Bibliography and Epitome*

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

Insulin Coma Therapy in Schizophrenia

1. Insulin coma therapy at the Pennsylvania Hospital produced an immediate improvement or remission in 67·7 per cent. of 780 patients treated between 1936 and 1951.

2. At least 334 patients, or 63·3 per cent. of all patients who originally improved, had a relapse; 44 per cent. of all these relapses occurred within 30 days, and 78 per cent. within one year of treatment. A second insulin course brought about an improvement or remission in 52 per cent. of 122 patients who had relapsed.

3. Factors associated with the most favorable prognosis include: age over 16, psychosis of less than 6 months' duration, with a clinical picture of paranoid, catatonic, or undifferentiated schizophrenia; and if during treatment the patient receives at least 30 to 60 coma hours and gains more than 30 pounds in weight.

4. They conclude that insulin coma therapy is effective in restoring the schizophrenic patient to his prepsychotic adjustment. This restoration to health is not accompanied by a permanent correction of the factors that predispose the patient to regress to schizophrenia.

(Authors' Abstr.)

The EEG Changes in Unilateral and Bilateral Frontal Lobotomy

1. In cases of unilateral and bilateral frontal lobotomy, temporal slow wave activity was found to be a prominent feature, though more transient than the dominant frontal slowing. This non-frontal slowing may be interpreted as the result of cerebral edema and hippocampal herniation from operative manipulation.

2. There is an apparent correlation between the degree of slow activity in the postoperative EEG and clinical improvement, in that slight or severe degrees of slowing was found to be more conspicuous in those cases that exhibited little clinical improvement. In contrast, moderate slowing was associated with moderate to marked clinical improvement.

3. The frontal slow wave activity, though decreasing in prominence, persists in the majority of cases for at least 3 years and possibly longer.

(Authors' Abstr.)

The Effect of Adrenochrome and Niacin on the Electroencephalogram of Epileptics

1. Adrenochrome in dosages of 10 mgms. does not change the EEG of normal volunteers, but in 10, 25, and 50 mgm. doses increases the bilateral paroxysmal abnormalities in the EEG of epileptics, but has very little effect on the cortical focus itself.

2. Nicotinic acid given orally or intravenously in normal volunteers showed a slight shift in EEG frequency to the fast side; in epileptics the drug considerably decreases the bilateral diffuse paroxysmal abnormalities (except in true idiopathic epilepsy), but has very little influence on the focus itself.

3. The mode of action of the above-named drugs is discussed.

4. A tentative explanation is offered as to the genesis of the paroxysmal EEG disturbance in schizophrenia.

(Authors' Abstr.)

MARCH

APRIL

The Limbic System ("*Visceral Brain*") *and Emotional Behavior*

Experimentation of the last 15 years suggests that the limbic system, which anatomically is a common denominator in the brains of all mammals, is also, physiologically speaking, a common denominator of a variety of viscerosomatic and emotional reactions. In this paper, especial attention is given to the recent developments pertaining to the part of the limbic

system contained in the hippocampal formation. Bioelectrical studies are cited that provide further evidence that this part of the brain is afferently related to all the sensory systems. From these and other experiments concerned with ablation and stimulation, inferences are derived that give additional support to the theory that this region of the brain is concerned with the experience and elaboration of emotion.

(Author's Abstr.)

Amino Acids of the Cerebrospinal Fluid

The procedure for the identification and quantitative estimation of the free amino acids of the cerebrospinal fluid, using ascending two-dimensional paper chromatography, is given in detail.

Average losses during the procedure have been determined.

Spinal fluids from 26 surgical patients with no evidence of neurological disease have been analyzed by this procedure and compared with fluids from 12 well-authenticated cases of multiple sclerosis.

No significant quantitative difference, or any consistent qualitative difference, characterizes the amino acid pattern of the multiple sclerosis group.

Proline and methionine were identified in a small percentage of the fluids studied which contained red cells, but in no other fluids.

(Authors' Abstr.)

Studies on Headache

Eight persons subject to vascular headache of the migraine type had technically satisfactory studies made before, during, and after 26 headache attacks, with the following results:

1. Decreased rates of excretion of water, sodium, potassium, and creatinine were usually observed prior to and during the early phases of vascular headache of the migraine type.
2. Increased rates of excretion of water, sodium, and potassium were usual with subsidence of the headache attacks.
3. Creatinine excretion returned to "normal" values during subsidence of headache, with four exceptions. On these four occasions potassium excretion was high.
4. Weight gain prior to the headache attack was common but not invariable. It sometimes occurred well in advance (7 to 10 days) of the onset of headache.
5. Weight loss with subsidence of headache was usual. However it was sometimes delayed 24 to 48 hours.

It is concluded that the described fluid, electrolyte, and renal changes are not causally or mechanistically related to the onset, intensity, or duration of the migraine attack. Instead, they are manifestations of the widespread bodily changes accompanying adaptive reactions during and after stressful periods. The migraine attack is a concurrent, but independent, feature.

(Authors' Abstr.)

MARCH

Blood Platelets in Disseminated Sclerosis

In disseminated sclerosis the permanent changes are localized along the blood vessels, being associated with venules and veins. Histological examination of fresh foci do not reveal serious thrombotic changes, but often clots of blood platelets are seen in the central veins. In the present work the blood platelets in the circulating blood were examined with a view to variations in their number. The blood analyses were as far as possible extended over a fairly long period, as a rule up to one month, and in a single case six months. The values obtained were compared with corresponding values from a control and a normal series. In "stationary" disseminated sclerosis the authors found moderate fluctuations of the blood platelet number, somewhat greater than in the normal and the control series. During clinical activity there was a tendency to a low level, followed by a rise during improvement. The fluctuations proved to be considerably greater in patients with acute disseminated sclerosis than in patients with the stationary form or in normals, or in patients with other neurological disorders.

In principle, the curves run a similar course during infectious diseases and after tissue destruction, operations, etc. An increased tendency to agglutination is possibly also reflected in the blood platelet system.

The counts showed, furthermore, that in normals the variations in blood platelet number are much greater from subject to subject than from day to day in one subject.

Though the series under review does not allow of a simple comparison between the individual variations of the thrombocyte counts in patients with active and in patients with inactive disseminated sclerosis, the tendency toward a greater variability in the active group is so conspicuous that this question merits more thorough investigation.

(Authors' Abstr.)

Visual and Motor Instability in Multiple Sclerosis

In a fairly large group of patients with multiple sclerosis subjected to a standardized stress, the majority, or about 75 per cent., showed aggravation of symptoms, in some cases even considerable. The exacerbation occurred within 10 to 15 minutes. After the experiment was stopped, most patients returned to the status quo within 15 to 20 minutes, while others required a somewhat longer readjustment.

The symptoms apparently comprise the entire nervous system, including the visual function. Certain findings indicate that the visual impairment at least is not merely a nervous phenomenon, but that far more peripheral tissue changes may contribute. It is possible, but not yet proved, that peripheral changes also play a role in eliciting the other symptoms. Such a peripheral factor cannot be ruled out primarily in the frequently marked adynamia, which sometimes may be accentuated to total paralysis and may be characterized by features reminding one of myasthenia, e.g. ptosis, bulbar symptoms, hypotonia, and loss of tendon reflexes. Since, however, other signs were unmistakably of "central" origin—appearance of the Babinski toe sign and spontaneous nystagmus—it must be presumed that the clinical phenomena represent a widespread action upon the entire organism.

Heating of the nature described is a "stress" on the multiple sclerosis organism. It is well known that many multiple sclerosis patients have observed such exacerbations upon varied forms of stress, not the least by heating. The patients often report this spontaneously. These spontaneous statements were the very reason why the authors decided to investigate this aspect. Infectious diseases also aggravate the condition of sclerosis patients. Perhaps fever is the most important factor other than phenomena of more complicated nature, such as allergization.

In the experiments, unlike natural stress of spontaneous occurrence, the stress could be regulated and interrupted. Therefore, it has exerted its action within an extremely limited period.

As is well known, the physiological reaction to stress is a complicated one. Many factors are involved. As regards heating, they know that heating is the immediate cause of vascular dilation in the skin and in the central nervous system. The latter effect is known from a large number of animal experiments. Recently, Engel demonstrated such vascular dilatation also in the nervous system of man. This is, of course, of particular interest in connection with the present investigation, because various workers have shown that the pathological changes in multiple sclerosis are of perivenous localization. From the pathoanatomical point of view, multiple sclerosis is a kind of periphlebitis in which large plaques are formed by the confluence of numerous, small periphlebitic zones. It has been shown also that in fresh zones the dilated vessels are surrounded by edema. Marius Haarr (1951) has observed edema in the walls of the retinal vessels in multiple sclerosis.

The possibility of any development of edema in the parenchyma of the central nervous system must, however, be ruled out in the present experiments, considering that the symptoms subside in about 20 minutes. At any rate, such edema would have to be limited to the interstitial tissue. At the present time, it seems most reasonable to assume that an alteration takes place in the ion distribution in the membranes of the nervous system, of the eye and possibly of the neuromuscular apparatus, with a corresponding alteration in the membrane potentials.

The preliminary result of the present investigation is the finding that a certain proportion of patients with multiple sclerosis exhibit intermittent visual impairment which does not seem to be related to alterations in the optic nerve function. This impairment is elicited particularly by physical exertion or heat and may be induced or reproduced by exposing the patients to a certain degree of heating. Patients with multiple sclerosis present an abnormally high incidence of myopia, differing significantly from that in a Danish normal series. Lastly, fluctuations in the visual acuity are far commoner in myopic than in emmetropic or hypermetropic subjects.

(Authors' Abstr.)

Intravenous Hydrocortisone, Corticotropin and the Electroencephalogram

The intravenous administration of both corticotropin and hydrocortisone may induce an increase in theta activity (5 to 7 c/sec.) in the electroencephalogram, although hydrocortisone would seem to exert this effect more consistently and to a greater degree than does corticotropin.

The effect was somewhat greater in epileptic subjects with previously abnormal electroencephalograms. In two instances hydrocortisone produced an increased incidence of 2 to 3 c/sec. spike-wave seizure discharges.

Hydrocortisone produced essentially no change in serum sodium or chloride concentrations but did cause a significant elevation in serum potassium in five of the seven subjects studied. The electroencephalographic changes in these subjects could not be correlated with this electrolyte shift.

Corticotropin induced changes in the electroencephalogram in a patient with a functionally inactive adrenal cortex, suggesting that it may have a direct effect upon cerebral electrical activity.

(Authors' Abstr.)

Clinical Experience with Meratran

1. The pharmacology of a new central nervous system stimulant, Meratran, is reviewed briefly.

2. The therapeutic indications of this compound are roughly similar to those of the amphetamines.

3. It has benefited the group of narcoleptic patients studied.

4. The drug continues to prove of value in reactive depressions.

5. In institutionalized patients its use is advised in non-deluded schizophrenics having restriction of interest and depressive features, in long-term schizophrenics with deterioration, and in cases of psychomotor retardation with blocking of communication. In patients with active delusions, anxiety, and agitated behavior it is contraindicated.

6. In geriatric practice the depressed but otherwise organically fit older patient who cannot be inspired to continue normal activities can be helped by small doses of the drug.

7. Numerous other clinical conditions, ranging from drug-induced lethargy caused by anticonvulsants, antihistamines, chlorpromazine, rauwolfia compounds, etc., to "afternoon letdown", alcoholic hangover, the fatigue and depression encountered in diabetes, parkinsonism, and hepatitis, etc. have been benefited by the employment of small doses of Meratran, according to various investigators.

8. Selected cases of blepharospasm and spasmodic torticollis have been helped by this drug. Other patients of this type cannot tolerate the drug in therapeutically effective doses. The effect of Meratran in stammerers is being studied.

9. 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.

10. When anxiety or agitation comprise a sizable proportion of the clinical picture the drug should be used warily and with caution.

11. Effective dosage ranges (except in narcolepsy and motor tics) vary between 2·0 and 25·0 mg. daily.

12. The drug appears to be a true central nervous stimulant without effect on the autonomic nervous system, and therefore is not a member of the sympathomimetic group of compounds. Experimental evidence at this time points to the reticular formation of the upper brain stem and/or the septal area as the primary site of action of the drug.

13. Initial observations on other compounds closely related to Meratran chemically indicate that they may open up new avenues of investigation in the field of neuropharmacology.

(Author's Abstr.)

MARCH

VOL. 7 EEG CLIN. NEUROPHYSIOL. 1955

Electroencephalograms During Cycles of Addiction to Barbiturates in Man

1. The clinical and electroencephalographic changes which occur during chronic secobarbital intoxication and after abrupt withdrawal of this drug were studied experimentally in two groups of former narcotic addicts without previous histories of epilepsy or psychosis: group I, consisting of 14 individuals receiving 0·9 to 2·6 g. daily in divided doses for 33–89 days, and group II, including 21 individuals receiving 0·6 to 0·8 g. of the same drug for 38–58 days.

2. During the period of chronic intoxication, the subjects in group I displayed varying degrees of ataxia, dysarthria and other changes resembling those of cerebellar dysfunction, as well as marked changes in affect, sensorium and judgment. Concomitantly, electroencephalograms were characterized by mixed rhythmic fast and slow abnormalities, mainly in frontal and parietal tracings. Tolerance developed to the clinical effects of barbiturates, but not to the electroencephalographic effects. After abrupt withdrawal of barbiturates, varying degrees of anxiety, tremulousness, postural faintness, anorexia, insomnia, and weight loss developed in almost all the subjects. In addition, 79 per cent. exhibited 1–4 generalized convulsions on the second or third day of abstinence, and 65 per cent. displayed psychoses, generally in the form of agitated delirium, between the 4th and 7th day of abstinence. Concomitantly, marked changes appeared in the majority of electroencephalograms, generally in the direction of periodic hypersynchronization, and with the frequent appearance of mixed spike and slow wave or 4 c/sec. "spike-and-dome" paroxysmal discharges. After the 8th day, clinical recovery proceeded uneventfully, and electroencephalograms assumed a normal pattern in the majority of cases, with only mild abnormalities in the remainder.

3. During the period of chronic intoxication, the subjects in group II displayed mild or no evidence of ataxia, etc. Concomitantly electroencephalograms were characterized by predominance of rhythmic fast activity in the frontal and parietal tracings. After abrupt withdrawal of barbiturates, abstinence phenomena were similar to but much milder than those observed in group I. Only 2 subjects exhibited seizures, and none developed psychosis. In general, concomitant alterations in the electroencephalograms were similar to but milder than those in group I, with two striking exceptions. In these, paroxysmal discharges were more common than in any record obtained in group I. Clinical recovery proceeded uneventfully, while electroencephalograms assumed normal patterns in about half of the group, with mild random abnormalities in the remainder.

4. No one-to-one correlations could be demonstrated between any given clinical state and any given electroencephalographic pattern. However, the occurrence of clinical seizures was most commonly associated with random spike, diffusely slow or paroxysmal activity in electroencephalograms, and slow abnormalities of various sorts predominated during periods of psychosis.

5. The electroencephalographic changes occurring during cycles of addiction to barbiturates are discussed with reference to possible neurophysiological mechanisms.

(Authors' Abstr.)

Studies of the Electroencephalogram of Normal Children: Comparison of Visual and Automatic Frequency Analyses

Electroencephalograms of 71 normal children in one-year age groups ranging from 1 to 10 years inclusive were recorded. In all instances right and left parieto-occipital recordings were subjected to frequency analysis by means of the Ediswan Walter analyser. The results of the analysis, presented in the form of a scattergram for each one-year age group, show (1) relative constancy (under basic conditions) of frequency analysis of one area and similarity of homologous areas; (2) great variability of analysis within single age groups; this has been illustrated by electroencephalograms representative of relatively mature (fast) and immature (slow) patterns in each age group; and (3) evidence of individuality of delta (1 to 3 c/sec.), theta (4 to 7 c/sec.) and alpha (8 to 12 c/sec.) which undergo complex changes with development.

Four subjects (5·6 per cent.) had grossly abnormal tracings. While 3 of these subjects had focal sharp-wave discharges, the fourth had a diffuse abnormality. Of the 3 subjects with focal sharp waves in their electroencephalograms, 2 had normal records 18 months later. It is concluded that sharp-wave foci in children may have a less serious prognostic significance than in adults.

The relative merits of visual and automatic analysis are discussed together with suggestions for the practical application of automatic analysis in pediatric electroencephalography. It is suggested that combination of the automatic-analyser tracing and the 8 traces of the standard recording may result in reaching or even exceeding the threshold of data saturation of the observer. Such a situation may require compromises aimed at simplifying the final presentation.

(Authors' Abstr.)

The Use of Frequency Analysis in the Interpretation of the EEGs of Patients with Psychological Disorders

1. A method of using frequency analysis of the rates of EEG wave forms has been described which appears to produce consistent and useful results.

2. This method, used in conjunction with EEG interpretation and with psychological data has demonstrated positive correlations between EEG pattern and psychological factors which appear to confirm and to establish more firmly the observations of previous authors. They are of clinical diagnostic use.

3. In the present study a comparison was made among three groups: patients in a mental hospital; inmates of a prison farm; and control "normals". EEG data and frequency analysis showed significant differences in the three groups.

4. These differences showed a more exact correlation with psychological criteria produced by the various tests given. In particular, anxiety and aggression were each factors related to specific EEG patterns.

(Authors' Abstr.)

Metrazol and Combined Photic-Metrazol Activated Electroencephalography in Epileptic, Schizophrenic, Psychoneurotic and Psychopathic Patients

1. Photic, Metrazol, and combined photic-Metrazol activation was carried out in 47 epileptic, 20 psychoneurotic, 30 psychopathic, and 53 schizophrenic patients.

2. Combined photic-Metrazol activation was found to be a valuable and easily controlled method for the demonstration of low myoclonic thresholds in 84 per cent. of patients with idiopathic epilepsy, and in 53 per cent. of schizophrenics. A low threshold was obtained in only 2 per cent. of patients with psychoneurosis and character disorder.

3. The pattern of EEG response is different in epileptic and non-epileptic patients.

4. Combined photic-Metrazol activation has definite diagnostic value as an aid in the evaluation of patients with suspected epilepsy.

5. Electro-shock treatment has the immediate effect of raising the myoclonic threshold in schizophrenic patients, but the effect is a temporary one.

(Authors' Abstr.)

Studies in the Processes of Aging: Electroencephalographic Findings in 400 Elderly Subjects

1. Electroencephalograms were obtained on 400 subjects over the age of 60 as part of a project dealing with aging of the central nervous system.

2. One hundred senile patients, without evidence of gross focal neurological disease revealed that 22 per cent. had normal records with a preponderance of diffuse and mixed abnormalities.

3. In 145 volunteers from the community without neurological disease, a high percentage of focal disturbances were found, and a gradient of decreasing EEG abnormality of all types was noted with higher socio-economic levels. Focal disturbances alone did not seem to cause psychological impairment.

4. Psychological test data correlate diffuse and mixed EEG abnormalities with the greatest degree of psychological deterioration.

5. Forty-five psychiatric patients with no evidence of brain damage revealed patterns of electroencephalographic abnormalities similar to the community group of volunteers, 60 per cent. of their records being normal. Diffuse fast wave disturbances were relatively more frequent among the abnormalities seen.

6. Ninety-four neurological cases showed the expected low incidence in normal records and a heavy preponderance of focal disturbances.

7. A gradient of decreasing normal records was noted in progressively older decades. Diffuse dysrhythmias which followed this trend were due to slow wave disturbances. The incidence of focal records did not appear to change in succeeding decades, but a definite increase in the proportion of severe foci was noted in progressively older decades.

8. Diffuse fast wave disturbances were not frequent, and showed a tendency to decrease in older patients, as did the proportion of severe fast disturbances. No fast wave abnormalities were seen in patients over the age of 79.

9. The high incidence of foci in this series could not alone be correlated with psychological test evidence of deterioration. When foci were associated with diffuse abnormalities, however, organic deterioration was definitely noted. Primarily left temporal foci were often clinically silent. The suggestion was made that hippocampal degenerations or beginning generalized vascular disease might be the cause.

10. It was suggested that temporal foci could be more easily elicited using the vertex as a reference electrode, as well as keeping the ears "untied" and ungrounded. Also important was the use of the low-lying anterior temporal lead.

(Authors' Abstr.)

VOL. 101 J. COMP. NEUR. DECEMBER, 1955

Neurosecretory Pathways Between the Hypothalamic Paraventricular Nucleus and the Neurohypophysis

A description is given of the neurosecretory pathways between the hypothalamic paraventricular nucleus and the neurohypophysis in dogs, as observed in serial sections stained following the chrome-alum-hematoxylin phloxine procedure.

The area traversed by the principal mass of neurosecretory fibers corresponds to that occupied by Greving's tractus paraventricularis cinereus.

Two additional neurosecretory pathways are described which are parts of the paraventriculo-hypophysial system. Both originate in the caudodorsal tip of the paraventricular nucleus.

One of these accessory bundles extends into the lateral hypothalamic area where it is found in relation to scattered nerve cells exhibiting neurosecretory phenomena. The bundle turns medialward, dorsal to the supraoptic nucleus, and joins the supraoptic-hypophysial tract.

The other bundle provides the shortest and most medial, direct, connection between the paraventricular nucleus and the neurohypophysis. After looping over the fornix, first dorsal then lateral, it crosses the substantia grisea centralis diagonally and enters the infundibular separate from and caudal to the supraoptic-hypophysial tract.

Search for evidence of termination of the fibers among the cells of the supraoptic nucleus was unsuccessful. It is concluded, therefore, that the fibers arising from the paraventricular nucleus and associated with neurosecretory material for the most part establish a direct connection of the paraventricular nucleus with the neurohypophysis.

(Author's Abstr.)

The Anatomy of the Primate Brachium Conjunctivum and Associated Structures

1. The brachium conjunctivum is composed of three limbs—the well-known crossed ascending limb, the less well-known descending limb (crossed) and the hithertofore unknown uncrossed ascending limb.

2. No myelinated uncrossed descending limb exists.

3. The first and third of these three limbs are distributed to the ventrolateral part of the thalamus and globus pallidus of their respective sides. The pallidal contribution, although previously postulated, is hardly known to most students of the cerebellum.

4. The crossed ascending limb traverses the region of the red nucleus.

5. The uncrossed does not but it does enter the arcuate nucleus which it probably penetrates to end in the ventrolateral part of the thalamus.

6. The brachium conjunctivum sends no myelinated fibers to the subthalamic nucleus and there does not appear to be any notable contribution to the substantia nigra.

7. Fibers travelling with the crossed ascending limb do, however, arise from the red nucleus and pass to the subthalamic nucleus.

8. The descending limb sends fibers to the superior central, reticulo-tegmental and magnocellular reticular nuclei of the pontine region, enters the cervical spinal cord and may send some fibers to the opposite side of this.

9. The descending limb contributes to the medial longitudinal fasciculus.

10. The brachium conjunctivum may also, according to another supplementary plan, be divided into three components: dorsal, intermediate and ventral.

11. The uncrossed ascending limb arises more particularly from the dorsal component and the descending limb from the dorsal and intermediate components.

12. While all components probably contribute to the crossed ascending limb those elements arising from the dorsal and intermediate components send relatively more fibers to the thalamus than to the globus pallidus whereas the reverse situation is true for those elements arising from the ventral component.

13. The contribution of the dorsal component to the crossed ascending limb traverses, most particularly, the dorsolateral part of the area of the red nucleus, the ventral traverses the ventromedial area and the intermediate component the central area.

14. The arrangements and relations of the limbs and components of the brachium conjunctivum have been described in the text and a plan has been presented for the purpose of enabling the investigator to determine what parts of the brachium will be rendered nonfunctional as the result of a lesion in any part of it.

15. The mammillary peduncle arises from the deep tegmental nucleus of Gudden, ascends between the interpeduncular nucleus and substantia nigra and enters the lateral mammillary nucleus.

16. No specific, independent ascending mammillo-penduncular tract appears to exist apart from the mammillary peduncle.

17. The pallido-interpeduncular system appears to be a pallido-nigric system in large part.

18. The dorsal supraoptic decussation arises from, or in close proximity to, the medial longitudinal fasciculus.

19. The ventral supraoptic decussation arises from the dorsomedial portion of the mesencephalic tegmentum.

20. The reader's attention is called to the fact that the correlation between the anatomic material and the physiologic circumstances which transpired is reported in Carrea and Mettler (1955). (Author's Abstr.)

Observations on the Intracortical Relations of the Climbing Fibers of the Cerebellum

The climbing fiber has been found to possess more extensive synaptic relations in the cerebellar cortex than previously believed.

1. At the level of the Purkinje cell bodies recurrent collaterals are seen to disappear into the neuropil plexus of the granule cell layer. The synaptic relations of this collateral are not known.

2. Some collaterals are observed to make contacts with adjacent Purkinje cell bodies or their primary and secondary dendrites.

3. Collaterals and terminals have been traced to stellate and basket cell somata and dendrites where they appear to make synaptic contacts via boutons-en-passage or end feet.

4. Ascending and descending collaterals of the axons of stellate cells and basket cells are observed to effect axon to axon contacts with the climbing fibers. Such contacts are effected by typical end feet, boutons-en-passage, or through complex inter-twining of the elements.

6. The climbing fiber has also been observed to establish contact by means of its collaterals with the dendrites of large short-axoned stellate cells of the granule layer and with parallel fibers.

7. The stellate and basket cells of the molecular layer appear to establish synaptic contact with each other forming neuronal chains of varying lengths. Recurrent axonal collaterals have been traced back to the cell of origin. Collaterals of stellate cell axons are also seen to terminate by end boutons or ring forms on Purkinje dendrites.

8. It is suggested that a series of feed backs from various stages of the intracortical pathways, i.e. recurrent collaterals of the climbing fiber, of the Purkinje cell axon, and the axon of the large stellate cells of the granule layer form a plexus which may regulate the threshold of this receptive layer.

9. On the basis of the fine structure of the climbing fiber and the synaptic relations which they have just reported, it appears that this fiber activates a group of neuronal chains of varying lengths. Most of these chains seem to form closed loops with collaterals so arranged that activation of efferent units may occur simultaneously with reactivation of the chain. Maximum activation of stellate chains probably occurs in the immediate vicinity of the climbing fiber.

10. Available neurohistological and neurophysiological data suggest that the climbing fiber and the elements it activates may be responsible at least in part for the phenomenon of cerebellar localization. The hypothetical nature of this suggestion and the need for electrophysiological elucidation are stressed. (Author's Abstr.)

VOL. 52 J. GEN. PSYCHOL. JANUARY, 1955

pH of Cerebral Cortex during Induced Convulsions

1. The pH of the cerebral cortex was measured with membranes and capillary glass electrodes, and correlated with changes in cortical electrical activity induced by asphyxia, CO_2, Metrazol and nitrogen mustard.

2. During Metrazol seizures, cortical pH declined from approximately 7·3 to 7·0, and was neither preceded nor followed by an alkaline shift.

3. Acute asphyxia caused a fall of pH from 7·3 to 7·1. Hyperventilation produced a rise from 7·3 to 7·45.

4. Inhalation of 30 per cent. CO_2—70 per cent. O_2 during Metrazol seizure caused a fall of pH to 6·4 Metrazol discharge disappeared at pH 6·9 and reappeared at 6·7 when CO_2 inhalation was discontinued.

5. Nitrogen mustard seizure activity did not appear until after the cortex had been made acid (pH 6·6) by CO_2 inhalation, and the CO_2 then discontinued.

6. The implications of these findings are briefly discussed. (Authors' Abstr.)

Effect of Bilateral Ablation of Cingulate Area on Behaviour of Cats

1. In cats, bilateral ablation of the cingulate area in the frontal lobe produces a syndrome characterized by confused, perseverative, obsessive behaviour, and a plastic tendency whereby the animal may be posed for long periods of time in bizarre positions.

2. There is also evidence of change in emotional status such that rage reactions are more easily elicited.

3. This syndrome does not appear following removal of any other cerebral cortical area but it is intensified and prolonged by the additional removal of the frontal poles or of additional tissue from the mesial surface of the frontal poles.

4. Bilateral ablation of the motor areas, although it abolishes placing and hopping responses and results in consequent postural disability, does not produce the confusional and plastic condition which follows bilateral ablation of the cingulate areas.

5. The syndrome which follows bilateral cingulate ablation is similar to that described by Barris in 1937.

6. This syndrome has also some of the elements of postural confusion and of apraxia described in man following similar lesions. It is suggested that the hypomotility and inertia described by others in man and monkey as related to cingulate ablation may be the result of some motor element or dyspraxia. (Author's Abstr.)

VOL. 18 J. NEUR. NEUROSURG. PSYCHIAT. 1955

Variations in the Basophilia of Nerve Cells Associated with Increased Cell Activity and Functional Stress

After staining nerve cells with gallocyaninchromalum, a quantitative and stoicheiometrical staining reaction for nucleic acids, the cell pictures exhibit marked changes with variations in the functional and pathological activity of the cells. These changes consist in variations in the basophilia of the cytoplasm, nucleus, nucleolus, and nuclear membrane, accompanied by alterations in the form of the cell body and nucleus, and size of the nucleolus, as well as characteristic changes in the distribution of the basophilic elements in the cytoplasm and displacement of the nucleus inside the cell body. The fundamental cell stages of basophilia (chromoneutrality, hyperchromasia, chromophobia, chromophilia) are described.

Spontaneous variations in the basic staining reaction of the nerve cells constantly occur in the central nervous systems of normal animals and man, but are greatly enhanced by experimental procedures or in disease.

Chromophobia in certain human cases of patho-functional stress (acute delirium, death from convulsant treatment, traumatic epilepsy), as well as in the ganglion cells of Aplysia after electric stimulation is described.

All the evidence indicates that the cell pictures of chromophobia are to be interpreted as structural correlates of increased activity and abnormal neuronal discharge. Certain characteristic cell pictures provide strong evidence in support of the theory (Einarson, 1933, 1935) that the nucleic acid of the cytoplasm is formed primarily round the nucleolus inside the nucleus and then diffuses through the nuclear membrane to become a constituent of the basophilic elements in the cytoplasm.

(Authors' Abstr.)

Unusually Severe Lesions in the Brain Following Status Epilepticus

The case has been described of a boy who at the age of 9 became ill with Still's syndrome. In the course of this illness he suddenly went into status epilepticus, which was followed by three days' coma and pneumonia. On recovery from the acute episode he was found to be demented. Subsequently he had grand mal, petit mal, and also what may be described as temporal lobe seizures. He died 12 months after the first epileptic seizure.

At necropsy he showed widespread damage in the brain due mainly to circulatory and anoxic disturbances associated with the first status epilepticus. The lesions were most severe in the first temporal convolution and adjacent Sylvian regions. Ammon's horn and the hippocampal gyrus, the medial orbital and the anterior cingular regions. The amygdaloid nucleus showed extensive incomplete softening.

The pathogenesis and functional significance of the lesions are discussed. Particular attention is drawn to the combination of lesions in the first temporal convolution and hippocampus, which Earle, Baldwin and Penfield regarded as specific to herniation and anoxia at birth.

Special reference is made to the involvement of the amygdaloid nucleus.

(Authors' Abstr.)

Prefrontal Leucotomy and the Anticipation of Pain

In order to test the hypothesis that prefrontal leucotomy relieves painful conditions by reducing the anticipatory element of fear a pain-expectancy test was devised. The relative disturbance caused by a painful shock and by a preceding warning light was estimated by measuring the ratio of the psychogalvanic responses aroused by these two stimuli. Twelve of the 13 patients examined showed post-operatively an increase in this ratio which indicates a relative reduction in the autonomic disturbance caused by the warning signal. It was shown that this reduction in the anticipatory fear associated with a painful stimulus was not due to an alteration in the perception of pain or to a reduction in the amount of pain tolerated during the test.

One subject, who had been relieved by leucotomy of a totally incapacitating preoccupation with a post-herpetic neuralgia, is reported in detail.

(Authors' Abstr.)

Intellectual Changes Following Temporal Lobectomy for Psychomotor Epilepsy

Testing of patients undergoing temporal lobectomy for psychomotor epilepsy suggests that following the operation:

1. General intelligence is relatively unimpaired.
2. Specific abilities may be impaired, at least for some time.
3. A significant learning disability may result.
4. The disability is strongly associated with lesions of the dominant hemisphere.
5. The disability may still be present a year after operation.
6. The learning disability is not a function of the level of intelligence of the patient or of intellectual changes following operation.

(Authors' Abstr.)

Effects of Photic Stimulation During Sleep

The photic responses of five normal persons were investigated electroencephalographically during sleep. Photic responses were observed in all instances by means of automatic low frequency analysis. The responses tended to decrease with the deepening of sleep.

Next, the effect of light stimulation on 30 epileptic patients sensitive to light and 46 who were not sensitive to light was investigated during sleep. The sensitivity to light tended to be unchanged, reduced, or absent during sleep. The responsible factors seem to be the severity of the pathologic process and the effect of premedication necessary to induce sleep in some cases. Patients severely sensitive to light tended to remain light sensitive to the same degree in spontaneous sleep, while in medicated sleep a reduction or absence of these pathologic responses occurred. Patients mildly sensitive to light lost their light sensitivity even in spontaneous sleep. In no instance did sensitivity to light increase compared with that in the waking state. None of the 46 epileptic patients who were insensitive to light in the waking state became sensitive to it during sleep.

Seizure discharges in the electroencephalogram which produced clinical manifestations in the waking state became less effective in producing outward signs during sleep.

In two cases focal occipital sharp waves could be triggered by the flashing light during the waking state and during sleep.

The optic pathways to the cortex apparently remain patent during sleep although the threshold to stimuli rises. This rise in threshold may occur at the level of the lateral geniculate body.

(Authors' Abstr.)

APRIL

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Study of Correlations between Electroencephalographic and Psychological Patterns in Emotionally Disturbed Children

1. The high percentage of abnormal EEG's in childhood schizophrenia (78·6 per cent.) suggests an organic basis or component in this particular condition. An EEG abnormality rate of 73·4 per cent. in the group of primary behavior disorders is in agreement with the findings of previous similar studies, and also suggests the probability of a defect or developmental retardation in the cerebral structure.

2. There is no apparent relationship between abnormality of the EEG and specific types of behavioral patterns such as extreme passivity, aggressiveness, or hyperactivity. Early head trauma and serious illness were also found with the same incidence among children of the emotionally disturbed group with normal EEG's as among the abnormal. Neither is there any apparent relationship between the EEG and specific emotional traits as suggested in the Rorschach test, with the possible exceptions of the apperceptive approach and form quality.

3. The greater the cerebral dysfunction, as indicated by the EEG, the more abnormal do we find specific psychological variables dealing with perception, perceptual-motor functions, and the body image.

4. Gross distortions in visual motor Gestalt functions, in body image, and in perceptual and motor functions in general appear related to foci and asymmetries in the EEG, most notably in the occipital areas.

5. The alpha percentage may be related to the accuracy of form perception as reflected by the Rorschach test. This accuracy of perceptual association appears to become impaired in the presence of foci in the EEG, especially occipital foci.

6. The results of the study tend to support Schilder's contention that organic damage to the brain causes a disturbance in perception and motility and therefore adversely affects the body image.

(Authors' Abstr.)

An Experimental Study of the Etiology of "Rum Fits" and Delirium Tremens

1. Ten healthy morphine addicts who had been abstinent from narcotics for at least 3 months volunteered for a study of chronic intoxication with alcohol. The objective was to maintain each subject continually in the maximum state of intoxication compatible with safe

ambulatory management for a period of 6 to 13 weeks, and then to discontinue alcohol abruptly.

2. Alcohol was given orally at intervals of 1 or 2 hours from 6 a.m. to 12 midnight, with supplementary drinks at 2 a.m. or 3 a.m., and in an average daily dose of 266 to 489 ml. of 95 per cent. ethyl alcohol for 7 to 87 days.

3. Convulsions and delirium did not appear during the period in which patients were consuming large amounts of alcohol sufficient to maintain high blood alcohol levels.

4. Three patients withdrew from the experiment after 16 days of drinking, or less, and one after 34 days of drinking. The symptoms following discontinuance of alcohol by these patients were mild, consisting chiefly of tremulousness, nausea, perspiration and insomnia, and of brief duration.

5. Six of the patients drank for 48 to 87 days. Following abrupt withdrawal of alcohol, all developed tremors, marked weakness, nausea, vomiting, diarrhoea, hyperreflexia, fever and hypertension. Two of these six patients had seizures; three had a frank delirium (one of these was receiving large amounts of barbiturates at the time delirium occurred); two had transient visual or auditory hallucinations or both; and one escaped both convulsions and hallucinations. These phenomena occurred despite the ingestion of an adequate diet, with multiple vitamin supplements, throughout the periods of intoxication and withdrawal.

6. The intensity of symptoms following withdrawal of alcohol appeared to be correlated roughly with amount of alcohol consumed and with the length of the period of intoxication.

7. A characteristic electroencephalographic pattern was obtained during chronic intoxication with alcohol and during the withdrawal period. Early during chronic intoxication, the EEG's were generally slowed whenever the patients had high blood alcohol levels and were showing clinical evidence of intoxication. Later during chronic intoxication, the EEG's were not as slow, even though blood alcohol levels were higher than during the early part of the period of intoxication. Following withdrawal of alcohol, the EEG first became normal. Between the 16th and 33rd hours of abstinence, the percentage of alpha activity declined and random spikes and bursts of slow waves were observed.

8. The concentration of alcohol in the blood (usually determined with an automatic breathmeter) was followed in three of the patients. As long as the patients were drinking between 397 and 466 ml. of alcohol daily or less, blood alcohol levels were less than 50 mg. per 100 ml. and clinical evidence of intoxication was not present. Elevation of the alcohol intake to between 430 and 479 ml. per day was followed by a rise in blood alcohol levels to between 150 and 250 mg. per 100 ml., accompanied by evidence of marked intoxication. When the dosage of alcohol which initially caused high blood alcohol levels was maintained, the concentration of alcohol in the blood fell slowly and nearly reached zero. A small increase in the dosage of alcohol and a change in the schedule of drinking was followed by a second elevation in the blood alcohol concentrations. Thereafter blood alcohol levels did not fall until alcohol was withdrawn.

9. No evidence of residual impairment could be detected 3 months after discontinuance of drinking, as judged by physical, psychiatric, psychological, laboratory, and electroencephalographic examinations.

(Authors' Abstr.)

The "Craving" for Alcohol. Formulation of the Joint Expert Committees on Mental Health and on Alcohol

The terms craving, irresistible desire, need, and sometimes appetite, have been employed in the alcohol literature to explain certain or all forms of abnormal drinking behavior seen in alcoholics.

There exists a variety of alcoholic drinking behavior which specifically suggests "craving" in the vernacular sense, but closer analysis reveals that different mechanisms are at work and that a term such as "craving" with its everyday connotations should not be used in the scientific literature to describe them if confusion is to be avoided.

The onset of the excessive use of alcohol, the drinking pattern displayed within an acute drinking bout, relapse into a new drinking bout after days or weeks of abstinence, continuous daily excessive drinking and loss of control, are all behaviors which have been claimed to be manifestations of "craving" of the same order.

"Craving" and its alternative terms have been used to explain drinking arising from (*a*) a psychological need, (*b*) the physical need to relieve withdrawal symptoms, or (*c*) a physical need which originates in physiopathological conditions involving metabolism, endocrine functions, etc., and existing in the alcoholic before he starts on his drinking career or developing in the course of it.

It has been pointed out by some investigators that a physical craving for alcohol, as indicated by withdrawal symptoms, is seen immediately following withdrawal of alcohol only after prolonged, continuous and heavy use; such a physical craving cannot be postulated as the cause of the resumption of drinking after a considerable period of abstinence when withdrawal symptoms are no longer present.

The Joint Committees feel that a sharp distinction should be drawn between (*a*) the processes operative immediately after withdrawal of alcohol in the situation described above, and (*b*) those which lead to resumption of drinking after the disappearance of withdrawal symptoms.

Since, on the interruption of continuous drinking, the distressing withdrawal symptoms provoke the alcoholic to seek relief from them by the use of more alcohol, the Joint Committees would prefer to refer to this condition as a physical dependence on alcohol.

During a period of abstinence, even in the absence of withdrawal symptoms, one observes clinically the building up of psychological tension which provokes a pathological desire for alcohol as a means of relieving this tension; in this condition the individual may be said to be psychologically dependent on alcohol.

It must be pointed out, however, that mounting psychological tension is not the only cause of resumption of drinking. It can also be caused by social pressure to drink, or sometimes even by the accidental ingestion of alcohol.

In addition, a physiopathological condition (other than physical dependence) cannot be excluded as one of the factors which may lead to the resumption of drinking after days or weeks of abstinence.

In all alcoholics, regardless of whether they have an abnormal disposition or suffer from any acquired mental disorder, one observes a weakening of that part of the higher personality from which the inhibition of primitive tendencies derives. As a result, there appears a release of the primitive side of the personality. The pathological desire for alcohol therefore becomes more evident as the inhibiting forces weaken and ultimately fail.

There is also a relatively small group of drinkers in whom the pathological desire for alcohol appears practically at the beginning of their drinking career, instead of after many years, and can thus lead to a rapid development of alcoholism. Among these will be found certain types of psychopath (e.g. the volitionally weak and the impulsive personalities). It may occur also in certain cases of somatic or mental disorder (for instance, in post-concussion states, epilepsy, certain psychoses, and oligophrenia). There is, however, a minority in this group who show none of these conditions and yet manifest a pathological desire for alcohol from the beginning of their drinking history.

The Effects of Solid Food and of Alcoholic Beverages, especially Wine, on the Excretion of Hippuric Acid

The experiments described herein were carried out in healthy young subjects in order to study the effects of alcoholic beverages, especially wine, on the excretion of hippuric acid following the ingestion of sodium benzoate. The urinary excretion of hippuric acid was studied for a period varying from 6 to a maximum of 10 hours under the following experimental conditions: (1) on an empty stomach, (2) after a meal without wine, (3) after a meal with wine, (4) after an aqueous solution of ethyl alcohol on an empty stomach, and (5) after wine on an empty stomach.

1. The administration of the test dose of 6 g. of sodium benzoate after a meal caused a higher excretion of hippuric acid than that observed following its administration on an empty stomach.

2. Wine ingested on an empty stomach did not substantially affect the total amount of hippuric acid excreted following the administration of sodium benzoate but did delay and prolong its excretion.

3. Ethyl alcohol in aqueous solution definitely decreased the total amount of hippuric acid excreted after the administration of sodium benzoate, and also delayed and prolonged its excretion.

4. Wine with a meal caused a marked increase in the excretion of hippuric acid as well as an earlier and more prolonged period of hyperhippuricuria.

(Authors' Abstr.)

1. Physiology, Biochemistry, Pathology, etc.

Biochemistry of the Brain. Skvirskaya, E. B. [*Nauka y Zhytya*, **5**, 20–2 (1953); *Referat. Zhur., Khim.*, No. 6787 (1953).]

Brief and popular review of the data on the metabolism in the brain and on the chemistry of transmission of a nerve stimulus.

M. Hoseh (Chem. Abstr.)

Physiological Factors Influencing Brain Glycogen of the Mouse. Chance, M. R. A., and Walker, A. P. (Univ. Birmingham, Engl.). [*J. Endocrinol.*, **10**, 316–24 (1954); *cf. C.A.* 45, 5317*d*].

Intravenously injected glucose increased brain glycogen concentration (I) of the mouse and caused a 40 mg. per cent. increase in blood glucose. Injection of the anti-insulin principle of the anterior pituitary also increased (I), as did adrenaline. Neither insulin, cortisone, deoxycorticosterone glucoside, nor fasting affected (I). During metrazole-induced convulsions, none of these substances influenced (I) significantly, except for insulin, which reduced (I) with the characteristic decrease in blood glucose. The changes in blood glucose with (I) with some types of activity are presented, and it is concluded that they represent independent responses resulting from central nervous activity.

KATHRYN KNOWLTON (Chem. Abstr.)

Microchemical Investigation of Oxalic Acid in Cerebrospinal Fluid. Berisso, Benjamin. [*Pubs. inst. invest. microquim., Univ. nacl. litoral (Rosario, Arg.)*, **17**, 235–42 (1953).]

Various methods are studied for identifying oxalic acid in the cerebrospinal fluid, involving the formation of crystals. Such reagents as $Sr(NO_3)_2$, $CdSO_4$, and yohimbine-HCl are used, and the sensitivity of the reaction, interferences, and physical characteristics of the oxalate formed are reported.

R. B. BRADSTREET (Chem. Abstr.)

Metabolism of Nucleic Acids in the Liver and CNS. Chepinoga, O. P., Skvirskaya, E. B., Ruskina, L. P., and Siliech, T. P. (Biochem. Inst. Acad. Sci. Ukr. S.S.R., Kiev). [*Ukrain. Biokhim. Zhur.*, **24**, 177–85 (in Russian, 185–7), (1952); *cf. ibid.*, **23**, *No.* 3 (1951).]

Brain and liver nucleic acid metabolism was studied in 150-g. white rats as follows: (1) controls; (2) after partial liver excision; (3) during prolonged narcosis; (4) a combination of (2) and (3). The left lower portion of the liver (about one-third of the total liver wt.) was removed under ether. Sodium medinal (15 mg./100 g. wt., 3–4 times daily) was used for narcotic sleep induction. Determined were: total nucleic acid (NA) P, ribonucleic acid (RNA) P, deoxyribonucleic acid (DNA) P, ribonuclease (RNAase) and deoxyribonuclease (DNAase) in liver and brain tissues. With (2) a decrease in NA P resulted in both brain and liver, enzyme activity increasing except for DNAase in the liver where it decreased. In (3) the effect on the CNS led to lowered NA P in brain and liver, and decreased enzyme activity except for DNAase of the brain which increased. (4) Was not the summative effect of (2)+(3) since the new metabolic pattern from (2) is further changed by (3). A modified Schmidt-Tannhauser method (cf. Chepinoga, Skvinskaya and L. P. Rukina, *Ukrain. Biokhim. Zhur.*, **23**, No. 3 (1951)) was used for total NA P. DNAase was determined viscometrically. A RNAase determination was developed based upon the Kunitz method (C.A.34, 7944[4]) as follows: Determination A: 0·5 ml. of 0·1 M acetate buffer (pH 6·4), 0·5 ml. of 1-hr. 1:10 aqueous extract of minced tissue, and 1·0 ml. 0·4 per cent. Na salt of RNA. Determination B: 0·5 ml. of 0·1 M acetate buffer (pH 6·0), 0·5 ml. of extract, and 1·0 ml. H_2O. All samples were incubated 1 hr. at 37°, 2·0 ml. of 0·35 per cent. uranyl acetate with 5 per cent. CCl_3COOH added, left an additional 30 min. at 37° to precipitate proteins and remaining RNA, and then filtered. One ml. of filtrate was digested with 0·15 ml. of concentrated H_2SO_4 and P. determined colorimetrically, comparing both A and B against their respective controls.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Exchange of Substances in the Brain During Excitation. Palladin, A. V. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova*, **3**, 801–8 (1953).]

Rabbits were administered subcutaneously in a single dose pervitin, 5–8 mg./kg., or metrazole, 50–70 mg./kg., and beheaded 1, 2, or 4 hrs. after the injection. The brain was removed and frozen in liquid air. To prevent effects of beheading on labile P compounds, the rabbits were first instantly killed by intravenous injection of 1 ml. of 10 per cent. hexonal. Adenosinetriphosphate (A.T.P.) and inorganic P were determined. Injection of pervitin lowers ATP concentrations 1 hr. after injection, and raises the concentration of inorganic P. The values for both return to normal within 4 hrs. Metrazole raises ATP and lowers the inorganic P concentration 1 hr. after injection, the values becoming normal within 4 hrs. P^{32} was injected simultaneously with pervitin or metrazole, and relative specific activities of P^{32} of ATP and inorganic P in the brain were determined 1–4 hrs. after injection. With pervitin there was an increase in the ATP exchange; after metrazole, lowered exchange of ATP with no variation up to 4 hrs. No changes in the phospholipide content was noted after either pervitin or metrazole. By employing P^{32}, however, after pervitin administration the extent of incorporation of P^{32} into saturated phospholipides is greatly increased 1 hr. after the injection, returning to normal within 4 hrs. The incorporation of P^{32} into unsaturated phospholipides after pervitin is somewhat above normal, falling below normal within 4 hrs. Pervitin stimulates the central nervous system, thereby raising its working capacity, while metrazole stimulates the brain without raising its working capacity. Chronic overstimulation by means of daily application of electric current for 1–1·5 months to rats or by production of insomnia in rats for 3 days lowered the ATP of the brain. Glycogen content is unaltered in insomnia, but in overstimulation by electric current it is somewhat increased, accom-

panied by lowering of the activity of phosphorylase. During overstimulation by electric current in rats there is no change in the level in ribo- or deoxyribosenucleic acid in the brain, but the activity of deoxyribonuclease is lowered. By means of P^{32} it was shown that the exchange of the nucleic acids during overstimulation is reduced, suggesting lowered synthesis of proteins in the brain during overstimulation. These and previous data are inconsistent with the view that the level of deoxyribosenucleic acid in the cell nucleus is constant, and that it plays a role only during division. Changes in the activity of deoxyribonuclease correspond with the appearance of new functions, being connected with an increase in differentiation of organs and tissues.

J. A. STEKOL (Chem. Abstr.)

Action of Diet on the Level of Pyruvic and Lactic Acids in Blood and Cerebrospinal Fluid in Mental Diseases. De Franciscis, P., and Lampitella, P. [*Boll. soc. ital. biol. sper.*, **29**, 260–3 (1953).]

The diet of psychiatric patients was found to be deficient in lipides, Ca, P and vitamins. These patients had, as was shown in a previous study, increased levels of pyruvic acid in blood (I) and cerebrospinal fluid (II). In (II) the lactic acid content was increased up to 50 per cent. After the diet of 10 patients was balanced to normal requirements for 3 months, determinations were made on (I) and (II) of pyruvic and lactic acids. It was found that: lactic acid in (I) and (II) was normal; pyruvic acid was less than in the patients with the deficient diet.

J.C.C. (Chem. Abstr.)

Total Lipide and Plasmalogen Contents of the Brain in Experimental Hyperthyroidism. Minder, W. H., and Abelin, I. (*Univ. Bern. Switz.*). [*Helv. Physiol. et Pharmacol. Acta*, **12**, 63–73 (1954 (in German).]

In rats with hyperthyroidism induced by feeding thyroid material for 10–28 days there was no change or perhaps a slight increase in total lipides of the brain. Another group fed a high-fat diet for 1– days showed no change in total brain lipides. No change in plasmalogen content was observed in either group.

L. E. GILSON (Chem. Abstr.)

Phosphocreatine and Adenosinetriphosphate (ATP) Changes in Brain Cortex after Electroconvulsions. Minaev, P. F., and Kurokhtima, T. P. (*Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., Moscow*). [*Ukrain. Biokhim. Zhur.*, **21**, 359–62 (1949) (in Russian).]

The content of phosphocreatine (I) and of ATP (II) decreases sharply after convulsions and before a second stimulus in effective, excitability of the cortical motor zone decreasing sharply at the same time; 30 min. after termination of convulsions, the contents of (I) and of (II) in the cortex return to normal, by which time excitability of the cortex has been considerably restored. Trephination of the dog skull was carried out under morphine-ether-chloroform or ether-chloroform; 30 min. after incision of the dura mater, excitability of the cortical motor zone was determined by a constant current from Ag electrodes of a chronaximeter, and was established by contraction of the hind paw extensor muscles. Having determined excitability, a portion of the cortex was excised from one control lobe by a surgical spoon chilled in liquid air and the sample frozen in liquid air, no more than 2–3 sec. lapsing from moment of sampling to immersion in liquid air. Five minutes after the excision, convulsions were produced by electric current, one electrode on the lower lip, the second on the neck muscles. Duration of the irritation was 2–3 sec., with 1-min. intervals between convulsions. It was not possible to obtain more than 5–12 seizures in a row, the last attacks being short and weak. Convulsions having ceased, a portion of cortex from the 2nd lobe was similarly extended, frozen, and the excitability determined every 5–10 mins.; 30 mins. after termination of convulsions, one more portion of cortex was excised and frozen. Each of the 3 portions of cortex were ground to a powder while frozen and cooled-8 per cent CCl_3COOH was added (1:10). The following P compounds were determined in the filtrate: (1) inorganic P, after precipitation with Mg. mixture, (2) some inorganic P+phosphocreatine P, (3) P after 10-min. hydrolysis in 1N HCl at 100°. P. was determined colorimetrically according to Fiske and SubbaRow in a step photometer.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Adenosinetriphosphate (ATP) and Phosphocreatine Changes in Brain Cortex after Corazole Convulsions. Levyant, M. I., Malkiman, I. I., and Kamenetskaya, B. I. (*Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., and Central Inst. Psychiat., Moscow*). [*Ukrain. Biokhim. Zhur.*, **21**, 363–7 (1949) (in Russian).]

There is a considerable decrease in ATP (I) and phosphocreatine (II), an increase of inorganic P, and excitability of the cerebral motor zone is sharply depressed; this is in accord with the hypothesis that ATP is an energy source of cortical excitation. Bilateral trephinations of dogs under morphine-ether narcosis were made, and the dura removed; 1·5–2 hrs. after operation, when the dog showed pupillary reflexes, 1–1·5 g. of cortex was excised and immediately immersed in liquid air. After 1 hr. 0·25 ml. of 10 per cent. corazole soln./kg. wt. was injected intravenously via a glass cannula in the femoral vein. Following

a latent period of 15–20 sec., tonic and then clonic convulsions of 2–3 min. duration set in, immediately after which a second symmetrical sample was excised. One hour after the second sample, a series of consecutive convulsions were induced, corazole being injected immediately after cessation of convulsions, and a third sample was taken. Rheobase for the normal motor zone was also determined. After single and multiple attacks, excitability was determined by a chronaximeter, the active electrode (a swab moistened in Ringer solution and connected by a thin Ag rod) being placed on the motor zone, the indifferent electrode (Ag tube) being placed in the rectum. Excitability was established by threshold contraction of the extensor muscles of the hind contralateral limb. Samples were analyzed for inorganic P, (I) and (II). Frozen samples were powdered and then ground in a porcelain mortar with 4 per cent. CCl_3COOH (1:4), protein precipitation, being limited to 10 min. to avoid rupture of labile P compounds (II). (I) was precipitated in 1 filtrate by additions of 25 per cent. mercuric acetate (0·25 ml./3 ml. of CCl_3COOH filtrate). To a second portion of filtrate (1 ml.) NaOH was added to a light phenolphthalein pink, followed by 0·2 ml. of 25 per cent. barium acetate. Inorganic P was determined in the precipitate and (II) in the centrifugate.

CLAYTON HOLOWAY (Chem. Abstr.)

Effect upon Depleted Nerve Centers of Adenosinetriphosphate (ATP) Introduced into the Brain Ventricles. Minaev, P. F. (Inst. Biol. and Med. Chem., Acad. Med. Sci. U.S.S.R., Moscow). [*Ukrain. Biokhim. Zhur.*, **21**, 368–73 (1949) (in Russian).]

Injection of ATP into the ventricles changes the composition of nerve centers depleted by epileptic seizures, enabling them to regain activity toward electrical stimulation. After exclusion of brain glycolysis by monoiodoacetate inactivation, and after failure of the animal to react to electrical stimulation by manifesting epileptic convulsions, the introduction of ATP into the brain ventricles makes it possible for convulsions to begin anew.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Glycogen in the Brain Cortex under Normal and Pathologic Conditions. Shabadash, A. L. [*Ukrain. Biohkim. Zhur.*, **23**, 360–3 (1951) (in Russian).]

A didactic comparative discussion of microscopic and biochemical data previously recommended given by S. and others.

B. S. LEVINE (Chem. Abstr.)

Tweens as Substrates for Determination of the Lipase Activity of Brain. Bozzetti, E. [*Boll. soc. ital. biol. sper.*, **28**, 1087–9 (1952).]

Tweens 20, 40, 60, and 80, of the Atlas Powder Co., proved to be good substrates for quantitative determination of the lipase activity of brain tissues. The values obtained are lower than those obtained with tributyrin as substrates; tributyrin is considered not to be a substrate for lipase.

B.A. (Chem. Abstr.)

Phosphatase and Lipase Activity of the Brain. Bozzetti, E. [*Boll. soc. ital. biol. sper.*, **28**, 1089–90 (1952).]

Stress is laid upon the importance of stipulating the incubation time when carrying out a quantitative determination of phosphatase activity in the brain. Oscillations in values were paralleled by similar changes in lipase activity as found when using Tweens as substrate. There was direct proportionality between variations in the values obtained for alkaline phosphatase and those for lipase when acting upon polyoxyethylene sorbitan monolaurate (Tween 20). Such variations were not found with Tween 80 (polyoxyethylene sorbitan trioleate) and olive oil.

B.A. (Chem. Abstr.)

Brain Phosphorylases During Insulin Intoxication. Khaikina, B. I., and Goncharova, K. O. (Inst. Biochem. Acad. Sci. Ukr. S.S.R., Kiev). [*Ukrain. Biohkim. Zhur.*, **22**, 92–8 (99–100, in Russian) (1950); *cf. C.A.* 48, 6535a.]

The addition of insulin to enzymic brain preparations *in vitro* increases phosphorylase activity toward polysaccharide synthesis, but does not affect phosphatase activity. The introduction of large insulin doses during convulsions affects phosphatase and phosphorylase activities as follows: (1) phosphatase action is blocked; (2) phosphorylase activity in favour of synthesis remains at high level; at the same time, however, the polysaccharide synthesis mechanism decreases, e.g., at pH 6·2 polysaccharide synthesis is low in the absence of a seeder; (3) phosphorylase activity in favour of breakdown is somewhat increased.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Factors Affecting Rat-brain Phosphatase Activity in Fresh Tissue Suspensions and in Histochemical Methods. Pratt, O. E. (Maudsley Hosp., London). [*Biochim. et Biophys. Acta*, **14**, 380–9 (1954) (in English); *cf. C.A.* 47, 12455h.]

A study was conducted to determine the effects of Pb++, Ca++, Mg++ and of the procedure for tissue preparation on the activity of acid phosphatase, alkaline phosphatase (I), adenosine-5′-phosphatase, adenosinetriphosphatase (II) and thiamine pyrophosphatase in rat-brain suspensions and in histochemical enzyme localization methods. Ca++ activates (I). Pb++

generally inhibits the other enzymes in the histochemical system, but if its concentration is too low inorganic phosphate can be lost from the tissue, resulting in artefacts. Ca++ and Mg++ influence enzyme activity in the histochemical system in much the same way as they do in fresh tissue suspensions, except that (II) activation by Mg++ is reduced greatly by Pb++ present in the histochemical system.

MORTON PADER (Chem. Abstr.)

Metabolism of Glutamic Acid-1-C^{14} and Aspartic Acid-4-C^{14} in Rat Brain and Kidney Homogenates. Rayford, Claudia Ratcliff and Friedberg, Felix (Catholic Univ. of Amer., Washington, D.C.). [*Biochem. et Biophys. Acta*, **14**, 390–6 (1954) (in English).]

Whole rat kidney and brain homogenates utilize only the L-form of aspartic acid (I) and glutamic acid (II). Brain homogenate supernatant, however, may utilize a small amount of D-isomer. Whole rabbit kidney homogenate dissimilates D-I. Adenosinemonophosphate (AMP) and adenosinetriphosphate (ATP) inhibit (I) oxidation by kidney homogenate, but AMP stimulates it in brain. Diphosphopyridine nucleotide (DPN), triphosphopyridine nucleotide (TPN), pyruvate, and α-ketoglutarate increase dissimilation of (I) by both kidney and brain homogenates. AMP, ATP, DPN, TPN and oxalacetate stimulate (II) catabolism by rat kidney and brain homogenates. (I) and (II) oxidation by various tissues decreases in the order; liver, kidney, brain, spleen. Blood has no oxidizing activity. Oxidation rate is low in foetal liver, livers of Walker tumorbearing hosts, and in tumor tissue itself.

MORTON PADER (Chem. Abstr.)

The Relation Between the Oxidation of Glutamic Acid and the Synthesis of Acetylcholine in Brain Extracts. Kometiani, P. A. (Inst. Physiol. Acad. Sci. Georgian, S.S.R., Tiflis). [*Soobshecheniya Akad. Nauk Gruzin. S.S.R.*, **12**, *No.* 9, 531–8 (1951) (in Russian).]

In homogenates of rat brain the synthesis of acetylcholine (I) and phosphorylcholine (II) was slightly greater under aerobic than anaerobic conditions. With acetone powder extract of rat brain anaerobic conditions gave a great synthesis of (I). When ATP (adenosinetriphosphate), (II), and choline were all present in the reaction medium the highest synthesis of (I) was achieved. Omission of choline reduced the synthesis of (I) approximated 50 per cent. while omission of ATP lowered it by 95 per cent. When acetone powder extract was used, maximum synthesis of (I) was obtained on addition of diphospho-pyridine nucleotide, diaphorase, cytochrome oxidase, and cytochrome c. Niacinamide did not affect the synthetic rate. It was concluded that (II) plays an important role in the synthesis of (I) in brain tissue and *in vivo* the supply of (II) is maintained by formation of ATP with glutamic acid furnishing the energy source *via* oxaloacetate and the citric acid cycle.

JAY L. ROTH (Chem. Abstr.)

Ammonia-formation Systems in Brain Tissue. Tsukada, Yasuzo and Takagaki, Genkichiro (Keio Univ., Tokyo). [*Nature*, **173**, 1138–9 (1954).]

A homogenate prepared from instant-frozen guinea pig brain was incubated without substrate at 37°. After 10 min., a considerable amount of NH_3 was formed, glutamic acid as the source. Incubation for 30 min. showed that glutamine functioned as an NH_3-binding system rather than an NH_3-forming system. The NH_3 sources at this second stage were both glutamic acid and adenylic compound. After 50–90 min. incubation, NH_3 formation continued and glutamine decreased slowly. In this last period glutamine deamination was more active than glutamine synthesis.

J. D. TAYLOR (Chem. Abstr.)

The Localization of Abscesses in Brain with Radioactive Iodine. Burian, K., and Hoffmann-Credner, D. (2. Universitatsklinik, Vienna). [*Wien. Z. Nervenehilk. u. Grenzgebiete*, 306–14 (1953).]

Experiments with cats with artificially produced abscesses in brain *in vivo* showed that delivered I^{131} is stored in the abscesses and therefore may be located with sufficiently improved Geiger-Müller counters.

H.R.L. (Chem. Abstr.)

Encephalography in Vitamin B_1 Deficiency and Thiamine Shock. Mouriquand, G., Courjon, Jean, Edel, V., and Bonnet, H. [*Bull. acad. natl. med. (Paris)*, **136**, 580–5 (1952).]

Deficiency was produced in pigeons. Shock conditions developed after rapid intramuscular injection of 100 mg. thiamine in normal and deficient birds. In deficiency the changes in vestibular chronaxie precede by several days the appearance of electroencephalic changes. In thiamine shock, both effects coincide initially, but the electroencephalogram is delayed in its return to normal values as compared with the chronaxie. The disturbances caused by the shock are more clearly evidenced in the electroencephalogram.

A. E. MEYER (Chem. Abstr.)

Effect of Acetylcholine on the Electrical Activity of Peripheral Nerve. Legouix, Jean Paul and Minz, Bruno. [*Compt. rend.*, **238**, 1609–11 (1954).]

When the sciatic nerve of the pithed perfused frog was stimulated, the electrical activity of the peripheral branch of the nerve was recorded with the aid of an oscillograph. The

electrical activity was greatly enhanced and the amplitude of the maximum action potential was decreased if the perfusing Ringer solution contained equal parts of eserine and acetylcholine at 10^{-9} concentration.

W. DONALD GRAHAM (Chem. Abstr.)

Wallerian Degeneration in the Rat. The Effect of Age on the Concentration of Nucleic Acid and Phospholipide in Intact and Sectioned Nerves. Mannell, W. A., and Rossiter, R. J. (Univ. Western Ontario, London, Ca.). [*J. Exptl. Biol.*, **31**, 198–207 (1954).]

The concentrations of nucleic acid and phospholipide were correlated negatively with the weight of the sciatic nerve. After nerve section there was an increase in the concentration of nucleic acid and a decrease in the concentration of phospholipide. These changes took place more rapidly in smaller nerves from younger animals.

L.P.T. (Chem. Abstr.)

Content of Glycogen and Fermentable Sugar in the Brain During Abolition and Restoration of Life in the Organism. Gaevskaya, M. S. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova*, **3**, 617–25 (1953).]

The brain of dogs, under ether, was exposed, and the animals were killed by bleeding from the hip artery. After 6 min. (time of clinical death) the animals were revived by blood transfusion and artificial respiration. No glucose was added to the transfused blood; adrenaline was added in the concentration of 1:1,000. Before bleeding, all dogs received heparin intravenously. The brain tissue was removed and frozen in liquid N_2, ground, and divided into two portions. One was analyzed for glycogen, the other for fermentable sugar and lactic acid. These were determined in the blood also. The glycogen content of the brain of the dying dog began to decrease in the first 3 mins. of "clinical death", reaching 10–30 mg. per cent. in the 5–6th min. During revival, the glycogen content of the brain did not reach normal levels until the lactic acid content of the brain became normal. Three to 6 hrs. after revival, when the sugar and lactic acid levels in the brain reached normal values, the glycogen content of the brain increased, returning to normal levels on the 3rd day. In the sixth minute of clinical death the brain retains some ability to ferment sugar. The quantity of nonfermentable sugar in the brain is independent of total reducing substances and of the state of the animal during death or revival.

J. A. STEKOL (Chem. Abstr.)

Laboratory Reports on Gargoylism. Sartori, Ernesto (*Univ. Padova, Italy*). [*Atti soc. med.-chir. Padova*, **30**, 265–7 (1953).]

In 2 cases of gargoylism, serum mucoproteins calculated as tyrosine were 5·50 and 5·35 mg. per cent. compared with $3{\cdot}38 \pm 0{\cdot}27$ for normal adults and 2·50 to 3·50 for control babies of the same age. There was also a greater elimination of 11-oxycorticosteroids, i.e. 1·40, 1·35, 1·25 mg./24 hrs. compared with controls 0·30, 0·60 mg.

M.E. (Chem. Abstr.)

2. Pharmacology and Treatment.

Effect of Tetraethylthiuram Disulfide (Antabuse) on the Alcohol Metabolism in vivo. Nowinski, Wiktor W., and Ewing, Paul L. (*Univ. of Texas Med. Branch, Galveston*). [*Texas Repts. Biol. Med.*, **11**, 597–601 (1953).]

In pigeons fed Antabuse for several days and then given a single injection of EtOH, AcH accumulates in the blood in amounts comparable to those obtained in man. Since pigeon liver is devoid of xanthine oxidase, the effect of Antabuse cannot be based on inhibition of this enzyme, but must affect other enzymes concerned with the breakdown of AcH.

F.B.M. (Chem. Abstr.)

Convulsant Action of P-aminosalicylic Acid. Scarinci, V. (*Univ. Bologna*). [*Arch. sci. biol.* (*Italy*), **36**, 394–404 (1952).]

P-Aminosalicylic acid (I) applied directly to various regions of the nervous system in the toad (*Bufo viridis*), the frog (*Rana exculenta*), the pigeon, the rabbit, and the dog produced an epileptic state or hyperexcitability followed in some cases by a flaccid paralysis. These effects were not caused by the osmotic pressure of the solutions applied since solutions of NaCl and of Na salicylate at the same concentration produced no effect. The pronounced action on the nervous system appeared to be associated with the molecular configuration of the molecule. An NH_2 group para to the carboxylic group seems to be the structure responsible for the neurotropic properties of (I). Reactions to (I) depended both on the species and on the region applied. Local application to the dorsal surface of the spinal cord of the toad produced in order, increase in reflex excitability, tetanus, and finally flaccid paralysis. In both the frog and the toad (I) applied locally to the bulb caused paralysis. In dogs application of (I) to various regions of the brain caused clonus in the muscles under control of that region. Application to the zygomatic-temporal region decreased chronaxy in the area controlled by this region. Dogs made susceptible by pharmacological means to reflex epilepsy were easily put into an epileptic state by (I). In thalamic pigeons application of (I) to the optic lobes followed by the stimulation of reflexogenic cutaneous areas produced an epileptic state.

Epilepsy could not be induced after the lobes were removed. Application of (I) to the area of the cerebral cortex controlling the mouth region of the rabbit produced epileptiform electrical responses measurable by electrical recordings. Epileptic reflexes of the Jacksonian type were also produced in the mouth region without any reflex cutaneous stimulation. In general, the action of (I) was similar to that of strychnine.

NELLIE M. PAYEN (Chem. Abstr.)

Induction of Cortical Convulsion Current Centers by Narcotic and Hypnotic Agents and the Relation of the Focal Activity to the Convulsion Excitability of the Brain Cortex. Caspers, Heinz (Univ. Munster. Westfalen, Ger.). [*Z. ges. exptl. Med.*, **122**, 142–66 (1953).]

The effect of Et_2O, luminal, and evipan was studied electroencephalographically in rats. The drugs induced latent convulsion centers. The focal activity was related to the cortex excitability.

JOHN H. WEISBURGER (Chem. Abstr.)

Action of Nicotine and of Central Ganglioplegics on the Electrical Activity of the Brain. Longo, V. G., Berger, G. P. v., and Bovet, D. (Ist. super. sanita, Rome). [*J. Pharmacol. Exptl. Therap.*, **111**, 349–59 (1954).]

The effects of nicotine, Parpanit, Parsidol, Largactil, and Artane on the electroencephalogram of the rabbit are described.

L. E. GIBSON (Chem. Abstr.)

The Physiological Changes in Rabbit Induced by Electro-shock and the Influence of Several Drugs Thereupon. Kan, Noboru (Totori Univ. School Med.). [*Folia Pharmacol. Japan*, **48**, 42–51 (1952); *Breviaria*, 3–4 (in English).]

In rabbit 5 v. a.c. for 30 sec. did not cause an effect, 10 v. for 1 sec. gave varied results, and 15 v. for 1 sec. gave typical convulsion by electroshock; with d.c. the minimum effective amount was 40 v. for 1 sec. Repeated treatment produced resistance in rabbit against electroshock. Previous anesthesia with ether, urethan, and evipan Na produced some resistance against electroshock and mitigated the convulsion induced; morphine increased the degree of convulsion. $NaHCO_3$ sensitized the rabbit to electroshock and caused a stronger convulsion. Atropine, adrenaline, and pilocarpine slightly influenced the convulsion induced by the electroshock. The electroshock immediately influenced slightly, then decreased the leucocyte number, and the original level returned in 2 hours. The lymphocytes increased immediately, decreased, and then increased; pseudoeosinophil cells showed a reverse process to the lymphocytes. The blood pigment increased immediately, decreased, and finally increased to above the original level. Previous administration of drugs slightly influenced these effects, and those intensifying the convulsion increased the leucocyte number for a time. Respiration of rabbit was halted for 25 seconds after the electroshock and recovered with considerable agitation; the above drugs showed slight influence on this effect. The blood pressure increased with the convulsion by electroshock, gradually decreased, and then increased to normal; during the convulsion the cardiac movement was temporarily halted or decreased in activity. Compressing the abdominal aorta or removing intestine, spleen, and pancreas made the change in the blood pressure small, and removing the adrenal gland or administration of ergotamine did not allow the blood pressure to increase to the original level. Anesthesia by ether, $CHCl_3$ urethan, evipan Na, and alcohol decreased the blood pressure increase by the electroshock and morphine and $NaHCO_3$ intensified the increase. Administration of exciting agents caused temporary decrease of the blood pressure just after the electroshock. When the convulsion by the electroshock was eliminated by curare, the increase of blood pressure almost disappeared, indicating that the increase at the convulsion stage is due to the increase of resistance of the blood vessels by convulsion; contraction of blood vessels of central nervous nature may also participate in it. It was suggested that the blood-pressure decrease following the above increase is due to decrease of blood-vessel resistance due to muscular slackening together with the blood-vessel dilation of central nervous nature; participation of suppression of cardiac movement and acetylcholine formation was also suggested. The final increase of the blood pressure is chiefly due to adrenaline secretion by adrenal gland and sometimes to central excitement. The intestinal movement was temporarily inhibited by the electroshock; this was due to adrenaline secretion since previous removing of the adrenal gland or administration of ergotamine did not produce this effect. Inhibition of the intestinal movement by anesthetizing agents is eliminated by the electroshock in some cases. In parellel to the convulsion the brain wave was agitated by the electroshock. The changes induced by the electroshock in rabbit may be partially caused by the convulsion and partially by the excitement in the autonomic nerve center. Curare affected the former and ergotamine the latter; anesthetizing and exciting agents influence both. It was indicated that the effect of the electroshock is so great that small amounts of drugs did not much influence it.

SHOZABURO KITAOKA (Chem. Abstr.)

Tissue Distribution of a New Central Convulsant, 10-(2-dimethylaminopropyl)-9-acridanone. Mayer, S. E., and Bain, J. A. (Univ. of Illinois Med. Coll., Chicago). [*J. Pharmacol. Exptl. Therap.*, **111**, 210–23 (1954).]

The compound is a potent convulsant agent. In the symptoms it produces it resembles pentamethylenetetrazole. A sensitive specific method based on fluorescence is described for determination of its concentration in tissues. Intravenous injection of threshold doses in rats and cats results in marked concentration of the drug in brain and kidney. The concentration in the cerebral cortex is approximately 17γ/g. of tissue when seizures are produced. Examination of the distribution in the central nervous system showed a correlation between the numbers of cell bodies in a given portion of the neuraxis and the amount of uptake of the drug.

L. E. GILSON (Chem. Abstr.)

The Effect of Central-nervous-system-stimulating Pharmacological Substances on the Absorption of Radioactive Iodine and on the Synthesis of Thyroxine of the Thyroid Gland. Kolli, E. A. (All-Union Inst. Exptl. Endocrinol., Moscow). [*Biokhimiya*, **19**, 273–9 (1954).]

Caffeine doses (5–128 mg.) and phenamine doses (0·03 mg.) augmented the absorption of radio-I by the thyroid gland. The effect becomes apparent on the third day and lasts for 8–10 days after drug administration. Beyond this period a reduction in absorption of the radio-I is accompanied by an increase in the weight of the thyroid gland and in the amount of organically bound I, causing an augmentation in the process of hormone generation and a consequent increase in the accumulation of thyroxine in the thyroid gland. High doses of caffeine and of phenamine are less effective than moderate doses.

B. S. LEVINE (Chem. Abstr.)

Action of Caffeine on the Spinal Reflexes in the Curarized and Decerebrate Frog. Gualtierotti, Torquato (Univ. Milan). [*Atti accad. nazl. Lincei, Rend., Classe sci. fis., mat. e nat.*, **16**, 384–6 (1954).]

The main effect of caffeine on the central nervous system consists in facilitating the convergence of sensory and motor impulses by decreasing the synaptic delay and producing a synchronized bombardment of the neurons. This produces a more accentuated basal depolarization of the medulla and an increasing synchronization of the synaptic potentials characterized by the appearance of a wave of larger amplitude and shorter duration, and caffeine and strychnine action is discussed.

A.E.M. (Chem. Abstr.)

The Activity of Some Central Depressant Drugs in Acute Decorticate and Diencephalic Preparations. Dasgupta, S. R., Mukherjee, K. L., and Werner, G. (School Trop. Med., Calcutta). [*Arch. intern. pharmacodynamie*, **97**, 149–56 (1954).]

Decorticate and diencephalic cats are much more sensitive to the depressant effects of R.P. 4560 and Pentothal than are normal cats. The effect of R.P. 4560 is especially enhanced. Transection of the base of the frontal lobes in front of the optic chiasma causes similar behavior changes as a decortication but the hypersensitivity to drugs is absent.

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

Some Pharmacodynamic Properties of Chlorpromazine. Reuse, J. J. (Univ. Brussels, Belg.). [*Compt. rend. soc. biol.*, **148**, 192–3 (1954).]

The adrenolytic, ganglioplegic, and antihistaminic actions of chlorpromazine are described.

L. E. GILSON (Chem. Abstr.)

The Interaction of Barbiturates With Serum Albumin and Its Possible Relation to Their Disposition and Pharmacological Actions. Goldbaum, Leo R., and Smith, Paul K. (George Washington Univ., Washington, D.C.). [*J. Pharmacol. Exptl. Therap.*, **111**, 197–209 (1954).]

Ultrafiltration studies show that the reversible binding to bovine albumin of numerous common barbiturates is related to the length and nature of the side chains. Binding is related to pH and is maximal at pH 7·8–8·0. With increasing drug concentration the fraction bound decreases but the total amount bound increases. With increasing protein concentration the fraction of drug bound approaches a maximum. Thiopental is more strongly bound than comparable barbiturates and will partially displace them from serum albumin. It in turn can be displaced by Na lauryl sulfate. Rabbit tissue homogenates can bind larger fractions of barbiturates than can be accounted for by their serum albumin content. The extent of bindings *in vitro* seems related in part to the distribution of the drugs *in vivo*. The extent of protein binding correlates fairly well with the known pharmacological properties of the drugs.

L.E.G. (Chem. Abstr.)

The Effect of Caffeine on Activity of the Higher Nervous System in Mice. I. Use of Various Single Doses of Caffeine. Vikt. K. Fedorov. [*Zhur. Vysshei Nervnoi Deyatel. im. I.P. Pavlova*, **3**, 626–35 (1953).]

Caffeine in doses of 0·01–0·07 mg. per mouse increases responses to conditioned reflexes with no after-effects of caffeine on the animal. Doses of 0·1–0·7 mg. per mouse produce a

sharp initial response, followed by a depressing effect; 2–3 days later the responses return to normal. Doses of 1–5 mg. per mouse produce effects similar to those of medium doses, but more sharply defined, which last for up to 10 days. Chronic administration of medium and large doses of caffeine for up to 2–4 months lowers significantly conditioned reflex activity in mice, owing in part to the effects of all the procedure of administration of caffeine to mice. In all cases caffeine was fed to mice with small amounts of food, which was consumed in 2–3 minutes.

J. A. STEKOL (Chem. Abstr.)

Effects of Adenosinetriphosphate on Electrical Activity of the Brain During Preconvulsive and Convulsive Phases Induced by Various Convulsants. Torda, Clara (*Cornell Univ. Med. Coll., New York, N.Y.*). [*Am. J. Physiol.*, **178**, 123–8 (1954); *cf. C.A.* **47**, 7677a).]

Adenosinetriphosphate (ATP) induced a temporary inhibition of the changes of the cerebral activity caused by physostigmine salicylate during both the preconvulsive and convulsive phases. Physostigmine apparently acts mainly through an increase of the acetylcholine content of the brain. ATP inhibited some of the changes induced by pentylenetetrazole (I) and did not modify others. (I) induces convulsions by the interaction of at least 2 mechanisms; an increase of the acetylcholine content of the brain and another, not yet identified, process. It is suggested that the spiking and increase of the voltage of the brain waves induced by acetylcholine are interrelated with a metabolite appearing during the resynthesis of ATP. One of the mechanisms through which a dynamic equilibrium between the content of ATP and acetylcholine in the brain is maintained was described. This regulation results from the property of ATP to increase acetylcholine synthesis and the property of acetylcholine to increase splitting of ATP by adenosinetriphosphatase.

E. D. WALTER (Chem. Abstr.)

Narcotics and Brain Respiration. Ghosh, J. J., and Quastel, J. H. (*Montreal Gen. Hosp., Can.*). [*Nature*, **174**, 28–31 (1954).]

The increased respiration of rat brain cortex *in vitro*, brought about by K ions or 2,4-dinitrophenol (I), is suppressed or eliminated by the presence of pharmacologically active concentrations of phenobarbital, thiopental, and chloretone. The increased sensitivity of the respiration of stimulated brain cortex to narcotics is due to a retarding effect of the narcotics on a specific phase of nerve respiration that is K-sensitive and concerned with glucose (or pyruvate) oxidation. This phase is not prominent in a resting, unstimulated nerve, the respiration of which is made up largely of processes that are unresponsive to K or insensitive to low concentrations of narcotics. This phase, however, becomes an important aspect of the respiration of stimulated nerve. The presence of EtOH at 0·1 per cent. brings about 20 per cent. inhibition of the respiration of rat brain cortex stimulated by K or (I). The same concentration of EtOH increases the respiration of unstimulated brain cortex, probably by undergoing an oxidation, which is obscured by the stimulation of respiration in a glucose medium by the addition of K ions or (I).

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