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Clinical Studies on α(2-Piperidyl) Benzhydrol Hydrochloride, a New Antidepressant Drug

1. The pharmacology of a new antidepressant drug, Meratran, is reviewed briefly.
2. Clinical trial in 320 cases disclosed that the therapeutic indications of this compound are roughly similar to those of the amphetamines.
3. Reactive depressions responded effectively in 90 per cent. of the author's relatively small series.
4. Endogenous depressions responded favorably in 65 per cent. of the author's cases.
5. The drug has proved valuable in office practice because the appetite loss and the cardiovascular pressor reactions sometimes observed after the administration of the amphetamines are not encountered. In addition, the drug seldom interferes with nocturnal sleep, and when it produces anxiety side reactions these are less severe and less disturbing subjectively than those encountered with the amphetamines.
6. When anxiety or agitation comprise a sizable proportion of the clinical picture the drug should be used with caution.
7. Preliminary observations indicate that the drug may have therapeutic usefulness, in addition to the depressive states, in some of the tics, in narcolepsy, and as an adjunct in the management of certain epileptics.
8. Effective dosage ranges (except in narcolepsy) vary between 3·0 and 25·0 mg. daily.
9. Wider clinical trial of this compound appears justified.

(Author's Abstr.)

* A number of abstracts in this section are reproduced from *Chemical Abstracts*. To the Editors of this Journal we extend our grateful thanks.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

The Effect of Meratran on Twenty-five Institutionalized Mental Patients

A study was conducted on 25 institutionalized psychotic patients with chronic courses, selected because of their depressive and/or regressive symptoms.

Meratran was found to be a central nervous system stimulant useful in the field of psychiatry and with certain indications and contraindications: (1) indications: (*a*) schizophrenics without delusions having restriction of interest and activity and with depressant features, (*b*) psycho-motor retardation and/or blocking of communication, (*c*) long-term hospitalized schizophrenics with severe deterioration; (2) contraindications: (*a*) patients with delusions, (*b*) patients with anxiety, (*c*) disturbed patients with cerebral arteriosclerosis.

(Authors' Abstr.)

Stimulation of the Amygdaloid Nucleus in a Schizophrenic Patient

The patient's principal response with this stimulation was a reaction of rage appearing when the current approached an intensity of 5 ma. When the current was reduced to 4 ma., the rage disappeared and the patient was able to discuss it quite objectively. The rage returned each time that the current was increased to 5 ma. and similarly disappeared when the current was reduced to 4 ma. The patient states that she was perfectly aware of her feelings but described them as unusual for her. During the periods when the current was below threshold she was rather amused by her reaction. At various intervals repeat X-rays were obtained which indicated that the electrodes had not shifted. Despite this, on subsequent treatment utilizing the same parameters of stimulation, the patient developed intense fear with an impulse to run. The common feature was a strong emotional response.

(Authors' Abstr.)

JUNE

Experimental Psychiatry. II. Clinical and Physio-Chemical Observations in Experimental Psychosis

1. Experimental psychiatry, i.e. the comprehensive study of experimentally produced psychosis, is important for the advancement of psychiatry.

2. The diethylamide of d-lysergic acid (LSD) has proven an excellent tool for investigation of experimentally produced psychotic-like manifestations.

3. Clinical, psychological, physiological and biochemical evidence is offered which indicates that the adrenalin system is involved in the LSD-produced emotional and psychotic phenomena.

4. Theoretical reflections concerning the enzymatic adrenalin system as the basis of the development of schizophrenia and other psychoses are reported.

(Authors' Abstr.)

Chlorpromazine Treatment of Mental Disorders

Chlorpromazine has a diverse pharmacological action on the human organism. A considerable body of evidence has been accumulated pointing to its therapeutic efficacy in many kinds of mental disorders. It is a drug of low toxicity even in large doses and one which may be administered over long periods of time without an undesirable increase of tolerance.

It appears to be a highly effective agent for controlling psychomotor excitement of all kinds without the undesirable effects of the standard methods and maintaining the patient in a fairly accessible state at all times. Its action on other types of mental illness is not so remarkable but is certainly worthy of further investigation, particularly in the chronic schizophrenic patients in whom most treatments are unrewarding. Facilitation of communication together with a remarkable objectivity towards significant ideas and feelings has occurred in many of this group.

Speculation about the mode and site of action of the drug seems premature but such evidence as there is suggests that it is a subcortical one. While in the initial states of treatment there is a definite resemblance in the behavior of these patients to those who have been lobotomized there are none of the deficit found in the latter. Neither the dosage nor the mode of administration of the drug is in any way standardized. The initial results obtained in Europe and this country have been satisfactory enough to justify a thorough clinical investigation of chlorpromazine and a search for even more powerful related compounds.

(Author's Abstr.)

VOL. 112 JULY

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Diagnostic Aspects of a Study of Intracellular Phosphorylations in Schizophrenia

1. This test affords a means for study of intracellular biochemical changes.

2. Proceeding from the fact that it has given quite uniform results in a fairly large healthy control group of persons and that different results are obtained in the cases of some clinically psychotic patients we may classify the test results of the first group as normal and of the second group as pathological.

3. The test gives normal response in the cases of most of our patients diagnosed clinically as suffering from psychiatric conditions other than schizophrenia as well as in diabetics and hyperthyroid cases.

4. Pathological test results are obtained chiefly within the schizophrenic range of diagnoses but some of the most clinically characteristic schizophrenics give normal results with this test.

5. Present indications are that there is some factor present within the group of schizophrenic spectrum cases which is common to many of these cases but that the central group of well confirmed, long-term cases of schizophrenia is itself not positively distinguishable by this means.

6. At the present state of the investigation the cases showing "normal type" enzymatic response can be tentatively characterized by the lack of the symptomatology of an acute psychotic attack of a sudden onset as it is typical in cases described as simple schizophrenia.

(Authors' Abstr.)

VOL. 9 AM. J. PSYCHOTHER. APRIL, 1955

JULY

VOL. 1 ARCH. CRIM. PSYCHODYN. 1955

VOL. 73 ARCH. NEUR. PSYCHOL. APRIL, 1955

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Semen Dyscrasia in Schizophrenia

Schizophrenics manifest many systemic disturbances of their physiologic functions.

The semen and its cytology are sensitive to general physiologic changes and are as deserving of study as any of the other body fluids.

The number of seminal analyses reported are too few to permit any conclusions as to either the genesis of schizophrenia or the etiology of spermatic monstrosities.

The results suggest the presence in schizophrenia of an X substance, which deranges spermatogenesis and produces the appearance of abnormal forms of spermatozoa.

(Author's Abstr.)

Stimulation of Suprabulbar Reticular Formation

Stimulation of the suprabulbar reticular formation produced a facilitation of flexor and extensor monosynaptic reflexes which was greatest during stimulation, which decreased markedly immediately after cessation of stimulation and then developed a late phase which persisted for two and a half to four and a half minutes.

The polysynaptic reflex evoked by simulation of a skin nerve was inhibited, and the polysynaptic components of mixed-nerve-evoked reflexes were frequently inhibited by stimulation of points which caused facilitation of the monosynaptic reflex. In about 50 per cent. of the cases, however, the polysynaptic element of the mixed-nerve reflex was facilitated, but not to as great a degree as was the monosynaptic component.

Antidromic potentials obtained from the cord segment transmitting the testing reflex were facilitated by reticular formation stimulation.

Dorsal root reflexes and the intermediary element of the cord potential were suppressed by reticular formation stimulation which facilitated the monosynaptic reflex.

The late facilitation produced by stimulation of the reticular formation resembled in amplitude and duration the post-tetanic potentiation produced by stimulation of muscle afferents. These two types of facilitation summated when elicited simultaneously. The presynaptic effect of one (post-tetanic potentiation) conceivably summated with the postsynaptic effects of the other.

The decrease in latency of the monosynaptic reflex during the periods of facilitation produced by reticular formation stimulation was explainable by a decrease in excitation time, as shown by the orthodromic focal potential recorded from the motoneuron pool.

A production of oscillations or fluctuations in reflex spike height by reticular formation stimulation was observed, and its possible implication in relation to the problem of tremor was noted.

Stimulation of certain areas in the reticular formation produced a mixture of facilitatory and inhibitory effects, requiring more study.

Stimulation of the pyramid, unlike stimulation of the reticular formation, produced facilitation which lasted for only a brief interval after stimulation.

Recording potential difference between the central and the peripheral portion of a ventral root by means of a direct-coupled amplifier showed that depolarizing forces act upon the motoneuron pool during periods of facilitation.

Decerebration and decerebellation reduced the amplitude and duration of the late phase of facilitation following reticular formation stimulation.

It is possible that the late and prolonged phase of facilitation is due to prolonged discharge from the reticular formation. Conclusive evidence of this was not obtainable by the methods employed.

(Authors' Abstr.)

Validity of Rorschach Test as Measure of Psychological Effects of Brain Damage

In an experiment designed to investigate the validity of Rorschach test indications of brain damage and to explore further the intellectual and affective changes associated with brain damage, the Rorschach test was individually administered to 50 persons with proved brain damage or dysfunction and 50 matched controls with negative neurological and anamnestic findings. The subjects in the two groups were very closely matched in pairs on the basis of color, sex, chronological age, and years of formal education. In the brain-damaged group the cerebral lesions were heterogenous with respect to type, location, and extent. The control group included a substantial proportion of paraplegic and neurotic patients to minimize the possibility that intergroup differences might be attributed to hospitalization, chronic illness, and affective disorders.

The results indicated thorough-going suppression of mean values for the brain-damaged group on quantitatively scored Rorschach variables. In 18 of 21 instances, statistical comparisons indicated that the means for the brain-damaged group were significantly lower than those for the controls. The consistency with which the differences reached statistically significant levels suggested that brain damage causes a generalized suppression of personality factors.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Variables supposedly relating primarily to either intellectual or affective functions were significantly reduced. Evaluation of the frequency of occurrence of Rorschach test "signs" of brain damage indicated that they have some value in differentiating the groups. The brain-damaged patients tended to give less realistic associations, repeated responses without regard for form, often recognized the inadequacy of responses but were unable to improve or withdraw them, tended to give more concrete responses, were less able to define associations clearly, tended to withdraw from the problem and then reapproach it apparently in an effort to regain a new set, were less able in giving more than one association to a single stimulus complex, more frequently seemed to distrust their ability and sought help from the examiner, and sometimes engaged in overt catastrophic emotional reactions as their difficulty with the test situation mounted. The ability to identify reliably these indications of brain damage in an individual Rorschach protocol is dependent to a heavy extent upon the examiner's experience. In addition, it should be noted that differences in the occurrence of these signs between the group with and the group without brain damage seemed to appear only to a matter of degree. They do not constitute a basis for perfect discrimination even in the hands of an experienced examiner.

The same groups of patients were previously compared on Halstead's test of biological intelligence. The Halstead Impairment Index, as well as 8 of his 10 "discriminating" tests, yielded results which differentiated the groups at much more extreme confidence levels than were obtained with the Rorschach test. In spite of the considerably closer approach to perfect differentiation of the patients according to diagnosis obtained with Halstead's test, the availability and widespread use of the Rorschach test, together with the relatively encouraging results obtained, suggest the value of further investigation of the psychological effects of brain damage with this test.

(Author's Abstr.)

MAY

Use of Large Doses of Cortisone in Schizophrenia

Nine nondeteriorated schizophrenic women were given 500 mg. of cortisone daily for from 4 to 10 weeks. These patients were studied intensively from the psychiatric, physical, and laboratory points of view.

1. Three patients showed slight and transient psychiatric improvement. Five were definitely made worse. One seemed unaffected. Many showed an increase in psychomotor activity.

2. No significant long-standing beneficial therapeutic results were obtained with use of cortisone alone. Cortisone did not appear to work synergistically with electroshock therapy.

3. Six patients revealed clinically demonstrable physical changes. Two showed a modified Cushing syndrome.

4. No significant alterations in electrolytes or other blood chemistry studies were seen. A significant eosinophile drop occurred in six patients. Two showed a significant drop in basal metabolic levels.

Several theoretical possibilities as to why all the patients did not show more pronounced evidence of hyperadrenalism are suggested.

(Authors' Abstr.)

Epinephrine-Mecholyl Test (Funkenstein Test)

Statistical study of 201 consecutive patients confirms the basic thesis proposed by Funkenstein and associates that prognostic implications can be derived from the epinephrine-Mecholyl test.

The recovery potential of the patients is shown to be positively correlated with the intensity of the autonomic response elicited. The recovery potential is high in patients with a greatly enhanced response to Mecholyl, either in cholinergic-muscarinic or in adrenergic-nicotinic direction, slightly less in patients with a moderately enhanced response, low in patients in whom one of the responses (that to epinephrine) is below par, and intermediate in those patients whose autonomic responses do not significantly differ from those of normals not under stress.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Absence of epinephrine-precipitable anxiety is prognostically favorable in cholinergic (muscarinic) overreactors, while presence of epinephrine-precipitable anxiety is prognostically favorable in the adrenergic (nicotinic) overreactors.

To electroshock therapy—of which a combined convulsive-nonconvulsive variant was employed similar to the combination of these modalities in electronarcosis—the most marked cholinergic and adrenergic overreactors responded best. Of the patients whose response to epinephrine was inadequate, none recovered with electroshock and/or psychotherapy, electroshock, as well as psychotherapy, being entirely ineffective in that group. The only Group V patients who achieved recovery were the two patients treated with insulin coma.

Epinephrine-precipitable anxiety nowhere represented a prognostically favorable item for response to electroshock therapy; however, it was less of a liability in our patients receiving combined convulsive-nonconvulsive treatment than in the patients treated with purely convulsive electroshock reported by Funkenstein and associates. In the combined Groups I–V, epinephrine-precipitable anxiety was thus eliminated as a liability altogether; the recovery rate of the patients with combined convulsive-nonconvulsive treatment (modified electronarcosis) was about equal for the subgroup with and for the subgroup without epinephrine-precipitable anxiety.

For Group IV, the recovery rate with psychotherapy was equal to that with electroshock therapy. Electroshock should therefore not be administered to Group IV patients except for purely symptomatic relief and should not be counted on to contribute to the ultimate recovery of the patient. This appears to depend upon the success of the psychotherapeutic work with the patient.

Epinephrine-precipitable anxiety is a prognostically favorable item for patients undergoing insulin therapy.

In the most favorable and the most unfavorable blood pressure reaction groups the predictive value of the epinephrine-Mecholyl test exceeds the predictive value of clinical diagnosis.

(Author's Abstr.)

Subcortical Connections from Temporal Cortex of Monkey

Connections from different parts of the temporal lobe to the basal ganglia, amygdala, and rhinencephalic cortex have been studied in the monkey by strychnine neuronography, evoked potential, and propagated seizure techniques. A preferential propagation was found from the temporal pole (TG) and from the superior temporal gyrus (TA) to the homolateral putamen, globus pallidus, amygdala, hippocampus proper, and hippocampal gyrus. Little or no propagation of activity to these structures was manifested upon stimulation of the second temporal gyrus (TE).

The findings indicate close functional relationships between the tip and the superior gyrus of the temporal lobe, and suggest a fundamentally different mode of organization of connections, and hence of function, of the second temporal gyrus.

Abundant and relatively direct connections from the tip and superior temporal gyrus to subcortical and rhinencephalic structures may help to clarify the role of these cortical areas in somatic, autonomic, and psychic spheres.

The facile propagation of seizure discharge initiated in the temporal tip and superior temporal gyrus to the amygdala may support recent proposals for an equivalent potentiality of both temporal cortex and amygdala in the genesis of psychomotor types of epilepsy. The present observation that evoked after-discharge is transmitted with equal facility to the putamen and globus pallidus raises the question of whether the basal ganglia, together with the amygdala, may participate in seizure activity during a psychomotor fit.

(Authors' Abstr.)

JUNE

Treatment of Multiple Sclerosis with Low-fat Diet

Five and one-half years' experience with a low-fat diet in the treatment of multiple sclerosis is summarized. This diet appears to lessen the severity of the disease by reducing the frequency and severity of the exacerbations. Its usefulness is greatest early in the disease, before significant disability and a steady progression of symptoms have developed. The period of observation has now been sufficiently long to give us some confidence in our observations, although we must not overlook the fact that since we are dealing with a disease having an average duration of perhaps 20 to 25 years, any conclusion concerning its therapy must still be tentative.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

The mechanism by which the fat intake might influence the disease is discussed. Serious consideration is given to the hypothesis that patients with multiple sclerosis have a basic defect in the suspension stability of their blood, which is upset by the hyperlipemia following heavy fat meals.

(Author's Abstr.)

Antibrain Antibodies in Multiple Sclerosis

The complement fixation tests with the solutions of Folch-Lees proteolipides A, B and C, used as antigens, gave negative results.

The combined number of positive complement fixation tests with the multiple sclerosis brain antigens was 83·3 per cent. in multiple sclerosis patients.

The combined number of positive complement fixation tests in the control group was 42·6 per cent.

The difference between the number of positive complement fixation tests in multiple sclerosis sera and the number of those in normal sera was 40·7 per cent., a difference which is statistically valid.

The observation that the addition of normal sera to the positive multiple sclerosis sera reduces the positive reaction to a negative one, or to a much weaker one, led to a hypothesis that a substance is added capable of neutralizing the complement-fixing bodies, thereby liberating the complement.

This finding led to the selection of donors on the basis of this test for the treatment of the multiple sclerosis patients with blood transfusions.

(Author's Abstr.)

Intellectual and Affective Functions in Multiple Sclerosis

Widely divergent estimates have been reported regarding the incidence and extent of intellectual impairment in persons having multiple sclerosis. Some are based upon clinical impressions only; others are conclusions reached by the use of single psychological tests or batteries which have proved of inconsistent validity in organic brain damage. In the present study, an extensive series of tests was used; the results were analyzed statistically, and the findings were correlated.

Three groups of 13 patients each were used. One was composed of an unselected series of patients with multiple sclerosis; a control group consisted of patients with proved brain damage, and another control series was made up of patients having no history or evidence of damage to the brain. Each patient was matched with a corresponding one in the other groups on the basis of color, sex, age, number of years of formal education, and Wechsler-Bellevue full-scale Intelligence Quotient.

The Tests administered to each patient were the Minnesota Multiphasic Personality Inventory, Halstead's tests for measurement of biological intelligence, and the Rorschach Test. Halstead has presented evidence indicating that his battery measures aspects of intelligence which are particularly susceptible of impairment with brain damage, but are not closely correlated with I.Q. measures.

The profiles of all three groups were similar on the Minnesota Multiphasic Personality Inventory and were quite typical of neurotic disturbances. On the other hand, Halstead's battery indicated severe and parallel intellectual impairment in a high percentage of patients in both the multiple sclerosis group and the group with brain damage. The Rorschach Test indicated similar impairment, but of less striking magnitude. The findings in the group without damage to the brain, in contrast, were generally within the normal range.

Although the samples are small, the results indicate a statistically valid trend which warrants similar investigations of larger series.

(Authors' Abstr.)

VOL. 74 JULY

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Variations in the Plasma Fibrinogen During the Course of Multiple Sclerosis

On the basis of Putnam's theory that the characteristic plaques in multiple sclerosis are caused by thrombi in the small veins of the central nervous system, investigations have been made with a view to demonstrating factors which might explain the origin of these thrombi.

A rise in the plasma fibrinogen has been demonstrated in multiple sclerosis; this is of special interest in this connection, as a raised fibrinogen content increases the agglutinability of the thrombocytes.

The investigations here described seem to indicate that variations of the plasma fibrinogen occur in multiple sclerosis, and that exacerbations of the disease are accompanied by rises in the plasma fibrinogen.

This gives rise to the question of what importance may be ascribed to the plasma fibrinogen in the case of thrombus formation in plaques. Several conditions, however, seem to go against a possible primary importance of fibrinogen in this process. Thus, often a raised fibrinogen occurred without clinical signs of the formation of new plaques. A raised plasma fibrinogen is, moreover, found in other chronic diseases without this giving rise to an increased frequency of thrombus formation. The periodically raised plasma fibrinogen content, as well as the clinically demonstrable exacerbations, is most likely to be an accompanying phenomenon to the actual cause of the disease.

(Author's Abstr.)

Effects of Diphenylhydantoin (Dilantin) on Adrenal Cortical Function

Diphenylhydantoin (Dilantin) was administered orally for varying periods of time to 12 nonepileptic human subjects and their adrenocortical activity was estimated by measurements of urinary excretion of 17-ketosteroids and corticoids. During acute administration of the drug 17-ketosteroid excretion remained essentially unchanged, but the corticoid excretion increased; during prolonged administration the excretion of both decreased significantly. These findings suggest that diphenylhydantoin may have an initial stimulatory and a later depressant action on the adrenal cortex. The implications of the results are discussed with regard to convulsive states in general and the mode of action of diphenylhydantoin as an anticonvulsant.

(Author's Abstr.)

Language Disturbances in Cerebral Disease

In summary, it is suggested that in arteriosclerotic dementia, and probably also in a certain proportion of epileptic cases, the striking decline in vocabulary level which is observed is related to the presence of localized cerebral lesions causing a mild aphasic state which may escape clinical detection by gross clinical observation but which manifests itself in a characteristic pattern of psychologic test performance. It is probable that this relationship also holds for other organic defect states. This possibility indicates that one must be extremely cautious in designating "typical" test performance patterns in cerebral disease, and it emphasizes the necessity for further investigations of homogeneous groups of patients. From the observations which have been reported it seems evident that the assumptions underlying the application of many so-called deterioration scales are in need of revision.

(Author's Abstr.)

VOL. 78 **BRAIN** 1955

The Nature and Clinical Significance of Pigments in the Cerebrospinal Fluid

1. Oxyhaemoglobin, bilirubin and methaemoglobin are the pigments which commonly occur in coloured cerebrospinal fluid.

2. Oxyhaemoglobin appears at the onset of haemorrhage, progresses to a maximum the first few days and then gradually diminishes in amount. Bilirubin appears in two to three days

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

and increases in amount as oxyhaemoglobin decreases. Bilirubin persists for two to three weeks. Experiment *in vitro* suggested that only the action of living cells can produce bilirubin.

3. Methaemoglobin is found in fluids from subdural and intracerebral haematomas, craniopharyngiomas, and in fluids near encapsulated blood.

4. In cases in which there was obstruction to the flow of cerebrospinal fluid, cystic fluids and subdural effusions, the protein was elevated and bilirubin was the predominant pigment. The transudation of bilirubin complex from blood plasma is suggested in such situations.

5. In 10 of the 12 jaundiced patients, the spinal fluid was xanthochromic and bilirubin was the only pigment detected.

6. The benzidine, van den Bergh and potassium cyanide tests are useful simple confirmatory tests that can be performed in any ward laboratory when spectrophotometric methods are not available.

(Authors' Abstr.)

Neurological Deficiencies after Ablation of the Precentral Motor Area in Macaca Mulatta

These experiments were concerned with a reinvestigation of the function of the "motor" cortex studied in eight *Macaca mulatta*. Since the precentral motor area was defined as a functional unit that does not coincide with previous definitions of the "motor" cortex (Woolsey and Settlage, 1950; Woolsey *et al.*, 1952), this study was undertaken to determine the results of ablation of this area alone. The following conclusions were reached:

1. Precentral motor area lesions resulted in immediate severe voluntary impairment, hypotonia and diminished tendon reflexes in the extremities contralateral to the ablations; no ipsilateral deficits were observed.

2. Partial recovery of motor performance followed, and movements reappeared as soon at distal as at proximal joints; detectable impairments persisted at both.

3. Within two to twelve weeks the animals were able to pick up small stationary objects by apposition of thumb and index finger but after maximal recovery this manœuvre was accomplished with only approximately half normal speed.

4. No significant spasticity developed. In the arms the triceps and finger jerks passed through a transient phase of moderate hyperactivity.

5. Placing and hopping reactions returned after one to three weeks in the affected limbs, but they were performed persistently in a retarded, hypermetric manner. The responses were enhanced with excitement of the animal.

6. The abdominal reflexes on the side contralateral to the lesion were diminished for four to six weeks following the operation, but after this interval they appeared as active as normal.

7. The plantar reflex consisted of apposition of all toes instead of the normal active flexion of the toes and frequent withdrawal of the entire hind-limb.

8. Atrophy of about 10 per cent. appeared in the limbs opposite the lesion during the period of greatest disuse and completely subsided after maximal recovery of motor function was achieved.

9. No grasp reflexes were obtained, although the lesions included Vogt's dorsal and part of the medial area $6a\alpha$.

10. These experiments do not support the concept that all parts of the motor cortex exert some control over all parts of the body musculature.

(Author's Abstr.)

Neurological Deficiencies Following Supplementary Motor Area Lesions in Macaca Mulatta

The supplementary motor area was defined by electrical stimulation as a distinct somatotopically organized field (Woolsey *et al.*, 1950, 1952), and this investigation was undertaken to determine the neurological deficits produced by its removal. The results were derived from lesions restricted to the supplementary area and from ablations involving either the precentral or supplementary motor area with injury to the other area. Experiments were also performed to determine if extirpation of the portions of the histologically mapped "area 6" not included in the precentral motor area would demonstrate motor impairment. The results are as follows:

1. The supplementary motor is a bilateral functioning system, for greater deficits were obtained after simultaneous bilateral than after unilateral ablations.

2. Unilateral supplementary area lesions produced weak, transient grasp reflexes in the contralateral limbs, and within one week moderate bilateral hypertonia of the shoulders. No noticeable paresis was present.

3. Simultaneous bilateral supplementary area ablations yielded practically no paresis, but posture and tonus were disturbed. Immediately there was increased resistance to passive movements of the limbs, and during an interval from two to four weeks contractures supervened. The hypertonia was encountered in the flexor muscles. The tendon reflexes were hyperactive within a day to two weeks with some of them (finger and toe jerks) becoming clonic. The spasticity demonstrated topographical localization according to the portions of the areas removed. Grasp reflexes were present for three to five weeks.

4. When the supplementary area was removed bilaterally in two stages with over six months intervening between the operations, only slight increased resistance was located at the ankles. No hyperactive tendon reflexes appeared, and weak, temporary grasp reflexes were

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

observed after the second operation. This indicates that practically no release phenomena will follow the second operation provided a sufficient time interval intervenes between two such operations.

5. If no addition to a simultaneous bilateral supplementary lesion there occurred unilateral injury of the precentral hind-limb area, the immediate resistance and final contractures were less in the lower limb opposite the additional precentral ablation.

6. If with removal of the precentral motor area the supplementary area was damaged, there resulted localized increased resistance to passive movement according to the portions of the area encroached upon. This was true with unilateral and bilateral ablations.

7. The lesion involving unilateral precentral plus supplementary limb areas resulted in immediate hypotonic paresis and impairment of tendon reflexes. This stage of diminished reflex activity within two weeks merged into a state of increased reflex activity; the hypotonus changed to moderate increased resistance to passive movements in the fore-limb and to approximately normal tonus in the hind-limb. The experiment defined the supplementary motor area as concerned with controlling movement, for the paralysis observed was greater than after unilateral precentral motor removals.

8. The placing and hopping reactions persistently disappeared in the affected extremities following unilateral precentral plus supplementary lesions; but previous simultaneous or later removal of the limb area of the precentral or of the supplementary motor system in the opposite hemisphere permitted the reactions to be performed crudely in the affected extremity.

9. Ablation of "area 6" not included in the precentral or supplementary motor area resulted in no motor impairment of the limbs, no grasp reflex, and no hypertonia. This indicates that the only motor functional parts of "area 6" are those portions included in the precentral and supplementary motor area.

(Author's Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

VOL. 46 BR. J. PSYCHOL. MAY, 1955

AUGUST

VOL. 20 BULL. LOS ANGELES NEUR. SOC. JUNE, 1955

VOL. 16 DIS. NERV. SYST. APRIL, 1955

Complications of Chlorpromazine Treatment

Chlorpromazine deserves acceptance as a new form of psychiatric treatment.

To be really effective in schizophrenia it must be given in much larger doses than other investigators have considered safe.

There are many complications to chlorpromazine therapy. None appears to be dangerous and all may be managed satisfactorily by reduction of dosage or temporary withdrawal.

(Author's Abstr.)

MAY

JUNE

JULY

Oral Metrazol Therapy in Senility

Fifteen senile patients nearly all of them disorientated, confused, often restless, untidy and quarrelsome, received oral Metrazol therapy. Generally, 2 tablets of 1½ grains each were given 3 to 4 times a day. Twelve of the 15 patients were definitely improved even after so short

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

a time as 4 to 5 weeks. Usually demonstrable improvement occurred within 10–14 days after the therapy was started. Although 2 patients became definitely more alert mentally—one of them even requesting to go home and later discharged in his own cognizance. All the other 10 men became more amenable to ward care, so that restraint frequently could be dispensed with and the constant aimless wandering about the ward ceased.

What can be achieved with Metrazol therapy in mentally less confused cases remains to be seen. Judging from the results so far, Metrazol therapy certainly is of value to reduce the nursing difficulties inherent in the care of such senile cases. This in itself is no mean advantage which enables the personnel to give more time to those other patients who require special attention.

(Authors' Abstr.)

Clinical Comparison of Raudixin and Rau-sed in Chronic Mental Illness

Raudixin and Rau-sed were given to fifteen chronically disturbed mental patients. The clinical responses to either drug, in relation to hyperactivity, overtalkativeness, assaultiveness, destructiveness, agitation and tension were the same. There was no significant difference in decreases of blood pressure occasioned by either medication.

The authors feel that these drugs can be used with a marked degree of safety and that chronic mental patients may obtain considerable benefit from this treatment.

(Author's Abstr.)

VOL. 7 EEG CLIN. NEUROPHYSIOL. MAY, 1955

Hippocampal Seizure States in Guinea Pig

1. The electrical activity of hippocampus and isocortex in unanesthetized guinea pigs during resting state and in response to external stimulation is described. It is shown that there is a differential response of hippocampal and isocortical activity to complex environment stimuli.

2. Mechanical and electrical stimulation of the hippocampus induce local and propagated seizure discharges at relatively lower thresholds than stimulation of isocortex, striatum and thalamus.

3. The structure of the hippocampal seizure discharge as analyzed from combined ink-writer and cathode-ray oscillograph recordings is a composite of several activities of different frequency orders with relatively constant mutual phase relationships. In particular, the clonic stage is characterized by slow pulses of 0·3 to 5 c/sec., with superimposed waves of 10–30 c/sec., carrying on top of them brief spikes of 2·5 msec. duration. Each of these complex pulses is preceded by a shower of 100–200 c/sec. spikes. Periods of apparent silence are characterized by a deviation of the basis potential from the isoelectric line, of opposite polarity to the one exhibited during the clonic pulse. Gross spikes and spike-and-waves appearing at the onset of a "tonic-clonic" after-discharge are rarely observed in the hippocampus but are common in the epileptic activity of neocortex, striatum, amygdala and thalamus.

4. Hippocampal after-discharges spread widely over cortical and subcortical structures, as well as over the cerebellum. They show a preferential spread over the centrocaudal isocortex, often avoiding the rostral neocortex.

5. Unless unduly strong stimulation, resulting in a grand mal convulsion, is applied, there are only slight changes of behavior concurrent with the after-discharge: arrest of ongoing behavioral activity and decrease of reflex responses.

6. These various findings suggest that the hippocampus may play an important role in epilepsy in general. This structure may participate in, and may indeed initiate the manifestation of those forms of epilepsy which are chiefly characterized by disturbances of awareness and mental confusion.

(Authors' Abstr.)

Electrophysiological Studies on the Connections of the Amygdaloid Nucleus in the Cat. Part I: The Neuronal Organization of the Amygdaloid Projection System

1. The subcortical and cortical connections of the amygdaloid complex are studied in 23 cats using the technique of recording evoked potentials to single shock and repetitive electrical stimulation of the amygdala.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

2. The subcortical projection area of both baso-lateral and cortico-medial subdivision of the amygdala overlap widely. This subcortical projection field extends from the septum and the base of the head of the caudate nucleus back to the tegmentum mesencephali comprising essentially beside the just named structures the preoptic area, the hypothalamus, the subthalamus, the entopeduncular nucleus and some nuclei of the diffuse thalamic projection system.

3. Short latency responses on baso-lateral amygdaloid stimulation, most probably mediated directly without synaptic interruption, are found in the "primary projection field", which covers the basal part of the telencephalon medium and the adjacent rostro-basal pole of the diencephalon. From here responses are relayed to the remainder of the projection area—the "secondary projection field"—through short multisynaptic neuronal links. This "secondary projection field" comprises mainly the more caudal parts of the centro-basal core of gray matter extending from the hypothalamus to the tegmentum mesencephali. This latter area may eventually be activated through a more direct amygdalo-mesencephalic system by-passing the hypothalamus.

Short latency responses from the cortico-medial group extend further caudal into the hypothalamus than those observed on baso-lateral amygdaloid stimulation. It seems therefore that the "primary projection field" of the cortico-medial amygdaloid subdivision is more extensive. On the other hand no evidence is found for a tegmental projection of this nuclear subdivision.

4. Pathways from the baso-lateral nuclear group to their "primary projection field" in the subcortex do not run through the stria terminalis. This fiber bundle originates in the cortico-medial part of the amygdala and represents the main outflowing fiber path of this amygdaloid subdivision. The baso-lateral part uses shorter and more direct pathways to its "primary" subcortical projection area. However, there are intraamygdaloid association fibers through which over multi-synaptic relays the baso-lateral nuclei may discharge through the stria terminalis also.

5. The cortical projection area of the amygdala comprises neocortical, paleocortical and archicortical structures. The neocortical areas in connection with the amygdala are homologous with the anterior temporal and insular region in man.

Multisynaptic chains exist from the amygdala *via* the paleocortex of the piriform lobe to the archicortex of the hippocampus, which although very responsive to amygdaloid stimulation does not receive any direct fiber connection from the amygdala. The possibility of a recurrent firing of the hippocampus from the amygdala *via* the septum and ascending fornix fibers is also briefly discussed.

6. The fibers originating in the amygdala seem to belong mainly to the group of thinly myelinated and unmyelinated elements. Some of the properties of the amygdaloid projection system are best explained on the assumption that part of the neurones at least are comparable to autonomic elements of the C-fiber group.

7. The functional significance of the experimental data are briefly discussed. The wide variety of amygdaloid stimulation effects as observed by several authors becomes understandable in view of the data presented in this study, since they show that excitation originating in the amygdala impinges upon a wide subcortical area known to contain the central representations of various integrative mechanisms regulating somatic, autonomic, behavioral and electrographic activities.

8. The cortical projection pattern of the amygdala corroborates clinical electroencephalographic and electrocorticographic findings in cases of temporal lobe epilepsy with ictal automatism, where activation of epileptogenic activity in the anterior and mesial temporal as well as in the insular cortex is observed presumably from a primary source in the amygdaloid region.

(Author's Abstr.)

Electrophysiological Studies on the Connection of the Amygdaloid Nucleus in the Cat. Part II. The Electrophysiological Properties of the Amygdaloid Projection System.

1. The changes in excitability within the amygdaloid projection system were studied using the method of single shock and repetitive stimulation of the amygdala. As a routine the following technique was applied: first, the responses to 1 c/sec. single shock responses were observed and then the changes this response underwent during 10 c/sec. or 50 c/sec. repetitive stimulation were studied. At the end of the period of repetitive stimulation single shock stimulation at 1 c/sec. was immediately resumed in order to obtain information about facilitatory or inhibitory after-effects.

2. With this technique the following changes were observed: recruitment or obliteration during repetitive stimulation, often followed by potentiation in the post-tetanic single shock stimulation phase. Changes in latency—either decrease or increase—were seen to go along with these changes in excitability in many instances.

3. Recruitment was very often observed with 10 c/sec. repetitive stimulation. It was absent with 50 c/sec. stimulation. Recruitment was most prominent with long latency responses suggesting multisynaptic transmission and therefore was considered as an amplification process due to building up of a facilitatory state at successive synaptic stations.

The opposite process of building up of inhibitory phenomena leading to progressive obliteration of the response was occasionally seen also, though less frequently.

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Moreover, evidence was found that both processes may sometimes co-exist in a complex multisynaptic neuronal system. They become apparent when they show a different time course of development.

4. Potentiation, though maximal in multisynaptic chains of neurones, was however less dependent on the presence of repeated synaptic passages than recruitment. Potentiation may partly take place at the site of stimulation itself, though it is to undergo amplification when passing through successive synapses. Potentiation may reach its maximum with a certain delay after the end of repetitive stimulation, which is evidence of the presence of a co-existing state of inhibition decaying more rapidly than the facilitatory state. Signs that this inhibitory state is already present or developing during the preceding repetitive phase of stimulation are usually present.

Potentiation in the amygdaloid projection system seems to be due to summation of facilitatory states going along with progressive extension of the subliminal fringe with consecutive increase in number of firing neurones.

5. Changes in latency may go along with these excitability changes as expressed by recruitment, obliteration and potentiation. There is, however, no constant parallelism between increased excitability and shortening of latency, the opposite situation of a progressive lengthening of the latency together with building up of a heightened central excitation as in recruitment may also be seen.

6. The possible significance of these findings is briefly discussed. In view of the reported results excitation in the amygdaloid system must be considered as highly susceptible to fluctuations in excitability level according to the rate of firing. Connections from the amygdala to its projection areas seem therefore somewhat loose and flexible. The amygdala is thought to act in a modulatory way on complex somatic, autonomic and behavioral mechanisms integrated in subcortical structures. Additional evidence derived from findings of other authors is briefly summarized to corroborate this conception of the functional significance of the amygdala.

(Author's Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

An Experimental Study of Pathways from the Basal Ganglia

Lesions were placed in the basal ganglia in three specimens of *Macaca mulatta*. The animals were observed during a survival period of from two to 8 weeks. The brains were studied in Marchi preparations. The following results were obtained:

1. The origin of the ansa lenticularis is not confined to the medial division of the globus pallidus. Additional possible sources are the lateral division of the globus pallidus and the putamen. The tract may be joined by fibers from the temporal and insular cortex.

2. Fibers from the basal ganglia were followed into various areas of the dorsal and the ventral thalamus and the hypothalamus and into the red nucleus of the mesencephalon.

3. The origin of the lateral cortico-habenular tract is basal to the globus pallidus, presumably in the amygdala and the pyriform lobe cortex.

4. Small electrolytic lesions in the globus pallidus result in no detectable abnormalities in behavior in the macaque.

5. A lesion destroying the globus pallidus unilaterally and interrupting the fibers basal to the globus pallidus bilaterally produces a marked reduction in the monkey's willingness to move. Peculiar jerks occurred whenever this monkey was touched.

(Author's Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

The Inferior Olive. A Golgi Study

Detailed study of the inferior olive in a large group of animal and human brain stems, using the silver chromate impregnation method of Golgi, has revealed new information regarding the structure of this nucleus.

1. The cell population of the inferior olive is not homogenous in structure. Cells with large, simple and relatively unramified dendrite patterns occupy the caudal portions of the dorsal and medial accessory nuclei. Cells with smaller, highly ramified, spherical dendrite arbors of the type described by Ramon y Cajal are found in the rostral portions of the accessory nuclei and the phylogenetically newer primary olivary nucleus.

2. In preparations of human inferior olive, a large cell with very extensive dendrite distribution has been found in the center of the olivary grey matter.

3. In addition to the classical afferent arborizations, at least two new patterns of axon terminations have been described.

(*a*) The majority of fibers from the descending tract which enter the rostral pole of the olive terminate in simple bifurcating fibers bearing either small nodules or clusters of terminal buttons. Small numbers of fine fibers with similar patterns of termination enter the olive from the region of the white matter near the midline.

(*b*) Fibers of larger caliber enter the dorsomedial aspect of the nucleus and terminate on olive cell somata or on orange-staining bodies in clusters of terminal buttons or in more complex rosette forms. It is suggested that these fibers fractionate the olive cell pool by manipulating firing thresholds on the basis of impulse patterns from centers of higher integration. The question is raised whether this "feedback" type of circuit might not represent part of the basic pattern of the so-called relay nucleus.

4. A small number of efferent axons have been seen to leave the rostral pole of the olive and course cephalad.

5. The olivary neurophil is described in detail. Anatomical and functional evidence is presented which suggests that the olive may be especially adapted, through the configuration of its neuropil, to maintain a low threshold to afferent impulses.

6. Within the neuropil, many small nodules and oval bodies are seen, lying apparently free, or in contact with axonal or dendritic processes. The nature and function of these bodies is unknown.

7. Spherical, orange-staining bodies with rims of unstained refractile substance are described throughout the olive and in other parts of the nervous system. Many of the rosettes of the heavy afferent fibers appear to terminate on these bodies, which also make contact with various elements of the axonal and dendritic neuropil and with what are presumed to be astrocyte processes. The possible nature of these bodies is discussed and evidence is brought forward which indicates that they may belong to the group of oligodendroglia. If so, recent studies indicating the close relationship of neuroglia to acetylcholine esterase suggest that orange-staining body-neural relationships may furnish the anatomical substrate for one type of neurohumeral interaction in the central nervous system.

(Authors' Abstr.)

APRIL

Histochemical Studies of Glycogen of the Area Postrema and the Allied Structures of the Mammalian Brain

The area postrema and other paraventricular structures were studied, with the histochemical methods for glycogen, in the mouse, rat, hamster, guinea pig, rabbit, cat, dog, and man. The brains, after prompt excision from the animals, were fixed in Rossman's fluid, followed by embedding in paraffin. The sections were stained with the lead tetraacetate-Schiff method or the McManus method.

The area postrema and intercolumnar tubercle are provided with abundant sinusoidal blood vessels surrounded by conspicuous connective tissues, which are moderately positive but saliva-resistant, a reaction attributable to the presence of mucopolysaccharide.

The area postrema of all animals examined, excepting man, reveals the presence of variable amounts of glycogen granules. The most evident deposit was in the rabbit and hamster, the intermediate in the dog, pig and cat, and the least in the mouse, rat and guinea pig. The guinea pig shows, however, a prominent accumulation of glycogen in the outskirts of this area. The glycogen particles are observed to be mainly located either around the blood vessels or on the intercellular fibrillar structures.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

A moderate deposition of glycogen is demonstrated within the ependymal cells and adjacent neuropil of the supraoptic crest in the mouse and rat, while none is found in the hamster. The elongated ependymal cells of the subcommissural organ contain a moderate amount of glycogen in the mouse, rat and hamster. The intercolumnar tubercle shows a small amount of glycogen in the hamster.

(Author's Abstr.)

Organization of the Cerebral Cortex. III. A Study of Aging in the Human Cerebral Cortex

The quantitative changes in cell number with increasing age were investigated according to the method of Bok. Sections of cortex were removed from a human series extending from birth to 95 years.

The counting of cortical cells and rank correlation of cell number with age indicate that the greatest decrease in cell number with increasing age occurred in the superior temporal gyrus followed by the precentral gyrus and then the area striata. The postcentral gyrus showed the least change in cell number. It was noted that, at least between the newborn and 16 to 21 year old group, the decrease in cell number was an apparent rather than a real decrease. The factors responsible for this were discussed. In the precentral gyrus, a differentiation of the cortical layers was observed from the superior to the inferior extent of the gyrus. The portion closest to the lateral fissure reveals a stratification. The superior portion is not delineated in this way.

Whereas all the cortical layers show a decrease in cell number with age, external and internal granular layers are particularly affected. The dominant cell type in these layers in the newborn is the granule cell. In the older age groups these layers contain more small pyramidal cells than granule cells.

(Author's Abstr.)

VOL. 48 **J. COMP. PHYSIOL. PSYCHOL.** APRIL, 1955

JUNE

VOL. 18 **J. NEUR. NEUROSURG. PSYCHIAT.** MAY, 1955

The Association of Dementia with Radiologically Demonstrated Cerebral Atrophy

In routine clinical practice at least 85 per cent. of 68 cases of unexplained dementia in later life showed evidence of cerebral atrophy in the A.E.G.

In 213 A.E.G.s performed in the investigation of cases without dementia 11 per cent. showed an unexplained cerebral atrophy, and these were most commonly associated with epilepsy of late onset.

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Features of the A.E.G. that suggest an associated dementia are cortical sulci greater than 0·5 cm., air trapped in the insular region, and enlargement of the lateral ventricles particularly marked in the region of the trigone.

(Author's Abstr.)

JULY

VOL. 14 J. NEUROPATH. EX. NEUR. APRIL, 1955

VOL. 18 J. NEURO-PHYSIOL. MAY, 1955

JULY

VOL. 12 J. NEUROSURG. MARCH, 1955

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

MAY

JULY

VOL. 23 J. PERSONAL. JUNE, 1955

VOL. 19 J. PROJ. TECHN. JUNE, 1955

VOL. 20 J. SPEECH HEAR. DIS. MARCH, 1955

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

JUNE

VOL. 5 NEUROL. JUNE, 1955

Examinotion of the Sensory System in Patients After Hemispherectomy

Following hemispherectomy these patients seemed to experience only a minimal reduction in their sensory perception. The reason the loss is relatively minimal after excision of cerebral areas generally considered necessary for the recognition and discrimination of stimuli is not entirely established. The thalamus unquestionably acts as the primary, and probably major, receptive center for perception of pain, temperature, and light touch stimuli. These modalities of sensation remained nearly intact after hemispherectomy. Finer discriminative powers are lost to some extent but not entirely. Tests for stereognosis are only minimally less accurately completed on the involved than on the uninvolved side. This is believed due to the assumption by the remaining (and since early childhood the dominant) hemisphere of these functions usually carried out by the contralateral sensory areas. Nielson has alluded to this assumption of function by his statement that aphasia does not develop in infants from a unilateral lesion regardless of laterality. Similarly, patients with destruction of the internal capsule by vascular lesions (producing anatomically a lesion comparable to a hemispherectomy) retain no such sensory perceptive powers as do these patients with hemispherectomies. An alternative possibility is that in the thalamus there is an ability to discriminate stimuli on a spatial basis. Such localization has been demonstrated in macaques. However, the cortex undoubtedly functions to delineate better such tactile stimuli. It is emphasized that in the interpretation of these data it must not be forgotten that the patients in this series were handicapped pre-operatively and had been so handicapped for many years. It is believed that because of this fact transference of these data to patients without long standing pre-existing neurologic functional loss cannot be done.

(Authors' Abstr.)

JULY

The Hypothalamic Syndrome in Rats with Experimental Lesions

Lesions were placed in the hypothalami of Sprague-Dawley rats by means of electrodes inserted perpendicular to the midsagittal plane of the brain. Some with low colonic temperatures died of starvation. Others (15 rats) exhibited hyperphagia, polydipsia, obesity and sham rage; none of these showed changes in colonic temperatures. The female rats in which the estrus cycles were studied showed disturbances of the cycle.

The lesions responsible for obesity were bilaterally symmetrical, either filiform, umbonate, spindle-shaped, or cylindrical, sometimes bridging the third ventricle, in the anterior portion of the ventrotuberal hypothalamus. Large and extensive lesions of the anterior hypothalamus were usually necessary to produce the obese condition or changes in estrus cycles; small lesions in this area failed to produce these conditions. Midtuberal lesions of the hypothalamus need not be large. It was found that thread-like lesions, provided they damage part of the ventromedial nuclei and the areas immediately lateral to these nuclei, were sufficient to produce the obese condition without changes in estrus cycles or colonic temperatures.

(Author's Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Ballism Associated with Partial Destruction of the Subthalamic Nucleus of Luys

A case of ballism occurring in a 72 year old hypertensive male controlled after ventrolateral cordotomy was reported clinically and pathologically. Death resulted from bronchopneumonia 23 days after onset of the dyskinesia. Sections of the brain were studied by the Marchi method. The lesion, destroying approximately 31 per cent. of the right subthalamic nucleus, was located in the lateral half of the nucleus rostrally and in the dorsal half of the nucleus caudally. No definite conclusion regarding somatotopical localization within the subthalamic nucleus could be drawn from this case.

The following conclusions were drawn:

1. The limit of physiologic safety for the human subthalamic nucleus is of the same order as in the rhesus monkey despite its absolute size, being approximately 15 times as large (relative size is about the same).

2. Pre-existing striatal deficit contralateral to a lesion of the subthalamic nucleus apparently does not prevent the appearance of ballism in man.

3. The primary blood supply of the subthalamic nucleus is probably derived from branches of the posterior cerebral artery.

4. The possibility that localized lesions of the spinal cord may abolish ballistic activity without producing signs of symptoms of pyramidal deficit is suggested by the case reported here. An attempt to confirm this result would seem worthwhile.

(Author's Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Chlorpromazine in the Management of Acute Alcoholic States

Experience with chlorpromazine hydrochloride in 164 alcoholic patients is reported.

In relatively large doses this drug possesses properties that make it extremely helpful in the management of acute alcoholic states. It produces immediate control of motor excitement and of nausea and vomiting, permits a restful, relaxed sleep, and contributes to the relief of tension and anxiety. The patient is able to retain fluids and nourishment, can be readily aroused for appropriate nursing care, and thus is quickly able to return to a state of physiological normalcy.

No addiction to the drug has been noted. There are few unpleasant side effects. During initial therapy, orthostatic hypotension of moderate degree is fairly common. Occasionally the hypotension may be severe. Thus, the blood pressure of patients treated with chlorpromazine should be closely followed, particularly when large doses are given, and the patients should be kept in a recumbent position.

(Authors' Abstr.)

1. Biochemistry, Physiology, Pathology, etc.

Formation of Ammonia in Brain Tissue and Adenylic Acid Deaminase. Tsukada, Yasuzo and Takagaki, Genkichiro. [*Kagaku* (*Science*), **24**, 572 (1954).]

When tissue homogenates from guinea pig brain were incubated at 37° and pH 7·0, rapid increase of NH_3 and concomitant decrease of glutamic acid (I) were observed. The amount of NH_3 formed was fully accounted for by the decrease of (I). With longer incubation periods adenine derivatives were deaminated to form inosine derivatives, but the deamination was not observed with brain slices; therefore adenylic acid deaminase was considered to be inactive in slices, showing a difference from the enzyme system in a homogenate. Amination of inosinic acid to adenylic acid did not occur in brain slices even in the presence of inosinetriphosphate (ITP) and glutamine. Addition of (ITP), however, increased formation of NH_3 even in brain slices. The effect of (ITP) may be due to activation of glutaminase, rather than to amination of inosine derivatives.

T. KOBAYASHI (Chem. Abstr.)

The State of Cholesterol and Phospholipides in the Brain Tissues of Animals. Nedzvetskii, S. V., and Ratnitskaya, S. S. [*Biokhimiya*, **19**, 677 (1954).]

Blood vessels and dura of cattle brains were removed. Tissues were ground with glass in 0·9 per cent. NaCl and centrifuged. The supernatant was designated as extract 1 and the sediment subjected to a second similar extraction and centrifugation. The second supernatant was designated as extract 2. The sediment was then extracted twice with 7 per cent. NaCl and residue ground in 0·25 per cent. NaOH. Extractions thus obtained which gave the biuret reaction were tested for content of cholesterol and phospholipides. Tests were also made to determine whether the cholesterol and phospholipides are in combination with the proteins of the brain tissues. It was shown that by the NaCl solvents 24–27 per cent. of the cholesterol is

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

extracted from the gray matter of the brain, 6–8 per cent. from the white matter, and 11–18 per cent. from the cerebellum. In these extractions the cholesterol is in combination with the brain proteins. By the same processes 33–45 per cent. of the phospholipides are extracted from the gray matter, 27–33 per cent. from the white matter, and 36–45 per cent. from the cerebellum. About 50 per cent. of the phospholipides thus extracted are not in union with the proteins, or united in only a weak manner. The 0·25 per cent. aqueous solution of NaOH extracts the remainder of the cholesterol and phospholipides which are in combination with the brain tissue proteins. These are easily precipitated by HCl and again redissolved by NaOH without any change in their original complex-structure.

B. S. LEVINE (Chem. Abstr.)

The Thiamine Dehydrogenase Content of the Nervous System. Titaev, A. A. [*Biokhimiya*, **19**, 645 (1954).]

In the nervous system of invertebrates, thiamine dehydrogenase (TD) is more active than in the brain of vertebrates. (TD) is evenly distributed over all parts of the brain of the fish. In the brains of mammals, including man, (TD) is concentrated mostly in the posterior part of the hypothalamus; in vertebrates the highest concentration is found in the hypophysis. There is a gradual diminution of (TD) concentration in the brain of vertebrates from fishes to mammals, especially in the anterior part of the brain. It is completely absent in the cortex of the brain hemispheres at the higher stages of evolutionary development of vertebrates. In the embryo (TD) is found in approximately the same concentration in the hemispheres as in other parts of the brain. One of the reasons for the high activity of (TD) in the nervous system of invertebrates (and plants) is the presence of polyphenol oxidase, which hastens the (TD) reaction as a result of adrenaline oxidation. It is suggested that a close connection exists between the function of the (TD) system and the vegetative part of the nervous system.

B. S. LEVINE (Chem. Abstr.)

Influence of Bicarbonate Ions on the Glycolysis of Brain Suspensions. Keller, Herbert. [*Hoppe-Seyler's Z. physiol. Chem.*, **299**, 93 (1955).]

Under aerobic conditions HCO_3^- accelerated lactate formation and reversed its retardation by adenosinetriphosphate. Under anaerobic conditions the effect of HCO_3^- was smaller. The inhibitory action of creatine phosphate on lactate formation was augmented by HCO_3^-.

ERICH HEFTMANN (Chem. Abstr.)

The Ionic Permeability of Nerve Membranes. Keynes, R. D. [*Recent Develop. Cell Physiol., Proc. 7th Symposium Colston Research Soc. Univ. Bristol*, 43–9, (1954).]

A review of current concepts and the evidence therefore of the part played by ion movements in the conduction of the nerve impulse and the relation between nerve function and metabolism.

J. A. BAIN (Chem. Abstr.)

Beriberi Toxin. 1. *Matusda, Shin.* [*Vitamins (Japan)*, **5**, 207 (1952).]

When chicks were bred on diets deficient in thiamine, beriberi toxin appeared in the plasma, and by the injection of this plasma to chicks bred on the low-thiamine diets, these chicks contracted beriberi. It was assumed from the histological studies that this toxin was the abnormal metabolite produced in viscera owing to the beriberi disease.

HIROYASU FUKUBA (Chem. Abstr.)

Cortical and Cerebral Convulsions Caused by Bile and Bile Salts. Takeda, Tatsuo. [*J. Physiol. Soc., Japan*, **16**, 747 (1954).]

Bile of cow, dog, cat and toad produced cerebral clonic convulsions in rats. Among the bile salts, deoxycholate and warmed trihydroxycholate caused clonic convulsions, while 3-hydroxy-7-ketocholate induced clonic and tonic convulsions. Although choleic acid alone showed no effect, it could suddenly become active by addition of butyric acid.

ITIRO TYUMA (Chem. Abstr.)

Iodine Content of the Central Nervous System of Cats After Thyroidectomy. Tutaev, G. V., and Isichenko, N. A. [*Byull. Eksptl. Biol. i Med.*, **32**, *No.* 9, 38 (1954).]

Iodine content of the central nervous system was determined at various periods following operation. Control tests were run on normal animals and showed the distribution of (I) in the different areas of the brains in descending order: cortex, cerebellum, pons, and medulla oblongata; 5–7 days following the operation the (I) decreases in the following increasing order: cortex, cerebellum, pons, and medulla oblongata; 15–20 days later the level of (I) is unchanged in medulla oblongata, higher in cortex and pons, and lower in cerebellum; 30–50 days later the largest amount of (I) is found in pons and medulla oblongata, the least in cerebellum and cortex. After 60–120 days the largest amount is found in cortex. Thus the cortex, despite its depleted (I) content, retains its leading position among the four brain areas.

A. S. MIRKIN (Chem. Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Behavior of Some Phosphate Esters in Brains at the Start of Convulsions Induced by Fluorocitrate and Fluoroacetate. Dawson, R. M. C., and Peters, R. A. [*Biochim. et Biophys. Acta*, **76**, 254 (1955).]

Young rats were administered fluoroacetate (I) intraperitoneally or fluorocitrate intracerebrally and phosphate esters and citrate were determined in the brain, kidney and heart at the start of convulsions. Marked changes were not observed in the levels of 10 min.–labile P. Small, significant decreases were noted in the cerebral levels of phosphocreatine and labile nucleotide P in animals administered (I). Citrate levels increased. The experiments showed no evidence that convulsive discharge in (I) poisoning can be initiated by a lack of water-soluble energy-rich P esters in the brain but the possibility of localized depletion was not excluded.

MORTON PADER (Chem. Abstr.)

Importance of the Determination of Citric Acid of Cerebrospinal Fluid in Various Affections of the Nervous System in Children. Crisalli, Mary and Capra, Carlo. [*Minerva pediat.*, **6**, 424 (1954).]

In 12 normal children (8 months–11 years), the citric acid (I) content of the cerebrospinal fluid averaged 2 mg. per cent. (I) (for a total of 58 patients with acute, chronic and degenerative diseases of the nervous system) was very high in tuberculous meningitis, inversely proportional to the glucose content, high in serous meningitis and poliomyelitis, and higher the more evolutive the process in progressive degenerative encephalitis and in cases of tumor.

C. SCANDURA (Chem. Abstr.)

Behavior of the Glucose Contents of Blood and Cerebrospinal Fluid After Sugar Administration to Patients with Hydrocephalus. Gueli, U., et al. [*Riv. pediat. siciliana*, **8**, 1 (1953).]

In 6 of 8 children with hydrocephalus, the (basally lower) blood glucose curve (I) after the administration of 4 g. glucose/kg. body weight was like that of healthy controls; that of the (basally higher) cerebrospinal fluid glucose had a behavior opposite to (I) and was different from controls.

C. SCANDURA (Chem. Abstr.)

The Iodine Content of the Central Nervous System and Thyroid Gland of the Hypophysectomized Cats. Tutaev, G. V., and Isichenko, N. A. [*Byull. Eksptl. Biol. i Med.*, **38**, *No.* 10, 42 (1954).]

After hypophysectomy the (I) content of the brains of the animals which were operated on was 61·7 γ/100 g. while that of normal animals was 265·6. On the other hand, the (I) content of the thyroid gland increased as compared with that of normal animals. However, this increase is found only after a long period following the operation. The first few days it is decreased. Despite the eventual increase of the (I) content of the thyroid gland that of the brain remains low which emphasizes the very important role played by the hypophysis in the metabolism of (I) in the central nervous system.

A. S. MIRKIN (Chem. Abstr.)

Phospholipide Fractions in Multiple Sclerosis and Normal Serum. Bernsohn, Joseph and Namajuska, Izolina. [*Proc. Soc. Exptl. Biol. Med.*, **88**, 124 (1955).]

Determinations on normal serum for cephalin, lecithin and sphingomyelin by the methods described gave values of 9·4 per cent., 6·5 per cent. and 19·7 per cent., respectively, of the total phospholipides. In serums of multiple sclerosis patients the distribution was similar, although the total phospholipide content of the serum was a little below normal.

L. E. GILSON (Chem. Abstr.)

Carbohydrate Metabolism in Brain Disease. IV. Effect of hydrocortisone and corticotropin (ACTH) on the Metabolic Effects of Administered Glucose in Patients with Chronic Schizophrenic and Manic-depressive Psychoses. Henneman, Dorothy H. [*Arch. Internal Med.*, **95**, 241 (1955).]

The changes in the blood concentration of glucose and of lactic, pyruvic, citric, and α-ketoglutaric acids after the administration of glucose were studied in patients with chronic psychoses. The changes induced by the administration of corticotropin or hydrocortisone prior to the administration of glucose suggest that these hormones inhibit the metabolic pathways whereby pyruvate and lactate enter the tricarboxylic acid cycle and potentiate the pathways whereby citrate is utilized.

EDWARD J. VAN LOON (Chem. Abstr.)

Relation Between Age and Cholinesterase Activity in Several Rabbit Brain Areas. Aprison, M. H., and Himwich, H. E. [*Am. J. Physiol.*, **179**, 502 (1954).]

The cholinesterase (ChE) activities were determined in the frontal cortex, caudate nucleus, superior colliculus, and medulla oblongata of the growing rabbit brain. All (ChE) activities were low during gestation and rose to maximal values at different periods after birth. First the medulla oblongata increased to a maximum at 15 days and following an early rapid fall stabilized at an intermediate value. The superior colliculus was the next to attain a maximum at approximately 8–9 months after which there was a slow decrease during the rest of the time interval studied. The caudate nucleus and frontal cortex were the last to reach a maximum at approximately 18 months.

E. D. WALTER (Chem. Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Effect of Adrenocorticotropin on Some Aspects of Brain Metabolism and Electroencephalogram. Torda, Clara. [*Congr. intern. biochim., Résumés, communs.*, 2e *Congr., Paris*, 65 (1952).]

The data of 2 other papers are summarized and discussed. The increased electrical activity of the brain after administration of adrenocorticotropin is relatively independent of changes in blood circulation and in concentration of Na and K. It is probably due to increased NH_3 in the brain.

W. C. TOBIE (Chem. Abstr.)

Enzyme Concentrations in the Brain and Adjustive Behavior Patterns. Krech, David, et al. [*Science*, **120**, 994 (1954).]

Rats were grouped according to spatial or visual preference on the basis of their performance in a standardized insolvable maze. The animals were later killed, and tissue was taken from their visual (I), somesthetic (II), and motor areas (controls) and analyzed for their cholinesterase (ChE) content. It was found that ChE was 20 per cent. lower in (I) than in (II) ($P=0{\cdot}001$). The spatial group showed a significantly higher (ChE) content than the visual group. The visual group showed a progressive and statistically significant increase in ChE activity from (I) through (II) to the motor area.

J. D. TAYLOR (Chem. Abstr.)

Distribution of Substance P and Choline Acetylase in the Brain. Zetler, Gerhard and Schlosser, Lucie. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **224**, 159 (1955).]

Eleven areas in each of 10 brains from cattle were investigated for substance P and 22 different areas in 10 human brains. The highest concentration was found in the substantia nigra, the second highest in the ala cinerea. The presence of enteramine can erroneously cause a high reading for substance P. This was avoided by the use of the isolated guineapig ileum by Gaddum's method. Since in the investigation for choline acetylase in human brains autolytic processes interfere, the effect of autolysis was determined with rat brains as test substance. Autolysis caused in every instance a decrease in choline acetylase activity. The localization of choline acetylase was investigated in human and dog brains. Areas with high choline acetylase contained little substance P and *vice versa*. This is not caused by an inhibition of choline acetylase by substance P since there is no interference if both are mixed. Substance P occurs chiefly in areas with a small content of cholinergic neurons.

A. E. MEYER (Chem. Abstr.)

Effects of the So-called Emotional Stimulation of an Animal on the Functional State of the Thyroid Gland. Amiragova, M. G. [*Doklady Akad. Nauk. S.S.S.R.*, **99**, 325 (1954).]

Emotional stimulation of experimental animals (dogs) leads to repression of the ability of the thyroid to accept iodine from the surrounding medium; this state of the thyroid becomes normal after 4 hours following the stimulation. Cats gave a similar response. Emotional stimulation increases the secretion of thyroid products into the blood. The determinations were made by detection of radioiodine, I^{131}, which was introduced per os or intraperitoneally. The emotional stimulation was produced by teasing a cat with a dog and *vice versa*.

G. M. KOSOLAPOFF (Chem. Abstr.)

Inositol in Brain Metabolism. Kerken, H., and Maibauer, D. [*Klin. Wochschr.*, **32**, 1113 (1954).]

The inositol (I) content of brain, sympathetic ganglia, liver, pancreas, thyroid, adrenal, and kidney were determined microbiologically. The (I) content of cerebrospinal fluid is 3 times as high as that of serum, and brain tissue has an active (I) metabolism.

E. HEFTMANN (Chem. Abstr.)

Influence of the Hypothalamus on the Blood Lipides. Inoue, K., et al. [*Med. J. Osaka Univ.*, **5**, 475 (1954).]

When the ventromedial hypothalamic nucleus of the rabbit was stimulated electrically, the total cholesterol of rabbit serum decreased 6–28 per cent. at about 60 minutes, and the lipide P and total lipide decreased in about half of the animals. When the lateral nucleus was stimulated, these values were unchanged or increased. 42 references.

A. DIETZ (Chem. Abstr.)

Inhibitory Effect of Malonate on the Respiration of Brain Tissue with Special Reference to the Potassium Effect. Kimura, Y., and Niwa, T. [*Nature*, **171**, 881 (1953).]

Guinea pig brain cortex slices respiring in Krebs-Ringer-phosphate solution in the presence of $0{\cdot}1$ M KCl are acutely susceptible to malonate (10^{-3}M) as contrasted with normal respiration which is quite resistant to malonate. The possibility is suggested that in KCl-saline solution, either the Krebs cycle is the main pathway of brain tissue respiration or the Krebs cycle, which is masked in some way or other under normal conditions, is opened up and brought into operation by the addition of excess K.

J. D. T. (Chem. Abstr.)

Integration of the Bioelectric Activity of the Brain in Relation to Compensating Oscillograms in Man. Schminke, G. A. [*Byull. Eksptl. Biol. i Med.*, **38**, *No.* 11, 71 (1954).]

B. S. L. (Chem. Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

2. Pharmacology and Treatment

Laboratory and Clinical Observations on Chlorpromazine (SKF-2601-A)—Hemodynamic and Toxicological Studies. Moyer, J. H., et al. [*Am. J. Med. Sci.*, **227**, 283 (1954).]

In laboratory studies on dogs, chlorpromazine (I) was a hypotensive agent decreasing peripheral resistance with a variable effect on cardiac output, and no evidence of acute renal toxicity or renal hemodynamic alterations. When injected into dogs it appeared to increase Na and water excretion. In clinical studies, the only suggestive evidence of toxicity consisted of alterations of the electrocardiograms of 2 seriously ill patients. The more intensive response to (I) that was noticed in patients with hepatic disease suggests that biotransformation of (I) may occur in the liver.

MARION HORN PESKIN (Chem. Abstr.)

Action of Camphor on the Synapses in the Motor and Autonomic System. Rohr, H. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **224**, 327 (1955).]

Experiments on frogs and mammals showed that the paralytic effect of camphor is not based on a curare-like action at the neuromuscular synapses. Experiments with the isolated perfused frog heart with stimulation of the vagal area showed on application of camphor, of the antagonistic system camphor-dihydroergotamine, and of camphor-prostigmine that the inhibition of the vagus by camphor is only an apparent vagus paralysis. Concentrations of camphor, efficacious on the frog heart, cause in dogs, cats, and rabbits convulsions. Lower doses influence the vagus stimulation only if afferent vagus condition is preserved.

A. E. MEYER (Chem. Abstr.)

The Blood Brain Barrier—the Effect of Acidic Dissociation Constant on the Permeation of Certain Sulfonamides into the Brain. Goldsworthy, Patrick D., et al. [*J. Cellular Comp. Physiol.*, **44**, 519 (1954).]

In mature, male rats, 1 hour after intraperitoneal injection, those sulfonamides with pK_a values below 8 gave a brain to blood concentration ratio of approximately 0·1. The ratios increased to 0·36–1·0 through the range of pK_a 8 to 10·5 and then decreased as pK_a increased. There was no correlation between molecule weight or lipide solubility of the sulfonamides and their distribution.

H. L. MASON (Chem. Abstr.)

Factors Involved in Drug-produced Model Psychoses. Fisher, R. [*Experientia*, **10**, 435 (1954) (in English).]

There is a close inverse correlation between the single dose required to produce psychoses and the affinity for wool for mescaline-HCl, Methedrine-HCl, methanol tartrate of lysergic acid monoethylamide, and methanol tartrate of lysergic acid diethylamide.

D. S. FARNER (Chem. Abstr.)

Changes of Behavior and Electroencephalogram in Rhesus Monkeys Caused by Chlorpromazine. Das, N. N., et al. [*Arch. intern, pharmacodynamie*, **99**, 451 (1954).]

Chlorpromazine injected into monkeys produced striking behavior changes, so that fierce animals became somnolent and showed almost complete akinesia. The electroencephalograms were characterized by high voltage, slow electric activity over the whole cortex. Probably the drug suppresses the action of the awakening "upward discharge" of the ascending reticular formation.

M. L. C. BERNHEIM (Chem. Abstr.)

Pharmacological Properties and Application of the New Drug Pachycarpin. Mashkovskii, M. D., and Kryshova, N. A. [*Sovet. Med.*, 1953, *No.* 2, 36–8; *Referat. Zhur. Khim.*, 1954, *No.* 20290.]

Pachycarpin (I) inhibits conduction transfer of nervous stimulation through the vegetative ganglia, stimulates contraction of the uterus, intensifies protective-inhibitory processes in the cerebral cortex, and possesses low toxicity. (I) is also effective in some cases of arterial and muscular disorders as well as in sympathetic ganglion disorders. Limits of the medical application of (I) are indicated.

E. WIERBICKI (Chem. Abstr.)

Chlorpromazine as a Therapeutic Agent in Clinical Medicine. Moyer, John, et al. [*Arch. Internal Med.*, **95**, 202 (1955).]

Chlorpromazine is an effective inhibitor of psychomotor excitement and agitation and appears to have some anticonvulsant activity. It is also an effective anti-emetic agent.

EDWARD J. VAN LOON (Chem. Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press

Effect of Chlorpromazine on the Electric Activity of the Cerveau Isolé. Das, N. N., et al. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **224**, 248 (1955).]

Mesencephalic transection (cerveau isolé) of the brain stem was carried out in cats at the collicular level and the electric waves were taken from the surface of the frontal and occipital lobes of the cortex. Doses of 0·2–0·5 mg./kg. chlorpromazine caused marked changes in the electrocorticogram of the thalamo-cortical system. The spindles and slow waves, characteristic for the preparation disappeared a few minutes after the injection. In some experiments there appeared temporarily spikes and waves.

A. E. MEYER (Chem. Abstr.)

Treatment of Epilepsy with Cation Exchangers. Mertens, H. G., et al. [*Klin. Wochschr.*, **33**, 35 (1955).]

Withdrawal of Na by feeding of cation-exchange resins has favorable clinical results n epilepsy.

ERICH HEFTMANN (Chem. Abstr.)

Applicability of Dormiphen for Sleep Therapy from the Pharmacological Point of View. Sobek, Vojtech. [*Casopis Lekaru Ceskych*, **93**, 532 (1954).]

Among the narcotics studied, Amytal Na (I) and Dormiphen (cyclohexenyl-ethylbarbituric acid) (II) were more toxic than Bromisoval (III) and Evipan (IV) in mice (LD_{50} 0·27 for (I) and 0·32 g./kg. for (II)). Chronic toxicity tests showed no significant differences. The hypnotic activity of (III) and (IV) is less than that of (I) and (II). There was no remarkable difference between (I) and (II) as far as the influence on blood pressure, body temperature, and glycemic curve was concerned. The activity of (II) decreased during long-term administration. (II) can be substituted by (I) for the purposes of sleep therapy, (II) can be used as an adjuvant.

IVO M. HAIS (Chem. Abstr.)

https://doi.org/10.1192/bjp.102.426.181 Published online by Cambridge University Press