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# The Subthalamic Nucleus

## Part I: Development, Cytology, Topography and Connections

With 29 Figures



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## **Abstract**

This monograph (Part I of two volumes) on the subthalamic nucleus (STN) accentuates the gap between experimental animal and human information concerning subthalamic development, cytology, topography and connections. The light and electron microscopical cytology focuses on the open nucleus concept and the neuronal types present in the STN. The cytochemistry encompasses enzymes, NO, glial fibrillary acidic protein (GFAP), calcium binding proteins, and receptors (dopamine, cannabinoid, opioid, glutamate,  $\gamma$ -aminobutyric acid (GABA), serotonin, cholinergic, and calcium channels). The ontogeny of the subthalamic cell cord is also reviewed. The topography concerns the rat, cat, baboon and human STN. The descriptions of the connections are also given from a historical point of view. Recent tracer studies on the rat nigro-subthalamic connection revealed contralateral projections. Part II of the two volumes (volume 199) on the subthalamic nucleus (STN) starts with a systemic model of the basal ganglia to evaluate the position of the STN in the direct, indirect and hyperdirect pathways. A summary of *in vitro* studies is given, describing STN spontaneous activity as well as responses to depolarizing and hyperpolarizing inputs and high-frequency stimulation. STN bursting activity and the underlying ionic mechanisms are investigated. Deep brain stimulation used for symptomatic treatment of Parkinson's disease is discussed in terms of the elements that are influenced and its hypothesized mechanisms. This part of the monograph explores the pedunculopontine–subthalamic connections and summarizes attempts to mimic neurotransmitter actions of the pedunculopontine nucleus in cell cultures and high-frequency stimulation on cultured dissociated rat subthalamic neurons. STN cell models – single- and multi-compartment models and system-level models are discussed in relation to subthalamic function and dysfunction. Parts I and II are compared.

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## Abbreviations

A	Fields of Sano
A	Adenosine receptor
A8,A9	Catecholaminergic areas
ABC	Avidin-biotin-HRP complex
Alent	Ansa lenticularis (Fig. 2)
AMPA	$\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid
Am(g)	Amygdala
Apt	Anterior pretectal nucleus: AD, AM, AV indicate the dorsal, medial, ventral parts
APV	D-2-Amino-5-phosphono-valerate
AWSR	Array-wide spiking rate
AV	Anterior thalamic nucleus
BAPTA	1,2-bis(2-Aminophenoxy)-ethane- <i>N,N,N',N'</i> -tetraacetic acid
bc	Brachium conjunctivum
bci	Brachium of the colliculus inferior
BDA	Biotinylated dextran amine
BG	Basal ganglia
BI	Burst index
BIP	Burst intensity product
bp	Brachium pontis
CaBP	Calcium binding proteins
CB	Cannabinoid receptor
CB	Calbindin
CC	Corpus callosum
cd	Nucleus caudatus
Ce	Capsula interna (Fig. 2)
ChII	Chiasma opticum
CG	Central grey
Ci	Capsula interna (also Fig. 2)
ci	Capsula interna
Cl	Corpus Luysii

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cl	Contralateral
cla	Clastrum
Cm	Corpus mamillare (Fig. 2)
CM	Centre median
Cml	Ganglion laterale corp. mamillare (Fig. 2)
Cmm	Ganglion mediale corp. mamillare (Fig. 2)
Coa	Commissural anterior (Fig. 2)
Coha	Commissura hypothalamica anterior (Fig. 2)
Cop	Commissura posterior
Cospm	Commissura supramamillaris (Fig. 2)
cp	Pedunculus cerebri
CR	Calretinin
Cu	Cuneiform nucleus
Csth	Corpus subthalamicum (Fig. 2)
ctb	Central tegmental tract of von Bechterew
ctt	Central tegmental tract
δ	Opioid receptor
d	Vesicle containing dendrites
D	Dopamine receptor
DA	Dopamine
Dbc	Decussation of brachium conjunctivum
DBS	Deep brain stimulation
dcv	Dense core vesicle terminals
DIV	Days in vitro
Dlx1/2	Homeobox gene
DNQX	6,7-Dinitroquinoxaline-2,3-dione
E	Embryonic day
EP	Nucleus entopeduncularis
F1	Flat type 1 (boutons)
F2	Flat type 2 (boutons)
Fhy	Fasciculus hypophyseos (Fig. 2)
Fmp	Fasciculus mamillaris princeps (Fig. 2)
Fo	Fornix (Fig. 2)
Fsp	Fasciculus subthalamicopeduncularis (Fig. 2)
fp	Fibrae perforantes (Fig. 2)
frtf	Fasciculus retroflexus Meynerti (Fig. 2)
Fu	Fasciculus uncinatus (Fig. 2)
GABA	γ-Aminobutyric acid
GAD	Glutamic acid decarboxylase
GAT	Specific high-affinity GABA uptake protein

GC	Gyrus cinguli
GCA	Gyrus centralis anterior
GCP	Gyrus centralis posterior
Gem	Ganglion ectomamillare (Fig. 2)
GF	Gyrus fusiformis
GH	Gyrus hippocampi
Ghb	Ganglion habenulae (Fig. 2)
gl	Corpus geniculatum
Glp	Glandula pinealis (Fig. 2)
glp	Globus pallidus (Fig. 2)
Glu	Ionotropic glutamate receptor
GP	Globus pallidus
GPe	Globus pallidus externus
GPi	Globus pallidus internus
H,h	H (Haubenfelder) fields of Forel (also Fig. 2)
5HT	5-Hydroxytryptamine
HRP	Horseradish peroxidase
HVA	High voltage activated currents
I	Insula Reilii (Fig. 2)
i	Nucleus internus gangl. med. corp. mamillaris (Fig. 2)
il	Ipsilateral
Ins	Insula
ISI	Interspike interval
κ	Opioid receptor κ
Kv3	Type delayed rectifier
L	Calcium channel type
ll	Lemniscus lateralis
Lm	Lemniscus medialis (also Fig. 2)
Lmi	Lamina medullaris interna
Lmm	Lamina medullaris medialis (Fig. 2)
Lml	Lamina medullaris lateralis (Fig. 2)
Lp	Posterior limitans thalamic nucleus
LPC	Gyrus paracentralis
LPI	Lobulus parietalis inferior
LR1	Large round type 1 (bouton)
LR2	Large round type 2 (bouton)
LTS	Low-threshold spike
μ	Opioid receptor μ
M,m	Cholinergic receptor

MEA	Midbrain extrapyramidal area
MEA	Multi-electrode array
mGlu	Metabotropic glutamate receptor
ml	Medial lemniscus
mlf	Fasciculus longitudinalis medialis
MPTP	1-Methyl-4-phenyl-1,2,3,6 tetrahydropyridine
mV	Motor nucleus of the nervus trigeminus
N	Calcium channel type
N	Substantia nigra
Nam	Nucleus amygdaliformis (Fig. 2)
Nans	Nucleus ansae lenticularis Meynerti (Fig. 2)
Narc	Nucleus arcuatus thalami (Fig. 2)
Nc	Nucleus caudatus (Fig. 2)
Nci	Nuclei of the colliculus inferior
NcM	Nucleus commissurae Meynerti (Fig. 2)
Ndd	Nuclei dorsales disseminati thalami (Fig. 2)
Neop	Nucleus of Darkschewitsch (Fig. 2)
NGF	Nerve growth factor
Ni	Substantia nigra
Nic	Substantia nigra pars compacta
Nir	Substantia nigra pars reticulata
Nkx-2.1	Homeobox gene
Nl	Nucleus centralis thalami (Fig. 2)
Nld	Nucleus lateralis dorsalis thalami (Fig. 2)
Nlv	Nucleus lateralis ventralis thalami (Fig. 2)
Nlve	Nucleus lateralis ventralis ext. thalami (Fig. 2)
Nlvi	Nucleus lateralis ventralis int thalami (Fig. 2)
Nm	Nucleus medialis thalami (Fig. 2)
Nmi	Nucleus mamilloinfundibularis (Fig. 2)
NMDA	<i>N</i> -Methyl-D-aspartate
NO	Nitric oxide
NOS	Nitric oxide synthase
NP	Pontine nuclei
Nso	Nucleus supraopticus
NR	Subtypes NMDA receptor
Ntg	Nucleus ruber tegmenti (Fig. 2)
Ntgd	Nucleus ruber tegmenti pars dorsalis (Fig. 2)
NIII	Nucleus oculomotorius
NVme	Mesencephalicus trigeminal nucleus
6-OH-DA	6 Hydroxy dopamine
ot	Tractus opticus
$\omega$ -CgTX	$\omega$ -Conotoxin
$\omega$ -AgTX	$\omega$ -Agatoxin

P	Postnatal day
P	Calcium channel type
pale	Globus pallidus externus
pali	Globus pallidus internus
parahip	Parahippocampal gyrus
PBP	Parabrachial pigmented nucleus
pc	Pedunculus cerebri
Ped	Pedunculus cerebri
Pl	Nucleus paralemniscalis
Pp	Pes pedunculus
PPN	Nucleus tegmenti pedunculopontinus
ppci	Capsula interna pars peduncularis
Pu	Putamen (Fig. 2)
Pul	Pulvinar (Fig. 2)
put	Putamen
PV	Parvalbumin
Q	Calcium channel type
R	Calcium channel type
R	Nucleus ruber
RE	Thalamo-reticular cells
RT	Nucleus reticularis thalami
Ru	Nucleus ruber
SC	Colliculus superior
SEM	Scanning electron microscopy
Sg	Suprageniculate nucleus
Shh	Sonic hedgehog
Smg	Gyrus supramarginalis
SN	Substantia nigra
SNC	Substantia nigra pars compacta
SNL	Substantia nigra pars lateralis
SNr	Substantia nigra pars compacta
Sns	Substantia nigra Soemmeringi (Fig. 2)
Spa	Substantia perforata anterior (Fig. 2)
SR	Small round boutons
St	Stria cornea (Fig. 2)
st	Spinothalamic tract
Stri	Stratum intermedium pedunculi (Fig. 2)
Strz	Stratum zonale thalami (Fig. 2)
STN	Subthalamic nucleus
T	Calcium channel type
t	Türck's part of cerebral peduncle

T1-3	Temporal gyri
TII	Tractus opticus
Tbc	Tuber cinereum (Fig. 2)
TC	Thalamo-cortical cells
TcTT	Tractus corticotegmentothalamicus Rinviki
TEA	Tetraethylammonium chloride
Tgpp	Nucleus tegmenti pedunculopontinus
Tpt	Tractus peduncularis transversus (Fig. 2)
Tri	Trigonum intercrurale
Tt	Taenia thalami
TTX	Tetrodotoxin
Un	Uncus
Va	Fasciculus mammillothalamicus (Fig. 2)
VA	Ventral anterior thalamic nucleus
VE	Nuclei ventralis thalami
Vim	Nucleus ventralis intermedius thalami
VM	Ventral medial thalamic nucleus
Voa	Nucleus ventro-oralis anterior
Vop	Nucleus ventro-oralis posterior
VPI	Nucleus ventralis posterior inferior thalami
VPL	Nucleus ventralis posterior lateralis thalami
VPM	Nucleus ventralis posterior medialis thalami
VTA	Ventral tegmental area
VIII	Ventriculus tertius (Fig. 2)
Wnt-3	Homeobox gene
Zi	Zona incerta (also Fig. 2)
II	Optic tract
3D	Three dimensional
IV	Nervus trochlearis