

HANDBOOK OF NEUROCHEMISTRY

Edited by Abel Lajtha

2

**STRUCTURAL
NEUROCHEMISTRY**

HANDBOOK OF NEUROCHEMISTRY

Edited by Abel Lajtha

*New York State Research Institute
for Neurochemistry and Drug Addiction
Ward's Island
New York, New York*

VOLUME II

STRUCTURAL NEUROCHEMISTRY

 PLENUM PRESS • NEW YORK—LONDON • 1969

Contributors to this volume:

- | | |
|---------------------|---|
| Leo G. Abood | Center for Brain Research and Department of Biochemistry, University of Rochester, Rochester, New York (page 303) |
| C. W. M. Adams | Sir William Dunn Professor of Pathology, Guy's Hospital Medical School, London University, and Honorary Consultant Morbid Anatomist, Guy's Hospital, London, Great Britain (page 525) |
| Joseph Altman | Laboratory of Developmental Neurobiology, Department of Biological Sciences, Purdue University, Lafayette, Indiana (page 137) |
| Samuel H. Barondes | Departments of Psychiatry and Molecular Biology, Albert Einstein College of Medicine, Bronx, New York (page 435) |
| S. Berl | Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, New York (page 447) |
| D. D. Clarke | Chemistry Department, Fordham University, New York, New York (page 447) |
| T. Z. Csáky | Department of Pharmacology, University of Kentucky College of Medicine, Lexington, Kentucky (page 49) |
| H. F. Daginawala | Department of Pediatrics, The University of Texas Medical Branch, Galveston, Texas (page 241) |
| Hugh Davson | Department of Physiology, University College, London, England (page 23) |
| Eduardo De Robertis | Instituto de Anatomia General y Embriologia, Facultad de Medicina Universidad de Buenos Aires, Buenos Aires, Argentina (page 365) |
| B. Droz | Departement de Biologie, Commissariat a l'Energie Atomique, Saclay, France (page 505) |

K. A. C. Elliott	Department of Biochemistry and the Montreal Neurological Institute, McGill University, Montreal, Canada (page 103)
Ezio Giacobini	Department of Pharmacology, Karolinska Institutet, Stockholm, Sweden (page 195)
John A. Harvey	Department of Psychology, University of Iowa, Iowa City, Iowa (page 115)
Robert Katzman	The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, New York (page 11)
G. A. Kerkut	Department of Physiology and Biochemistry, Southampton University, Southampton, England (page 539)
Edward Koenig	Department of Physiology, State University of New York at Buffalo, Buffalo, New York (page 423)
Harold Koenig	Neurology Service, V. A. Research Hospital, and Department of Neurology and Psychiatry, Northwestern University Medical School, Chicago, Illinois (page 255)
Giulio Levi	Center of Neurobiology, Department of Biochemistry, Istituto Superiore di Sanita, Rome, Italy (page 71)
Richard N. Lolley	Neurochemistry Laboratories, Veterans Administration Hospital, Sepulveda, California, and Department of Anatomy, UCLA School of Medicine, Los Angeles, California (page 473)
P. Maxcy, Jr.	Department of Pediatrics, The University of Texas Medical Branch, Galveston, Texas (page 241)
Henry Mcllwain	Department of Biochemistry, Institute of Psychiatry, British Postgraduate Medical Federation, University of London, Maudsley Hospital, London (page 115)

Hanna M. Pappius	The Donner Laboratory of Experimental Neurochemistry, Montreal Neurological Institute, and Department of Neurology and Neurosurgery, McGill University, Montreal, Canada (page 1)
Giuseppe Porcellati	Department of Biological Chemistry, University of Pavia, Pavia, Italy (page 393)
D. A. Rappoport	Department of Pediatrics, The University of Texas Medical Branch, Galveston, Texas (page 241)
Georgina Rodríguez de Lores Arnaiz	Instituto de Anatomía General y Embriología, Facultad de Medicina Universidad de Buenos Aires, Buenos Aires, Argentina (page 365)
Steven P. R. Rose	Medical Research Council Metabolic Reactions Research Unit, Department of Biochemistry, Imperial College, London, England (page 183)
Herbert Schimmel	The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, New York (page 11)
V. P. Whittaker	Department of Biochemistry, University of Cambridge, Cambridge, England, and New York State Institute for Basic Research in Mental Retardation, New York, New York (page 327)

PREFACE

That chemicals (although not always called by this name) affect the brain and its functions, such as behavior, has been known for thousands of years. It is therefore surprising that the concept that chemical mechanisms are at least partially responsible for the complex functions of the brain is so recent. Investigation of the closely interlinked biophysical and biochemical properties of the nervous system has achieved many notable successes in recent years and is the most exciting development in 20th-century science.

Although all the morphology, the activity, and the alteration of the brain, whether bioelectric, biochemical, pathological, or structural, constitute an organic and indivisible whole, the ambition of the *Handbook* is to look at only a few aspects of this whole and to focus the discussions on the experiments that the neurochemists have performed.

Neurochemical study of the nervous system has, perhaps of necessity, gone through several phases: the first phase was more analytical and involved study of the composition of the tissue; the second, more recent phase clarified many of the metabolic sequences that occur in this tissue. Clearly, both were essential, but they showed that additional approaches are necessary. The present phase seems to be the study of control processes; present interest focuses on what determines, in a qualitative and quantitative fashion, the processes occurring in the nervous system. Perhaps the next phase will be the study of function, the study of the final stage of integration.

With the great speed of advance of knowledge in our field, it is difficult not to be an optimist. We now talk about things even as complex (and not so long ago seemingly unapproachable) as memory, learning, sleep, emotion, discrimination, and pain, and we not only talk about them but also devise meaningful experiments to study these extremely complex phenomena.

Not only can we study such complex phenomena as outside observers, but also we can manipulate them in a number of ways in order to understand them. It is hardly necessary to emphasize here that it may be too ambitious even at our present stage of knowledge to hope that this book will help in understanding the complexities of the nervous system; what we can hope is that it will help to formulate further research.

The divisions of the various volumes of the *Handbook* are not very sharp; still, the present volume emphasizes structural aspects of neurochemistry. Structural aspects are hardly more important or more complex in any other

organ than in the nervous system. This seems to be not only one of the most structurally complex organs, but also one whose structure obviously has great significance for its function and whose mechanisms clearly cannot be understood without understanding the various structures where these mechanisms proceed. Life in all its aspects has great unity, and the facts we learn not only are clearly important for brain research in particular, or for the function of the nervous system, but also have a broader meaning for our concepts of living organisms as a whole. Therefore, from structural as well as other aspects, the results of brain research are applicable to, and contribute to, other disciplines.

It was pointed out in the first volume of this *Handbook*—and, unfortunately, it can be pointed out in any of the future volumes as well—that because of the practical necessity to limit the size of the volumes a great many important contributions could be only very briefly discussed, some not at all. The decision of what to include or exclude was often somewhat arbitrary. For this, mostly the editorial scissors (or short-sightedness) can be blamed, but perhaps it will serve as an excuse that the book is planned as a starting point of, rather than a substitute for, the future search for the wealth of information that has been written in the original publications or in the many reviews.

Among the purposes of the *Handbook* is to attract new talent to the field of brain research by giving to the reader a brief look at what the workers in this area have found out and what questions have been asked, even in a tentative way. Hopefully, many will carry this work further, at times even proving that in the past the wrong questions were asked.

The task, of course, is formidable. The structure proves to be more complex the more we investigate it: the more we find out about the brain, the more we realize what there is to be found out. But what is most significant, the task ahead, which not so long ago seemed impossible, seems less forbidding. We still know very little, but all the facts that seem to be established seem to form a reasonable complex, where all the parts fit and where what we have found so far seems to make sense. There is very little, if any, evidence that would indicate that it is impossible to understand brain function in even its most intricate details. Obviously, the neurochemists who wrote the chapters of these volumes hope that their work will contribute to this understanding. The editor has no doubt that it will and that the fuller understanding of the brain will be one of mankind's greatest achievements.

Abel Lajtha

New York, New York
February 1969

CONTENTS OF VOLUME I: Chemical Architecture of the Nervous System

Chapter 1

Inorganic Constituents by Donald B. Tower

Chapter 2

Carbohydrates by H. S. Bachelard

Chapter 3

Amino Acids by Williamina A. Himwich and Harish C. Agrawal

Chapter 4

Peptides by John J. Pisano

Chapter 5

Proteins by Samuel Bogoch

Chapter 6

Acidic Proteins by Blake W. Moore

Chapter 7

Nucleic Acids by D. A. Rappoport, R. R. Fritz, and J. L. Myers

Chapter 8

Lipids by George Rouser and Akira Yamamoto

Chapter 9

Myelin by Lewis C. Mокrasch

Chapter 10

Sterols by R. Paoletti, E. Grossi-Paoletti, and R. Fumagalli

Chapter 11

Glycoproteins by Eric G. Brunngraber

Chapter 12

Mucopolysaccharides by Richard U. Margolis

Chapter 13

Iron by Ole J. Rafaelsen and Bent Kofod

Chapter 14

Gray-White Matter Differences by Jørgen Clausen

Chapter 15

Cerebral Metabolism *in Vivo* by William Sacks

Chapter 16

Enzymes by N. Seiler

Appendix

Subject Index

CONTENTS OF VOLUME III: Metabolic Reactions in the Nervous System

Chapter 1

Carbohydrate Metabolism by R. Balázs

Chapter 2

Glycogen Metabolism by R. V. Coxon

Chapter 3

Cytochromes and Oxidative Phosphorylation by C. L. Moore and P. M. Strasberg

Chapter 4

Phosphatases by S. R. Cohen

Chapter 5

Peptide Hydrolases by N. Marks

Chapter 6

Biochemistry of Selected Amino Acids by H. J. Strecker

Chapter 7

Metabolism of Aromatic Amino Acids by G. Guroff and W. Lovenberg

Chapter 8

Sulfur Amino Acids by M. K. Gaitonde

Chapter 9

γ -Aminobutyric Acid by C. F. Baxter

*Chapter 10***Glutamate and Glutamine** by C. J. Van den Berg*Chapter 11***Glycine: Its Metabolic and Possible Transmitter Roles** by M. H. Aprison, R. A. Davidoff, and R. Werman*Chapter 12***Deamination of Nucleotides and the Role of Their Deamino Forms in Ammonia Formation from Amino Acids** by H. Ch. Buniatian*Chapter 13***Cerebrosides and Sulfatides** by N. S. Radin*Chapter 14***Gangliosides** by L. Svennerholm*Chapter 15***Sphingomyelin: Enzymatic Reactions** by A. Rosenberg*Chapter 16***Metabolism of Phosphoglycerides** by R. J. Rossiter and K. P. Strickland*Chapter 17***Metabolism of Phosphoinositides** by J. N. Hawthorne and M. Kai*Chapter 18***Lipid Haptens** by M. M. Rapport*Chapter 19***Fatty Acids** by A. F. D'Adamo, Jr.*Chapter 20***Cholesterol Metabolism** by A. N. Davison*Chapter 21***Metabolism of Myelin Constituents** by F. N. LeBaron

FURTHER VOLUMES

VOLUME IV: Control Mechanisms in the Nervous System

VOLUME V: Metabolic Turnover in the Nervous System

VOLUME VI: Alterations of Chemical Equilibrium in the Nervous System

VOLUME VII: Pathological Chemistry of the Nervous System

CONTENTS

Chapter 1

Water Spaces	1
by Hanna M. Pappius	
I. Introduction	1
II. Definition of Spaces	1
III. Problems of Methodology	2
A. General	2
B. Experiments <i>in Vivo</i>	2
C. Experiments <i>in Vitro</i>	3
IV. Chemically Determined Spaces	3
A. Spaces <i>in Vivo</i>	3
B. Spaces <i>in Vitro</i>	6
C. Summary	7
V. Extracellular Space Determined by Electrical Impedance Measurements	7
VI. Electron Microscopy and Extracellular Spaces in Cerebral Tissues	8
VII. Abnormal Spaces	8
VIII. Conclusion	9
IX. References	9

Chapter 2

Water Movement	11
by Robert Katzman and Herbert Schimmel	
I. Analogy with Lipid Bilayers	11
II. Diffusion of Labeled Water Between Blood and Brain	12
III. Flux of Water Between Blood and Brain Under Hydrostatic or Osmotic Pressure Gradients	12
IV. Comparison of Osmotic and Diffusional Flow	13
V. Effect of Volume Diffusion on Half-Times	15

VI. Prediction of Effects of Osmotic Treatments	16
VII. Relationship of Changes in Brain Water to Changes in Intracranial Pressure—Clinical Applications	20
VIII. References	21

Chapter 3

The Cerebrospinal Fluid	23
by Hugh Davson	
I. Location	23
II. Origin and Fate	23
III. Functional Insulation from Blood	25
IV. Chemical Composition	26
A. Protein	27
B. Crystalloids	27
V. Relation of Cerebrospinal Fluid to Brain and Cord	30
A. Regional Variations in Composition	32
B. Freshly Secreted Cerebrospinal Fluid	33
C. Secretion of Extracellular Fluid	33
D. Lymphatic Role of the Cerebrospinal Fluid	35
VI. Blood-Brain Barrier	38
A. Goldmann's Experiments	39
B. Sugars and Amino Acids	40
C. Cerebral Edema	41
VII. General Conclusions	43
VIII. References	43

Chapter 4

Choroid Plexus	49
by T. Z. Csáky	
I. Introduction	49
A. Morphology	49
B. Metabolism and Enzyme Content	51
C. Function	51
II. Experimental Techniques	52
A. <i>In Vitro</i> Technique	52
B. <i>In Vivo</i> Technique	53
III. Blood-to-CSF Transport	53
IV. Mechanism of CSF Formation by the Choroid Plexus	54
V. Permeability to Water	55

VI. Apparent Uphill Movement of Water	56
VII. Transport of Electrolytes	56
A. Sodium	56
B. Potassium	57
C. Calcium and Magnesium	58
D. Chloride	58
E. Iodine, Bromides, and Thiocyanate	59
VIII. Transport of Nonelectrolytes	59
IX. Energy-Dependent Accumulation of Substances in the Choroid Plexus	60
X. Transport from the CSF into the Blood	61
XI. Pinocytosis	62
XII. Effects of Drugs on Choroidal Transport	62
A. 2,4-Dinitrophenol (DNP)	63
B. Digitalis	63
C. Acetazolamide (Diamox)	64
XIII. References	65

Chapter 5

Spinal Cord

by Giulio Levi

I. Introduction	71
II. Inorganic Constituents	71
III. Carbohydrates	73
A. Carbohydrate Levels and Transport	73
B. Enzymes of Glucose and Glycogen Metabolism	75
C. Enzymes of Krebs Cycle and Respiratory Enzymes— O ₂ Uptake	75
IV. Lipids	76
A. Lipid Composition of Spinal Cord	76
B. Developmental Changes in Spinal Cord Lipids	79
C. Phosphorylated Compounds Related to Phospholipids	79
D. Prostaglandins	82
V. Proteins	82
A. Amino Acids	82
B. Peptides	84
C. Proteins	85
VI. Phosphorus, Labile Phosphates, and Nucleic Acids	87
VII. Pharmacologically Active Substances	88
A. Acetylcholine and Related Enzymes	88
B. Monoamines and Related Enzymes	89
C. Polyamines	92

VIII. Hydrolases and Carbonic Anhydrase	92
A. Phosphohydrolases	92
B. Nonspecific Esterases	93
C. Carbonic Anhydrase	93
IX. Vitamins	93
X. Concluding Remarks	94
XI. References	95

Chapter 6

The Use of Brain Slices. 103

by K. A. C. Elliott

I. Introduction	103
II. Permissible Thickness	103
III. Preparation and Weighing of Slices	104
IV. Suspending Media	107
V. Methods of Study	108
VI. Criticism	108
VII. Types of Information Gained with Slices	110
VIII. Further Developments	112
IX. References	113

Chapter 7

Electrical Phenomena and Isolated Tissues from the Brain. 115

by John A. Harvey and Henry McIlwain

I. Introduction	115
II. Techniques	115
A. Tissue Preparation	115
B. Incubation Conditions	118
C. Calculations	121
III. Ion Exchange	123
A. Maintenance of Normal Ionic Gradients	123
B. Ion Content and Fluxes Under Normal Conditions	125
C. Effects of Electrical Stimulation on Ion Movement— Recovery	125
D. Associated Phenomena	127
IV. Consequent Metabolic Changes	129
V. Associated Electrical Phenomena	129
A. Resting Membrane Potential	129
B. Electrical Responses to Stimulation	131
VI. References	134

*Chapter 8***DNA Metabolism and Cell Proliferation** 137
by Joseph Altman

I. Introduction	137
A. Classical and Modern Views of Cell Proliferation in the Brain	138
II. Biochemical Studies of DNA Metabolism	143
A. Estimates of Cell Concentration in the Brain	143
B. Some Shortcomings of the Technique	146
III. Thymidine- ³ H Autoradiography	146
A. Technique of Thymidine- ³ H Autoradiography	147
B. Evaluation of Autoradiograms	149
IV. Cell Proliferation in the Embryonic Nervous System	153
A. Cell Proliferation in the Primitive Neuroepithelium	153
B. Cell Proliferation in the Secondary Germinal Matrix	155
V. Regional Studies of Postnatal Cell Proliferation in the Brain	158
A. Postnatal Neurogenesis	158
B. Postnatal Gliogenesis	167
C. Meninges, Capillaries, and Choroid Plexus	168
VI. Conditions Altering Cell Proliferation in the Brain	169
A. Pathological Effects	170
B. Behavioral Effects	173
VII. References	174

*Chapter 9***Neurons and Glia: Separation Techniques and Biochemical Interrelationships** 183

by Steven P. R. Rose

I. Introduction	183
II. Methodology	183
A. Separation	184
B. Isolation	184
C. Nature of the Isolated Cells: Comparison with Microdissection Techniques	185
D. Choice of Method	186
III. Biochemical Data	186
A. Chemical Differences	186
B. Enzymatic Differences	187
C. Metabolic Differences	188
IV. Neuronal-Glial Interrelationships	189
V. Note added in Proof	191
VI. Reviews	191
VII. References	191