

**Elektronenmikroskopie des zentralen und
peripheren Nervensystems**

**Electronmicroscopy of the Central and
Peripheral Nervous System**

Zellbiologie und Zellkultur des Nervengewebes

Biology and Culture of the Nervous Tissue

**Vol. II
Thema II und III**

MIT 237 ABBILDUNGEN

19



62

GEORG THIEME VERLAG · STUTTGART

This work was published with the partial support of the National Institute of Neurological Diseases and Blindness and the World Federation of Neurology.

Alle Rechte, insbesondere das Recht der Vervielfältigung und Verbreitung sowie der Übersetzung in fremde Sprachen, vorbehalten. Kein Teil des Werkes darf in irgendeiner Form (durch Photokopie, Mikrofilm oder ein anderes Verfahren) ohne schriftliche Genehmigung des Verlages reproduziert werden.

© Georg Thieme Verlag, Stuttgart 1962 · Printed in Germany.

Satz und Druck: Darmstädter Echo GmbH., Darmstadt.

**IV. INTERNATIONALER KONGRESS
FÜR NEUROPATHOLOGIE**

**IV. INTERNATIONAL CONGRESS
OF NEUROPATHOLOGY**

PROCEEDINGS

Vol. II

IV. INTERNATIONALER KONGRESS FÜR NEUROPATHOLOGIE

IV. INTERNATIONAL CONGRESS OF NEUROPATHOLOGY

VOM 4.—8. SEPTEMBER 1961

MÜNCHEN

PROCEEDINGS

IN DREI BÄNDEN

Vol. II

Thema II und III

EDITOR

PROF. DR. H. JACOB

MARBURG/LAHN

19



62

GEORG THIEME VERLAG · STUTTGART

INHALTSVERZEICHNIS

Thema II:

Elektronenmikroskopie des zentralen und peripheren Nervensystems

2nd Theme:

Electronmicroscopy of the Central and Peripheral Nervous System

A. HESS, Salt Lake City		A. L. WOOLF, Smethwick	
Structural Differences of Fast and Slow		The Ultrastructure of the Human	
Extrafusal Muscle Fibers and their		Motor End Plate as Seen in Muscle	
Nerve Endings	3	Biopsies	18
References	4	References	20
J. B. FINEAN, A. L. WOOLF, Birmingham		G. M. LEHRER, New York	
Electron Microscope Studies of Patho-		The Electronmicroscopic Localization	
logical Changes in Human Cutaneous		of Cholinesterase in Synaptic Struc-	
Nerve	4	tures	20
References	6	Methods and Materials	21
H. DE F. WEBSTER, Boston		Results	21
Experimental Diphtheritic Neuritis		Discussion	21
and Wallerian Degeneration: A Com-		J. M. BLUMBERG, S. I. ZACKS,	
parative Study of Demyelination Uti-		W. C. BAUER, Washington D.C.	
lizing Phase and Electron Microscopy	6	Ultrastructure of Neuromuscular Junc-	
C. COËRS, E. DE HARVEN, Bruxelles		tion in Myasthenia Gravis	22
La microscopie electronique de la		Discussion	24
jonction neuro-musculaire humaine .	7	S. I. ZACKS, J. F. METZGER,	
Observations	8	C. W. SMITH, J. M. BLUMBERG	
Terminaisons motrices	8	Localization of Ferritin-Labelled Bo-	
Appareils sous-neuraux	8	tulinus toxin in the Neuromuscular	
Conclusion	15	Junction of the Mouse	25
Bibliographie	16	Methods and Materials	25
W. C. BAUER, J. M. BLUMBERG,		Measurements of ferritin spacing .	25
S. I. ZACKS, Washington D.C.		Observations. Normal neuromuscular	
Short and Long Term Ultrastructure		junctions	25
Changes in Denervated Mouse Motor			
End Plates	16		

Botulinus toxin poisoned neuromuscular junction	25	E. DE ROBERTIS, Buenos Aires	
Ferritin-labelled botulinus toxin	27	Structure and Chemical Composition of Isolated Nerve Endings	54
Ferritin-injected mice	27	References	56
Protein ferritin	27		
The distribution of ferritin in mouse neuromuscular junctions poisoned with ferritin-labelled botulinus toxin	27	E. G. GRAY, London	57
Discussion	28	Electron Microscopy of Synaptic Organelles of the Central Nervous System	57
References	30	Method	57
		Observations. Presynaptic processes	57
S. L. PALAY, Bethesda		Synaptic membranes	60
Normal Fine Structure of the Central Nervous System	31	Post-synaptic process	60
		Conclusions	60
		References	61
J. F. HARTMANN, Minneapolis			
Identification of Neuroglia in Electron Micrographs of Normal Nerve Tissue	32	F. GULOTTA, J. CERVÓS NAVARRO, Bonn	
References	35	Beitrag zur elektronenmikroskopischen Kenntnis der Synapsen im Zentralnervensystem	61
E. DE ROBERTIS, Buenos Aires			
Fine Structure of Synapses in the CNS	35	F. S. VOGEL, L. KEMPER, New York	
Discussion	35	Modifications of Hortega's Silver Impregnation Methods to Assist in the Identification of Neuroglia with Electron Microscopy	66
The intersynaptic filaments	37	Methods	66
The subsynaptic web	37	Observations	67
References	38	Discussion	71
A. BAIRATI, Milano		References	71
Nature et structure submicroscopique des fibres gliales chez l'homme	38	A. BIRCH-ANDERSEN, VAGN DAHL, STEEN OLSEN, Kopenhagen	
I) Analyse polaroscopique	39	Elektronenmikroskopische Untersuchungen über die Struktur der Kleinhirnrinde des Menschen	71
II) Analyse chimique	40	Befunde	73
III) Analyse diffractographique aux rayons X	40	Literatur	77
Examens au microscope électronique	41		
Conclusions	41	S. DONAHUE, G. D. PAPPAS, New York	
Bibliographie	42	The Fine Structure of Capillaries in the Cerebral Cortex of Fetal and Adult Rats	77
H. RUSKA, Düsseldorf		References	80
Über funktionelle Konsequenzen der Vielphasigkeit der Zelle	42		
Literatur	49	E. ANDERSON, Iowa	
A. PETERS, Edinburgh		Fine Structure of Developing Spinal Ganglion Cells of Rats	80
Myelination in the Central Nervous System	50		
References	54		

C. E. LUMSDEN, R. PIPER, Leeds	A. Leptomeningeal reaction	125
Electron Microscopy of Nervous Tissue	B. Leukocytic reaction	126
Cultivated in Vitro	C. Neuronal reaction	127
81	D. Microglial reaction	128
	E. Macroglial and neuropil reaction	128
H. HAGER, München	F. Vascular reaction	128
Elektronenmikroskopische Befunde zur	References	129
allgemeinen Zytopathologie des zen-		
tralnervösen Gewebes		
85		
Literatur	K. BLINZINGER, München	
94	Zur Feinstruktur der Infiltratzellen und	
	der reaktiv veränderten glösen Grenz-	
L. ROIZIN, R. RUGH, M. KAUFMANN,	membranen bei Spätstadien der experi-	
R. ORES, New York	mentellen Kolimeningitis	130
Some Comparative Electron Micro-	Literatur	135
scope, Histopathology and Histoche-		
mical Studies of the Central Nervous		
System of Rats Following X-Irradiation	R. P. BUNGE, M. B. BUNGE, H. RIS,	
95	New York	
References	Electron Microscopic Observations on	
99	Normal, Demyelinating, and Remyeli-	
	nating White Matter	136
J. CEKVÓS NAVARRO, Bonn	References	142
Elektronenmikroskopische Befunde an		
Spinalganglienzellen der Ratte nach		
Ischiadikotomie		
99		
	H. J. LÖBLICH, München	
W. SCHLÖTE, München	Elektronenmikroskopische Befunde bei	
Zur Ultrastruktur primärer retrograder	akuter Kreislaufstörung im Hypo-	
Axonveränderungen nach experimen-	physen-Zwischenhirnsystem	142
teller Strangdurchtrennung am Rücken-	Literatur	149
mark der weißen Ratte		
105		
Literatur	J. E. GRUNER, Strasbourg	
112	La microscopie électronique en neuro-	
K. NIESSING, W. VOGEL, Marburg/Lahn	pathologie humaine: Biopsies céré-	
Das elektronenmikroskopische Bild der	brales, nerveuses et musculaires	150
Hirnrinde beim sogenannten Hirnödem	Iconographie	154
112		
Literatur	A. BISCHOFF, A. VOGEL, Zürich	
117	Elektronenmikroskopische Unter-	
G. ULE, Kiel	suchungen über degenerative Glia-	
Elektronenmikroskopische Studien zum	veränderungen. Ein Beitrag zum Pro-	
experimentellen Hirnödem	blem der degenerativen Entmarkungs-	
118	krankheiten	154
Literatur	Material und Methode	155
124	Befunde	155
	Diskussion	156
E. NELSON, Minneapolis	Literatur	159
Electron Microscopic Observations on		
Experimental Inflammatory Diseases	L. STOCKINGER, Wien	
of the Central Nervous System	Zur Elektronenmikroskopie lang for-	
124	molfixierten ZNS-Materials	160
Materials and methods		
125		
Results and discussion		
125		

A. MARTINEZ, Santiago de Chile	W. L. TAFURI, Belo Horizonte
Electron Microscopy of Human Atherosclerotic Cerebral Vessels	Beitrag zum Studium der Schädigungen des Plexus submucosus (Meissner) und myentericus (Auerbach) des Ileum, Caecum und Colon des Meerschweinchens (Cavia, Cobaya)
Materials and methods	185
Results	
Discussion	
References	
164	
165	
166	
169	
169	
KL. MANNWEILER, Hamburg	J. PICK, New York
Untersuchungen an menschlichen Hirntumoren und deren Grenzgebieten . .	Electron Microscopic Studies of Sympathetic Neurons in the Frog (Rana Pipiens)
170	190
J. KEPES, Kansas City	Comment on the Histologie of Sympathetic Neurons
Electron Microscopic Studies of Meningiomas	191
174	Observations with Electron Microscope
References	191
177	References
	196
W. WECHSLER, München	J. TAXI, Paris
Elektronenmikroskopische Befunde bei menschlichen und experimentell erzeugten Erkrankungen der quergestreiften Skelettmuskulatur	Étude au microscope électronique de synapses ganglionnaires chez quelques Vertébrés
178	197
Literatur	Bibliographie
185	202

Summary Theme II:

Electronmicroscopy of the Central and Peripheral
Nervous System

Von Dr. H. HAGER, München

INHALTSVERZEICHNIS

Thema III:

Zellbiologie und Zellkultur des Nervengewebes

3rd Theme:

Biology and Culture of the Nervous Tissue

C. M. POMERAT, Pasadena

Cinematography in the Service

of Neuropathology 207

1. The effect of electrolytes on cells
from nervous tissue 207

2. Psychotropic drugs in relation to
cells from nervous tissue 209

3. Electron microscopy of cell
cultures 211

4. Pathological lesions reproduced
in vitro 211

5. Viruses in brain tumors 214

6. Irradiation of nervous tissue 214

References 215

I. COSTERO, R. BARROSO-MOGUEL,

A. CHÉVEZ, México City

Aspects of the Pathology of the Chemoreceptors in the Carotid Body

Tumor 217

1. Chief cells 217

2. Argentaffin cells 221

3. Nerve fibers 224

4. Discussion 224

References 229

I. KLATZO, J. MIQUEL, R. OTENASEK,

Maryland

Uptake and Passage of Fluorescein

Labeled Serum Protein (FLSP) in Ner- vous Tissue 231

References 235

H. HYDÉN, Göteborg

Biochemical and Metabolic Differences between the Neuron and its Oligoden- droglia at Increased Neural Function 235

Technical aspects 236

ATPase activity and amount of ATP 237

RNA, proteins, lipids 239

Respiratory enzyme activity 239

Increased neuronal activity 239

Neuron-glia changes at the mole-
cular level at increased RNA-protein
synthesis 240

The effect of hypoxia 240

Theoretical considerations 241

References 241

J. NAKAI, Tokyo	I. PÁLYI, D. ÁFRA, Z. PÓBALAKY, L. ZOLTÁN, Budapest
Transformation and Multiplication of Neuroglia in Tissue Culture	Die Wirkung von Röntgenstrahlen auf den Phosphorstoffwechsel von Gliomen- kulturen
Transformation of Glia	Methodik
Multiplication of Glia	Ergebnisse
Conclusion	Diskussion
References	Literatur
T. NAKAZAWA, J. TOMINAGA, K. YAMAUCHI, Tokyo	M. R. MURRAY, E. R. PETERSON, R. P. BUNGE, New York
Morphological Concepts of Astrocyte Based in Tissue Culture	Some Nutritional Aspects of Myelin Sheat Formation in Cultures of Central and Peripheral Nervous System
	Introduction
	Method and materials
	Observations
	References
L. LISS, Columbus, Ohio	T. YONEZAWA, M. B. BORNSTEIN, E. R. PETERSON, M. R. MURRAY, Kyoto and New York
Morphology of Nervous System Tumors in Vitro	Temporal and Spatial Distribution of Oxidative Enzymes (Cytochrome Oxi- dase Compared with Succine Dehy- drogenase and Diaphorases) during Myelin Formation and Maintenance
1. Astrocytoma	
2. Oligodendroglioma	
3. Ependymomas	
4. Glioblastoma	
5. Medulloblastoma	
6. Gangliocytoma or neuroblastoma	
7. Neurofibroma	
8. Craniopharyngioma	
9. Meningioma	
10. Melanoma	
O. PALACIOS, Hamburg-Eppendorf	E. R. PETERSON, T. YONEZAWA, M. R. MURRAY, New York
Neuroblastome in der Gewebekultur	Experimental Demyelination with Diphtherial Toxin in Cultures of Dorsal Root Ganglia
Literatur	
I. S. AKSEL, T. BALI-AYKAN, Istanbul	M. B. BORNSTEIN, S. H. APPEL, M. R. MURRAY, New York
Das Verhalten der durch Methyl- cholanthren erzeugten transplantier- baren Hirntumoren der Mäuse in Ge- webskulturen	The Application of Tissue Culture to the Study of Experimental "Allergic" Encephalomyelitis. Demyelination and Remyelination
Literatur	Methods
	Results
	Conclusion
	References

S. H. APPEL, M. B. BORNSTEIN, B. C. SEEGAL, M. R. MURRAY	M. OKAMOTO, K. OGAWA, Kyoto
The Application of Tissue Culture to a Study of Experimental Allergic Encephalomyelitis: Immunological Ob- servations	Cytochemistry of Cultured Neural Tissue
283	291
Methods	EBBA LUND, E. LYCKE, P. SOURANDER, Gothenburg, Schweden
283	A Cinematographic Study of Toxo- plasma Gondii in Cell Cultures
Results	293
1. Patterns of demyelination	References
283	293
2. Fluorescent antibody studies	E. KOVÁCS, München
284	Biochemical and Morphological Studies, "in vitro", on Cells Infected with Virus Nucleic Acids
Conclusions	294
284	Discussion
References	297
285	Conclusions
L. L. ROSS, M. B. BORNSTEIN, New York	297
The Application of Tissue Cultures to the Study of Experimental "Allergic" Encephalomyelitis. III. Electron Micro- scopic Observations of Demyelination and Remyelination	References
285	298
G. P. MARCONI, A. PARRINI, G. PESSINA, Firenze	T. NAKAZAWA, R. MIH, Tokyo
Su alcune circostanze concomitanti la formazione di mielina in gangli spinali di embrioni di pollo coltivati in vitro	On the Problem of Systembuilding Mechanism of Peripheral Nerve
288	298
Materiale e metodi	E. E. MANUELIDIS, New Haven, Conn.
288	Experiments with Tissue Cultures and Heterologus Transplantation of Glio- blastoma Multiforme
Risultati	300
288	References
Discussione	304
290	

Summary Theme III:

Biology and Culture of the Nervous Tissue

Von G. KERSTING, München

**Elektronenmikroskopie des zentralen und
peripheren Nervensystems**

**Electronmicroscopy of the Central and
Peripheral Nervous System**

Zellbiologie und Zellkultur des Nervengewebes

Biology and Culture of the Nervous Tissue

**Vol. II
Thema II und III**

MIT 237 ABBILDUNGEN

19



62

GEORG THIEME VERLAG · STUTTGART

Structural Differences of Fast and Slow Extrafusar Muscle Fibers and their Nerve Endings

By A. HESS, Salt Lake City

Muscle fibers were fixed in *Susa* or *Dalton's* fluid, embedded in plastic, and longitudinal and cross sections were studied in the phase contrast and electron microscopes. Other muscle fibers were fixed in glyoxal, teased and stained for cholinesterase. Some of the teased muscle fibers stained for cholinesterase were refixed in *Dalton's* fluid, embedded in plastic, and viewed in the electron microscope.

Fibrillenstruktur muscle fibers have regular fibrils, each surrounded by sarcoplasm and granules. The Z-disk runs straight across the width of the fibril. These are the twitch or "fast" fibers. Felderstruktur muscle fibers have irregular fibrils apparently joining each other at certain points along the length of the fibrils, the fibrils are not regularly surrounded by sarcoplasm and granules, and the Z-disk appears zigzag across the width of the fibril.

End plate or "en plaque" nerve endings are the ordinary kind of ending and usually occur one per muscle fiber on Fibrillenstruktur muscle fibers only. Several "en grappe" terminations occur on each muscle fiber and only on fibers of Felderstruktur.

Frogs. Fibrillenstruktur and Felderstruktur muscle fibers occur in the tonus bundle of the iliofibularis muscle; only fibers of Fibrillenstruktur are found in portions of the iliofibularis muscle without the tonus bundle. The "en plaque" endings in the tonus bundle are most frequently relatively short, branched and variable in structure, while those in other portions of the iliofibularis muscle are generally long and are the typical "Endbüschel" of frog muscle. "En grappe" endings are found only in the tonus bundle. The distance between the multiple "en grappe" endings on a single Felderstruktur muscle fiber is very irregular and can vary from 60 μ to more than 1 millimeter.

Chickens. The posterior latissimus dorsi of the chicken from hatching to one week of age, from 2 to 3 months of age, and adult, consists almost entirely of muscle fibers of Fibrillenstruktur type which have one ordinary end plate on each fiber. There are, however, a few fibers which receive several "en grappe" terminations in the posterior latissimus dorsi and are probably of Felderstruktur type. The anterior latissimus dorsi of such chickens consists entirely of muscle fibers of Felderstruktur. Several "en grappe" terminations are found on each of these muscle fibers, occurring regularly along the length of the muscle fiber and separated by distances of about 250 μ —350 μ in 1- to 7-day-old chickens, and by about 1,000 μ in adults. The biventer cervicis consists of mixed Fibrillenstruktur and Felderstruktur muscle fibers, the former with one end plate type ending per muscle fiber and the latter with several "en grappe" terminations on each muscle fiber.

2nd THEME:

**Electronmicroscopy of the Central and Peripheral
Nervous System**

THEMA II:

**Elektronenmikroskopie des zentralen
und peripheren Nervensystems**

Mammals. Fibrillenstruktur and Felderstruktur muscle fibers occur in the extraocular muscles of the guinea pig. In addition, thin muscle fibers with concentrations of mitochondria on the borders of the fiber are found on the periphery of extraocular muscles. Most of these latter fibers are Felderstruktur, some are Fibrillenstruktur. "En plaque" endings occur only on fibers of Fibrillenstruktur and have interlacing fingerlike processes on a compact portion of the muscle fiber. "En grappe" endings occur only on fibers of Felderstruktur and are seen as clusters or collections of droplets of stained material and are indeed "grape-like" or can appear simply as a darkly stained spot of material on the muscle fiber. The spots of stained material occur irregularly spaced from each other; the more delicate clusters of droplets cover extensive lengths of muscle fibers and appear on some stretches of muscle to be practically continuous from one ending to the next. It is suggested that the "en grappe" endings appearing as irregularly spaced spots occur on the thin Felderstruktur muscle fibers which have concentrations of mitochondria in their borders and which are located on the periphery of the extraocular muscles, while the more delicate and extensive "en grappe" endings occur on the other larger Felderstruktur fibers in the interior of the muscle.

References

- Hess, A.: The structure of extrafusal muscle fibers in the frog and their innervation studied by the cholinesterase technique. *Amer. J. Anat.* 107, 129—152 (1960); Structural differences of fast and slow extrafusal muscle fibres and their nerve endings in chickens. *J. Physiol. London* 157, 221—231 (1961). The structure of slow and fast extrafusal muscle fibers in the extraocular muscles and their nerve endings in guinea pigs. *J. Cellul. Comp. Physiol.* 58, 63—80 (1961).

Electron Microscope Studies of Pathological Changes in Human Cutaneous Nerve

By J. B. FINEAN and A. L. WOOLF, Birmingham

Dr. Finean and I are reporting here the results of what we believe to be the first systematic study of the ultrastructure of normal and abnormal cutaneous nerves. That such a study has not previously been conducted is surprising in view of the ease with which small branches of cutaneous nerves may be sampled in the course of muscle biopsies which today are being carried out with increasing frequency. We have taken specimens from over 100 patients, the nerve used being most commonly a branch of the antebrachial cutaneous nerve of the forearm removed in the course of a biopsy of palmaris longus or flexor carpi radialis. A 2 cm. length of nerve was divided into 4 pieces placed in saline, osmic acid, potassium permanganate and formol saline for haematoxylin and eosin staining, respectively. The specimen in

saline was examined by low-angle X-ray diffraction. This appears to be a valuable technique for early determination of the amount of myelin present. In 15 cases we encountered abnormal diffraction patterns (*Finean and Woolf, 1961a*). The abnormal patterns were seen in patients with histologically normal nerves, but we have also encountered an abnormal pattern in three cases in which paraffin and electron microscope sections showed marked degenerative changes.

Electron microscopy was carried out on the specimens fixed in osmic acid and potassium permanganate. So far about 50 preparations have yielded useful electron microscopic data and 15 have been studied in detail (*Finean and Woolf, 1961a and b*). We have particularly carefully studied the myelin layering and have found no difference in cases where the nerve was thought on clinical grounds to be normal, from that encountered in other mammalian peripheral nerves (*Fernández-Morán, 1957; Fernández-Morán and Finean, 1957; Finean and Robertson, 1958; Robertson, 1959, 1960; Sjöstrand, 1960*). In some cases suspected clinically of sensory denervation, striking changes in the myelin layering were observed (*Finean and Woolf, 1961a and b*). There was a tendency for the myelin layers to roll up and form droplets. In some fibres the axon was shrunken or had actually disappeared suggesting that the changes in the myelin might be secondary to axonal degeneration. In another case the axons had apparently been more resistant, since axons larger than those normally found unmyelinated, could be seen devoid of myelin cover or with only a few laminae which were thought to represent abortive attempts at myelin regeneration.

The unmyelinated nerve fibres were particularly interesting especially in view of the impossibility — apart from the crude demonstrations of silver impregnation — of studying them without the electron microscope. We were particularly impressed by the remarkable variation in diameter of the non-myelinated axons some of them being only $0.1\ \mu$ in diameter and almost certainly invisible with the light microscope even when impregnated with silver. The axons also varied markedly in outline and electron density. The interpretation of these variations in terms of function — sensation conducted, autonomic fibres, etc., — has still to be made.

The number of axons in an individual Schwann cell also varied considerably and was particularly high in infancy. Where myelinated nerve fibres were markedly reduced in number or were completely absent, as in a case of sensory neuropathy, the unmyelinated fibres appeared correspondingly more numerous suggesting that a degree of axonal sprouting had occurred. However, such a conclusion cannot be considered proven until quantitative studies of the normal and abnormal nerves have been carried out. Another feature suggesting regenerative sprouting was the finding of myelinated sheaths of normal thickness around axons of unusually small calibre in a case of Guillain-Barré syndrome with evidence in other fibres of axonal degeneration. Here again, however, statistical studies are required.

These investigations are only in a very preliminary stage but it is already obvious, that electron microscopy will be of the greatest value in extending the meagre information provided by the light microscopy of pathological specimens of human cutaneous nerves.