5 Anhang

5.1 Zusammenfassung

Die dopaminergen Neurone im motorischen und limbischen Mesencephalon sind wichtige regulatorische Stationen in den parallel verlaufenden Basalganglienschleifen. Störungen dieser Neuronen führen zu wichtigen psychischen und motorischen Erkrankungen. Mit bisherigen Therapieansätzen ist es nicht möglich, selektiv nur die psychischen oder motorischen Schleifen zu beeinflussen. Eine Möglichkeit zur Unterscheidung dieser beider Neuronengruppen für zukünftige pharmakologische Therapieansätze könnte über die Beeinflussung von Ionenkanälen erfolgen.

Aus diesem Grund wurde in der vorliegenden Arbeit die Verteilung der Kir3-Kanalproteine im motorischen und limbischen Mesencephalon der Ratte untersucht.

Es wurden Antikörper gegen die vier Mitglieder der Kir3-Familie gewonnen und anschließend gereinigt. Die gereinigten Antikörper wurden in immuncytochemischen Färbungen eingesetzt, um sowohl lichtmikroskopisch als auch elektronenmikroskopisch die Verteilung der Kir3-Kanalproteine in den dopaminergen Neuronen des ventralen Mesencephalons zu untersuchen.

Es gelang alle vier Kanalproteine in diesem Gebiet nachzuwiesen. Sie unterscheiden sich sowohl in ihrer Häufigkeit als auch in ihrer ultrastrukturellen Verteilung. Eine Sonderstellung nimmt das Kanalprotein Kir3.2 ein. Von den vier Kanalproteinen ist es das einzige, dass nicht nur innerhalb von dopaminergen Neuronen (oft in der Nähe des ERs), sondern auch an der Cytoplasmamembran nachgewiesen werden konnte. Zusätzlich ist dieses Protein heterogen verteilt, es weist einen Gradienten zwischen dem lateralen motorischen und dem medial gelegenen limbischen Mesencephalon auf.

Die Ergebnisse der vorliegenden Arbeit lassen es möglich erscheinen, dass die zukünftigen Behandlungen von Störungen der dopaminergen Neurone im motorischen und limbischen Mesencephalon durch eine zusätzliche Beeinflussung von Kir3.2-Kanälen selektiver und mit weniger Nebenwirkungen erfolgen kann.

5.2 Abkürzungen

α	anti, Präfix vor Antikörpern
5-HT	5-Hydroxytryptamin (Serotonin)
A	Adenin
BCA	Bicinchonin Säure
BCIP	5-Brom-4-Chloro-3-Indolyl-phosphat
bp	Basenpaare
BSA	engl. bovin serum albumin (Rinderserum-Albumin)
C	Cytosin
CCK_8	Cholecystokinin 8
ChAT	Cholinacetyltransferase
CLi	Nucleus caudalis linearis
D	Asparaginsäure
Da	Dalton
DA	Dopamin
DAB	Diaminobenzidin
DHFR	Dihydrofolat-Reduktase
DLG	engl. Drosophila lethal(1)discs large-1 tumor suppressor protein
DNA	Desoxyribonucleinsäure
dNTP	Desoxynucleosidtriphospat
E	Glutamat
EDTA	Ethylendiamintetraessigsäure
G	Guanin
GABA	gamma-Amino-n-Buttersäure
GAD	Glutamatdehydrogenase
GPi	Globus pallidus pars interna
GPe	Globus pallidus pars externa
IF	Nucleus interfascicularis
Ig	Immunglobuline
IPTG	Isopropyl-β-D-thiogalactosid
K	Lysin
kb	Kilo-Basenpaare
kDa	Kilo-Dalton

Kir	engl. Inwardly rectifying potassium (K) channel (einwärtsgleichrichtender Kaliumkanal)
LB	engl. Luria broth (Bakterienmedium)
LMW	engl. Low Molecular Weight (Molekulargewichts-standard)
NBT	Nitroblautetrazoliumchlorid
NK-B	Neurokinin-B
NT	Neurotensin
$OD_{.... nm}$	Optische Dichte bei ..... nm
PaP	Nucleus parapeduncularis
PBPL	Nucleus pigmentosus parabrachialis pars lateralis
PBPM	Nucleus pigmentosus parabrachialis pars medialis
PDZ	eine zuerst in folgenden Proteinen gefundene Domäne: PSD-95 (SAP-90), DLG und ZO-1
PAGE	Polyacrylamid-Gelelektrophorese
PCR	Polymerase-Kettenreaktion
PBS	Phosphat gepufferte Saline
PN	Nucleus paranigralis
PIP_2	Phosphatidylinositol(4,5)–bisphosphat
R	Arginin
RLi	Nucleus rostralis linearis
SDS	engl. Sodium dodecylsulfate (Natriumdodecylsulfat)
SN	Substantia Nigra
SNc	Substantia Nigra pars compacta
SNcd	Substantia Nigra pars compacta, dorsalis
SNcv	Substantia Nigra pars compacta, ventralis
SN_L	Substantia Nigra pars lateralis
SNr	Substantia Nigra pars reticulata
SP	Substanz P
S	Serin
SUR	engl. sulfonylurea receptor (Sulfonylharnstoff Rezeptor)
T	Thymin
TASK	engl. TWIK-1-related acid sensitive K^+ channel
TEMED	N,N,N′,N′,-Tetramethyethylendiamin
TH	Tyrosinhydroxylase
TOSS	engl. TWIK-originated similarity sequence
TRAAK	engl. TWIK-related arachidonic acid-stimulated K^+ channel
TREK	engl. TWIK-1-related K^+ channel

Tris	Tris(hydroxymethyl)-aminomethan
TWIK-1/-2	engl. tandem of p-domains in a weak inward rectifying K^+ channel
U	engl. unit (Einheit zur Kennzeichnung der Enzymaktivität)
V	Valin
VAChT	Vesikulärer Acetylcholin Transporter
VTA	engl. Ventral Tegmantal Area (Area tegmentalis ventralis)
... × g	...fache der Erdbeschleunigung
ZNS	zentrales Nervensystem

Alle nicht aufgeführten Abkürzungen physikalischer Größen und deren Eineiten entsprechen dem SI-System (*Systeme International D´Unites*).

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5.4 Publikationen

5.4.1 Veröffentlichung

Schmidt,K., Eulitz,D., Veh,R.W., Kettenmann,H. & Kirchhoff,F. (1999) Heterogeneous expression of voltage-gated potassium channels of the shaker family (Kv1) in oligodendrocyte progenitors. *Brain Res.*, **843**, 145-160.

5.4.2 Posterbeiträge

Eulitz, D., Thomzig, A., Karschin, A. und Veh, R. W. “Regional, Cellular, and Subcellular Localization of Kir3.0 Channel Proteins in Rat Brain”. 14. Arbeitstagung der Anatomischen Gesellschaft, Würzburg. 1997. Annals of Anatomy, Supplement 180 (1998).

Eulitz, D., Thomzig, A. und Veh, R. W. “Chemoarchitecture und Subnuclear Composition of the Basal Mesencephalon (VTA/SNc Complex) in Rat and Mouse”. 15. Arbeitstagung der Anatomischen Gesellschaft, Würzburg. 1998. Annals of Anatomy, Supplement 181 (1999).

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5.5 Lebenslauf

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5.6 Danksagung

Die vorliegende Arbeit wurde in der Arbeitsgruppe „Elektronenmikroskopie und molekulare Neuroanatomie“ am Institut für Anatomie der Charité durchgeführt. Bedanken möchte ich mich bei Prof. Dr. R. W. Veh für die Bereitstellung des interessanten Themas.

Ich danke den Mitarbeitern der Arbeitsgruppe für das freundschaftliche Klima und die gute Zusammenarbeit. Ich danke allen für die anregenden Diskussionen und die stets gewährte Hilfsbereitschaft, sie haben zum Gelingen der Arbeit beigetragen. Mein Dank geht auch an Dr. Thomas Jöns für das Lesen des Manuskripts.

Ich danke Rike für ihre Geduld und Hilfe.