



PROGRESS IN BRAIN RESEARCH

VOLUME 45

# PERSPECTIVES IN BRAIN RESEARCH

Proceedings of the 9th International Summer School of Brain Research,  
Organized by the Netherlands Central Institute for Brain Research, Amsterdam,  
and held at the Royal Netherlands Academy of Arts and Sciences at Amsterdam,  
The Netherlands on July 28 — August 1, 1975

EDITED BY

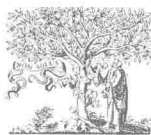
M. A. CORNER

AND

D. F. SWAAB

(J. Sels Assistant Editor)

*Netherlands Central Institute for Brain Research,  
IJdijk 28, Amsterdam (The Netherlands)*



ELSEVIER SCIENTIFIC PUBLISHING COMPANY  
AMSTERDAM/NEW YORK/OXFORD

1976

PUBLISHED BY:  
ELSEVIER/NORTH-HOLLAND BIOMEDICAL PRESS  
335 JAN VAN GALENSTRAAT, P.O. BOX 211  
AMSTERDAM, THE NETHERLANDS

SOLE DISTRIBUTOR FOR THE U.S.A. AND CANADA:  
ELSEVIER/NORTH-HOLLAND INC.  
52 VANDERBILT AVENUE  
NEW YORK, N.Y. 10017, U.S.A.

Library of Congress Cataloging in Publication Data

International Summer School of Brain Research,  
9th, Amsterdam, 1975.  
Perspectives in brain research.

(Program in brain research ; v. 45)  
Includes index.

I. Brain--Congresses. I. Corner, M. A.  
II. Swaab, D. F. III. Amsterdam. Nederlands  
Centraal Instituut voor Hersenonderzoek. IV. Title.  
V. Series: [DNLM: 1. Brain--Congresses.  
2. Research--Congresses. WL FR667J v. 45 / WL20  
I614 1975p]  
QP376.P7 vol. 45 599'.01'88 ' 76-49820  
ISBN 0-444-41457-6

WITH 176 ILLUSTRATIONS AND 22 TABLES

© ELSEVIER/NORTH-HOLLAND BIOMEDICAL PRESS, 1976

ALL RIGHTS RESERVED.  
NO PART OF THIS PUBLICATION MAY BE REPRODUCED, STORED IN A  
RETRIEVAL SYSTEM, OR TRANSMITTED, IN ANY FORM OR BY ANY MEANS,  
ELECTRONIC, MECHANICAL, PHOTOCOPYING, RECORDING OR OTHERWISE,  
WITHOUT THE PRIOR PERMISSION OF THE COPYRIGHT OWNER.

PRINTED IN THE NETHERLANDS

PROGRESS IN BRAIN RESEARCH  
VOLUME 45  
PERSPECTIVES IN BRAIN RESEARCH

# PROGRESS IN BRAIN RESEARCH

## ADVISORY BOARD

W. Bargmann	Kiel
H.T. Chang	Shanghai
E. De Robertis	Buenos Aires
J.C. Eccles	Buffalo (N.Y.)
J.D. French	Los Angeles
H. Hydén	Göteborg
J. Ariëns Kappers	Amsterdam
S.A. Sarkisov	Moscow
J.P. Schadé	Amsterdam
F.O. Schmitt	Brookline (Mass.)
J.Z. Young	London

## List of Contributors

- J. ARIËNS KAPPERS, Netherlands Central Institute for Brain Research, Amsterdam, The Netherlands.
- G.P. BAERENDS, Zoological Laboratory, University of Groningen, Groningen, The Netherlands.
- R. BALÁZS, Medical Research Council, Developmental Neurobiology Unit, Carshalton, Surrey, Great Britain.
- P. BARTS, Institute of Medical Physics TNO, Utrecht, The Netherlands.
- B. BOHUS, Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands.
- V. BRAITENBERG, Max-Planck-Institute for Biological Cybernetics, Tübingen, G.F.R.
- W. BURR, Institute of Medical Physics TNO, Utrecht, The Netherlands.
- M.A. CORNER, Netherlands Central Institute for Brain Research, Amsterdam, The Netherlands.
- O. CREUTZFELDT, Max-Planck-Institute for Biophysical Chemistry, Dept. of Neurobiology, Göttingen, G.F.R.
- G.S. DAWES, The Nuffield Institute for Medical Research, University of Oxford, Oxford, Great Britain.
- R.M. GAZE, National Institute for Medical Research, London, Great Britain.
- W.H. GISPEN, Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands.
- E.G. GRAY, University College London, Dept. of Anatomy, London, Great Britain.
- E. van HEUSDEN, Institute of Medical Physics TNO, Utrecht, The Netherlands.
- R.A. HOPE, National Institute for Medical Research, London, Great Britain.
- H. HYDÉN, University of Göteborg, Institute of Neurobiology, Göteborg, Sweden.
- R. LEVI-MONTALCINI, Lab. of Cell Biology, Rome, Italy and Dept. of Biology, Washington University, St. Louis, Mo., U.S.A.
- F.H. LOPES DA SILVA, Institute of Medical Physics TNO, Utrecht, The Netherlands.
- J. OLDS, California Institute of Technology, Division of Biology, Pasadena, Calif., U.S.A.
- B.T. PICKERING, University of Bristol, Dept. of Anatomy, Bristol, Great Britain.
- J.S. ROBINSON, The Nuffield Institute for Medical Research, University of Oxford, Oxford, Great Britain.
- S.P.R. ROSE, The Open University, Brain Research Group, Milton Keynes, Bucks., Great Britain.
- A. van ROTTERDAM, Institute of Medical Physics TNO, Utrecht, The Netherlands.
- B. SCHARRER, Albert Einstein College of Medicine, Dept. of Anatomy, Bronx, N.Y., U.S.A.
- J. SCHERRER, University of Paris, Medical Faculty, Pitié Salpêtrière, Lab. of Physiology, Paris, France.
- R.W. SPERRY, California Institute of Technology, Division of Biology, Pasadena, Calif., U.S.A.
- W. STORM VAN LEEUWEN, University Hospital Utrecht, Dept. of Clinical Neurophysiology, Utrecht, The Netherlands.
- L. SVENNERHOLM, University of Göteborg, Dept. of Neurochemistry, Psychiatric Research Centre, Göteborg, Sweden.
- I. URBAN, Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands.
- H. VAN DER LOOS, University of Lausanne, Medical Faculty, Institute of Normal Anatomy, Lausanne, Switzerland.
- P.D. WALL, University College London, Cerebral Functions Research Group, Dept. of Anatomy, London, Great Britain.
- P.A. WEISS, Rockefeller University, New York, N.Y., U.S.A.

- V.P. WHITTAKER, Max-Planck-Institute for Biophysical Chemistry, Dept. of Neurochemistry, Göttingen, G.F.R.
- D. de WIED, Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands.
- T.J.B. van WIMERSMA GREIDANUS, Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands.
- J.Z. YOUNG, University College London, Dept. of Anatomy, London, Great Britain.

## Introduction

“Perspectives in Brain Research” was the theme of the 9th in a series of International Summer Schools organized by the Netherlands Central Institute for Brain Research in Amsterdam. The series was started in the early 1960s on the initiative of Dr. J.P. Schadé, shortly after the assumption of the directorate of the Institute by Dr. J. Ariëns Kappers, until then Professor of Anatomy at the University of Groningen. The fact that Prof. Ariëns Kappers was a close relative of C.U. Ariëns Kappers, the founder and first director of the same institute, lent a unique flavor to the occasion of his retirement in the Summer of 1975. It seemed to us, therefore, that there existed a certain appropriateness for choosing a more general theme than had been the case in previous Summer Schools: one that would complete a cycle, as it were, by pausing to consider where the outstanding unsolved questions in experimental neurobiology now lie, almost 70 years after Prof. Ariëns Kappers’ initiative in stimulating basic research in this field.

Such an assessment was all the more appropriate at this time, since the Brain Research Institute was itself deeply engaged in re-evaluating its own research activities in terms of a collaborative multidisciplinary approach. An explosive growth in the previous decade had left the Institute in possession of material, as well as theoretical, facilities necessary for handling the challenges posed by the study of the nervous system. What was still needed was a well-founded consideration of the direction(s) in which a concerted effort could best be made. Little did any of us anticipate then that a special poignancy was soon to be added to the occasion of the second Prof. Ariëns Kappers’ retirement: a ministerial decision to terminate the very existence of the institution which the first Prof. Ariëns Kappers had created so many years before. The cycle was indeed to be completed, but with a vengeance! This danger since seems to have been averted by a hairsbreadth, for which we warmly thank our scientific colleagues throughout the world — whose overwhelming response against this decision last year proved to have played a decisive part in persuading the Dutch parliament to reconsider the liquidation order.

As regards the present volume, we started out by trying to have represented as many as possible of the areas deemed to be of major importance for neuroscience research in the coming years. In addition to the gaps which are undoubtedly present in this conception owing to our own limitations of imagination, there are also some unavoidable lacunae resulting from our failure to have approached in time all the potential contributions for each of the desired topics. The coverage was of course in practise still further thinned by the human impossibility of adequately covering any of the assigned themes within the limited time and space available. Nevertheless, we hope that the missing intellectual fare will only have caused the mesh of the proffered “net” of ideas to become somewhat less fine, without rupturing its overall structural integrity.



The material is presented under five main headings, each of which is subdivided into four chapters. Twenty distinguished investigators present their ideas about the direction their fields are (or ought to be) moving; in many cases the authors' own most recent findings themselves vividly illustrate the power of the research proposals being made. Starting from those molecular processes in nervous tissue which are most closely related to the chemistry of living cells in general, we progress to a detailed consideration of a more specialized biochemical mechanism: neuronal production of hormones and responses to them, in turn. The subject of nervous systems as information-processing networks is then arbitrarily subdivided into a part dealing with morphological, and another concerning physiological organization, before winding up the main body of the book with a section treating the biological *raison d'être* of all these masterpieces of natural design: their own perpetuation (and ultimately evolution) through the generation of motor activities adapted to the exigencies of environmental challenges.

In the introductory section of the book Prof. Weiss presents an extensive survey of the many basic challenges still remaining to neuroscience research, putting the spotlight on a number of persistent problems, some of which in fact touch the mysteries of life processes in general. Prof. Young then offers us an assessment of some methodological problems inherent in the strategy of looking to "simpler" living forms for suitable models of more general biological phenomena. At the end of the volume the reader is treated to two attempts to look beyond elemental brain processes and structural entities, into a qualitatively distinct domain: the integrated functioning of this most complicated of all organ systems. We are most fortunate here in having two experimental neurologists of the stature of Profs. Creutzfeldt and Sperry to take on the perhaps thankless task of trying to conceptualize the immense difficulties even in usefully formulating such questions for scientific purposes.

Before concluding, it is worthwhile mentioning that one cannot but be struck by the frequency with which classic problems from *developmental* neurobiology — e.g., "plasticity" in its many guises, "tropisms" and trophic interactions among nerve cells — keep popping up, far exceeding the emphasis which we had allocated to ontogeny when planning the symposium. This fact only underscores our own conviction at the Amsterdam Institute that brain maturation and adaptation, and the host of factors which regulate their course and expression throughout the life cycle, constitute perhaps the most imminently fruitful source of current research possibilities. Both C.U. Ariëns Kappers and his co-worker (and eventual successor) S.T. Bok, were already convinced on this point in their own time, so that the developmental approach to the nervous system is in fact a research tradition of long standing at the "Brain Institute".

## Acknowledgements

We are pleased to acknowledge the generous financial support given to the Summer School by all of the following:

Ahrin B.V.	'A. de Jong T.H.' B.V.
B.V. Metaalindustrie v/h Beyer & Eggelaar	Laméris Instrumenten B.V.
Brunschwig Chemie B.V.	L.K.B.-Produkten B.V.
Ciba-Geigy B.V.	Ministry of Education and Science
Eiga B.V., Medische Instrumentenhandel	Van Oortmerssen B.V. Wetenschappelijke Instrumenten
Elmekanic B.V.	Simac Electronics B.V.
European Training Programme in Brain and Behaviour Research	Organon Nederland B.V.
Gist-Brocades N.V.	Philips-Duphar B.V.
Hoffmann-La Roche B.V.	Dr. Saal van Zwabenberg Foundation
Hope Farms B.V.	Schering Nederland B.V.
C.H. van den Houten Fund	Shell Nederland B.V.
IBM Nederland N.V.	P.M. Tamson B.V.
	World Federation of Neurology

The editors would also like to acknowledge the following publishers, and all the authors involved, for their cooperation in allowing the reproduction of figures originally appearing in their own publications.

Academic Press, for two figures in the article of Lopes da Silva et al. (from *Progr. theoret. Biol.*, 2, 1972); for Fig. 8 of Olds (from *Pleasure, Reward, Preference*, 1973, Ch. 2) and Fig. 5 of Baerends (from *Fish Physiology*, Vol. 6, 1971); *Acta Paediatrica Scandinavica*, for Fig. 4 (from *Acta paediat. (Uppsala)*, 63, 1974) and Fig. 6 of Svennerholm (from *Acta paediat. (Uppsala)*, 64, 1975); American Association for the Advancement of Science, for Fig. 8 of Van der Loos (from *Science*, 179 (1973) 395–398) and Fig. 31 of Weiss (from *Science*, 167 (1970) 979–980); American Physiological Society, for Fig. 9 of Olds (from *J. Neurophysiol.*, 36, 1973); *Arch. ital. Biol.*, for Fig. 5 of Levi-Montalcini (from *Arch. ital. Biol.*, 113, 1975); E.J. Brill (Publishers), for Figs. 3, 6 and 7 of Baerends (from *Behaviour*, Suppl. 17, 1970); Cambridge University Press, for Fig. 1 of Dawes and Robinson (from *Foetal and Neonatal Physiology*, 1973); Cold Spring Harbor Symposia on Quantitative Biology, for various portions of text and figures in Whittaker (from *Cold Spr. Harb. Symp. quant. Biol.*, Vol. 40, 1975); Federation of American Societies for Experimental Biology, for Table VI of Svennerholm (from *Fed. Proc.*, 32, 1973); Macmillan Journals Ltd., for Table III of Svennerholm (from *Nature (Lond.)*, 257, 1975); National Academy of Sciences, for Fig. 9 (from *Proc. nat. Acad. Sci. (Wash.)*, 67, 1970) and Fig. 5 of Hydén (from *Proc. nat. Acad. Sci. (Wash.)*, 71, 1974); *Neurobiology* for Figs. 2, 3 and 4 (from *Neurobiology*, 4, 1974) and Fig. 8 of Hydén (from *Neurobiology*, 5, 1975); Neuroscience Research Program, for

Fig. 1 of Gray (from *Neurosci. Res. Prog. Bull.*, 6, 1968); New York Academy of Sciences, for Fig. 6 of Pickering (from *Ann. N.Y. Acad. Sci.*, 248, 1975); Raven Press, for Figs. 2, 3, 4 and 7 of Olds (from *Biological Foundations of Psychiatry*, 1976). Rockefeller University Press, for Fig. 2 of Gray (from *J. Cell Biol.*, 46, 1970); J. Saunders Co., for Fig. 2 of Svennerholm (from *Med. Clin. N. Amer.*, 53, 1969); Springer-Verlag, for Fig. 8 of Whittaker (from *J. neural. Trans.*, Suppl. XII, 39, 1974) and Fig. 5 of Pickering (from *Cell Tiss. Res.*, 156, 1975); and University of Chicago Press, for Fig. 3 of Weiss (from *Genetic Neurobiology*, 1950).

# Contents

List of Contributors . . . . .	v
Introduction . . . . .	vii
Acknowledgements . . . . .	ix
Session I — Prologue	
A glance at some problems facing brain research today J. Ariëns Kappers (Amsterdam, The Netherlands) . . . . .	3
Neurobiology in statu nascendi P.A. Weiss (New York, N.Y., U.S.A.) . . . . .	7
Are invertebrate nervous systems good models for the functional organization of the brain? J.Z. Young (London, Great Britain) . . . . .	39
Session II — Brain as a Tissue	
Tissue fractionation methods in brain research V.P. Whittaker (Göttingen, G.F.R.) . . . . .	45
Functional biochemistry of neurons and glial cells S.P.R. Rose (Milton Keynes, Great Britain) . . . . .	67
Plastic changes of neurons during acquisition of new behavior as a problem of protein differentiation H. Hydén (Göteborg, Sweden) . . . . .	83
Molecular neuropathology L. Svennerholm (Göteborg, Sweden) . . . . .	101
Session III — Brain—Hormone Interactions	
Neurosecretion — comparative and evolutionary aspects B. Scharer (Bronx, N.Y., U.S.A.) . . . . .	125
Hormones and brain development R. Balázs (Carshalton, Great Britain) . . . . .	139
The molecules of neurosecretion: their formation, transport and release B.T. Pickering (Bristol, Great Britain) . . . . .	161
Vasopressin and memory consolidation D. de Wied, Tj.B. van Wimersma Greidanus, B. Bohus, I. Urban and W.H. Gispen (Utrecht, The Netherlands) . . . . .	181

## Session IV — The Brain as a Structural System

Real neural networks	
V. Braitenberg (Tübingen, G.F.R.) . . . . .	197
Problems of understanding the substructure of synapses	
E.G. Gray (London, Great Britain) . . . . .	207
The nerve growth factor: its role in growth, differentiation and function of the sympathetic adrenergic neuron	
R. Levi-Montalcini (Rome, Italy and St. Louis, Mo., U.S.A.) . . . . .	235
Neuronal circuitry and its development	
H. Van der Loos (Lausanne, Switzerland) . . . . .	259

## Session V — The Brain as a Functional System

Models of neuronal populations: the basic mechanisms of rhythmicity	
F.H. Lopes da Silva, A. van Rotterdam, P. Barts, E. van Heusden and W. Burr (Utrecht, The Netherlands) . . . . .	281
Organization of spontaneous electrical activity in the neocortex	
J. Scherrer (Paris, France) . . . . .	309
The formation of continuously ordered mappings	
R.M. Gaze and R.A. Hope (London, Great Britain) . . . . .	327
Plasticity in the adult mammalian central nervous system	
P.D. Wall (London, Great Britain) . . . . .	359

## Session VI — Neural Control of Behavior

Rhythmic phenomena in prenatal life	
G.S. Dawes and J.S. Robinson (Oxford, Great Britain) . . . . .	383
EEG and behavior	
W. Storm van Leeuwen (Utrecht, The Netherlands) . . . . .	391
Brain stimulation and the motivation of behavior	
J. Olds (Pasadena, Calif., U.S.A.) . . . . .	401
On drive, conflict and instinct, and the functional organization of behavior	
G.P. Baerends (Groningen, The Netherlands) . . . . .	427

## Session VII — Epilogue

The brain as a functional entity	
O. Creutzfeldt (Göttingen, G.F.R.) . . . . .	451
A unifying approach to mind and brain: ten year perspective	
R.W. Sperry (Pasadena, Calif., U.S.A.) . . . . .	463
The nature of consciousness: some persistent conceptual difficulties and a practical suggestion	
M.A. Corner (Amsterdam, The Netherlands) . . . . .	471
Subject Index . . . . .	477

## SESSION I

### PROLOGUE



# A Glance at Some Problems Facing Brain Research Today

J. ARIËNS KAPPERS

*Netherlands Central Institute for Brain Research,  
Amsterdam (The Netherlands)*

The present volume contains the proceedings of the Ninth Summer School of Brain Research of our Institute, held from July 28–August 1, 1975 at the Royal Netherlands Academy of Arts and Sciences, Amsterdam, and organized by Drs. Corner and Swaab. I am deeply grateful to them for devoting so much of their time and energy in performing this complicated task, but which, in addition, could never have been accomplished so well without the invaluable help of Miss Sels.

The general topic chosen was: "Perspectives in Brain Research", which means that recently acquired knowledge in certain aspects of neurobiology will be presented, with the emphasis being upon future research possibilities. That only some of the many interesting neurobiological subjects will be dealt with during this meeting is of course unavoidable for practical reasons.

The choice of the general topic has perhaps not been entirely gratuitous: perspectives, being vistas and possibilities of future development, are for a large part projections from what has been going on in the past. For me, personally then, officially participating for the last time in an International Summer School, the continuation of past activities into times still to come becomes an especially appropriate theme. For the institute too, this is a natural moment for reflection upon its future course, and I suppose that all this has been at the back of the mind of the organizers.

During the 45 years comprising my active research life, and especially after World War II, the neurosciences have made an astonishing and most dramatic progress. I vividly remember the words of the grand old man of Dutch neurohistology, Professor Boeke from Utrecht, in summarizing the proceedings of the first meeting of neurobiologists (1955). He gave expression to his amazement and admiration that so much new and integrated knowledge had been gathered in such a relatively short time, and that so much had been contributed to the solution of problems on which he had worked during a life-time. He ended by stating that he hoped that not all problems would find their final solution in the end and that it would remain possible to wonder and accept wonders. I do not think that the people present at this meeting live in the expectation that very soon we will know all that there is to know about the brain. On the contrary, modern workers are more conscious than ever of the intricacy of the problems involved in the study of living matter, and especially



of nervous tissue. They are very much aware that the solution of one problem inevitably opens up many more questions which deserve to be solved. Moreover, I am not of the opinion that even exhaustive knowledge of the facts, and of their structural and functional interrelationships, would ever necessarily preclude our wonderment that these facts and relationships indeed exist — even if one were to accept the somewhat naïve hypothesis that the cosmos, including man, has evolved entirely due to chance processes.

I would like to dwell shortly here on some problems which are a natural consequence of the rapid progress made in the neurosciences. The wide field of neurobiology has now been more or less split up in many super-specializations. This differentiation is inevitable and necessary, but also offers its own problems. Ever larger numbers of neuroscientists produce an ever faster growing number of papers, published in ever increasing numbers of journals. Therefore, it has become very difficult for young research workers, not to mention old ones, to get even an idea of what is going on in every region of this broad field. For those scientists who desire to integrate the knowledge obtained by workers in a variety of related fields into their own thinking, and whose mind is more inclined to synthesis than to particularization, the struggle is often fierce. Time to read and think is scarce, the more so when the research worker has also to be a teacher, an organizer or an administrator. As a result, scientists are now in the habit of scarcely reading papers published earlier than at most 15 years ago, even when these are highly relevant to their current investigation. The consequence is that facts, known for a long time, sometimes are not used in new work because they are entirely unknown to the young research worker. Several times it has struck me that scientific discoveries made long ago were “discovered” again and presented as new findings!

Another very recent problem related to the rapid advancement of the neurosciences on the one hand, and the development of general affairs in this world on the other, is that young scientists in the developing countries rightly want to be introduced to the latest knowledge and technical methods in the field of neurobiology. Here gaps have to be filled quickly and thoroughly, often without optimal knowledge of basic facts. Much earlier knowledge and interpretation of facts have become obsolete, however, while not all facts are of fundamental importance — especially when practical application of neuroscience is what is wanted most. Some of these problems can therefore be solved by good courses in neurobiology in which basic facts are blended with recent discoveries. Organizations like the International Brain Research Organization and the World Health Organization, to mention only two, are very much aware of this important task and do whatever is possible in view of restrictions on manpower and money.

Looking back at the many years I was involved in the study of the nervous system I feel that I cannot be grateful enough for living during a period in which I was able to do research more or less freely. Times are rapidly changing, however, and there is an increasing tendency to curtail the further development of basic scientific research. There is a certain distrust of the community of pure scientists insofar as their activities do not lead immediately to some kind of tangible, practical result. More often than in earlier times, science as such is considered to be a financial and social luxury, rather than a cultural activity of