Part III.—Bibliography and Epitome.*

ACTA NEUR. PSYCHIAT. BELG.

VOL. L. DECEMBER, 1950.

Semiology of Encephalo-trigeminal or Encephalo-cranio-facial Angiomatosis. *Myle, G.* 713

VOL. LI. JANUARY, 1951.

Glutamic Acid in Mental Defectives. *Horen, H.* 1
Injury to the Spinal Cord, V, VI and VII. *André, M-J., et al.* . . 9, 17, 23
Multiple Cerebral Tumour with the Syndrome of Foster Kennedy. *Brihaye, J., et al.* 28

ACTA PSYCHIAT. NEUROL.

VOL. XXV. 1950.

The Filling of Subarachnoidal Spaces over the Convexity in Encephalograms of Normal and Tumour Cases. *Bonkálo, A.*. 323
Personality Aptitude and Physical Make-up. *Brattgard, S-O.* . . . 339
Meningo-encephalo-myelitis in a Patient with Hyperglobulinemia and Allergic Symptoms. *Esmach, O.* 355
The Effect of Hypoglycaemic Treatment on the Heart as shown by the E.K.G. *Hasché, E.* 363
Problems Associated with Senile Dementia. *Houge, N. H.*. 377
Remarkable Patients to whom Hypnosis brought Relief. *Koster, S.* . . 393
A Contribution to the Study of Friedreich's Disease. *de Lehocztky, T.* . 401
A Vestibulo-cerebellar Arrest of Development in a Widespread Osteo-neural Dysgenesis. *Martin, F.* 415
On Serum Copper in Patients with Schizophrenia. *Munch-Petersen, S.* . 423
A Case of Internuclear Ophthalmoplegia with Autopsy. *Sahlgren, E., and Hofman-Bang, E.* 429
The Isolation from the Blood of Chronic Schizophrenic Patients of Compounds Active in Radioactive Phosphate Turnover. *Ostrom, A., and Strang, O.* 437
Lumbar Prolapsed Disc. *Busch, E., et al.* 443

ACTA PSYCHIAT. NEUR., SUPPL.

1950.

A Study of Epilepsy. *Alström, C. H.* . . . . . No. 63
The Central Nervous System during Insulin Shock. *Lorentzen, K. A.* . ,, 64
Specific Dyslexia. *Hallgren, B.* . . . . . ,, 65
Late Prognosis in Meningococcal Meningitis. *Trolle, E.* . . . . ,, 66

ACTAS LUSO-ESPAN. NEUR. PSIQUIAT.

VOL. IX. AUGUST, 1950.

Therapeutic Observations on the Use of the Dinitriles. *Ortuno, A. E.*. . . 161
The Existential Psychoanalysis of Jean Paul Sartre. *Martin-Santos, L.* . 164
Kurt Schenider and Recent Psychiatric Nosology. *Solé Sagarra, J.* . . 179
Alterations in Space and Time during Experimental Parpanit Intoxication. *de la Vega, P.* 183
The Personality and Ideas of Viktor v. Weissäcker. *Rof Carballo, J.* . . 191
Medical Anthropology. *v. Weissäcker, V.*. 195

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https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

NOVEMBER.

Organic and Psychological Effects from Light in Therapy. *Fernandes, B.* . 261
A Study of the Organization of Hygiene in the Development of Psychiatric Processes. *Guzzia Aizpún, F. J., and Abella Gibert, D.*. 280
Oswald Bumke, His Work and its Influence on Modern Psychiatry. *Mikorey, M.* 300
Electroshock and Epilepsy. *Ardid, R. R.* 312
The Action of Mesantoin and of Glutamic Acid on Electroshock and on Coma from Ammonium Chloride. *Orrego, R. T., and Offermanns, J. L.* . . . 324

AM. J. MENT. DEF.

VOL. LV. JANUARY, 1951.

Postnatal Cerebral Trauma as an Etiological Factor in Mental Deficiency. *Boldt, W. H.* 345
A Treatise of Sterilization. *Vischi, G. J.* 366
Changes in the Crystalline Lens in Mongoloids. *Igersheimer, J., and Mautner, H.* 370
Nineteen Years' Experience with a Special Sterilization Act in Indiana. *Harshman, L. P.* 377
Kansas Sterilization Law as it Applies to the State Training School. *Tune, L. C.* 381
The Hearing of Mental Defectives. *Birch, J. W., and Matthews, J.* . . 384
Motor Proficiency and Intelligence. *Sloan, W.*. 394

AM. J. ORTHOPSYCHIAT.

VOL. XXI. JANUARY, 1951.

Group Dynamics. *Ackerman, N. W., et al.* 1
The Use of Films in Psychotherapy. *Prados, M.* 36
Mental Health Films in Community Education. *Middlewood, E. L.* . . 47
The Use of Case Material in Supervision. *Lehnert, B.* 54
Family Structure and Psychic Development. *Henry, J., and Warson, S.* . 59
Appraising the Contribution of the Mental Hygiene Clinic to its Community. *Gardner, G. E., et al.* 74
Indications for Mental Health Planning for Children in Israel. *Alt, H.* . 105
The Michigan Picture Test. *Hartwell, S. W., et al.* 124
The Contribution of Psychiatry to Child Health Services. *Senn, M. J. E.* . 138
Mental Evaluation of Children with Expressive Handicaps. *Doll, E. A.* . 148
A Case of Pseudoschizophrenia in a Child. *Rank, B., and Kaplan, S.* . . 155

AM. J. PSYCHIAT.

VOL. CVII. JANUARY, 1951.

Administrative Aspects of a Teaching Hospital. *Kohl, R. N.* . . . 481
Psychiatric Aspects of Civilian Defence. *Fantl, K.* 488
Psychiatry for Executives. *Laughlin, H. P., and Hall, M.*. 493
The Use of a Modified T.A.T. in a Neuropsychiatric Clinic in a General Hospital. *Smith, J. A., et al.* 498
Psychomotor Epilepsy as a Manifestation of Subdural Hematoma. *Levin, S.* 501
Review of Psychiatric Progress in 1950 503

FEBRUARY.

Displacement and Migration. *Tyhurst, L.* 561
Objective Evaluation of Personality Tests. *Zubin, J.* 569
Uses of the T.A.T. *Murray, H. A.*. 577
The Predictive Value of the Brief Psychiatric Interview. *Wittson, C. L., and Hunt, W. A.* 582
Narcoanalysis and Truth. *Redlich, F. C., et al.*. 586
The Crime of Menticide. *Meerloo, J. A. M.* 594
What the Public Thinks of Psychiatry. *Bingham, J.*. 599
The Volunteer Worker and the Psychiatric Hospital. *Fechner, A. H., and*

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

Parke, J. H. 602
Experimentally Produced Psychoses. *Hoch, P. H.* 607
A Study of Dreams in Schizophrenia and Allied States. *Noble, D.* . . 612
Ego Development and Psychoanalytic Technique. *Loewenstein, R. M.* . 617

AM. J. PSYCHOTHER.

VOL. IV. OCTOBER, 1950.

The Therapeutic Situation as it Concerns the Family. *Muncie, W.* . . 595
The Brunhild Complex. *Jolowicz, E.* 610
A Combined Approach to the Study of Treatment of Disturbed Children. *Lowenfeld, M.* 627
Experimentally Induced Dreams as Psychotherapeutic Aids. *Regardie, F. I.* 643

AM. PRACTIT.

VOL. II. JANUARY, 1951.

Muscular Dysfunction under Emotional Stress. *Jonas, A. D.* . . . 36

ANN. MÉD.-PSYCHOL.

VOL. CIX. JANUARY, 1951.

Cybernetics. *Dubouloz, P., and Corriol, J.* 1
Cybernetics. *Cossa, P.* 11
Accidents and Incidents in Insulin Treatment. *Billet, J., et al.* . . . 23

ARCH. INTER. STU. NEUR.

VOL. I. JUNE, 1950.

The Nervous System and General Physiopathology. *Meco, O.* . . . 5
Action of Synthetic Curarising Agents on the E.E.G. of Rabbits. *Bertrand, I., et al.* 21
New Conceptions of the Tele-diencephalic Vegetative Nervous System. *Maxia, C.* 31
Connections and Organization of the Thalamus. *Gerebtzoff, M. A.* . . 53
The Localization in the Central Nervous System Responsible for the Tonic and Clonic Phase of Epileptic Convulsions. *Siracusano, F., and Perroni, G. B.* 65
Impulsions. *Ey, H.* . . . . . 75 and 86
Idiocy of Cortical Origin. *Fattovich, G.* 107
An Attempt at Reconstruction of the Motor Type before Illness of the Parkinsonian Encephalitic. *Nistri, M.* 123
Subependymal Spongioblastoma. *Gerebtzoff, M. A., and Nizet, E.* . . 133
A Study of the Lipides in the Nervous System. *Brante, G.* . . . 141

DECEMBER.

Anatomical and Functional Structure of the Respiratory Centre. *Wyss, O. A. M.* 1
The Effect of Saponine and Several Other Chemicals upon the Action Current led through the Myelin Sheath. *Tasaki, I., and Ushiyama, J.* . 26
Hypophyseal Radio-haemorrhage. *Lehoczky, T.* 31
Some Remarks on the Paths of the Sympathetic Nervous System in Man. *Wrete, M.* 45
Histiocyte Activity in Peripheral Nerves in Various Experimental Conditions. *Macchi, G., and Nistri, M.* 54
Reflex Reactions in Localized Paramyoclonia under Narcosis. *Meco, O.* . 89
The Pathogenesis of Impulsions. *Ey, H.*. 104

ARCH. NEUR. PSYCHIAT.

VOL. LXIV. DECEMBER, 1950.

Capacity of Reinnervated Muscles to Function Efficiently after Prolonged Denervation. *Sunderland, S.* 755
The Syndrome of Anosognosia. *Weinstein, E. A., and Kahn, R. L.* . . 772

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

One Operation Cures Three People: Effect of Prefrontal Leukotomy on a Case of *Folie à Deux et Demie*. *Partridge, M.* 792
*Some Biochemical Changes Observed during Agene(R)-Induced Convulsions. *Belford, J., and Bonnycastle, D. D.* 797
Cecile and Oskar Vogl. *Olszewski, J.* 812
Petit mal Epilepsy Occurring in Status. *Tucker, W. M., and Forster, F. M.* . 823
*Temperature Regulation in Schizophrenia, I and II. *Buck, C. W., et al.* . 828
Effect of Stimulation of Area 4S on Fasciculations. *Madow, L., et al.* . . 843
Brain Revascularization after Carotid-jugular Anastomosis Assessed by Angiography. *Tarlow, I. M., et al.* 847
Further Experiences in Treatment of Septic Meningitis with Bacitracin. *Teng, P.* 861

Some Biochemical Changes Observed during Agene(R)-Induced Convulsions.

It is shown that there are biochemical changes in the blood of dogs exhibiting canine " epilepsy " induced by agene(R)-treated proteins that are similar to those reported to occur in human epilepsy.

The observed changes, which are described in detail, are briefly as follows :—

1. Glucose :

(*a*) A significant decrease in venous glucose prior to the first convulsive attack.

(*b*) A significant rise in both arterial and venous glucose during the convulsion. The arterial glucose is lower than normal in the interparoxysmal stage.

2. Serum potassium and magnesium : A rise in the interparoxysmal stage.

3. Carbon dioxide : A decrease in both the arterial and the venous blood during the convulsive attack, with persisting levels below normal in the venous blood in the interparoxysmal period.

4. Calcium oxygen and cholinesterase : No changes at any stage.

5. Serum inorganic phosphorus : Whereas the serum inorganic phosphorus was not found to change significantly, there was a suggestive rise at the time of the convulsive attack. (Authors' abstr.)

Temperature Regulation in Schizophrenia : 1. Comparison of Schizophrenic and Normal Subjects. 2. Analysis by Duration of Psychosis.

This investigation has been concerned with homeostatic function of the autonomic nervous system in schizophrenia. Temperature regulation was selected for study as a suitable example of homeostatic activity.

The investigation was divided into two parts. In the first a comparative study of the diurnal temperature cycle and the temperature response to heat and cold was made in a group of normal subjects, and in a series of 40 schizophrenic patients prior to the operation of lobotomy.

In the second part, the status of temperature regulation according to the duration of the psychosis was analyzed. For the analysis of the diurnal temperature cycle, a larger series of patients was studied, in order to include patients at the two extremes of the duration range.

The findings in this investigation have indicated that homeostatic autonomic function, if adequately represented by temperature regulation, is disturbed in schizophrenia, particularly during that period in which the psychosis, although definitely established, is relatively early and acute.

The interpretation of these results is discussed, the apparent relation between the course of the psychic and that of the physiological characteristics of the disease being stressed. (Authors' abstr.)

JANUARY.

VOL. LXV. 1951.

*Poliomyelitis : IV. A Study of the Midbrain. *Matzke, H. A., and Baker, A. B.* 1
Neurological Complications of Rabies Vaccine. *Latimer, F. R., et al.* . . 16
Cerebral Circulation in Postencephalitic Paralysis Agitans. *Shenkin, H. A., and Yaskin, J. C.* 29

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

Motivations in the Rehabilitation of Paraplegias. *Manson, M. P.* . . 34
Testing Visual Fields by Flicker Fusion. *Miles, P. W.* 39
*Lobotomy and Psychopathology. *Reiner, E. R., and Sands, S. L.* . . 48
*Value of Convulsive Therapy in Juvenile Schizophrenia. *Levy, S., and Southcombe, R. H.* 54
*Pneumoencephalographic Changes following Prefrontal Leukotomy. *Mescham, I., and Scruggs, J. B.* 60

Poliomyelitis : IV. A Study of the Midbrain.

1. The midbrain, although frequently involved in bulbar poliomyelitis, is never as severely implicated as the lower region of the brain stem.

2. Within the midbrain the severest involvement is generally observed within the oculomotor nuclei, the substantia nigra and the tegmental nuclei.

3. There are three sets of tegmental nuclei within the midbrain—the lateral, the ventral and the dorsal tegmental nuclei. Structurally these cells do not resemble the reticular cells of the medulla, but seem to be much more similar to the cells of the substantia nigra, to which they appear related.

4. Clinically, little evidence can be observed in patients with bulbar poliomyelitis to indicate extensive involvement of the tegmental nuclei.

5. In spite of the frequent and extensive involvement of the substantia nigra, little evidence of implication of the extrapyramidal system can be detected in cases of bulbar poliomyelitis. This is assumed to be due to the acuteness of the illness and the rapid fatality in these cases.

6. The oculomotor nuclei of the midbrain are only moderately implicated in bulbar poliomyelitis, and their involvement appears to correlate fairly well with ocular symptoms. (Authors' abstr.)

Lobotomy and Psychopathology.

The authors have demonstrated how the Malamud-Sands clinical psychiatric rating scale may be used in evaluation of the effects of lobotomy on the psychopathology of a group of 31 psychotic patients. Their analysis revealed that certain behavior patterns were favorably, and others were adversely, affected. Certain phenomena regarded by some investigators as unalterable were found to be influenced by this treatment. (Authors' abstr.)

Value of Convulsive Therapy in Juvenile Schizophrenia.

On the basis of the present study, the conclusion seems justifiable that the convulsion therapies do not appear to influence the course of schizophrenia when occurring in patients before the age of 18 years. Juvenile schizophrenia tends to run a malignant course. (Authors' abstr.)

Pneumoencephalographic Changes following Prefrontal Leukotomy (Freeman-Watts Technic).

Nineteen unselected cases in a series of 32 consecutive leukotomies were studied by pneumoencephalograms shortly before and up to 20 months after operation. The leukotomies were performed in accordance with the Freeman-Watts technic on patients with refractory psychoses of varying age groups.

The pneumoencephalographic changes in these 19 cases have been described in considerable detail. In nine of these the pre-operative pneumoencephalograms were normal in all respects. In five of these nine cases post-operative studies showed diffuse dilatation of the ventricles, and in all of the nine there was a significant absence of air in the subarachnoid space surrounding the brain. In one case there developed a large porencephalic cyst, occupying almost all of one frontal lobe.

In five cases the ventricles appeared normal pre-operatively, but there was an increase in the sulcal markings. Post-operatively the ventricles also showed progressive dilatation with obliteration of the subarachnoid space surrounding the brain. In one of these five a porencephalic cyst also developed. In the remaining five cases studies pre-operatively there was diffuse or localized ventricular dilatation. In four of these there developed frontal porencephalic cysts, progressive ventricular dilatation and obliteration of the subarachnoid space surrounding the brain.

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The related pathologic changes found in five of seven cases in which autopsy was performed were as follows: (*a*) cystic necrosis of the frontal lobes, (*b*) atrophy and gliosis throughout the brain, (*c*) meningeal thickening, scarring and hemorrhages, (*d*) generalized enlargement of the ventricles, most prominent in the frontal horns, and (*e*) cystic degeneration of the thalamus and basal ganglia, particularly in the nucleus medialis dorsalis of the thalamus.

The hydrocephalus described as a roentgenographic finding is probably due to a combination of cerebral gliosis and atrophy and a decrease in the absorptive function of the arachnoidal granulations. It may also be related to some extent to obstruction to the free egress of spinal fluid between the basal cisterns and the subarachnoid space overlying the brain.

Porencephalic cysts occurred with greater frequency in those cases in which dilatation of the anterior horns of the lateral ventricles was present pre-operatively, either as a localized dilatation or as a part of generalized enlargement of the ventricular system. The authors feel that this incidence is easily explained by the fact that the anterior horns of the dilated ventricles are more easily penetrated by the leukotome at operation.

These findings are consistent with those in the cases reported in the literature.

To prevent this occurrence, the authors suggest that pneumoencephalographic studies be included in the pre-operative work-up in all cases of prefrontal leukotomy. In those cases which show dilatation of the frontal horn of the ventricle, the surgical technic should be modified accordingly. (Authors' abstr.)

FEBRUARY.

Tuberculomas of the Brain. *Asenjo, A., et al.* 146
Encephalitic Form of Metastatic Carcinoma. *Madow, L., and Alpers, B. J.*. 161
*Effects of C10 and *d*-Tubocurarine on Electroconvulsions. *Margolis, L. H., et al.* 174
*Effect of Prefrontal Lobotomy on Temperature Regulation in Schizophrenic Patients. *Buck, C. W., et al.* 197
*Clinical and Psychological Investigation of Prefrontal Lobotomy in Chronic Schizophrenia. *Carscallen, H. B., et al.* 206

Effects of Decamethonium Bromide (C10) *and* d-*Tubocurarine on Electroconvulsions.*

The "curarizing" effects of *d*-tubocurarine chloride and decamethonium bromide (C10; decamethylene-1, 10-bistrimethylammonium dibromide) were compared in a group of 50 patients undergoing electric convulsion therapy for various psychiatric disorders.

The "curarization" effects of the two drugs were essentially similar in 66 per cent. of the patients. In 20 per cent. adequate relaxation could be produced with decamethonium bromide, whereas respiratory distress without optimal "curarization" was produced with *d*-tubocurarine chloride. In 14 per cent. optimal relaxation without respiratory distress could not be obtained with either drug. In no case did *d*-tubocurarine chloride produce optimal "curarization" without the same effect being achieved with decamethonium bromide.

There was no significant correlation between tolerance to one drug and that to the other, or between adequacy of response or degree of tolerance to either drug and the age and weight of the patient.

No complications, such as compression fractures or dislocations, were encountered in any patient even when the dose of the drug was insufficient to produce complete relaxation.

Decamethonium bromide is an improvement over *d*-tubocurarine chloride in modifying electric convulsion therapy in that histamine-like reactions are absent, the duration of paralysis is shorter and respiratory distress with intensely "relaxing" doses is less frequent. (Authors' abstr.)

Effect of Prefrontal Lobotomy on Temperature Regulation in Schizophrenic Patients.

In this report post-lobotomy changes in temperature regulation are described for a group of 40 schizophrenic patients. These changes brought the patients closer to the normal through a lessening of irregularity and rigidity in the pattern of temperature regulation. The post-operative change was greater in those

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subjects who differed most from the normal before operation, namely, in the group with relatively early psychoses.

In the interpretation of these findings, it is suggested that the pre-operative abnormalities result from the disturbing influence of the prefrontal cortex on lower autonomic centers. This disturbance would appear to diminish naturally as the psychosis approaches chronicity, and to be removed artificially by lobotomy.

(Authors' abstr.)

ARCH. NEURO-PSIQUIAT.

VOL. VIII. SEPTEMBER, 1950.

Surgery of the Sympathetic and Cerebral Lesions of Ischaemic Origin. *Wertheimer, P., and Mansuy, L.* 205
Syndromes of the Red Nucleus. *Tolosa, A., and Canelas, H. M.* . . . 211
An Infiltrating Glioma of the Brain Stem Simulating Encephalitis. *Filho, R. M., and Pimenta, A. M.* 227
Fronto-callosal Apraxia. *Tolosa, A., et al.* 235
Posterior Hernias of the Intervertebral Disc Erroneously Blamed for Neuralgia. *Gama, C.* 243
Lipoids and Inorganic Phosphorus in Neuranemia. *Canelas, H. M.* . . 249

ARCH. PSICHOL. NEUR. PSICHIAT.

VOL. XI. OCTOBER, 1950.

The Theory of Instincts and the Experimental Psychodiagnosis of Szondi. *Costa, A. M.* 407
Animal Psychology and its Problems. *Zunini, G.* 437
Observations on "The Construction Cube" of Knox-Pintner in Children of Different Ages. *Reda, G. C.* 459
Delirium and Bodily Dysgnosia. *Morselli, G. E.* 476

DECEMBER, 1950.

The Psychology of the Frontal Region in the Progress of Psychiatry. *Gemelli, A.* 517
Considerations on Olfactory Hallucinations. *Balduzzi, E.* 545
Statistical Research on Szondi's Test. *Remondins, C.* 578
The Action of Some Synthetic Anti-histamines in Agitated States. *Priori, R., and Semerari, A.* 585

ARQ. NEURO-PSIQUIAT.

VOL. VIII. DECEMBER, 1950.

Anatomo-clinical Contribution to the Modern Conception of Epilepsy. *Velasco, O. P.* 301
The Two Types of Induced Muscular Activity. *Barraquer-Bordas, L.* . . 335
A Contribution Towards the Study of the Psychopathology of Aphasia in Children. *Lefevre, A. B.* 345

BRAIN.

VOL. LXXIII. 1950.

Adult Toxoplasmosis in One Family. *Campbell, A. M. G., and Clifton, F.* . 281
Late Infantile Metachromatic Leuco-encephalopathy with Primary Degeneration of the Interfascicular Oligodendroglia. *Russell Brain, W., and Greenfield, J. G.* 291
*The Origin, Course and Termination of the Prefronto-Pontine Tract in the Human Brain. *Beck, E.* 368
E.E.G. in Subacute Progressive Encephalitis. *Cobb, W., and Hill, D.* . . 392

The Origin, Course and Termination of the Prefronto-Pontine Tract in the Human Brain.

(1) Six cases have been presented showing circumscribed, essentially prefrontal lesions, a fact confirmed by cytoarchitectonic examination. They have been compared with 22 further cases, in many of which the lesion includes anterior portions of area 6/FB.

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(2) The existence of a prefronto-pontine bundle arising from granular prefrontal cortex has been established in three hemispheres, in which the primary lesion terminates at a level anterior even to the dysgranular area 8/FC, and where the entire frontal lobe posterior to the leucotomy cut is free from any significant incidental lesion. In these three cases the degenerated tract can be traced through the internal capsule and the medial portion of the cerebral peduncle to its termination within the medial fascicles of the pons. The nerve cells surrounding these fascicles display transneuronal degeneration. All but one of the remaining 25 cases show degeneration of the prefronto-pontine and/or fronto-pontine tracts.

(3) The prefronto-pontine tract is shown to be derived from the dorsal as well as from the lateral convexity of the prefrontal region. The extreme pole and the entire orbital surface do not contribute.

(4) The question whether the cingular suppressor area contributes to the prefronto-pontine tract cannot be decided on the present material.

(5) A certain overlap of thicker fibres from dysgranular and agranular areas seems to exist in Arnold's bundle, which would therefore be better classified as a tract carrying simultaneously prefronto-pontine, as well as fronto-pontine components. This is in agreement with experimental evidence in the literature.

(6) The size of the degenerated area within the cerebral peduncle varies in proportion to the extent of the lesion from a medial one-sixth in those cases with exclusively prefrontal involvement to a medial one-fifth in those with additional damage to anterior zones.

(7) No cortico-nigral fibres originate anterior to area 6/FB.

(8) It is suggested that individual variations may exist regarding the fibre composition of the fronto-pontine system. One case with complete absence of at least the anterior component of this system is described in detail. A bilateral occurrence of this and similar anomalies has been noted. (Author's abstr.)

BR. J. MED. PSYCHOL.

VOL. XXIII. 1950.

A Psychiatric Study of Indian Soldiers in the Arakan. *Williams, A. H.* . 130
The Personality of Dyspeptics, with Special Reference to Gastric and Duodenal Ulcer. *Hamilton, M.* 182
Group Therapy. *Foulkes, S. H.* 199
Frontal-lobe Function. *Lindsay, J. S. B.* 206
Is a Social Psychiatry Possible? *Miller, E.* 213

VOL. XXIV. 1951.

Methodology and Research in Psychopathology. *Rickman, J., et al.* . . . 1
The Scientific Testing of Psycho-analytic Findings and Theory. *Stengel, E., et al.* 26
Pregnancy as a Precipitant of Mental Illness in Men. *Freeman, T.* . . . 49
Notes on the Post-insulin Analysis of a Schizophrenic Man. *Metman, P.* . 55
The Wonderful Freshness of Memories in Hysteria. *Russell-Davies D.* . 64

BR. J. PSYCHOL.

VOL. XLI. DECEMBER, 1950.

The Comparative Study of "Conflict" and "Experimental Neurosis." *Russell, R. W.* 95
The Effect of Names and Title upon the Serial Reproduction of Pictorial and Verbal Material. *Hall, K. R. L.* 109
Incentives. *Bartlett, F. C.* 122
A Comparative Study of Rumours and Reports in Earthquakes. *Prasad, J.*. 129
How Adolescents Think of Peoples, I. *James, H. E. O., and Tenen, C.* . . 145
Emotional Attitudes Towards the Family of Normal, Neurotic and Delinquent Children, II. *Jackson, L.* 173
The Sex Factor in the Cattell Intelligence Tests, Scale III. *Fitt, A. B., and Rogers, C. A.* 186

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

BULL. LOS ANGELES NEUR. SOC.

VOL. XV. DECEMBER, 1950.

*Frontal Lobe Functions and Intelligence. *Halstead, W. C.* . . . 205
*Frontal Lobes and Emotion. *Nielsen, J. M.* 213
Mass Action *versus* Mosaic Function of the Frontal Lobe. *Freeman, W.* . 220
Prefrontal Lobotomy. *Putnam, T. J.* 225

Frontal Lobe Functions and Intelligence.

Some conceptual and methodological difficulties which are retarding progress in understanding brain and behaviour in general and frontal lobe functions in particular are pointed out. These include difficulties in establishing a suitable unit of behaviour, in specifying the " lesion," in calibrating the behavioural scales, and in controlling learning effects in repeated measurements.

Attention is directed to Binet's distinction between intellectual level and intellectual activity. It is suggested that level is homologous with the cerebral power factor P, while activity is homologous with the abstraction activity factor A. These factors have been identified by the writer as components of biological intelligence.

The possibility remains to be explored that psychosurgery is effective by establishing a more " optimal " balance in the ratios between power factor P and abstraction activity A. (Author's abstr.)

Frontal Lobes and Emotion.

The frontal lobes are profoundly concerned with emotions by virtue of the cingulate gyrus-orbital cortex connections and the orbital cortex-temporal lobe connections. In general, the cingulate gyrus probably serves the function of recognition of instinctive drives and their effects which is tantamount to recognition of emotion. The orbital cortex is essential to introspection and wisdom. The frontal-temporal connections are essential to normal instinctive behaviour. A lesion in any of those locations profoundly disturbs instincts and emotions. (Author's abstr.)

CERVELLO.

VOL. XXVI. NOVEMBER, 1950.

Pneumoencephalotherapy in Schizophrenia. *Satta, A., and Crosa, G.* . . . 329
The Action of Adrenocorticotrophic Hormone in the C.S.F. of Subjects after E.C.T. *Poloni, A.* 335
Observations on the Behaviour of Morphine, Methedrine and Heroin Addicts during Treatment by the " Ottonello Method." *Mattioli-Foggia, C.* . 349

VOL. XXVII. JANUARY, 1951.

Considerations on Some Cases of Internal Frontal Hyperostosis. *Fattovich, G.* 1
Neuroepitheliomata of the Fourth Ventricle. *Ferrara, A.* 32

CONF. NEUROL.

VOL. XI. 1951.

Cranial Radiography and Oto-Neuro-Ophthalmology. 1
Psycho-surgery in Hungary. *de Lehoczky, T.* 36
Synopsis of E.E.G. Part II. *Barnes, T. C.* 40

DIS. NERV. SYST.

VOL. XI. DECEMBER, 1950.

Evaluation of Vitamin E Therapy in Psychiatric Disorders. *Stone, S.* . 355
Intracerebral Vascular Pseudocalcification Associated with Schizophrenia. *Mulder, D. W., and Denst, J.* 362
Convulsive Effects of Electroencephalostimulation by Manually Controlled " B.S.T." *Liest, L. J.* 367
The Concept of Psychopathic Personality. *Revitch, E.* 369
Planning a Mental Hospital of Fifteen Hundred Beds. *Hamilton, S. W., and Corcoran, M. E.* 373

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

JANUARY.

VOL. XII. 1951.

Role of the Psychiatrist in the Rehabilitation of the Disabled Veteran. *Cohen, N.* 3
Vibratory Sense—a Non-specific Sensory Modality. *Jackson, I. J.* . . 10
The Sentinel Asleep on Post. *Levin, M.* 15
Twelve-year Resumé in a Clinic for Epilepsy. *Arieff, A. J.* . . . 19

EDUC. PSYCHOL. MEASMT.

VOL. X. 1950.

Some Statistical Problems in Clinical Research. *Holt, R. B.* . . . 609
Predicting Academic Achievement with a New Attitude. Interest Questionnaire I. *Myers, R. C., and Schultz, D. G.* 654
Patterns of Response in Level of Aspiration Tasks. *Cohen, L. D.* . . 664
Evaluation of an Optometric Test. *Lauer, A. R., and Michael, W. B.*. . 685
Relation of Cynicism to Certain Student Characteristics. *Leidt, C. O., and Fritz, M. F.* 712

E.E.G. CLIN. NEUROPHYSIOL.

VOL. II. NOVEMBER, 1950.

The Electrical Activity of the Mammalian Olfactory Bulb. *Adrian, E. D.* . 377
Interpretations of Prolonged Rhythmic Reactions of the Sensory Areas of the Cerebral Cortex. *Bremer, F., and Bonnet, V.* 389
The Effects of Polarizing Current on Cell Potentials and Their Significance in the Interpretation of Central Nervous System Activity. *Bishop, G. H., and O'Leary, J. L.* 401
Autogenetic Inhibition. *Giant, R.* 417
Synchronous Activity in Normal and Atrophic Muscle. *Buchthal, F., and Madsen, A.* 425
*Spontaneous Electrical Activity of the Spinal Cord. *ten Cate, J.* . . 445
Fibre Type and Frequency Effect as Factors Determining Response to Afferent Stimulation. *Wyss, O. A. M.* 453
Effects at Different Frequencies of Cerebellar Stimulation upon Postural Tonus and Myotatic Reflexes. *Moruzzi, G.*. 463
*The Stability of a Randomly Assembled Nerve-network. *Ashby, W. Ross* . 471
*Behavioral and E.E.G. Changes following Chronic Brain Stem Lesions in the Cat. *Lindsley, D. B., et al.* 483

Spontaneous Electrical Activity of the Spinal Cord.

1. The isolated spinal cord of frogs and cats shows spontaneous electrical activity which can be registered without difficulty. In the electrochordogram it is possible to distinguish slow and fast waves.

2. A single isolated segment of the frog's spinal cord also shows spontaneous electrical activity.

3. The spontaneous electrical activity is maintained at a relatively high level by stimuli which are transmitted from the skin and muscles of the spinal cord. After section of all the spinal nerves, peeling-off of the skin and elimination of proprioceptive stimuli by injection of curare, the spontaneous electrical activity diminishes considerably.

4. The spontaneous electrical activity of the spinal cord is also influenced by the brain. Both the nuclei of the brain stem and the motor cortex of the cerebral hemispheres play an important part in this respect. (Author's abstr.)

The Stability of a Random Assembled Nerve-network.

As part of a program for studying cerebral dynamics, an analysis has been made of the general problem of how a system will behave if it is formed by the random assembly of many parts. In particular it was hoped that the investigation would throw light on the significance of the oscillations seen in the electro-encephalogram.

Several methods were used. The homeostat was used extensively to explore

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the possibilities, and the mathematical methods were used to extend the range. These methods are considered to provide the appropriate symbolism for the study of " open " physical systems.

The facts have led to the following conclusions :

(1) The stability of the whole is not deducible from the stabilities of the parts. Examples are given showing that parts all unstable may form a stable whole, and the converse.

(2) If a single part becomes intrinsically very stable it tends to become constant and to lose its effect on the behaviour of the whole.

(3) If all the parts become very stable intrinsically, the whole becomes equivalent to a collection of isolated parts.

(4) Increasing the richness of connections between parts usually decreases the chance of stability.

(5) Stability and instability are not possibilities of equal likelihood ; there is a bias towards instability. In many typical cases the chance that a random assembly of n parts will be stable falls off as $(\frac{1}{2})^n$.

(Author's abstr.)

Behavioural and E.E.G. Changes following Chronic Brain Stem Lesions in the Cat.

The effect upon behaviour and the E.E.G. of chronic lesions in the rostral brain stem has been studied in a series of cats.

Of lesions in sensory paths in the periaqueductal grey, or in the midbrain tegmentum and basal diencephalon, only the latter, in a position to interrupt the ascending reticular activating system, were followed by chronic somnolence and E.E.G. synchrony.

Activation of the synchronized E.E.G. by somatic and auditory stimulation was still possible either after the reticular activating system or after long sensory paths had been interrupted immediately behind the thalamus. Collateral sensory excitation of the reticular activating system in the lower brain stem, and the direct arrival of afferent impulses at some site above the midbrain, thus serve equally well to induce E.E.G. arousal, but only in the former instance does prolonged wakefulness follow.

Poverty of behaviour after lesions of the reticular activating system suggests that its influences may be directed both cephalically to activate the E.E.G. and caudally to facilitate motor activity, in maintaining the waking state.

(Authors' abstr.)

ENCÉPH.

VOL. XXXIX. 1950.

Familial Myoclonic Epilepsy, etc. *van Leeuwen, A., et al.* 449
The Results of Prefrontal Lobotomy. *Orthmayr, A.* 472
Results of Examination by Means of Intelligence Tests and the Rorschach Test after Lobotomy. *Jakob, I.* 482
Mathematical Explanations in a Case of Paranoia. *Bessiére, R., and Zaborowski, M.* 500
The Brain Considered as the Principal Seat of Hysterical Phenomena. *Salmon, A.* 511
Anorexia Nervosa of " Complex " Origin. *Scouras, Ph.* 545
A New Method of Shock Therapy, Photo-shock. *Gastaut, H., et al.* . . 554
Three Cases of Concordant Epilepsy in Twins. *Kammerer, T.* 568
Psychosomatic Studies. *Faure, J.* 580

ÉVOL. PSYCHIAT.

1950.

The Psychopathology of Confusion States. Discussion by *Abely, Baruk, et al.* 531
Refusal and Psychotherapy. *Aubin, H.* 565
Aggression and Delusion. *Van der Horst.* 591
Indications and Mechanism of Abreaction and its Relation to Shock-therapy. *Sargant, W.* 607

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

GIORN. PSICHIAT. NEUROPAT.

VOL. LXXVIII. 1950.

A Clinical Contribution to the Study of Olivo-ponto-cerebellar Atrophy. *Padovani, G.* 259
Consideration of the Response of Subjects Before and After Barbiturate Narcosis. *Casati, O.*. 279
A Case of Reticulo-sarcoma of the Dura Mater. *Delfini, C.* 289
The Influence of Electro-shock on Experimental Arterio-sclerosis with Adrenalin. *Delfini, C.* 305
The Association of Suprarenal Cortical Hormone-Ascorbic Acid in the Cure of Mental Illness. *Castelletti, V., and Bonfanti, G.* 327

IND. J. NEUR. PSYCHIAT.

VOL. II. 1950.

Problem of Mental Health in India. *Hasib, S. A.* 75
Present Day School of Thought in Psychiatry. *Davis, R. B.* 83
Primogeniture and Schizophrenia. *Chondbury, A. K. R.* 88

INTERNAT. J. PSYCHOANAL.

VOL. XXXII. 1951.

Transference of Reality. *Nunberg, H.* 1
Ego and Reality. *Loewald, H. W.* 10
Some Criteria for the Timing of Confrontations and Interpretations. *Devereux, G.* 19
On Counter Transference. *Reich, A.* 25
Counter-transference and the Patient's Response to it. *Little, M.* . . 32
The Role of " Displacement " in Agoraphobia. *Katan, A.* 41

INDIV. PSYCHOL. BULL.

VOL. VIII. 1950.

The Concept of " The Unconscious." *Bruck, M. A.* 81
The Myth of " The Unconscious." *Beecher, W.* 99
Early Childhood Memories of Mental Patients. *Friedmann, A.* . . . 111
The Ageing and the Aged. *Ginzberg, R.* 117
A Comparative Study of a Non-blood Related and a Blood Related Case of *Folie à Deux. Kramer, H. C.* 131
The Child and His Name. *Plottke, P.* 150

J. CLIN. PSYCHOL.

VOL. VII. JANUARY, 1951.

Current Mental Hygiene Practice. *Tyson, R.* 2

J. COMP. NEUR.

VOL. XCIII. DECEMBER, 1950.

A Retrograde Cell Degeneration. Study of the Cortical Projection Field of the Pulvinar in the Monkey. *Chow, K. L.* 313
The Morphogenesis of the Cetacean Cerebellum. *Jansen, J.* 341
Denervation Atrophy of the Distal Stump of a Severed Nerve. *Sunderland, S., and Bradley, K. C.* 401
Endoneural Tube Shrinkage in the Distal Segment of a Severed Nerve. *Sunderland, S., and Bradley, K. C.* 411
The Relationships between Some Sulci of the Brain and the Coronal and Sagittal Sutures in the *Macaca mulatta. Clark, G.* 421
Fiber Analysis of the Basal Ganglia. *Verhaart, W. J. C.* 425

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

J. COMP. PHYSIOL. PSYCHOL.

VOL. XLIV. FEBRUARY, 1951.

A Survey of Delayed Response Performance by Normal and Brain-damaged Monkeys. *Meyer, D. R., et al.* 17
The Role of Amino-Acid Supplementation and Dietary Protein Level in Serial Learning Performance in Rats. *Pilgrim, F. J., et al.* 26
Are Localized CRs Lost or Eradicated following Unilateral Cortical Damage? *Kellogg, W. N., and Hovorka, E. J.* 37
A Comparison of the Effects of E.C.T. and E.N. upon the Learning Ability of Young Rats. *Bernberg, R. E.* 50
The Effects of Infantile Stimulation upon Later Emotional Stability in the Mouse. *Hall, C. S., and Whiteman, P. H.* 61
A Conditioned Response Technique to Investigate " Experimental Neurosis " in the Rat. *Bijou, S. W.* 84
Some Effects of E.C.T. on a Conditioned Emotional Response. *Hunt, H. F., and Brady, J. V.* 88

J. EX. PSYCHOL.

VOL. XL. DECEMBER, 1950.

Involuntary Motions of the Eye during Monocular Fixation. *Ratliff, F., and Riggs, L. A.* 687
The Generalization of an Instrumental Response to Stimuli Varying in the Size Dimension. *Grice, G. R., and Saltz, E.* 702
The Effect upon Level of Consummatory Response of the Addition of Anxiety to a Motivational Complex. *Amsel, A.* 709
Eyelid Conditioning as a Function of the Inter-Trial Interval. *Spence, K. W., and Norris, E. B.* 716
Transfer of Training to a Motor Skill as a Function of Variation in Rate of Response. *Baker, K. E., et al.* 721
The Effect of Increased Positive Radial Acceleration upon Discrimination Reaction Time. *Canfield, A. A., et al.* 733
The Perception of the Vertical, IV. *Passey, G. E.* 738
The Perception of Obstacles by the Blind. *Worchel, P., et al.* 746
Mixed Distribution of Practice in Mirror Drawing. *Tsao, J. C.* 752
An Evaluation of Experimental Methods of Time Judgment. *Clausen, J.* . 756
A Further Test of the Ability of Rats to Learn the Location of Food when Motivated by Thirst. *Kendler, H. H., and Kanner, J. H.* 762
A Re-Examination of the Effect of Monetary Reward and Punishment on Figure-Ground Perception. *Rock, I., and Fleck, F. S.* 766
Acquisition of Motor Skill, III. *Ammons, R. B.* 777
An Experimental Study of Learning under an Irrelevant Need. *Maltzman, I. M.* 788
The Effect of Intermittent Reinforcement on the Change in Extinction Rate following Successive Reconditionings. *Perkins, C. C., jun., and Cacioppo, A. J.* 794
The Inter-Relationship of Operant Level, Extinction Ratio and Reserve. *Bullock, D. H.* 802

J. GEN. PSYCHOL.

VOL. XLIV. JANUARY, 1951.

Direct and Indirect Measures of Psychological Deficit in Multiple Sclerosis, I and II. *Canter, A. H.* . . . . . 3 and 27
Medical and Philosophical Results of the Method of Hypnotical Self-Observation. *Kohnstamm, O.* 71
Hypnosis in Relation to the Word Association Test. *Kline, M. V., and Schneck, J. M.* 129

J. GENET. PSYCHOL.

VOL. LXXVII. DECEMBER, 1950.

College Survivals and Non-Survivals at Marginal Test Levels. *Wells, F. L.* . 153
Some Projective Functions of Simple Geometrical Figures. *Wells, F. L.* . 187

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

Hoarding Behavior in the Golden Hamster. *Smith, W. I., and Ross, S.* . 211
The Development of Visuo-motor Performance on the Marble Board in Normal Children. *Crain, L., and Werner, H.* 217
Aspects of the Psychology of Meaning. *Pickford, R. W.* 231
An Experiment on the Identification of Body Odor. *Morlan, G. K.* . . 257
Instruction Time in Certain Multiple Choice Tests. *Wells, F. L.*. . . 267
An Experimental Test of Latent Learning in a Relatively Free-Choice Situation. *Shaw, M. E., and Waters, R. H.* 283
The Sociology of Perception. *Child, H.* 293
Performance of Normal and Brain-operated Monkeys on Mechanical Puzzles with and without Food Incentive. *David, R. T., et al.* 305
The Differential Decline of Subtest Scores of the Wechsler-Bellevue Intelligence Scale in 60–69 year old Individuals. *Fox, C., and Birren, J. E.* . . 313

J. NERV. MENT. DIS.
VOL. CXII. DECEMBER, 1950.

The Psychology of Gesture. *Marañon, G.* 469
*Reitman's Pin-Man Test. *Reitman, F., and Robertson, J. P. S.*. . . 498
*The Anticonvulsive Action of Histamine and other Vasodilating Drugs on Experimental Convulsions in Man. *Kaytor, F.* 511
A Psychosis with Barbiturate Withdrawal. *Hewitt, R. T.* 526

Reitman's Pin-Man Test. A Means of Disclosing Impaired Conceptual Thinking.

(1) Reitman's Pin-Man Test is described and the method of scoring it discussed in detail. It is taken to measure simultaneously the subject's capacity for abstract thinking, for empathy and for perceptually organizing material shown to him.

(2) It is demonstrated statistically that the test effectively distinguishes between deteriorated and non-deteriorated subjects, and gives consistent results when repeated with the latter.

(3) The test appears a satisfactory means, therefore, of registering changes in conceptual thinking, concreteness of outlook, emotional understanding, etc., either under the influence of a disease process, or following treatment, such as a prefrontal leucotomy. (Authors' abstr.)

The Anti-convulsive Action of Histamine and of Other Vasodilating Drugs on Experimental Convulsions in Man.

The anti-convulsant action of histamine and of other vasodilating drugs on metrazol and electric convulsions has been examined in 42 patients on 170 occasions.

The results prove unquestionably that the anti-convulsive action of histamine is powerful for metrazol seizures. The anti-convulsive action of acetylcholine bromide was about 80 per cent. that of carbaminoylcholine (Doryl) to 37 per cent., that of amyl nitrite to 30 per cent., in comparison to that of histamine. Nicotinic acid and nitroglycerine were not capable of inhibiting convulsions at all.

The anti-convulsive action of histamine is in proportion to the amount of the drug used, and it lasts a very short time, 25 to 40 seconds, during the sharpest fall of blood pressure caused by the drug.

The anticonvulsive action of histamine is not inhibited by adrenalin and ergotamine tartrate.

On the basis of the author's experiments and some literary data the author states that the anti-convulsive action of certain vasodilator drugs examined by him are not induced by cerebral vascular changes caused by them, nor is the metrazol seizure. The anti-convulsive effect seems to result from a special action exerted on physico-chemical processes (permeability, polarization) of the nerve cell membrane directly. Histamine and acetylcholine are most capable of exerting such action.

The author has not succeeded in inhibiting electric seizures by histamine. For this reason it seems possible that the pre-convulsive mechanism of the metrazol seizure is of a different nature from that of the electric seizure.

(Author's abstr.)

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VOL. CXIII. JANUARY, 1951

Conditioning of Respiration and its Psychosomatic Implications. *Freedman, B.* 1
Bilateral Symmetrical Necrosis of the Corpora Striata. *Hawke, W. A., and Donohue, W. L.* 20
The Technique of Histamine Biochemotherapy and Suggestions for its Use in Psychiatry. *Sackler, M. D., et al.* 40
The Influence of Frontal Topectomy upon Gastric Secretion. *Carpenter, M. B.* 52
Paralysis from Tetanus Antitoxin. *Davis, L. B.* 61

FEBRUARY.

Excessive Hunger as a Symptom of Cerebral Origin. *Kirschbaum, W. R.* . 95
Tuberculosis in Mental Hospitals. *Wassersug, J. D., and McLaughlin, W. F.* 115
The E.C.G. in Psychiatric Patients. *Oltman, J. E., and Friedman, S.* . . 127
The Relationship of the Vegetative Nervous System to Uremia. *Hess, L.* . 136
Mood, Anger and Somatic Dysfunction. *Harris, I. D.* 152
Comparison of Insulin Coma Therapy and Electronarcosis in Schizophrenia. *Reznick, S., and Arnett, V.* 159
Epilepsy and Arteriosclerosis. *Gordon, A.* 170

J. NEUR. NEUROSURG. PSYCHIAT.

VOL. XIII. NOVEMBER, 1950.

Infantile Hemiplegia Treated by Removing One Cerebral Hemisphere. *Krynann, R. A.* 243
Post-operative Intracranial Hypotension. *Chorobski, J.* 280
Electrical Activity of the Human Brain during Artificial Sleep. *Wyke, B. D.* 288
Familial Ataxia, Deaf-mutism and Muscular Wasting. *Matthews, W. B.* . 307
The Nailbed Capillaries in Disseminated Sclerosis. *Miller, J. H. D., and Harriman, D. G. F.* 312
*Memory Studies in E.C.T. *Williams, M.* 314

Memory Studies in Electric Convulsion Therapy.

Studies are described of the re-arousing of verbal responses by a series of pictures resembling, though not identical with, a series of pictures seen earlier. The subjects were 46 patients undergoing E.C.T. and 12 matched controls.

It was found that patients who were asked to give a verbal response to concrete pictures before a course of E.C.T. or during the early confusional period after it, gave the same verbal response more quickly than was expected to ambiguous pictures seen in the confusional state.

In well-orientated patients exactly the opposite effects were noted. If the patients were shown concrete pictures before the ambiguous ones, the ambiguous ones were responded to more slowly than if seen alone.

The relationship between these findings and some disturbances of memory noted in cases with known organic lesions is discussed, with references to further possible lines of research. (Author's abstr.)

J. NEUROPHYSIOL.

VOL. XIV. JANUARY, 1951.

*Dendritic Potential of Cortical Neurones Produced by Direct Electrical Stimulation of the Cerebral Cortex. *Chang, H-T.* 1
*An Observation on the Effect of Strychnine on Local Cortical Potentials. *Chang, H-T.* 23
Function of Meddulated Small-nerve Fibers in Mammalian Ventral Roots. *Kuffler, S. W., et al.* 29
*Role of Acetylcholine in Nerve Activity. *de Roetth, A., jun.* 55
*Effects of Combined Destruction of Frontal and Posterior "Associative Areas" in Monkeys. *Chow, K. L., et al.* 59
Limitations of Method of Strychnine Neuronography. *Frankenhaeuser, B.* . 73

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

Dendritic Potential of Cortical Neurons Produced by Direct Electrical Stimulation of the Cerebral Cortex.

1. From the observation of Golgi and Golgi-Cox preparations the general arrangement of cortical neurons has been described with special reference to the distribution of the apical dendrites of pyramids in the molecular layer. On the basis of this anatomical fact the local cortical response to a single electric shock applied to the cortical surface has been analyzed.

2. The cortical response as recorded with a unipolar electrode from the points within about 5 mm. away from the point electrically stimulated consists of two components; a sharp spike assignable to the dendritic potential, and a long-lasting slow wave representing the mass activity of the intracortical neurons.

3. The first component has a lower threshold and reaches its maximal magnitude sooner than the second component when the stimulus strength is gradually increased.

4. When the recording electrode penetrated into the cortex to a depth of about 1 mm. the polarity of the first component reversed while the second component remained, indicating that the first component is a process chiefly occurring in the superficial layer.

5. The interruption of the horizontal fibers by a shallow transverse incision between the stimulating and recording electrodes did not abolish the local cortical potential but reduced the amplitude, increased the latency and increased the initial positivity of the first component. An incision about 3 mm. deep, however, abolished the response completely.

6. The conduction velocity of nerve impulses propagating along the horizontal course of the apical dendrites as determined on the cortical surface is about 1 m. per second in cat, and 0·6–0·7 m. per second in monkey.

7. Differentiation and localization of the cortical dendritic potential were also made by the method of laminar blocking of the function of cortical neurons by superficial application of novocain on the cortex.

8. Anoxia produced by inhaling pure nitrogen abolished the second component earlier than the first, suggesting the occurrence of blockage at the axon-soma junction which prevented the passage of nerve impulses from the dendrites to the axon. (Author's abstr.)

An Observation on the Effect of Strychnine on Local Cortical Potentials.

The pattern of the local cortical potential could be modified by superficial application of strychnine on the cerebral cortex so that both the size and the promptness of onset of the second component were enhanced without significantly affecting the first component. When the action of strychnine was fully developed, the two components became fused into a single wave which, however, could be dissociated again into two temporally separated waves by reducing the stimulus strength. It is suggested that the effect of strychnine is probably to accelerate the process of impulse initiation of individual neurons in the central nervous system so as to increase the efficiency of summation, and to increase the chance of synchronization. (Author's abstr.)

Role of Acetylcholine in Nerve Activity.

By the use of DFP the minimum acetylcholine esterase activity required for maintaining pupillary function has been established. This result, considered as an isolated phenomenon, does not make possible a distinction whether synaptic transmission or axonal conduction is interrupted if the enzyme activity falls to a low level. However, the great variety of biophysical and biochemical facts accumulated during the last few years support the assumption of a similarity of the basic nature of the two processes. They have given a satisfactory explanation for the peculiarities observed at the synapse. There is no longer a basis to assume a special mechanism there as proposed in the original theories of chemical transmission. It thus appears justifiable to consider the minimum enzyme activity found as being part of the mechanism necessary to maintain synaptic transmission and axonal conduction.

The confirmation of the presence of choline acetylase in optic nerve fibers—in itself again not conclusive as evidence for the essentiality of acetylcholine in conduction—removes one of the main objections still maintained against Nachman-

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sohn's theory. The presence of the enzyme becomes pertinent in connection with the observation that all types of nerves, including the optic, contain acetylcholinesterase and that inhibitors of this enzyme block conduction.

(Author's abstr.)

Effects of Combined Destruction of Frontal and Posterior "Associative Areas" in Monkeys.

Four monkeys (*Macaca mulatta*) with bilateral parieto-temporo-preoccipital ablations were subjected to subsequent removal of frontal granular cortex. Tests and observations of sensory status and of discriminative capacities in vision, somesthesia and audition were made before and after the frontal operation. More complex functions (conditional reaction and delayed response) were also tested. Protocols were kept on general behavior and levels of activity. The effects of the additional prefrontal ablation are summarized below:

1. A decrease in visual acuity was found in one monkey, and a constriction of the visual field in another. No other primary sensory defects were observed.

2. Deficits in retention or relearning of some of the somesthetic discrimination problems (roughness and temperature) were found in two of the subjects. No deficits were demonstrable in the visual discrimination problems or in a learned auditory association.

3. Additional decrement on the conditional reaction problem resulted from the subsequent prefrontal excision.

4. Three animals failed completely on the problems requiring delayed response, and the fourth showed marked decrease in ability.

5. General activity was greatly increased in all animals.

These data, with those from previous experiments, are discussed in relation to the mode of representation of function in associative cortex. (Authors' abstr.)

J. NEUROSURG.

VOL. VIII. JANUARY, 1951.

Pathological Anatomy and Angiography of Intracranial Vascular Anomalies. *Sugar, O.* 3
Dural Sinus Venography as an Aid to Diagnosis in Intracranial Disease. *Ray, B. S., et al.* 23
The Hemodynamic Effect of Unilateral Carotid Ligation on the Cerebral Circulation of Man. *Shanklin, H. A., et al.* 38
Observations on the Interrelationships of Intracranial Pressure and Cerebral Blood Flow. *Ryder, H. W., et al.* 46
Surgical Experiences with Arteriovenous Anomalies of the Brain. *Bassett, R. C.* 59
Specific Treatment of Intracranial Aneurysms. *Poppen, J. L.* 75
Observations on Resection of the Superior Longitudinal Sinus at and Posterior to the Rolandic Venous Inflow. *Jaeger, R.* 103
Complications of Angiography. *Dunsmore, R., et al.*. 110
Complications of Ligation of the Internal Carotid Artery. *Voris, H. C.* . 119

J. NEUROPATH. EX. NEUR.

VOL. X. JANUARY, 1951.

Experimental Congenital Toxoplasmosis. *Cowen, D., and Wolf, A.* . . 1
Heterotopic Glial Nests in the Subarachnoid Space. *Cooper, I. S., and Kernohan, J. W.* 16
The Transplantation of Human Brain Tumors into Animal Hosts. *Martin, J.* 40
Histochemical and Quantitative Studies on Choline Esterase Distribution in Cervical Sympathetic Ganglia. *Hard, W. L., et al.* 48
Hypoglycemia from Islet Cell Tumor of Pancreas with Amyotrophy and Cerebrospinal Nerve Cell Changes. *Tom, M. I., and Richardson, J. C.* . 57
Hypoxemia and the Temperature of the Hypothalamus of the Cat. *Lowenbach, H.* 67
The Pyramidal Tract. *Lassek, A. M., and Shapiro, W. J.* 82

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

J. PERSONAL.

VOL. XIX. SEPTEMBER, 1950.

Individual Differences in Case of Perception of Embedded Figures. *Wilkin, H. A.* 1
Differences between the High and Low in Prejudice and their Implications for a Theory of Prejudice. *Lindzey, G.* 16
Value of Isolation Rigidity in Maintaining Integration in Seriously Disturbed Personalities. *Fisher, S., and R.* 41
Memory Dynamics, Projective Tests and Projective Interviewing. *Meltzer, H.* 48
On an Approach to Social Perception. *Luchins, A. S.* 64
The Influence of " Threat-Expectancy " on Perception. *Cowen, E. L., and Beier, E. G.* 88
The Effect of Prerecognition Hypotheses on Veridical Recognition Thresholds in Auditory Perception. *Blake, R. B., and Vanderplas, J. M.* . . . 95

J. PROJ. TECHNIQ.

VOL. XIV. DECEMBER, 1950.

The Validity of Human Form Drawings as a Measure of Personality Deviation. *Holzberg, J. D., and Wexler, M.* 343
The Rorschach Test as a Tool in Action Research. *Murray, V. F., and Joseph, A.* 362
Analysis of Group Rorschach of Physical Scientists. *Roe, A.* 385
The Use of Projective Techniques in the Evaluation of Neurosurgical Approaches to Psychiatric Treatment. *Ross, W. D., and Block, S. L.*. . . 399

J. SPEECH HEARING DIS.

VOL. XV. DECEMBER, 1950.

Paraphasia and Paralexia. *Schnell, H.* 291
Speech Therapy in a Psychiatric Hospital. *Buck, McK.* 307
A Case of Hysterical Aphonia in an Adult. *Bangs, J. L., and Freidinger, A.* 316
Stuttering Behavior and Learning. *Wischner, G. J.* 324
A Technique for Stutterers. *Froeschels, E.* 336
Flannel Chart Technique for the Rehabilitation of Speech and Hearing Disorders. *Enquist, L. E., and Wagner, C. F.* 338

J. PSYCHOL.

VOL. XXXI. JANUARY, 1951.

Recent German Theories of Stratification of Personality. *Gilbert, A. R.* . 3
New Perspectives in Behavior Study. *Syz, H.* 21
The Use of Extra-curricular Training Facilities in Undergraduate Departments of Psychology. *Staudt, V. M.* 29
On Emotions. *Goldstein, K.* 37
Studies of Manual Rotary Positioning Movements, I and II. *Chapanis, A.* 51 and 65
Illusions and Error. *Weinland, J. D.* 73
Differential Prognosis in a College Study Methods Course. *Tresselt, M. E., and Richlin, M.* 81
The Influence of Constitution and Environment upon the Development of Adopted Children. *Nieden, M. Z.* 91
Toward the Scientific Evaluation of Social Attitudes and Ideologies. *Rokeach, M.* 97
The Theory of Adaptive Differentiation. *Caldwell, W. E.* 105
Discriminability between Geometric Figures under Complex Conditions. *Sleight, S. B., and Mowbray, G. H.* 121
Need as a Determinant of Perception. *Chein, I., et al.* 129
Joint Effects of Cyclical Practice and Rest in Rotary Pursuit. *Conwell, H. R., and Ammons, R. B.* 137

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

NEUROPSIQUIAT.

VOL. I. JUNE, 1950.

The Progress of Psychiatry. *Kleist, K.* 209
Reflex Epilepsy Provoked by the Labyrinth. *Dimitri, V.* 223
Biological Studies on Genuine Epilepsy. *Moyans, B. A.* 230
Cerebral Cysticercosis. *Insausti, T.* 269
A Contribution to the Surgical Treatment of Chronic Schizophrenia. *Ipar, O. J.* 299

OCCUP. THER. REHAB.

VOL. XXIX. DECEMBER, 1950.

Rehabilitation of the Prefrontal Lobotomy Patient. *Rackow, L. L., and McGriff, D. L.* 329
The Value of Relaxation Procedures in the Treatment of Anxiety Tension States. *Bowman, H. D., et al.* 345

VOL. XXX. FEBRUARY, 1951.

Occupational Therapy in Psychiatry. *Dinis, J. S.* 1
Rehabilitation of the Hemiplegic with Orthopedic Disabilities. *Rudin, L., et al.* 14

PISANI.

VOL. LXIV. JANUARY–APRIL, 1950.

A Case of Sudden Death following a Psychic Trauma. *Stassi, M.* . . 61
A Case of Sudden Death from Injury to the Neck. *Stassi, M.* . . . 83
Epilepsy and Criminality. *Bonasera Vizzini, G.* 103
A New Reaction for the Estimation of General Intelligence (Test D-48). *De Franco, F., and Siracusano, F.* 139
Acetylcholine Therapy without Shock in Schizophrenia. *Santangelo, G.* . 145

PROC. ROY. SOC. MED.

VOL. XLIII. DECEMBER, 1950.

Discussion on the Treatment of Obsessional Neurosis 999

VOL. XLIV. 1951.

The Cerebral Basis of Consciousness. *Brain, W. R.* 37

PSYCHIAT.

VOL. XIII. NOVEMBER, 1950.

A Social Psychological Study of Incontinence. *Schwartz, M. S., and Stanton, A. H.* 399
A Philosophy of Personality. *Mullahy, P.* 417
Some Aspects of the Psychopathology of Schizophrenia. *Standish, C. T., et al.* 439
Hypotheses Concerning the Eastern European Jewish Family. *Landes, R., and Zborowski, M.* 447
Educational Therapy. *Riese, H.* 465
Status, Socialization and Interpersonal Relations of Mohave Children. *Devereux, G.* 489
Optima of Mental Health. *Smith, M. B.*. 503
German Words, German Personality and Protestantism Again. *Thorner, I.* 511

PSYCHOANAL. QUART.

VOL. XIX. OCTOBER, 1950.

General Problems of Acting Out. *Greenacre, P.* 455
Infant Memories and Constructions. *Schmideberg, M.* 468

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

Analysis of the Therapeutic Factors in Psycho-analytic Treatment. *Alexander, F.* 482
The Development of the Transference. *Macalpine, I.* 501
The Preconscious Mental Processes. *Kris, E.* 540
The Œdipus Triology. *Kanzer, M.* 561

PSYCHOSOM. MED.

VOL. XII. NOVEMBER–DECEMBER, 1950.

Psychodynamic and Esthetic Motivations for Plastic Surgery. *Hill, G., and Silver, A. G.* 345
The Role of Denial in Acute Post-operative Affective Reactions following Removal of Body Parts. *Rosen, V. H.* 356
Symptom Specificity and Bodily Reactions during Psychiatric Interview. *Malmo, R. B., et al.* 362
Psychophysiologic Relationship of Asthma and Urticaria to Mental Illness. *Funkenstein, D. H.* 377
Personality Factors in Neurodermatitis. *Allerhand, M. E., et al.* . . 386

VOL. XIII. JANUARY–FEBRUARY, 1951

Atopic Dermatitis. *Kepecs, J. G., et al.* 1
Relationship between Certain Emotional States and Exudation into the Skin. *Kepecs, J. G., et al.* 10
A Psychosomatic Theory of Thyrotoxicosis. *Ham, G. C., et al.* . . . 18
Life Situations, Emotions and Exercise Tolerance. *Duncan, C. H., et al.* . 36
Psychodynamics of Depression from the Etiologic Point of View. *Rado, S.* . 51
Prolonged Sneezing. *Murray, N., and Bierer, J.* 56

Q. J. EX. PSYCHOL.

VOL. III. FEBRUARY, 1951.

An Experimental Contribution to the Problem of Apparent Reality. *Phemister, M. R.* 1
Learning and Understanding. *Vernon, M. D.* 19
The Direction of Movement of Machine Controls. *Mitchell, M. J. H., and Vince, M. A.* 24
The Effect of Knowledge of Results on Learning and Performance, IV. *Dees, V., and Grindley, G. C.* 36
A Preliminary Report on a New Auditory After-Effect. *Deutsch, J. A.* . 43

Q. J. STUD. ALC.

VOL. XI. DECEMBER, 1950.

A Study of the Rate of Metabolism of Ethyl Alcohol. *Loomis, T. A.* . . 527
The Treatment of Alcoholism with Antabuse. *Crahan, M.* 538
Personality Traits and the Alcoholic. *Sutherland, E. H., et al.* . . . 547
Alcoholism in Industry. *Norris, J. L.* 562
The National Committee on Alcoholism. *Gardner, Y.* 567
Drinking Patterns of Italians in New Haven. *Williams, P. H., and Straus, R.* 586
Group Therapy in Alcoholism. *McCarthy, R. G.* 630

RASS. NEUR. VEGETAT.

VOL. VIII. OCTOBER, 1950.

Body Temperature and Toxic Conditions, I, II and III. *Donatelli, L., and Noferi, G.* . . . . . 221, 247, and 266
Variations in the Cutaneous Response to Intradermal Reactions in Various Lesions of the Nervous System. *Virgili, R., and Giunta, A.* . . . 288
The Behavior of the Cutaneous Reaction to Histamine in Peripheral Nerve Lesions. *Fontanari, D.* 300

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

The Influence of the Vegetative Nervous System on Intrathoracic Pressure. *Dal Co, C., and Cazzola, R.*. 338
A Contribution to our Knowledge of Acquired Hypertrophic Muscular Dystrophy. *Carrieri, G.* 353
Periodic Breathing in Hyperventilation during Intravenous Injection of Glucose Solution. *Francescon, M., and Gregoris, L.* 366

RASS. NEUROL. VEGETAT., SUPPL.

Meningeal Hemorrhage. *Noferi, G.*. . . . . No. 2

RASS. STUDI PSICHIAT.

VOL. XXXIX. SEPTEMBER–DECEMBER, 1950.

Facial Expression in Depression and in Schizophrenia. *Reale, G.* . . 631
Vertiginous Meniére-like Syndrome and Manifestations in the Optic Fundus. *Pierangeli, C. E., and Branchi, P. P.* 641
The Influence of Thiobarbiturate on Liver Function. *Giordano, A., and Befani, A.* 660
Meningo-cerebrospinal fluid and Neuraxial Pathology in Hyperdosage with Penicillin *via* the Suboccipital Route in Rabbits. *Linoli, O.* . . 669
Pharmacodynamic Research on Modifications of the Vegetative Nervous System after Prefrontal Lobotomy. *Coda, G.* 703
The Flocculation Reaction in the Plasma according to Di Maria's Alcohol Sublimate Method in Epileptics. *Befani, A.* 717
The Problem of Hypochondria. *Carelona, F.* 723
Transcerebral Electrotherapy at Low Intensity. *Riboli, B.* 742
Technique, Action and Indications for Narcosis Shock Therapy. *Traves, G., and Coda, G.* 750
Psychopathological Aspects of " Fear of Madmen." *Nistri, M.* . . . 760
Recent E.C.G. Observations in Acetylcholine Shock by Fiamberti's Method for the Cure of Schizophrenia and an Interpretative Hypothesis. *Serena, A.* 767
The Development of Delusions of Persecution in a Case of Relapsing Confusional Insanity. *D'Ormea, A.* 783

REV. NEUR.

VOL. LXXXIII. OCTOBER, 1950.

Meningiomas of the Posterior Fossa. *Petit-Dutaillis, D., and Daum, S.* . 241
The Treatment of Obstructive Internal Hydrocephalus by Ventriculostomy. *Krayenbuhl, H., et al.* 256
Pinealblastoma with Meningeal Invasion Diffuse Radiculitis. *Alajouanine, T., et al.* 268

REV. NEURO-PSIQUIAT.

VOL. XIII. MARCH, 1950.

Epilepsy following on Convulsant Treatment. *Delgado, H., and Sal y Rosas, F.* 1
The Intelligence and Personality of Cocaine Addicts. *Gutierrez-Noriga, C., and Zapata Ortiz, V.* 22
The Concept of Psychopathy. *Cason, H.*. 61

REV. NEURO-PSIQUIAT.

VOL. XIII. JUNE, 1950.

The Importance of Time in the Production of Syndromes of the Red Nucleus. *Trelles, J. O., and Roedenbeck, S. D.* 161
The Etiology of Acute Anterior Poliomyelitis. *Mendez, M.* 202

https://doi.org/10.1192/bjp.97.408.598 Published online by Cambridge University Press

REV. PSICOL. GEN. APPLIC.

VOL. V. JANUARY–MARCH, 1950.

Psychological Implications of Factorial Analysis. *Thurstone, L. L.* . . 19
The Rorschach Test. *Guera, A., and Lang, T.* 37
Preferences for Colour in Children and Students. *Rodriguez, J.* . . . 59
The Psychology of Industrial Apprenticeship. *Figuerido, C. A.*. . . . 69

APRIL–JUNE.

The Mechanics of Precision before the Psychology of Work. *Walther, L.* . 233
Immediate Auto-critical Control of the Rorschach Test. *Schachter, M.* . 247
Cerebral Hemispherectomy. *Obrador, S., et al.*. 259
The Nomenclature of the Rorschach Test and its Translation into Castilian. *Pentejo Sesena, J.* 277
The Interpretation of the Rorschach on Small Children. *Amor, C. S.* . . 307
The Physiopathology of Electro-shock. *Cerletti, U.* 335

RIV. PAT. NERV. MENT.

VOL. LXXI. 1950.

Psychosensory, Mesencephalic-diencephalic Syndrome of Lhermitte Type, etc. *Cargniello, D.* 391
Torsion Spasm. *Carrara, E.* 425
Gastric Function in Multiple Sclerosis. *Andreani, G., and Bagni, C.* . . 475
The Pathogenesis of Hypertrophic Osteoarthropathy of Pulmonary Origin. *Smorto, G., and Sciorta, A.*. 507
Papilloma of the Choroid Plexus. *Mastragostino, S.* 523
Semeiological Observations on Acute and Chronic Allergic Experimental Encephalomyelitis in the Monkey. *Cazzulo, C. L., and Ferraro, A.* . 533
Synopsis of the Neuropathology of Lightning. *Nistri, M.* 621

1. Biochemistry, Physiology, Pathology, &c.

Histochemical Distribution of Cholinesterase and Acid Phosphatase in the Prefrontal Cortex of Psychotic and Non-psychotic Patients. Pope, A., Meath, J. A., jun., Caveness, W. F., Livingston, K. E., and Thomson, R. H. [*Trans. Am. Neurol. Assoc.*, **74**, 147–53 (1949).]

Biopsy specimens excised from Brodmann's area 9 of the prefrontal cortex during the initial stages of prefrontal lobotomy showed greater cholinesterase activity and lower acid phosphatase activity in schizophrenics than in non-psychotics undergoing lobotomy for intractable pain. Acid phosphatase activity was greatest in axones and in the cell bodies of the larger cortical ganglion cells.

MARION HORN PESKIN (Chem. Abstr.).

Effect of Acetylcholine on the Resistance of Guinea-pigs to Anoxemia. Franck, C., Grandpierre, R., and Didon, P. (*Faculté Méd., Nancy, France*). [*66th Congr. French Assoc. Progress Sci., Sect. Pharmacol.*, 1947; *Toulouse méd.*, **49**, 10–13 (1948).]

Experiments made with dogs and rabbits (Cluzet *et al.*, *Comp. rend. soc. biol.*, **121**, 695 (1936); *Bull. acad. méd.* (*Paris*), **120**, 241 (1938); *J. physiol. et path. gén.*, **36**, 50 (1938), were performed with guinea-pigs. Acetylcholine increased their resistance to lack of O and to low pressures. G. SAG (Chem. Abstr.).

Effects of Anesthetics and Convulsants on Acetylcholine Content of Brain. Elliott, K. A. C., Swank, Roy L., and Henderson, Nora. (*McGill Univ. Montreal, Can.*) [*Am. J. Physiol.*, **162**, 469–74 (1950).]

Following administration of nembutal the acetylcholine (ACh) in rat or cat brain rises to a high maximum. It falls as anesthesia wears off, but can be raised again by further administration of the drug. Other anesthetics also increase the ACh level. Following metrazole or picrotoxin administration, the ACh level is lowered in nembutalized cats, but somewhat raised in unnarcotized cats.

E. D. WALTER (Chem. Abstr.).

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Anemia due to Acetylcholine. Fornaroli, P., and Antona, G. (Univ. Pavia, Italy). [*Boll. soc. ital. biol. sper.*, **25**, 1297–9 (1949).]

Injection of acetylcholine hypodermically in rats and rabbits causes hyperchromic anemia with diminution of the red cells to 2·5 million per cu. mm. in the rat and 1·5 million in the rabbit. The degree of anemia is proportional to the dose. Treatments with antipernicious anemia liver extract or with folic acid induces a prompt remission of the anemia. Treatments with liver extracts deprived of the antipernicious anemia factor or with extracts of kidney or spleen are ineffective.

M. Elliott (Chem. Abstr.).

Phenylpyruvic Oligophrenia. Mautner, Hans, and Quinn, Karl V. (Wrentham State School, Wrentham, Mass.). [*Ann. Paediat.*, **172**, 1–27 (1949).]

Large amounts of $NaHCO_3$ and vitamin C depressed excretion of phenylpyruvic acid. Tyrosine and glutamic acid effected no improvement.

Barbara R. Murray (Chem. Abstr.).

Excretion of Phenylalanine and Derivatives in Phenylpyruvic Oligophrenia. Jervis, Geo. A. (New York State Dept. of Mental Hyg., Thiells). [*Proc. Soc. Exptl. Biol. Med.*, **75**, 83–6 (1950).]

Quantitative data are presented on the urinary excretion of phenylalanine (I), phenylpyruvic acid (II), and phenyllactic acid by 20 patients (ages 2–42 years) affected with phenylpyruvic oligophrenia. The values, expressed as mgm. per gm. of total N, show no important differences from patient to patient kept on similar diets. High protein diet or ingestion of (I) or (II) increases the output. Sweat from 10 of the subjects contained 1·4–9·6 mgm. per cent. of (I) and 6–56 mgm. per cent. of (II).

L. E. Gilson (Chem. Abstr.).

Oligophrenia Phenylpyruvica. (II) Constancy of the Metabolic Error. Borek, Ernest, Brecher, Arthur, Jervis, Geo. A., and Waelsch, Heinrich. (Columbia Univ.). [*Proc. Soc. Exptl. Biol. Med.*, **75**, 86–9 (1950); *cf. preceding abstract.*]

No significant amounts of phenyllactic acid were found in the serums of 18 patients with phenylpyruvic oligophrenia. The free phenylalanine (I) concentrations of the serum were 19–38 mgm. per cent. No correlation was found between the degree of mental deficiency and the serum (I) concentration. Spinal fluid contained 6·1–8·2 mgm. per cent. of (I). It is suggested that although the increased amount of (I) is a result of metabolic error, its blood plasma level is determined by the ability of the kidney tubules to reabsorb (I). *Cf. C. A.*, **44**, 2590d.

L. E. Gilson (Chem. Abstr.).

Surface Tension of Spinal Fluid and the Phenomenon of "Antagonism." Piccardi, G., and Ferroni, E. (Univ. Florence, Italy). [*Sperimentale, Sez. chim. biol.* (**1**), 181–8 (1950).]

The surface tension of 2·5 c.c. spinal fluid poured on a watch glass was measured before and after addition of Na oleate. Following the known drop and "antagonistic" recovery of the dynamic surface tension three sharp minima in the curve were observed. Since a solution of trimethylcellulose (0·5 per cent.) gave minima similar to those of the spinal fluid, it is concluded that the phenomenon is due to the Na oleate. The minima are similar to those observed by Lecomte du Nouy by determining the tension as a function of dilution. Theory: The Na oleate is adsorbed on internal surfaces of the colloid.

A. E. Meyer (Chem. Abstr.).

The Proteins and the Hydrochloric Acid-collargol Reaction of the Cerebrospinal Fluid. Pérez-Tores, A., and Fontán J. L. Rivero. (Univ. Seville, Spain). [*Rev. clín. españ.*, **35**, 111–20 (1949).]

Spinal fluid from normal subjects and from patients with various types of meningitis and some miscellaneous diseases was examined. The amount of each protein fraction was determined by known methods and the HCl-collargol reaction of Riebeling (*C. A.*, **32**, 5488[5]) was applied. The shape of the curve obtained varied with the protein make-up of the fluid, especially with the relative, and at

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times absolute increase in euglobulins, and less frequently with the shift in the proportions of pseudoglobulin (I) and (II) present. The value of these determinations as an aid to diagnosis is discussed. L. E. GILSON (Chem. Abstr.).

The Indican Content of Cerebrospinal Fluid in Physiological and Pathological Conditions. Tinelli, Guiseppe (Univ. Bari, Italy). [*Policlinico (Rome), Sez. med.*, **52**, 69–78 (1945).]

By the Bohm and Gruner method (*C. A.*, **30**, 6404[6]) it was found: Normal subjects (20 cases), averaged 23·7γ per cent. (variations probably according to age); patients with nervous diseases (32 cases), meningitis (19 cases), nervous syphilis (11 cases), and metasyphilis (19 cases), respectively, 50·6, 56·7, 67 and 67·5γ per cent. Indican increase is due to both an increased passage from the blood to the cerebrospinal fluid through the altered blood-cerebrospinal barrier and to biochemical processes (protein fission) occurring in the same cerebrospinal fluid.
C. SCANDURA (Chem. Abstr.).

Examination of Cerebrospinal Fluid and Blood. Simplified Methods Derived from the Quantitative Gold Reaction. Lange, Carl, Miller, John K., and Harris, Albert H. (New York State Dept., Health, Albany). [*Am. J. Clin. Path.*, **20**, 872–6 (1950).] JOHN T. MYERS (Chem. Abstr.).

The Cerebrospinal Fluid in Multiple Sclerosis. Freedman, David A., and Merrit, H. Houston (Tulane Univ., New Orleans). [*Proc. Assoc. Research Nervous Mental Diseases*, **28**, 428–39 (1950).]

Review, with general discussion of chemical mechanism of colloidal reactions of cerebrospinal fluid. WARREN M. SPERRY (Chem. Abstr.).

Changes of Functional State of the Nervous System in Protein Deficiency. Dinerman, A. A., and Semenova, G. T. (1st Med. State Inst., Moscow). [*Arkh. Patol.*, **12**, No. 4 62–8 (1950).]

In rats protein starvation causes a severe instability of chronaxia analogous to that observed clinically in dystrophy. Caloric deficiency with full protein requirement alters chronaxia but slightly. The results are reversible by full diet.
G. M. KOSOLAPOFF (Chem. Abstr.).

Carbonic Anhydrase in the Brain of the Newborn in Relation to Functional Maturity. Ashby, Winifred, and Schuster, Ernest M. (St. Elizabeth Hospital, Washington, D.C.). [*J. Biol. Chem.*, **184**, 109–16 (1950); *cf. C. A.*, **43**, 4747*d*).]

Carbonic anhydrase appeared late in the cerebrum of the young of the dog, cat, rat and rabbit, but was present at birth in the young of the guinea-pig and cow, which are more mature when born, suggesting a correlation between the appearance of the enzyme in the cerebrum and the beginning of its functioning.
GEORGE K. DAVID (Chem. Abstr.).

Effect of Acute Hypoxia on the Motor Cells of the Spinal Cord. Krogh, Erik (Univ. Aarhus, Denmark). [*Acta Physiol. Scand.*, **20**, 263–92 (1950).]

Experiments were made on rabbits. Hypoxia was produced by clamping off aorta for varying lengths of time. Spasticity was examined electromyographically. The hyperactivity of the muscles of the lower extremities observed in hypoxemic rabbits is due to the preserved large motor cells in the anterior horn. In nearly every case these cells were found to be normal physiologically, but more chromophobic than in normal rabbits. The swollen, extremely chromatolytic cells are acutely degenerating cells which are dying following a stage of hyperactivity. The dead nerve cells disappear after 48–60 hours. Anoxemia damages more seriously neurons in the center of the anterior horn. S. MORGULIS (Chem. Abstr.).

Do Adrenergic Vasodilator Nerves Exist? Folkow, Björn, and Uvnas, Börje (Univ. Lund, Sweden). [*Acta Physiol. Scand.*, **20**, 329–37 (1950).]

From point of view of chemical transmission, sympathetic vasodilator nerves are cholinergic and adrenergic. Experiments on the action of atropine and eserine

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on vasodilator responses to stimulation show that skeletal muscles (cat) are supplied with sympathetic vasodilator fibers of cholinergic type. The existence of adrenergic vasodilator fibers is questioned, and it is suggested that this chemical transmission is exclusively cholinergic. Furthermore, since atropine completely annuls the vasomotor responses to stimulation of sympathetics while neo-antergan, even in doses which strongly antagonize the vasodilator action of histamine, produces no blocking, the hypothesis of the existence of vasodilator fibers of an histaminergic type in the sympathetic outflow finds no support. S. MORGULIS (Chem. Abstr.).

Sympathicomimetic Action of Brain Extracts. Holtz, Peter (*Karolinsches Inst., Stockholm*). [*Acta Physiol. Scand.*, **20**, 354–62 (1950).]

By two sensitive tests (blood pressure in cat and uterus of the rat), the sympathicomimetic action of brain extracts (beef, rabbit) was differentiated into adrenaline and arterenol actions. In both animals the two substances are present approximately in the same proportion (90 per cent. arterenol, 10 per cent. adrenaline), but whereas beef brain yields about 0·2γ the rabbit brain yields 2γ. Cocaine increases the pressor action of the extracts to the same extent as it does that of arterenol.

S. MORGULIS (Chem. Abstr.).

Survival and Revival of Nervous Tissues after Arrest of Circulation. Heymans, C. (*Univ. Ghent, Belg.*). [*Physiol. Rev.*, **30**, 375–92 (1950).]

Nervous tissue is more sensitive to lack of O and, therefore, to interruption of blood supply than are other tissues, and not all parts of the nervous system are equally affected; all can withstand complete anoxia up to five minutes, and none can survive more than 30 minutes. Within this time limit the survival is in this diminishing order: Respiratory, vasomotor or cardioregulatory center > palpebral pupillary centers > cortical centres. Sudden circulatory arrest may be treated by cardiac massage in case of cardiac standstill, or in case of ventricular fibrillation by electric shock, or by injection of procaine-HCl into the blood stream.

S. MORGULIS (Chem. Abstr.).

Effect of Partial Extirpation of Adrenals on the Higher Nervous Activity in Dog. (II) One-day Fast, Caffeine and Muscular Labor. Gzgzyan, D. M. (*Pavlov Evolut. Physiol. Inst., Acad. Med. Sci., U.S.S.R.*). [*Fiziol. Zhur.*, **36**, 261–70 (1950); *cf. ibid.*, **35**, 637 (1949).]

After partial removal of adrenals a one-day fast taking place in the most distinct period of changes of neural activity (2nd phase) causes a decline of conditioned reflexes, while unconditioned reflexes are stimulated. In the restorative phase after the operation, a one-day fast gives the same reactions as in controls. Feeding of caffeine in various doses leads to increased sensitivity to the drug. Light labor lowers, hard labor raises the level of stimulation of the central nervous system.

G. M. KOSOLAPOFF (Chem. Abstr.).

Nucleic Acids of the Brain during Prolonged Protein Starvation. Mandel, Lila, Jacob, Monique, and Mandel, Paul (*Univ. Strasbourg, France*). [*Compt. rend. soc. biol.*, **144**, 275–6 (1950); *cf. C. A.*, **44**, 8438*a*).]

L. E. GILSON (Chem. Abstr.).

Signal Transmission in Nerve. Muralt, Alexander v. (*Univ. Bern., Switz.*). [*Harvey Lectures, Ser.* **43**, 230–53 (1947–48).]

The conduction of the nervous impulse was studied by three approaches, i.e. the electric, the chemical, and the internal organization. The excitation wave is transmitted in jumps from one node to the next in medullated nerves. This method increases the speed of conduction. The internode is essential for the electrotonic spread of the stimulus. The newborn action potential is produced at the neighbouring node, and then jumps by spatial conduction from node to node. The production of the action current is derived from chemical reactions, and is accompanied by the release of acetylcholine and a thiamine compound. The internode is probably the locus for the production of free energy to the sites of excitation. From the cell body a nutritive influence is exerted which maintains the internal organization of the whole nerve and produces regeneration after injury.

JULIA O. HOLMES (Chem. Abstr.).

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Properties of Preparations from the Central Nervous System which Degrade Coenzymes (I) and (II); their Connection with Carbohydrate Metabolism. H. McIlwain (*Maudsley Hosp., London*). [*Biochem. J.*, **46**, 612–19 (1950).]

Phenosafranine (I) is a very potent inhibitor of cozymase degradation. Janus Green is another phenazine derivative which is very potent. (I) increases aerobic glycolysis of brain cortex almost to the anaerobic level without exerting much effect on respiration. (I) is now shown to be the most potent of phenazone compounds inhibiting degradation of cozymase. Nicotine, and even more so the structurally related compound, 4-(3-pyridyl)-4H-isoimidazole inhibit cozymase degradation. Although all substances inhibiting cozymase degradation release aerobic glycolysis, many do so without effect on cozymase degradation (KCl, CO, guanidines and amidines). Though it is not known whether continual breakdown and resynthesis of cozymase is involved in the reactions of carbohydrate metabolism and utilization in tissues, it is very probable that the enzyme, isolated from mammalian brain or spinal cord by extraction with H_2O or strong salt solutions, which degrades cozymase does play a specific role in carbohydrate metabolism in the brain. It is suggested that this may operate through the mechanism of phosphorylation which normally accompanies oxidation. S. MORGULIS (Chem. Abstr.).

Concentration or Exclusion of Some Heterocyclic Compounds by Brain Cortex, in Relation to Their Effects on Cardohydrate Metabolism. McIlwain, H., and Grinyer, I. (*Maudsley Hosp., London*). [*Biochem. J.*, **46**, 620–8 (1950).]

Some pyridine and phenazine derivatives which disturb the balance of carbohydrate and metabolism in slices of brain cortex also inhibit degradation of cozymase. The object was to find the concentrations at which these substances act upon each process separately. Slices of guinea-pig cortex absorb phenosafranine, diazine green, neutral red, and ethyl red from a glucose-saline medium aerobically until the concentration in the slice is 50–300 times greater than in the medium. Nicotine and nicotinamide are largely excluded from the slices. The absorption (max. rate about 1 micromole/g moist tissue wt./hr.) is greater aerobically with glucose than anaerobically and without glucose, the continued glucose metabolism being necessary for the tissue to hold phenazine or quinoline derivatives to the maximum extent. The substances increase aerobic glycolysis in concentrations which have no or little effect on respiration, while those which do not increase glycolysis have no or little action on cozymase degradation. Those of the former type have an unsubstituted pyridine N, and in the three position a substituent including the group $R_1R_2C–NHR_3$. The most active phenazine derivatives have basic substituents at 3 and 6, and a N-phenyl group. The concentrations of phenosafranine, diazine green, and neutral red (phenazine); ethyl red (quinoline) and nicotine and nicotinamide (pyridine) needed to increase aerobic glycolysis to a selected value and their effects on cozymase degradation are tabulated.
S. MORGULIS (Chem. Abstr.).

Mechanism of Inhibition of Anaerobic Glycolysis of Brain by Sodium Ions. Utter, M. F. (*Western Reserve Univ., Cleveland, Ohio*). [*J. Biol. Chem.*, **185**, 499–517 (1950); *cf. Racker and Krimsky, C. A.*, **40**, 1932.[3]]

The cord and medulla of cotton rats and the remaining brain tissue were homogenized separately, and extracts were prepared by centrifuging. Manometric studies were carried out in Warburg vessels, and individual enzymes of the glycolytic system were investigated in Thunberg tubes. Inhibition of acid production by Na in the presence of brain homogenate was strong when glucose was the substrate, but only slight when hexose diphosphate (I) was used. Even in the presence of (I), Na prevented utilization of inorganic phosphate and decreased that of glucose by both brain and cord homogenates. The effect on extracts was less marked. Inhibition was pronounced at a Na concentration of 0·035 M, and it increased rapidly with increasing concentration. High concentrations of K and Li were also inhibitory, as were low concentrations of Ca (0·02 M) and sulfate ion (0·04 M). The presence of Na had no effect on hexokinase, phosphohexokinase, or the coupled oxidation-phosphorylation reaction, but strongly inhibited the transfer of phosphate from phosphopyruvate to adenylic acid. FRED H. SNYDER (Chem. Abstr.).

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Cerebral Anoxia in Infantile Dehydration. Kerpel-Fronius, E., Varga, F., and Kun, K. (Univ. Children's Clinic, Pecs, Hung.). [Arch. Disease Childhood, **25**, 156–8 (1950).

The O_2 saturation of the blood of the longitudinal sinus was determined in 11 dehydrated infants. It decreased parallel to the gravity of the clinical condition. A close inverse correlation was found between the decrease of the O_2 saturation of the cerebral venous blood and anhydremic shock as measured by circulation time. Cerebral symptoms characteristic of a toxic condition in dehydration appeared when the O_2 saturation of the cerebral venous blood approached 25 per cent. Deep coma was observed when the latter decreased to less than 15 per cent. Thus, the cerebral symptoms of severe dehydration appear to be due to cerebral anoxia of the stagnating type. KATHRYN KNOWLTON (Chem. Abstr.).

The Vegetative Nervous System and Blood-sugar Regulation. Simon, Kurt (Med. Akad., Dusseldorf, Ger.). [Klin. Wochschr., **28**, 152–8 (1950).]

Results of tests show that all patients with acute illness within the cerebrum or cerebellum showed a reversal in curves from the expected norm after the administration of adrenaline as well as after the administration of insulin. The height of the paradoxical blood-sugar rise after the administration of insulin was dependent on the severity of the disease and on the rapidity of appearance of symptoms of cerebral damage. After improvement in condition the blood-sugar curve began approaching normal. After the brain injury had healed completely adrenaline and insulin injections yielded a normal blood-sugar curve.

RENATE H. MEDVED (Chem. Abstr.).

Cephalinase in Nervous Tissue. Tyrrell, L. W. (Whitchurch Hosp., Cardiff, Wales). [Nature, **166**, 310 (1950).]

A process is given whereby the P turnover rate in brain phospholipides is shown to occur mainly in the cephalin fraction. This is attributed to the possible presence of cephalinase which has little or no effect to the lecithin portion. Work was carried out on sterile rat brain tissue buffered at pH 7·5 and incubated at 37°.

A. B. S. (Chem. Abstr.).

The Chemistry of Myelination and Demyelination. Sperry, Warren M., and Waelsch, Heinrich (N.Y. State Psychiat. Inst., New York, N.Y.). [Proc. Assoc. Research Nervous Mental Diseases, **28**, 255–67 (1950).)]

Review. W. M. S.

The Behaviour of Potassium and Calcium in the Blood Serum in Epilepsy. Weinland, Wolf L. (Anstait, Bethel Bielefeld, Ger.). [Arch. Psychiat. Nervenbrankh., **183**, 731–8 (1950).]

K was determined 522 and Ca 489 times in the blood of 128 epileptics before, during, and after seizures. The results showed no definite relation between the concentrations of K and Ca, and the occurrence of epileptic seizures.

The Evaluation of Cerebral Processes by the Intravenous Insulin Functional Test of V. Falkenhausen and Gaida. Reiss, Ernest (Landeskrankenhaus, Detmold, Ger.). [Deut. Z. Nervenheilk., **164**, 303–16 (1950).]

The blood-sugar concentration (I) curve after insulin administration under standardized conditions was determined 172 times in 83 patients with various types of cerebral disease. The abnormal types of response were, no change in (I), a decrease in (I) without subsequent rise, and an increase in (I) without subsequent decrease during the 200 min. of observation. The abnormal responses are related to disturbances in the function of the hypophysis and hypothalamus.

WARREN M. SPERRY (Chem. Abstr.).

The Incidence and Significance of Hypoglycemia in Unselected Admissions to a Psychosomatic Service. Landmann, H. R., and Sutherland, R. L. [Am. J. Digestive Diseases, **17**, 105–8 (1950).]

A 5-hour glucose tolerance test was performed on 50 consecutive patients admitted to a psychosomatic service after a few days of well-balanced diet. Blood

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Ca and protein levels also were determined. In 44 per cent. of cases the blood sugar fell to hypoglycemic levels (below 70 mgm. per cent.) during the tolerance test. In 14 per cent. of cases there was a delayed insulin response.

W. E. C. (Chem. Abstr.).

Phosphatase of Brain Tissue. Binkley, Francis, and Olson, C. K. (*Univ. of Utah, Salt Lake City*). [*J. Biol. Chem.*, **186**, 725–30 (1950).]

A phosphatase (I) in purified condition was isolated from pig brain. This enzyme completely hydrolyzes inorganic pyrophosphate, and after 90 minutes' incubation removes approximately 50 per cent. of the terminal phosphate from adenosinetriphosphate. Preinoculation of (I) with Mg^{++} ions + glutathione (II) was more effective than preincubation with (II) alone. Prolonged preincubation with Mg^{++} ions made (I) about 55 per cent. as active as preincubation with (II) $+Mg^{++}$ ions. The activity of (I) is dependent upon the concentration of Mg^{++} ions between 0·0025 to 0·01 M; higher concentrations cause inhibition. Of other metals tested, only Mn^{++} ions + (II) exhibited an activating effect upon (I).

LAWRENCE ROSEN (Chem. Abstr.).

Role of Glutamic Acid in the Transport of Potassium in Brain and Retina. Terner, C., Eggleston, L. V., and Krebs, H. A. (*Univ. Sheffield, Engl.*). [*Biochem. J.*, **47**, 139–49 (1950).]

Slices of brain cortex (guinea-pig, rabbit) lose K ions by diffusion into the saline medium except under aerobic conditions and in the presence of both glucose and L-glutamate. Similarly retinas (ox eye) stored at 0° for 1–2 hours exchange nearly 50 per cent. of the K for Na, but the ionic concentrations are more or less restored during incubation provided both glucose and L-glutamate are present in the medium. However, the glucose could be replaced with lactic or pyruvic acid and the L-glutamate by L-aspartate. Since the latter is converted in brain or retina to glutamate, it is doubtful if the effect on K-ion diffusion is affected by the aspartate. Under anaerobic conditions glucose and glutamate have no significant influence on the K content of brain slices. It seems probable that while L-glutamate participates in the K transport, the glucose (or lactic and pyruvic acid) serve as sources of energy.

S. MORGULIS (Chem. Abstr.).

The Cerebral Blood Flow in Male Subjects as Measured by the Nitrous Oxide Technique. Normal Values for Blood Flow, Oxygen Utilization, Glucose Utilization and Peripheral Resistance, with Observations on the Effect of Tilting and Anxiety. Scheinberg, Peritz, and Stead, Euegne A. (*Duke Univ., Durham, N.C.*). [*J. Clin. Invest.*, **28**, 1163–71 (1949).]

The N_2O method was used for measuring cerebral blood flow in 20 normal young men in the supine position. In normal resting subjects 14 per cent. of the cardiac output is devoted to the cerebral circulation and 22 per cent. of the total O consumption is cerebral. Anxiety made no difference in cerebral metabolic function. Tilting normal subjects to the erect position caused a 21 per cent. fall in cerebral blood flow, a 23 per cent. fall in cerebral arterio-venous O difference, a 34 per cent. fall in effective arterial pressure, and a 10 per cent. fall in cerebral vascular resistance. Cerebral O utilization is relatively constant in the normal person under ordinary stresses. Its buffer system is flexible, allowing the cerebral arterio-venous O difference to compensate for relatively large changes in cerebral blood flow.

JOHN T. MYERS (Chem. Abstr.).

Change of Nitrogen Metabolism in Spinal Cord of Rabbits in Diphtheria. Promyslov M. Sh. (*Doklady Akad., Nauk, S.S.S.R.*, **73**, 775–7 (1950); *cf. C. A.*, **44**, 2107*h*).]

The character of N metabolism in the spinal cord of rabbit is of the same type as that of the brain proper. The extent of decomposition of N-containing substances increases exclusively at the expense of proteins, while metabolism of N-containing lipides is unaltered. Protein N declines in diphtheria, while residual N rises. H_2O content rises in the spinal cord, but drops in the brain.

G. M. KOSOLAPOFF (Chem. Abstr.).

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The Relation of the "Hydergin-glucose-test" to Psychic and Physical Status. Solma, Hugo (Psychiat. Clinic, Univ. Basel, Switzerland). [*Schweiz. Arch. Neurol. Psychiat.*, **65**, 311–29 (1950) (in *German*); *cf. C. A.*, **38**, 4600[6]).]

Glucose (I) tolerance was determined in 28 normal human subjects without, and 1 or 2 days later with, the intravenous injection of 0·3 mgm. hydergin (II), a mixture of DHO, DCS and DHK. (II) was given at the same time as the 20 g. dose of (I). (II) usually inhibited the rise in blood (I) concentration, but to a widely variable degree which was related to physical and psychic status. In subjects of the pyknic type the inhibition was less than in those of the leptosomic-asthenic type. In subjects with a passive psyche the inhibition was large, and in those with an active, vital psyche it was small.

WARREN M. SPERRY (Chem. Abstr.).

Biochemical Studies on the Action of the Nerve. (I) The Distribution of Cholinesterase in the Human Brain. Okinaka, Shigeo, Yoshikawa, Masaki, and Goto, Juya (Univ., Tokyo). [*Igaku to Seibutsugaku (Med. and Biol.)*, **17**, 82–5 (1950).]

Cholinesterase activities were determined in various parts of human brain by the method of Ammon (*C. A.*, **28**, 1724[6]). The results obtained agreed well with those by Nachmansohn (*C. A.*, **33**, 7322[8]).

MICHINORI NAKAMURA (Chem. Abstr.).

Brain Concussion and Blood Sugar. Mate, Istvan (Tudomanyegyetemi III, sz. Sebeszeti Klinika, Budapest, Hung.). [*Orvosi Hetilap*, **89**, 414–16 (1948).]

The blood sugar level was determined on 42 persons with brain concussion (I). In 9 cases this value was 140–160 mgm. per cent. Then a load was applied by dosing perorally 50 gm. dextrose. The sugar content of blood was determined every 30 minutes for 3 hours. Persons suffering from (I) showed blood sugar of 210–350 mgm. per cent. Persons showing normal blood sugar were free from (I). Blood-sugar values approached normal with disappearance of (I). The actual increase of blood sugar was not in proportion to the gravity of (I).

ISTVAN FINALY (Chem. Abstr.).

Biochemical Studies in Multiple Sclerosis. Jones, Harold H., Jones, Harold H., jun., and Bunch, Leitha D. (Winfield, Kan.). [*Ann. Internal Med.*, **33**, 831–40 (1950).]

In multiple sclerosis there is an abnormal response to oral glucose, the most striking evidence of which is blood elevation of pyruvic acid out of proportion to lactic acid. In cases in relapse, the fasting level of pyruvic acid is high and remains so throughout a glucose tolerance test. If the disease is less active, the disproportion of pyruvic to lactic acid does not appear until the 2nd, 3rd and 4th hour after glucose administration. Serum cholesterol is elevated and is higher in the active than in the quiescent case. Serum inorganic P level is low and P excretion is low when compared with urinary preformed creatinine, but after giving glucose urinary excretion of P is increased over the fasting state by 72, 24 and 25 per cent. at the 2nd, 3rd and 4th hours as compared to decrease of 31, 41 and 36 per cent. in controls. The urinary uric-acid creatinine ratio after glucose is lower than normal, being little different from the fasting level throughout the test.

JOHN T. MYERS (Chem. Abstr.).

Cerebral Blood Flow and Oxygen Consumption in Neurosyphilis. Patterson, John L. jun., Heyman, Albert, and Nichols, Fenwick T., jun. (Harvard Med. School, Boston, Mass.). [*J. Clin. Invest.*, **29**, 1327–34 (1950).]

Cerebral O consumption (CMRO), vascular resistance (CVR), and cerebral blood flow (CBF) were determined by the nitrous oxide method in 58 patients with neurosyphilis and in 16 controls. In patients with dementia paralytica, the CBF and CMRO were reduced, and the mean CVR was increased. There was a definite relation between mental deterioration and reduction in CMRO.

JOHN T. MYERS (Chem. Abstr.).

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2. Pharmacology and Treatment.

Pharmacological Action of β-phenylisopropylamine on the Nervous System. III. Action on Convulsive Activity in Cortical Motor Neurones. Scarinci, V. (Univ. Bologna, Italy). [*Boll. soc. ital. biol. sper.*, **25**, 217–19 (1949); *cf. C. A.*, **44**, 740*d*, 3141*a*.]

A 2 per cent. solution of β-phenylisopropylamine applied to the motor cortical zone in the dog, causes lowering of faradic excitability; a stronger (5 per cent.) solution has the optimum effect. Four medium-sized dogs were morphinized (thus suppressing all epileptic reflexes) and treated with the drug. Circumscribed application of the 2 per cent. drug, followed by stimulation of the cutaneous contralateral reflex area, gave a typical clonic reaction which persisted during the hyperactivity of the cortex. The details of the effects are given. The drug appears to excite cortical hyperactivity, which causes corticifugal convulsions. Possibly the convulsions are really present before the peripheral effects, but the corticifugal action may be affected by the spinal motorneurones, and thus cannot produce a motor effect. While convulsive activity is reinforced by a corticipetal impulse due to stimulation of the skin, the corticifugal effects may produce a motor response.
B. A. (Chem. Abstr.).

Glutamic Acid in the Treatment of Mentally Handicapped Children. A Review of the Background. Clapp, Roger W. (St. Louis Univ., St. Louis, Mo.). [*J. Missouri State Med. Assoc.*, **46**, 181–2 (1949).]

Biochemical, animal and clinical experiments suggesting that the administration of glutamic acid in large doses be used to improve mentally handicapped children and so facilitate teaching, are reviewed. Results of the administration of this substance to mentally dull children suggested that it is indicated only as an adjunct to teaching. RUTH BERGGREN (Chem. Abstr.).

Effect of Narcotics on Cell Respiration. Issekutz, B., jun., Lichtneckert, I., and Hetényi, G., jun. (Univ. Szeged, Hung.). [*Arch. intern. pharmacodynamic*, **83**, 33–48 (1950).]

Phenobarbital diluted to 2×10^{-3} decreases the O_2 uptake of surviving rat kidney slices and diaphragm by about 20 per cent. and inhibits the action of dinitrophenol on frog muscle, but urethan, morphine and scopolamine do not. The two last named cause some increased activity. In dogs, tissue respiration *in vivo* was not decreased by any of these drugs. M. L. C. BERNHEIM (Chem. Abstr.).

The Neuromuscular Blocking Action of Succinylcholine (Diacetylcholine). Castillo, Julio C., and De Beer, Edwin J. (Wellcome Research Labs., Tuckahoe, N.Y.). [*J. Pharmacol. Exptl. Therap.*, **99**, No. 4, Pt. 1,458–64 (1950).]

Succinylcholine resembles 2 molecules of acetylcholine linked together at the α-Me groups. It possesses the maximum neuromuscular blocking activity of its homologous series. It has 10 atoms (8C and 2O) interposed between the 2 quartenary N atoms, and thus approaches the favourable chain length found in decamethonium bromide. It exhibits a strong neuromuscular blocking action in the cat, rabbit and mouse, but the paralysis is of relatively short duration. The action is greatly prolonged by eserine. L. E. GILSON (Chem. Abstr.).

Effect of Insulin Hypoglycemia on Eosinophiles and Lymphocytes of Psychotics. Tsai, Shih Yuan, Bennett, Alene, May, Lawrence G., and Gregory, Raymond L. (Univ. of Texas Med. School, Galveston). [*Proc. Soc. Exptl. Biol. Med.*, **74**, 782–4 (1950).]

Insulin hypoglycemia causes in schizophrenics a significant eosinopenia and lymphocytopenia, which are considered to be indicative of adrenocortical stimulation. Insulin does not produce such changes if hypoglycemia is prevented by glucose administration. L. E. GILSON (Chem. Abstr.).

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Action of Phenamine on the Higher Nervous Activity in the Dog. Pavlov, B. V. (Pavlov Physiol. Inst., Acad. Sci. U.S.S.R.). [*Fiziol. Zhur.*, **36**, 271–82 (1950).]

Feeding 0·0025–0·5 mgm./kgm. phenamine 25–60 minutes before the experiments in which noises, light or touch stimuli were used for investigation of reflex activity in dogs, showed that 0·06 mgm. dosage gives optimum results in dogs with a weak nervous organization, while maximum doses are best for the better organized animals. These doses gave significant increase of conditioned salivary reflexes. The latent period was shortened in all cases. Under the action of the drug dogs which were normally restless in sound-proof boxes became quiet. Pulse rate usually rose, as did respiration. Frequent repetition of the drug eventually led to sharp reflex decline and refusal of food.

G. M. KOSOLAPOFF (Chem. Abstr.).

Neuromuscular Excitation: Responses of Normal and Denervated Mammalian Muscle to Bis (Trimethylammonium) Decane (C_{10}) and to d-Tubocurarine. Jarcho, L. W., Eyzaguirre, C., Talbot, S. A., Lilienthal, J. L., jun., and Leakins, E. (Johns Hopkins Univ., Baltimore, Md.). [*Am. J. Physiol.*, **162**, 475–88 (1950); *cf. C. A.*, **43**, 2329*e*.]

Bis (trimethylammonium) decane (C_{10}) depresses markedly the twitch tension of innervated rat muscle and causes asphyxial death unless respiration is artificially maintained. C_{10} reduces end-plate potential below the amplitude necessary for initiation of a prolonged electrical response in muscle fibers. C_{10} also reduces strength of contraction of denervated muscles stimulated directly; this action is blocked by *d*-tubocurarine. In both innervated and denervated muscle C_{10} depresses demarcation potentials. This action is also blocked by *d*-tubocurarine. Fibrillation potentials of denervated muscle are obliterated by C_{10} and partially suppressed by *d*-tubocurarine. It is suggested that both drugs are active at the motor end plate and also at undefined regions along the muscle fiber.

E. D. WALTER (Chem. Abstr.).

Narcotics and the Phosphates of Brain. Buchel, L., and McIlwain, H. (Univ. of London). [*Nature*, **166**, 269–70 (1950).]

Chloral and ethylbutylbarbituric acid cause a fall in cerebral respiration in guinea-pig cortex slices *in vitro* accompanied by a fall in phosphocreatine, and an increase of inorganic phosphate. WESLEY H. HARTUNG (Chem. Abstr.).

The Relation Between the Elicitation of Convulsions and the Inhibition of the Enzymic Decomposition of the Active Substance of Sensory Nerve Fibers by Several Drugs. Hellauer, H. F., and Umrath, K. (Univ. Graz, Austria). [*Z. Vitamin-Hormon- u. Fermentforsch*, **3**, 244–9 (1950) (*in German*); *cf. C. A.*, **43**, 5842*d*.]

The dilutions required to elicit convulsions in frogs were: strychnine (I) 1 : 1 : 10,000, picrotoxin (II) 1 : 4,000, brucine (III) 1 : 500, cardiazole (IV) 1 : 200. The dilutions required for complete inhibition of the enzymic decomposition of the sensory nerve fiber agent were: (I) 1 : 10,000, (II) 1 : 2,000, (III) 1 : 1,000, (IV) 1 : 250. The dilutions required for complete inhibition of cholinesterase, on the other hand, were: (I) 1 : 3,000, (II) 1 : 300, (III) 1 : 300, (IV) 1 : 500. This proves a relationship between the inhibition of the enzymic breakdown of the sensory nerve fiber agent, but not of acetylcholine, and the elicitation of convulsions. Simultaneous inhibition of cholinesterase by eserine affects the nature of the convulsions. ERICH HIRSCHBERG (Chem. Abstr.).

Evaluation of Curarizing Agents in Man. Unna, K. R., Pelikan, E. W., Macfarlane, D. W., Cazort, R. J., Sadove, M. S., and Nelson, J. T. (Univ. of Illinois, Coll. of Med., Chicago). [*J. Am. Med. Assoc.*, **144**, 448–54 (1950); *cf. C. A.*, **44**, 6517*d*.]

Two synthetic compounds with curare-like action, decamethonium bromide (I) and flaxedil (II) have been tested under a variety of conditions. (I) measured by its effect on grip strength, surpasses tubocurarine chloride (III) or (II) in potency. The different drugs have three different thresholds to paralyzing effects on the

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respiratory muscles, being lowest for (I) and highest for (II). The duration of the effect is longest for (III), and shortest for (II). Unlike the tubocurarine preparations, the effect of (I) is not cumulative. No antidote to (I) is known, while neostigmine methyl sulfate mitigates the effects of a subsequent injection of (III). Pretreatment with (III) greatly reduces the curarizing effects of subsequent injections of (I). S. MORGULIS (Chem. Abstr.).

Blood-sugar Curve in Electroshock. Valerio, Valerio, and Cataldi, Luigi (Univ. Naples). [*Riforma méd.*, **64**, 606–8 (1950).]

Within 10 to 30 minutes after initiation of shock treatment the blood sugar increases to a peak that corresponds to clinical hyperglycemia. A gradual fall to normal is succeeded after 3·5 hours by hypoglycemia that lasts to the end of treatment. A. E. MEYER (Chem. Abstr.).

The Mode of Action of Myanesin on the Central Nervous System. Henneman, Elwood, and Scherrer, Jean. [*Trans. Am. Neurol. Assoc.*, **74**, 208–11 (1949).]

MARION HORN PESKIN (Chem. Abstr.).

The Anti-convulsant Action of 2,2-Diethyl-1, 3-Propanediol and Some of its Homologs and Esters. Berger, F. M., and Ludwig, B. J. (Mount Labs., Inc., New Brunswick, N.J.). [*J. Pharmacol. Exptl. Therap.*, **100**, 27–37 (1950); *cf. C. A.*, **43**, 8546*g*.]

2,2-diethyl-1,3-propanediol (I) strongly antagonizes the convulsant and lethal effects of metrazole, strychnine and picrotoxin. These antagonistic effects occur with doses which do not exert a hypnotic or anesthetic action. (I) can be effectively administered enterally or parenterally. Its duration of action is short. (I) does not affect spinal reflexes and has little action on the spinal cord. It acts by a depressant effect on the forebrain and midbrain. (I) is partly conjugated in the body as an ether type glucuronide. Another portion is oxidized to α,α-diethylhydracrylic acid (II). The further oxidation product, diethylmalonic acid (III) was not found in the urine of patients receiving (I). (II) and (III) in doses of 400 mgm./kgm. had no anti-convulsant action. The 2,2-dimethyl, 2-methyl-2-ethyl, 2-methyl-2-propyl, 2-methyl-2-isopropyl, 2-methyl-2-butyl, 2-ethyl-2-butyl, 2-ethyl-2-phenyl, 2,2-dipropyl and 2,2-dibutyl homologs of (I) showed an anti-convulsant activity of a similar order to that of (I). None had a longer duration of action. (I) diacetate had a less intense but more prolonged action than (I). (I) monoacetate, succinate and dibenzoate showed no advantage over (I).

L. E. GILSON (Chem. Abstr.).

Anti-convulsant Properties of Benadryl and Pyribenzamine. Swinyard, Ewart A., Jolley, Joel M., and Goodman, Louis S. (Univ. of Utah, Salt Lake City). [*Proc. Soc. Exptl. Biol. Med.*, **75**, 239–42 (1950).]

Benadryl, pyribenzamine and dilantin all protected rats to a certain extent against electroshock convulsions, but had no preventive action against metrazole-induced convulsions. L. E. Gilson (Chem. Abstr.).

The Action of Hexachlorocyclohexane on the Central Nervous System (Warm-blooded Animals). Herken, Hans (Freie Univ., Berlin). [*Klin. Wochschr.*, **28**, 582–4 (1950).]

Aqueous suspensions of γ-hexachlorocyclohexane inhibit metrazole cramps in rats. The β-isomer postpones the onset of the cramps, while the α-isomer had no effect. In paraffin solution less cramp inhibition is experienced. Strychnine tetanus was prevented in some animals with gammexane. One large dose has more effect than several small ones, which points to an allobiotic action.

DORIT L. NOETHER (Chem. Abstr.).

The Spasm-preventing Effect of Histamine and Nicotinic Acid on Experimental Human Convulsions. Kajtor, Ferene (Univ. Debrecen, Hungary). [*Kiserletes Orvostudomany*, **2**, 206–17 (1950).]

Intravenous injections of 1·1–2·4 mgm. histamine (I) inhibited metrazole convulsions, but they were without effect against convulsions caused by electric

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shock. Nicotinic acid, nitroglycerine and adrenaline showed no preventive effects. The inhibiting effect of (I) was proportional to the dose and lasted for about 40 seconds. The simultaneous administration of (I) with metrazole inhibited convulsions; (I) was ineffective when given more than 40 seconds after the injection. The inhibiting effect of (I) is explained by the direct action on the nerve cells or through the autonomic nervous system. Acetylcholine bromide, carbamylcholine and amyl nitrite showed spasm-preventing effects similar to (I), but much weaker.
I. FINALY (Chem. Abstr.).

Lethal Barium Chloride Poisoning with Special Reference to Changes in the Cerebral Tissues. Fazekas, I. Gyula. [*Orvosi Hetilap*, **90**, 280–3 (1949).]

In 4 cases of poisoning from administration of 7 to 20 gm. $BaCl_2$, death occurred in 4·5–23 hrs. after intake. Severe changes occurred in the tissues of the central nerve system.
ISTVAN FINALY (Chem. Abstr.).

Pharmacology of the Nerve System Regulating Metabolism. Issekutz, Bela, sen., and Issekutz, Bela, jun. [*Orvosi Hetilap*, **90**, 257-63 (1949).]

Benzedrine phosphate, pulsoton, ephedrine and thyroxine increase the gas metabolism by excitation of the metabolism centers belonging to the sympathetic nerve system. This effect may be stopped by hypothalamic hypnotics, especially by morphine, scopolamine and dihydroergocornine. These latter agents were ineffective against adrenaline and 2,4-dinitrophenol, which directly increased cell oxidation.
ISTVAN FINALY (Chem. Abstr.).

Antabuse and the Metabolism of Alcohol. Newman, Henry W. (*Stanford Univ. School of Med., San Francisco*). [*Calif. Med.*, **73**, 137–40 (1950).]

Two dogs which received orally 0·5 gm. antabuse (I) (tetraethylthiuram) on the first day, 0·25 gm. on the 2nd, and 0·125 gm. daily for a week showed after injection of 1 gm./kgm. EtOH a normal blood concentration of EtOH, while their blood acetyldehyde (II) went up irregularly to 0·6 gm./100 c.c. Upon infusion of 185 mgm./kgm. (II), blood (II) increased to 2·0–4·0 mgm. Conclusion: (I) slows down the metabolism of (II).
F. FROMM (Chem. Abstr.).

Antabuse Therapy in Chronic Alcoholism. Dale, Paul W., and Ebaugh, Franklin G. (*Univ. of Colorado School of Medicine, Denver*). [*Am. J. Med. Sci.*, **220**, 103–9 (1950).]

A review of previous literature and a report of a new series of 29 cases in which "recovery" occurred in 9 and some improvement in 12. The action of tetraethylthiuram disulfide (antabuse) in producing unpleasant symptoms in persons taking alcohol is apparently due to formation of high blood levels of AcH from the alcohol. Caution is recommended, since several deaths have been reported during the course of an antabuse-alcoholic reaction. although few untoward reactions to antabuse alone have occurred.
MARION HORN PESKIN (Chem. Abstr.).

Effect of Tetraethylthiuram Disulfide (Antabuse) on Metabolism of Lactic Acid in the Human Organism. Jokivartio, E. (*Univ. Helsinki, Finland*). [*Acta Pharmacol. et Toxicol.*, **6**, 107–14 (1950).]

Treatment with antabuse prevented to a considerable but variable extent the rise in blood lactic acid which usually follows heavy muscular work by alcoholics and non-alcoholics.
L. E. GILSON (Chem. Abstr.).

New Parasympathetic Stimulant (Ethyl 3,3-Dimethyl-5-allylbarbituric Acid). I. Its Effect on Gastric Secretion. Ballem, C. M., Noble, R. L., and Webster, D. R. (*Can. Med. Assoc. J.*, **58**, 447–50 (1948).]

Na ethyl 3,3-dimethyl-5-allylbarbituric acid is a powerful stimulant to gastric secretion in dogs. The injection of 4 gm. per kgm. of body-weight, subcutaneously, in a 36-kgm. dog caused secretion of juice with a pH of 1·4 at the rate of 462 ml. per hour. The main action is on the acid- and mucus-producing cells, with a less marked action on the peptic cells. The action is central and is prevented by vagotony, tetraethylammonium chloride, or nembutal anesthesia. There is also an apparent paralysis of the nictitating membrane and reaction of the pupil, suggesting a depression of sympathetic function. Larger doses are followed by symptoms of excitement and inco-ordination.
B. A. (Chem. Abstr.).

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Action of Various Barbiturates on the Parenchymatous Organs in Narcosis of Long Duration. Carlon, C., and Mondini, P. (Univ. Padova, Italy). [*Giorn. ital. anestesiol.*, **15**, 282–6 (1949).]

Guinea-pigs were narcotized with farmotal, thionarcon or narconumal, with doses progressively less with time. Observations were made on liver, kidney and spleen for narcoses of 1–3 hours. Especially the liver and kidney showed diffuse congestion and degeneration of the epithelium. Narcosis with farmotal was rapid and profound, with no muscular tremor; breathing was faster, and respiration arrested after 120–150 minutes. Thionarcon gave superficial sleep even after 2–3 hours, and the animals reacted well to stimuli. With larger doses breathing was slowed down and respiration paralyzed. Narconumal was less toxic; narcosis was sufficiently deep but brief. Diffuse muscular tremors were observed. The animals breathed normally, but reacted to pain a few minutes after injection.

M. ELLIOTT (Chem. Abstr.).

Pain Relief with Hypnotic Doses of Barbiturates, and a Hypothesis. Keats, Arthur S., and Beecher, Henry K. (Harvard Univ. Med. School. Boston). [*J. Pharmacol. Exptl. Therap.*, **100**, 1–13 (1950).]

Chiefly discussion. Hypnotic doses of pentobarbital-Na given intravenously relieved post-operative pain in 50 per cent. of the patients treated. A hypothesis is presented to explain the analgesic properties of pentobarbital by depression of internuncial spread of pain impulses in the brain, and inhibition of the psychic phase of pain experience.

L. E. GILSON (Chem. Abstr.).

Rate of Penetration of Barbituric Acid Derivatives into the Brain. Butler, Thomas C. (Johns Hopkins Univ., Baltimore, Md.). [*J. Pharmacol. Exptl. Therap.*, **100**, 219–26 (1950).]

After intravenous injection of barbital and hexethal (ortal) in mice, the concentrations in the brain were determined by ultraviolet spectrophotometric methods which are described in detail. The concentration of barbital in the brain rises gradually for a considerable time after the injection. The increasing concentration corresponds closely with the increasing intensity of neurological effects. Hexethal, which shows immediate onset of anesthetic effects, attains its maximum concentration in the brain very quickly. It appears that the wide differences among the 5,5-disubstituted barbiturates with respect to the rate of onset of effects after intravenous injection are attributable to differences in rates of penetration into the brain.

L. E. GILSON (Chem. Abstr.).

The Excretion of Barbituric Acids during Continued Sleep Treatment of Schizophrenia. Staub, H. (Univ. Zurich, Switz.). [*Schweiz. Arch. Neurol. Psychiat.*, **65**, 330–70 (1950).]

As a treatment for schizophrenia various mixtures of barbital (I), phenobarbital (II), allobarbital (III), and sandoptal (IV), with and without urethan, novalgin, sympathol, dionine and scopolamine-HBr, were used, usually by intramuscular injection, to induce deep (6 cases), or twilight (3 cases) sleep, continued for periods of 12–14 days, except for one 9-day and one 28-day treatment. The excretion of (I), (II), (III) and (IV) in the urine was determined throughout the periods of treatment and for several days after. The urine was acidified, if necessary, with AcOH, concentrated in vacuum to a syrup, and extracted with EtOAc. The extract was evaporated, dissolved in a little water, acidified, saturated with NaCl, and extracted with Et_2O, which was evaporated. The residue was dissolved in 10 per cent. NaOH and extracted with Et_2O to remove alkaloids and neutral substances. The alkaloid solution was acidified with HCl, saturated with $NaHCO_3$, and extracted with Et_2O. The dried extract was sublimed in vacuum at 120–130°, and the crystal sublimate was dissolved in water. The solution was extracted with Et_2O, which was evaporated. The residue was weighed as total barbiturates (V). The unsaturated (III) or (IV) (they were not given together), was removed by chromate oxidation of the mixture, (I) and (II) were extracted, purified as before, and distilled by comparison of the m.p. with m.ps. of known mixtures of pure (I) and (II). The daily excretion of (V) was closely related to the volume of urine. There were wide variations in the percentages of the daily dose of (I), (II), (III) and (IV)

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excreted. The excretion in the after period varied widely among patients, but usually continued for several days. The total excretion for the entire period was about 70 per cent. of the amount given for (I), 40 per cent. for (III), and 20 per cent. for (II) and (IV). The findings are discussed in detail in relation to the type of therapy and the effect of alkaloids and other drugs.

The Distribution of Barbituric Acids in the Organism of Mentally Diseased Patients during Sleep Therapy. [*Ibid.*, 371–80.]

(V), (I), (II) and (III) were determined in some or all of 14 organs, blood, bile and bladder urine from three patients who had died during sleep therapy with a mixture of (I), (II) and (III) (*cf. C. A.*, **40**, 402[9] and above for methods used). Concentrations of each barbiturate tended to be similar in different organs of the same patient, but there were some exceptions. The lowest concentration of (I), (II) or (III) was 1·1 mgm., and the highest 17·4 mgm. per 100 gm. In one patient a concentration of 40·6 mgm. (V) per 100 gm. was found in the liver. Concentrations in the brain were generally similar to those found in other organs. The results are compared with the dosage of (I), (II), (III) and (IV), which had been given. WARREN N. SPERRY (Chem. Abstr.).

The Enzymic Mechanism of Barbiturate Action. Persky, H., Golstein, M. S., and Levine, R. (Michael Reese Hosp., Chicago). [*J. Pharmacol. Exptl. Therap.*, **100**, 273–83 (1950).]

The effect of pentobarbital on various enzyme systems was studied *in vitro*. Pentobarbital was shown to block the pyruvic acid oxidase system, most likely at the oxidation of the 2-carbon fragment. It does not block the oxidation of flavoprotein by either O or cytochrome c. It apparently blocks the essential SH groups of the dehydrogenase of the pyruvic acid system. The relation of this enzyme inhibition to narcosis *in vivo* is discussed.

L. E. GILSON (Chem. Abstr.).

Anti-convulsant Drugs. III. Some Allophanates. Spielman, M. A., Barnes, J. D., and Close, W. J. (Abbott Labs., North Chicago). [*J. Am. Chem. Soc.*, **72**, 2520–2 (1950); *C. A.*, **43**, 2169*c*.]

Thirty-six esters of allophanic acid were prepared and tested for anti-convulsant activity. The most active compounds were those derived from secondary and tertiary alcoholics of 5–7 C. The allophanates were mild hypnotics. HCNO was prepared by subliming $(HNCO)_3.2H_2O$ and passing same through a Pyrex tube in electric combustion furnace at dull, red heat, and then leading HCNO directly into the alcohol. A gentle current of CO_2 was used. Reaction required about 15 minutes. Receiver was removed, stoppered, and let stand 24 hours or longer, allophanate filtered and washed with little Et_2O, and crystallized from EtOH previously saturated with CO_2. Carbamates, as by-products, in part, caused low yields. A second method was illustrated by the addition to glacial AcOH and tertiary $C_5H_{11}OH$ of KCNO, portion-wise with stirring. Temperatures rose to 50° and then subsided. After standing several hours, mixture was diluted with H_2O and extracted with Et_2O, Et_2O washed with H_2O and evaporated and residue crystallized from EtOH, yielding tert-amyl allophanate, m. 166–8°. Results from KCNO were in general erratic and 3-Me-2-C_4H_9OH gave only carbamate. Anti-convulsant tests in mice were made by electroshock or by injection of metrazole in graded oral doses, usually 200, 400 and 800 mgm./kgm. Their low toxicity was evident in the virtual absence of any effects except depression. The compounds prepared were moderately hypnotic. None were considered worthy of clinical trial.

R. E. DUNBAR (Chem. Abstr.).

Effect of Convulsant and Anti-convulsant Agents on the Activity of Cytochrome Oxidase. Torda, Clara, and Wolff, Harold G. (Cornell Univ., Med. Coll., New York, N.Y.). [*Proc. Soc. Exptl. Biol. Med.*, **74**, 744–6 (1950).]

The activity of cytochrome oxidase preparations from rat liver or brain was considerably increased in the presence of the convulsant agents, acetylcholine, caffeine, camphor, DDT, Me salicylates, metrazole, picrotoxin, scilliroside and strychnine, in concentrations of 10^{-5} to 10^{-3} M. The activity was not significantly

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modified by choline or the anti-convulsant agents, hydantoin, methylphenylethylhydantoin, phenobarbital, Na phenylhydantoinate, and tridione, in 10^{-3} M and lower concentrations. Convulsant agents, therefore, activate at least two processes, a monoxidative mechanism that initiates the seizures and the oxidative recovery processes occurring during the convulsive seizures.

L. E. GILSON (Chem. Abstr.).

The Site of Action of Metrazole and Coramine. V. The Contrasting Basic Vegetative Action of both Drugs. Hahn, Fritz, Muller, Dieter, and Rummel, Walter (Med. Akad. Dusseldorf, Ger.). [*Arch. exptl. Path. Pharmakol.*, **209**, 312–24 (1950); *cf. C. A.*, **43**, 7137*e*.]

Frogs receiving coramine (I) in doses of 0·6 to 2·0 gm./kgm. were apathetic and flaccid with occasional convulsions. Their melanophores were dilated. Frogs receiving metrazole (II) in doses of 80–100 mgm./kgm. were active and excitable and their melanophores and skin muscles contracted. The effect of (I) on the melanophores was counteracted by (II) and adrenaline. N,N-diethy-3,5-dimethyl-4-isoxazol carboxamide and N,N,N′,N′-tetraethylphthalamide had a (I)-like action on the melanophores, while 4-cyclohexyl-3-ethyl-4,1,2,-triazone and pyramidone acted like (II) (IV).

VI. The Mechanism of the Blood Pressure Effect of Central Analeptics. Fritz, Hahn, and Rummel, Walter (Pharmakol. Inst. Med. Akad., Dusseldorf, Ger.). [*Ibid.*, 325–39.]

Metrazole (I) injections into the vertebral artery of cats anesthetized with 5 per cent. chloralose in 25 per cent. urethan, after vagotomy and severing of the carotid sinus nerves, produced no regular increase in blood pressure as seen after intravenous injections. Very often the effect was hypotonic and the hypertonic response either preceded or followed the hypotonic one. The equilibrium of the blood pressure regulating center in the medulla was considered responsible for the effect of an intravertebral injection of (I). Coramine (II) had a hypotonic effect after intravenous or after intravertebral injection. The effect of (II) probably is also referable to the blood pressure regulating center in the medulla. An initial hypertonic effect after intervertebral injection is more often seen with (II) than with (I), while the late hypertonic effect is rare and weak with (II). Picrotoxin and triazole derivatives behaved like (I). Caffeine and hexetone had no hypotonic action after intravenous injection. RICHARD F. RILEY (Chem. Abstr.).

A Comparison of the Anti-convulsant Action of Some Phenylhydantoins and their Corresponding Phenylacetylureas. Swinyard, Ewart A., Toman, James E. P., Jolley, Joel M., and Henrie, Madge (Univ. of Utah, Salt Lake City). [*J. Pharmacol. Exptl. Therap.*, **100**, 151–7 (1950).]

Phenylacetylurea and its homologs with Me, Et and Ph substituted on the α-*C* of the phenylacetyl group, and the corresponding phenylhydantoins were compared with respect to solubility in water, minimal neurological toxic dose in rats, ability to modify maximal electroshock seizure, anti-metrazole potency in rats, and ability to suppress induced hyperexcitability and hyperresponsiveness in frog sciatic nerve. All the compounds showed some anti-convulsant potency except the very insoluble diphenylacetylurea. There was no close correlation between solubility and pharmacological properties. The hydantoins were much more soluble than the phenylacetylureas. There was no remarkable difference in the toxicities and relative anti-metrazole activities of the two series. L. E. GILSON (Chem. Abstr.).

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