unfavourable. Of the remaining 41 the drinking patterns of 9 were not favourably affected by reserpine. In 2 of these 9 patients reserpine appeared to exacerbate the symptoms. In 32 cases reserpine seemed to help the patient achieve a measure of sobriety; 27 maintained sobriety for 12 months or longer; 3 for 6 months; and 2 for a 3-month period.

(Authors' Abstr.)

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