

Experimental Brain Research Supplementum 3

Gonadal Steroids and Brain Function

IUPS-Satellite-Symposium
Berlin, July 10-11, 1980

Edited by
W. Wuttke and R. Horowski

With 136 Figures and 10 Tables



Springer-Verlag Berlin Heidelberg New York 1981

Professor Dr. Wolfgang Wuttke
Max-Planck-Institut für biophysikalische Chemie
Abt. Neurobiologie
Postfach 968
3400 Göttingen

Dr. Reinhard Horowski
Department Klinische Neuropsychopharmakologie
Postfach 650 311
1000 Berlin 65

ISBN 3-540-10606-5 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-10606-5 Springer-Verlag New York Heidelberg Berlin

Library of Congress Cataloging in Publication Data.

Main entry under title:

Gonadal steroids and brain function.

(Experimental brain research. Supplement ; 3)

Includes bibliographical references and index. 1 Hormones, Sex--Physiological effect. 2. Brain. 3. Gonads. 4. Neuroendocrinology. I. Wuttke, W. II. Horowski, R. (Reinhard), 1944-. III. International Union of Physiological Sciences. IV. Series. [DNLN: 1. Gonads--Congresses. 2. Steroids--Physiology--Congresses. 2. Brain--Physiology--Congresses. Gonadotropins--Secretion--Congresses. WL 300 G635 1980]

QP572.S4G66 599.05'6 81-1677 AACR2

ISBN 0-387-10606-5 (U.S.)

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Printed in Germany

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Printing and Binding: J. Beltz, Hemsbach
2125/3321-543210

List of Senior Contributors

- BALL, P., Institut für Biochemische Endokrinologie, Arbeitsgruppe für Klinische Endokrinologie, Medizinische Hochschule Lübeck, 2400 Lübeck, FRG
- BARRACLOUGH, C.A., Dept. of Physiology, School of Medicine, University of Maryland, Baltimore, MD 21201, USA
- BAUER, K., Max-Volmer Institut, Abt. Biochemie, TU Berlin, Franklinstr. 29, 1000 Berlin 10, FRG
- BECKER, D., Institute for Psychology, Univ. Göttingen, 3400 Göttingen, FRG
- BLAKE, C.A., Department of Anatomy, University of Nebraska Medical Center, Omaha, NE, USA
- BREUER, H., Institut für Klinische Biochemie, Universität Bonn, 5300 Bonn, FRG
- DE COTTE, D.M., Department of Physiology, St. George's Hospital Medical School, London SW17, U.K.
- DÖCKE, F., Institute of Experimental Endocrinology, Humboldt University, Berlin, GDR
- DÖRNER, G., Institute of Experimental Endocrinology, Humboldt University, Berlin, GDR
- DONOVAN, B.T., Department of Physiology, Institute of Psychiatry, De Crespigny Par, London SE5 8AF, U.K.
- DÜKER, E., Max-Planck-Institute for Biophysical Chemistry, 3400 Göttingen, FRG
- FENSKE, M., Institut f. Tierzucht u. Haustiergenetik, Universität Göttingen, 3400 Göttingen, FRG
- GETHMANN, U., Kliniken für Frauenheilkunde und Geburtshilfe, Medizinische Hochschule Lübeck, 2400 Lübeck, FRG
- GHRAF, R., Institut für Physiologische Chemie, Fachbereich Theoretische Medizin, Universitätsklinikum Essen, 4300 Essen, FRG
- GILMORE D.P., Institute of Physiology, University of Glasgow, U.K.
- GORSKI, R.A., Department of Anatomy of the Brain Research Institute UCLA School of Medicine, Los Angeles, CA 90024, USA

HANCKE, J.L., Dept. Clinical Endocrinology, Medical School, 3000 Hannover, FRG

HIEMKE, C., Institut für Physiologische Chemie, Universitätsklinikum Essen, 4300 Essen, FRG

v. HOLST, D., Lehrstuhl für Tierphysiologie, Universität Bayreuth, 8580 Bayreuth, FRG

HOROWSKI, R., Research Laboratories of Schering AG, 1000 Berlin, FRG

JUNGBLUT, P.W., Max-Planck-Institut für experimentelle Endokrinologie, POB 61 03 09, 3000 Hannover 61, FRG

KAWAKAMI, M., Department of Physiology, Yokohama City University School of Medicine, Yokohama, Japan

KELLY, M.J., Department of Physiology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261, USA

KIRCHHOFF, J., Institut für Physiologische Chemie, Fachbereich Theoretische Medizin, Universitätsklinikum Essen, Hufelandstr. 55, 4300 Essen, FRG

KNOBIL, E., Department of Physiology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261, USA

KNUPPEN, R., Institut für Biochemische Endokrinologie der Medizinischen Hochschule Lübeck, Ratzeburger Allee 160, 2400 Lübeck, FRG

KOW, L.-M., The Rockefeller University, York Avenue & 66th Street, New York, NY 10021, USA

LADOSKY, W., Departamento de Fisiologia e Farmacologia Universidade Federal de Pernambuco, Recife, Brasil

LINTON, E.A., Department of Biochemical Endocrinology, Chelsea Hospital for Women, Dovehouse Street, London SW3 6LT, U.K.

MANISKY, T., Max-Planck-Institute for Biophysical Chemistry, 3400 Göttingen, FRG

McCANN, S.M., Department of Physiology, Southwestern Medical School, University of Texas, Dallas, TX, USA

McEWEN, B.S., The Rockefeller University, New York, NY 10021, USA

MEITES, J., Department of Physiology, Neuroendocrine Research Laboratory, Michigan State University, East Lansing, Michigan, MI 48824, USA

MOTTA M., Department of Endocrinology, University of Milano, 21, Via Andrea del Sarto, 20129 Milano, Italy

NESBITT, K., Department of Physiology, St. George's Hospital Medical School, London, U.K.

NEUMANN F., Research Laboratories of SCHERING AG, 1000 Berlin, FRG

PARVIZI, N., Institut für Tierzucht und Tierverhalten, FAL, Mariensee, 3057 Neustadt 1, FRG.

RUBERG M., Unité 159 de Neuroendocrinologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alésia, 75014 Paris, France

SAR, M., Department of Anatomy, University of North Carolina, Chapel Hill, NC 27514, USA

SAWYER C.H., Department of Anatomy and Brain Research Institute, UCLA School of Medicine, Los Angeles, CA 90024, USA

STUMPF, W.E., Department of Pharmacology, University of North Carolina, Chapel Hill, NC 27514, USA

WEINDL, A., Neurologische Klinik der Technischen Universität München, 8000 München, FRG

WUTTKE, W., Max-Planck-Institute for Biophysical Chemistry, 3400 Göttingen, FRG

Acknowledgements

The editors wish to express their gratitude to all persons who helped making the symposium and this book a success. In particular the assistance of Mrs. A. Scholz, R. Schley and H. Heinze (Schering) and of S. Schlette (Max-Planck-Institute for Biophysical Chemistry) is acknowledged. The patience of Mrs. B. Bartsch to type and of Dr. J. Ondo (visiting Professor Univ. South Carolina Med. School) to proofread all manuscripts was also of invaluable help. This symposium was only possible due to the financial generosity of the German Research Society, the Senator für Wirtschaft (Berlin) and the Schering Company. The fast processing of this book by the Springer-Company is encouraging to continue this inexpensive Symposium-Series in EXPERIMENTAL BRAIN RESEARCH.

W. Wuttke (Göttingen)

R. Horowski (Berlin)

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The Morphology of LRH and Oxytocin Neurons

A. Weindl and M.V. Sofroniew, München

Peptidergic neurons are involved in the regulation of gonadal steroids. The adenohipophyseal gonadotropic hormones luteinizing hormone (LH) and follicle stimulating hormone (FSH) are under the control of the decapeptide luteinizing hormone releasing hormone (LH-RH or LRH) produced by hypothalamic secretory neurons.

Other peptidergic neurons of the hypothalamus which are involved in reproductive functions and which also appear to be sensitive to gonadal steroids are neurons producing oxytocin. Oxytocin, an octapeptide produced in magnocellular perikarya of the supraoptic and paraventricular nucleus and transported within axons to the fenestrated capillaries of the neural lobe causes uterine contraction at term, and milk ejection. The secretion of oxytocin and its associated neurophysin (neurophysin I or estrogen-stimulated neurophysin) is influenced by estrogens (Robinson, 1978).

In this communication the morphology and distribution of neurons producing LRH and oxytocin, and their fiber connections to the hypophysis as well as to non-hypophyseal target areas in the brain of several mammals will be presented.

1. Material and Methods

Brains of tree shrews (*Tupaia belangeri*), a prosimian, and of rabbits fixed by perfusion with Bouin's solution were embedded in paraffin-paraplast and sectioned serially in the frontal, sagittal and horizontal plane. Details of the tissue preparation and of the unlabeled antibody enzyme immunohistochemical method used to

visualize LRH, oxytocin and neurophysin, as well as of the specificity tests of the antisera have been described previously (Sofroniew et al., 1979).

2. Observations

Perikarya containing LRH are widely distributed in the anterior hypothalamic/preoptic area of tupaia and rabbit. LRH perikarya often are bipolar or multipolar giving rise to two or several processes. Fig. 1 shows a LRH perikaryon in the anterior hypothalamic area of the rabbit. Two cell processes leave the perikaryon in opposite directions and have different calibers. The thin fiber directed caudally resembles an axon, the large fiber directed rostrally resembles a dendrite when compared to Golgi-impregnated neurons.

The main target of LRH fibers are the fenestrated portal capillaries of the external zone of the median eminence (Fig. 2a,b). In the external zone, LRH terminals are distributed laterally. Furthermore, LRH fibers are found in the stalk and proximal part of the neural lobe (Fig. 2c). In the preoptic region, LRH fibers run dorso-ventrally in the lamina terminalis and terminate at fenestrated capillaries of the organum vasculosum of the lamina terminalis (Fig. 3) where as in median eminence and neural lobe the blood-brain barrier for peptides and proteins is not present (Weindl and Joynt, 1972). In the subfornical organ, only a few LRH fibers terminate at capillaries (Krisch and Leonhardt, 1980; Weindl and Sofroniew, 1980), whereas no LRH fibers or cells are found in the area postrema and pineal organ, additional circumventricular organs lacking a blood-brain barrier,

In addition to vascular targets, LRH fibers are directed to neural targets inside and outside the hypothalamus (Fig. 8) where they form axosomatic contacts with other neurons. Areas where LRH fibers are found are: the mamillary and retromamillary area of the hypothalamus, the septum, the dorsal thalamus, the habenular region, the posterior commissure (Weindl and Sofroniew, 1980), the periaqueductal grey of the mesencephalon, the inferior colliculi (Fig. 5), the fasciculus retroflexus and the ventral hippocampus (Fig. 4). In the pigeon where groups of LRH perikarya are located

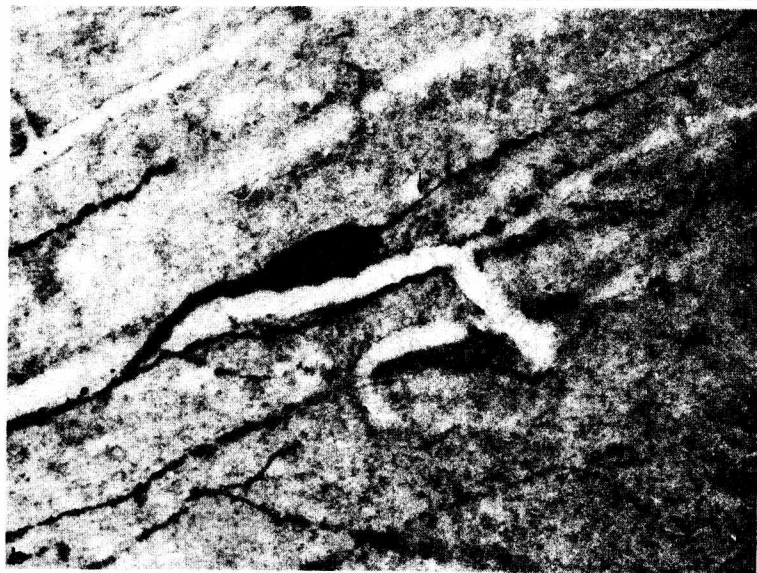
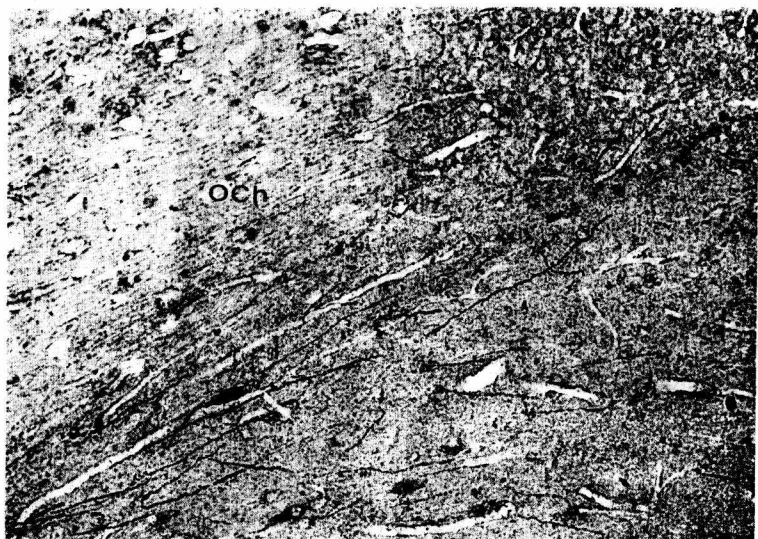


Figure 1a,b: Rabbit. Horizontal section through the anterior hypothalamus near the optic chiasm (OCh). LRH immunoperoxidase reaction. a. Survey. 133x. b. Detail of a. 350x. LRH perikaryon having two processes of different diameters. The rostrally directed thick fiber resembles a dendrite, the caudally directed thin fiber (+) resembles an axon



Figure 2a-c: *Tupaia belangeri*. Horizontal (a) and sagittal sections through the median eminence (b) and neurohypophyseal stalk (c). LRH immunoperoxidase reaction. LRH fibers terminate laterally in the external zone of the median eminence (ME) at portal capillaries in the vicinity of the pars tuberalis (PT) of the adenohypophysis (a,b). Other LRH fibers (+) continue into the stalk (St) and proximal part of the neural lobe (NL). IL intermediate lobe. PD pars distalis. a. 53x. b. 133x. c. 53x



Figure 3: *Tupaia belangeri*. Frontal section through the preoptic area and organum vasculosum of the lamina terminalis (OVLt). LRH immunoperoxidase reaction. LRH perikarya are located near the OVLt. LRH fibers are present in the preoptic area and the OVLt. 54x

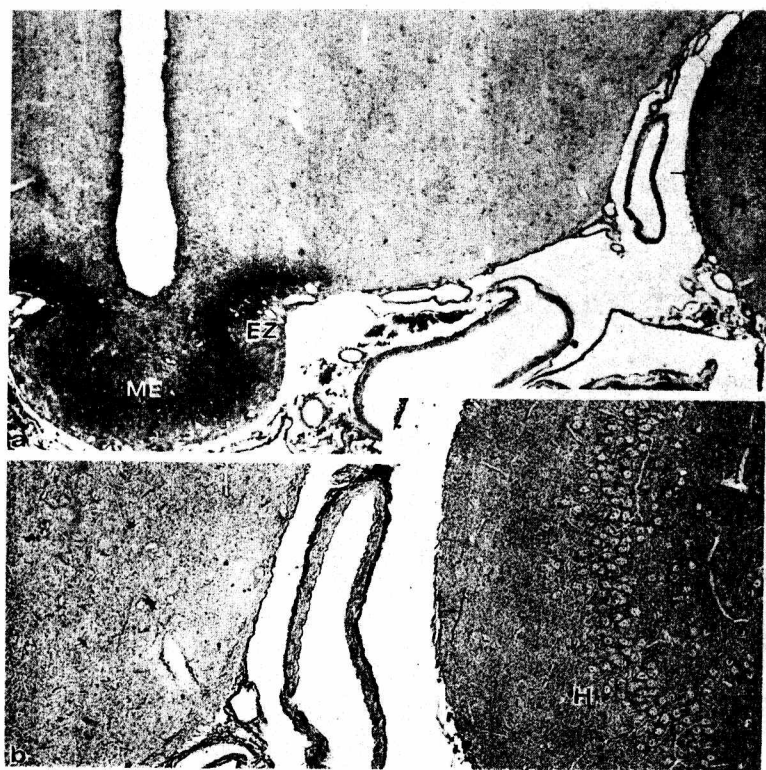


Figure 4a,b: Tupaia. Frontal section through median eminence, hypothalamus and neighbouring ventral hippocampus. LRH immunoperoxidase reaction. LRH fibers terminate in the lateral parts of the external zone (EZ) of the median eminence (ME). Extrahypothalamic LRH fibers are present in the ventral hippocampus ($\rightarrow$). a. Survey. 53x. b. Detail of a. 133x