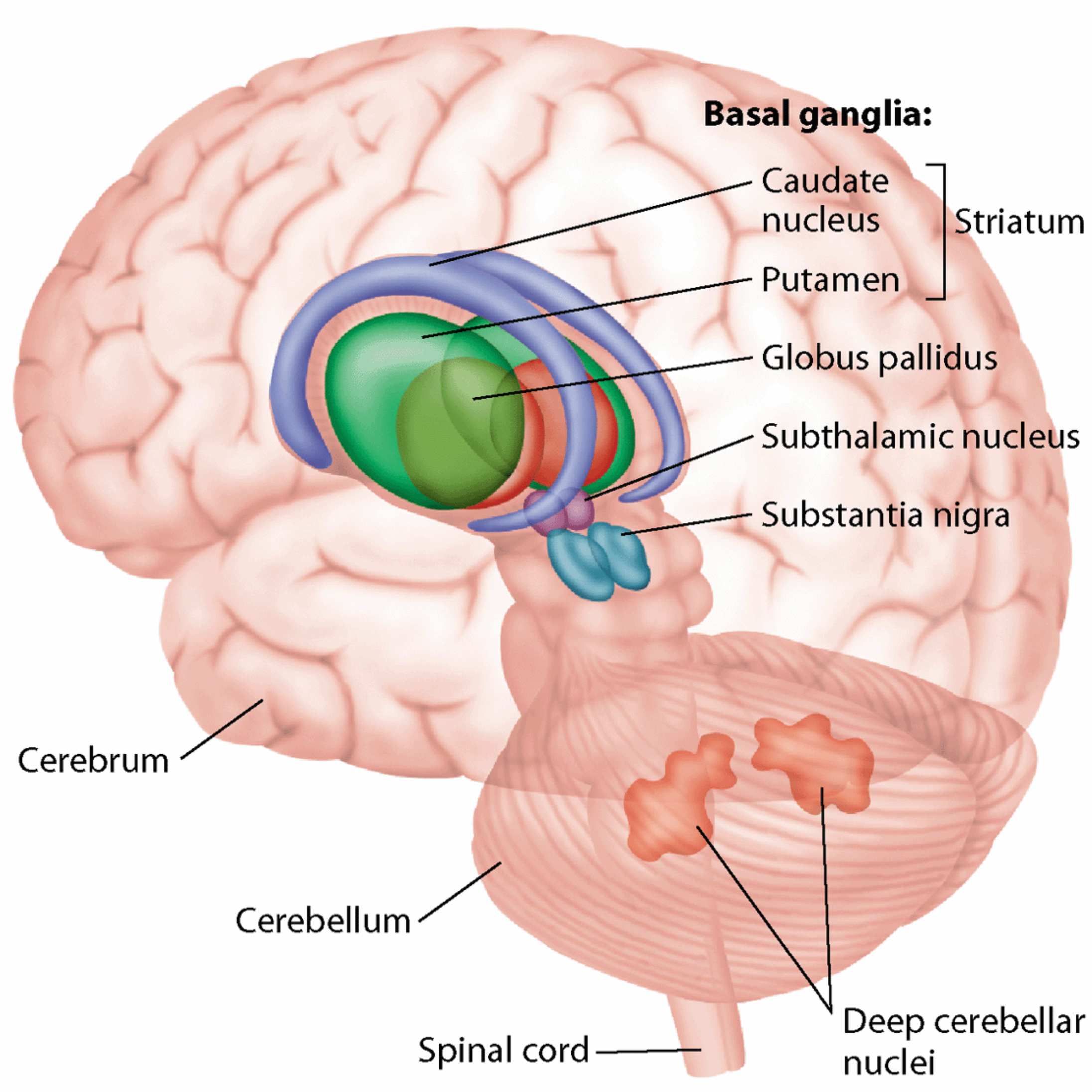
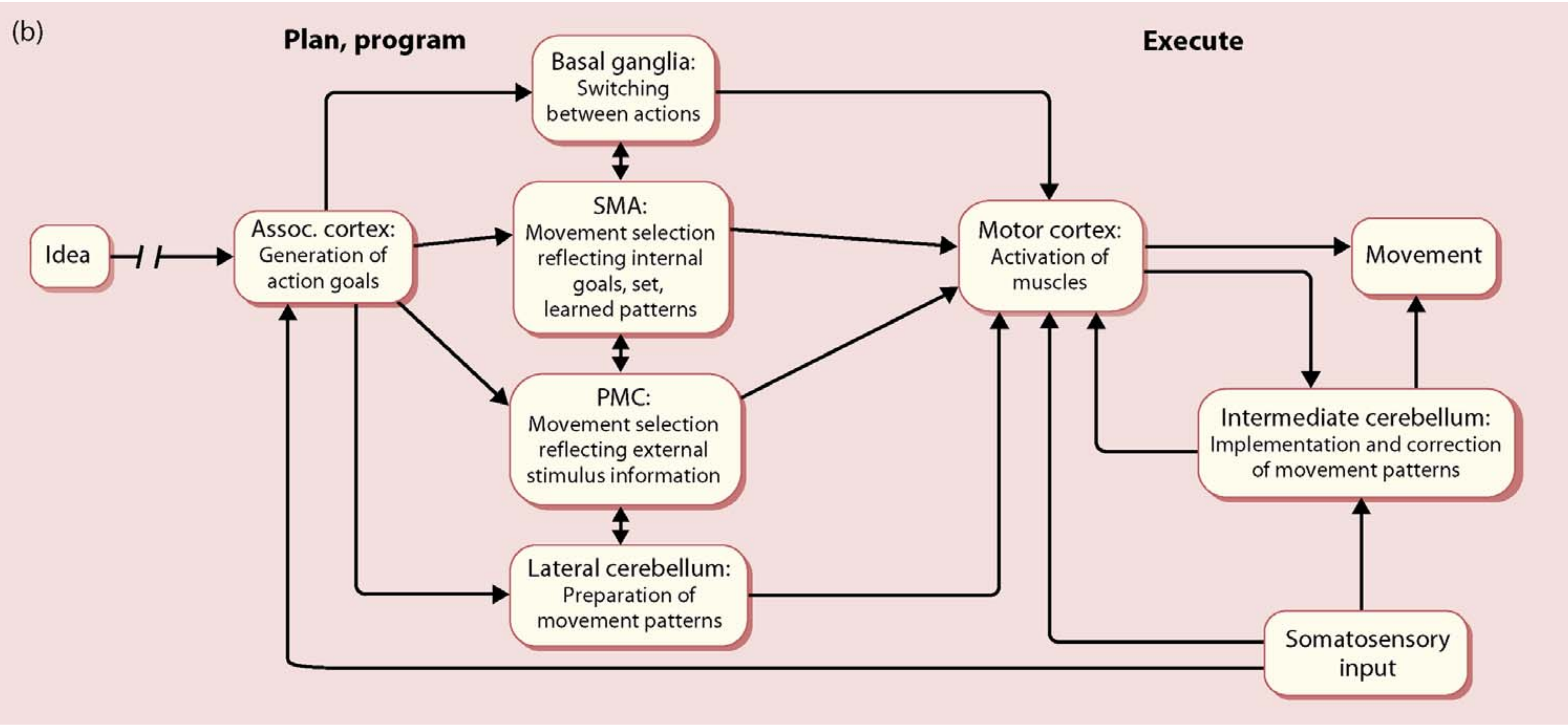
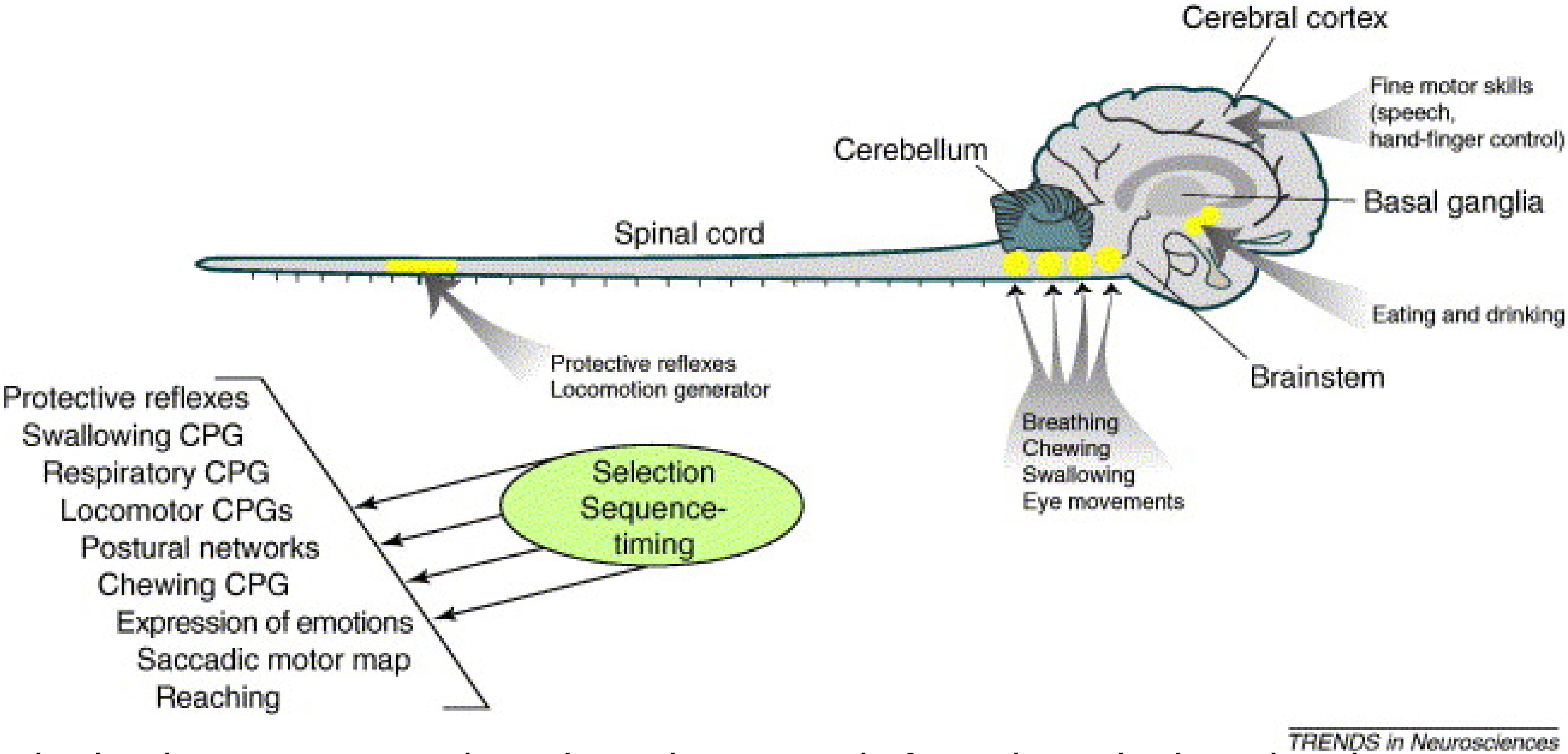
MOTOR SYSTEMS 2
BASAL GANGLIA

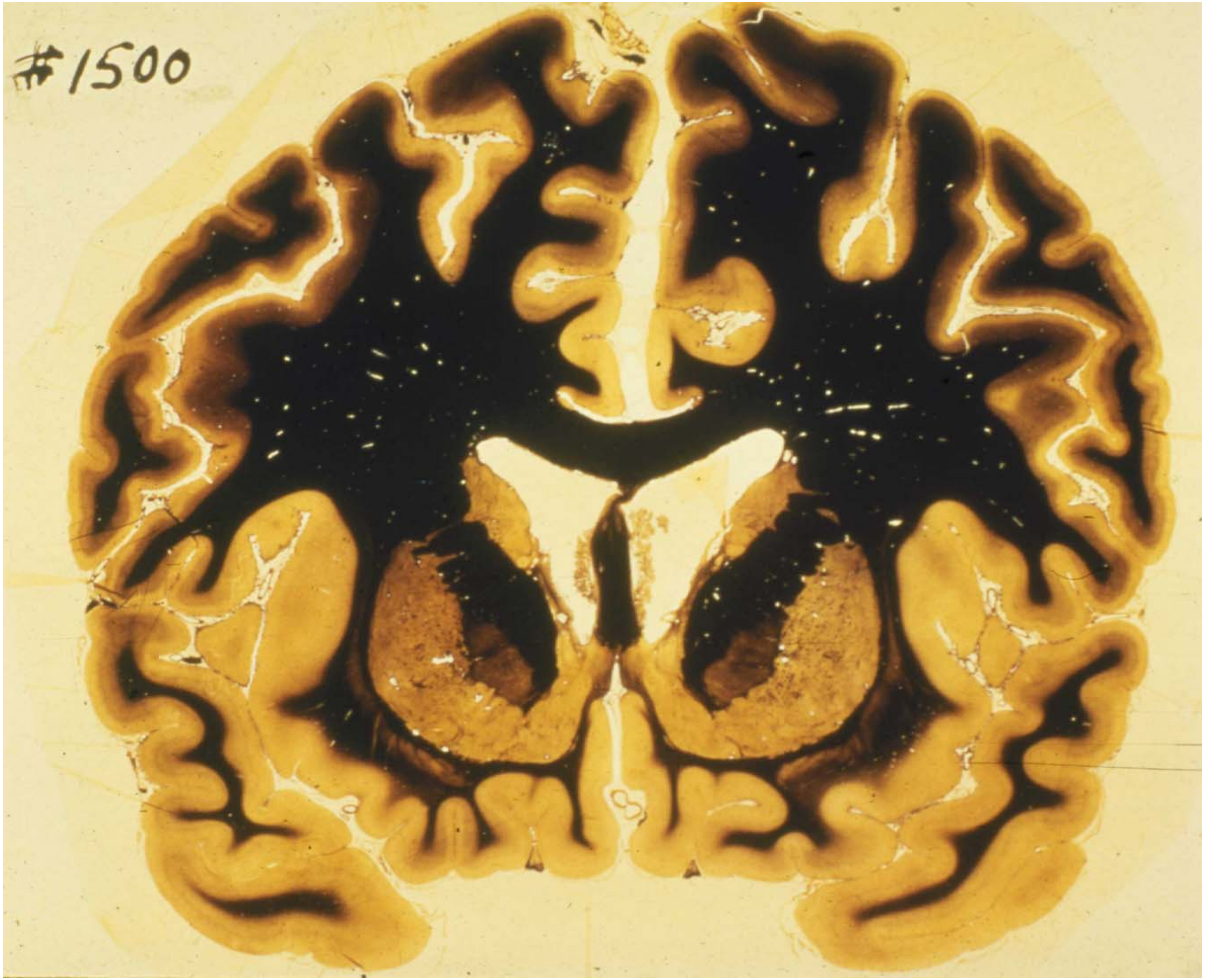



(b)
Plan, program
Execute
Basal ganglia:
Switching between actions
Idea
Assoc. cortex:
Generation of action goals
SMA:
Movement selection reflecting internal goals, set, learned patterns
Motor cortex:
Activation of muscles
Movement
PMC:
Movement selection reflecting external stimulus information
Intermediate cerebellum:
Implementation and correction of movement patterns
Lateral cerebellum:
Preparation of movement patterns
Somatosensory input

MECHANISM FOR SELECTION OF MOTOR PROGRAMS 1.



The basic motor repertoire. Along the neuraxis from the spinal cord to the upper brainstem, there are several neuronal networks or motor programs that when activated will produce different types of motor behaviour (drawing, upper right). They are composed of different networks that, for rhythmic motor patterns such as respiration, chewing and locomotion, are often referred to as central pattern generators (CPGs;yellow circles). Even more complex are the motor maps in tectum (superior colliculus) designed to control saccadic eye movements (Grillner et al, 2005)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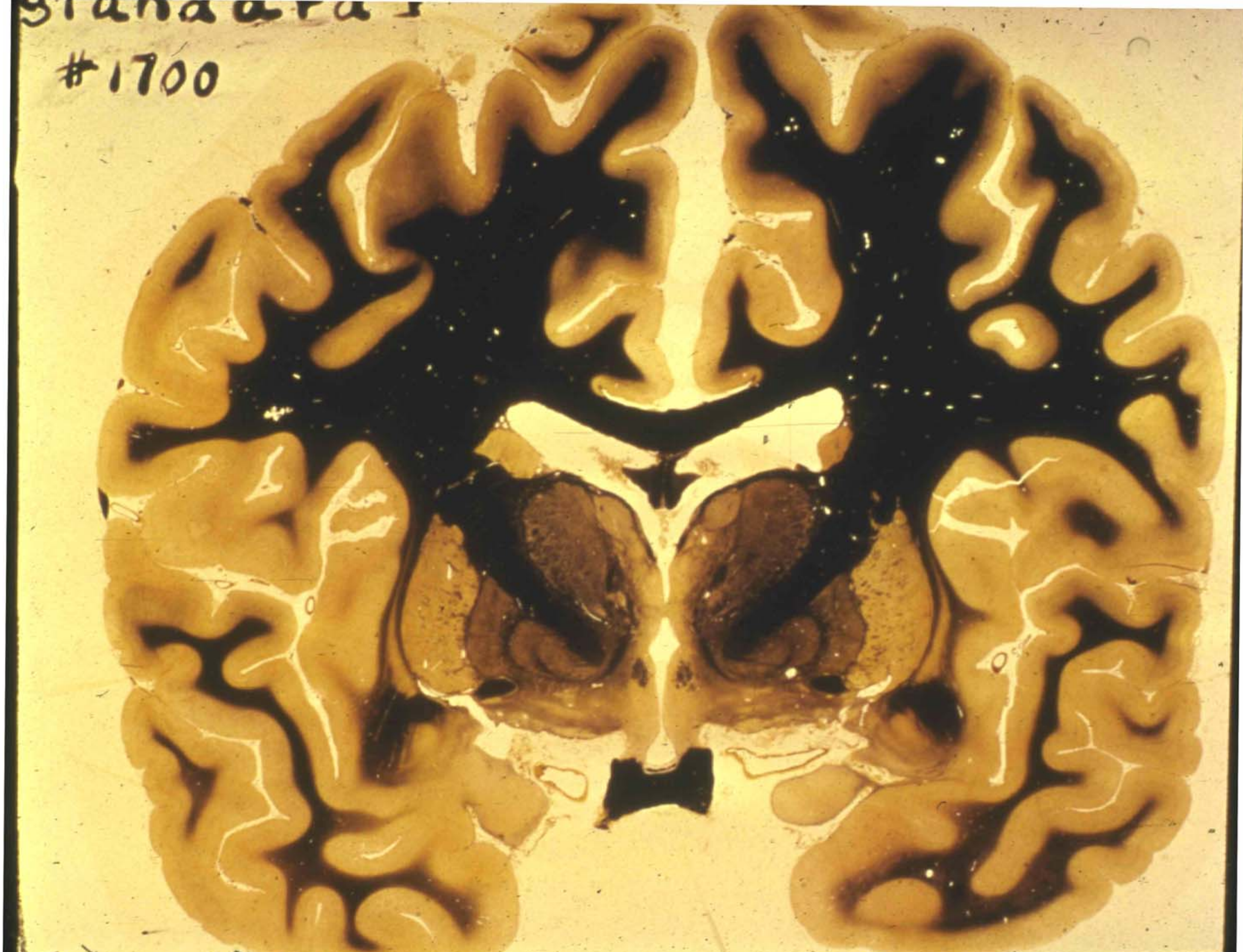
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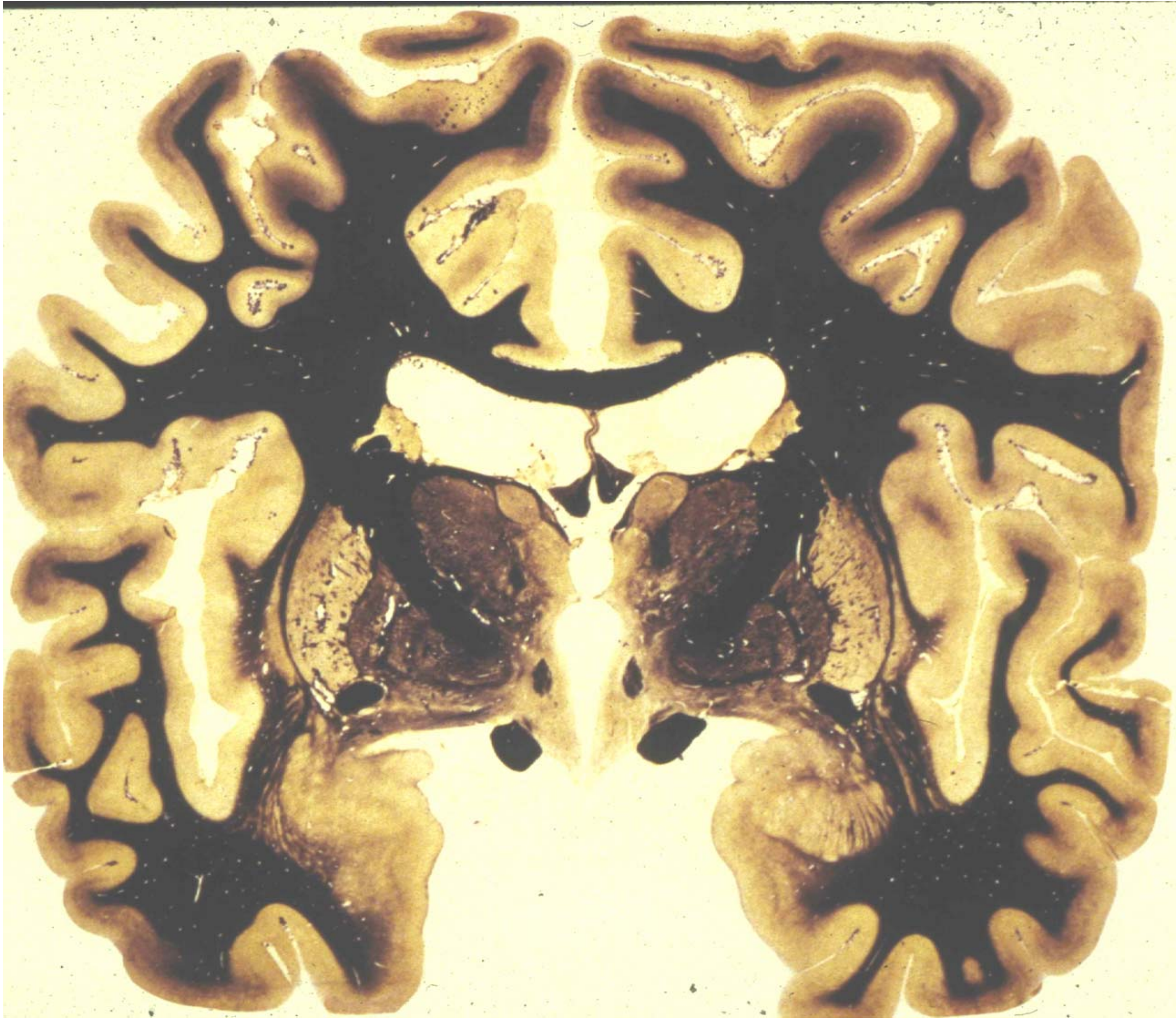

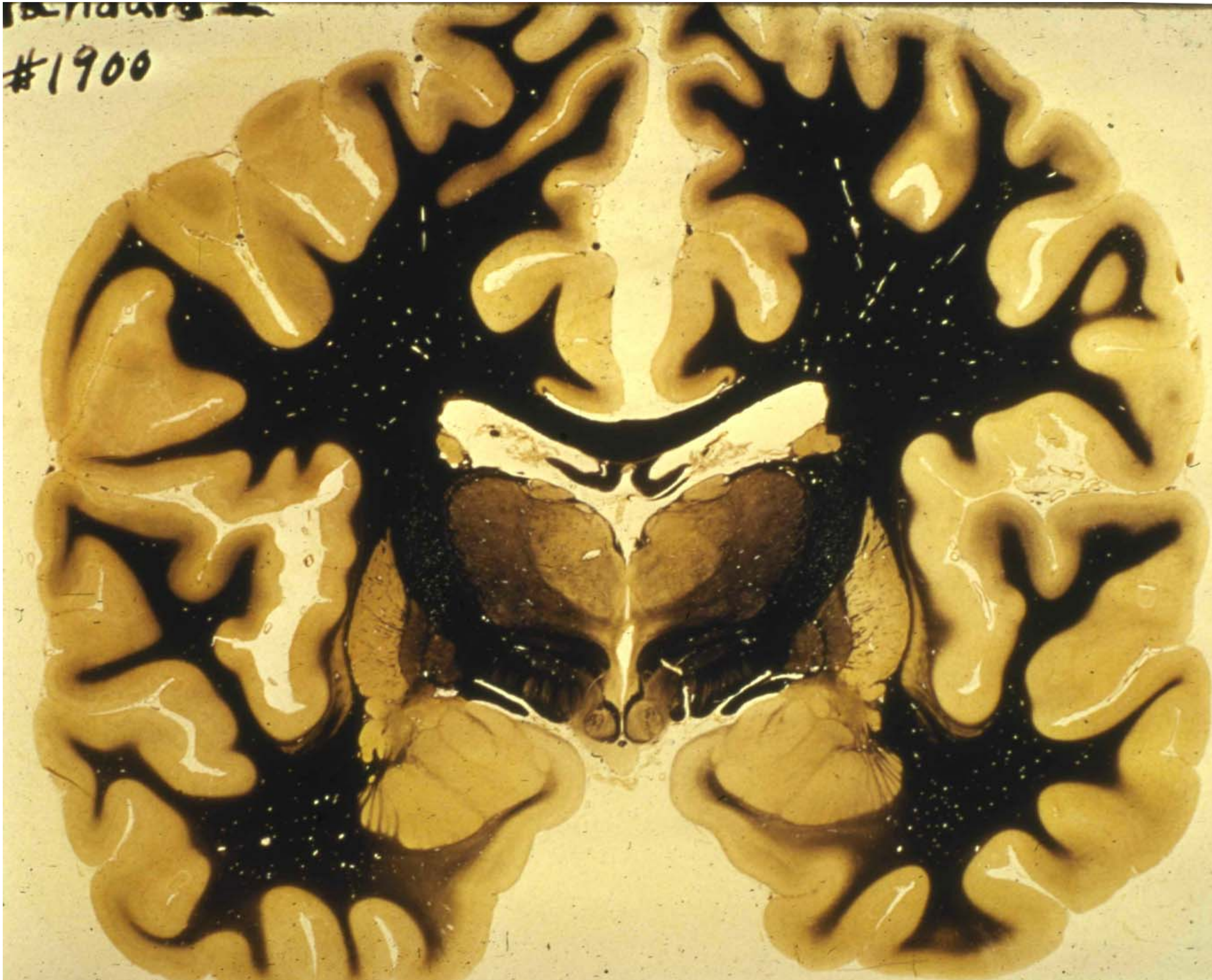
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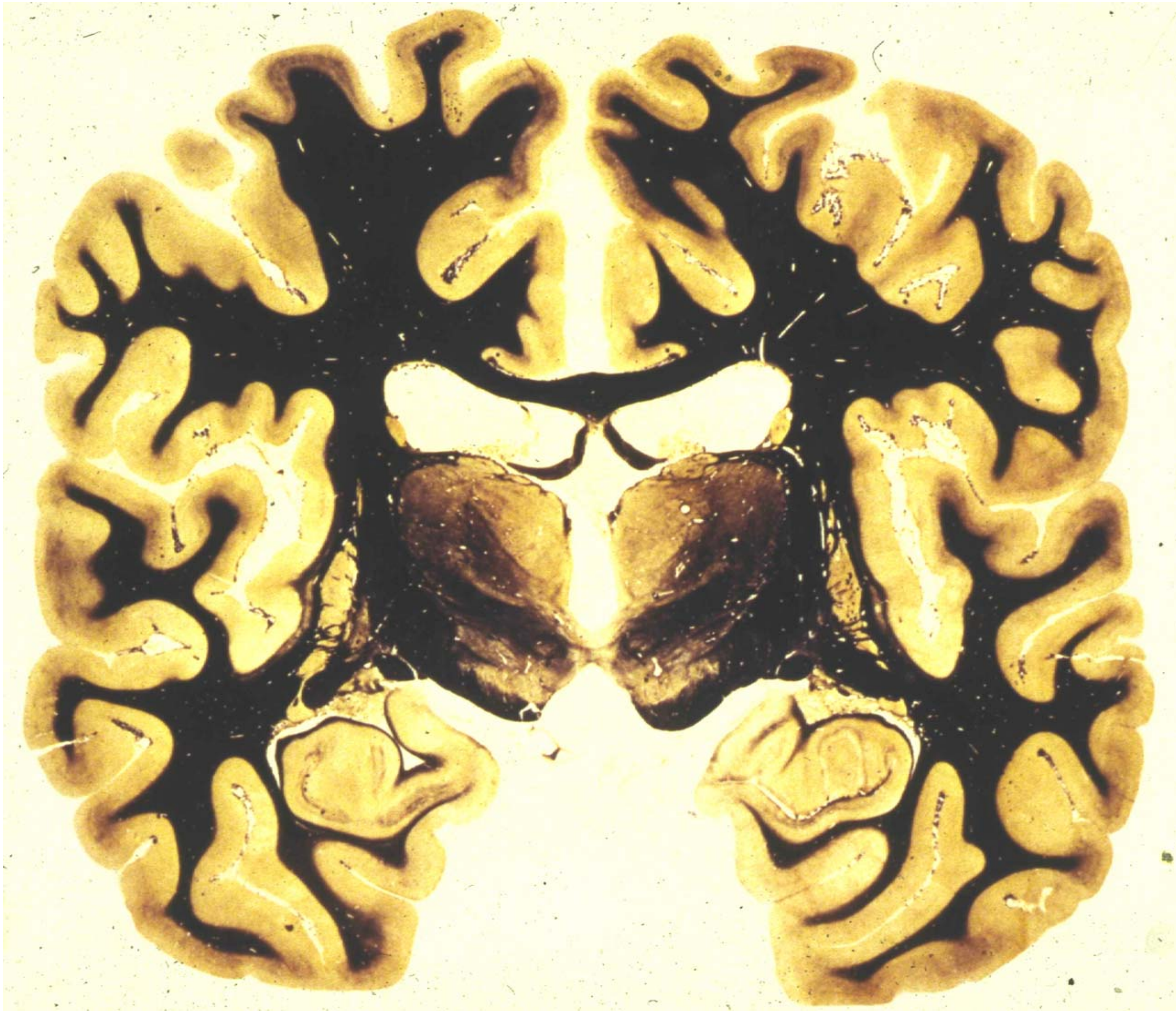
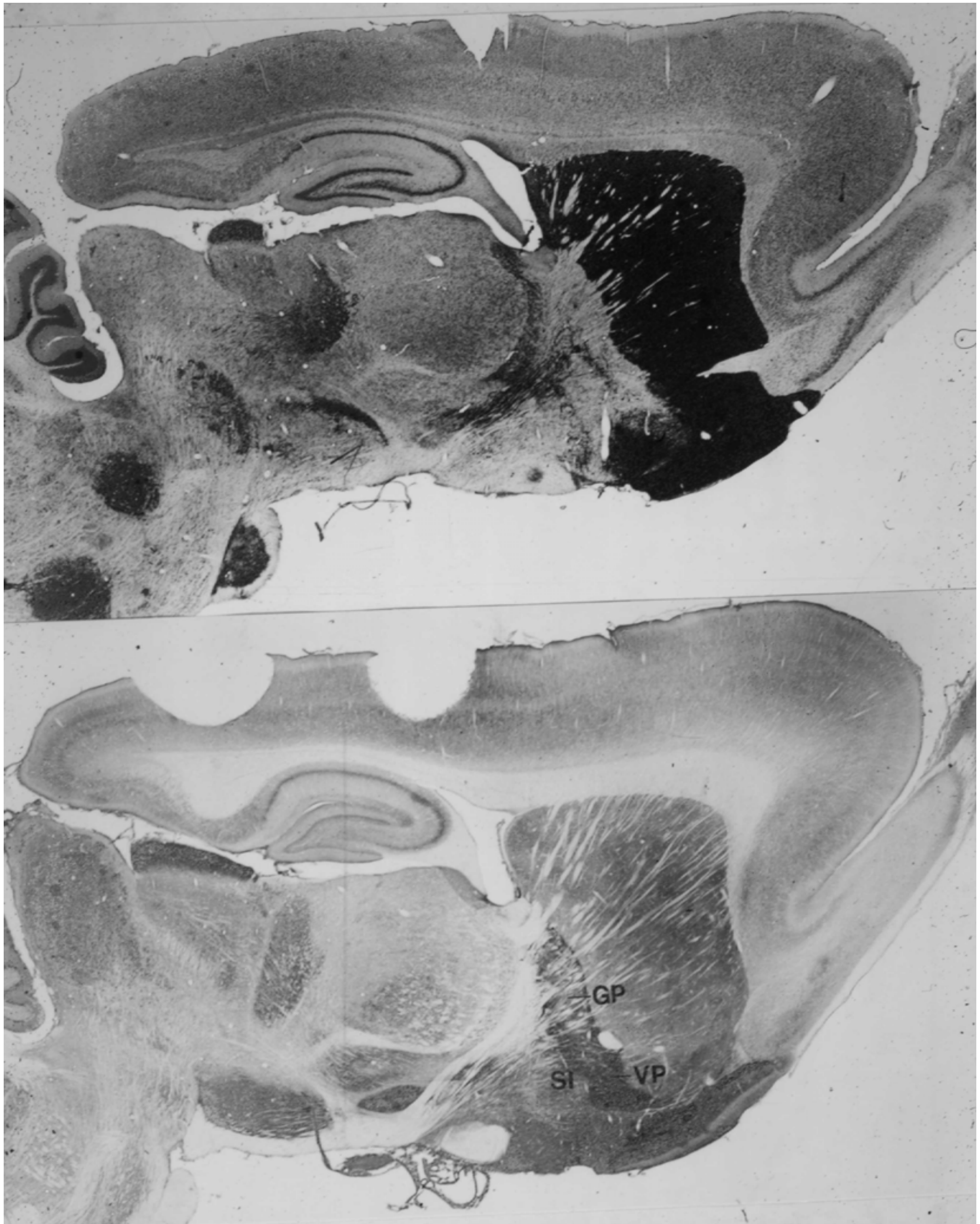


STRIATAL COMPARTMENTS 1: DORSAL-VENTRAL STRIATUM



DORSAL STRIATUM-

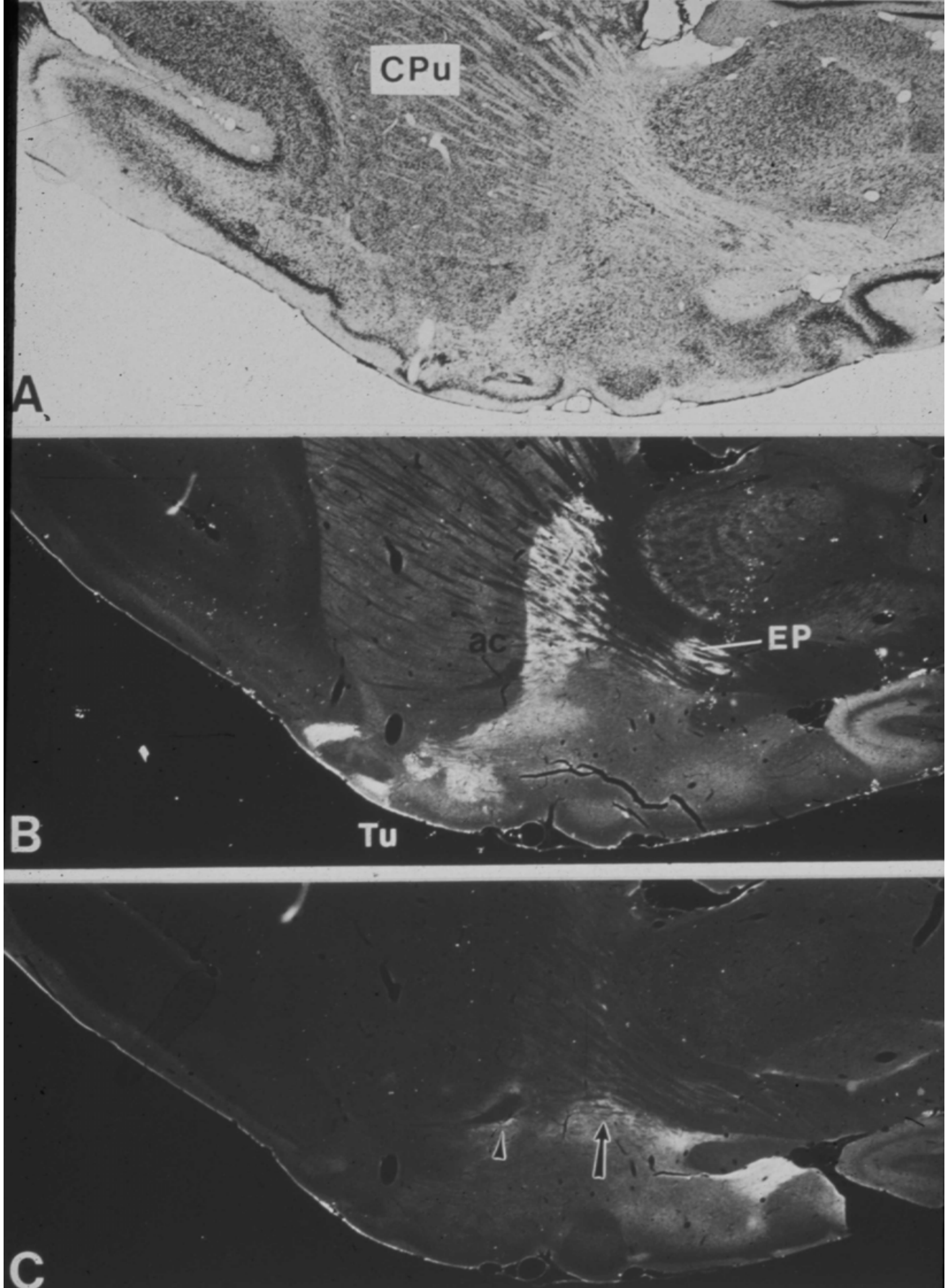
VENTRAL STRIATUM

ACHE

DORSAL PALLIDUM-

VENTRAL PALLIDUM

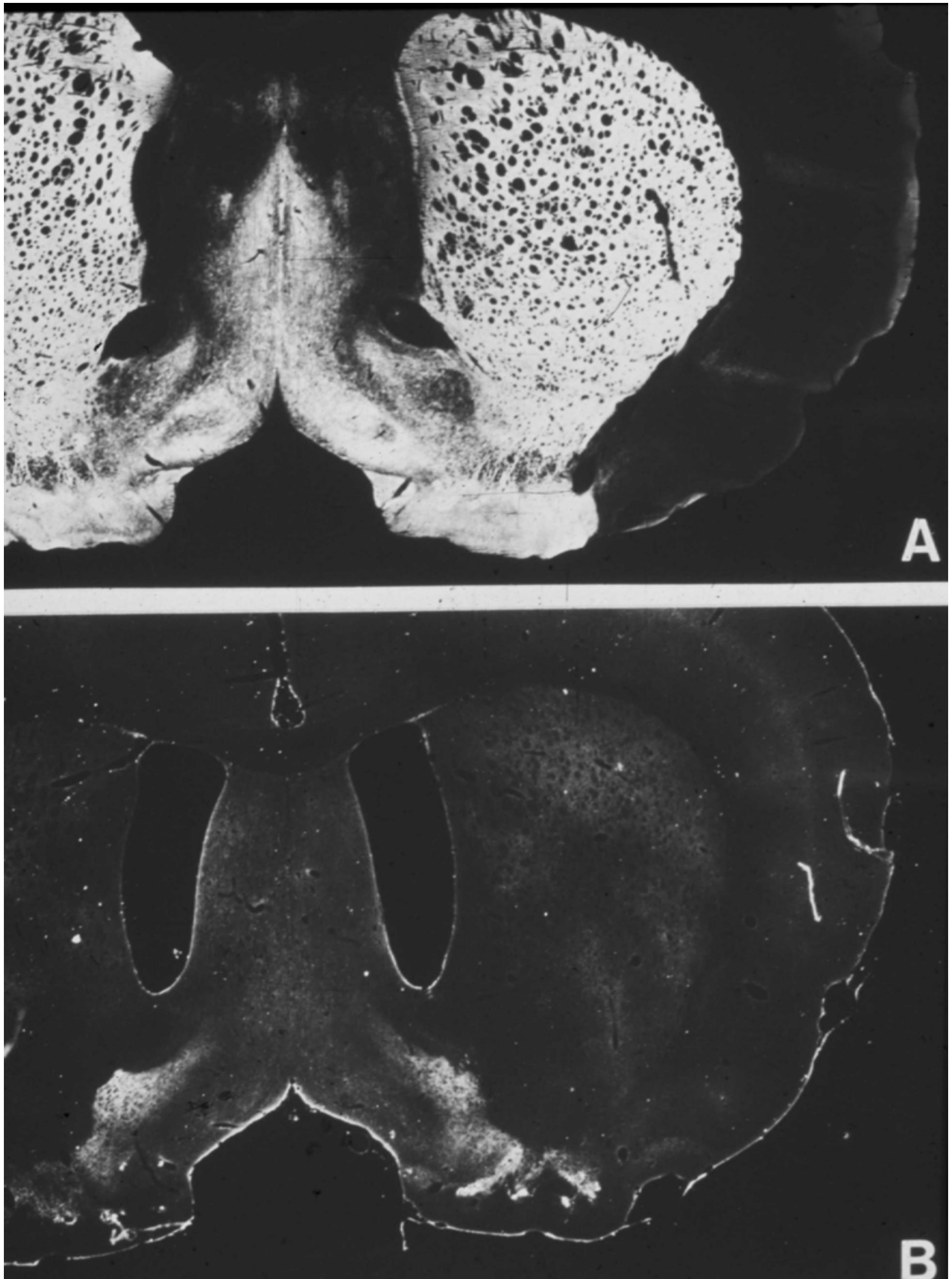
GAD

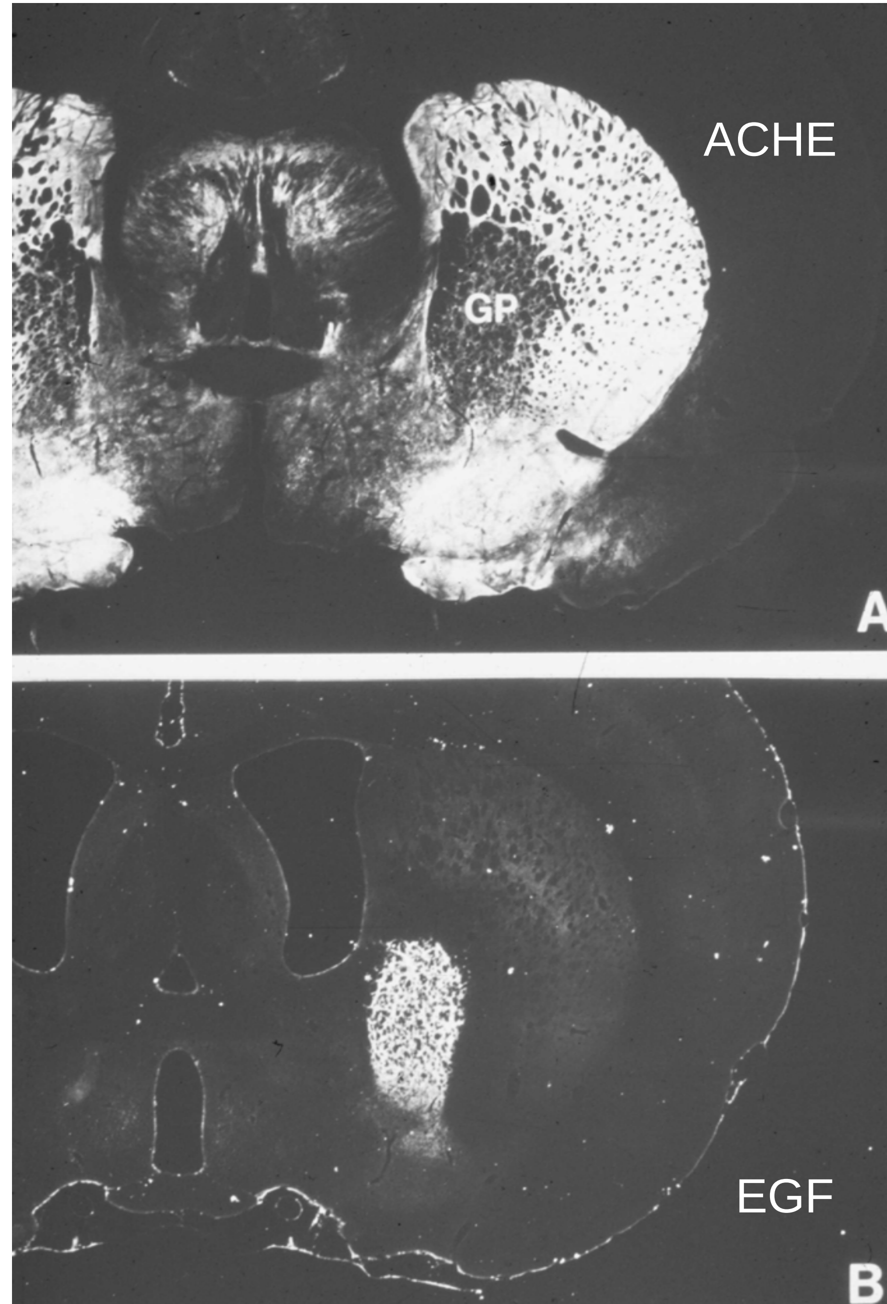


Nissl

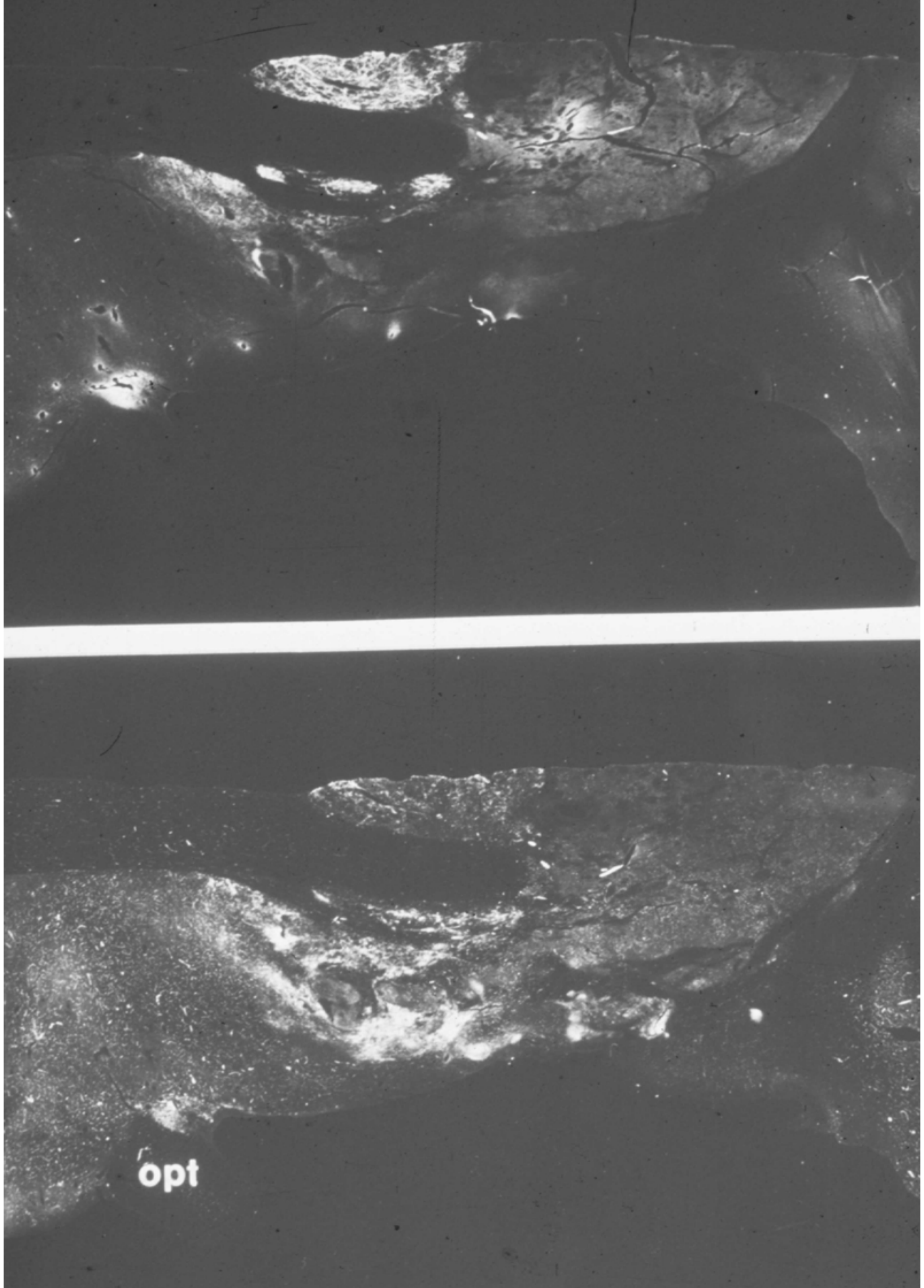
EGF

ANG


A
B

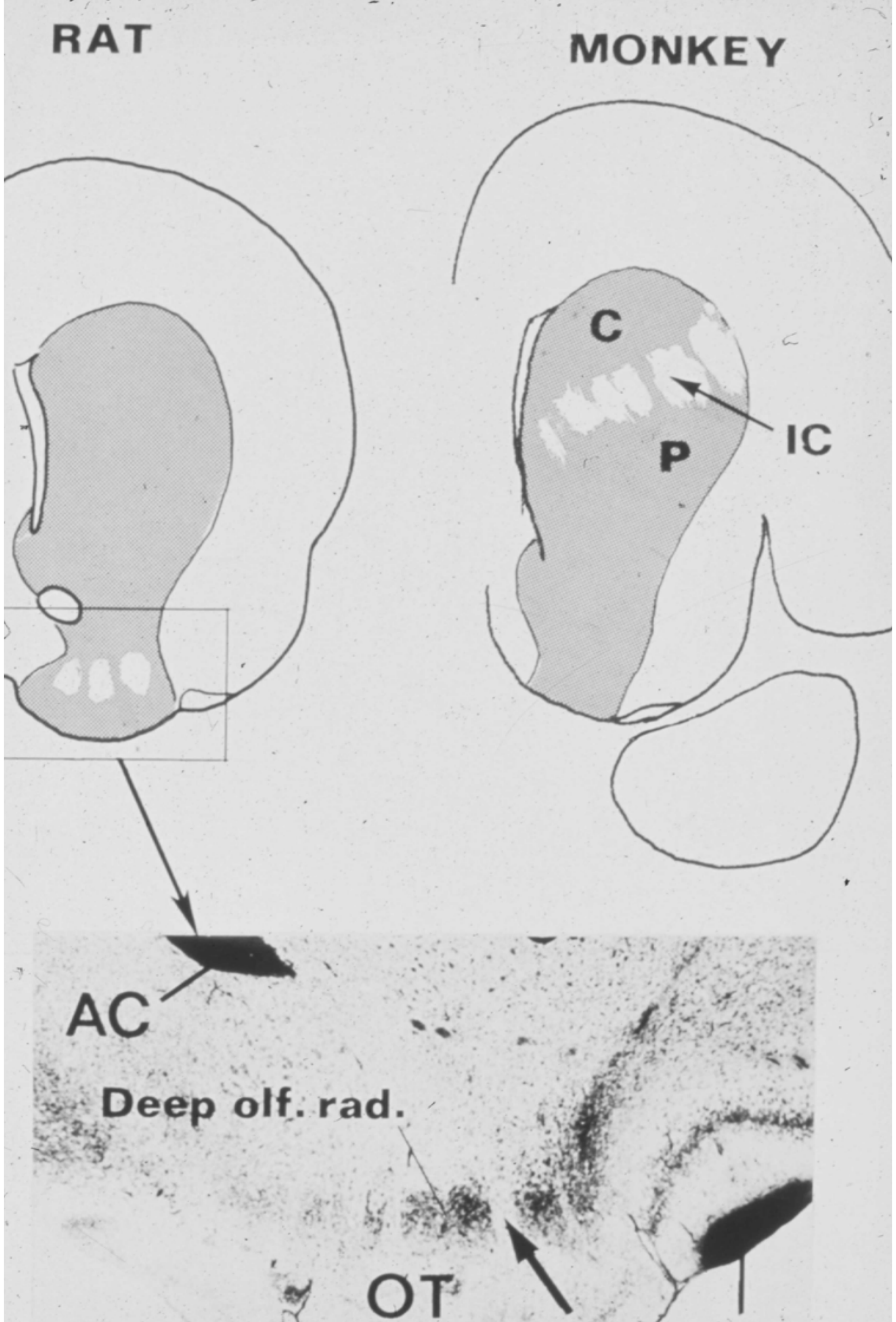

ACHE
GP
A
EGF
B

VENTRAL
PALLIDUM IN
HUMANS

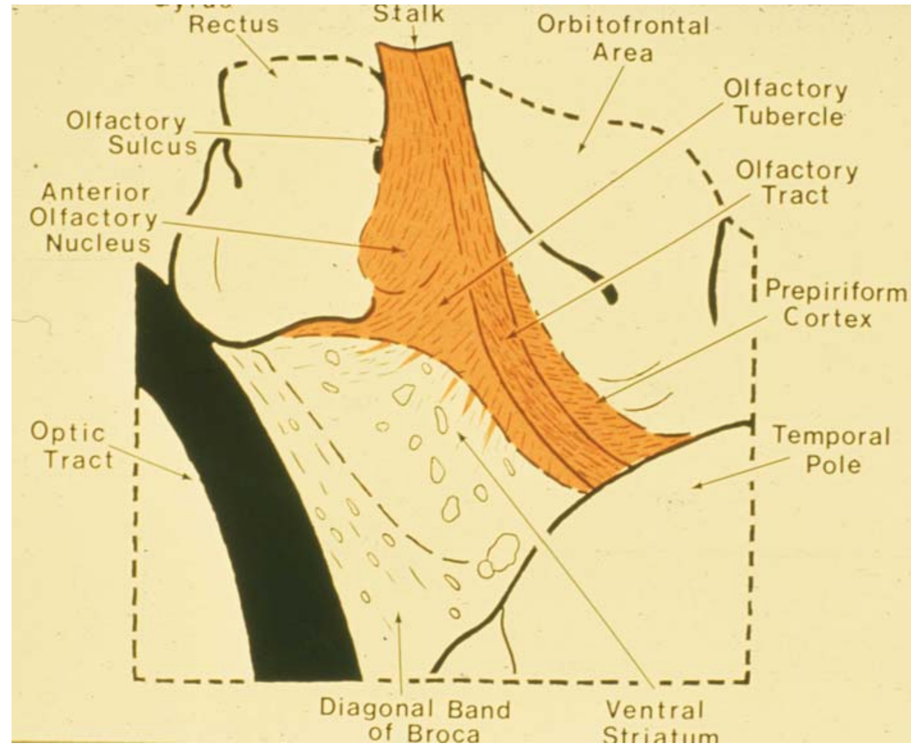


ENK

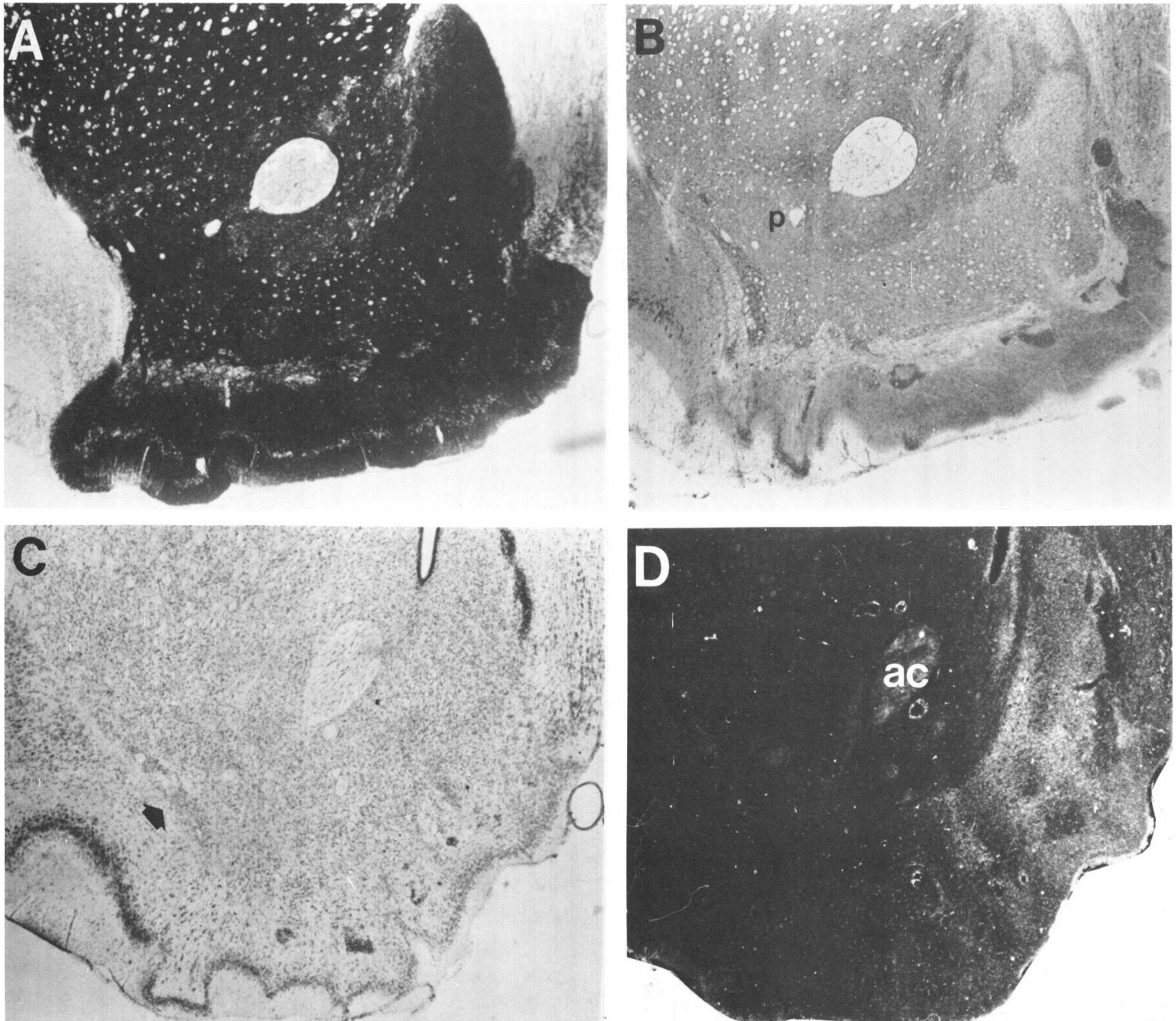
SP


RAT
MONKEY
C
P
IC
AC
Deep olf. rad.
OT

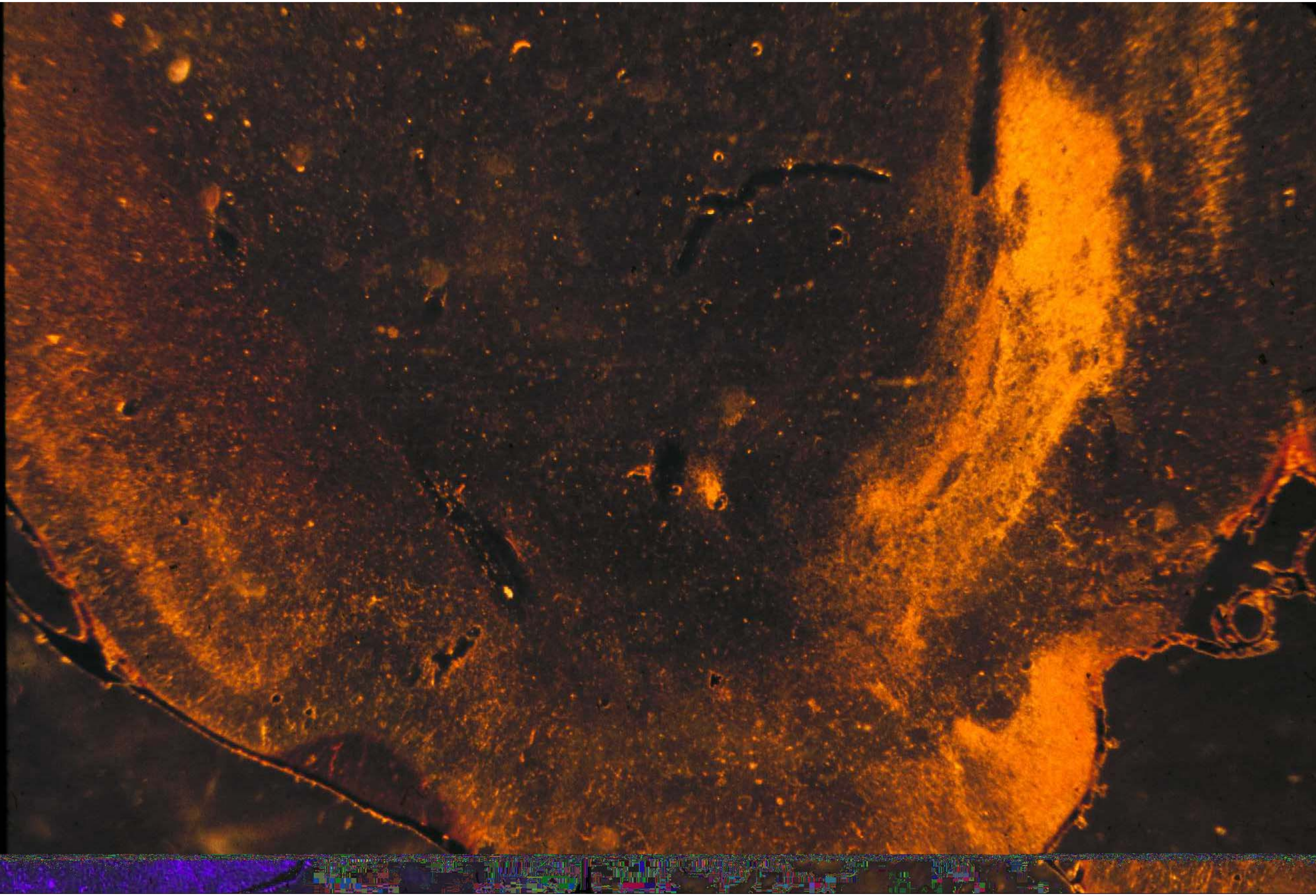
HUMAN


Rectus
Stalk
Orbitofrontal Area
Olfactory Tubercle
Olfactory Sulcus
Olfactory Tract
Anterior Olfactory Nucleus
Prepiriform Cortex
Optic Tract
Temporal Pole
Diagonal Band of Broca
Ventral Striatum

STRIATAL COMPARTMENTS 2; CORE-SHELL OF THE NUCLEUS ACCUMBENS



Zaborszky et al., (1985)

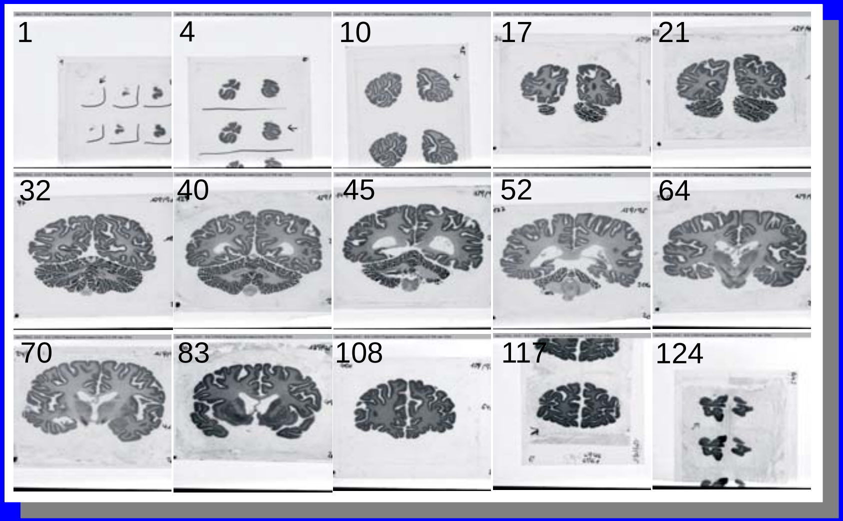


CCK distribution in the n. accumbens: the
shell is rich in CCK

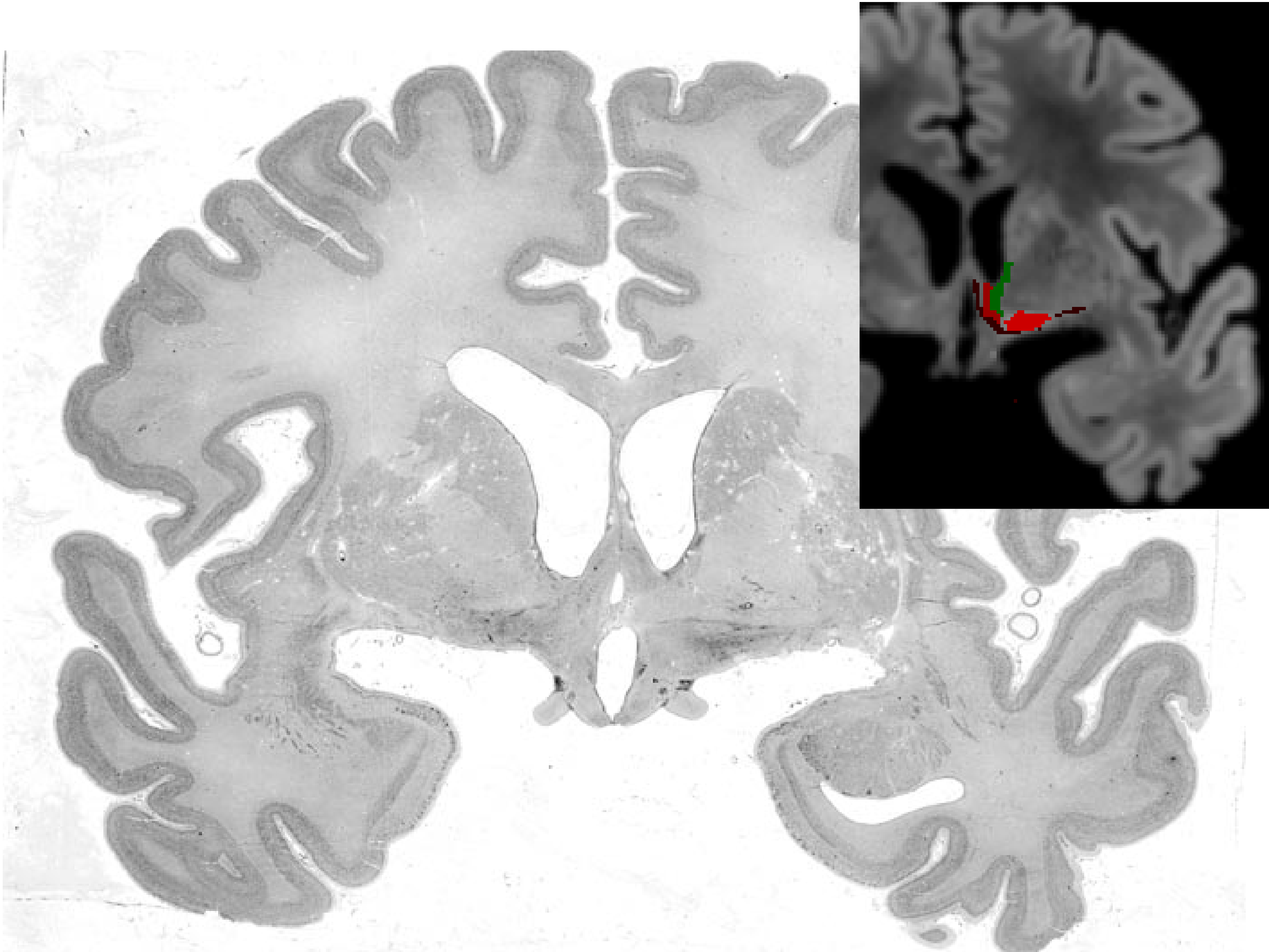
PROBABILISTIC MAPPING

MR

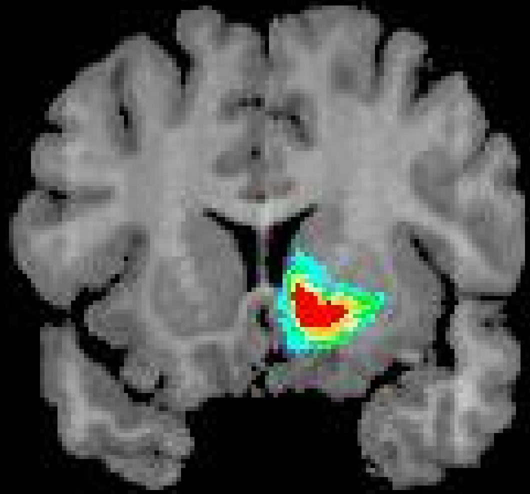
20μm

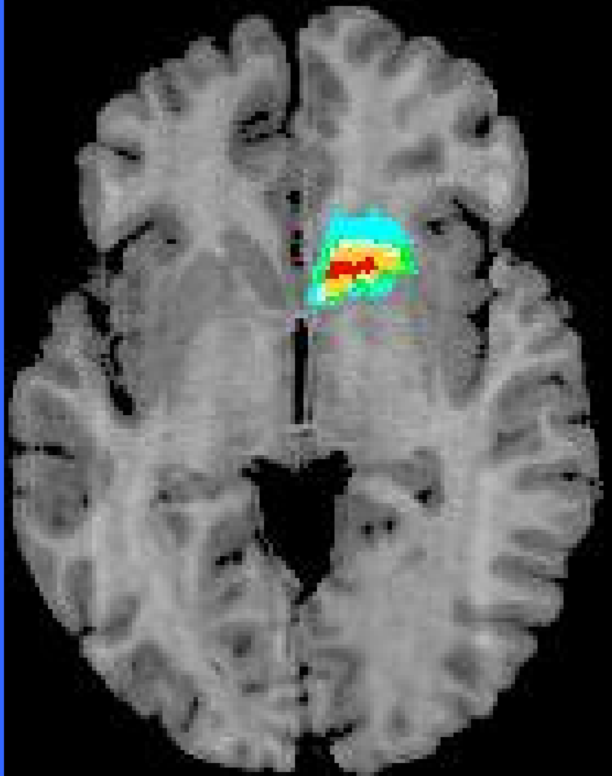


Histological sections (Merker‘s staining)



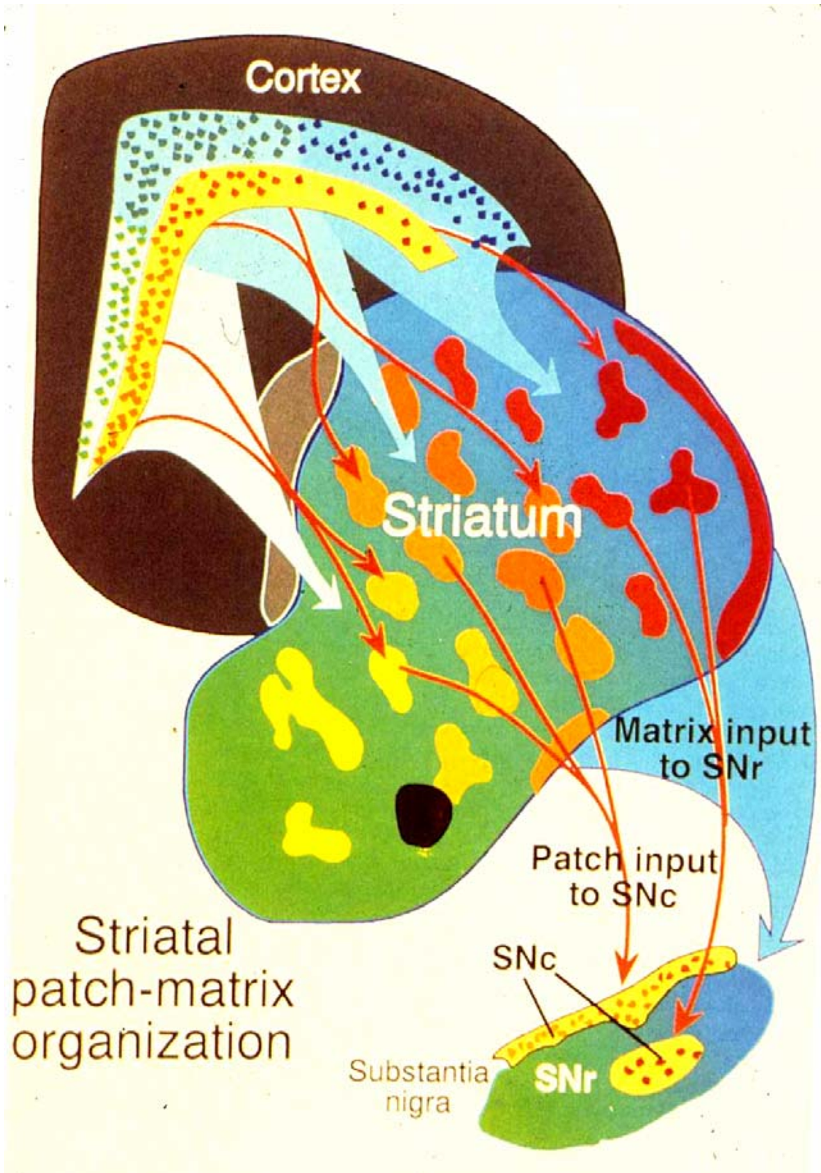
Probabilistic map of the nucleus accumbens





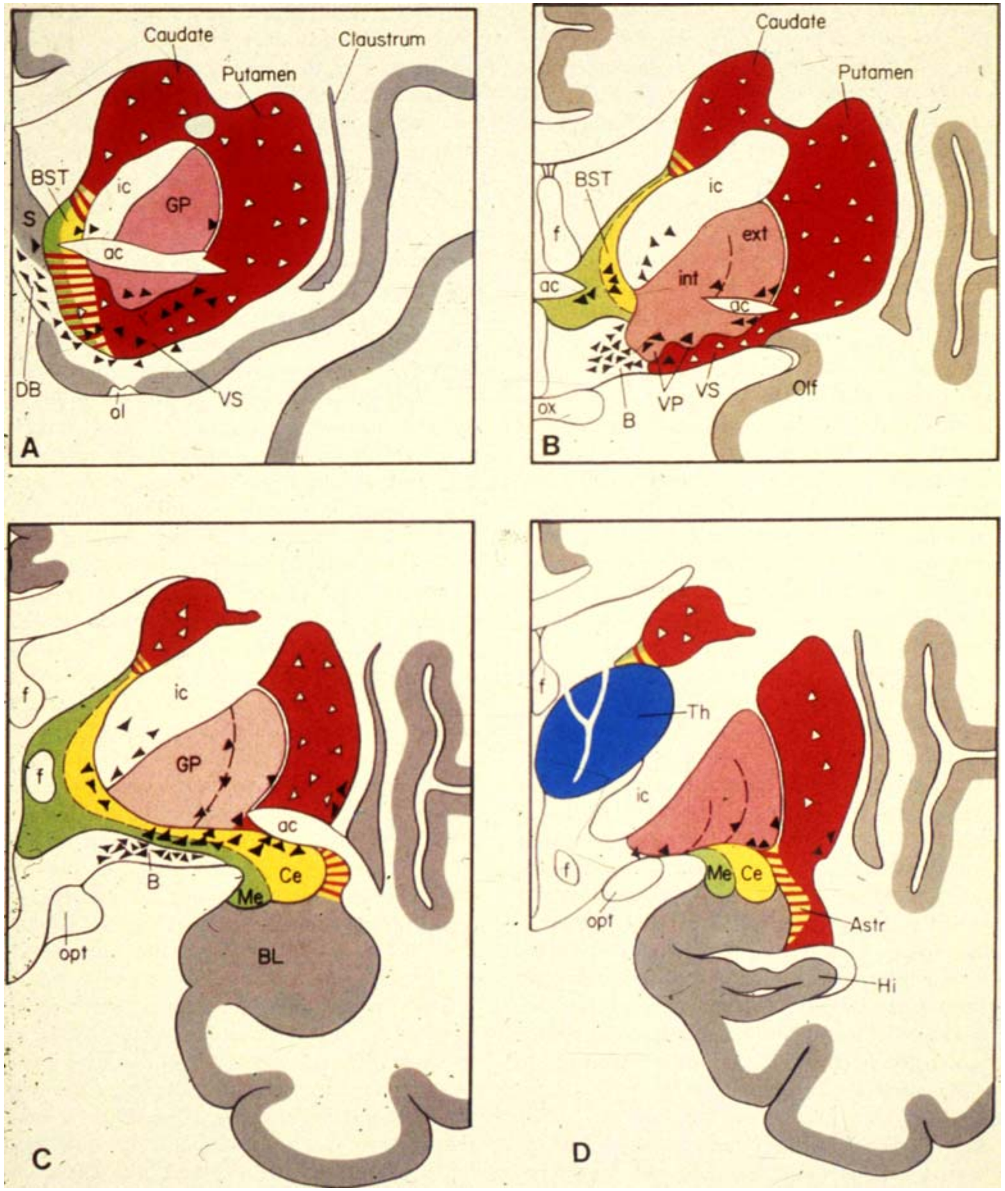
red voxels are common in all 5 brains;
brown voxels: 4 brains;
yellow voxels: 3 brains;
green voxels: 2 brains;
blue voxels: from individual brains

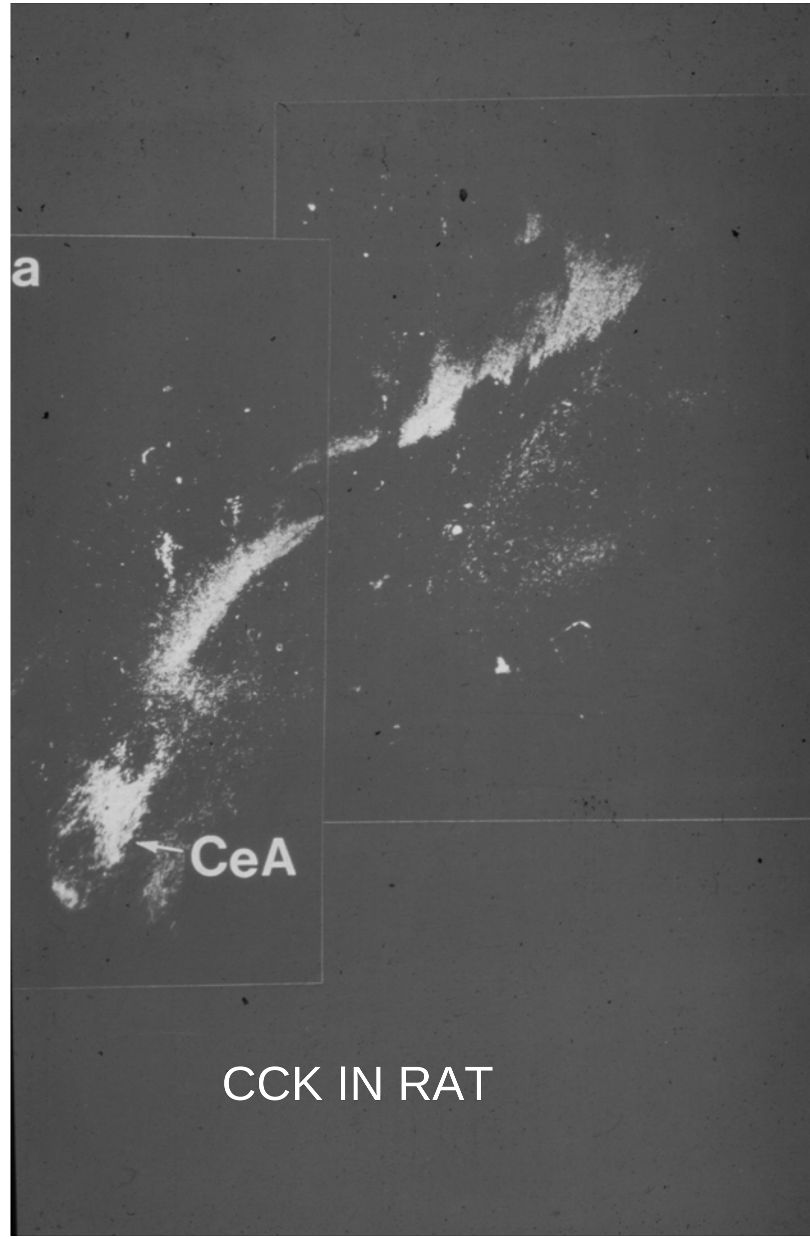
COMPARTMENTS IN THE STRIATUM 3: STRIATAL PATCH-MATRIX



Corticostriatal neurons in the deep parts of layer 5 of the cortex provide inputs to the striatal patch compartment, whereas superficial layer V neurons provide inputs to striatal matrix. Patch neurons provide inputs to dopaminergic neurons of the SNc. Matrix neurons provide inputs to locations of GABAergic neurons in the SNr (Gerfen)

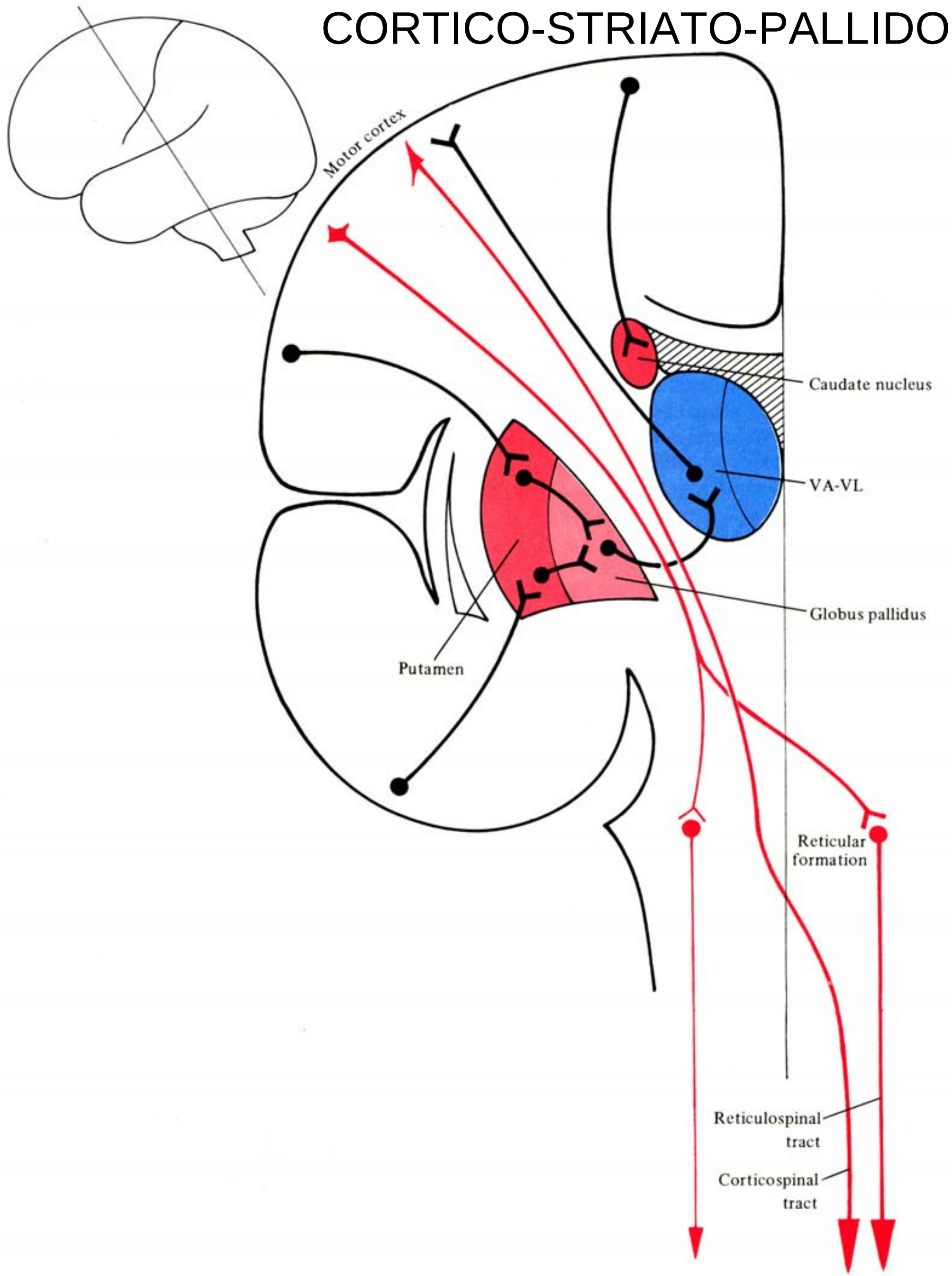
STRIATUM-NUCLEUS BASALIS-'EXTENDED AMYGDALA'





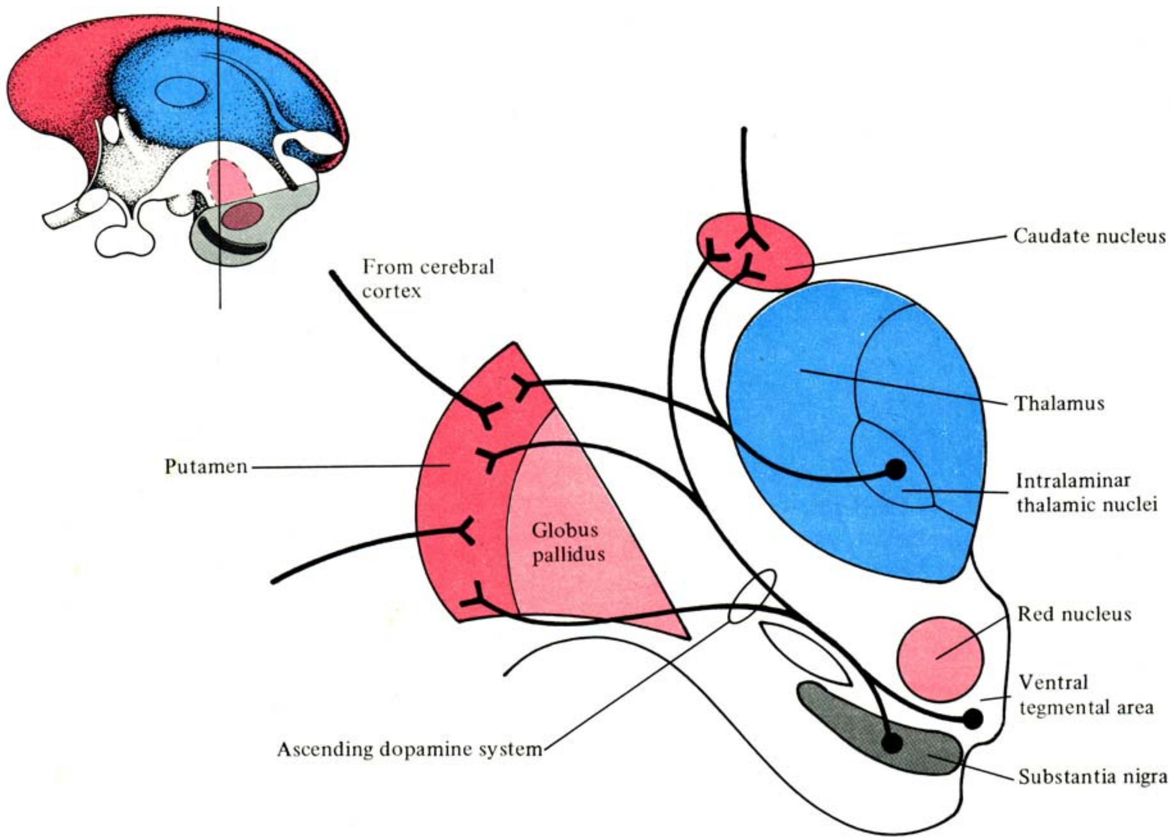
From: Heimer, De Olmos, Alheid and Zaborszky, 1991

CORTICO-STRIATO-PALLIDO-TAHALAMO-CORTICAL LOOPS



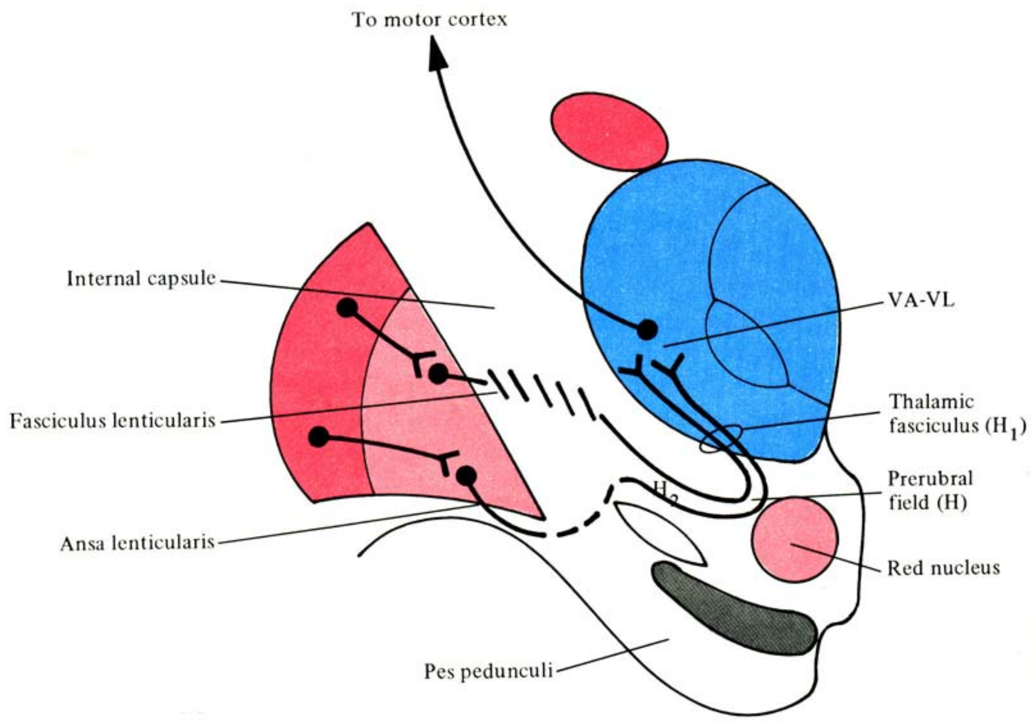
Schematic figure showing the cortico-strio-pallido-thalamic loop and its relationship to the descending corticospinal (pyramidal) and cortico-reticulo-spinal pathways (Heimer)

AFFERENTS TO THE STRIATUM



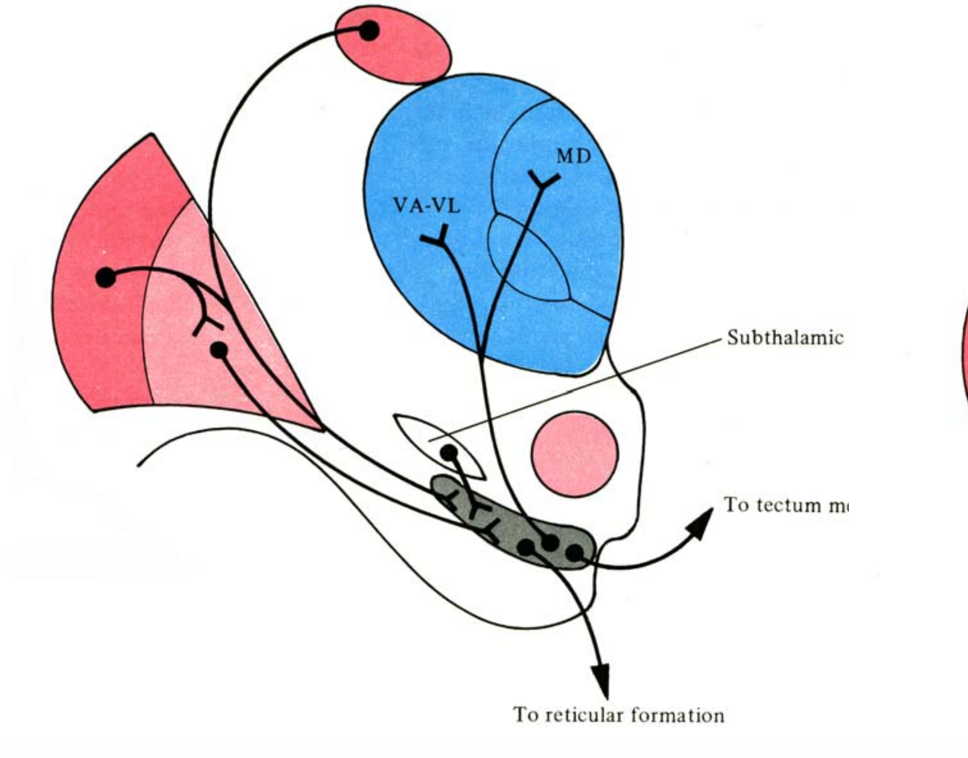
Afferent connections of the striatum (from cortex, thalamic intralaminar nuclei and the dopaminergic neurons of the SNC)

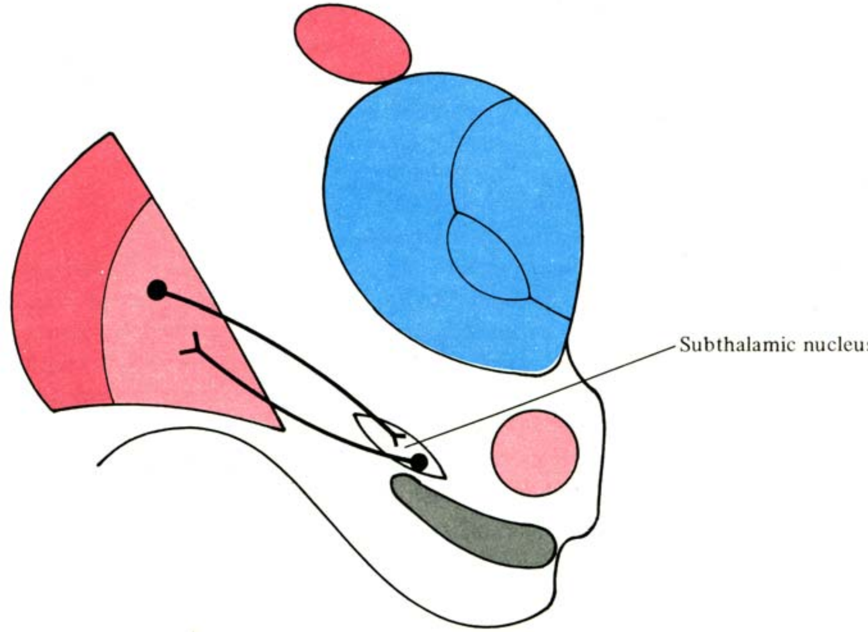
ANSA LENTICULARIS-FASCICULUS LENTICULARIS-THALAMIC FASCICULUS



The striato-pallido-thalamic loop (Heimer)

PARS RETICULATA OF THE NIGRA AND SUBTHALAMIC NUCLEUS

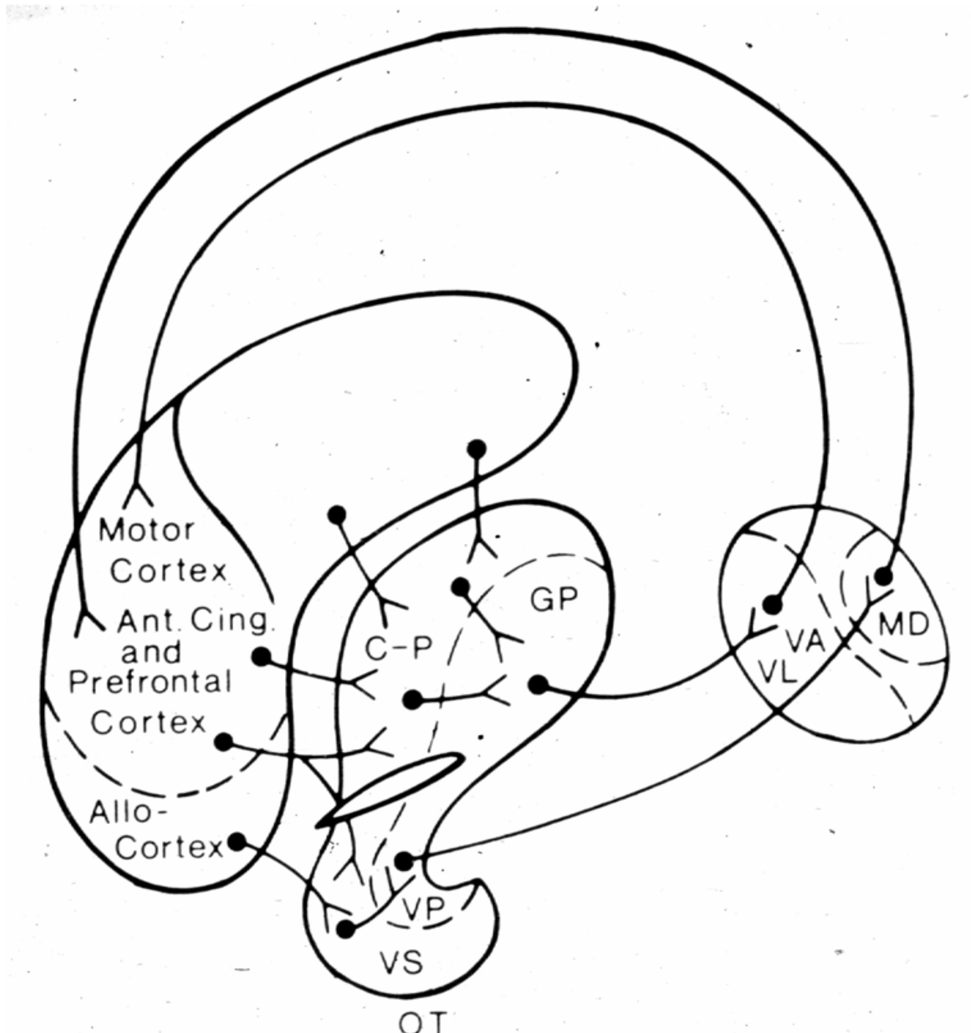




Afferents to and efferents from the pars reticulata (Heimer)

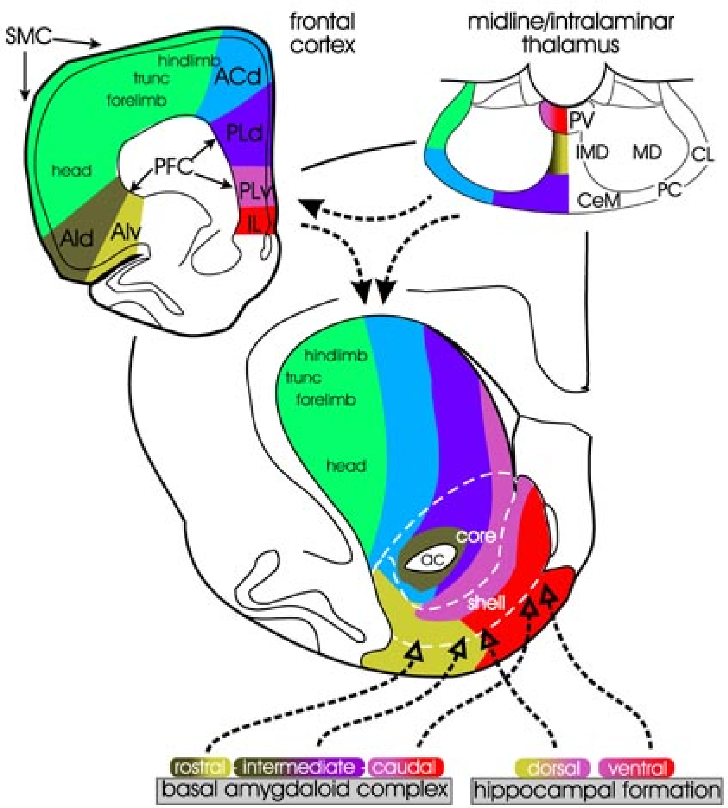
The pallido-subthalamic-pallido loop (Heimer)

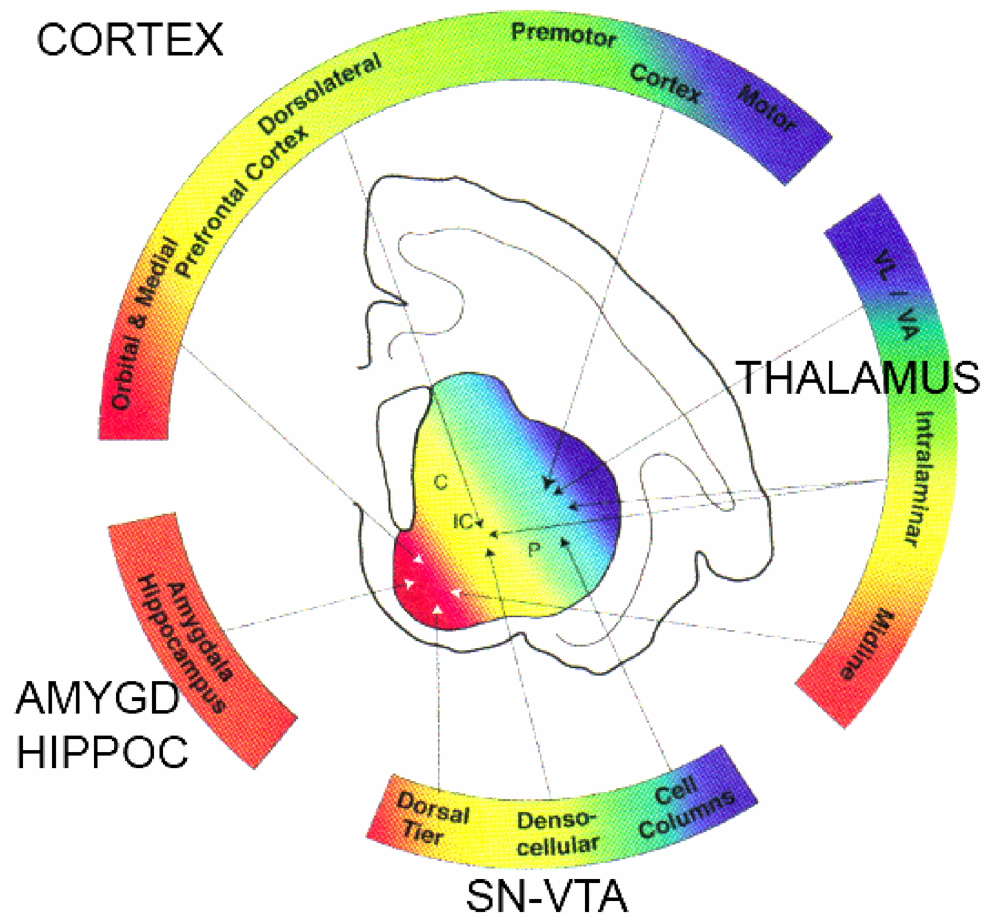
CORTICO-STRIATO-THALAMO-CORTICAL LOOPS: SIMILARITY BETWEEN DORSAL AND VENTRAL STRIATUM



Heimer et al., 1981

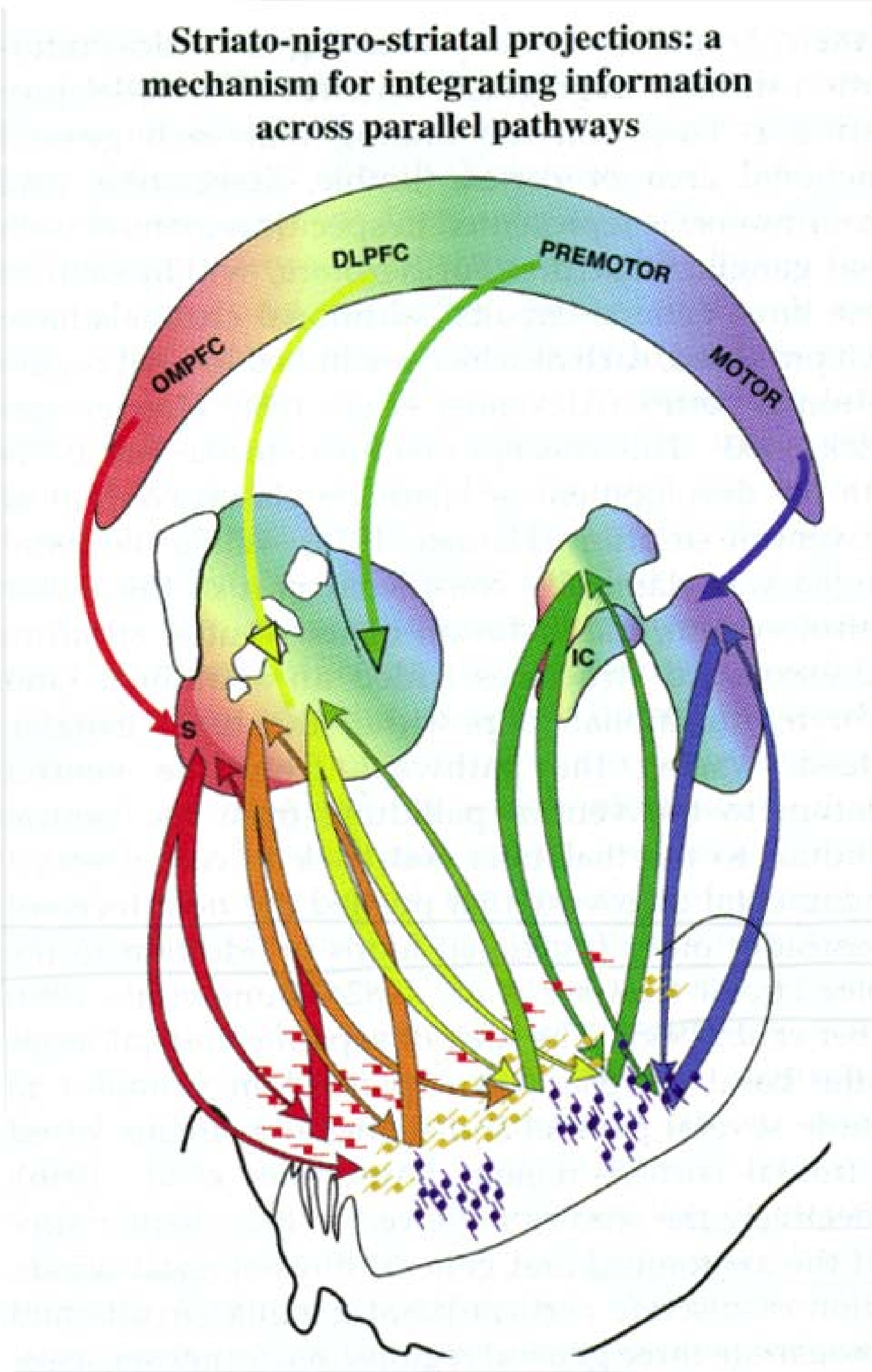
ORGANIZATION OF CORTICAL AND SUBCORTICAL INPUTS TO THE STRIATUM





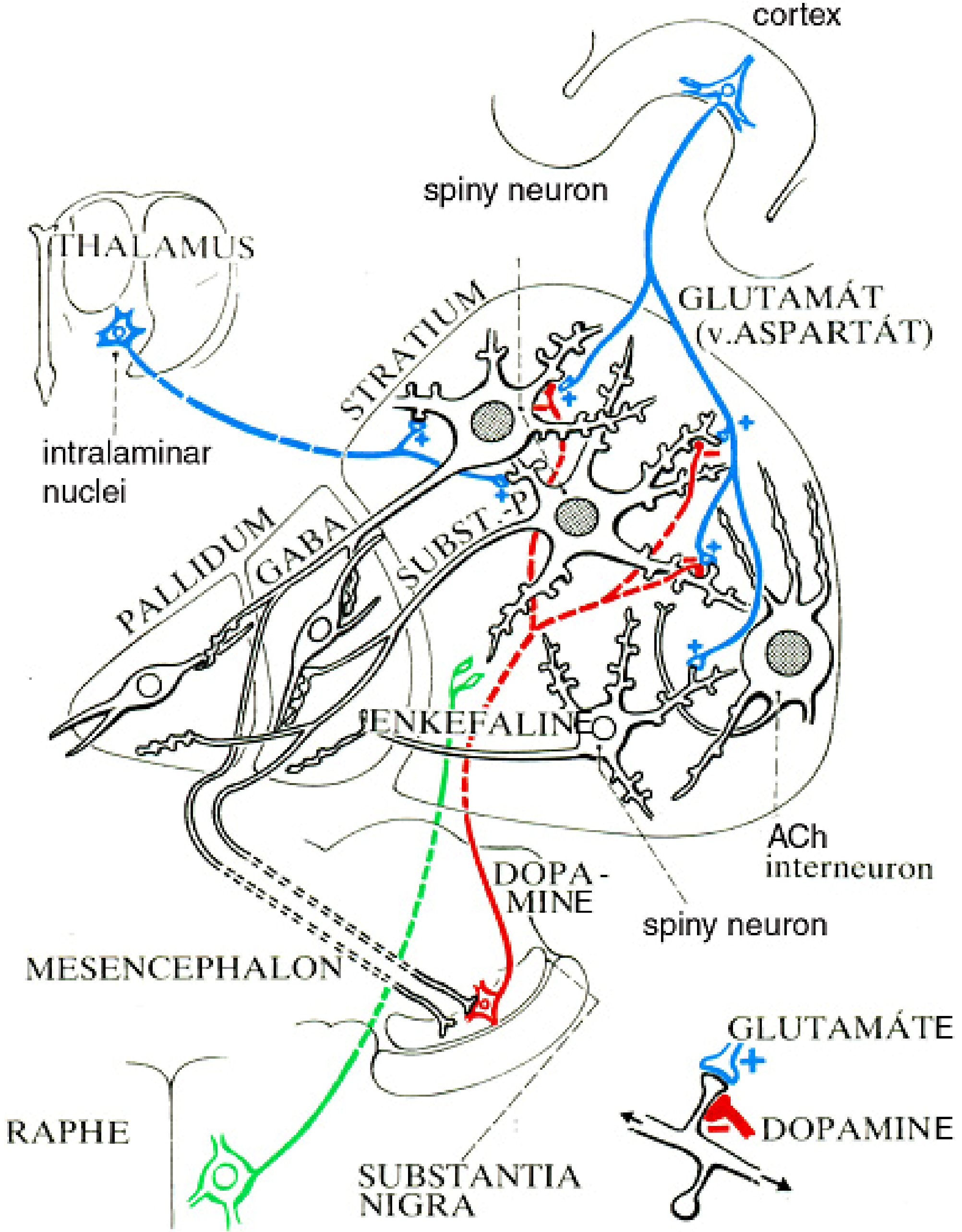
Voorn et al., 2004

Haber and Gdowski, 2004



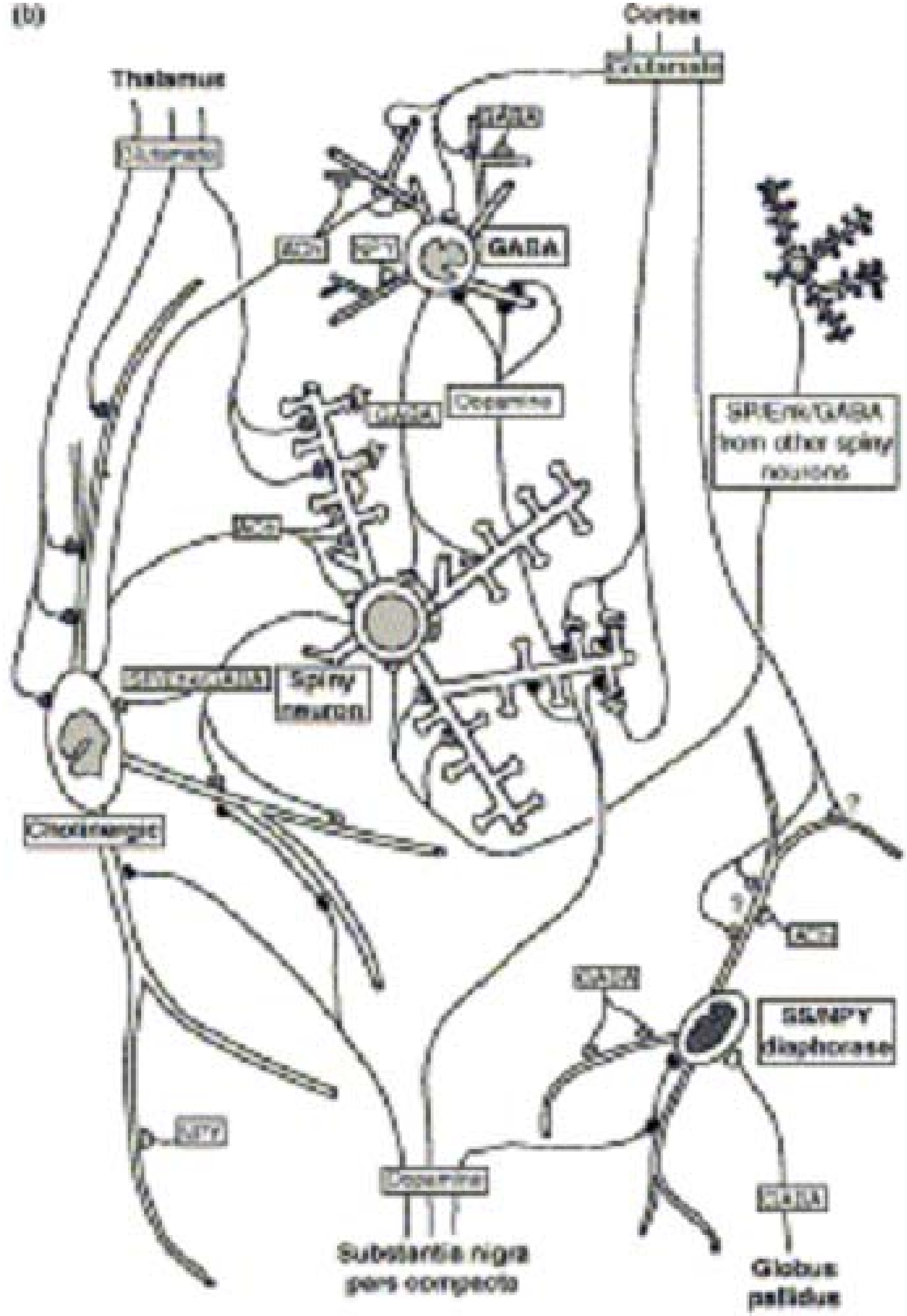
Projections from the shell target both the VTA and the ventromedial SNc (red arrows). From the VTA to the shell form closed loop. Projections from the medial SN feed-forward to the core forming the first part of a spiral (orange arrow). The spriral continues through the SNS projections (yellow and green arrows) with pathways originating in the core and projecting to more dorsally (blue). In this way ventral striatal regions influence more dorsal striatal regions via spiraling SNS projections. (From Haber and Gdowski, 2004)

SYNAPTOLOGY OF SOME OF THE BASAL GANGLIA CIRCUITRIES

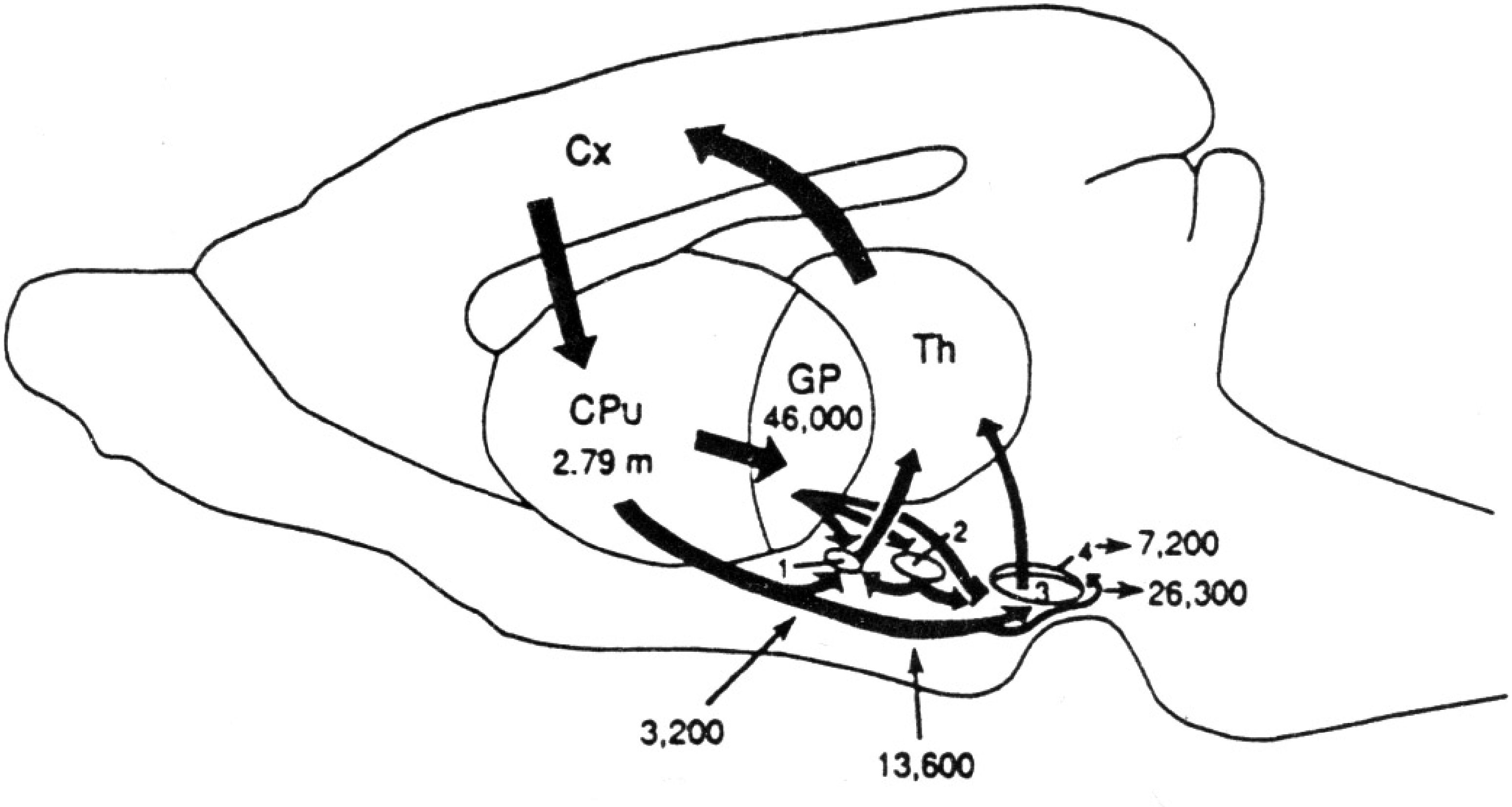


From Szentagothai

SYNAPTOLOGY OF SOME OF THE BASAL GANGLIA CIRCUITRIES



SOME NUMBERS…



Schematic diagram illustarting the total number of neurons within each subdivisions of the rat basal ganglia. 1=entopeduncular n. (internal pallidal segment); 2=subthalamic nucleus; 3=substantia nigra reticulata; 4=substantia nigra compacta

Convergence in striato-pallidal connections (Percheron)

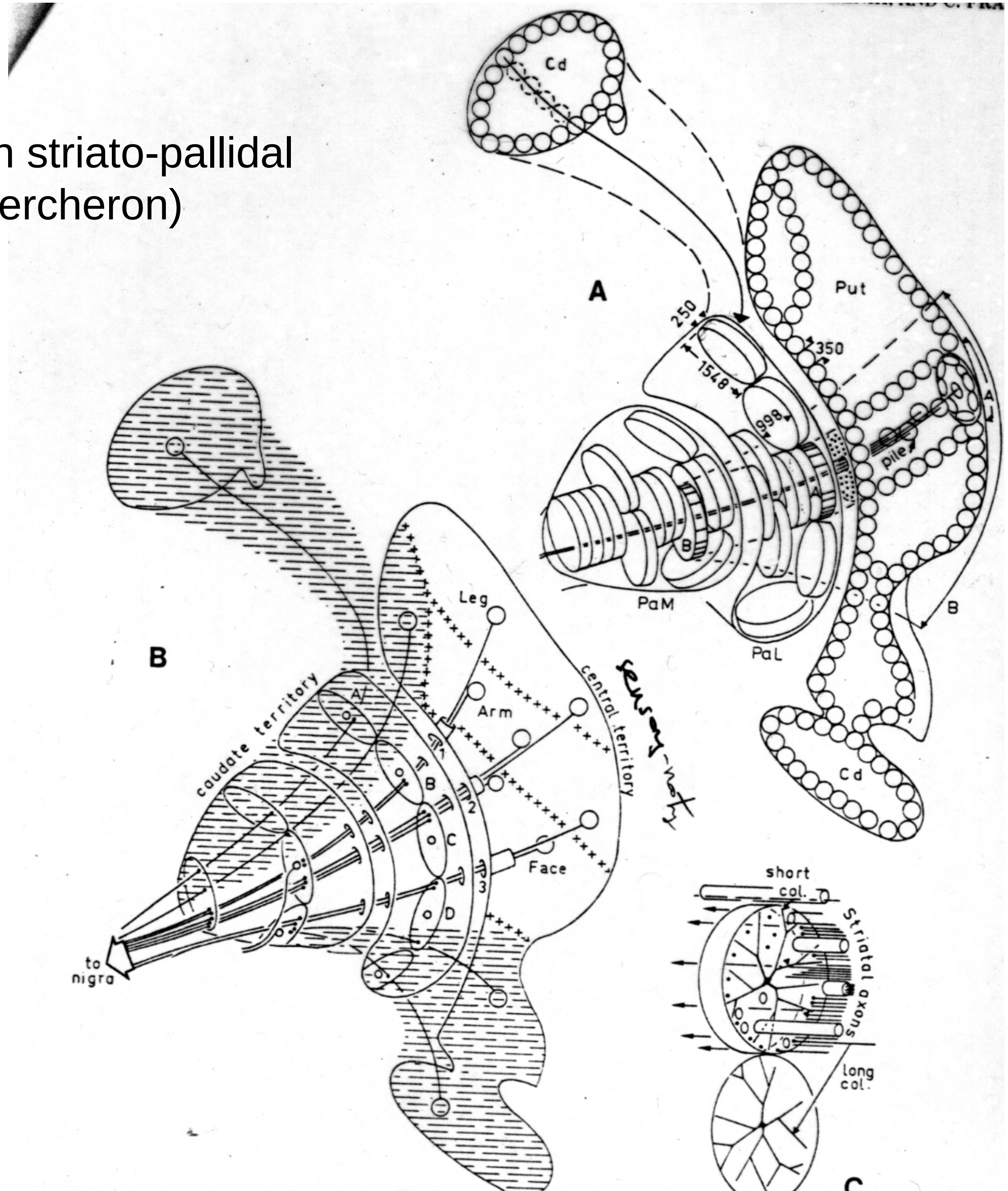
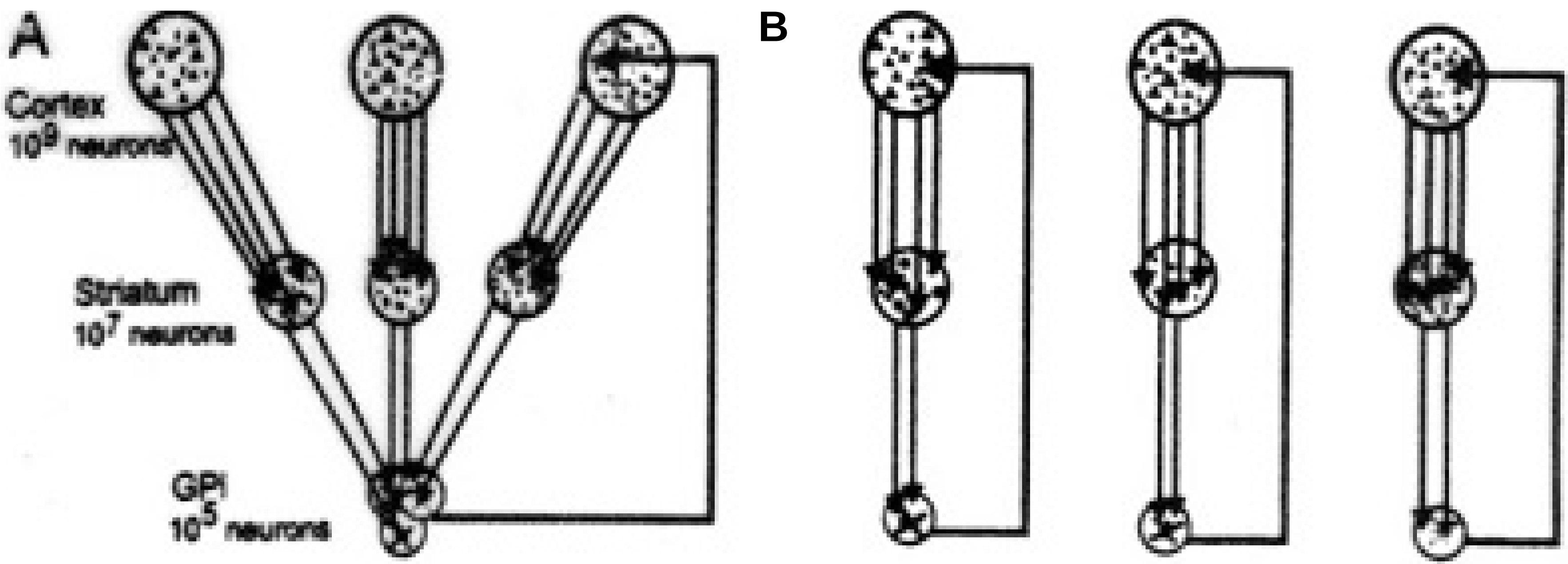
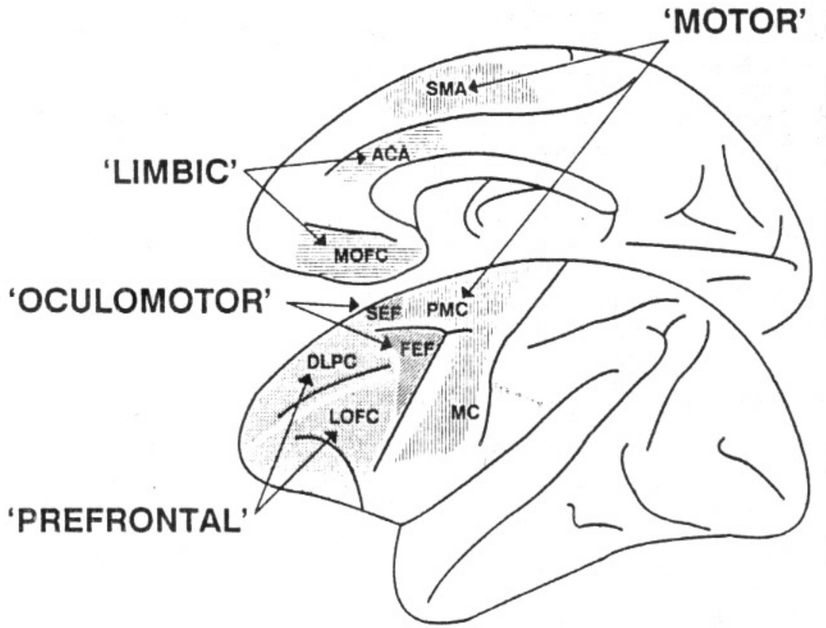


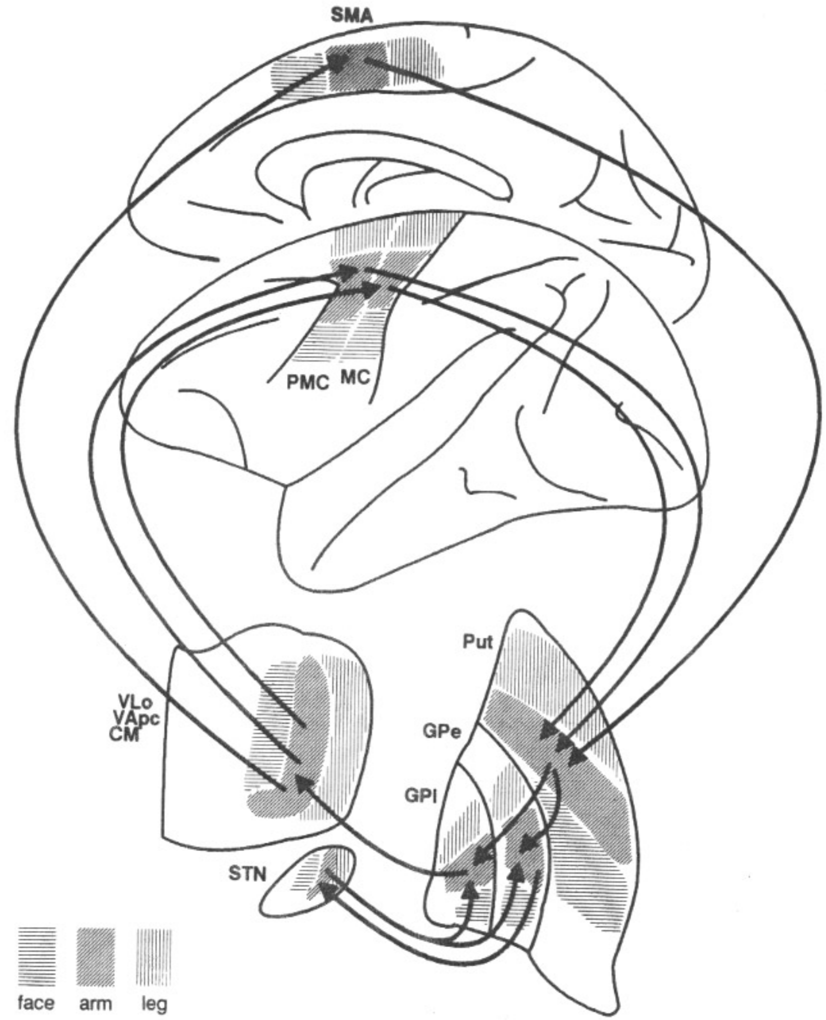
Fig. 7. Spatial model of the

PROCESSING CHANNELS IN THE BG: CONVERGENCE OR DIVERGENCE?



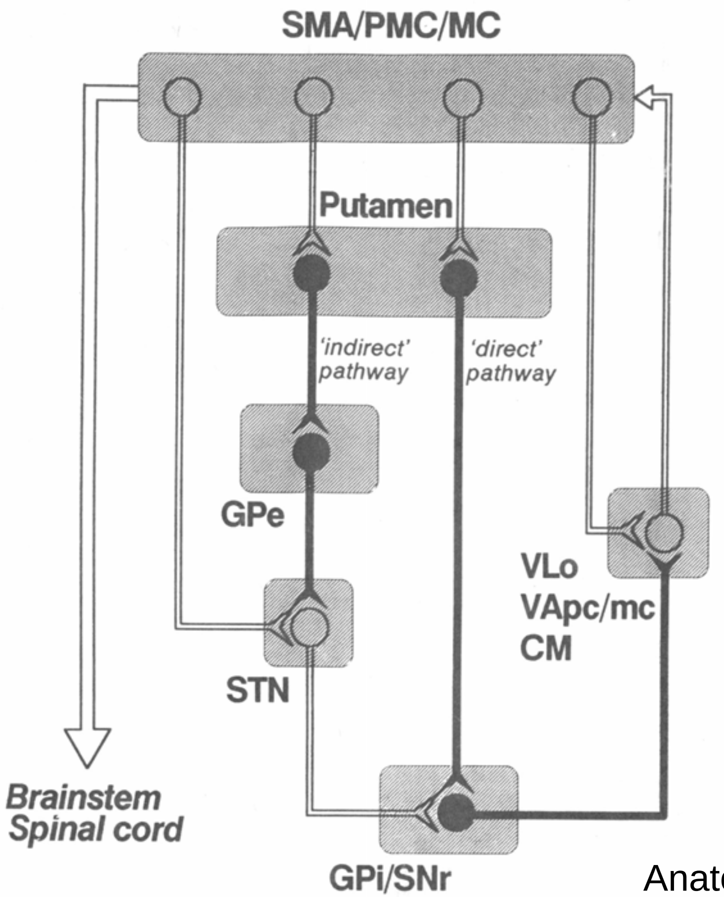
PARALLEL CIRCUITS LINKING BASAL GANGLIA AND CORTEX



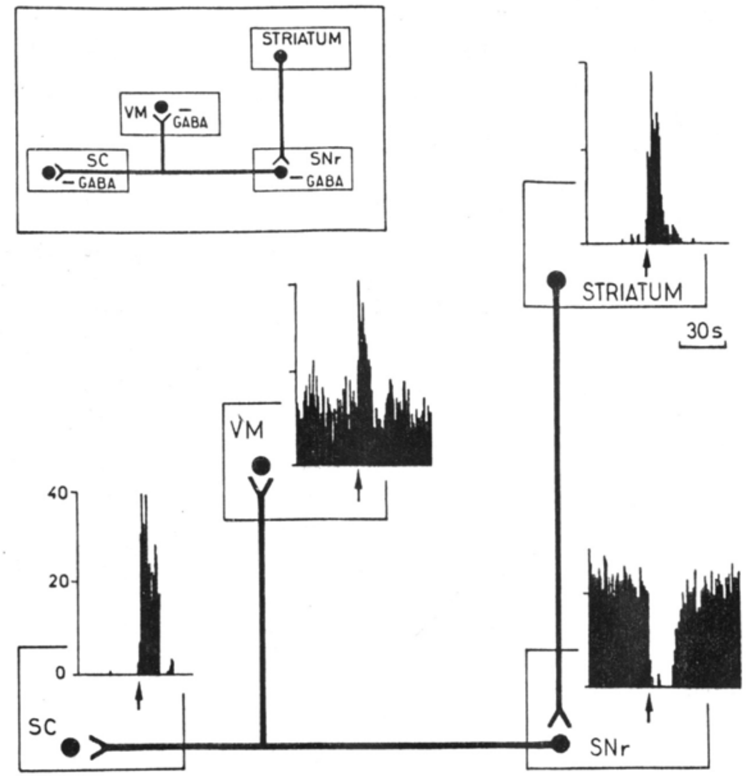


Schematic illustration of the cortical areas that receive the output of the separate basal ganglia-tahalamo-cortical circuits. ACA=anterior cingulate area; DLPC=dorsolateral, LOFC, lateral prefrontal, MOFC= medial orbitofrontal cortex. FEF= frontal; SEF=supplementary eye field

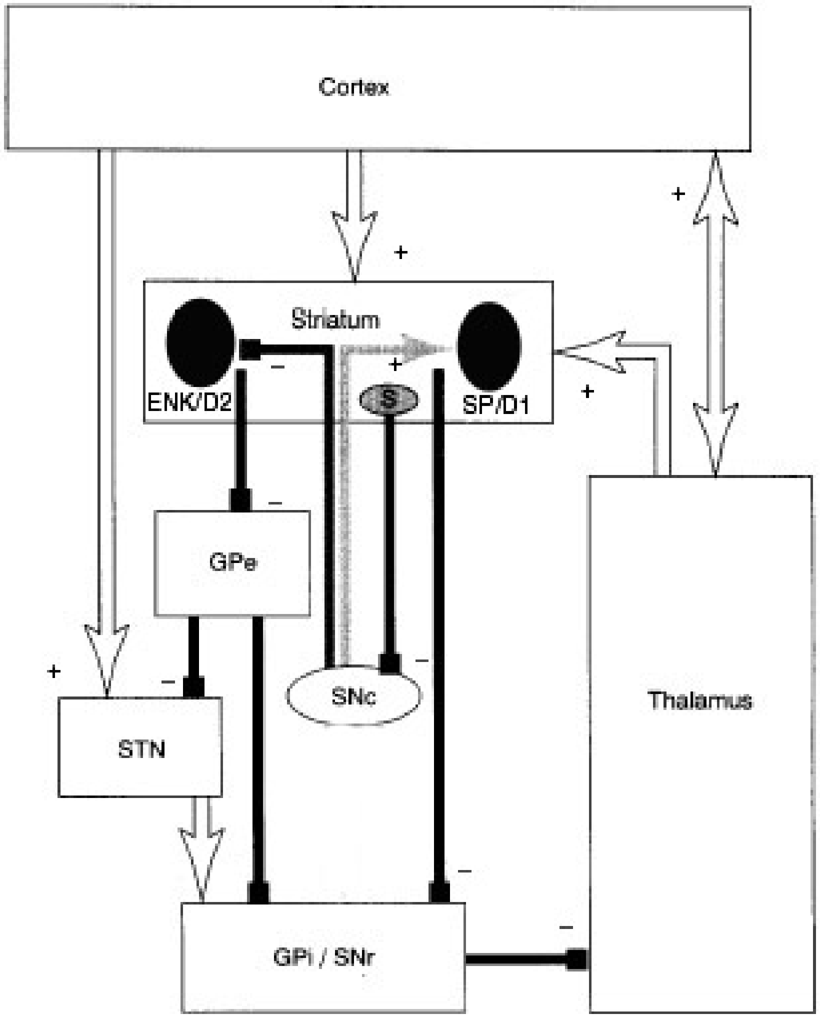
Somatiotopic organizaation of the 'motor' circuit. The arrows indicate the topographycally organized pathways that link the respective 'arm' representations at different stages of the circuit (Alexander and Crutcher, 1990)



Simplified diagram of the 'motor' circuit. Inhibitory neurons are filled, excitatory neurons are open (Alexander and Crutcher, 1990).



Anatomico-physiological organization of the striato-nigrofual ('direct')pathways to the ventromedial thalamic (VM) and to the superior colliculus (SC). The frequency histograms illustrate the sequence of electrophysiological events underlying the disinhibitory influence of the striatum. A striatal spike discharge, evoked by local application of glutamate, readily induces a clearcut silencing of the tonically active nigral neurons (SNr). Released from the potent nigral inhibition, collicular and thalamic cells are vigorously discharged (The arrow in each histogram indicates the onset of Glu injection in the striatum (Chevalier and Deniau, 1990)



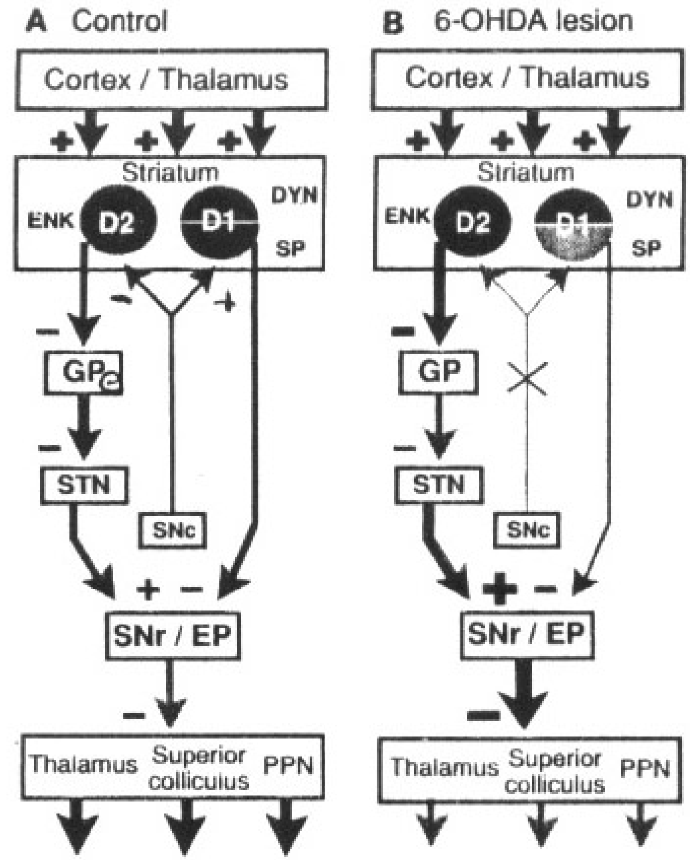
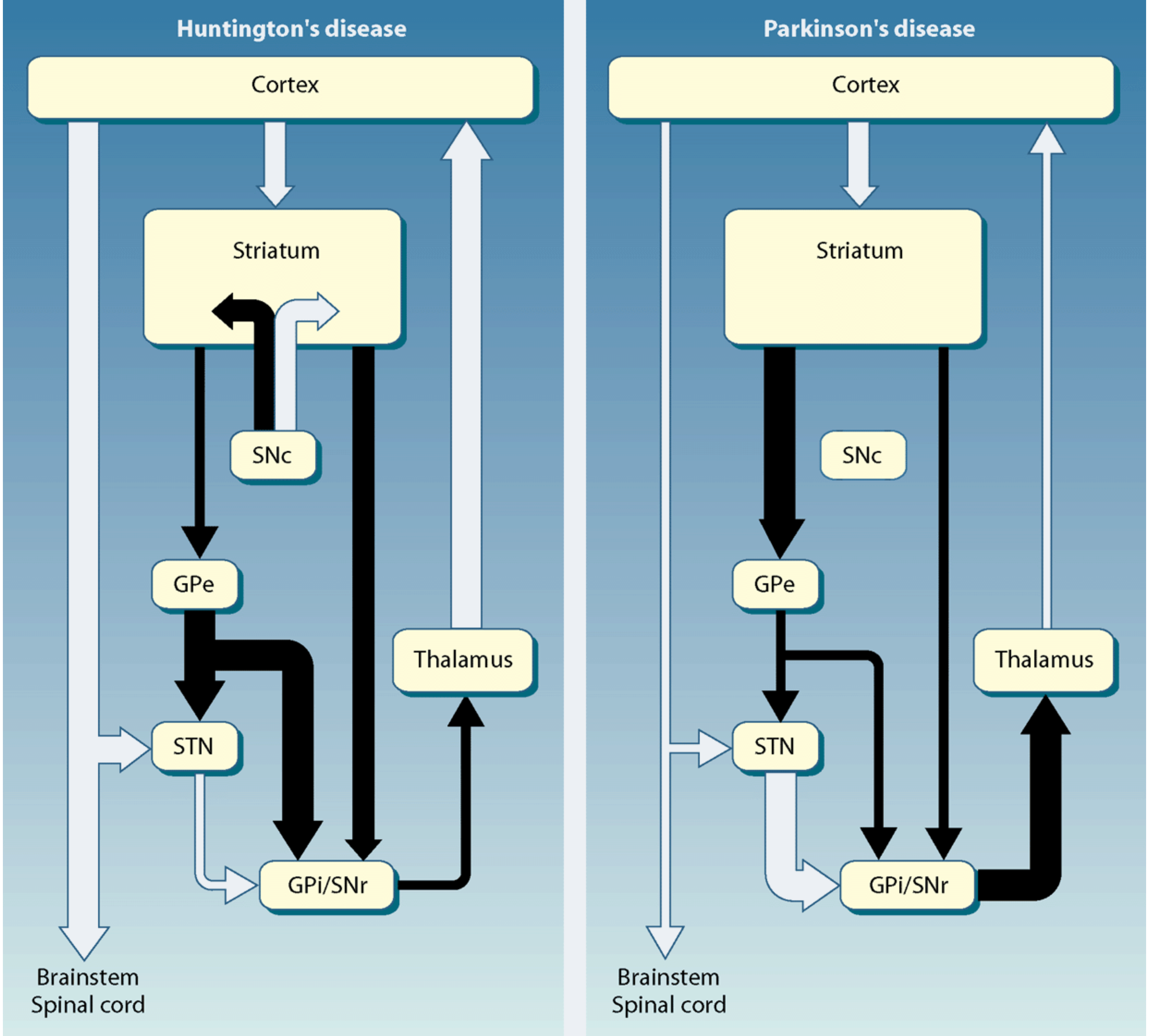
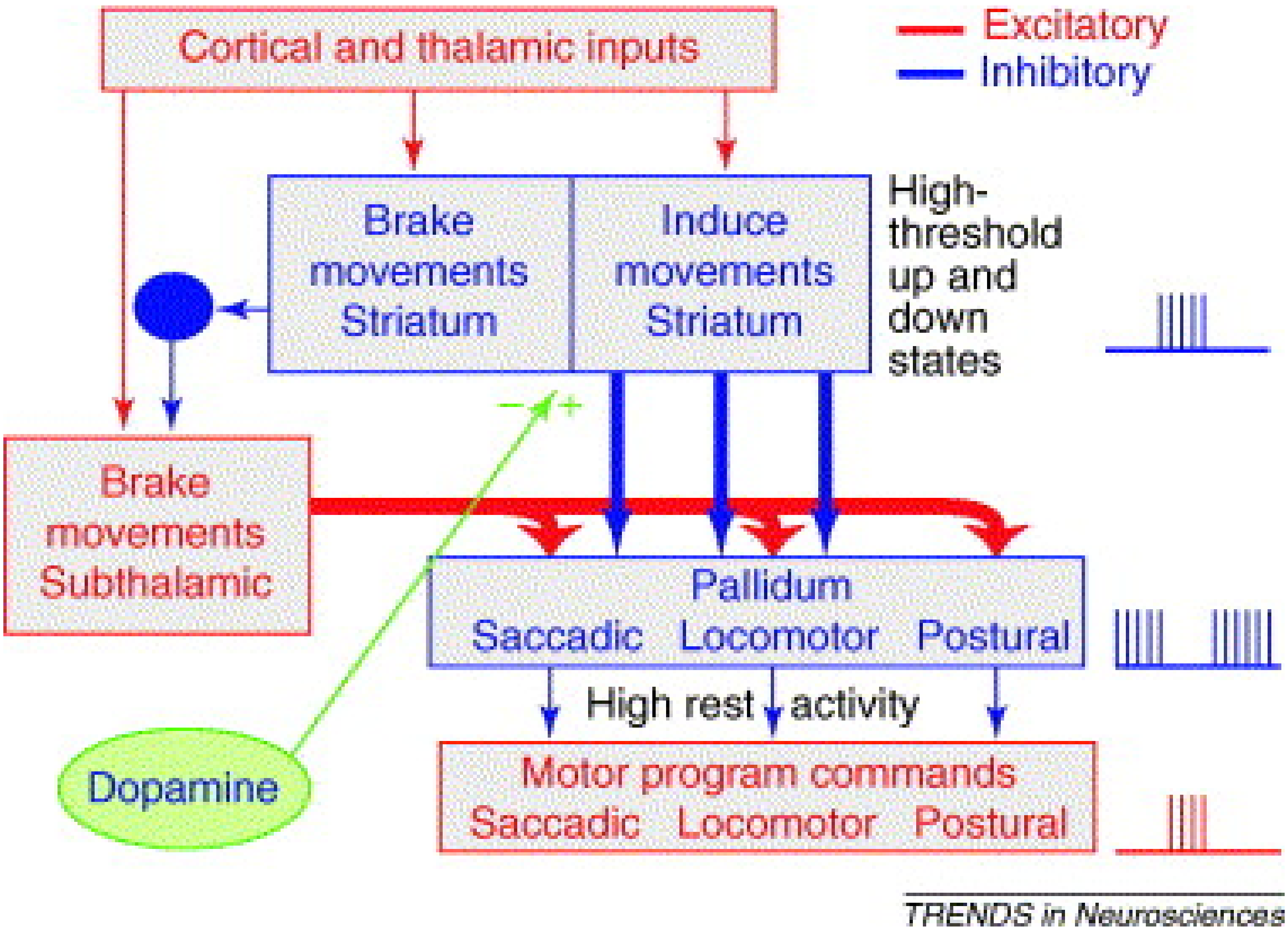


Diagram to explain changes of gene expression in basal gangila circuitry after 6-OHDA-lesion of the dopaminergic cells of the SN. This lesion result in increased ENK expression and activity of striatopallidal neurons. This results in increased firing of SNr-GABAergic neurons and diminished activity in thalamo-cortical axons.

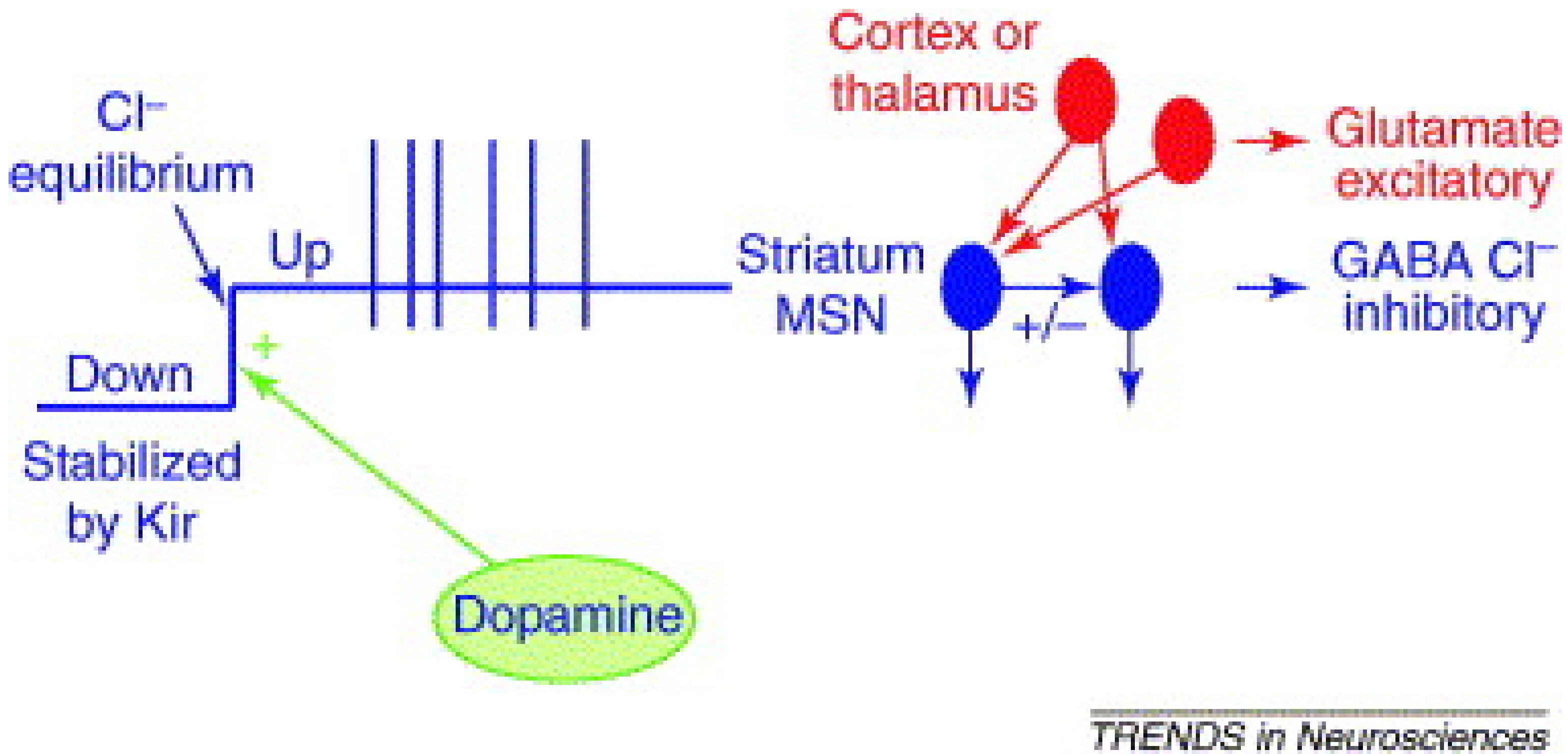

Huntington's disease
Cortex
Striatum
SNc
GPe
STN
GPi/SNr
Thalamus
Brainstem
Spinal cord
Parkinson's disease
Cortex
Striatum
SNc
GPe
STN
GPi/SNr
Thalamus
Brainstem
Spinal cord

MECHANISM FOR SELECTION OF MOTOR PROGRAMS 2.



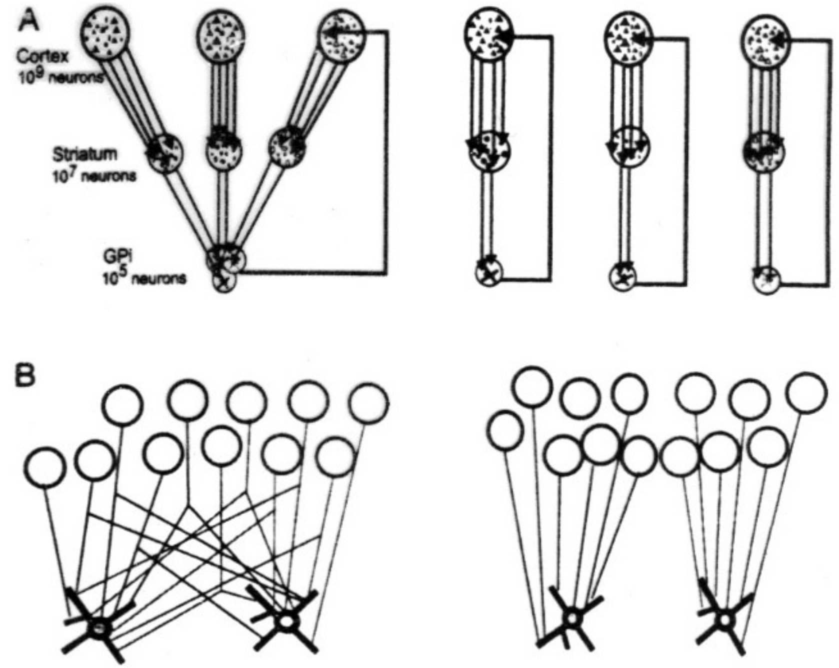
Grillner et al., TINS, 28:364, 2005

MECHANISM FOR SELECTION OF MOTOR PROGRAMS 3.



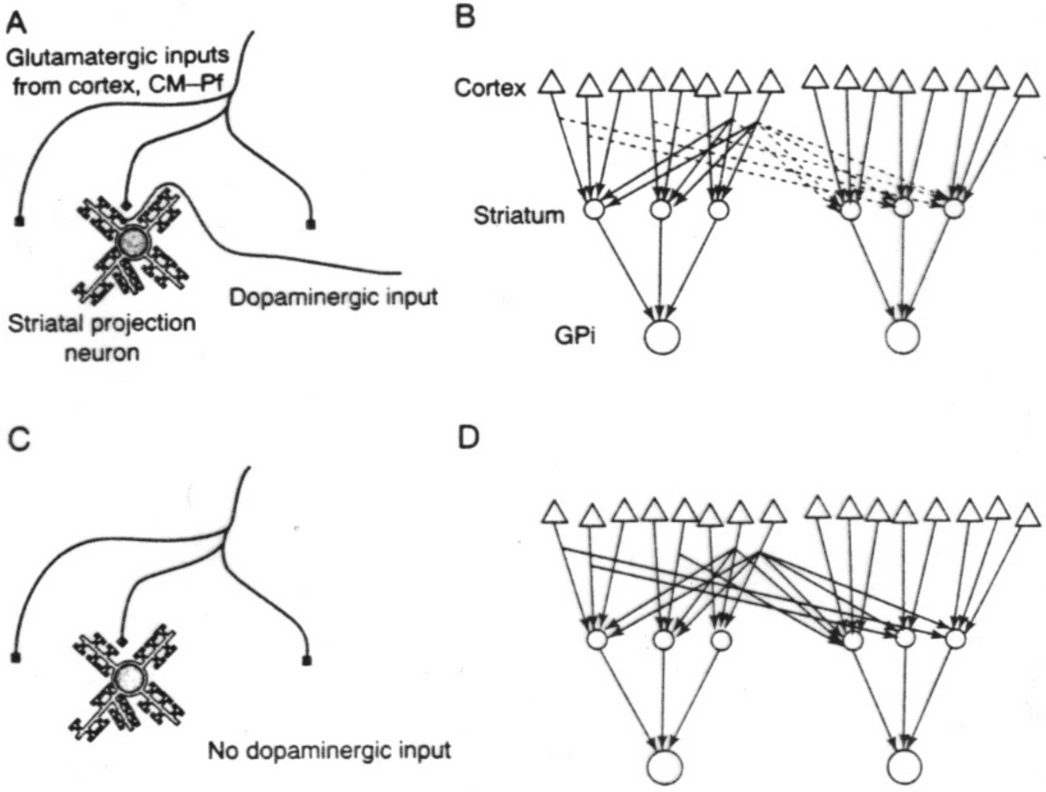
Important factors for the down and up states in medium spiny neurons. The transition from a down state to an up state is facilitated by dopamine, as indicated. MSN neurons thus have three states: a down state, an up state and, with further depolarization, a state in which they fire action potentials. From Gillner et al., 2005

PROCESSING CHANNELS IN THE BG



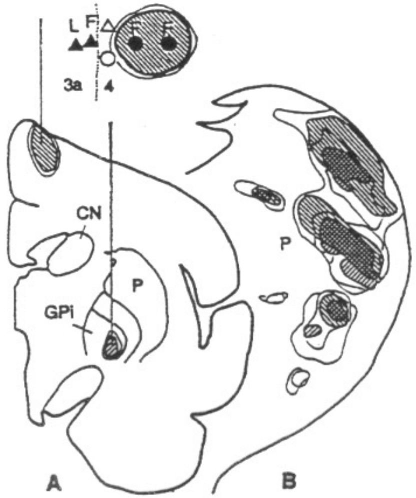
Conflicting views of information processing in the basal ganglia. Left old (convergent); Right: parallel processing. B: Zooming in the striatum-GPi connections according to the two models. According to the info-sharing, the two cells integrate the same information from many input sources. According to the segregared parallel model, there is no overlap in the incoming information to the two cells (Bergman et al., 1998).

PROCESSING CHANNELS IN THE BG:Putative Role of Dopamine Neurons

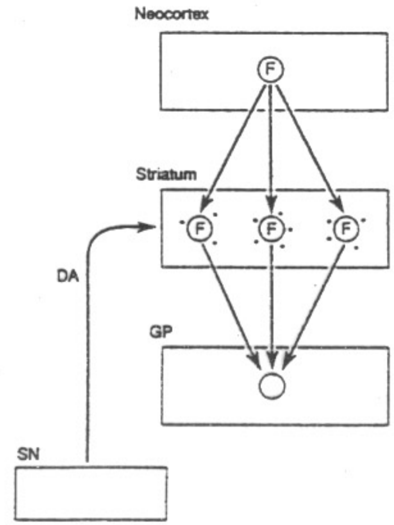


Dopamine modulation of functional connectivity in the basal ganglia. It is hypothesized that the main action of DA is to regulate the coupling level between the different subcircuits in the BG. In the normal state (A) DA endings on striatal spines can veto divergent glutamatergic inputs to the striatum thereby reducing the efficacy of cross-connections between channels. B: Diagrammatic model of the resulting segregated channels in the normal state. Broken arrows represent cross-channel connection with reduced efficacy. Following DA depletion (C) this segregation of afferent channels is lost, resulting in synchronized activation of pallidal cells (Bergman et al., 1998).

Divergent-reconvergent processing in cortico-striatal loops

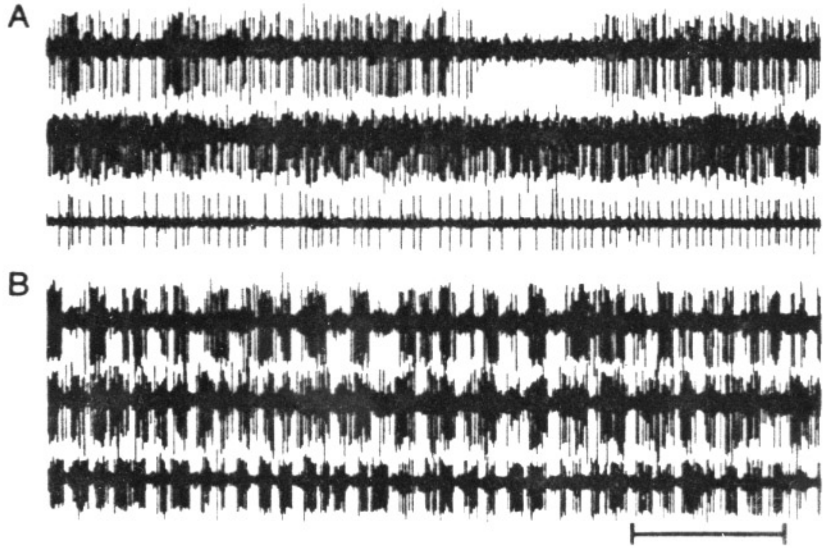


A: An injection of antergograde tracer was made in a small site in the motor cortex (area 4) representing the foot. In the same hemisphere , a small site in the pallidum was injected with retrograde tracer. Both the labeled axon projections from the cortex to terminal sites in the striatum and the labeled stratopallidal output cells are organized as sets of patches in the striatum. B The input clusters and output clusters overlap extensively (cross-hatching in B). Experiments using multiple-electrode recording suggest that during sensorimotor learning such distributed networks maybe coordinated by widely spaced striatal interneurons (possible cholinergic neurons) that acquire response properties on the basis of experienced reward (Graybiel et al., 1994).

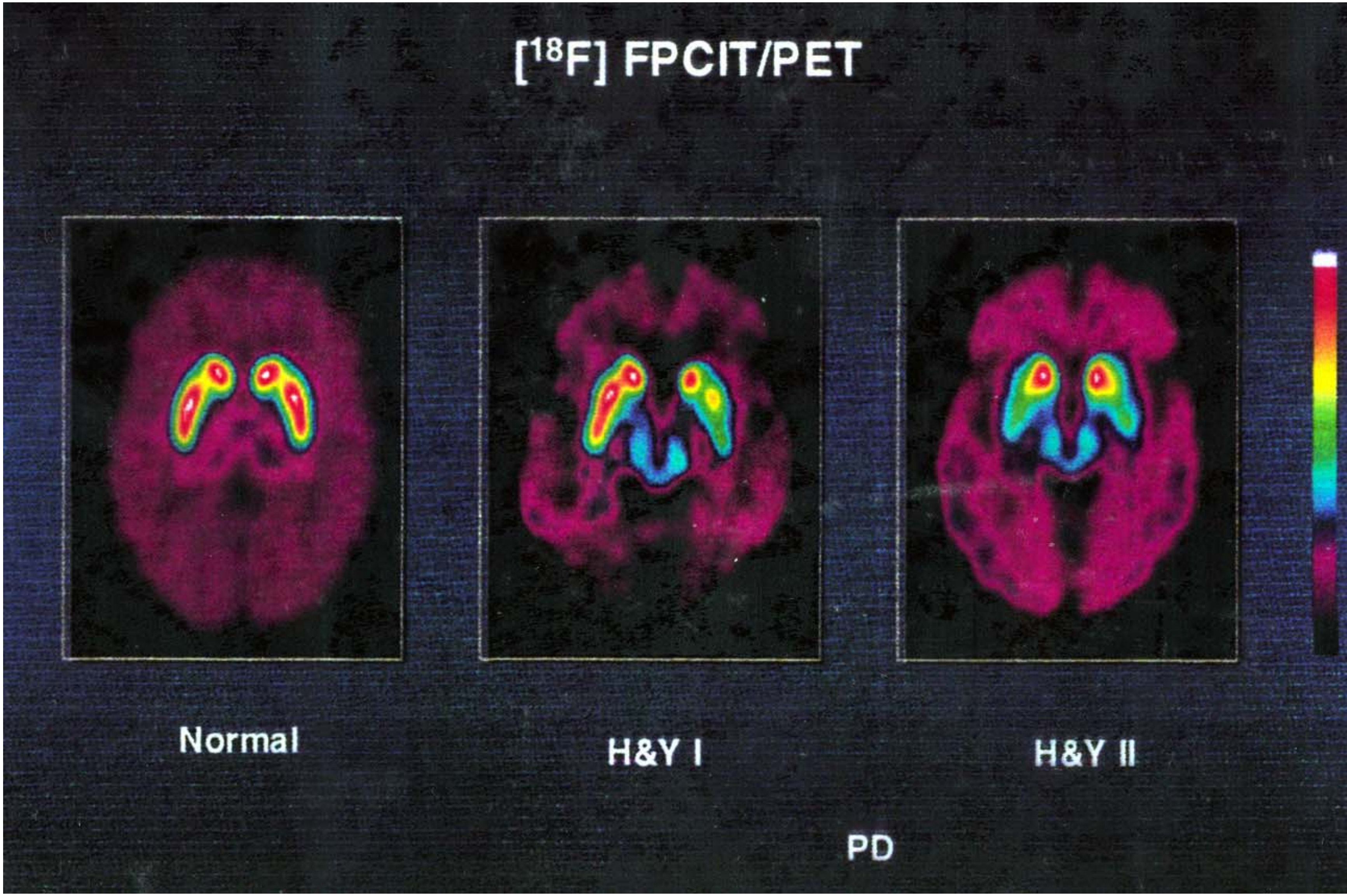


Model of divergent-reconvergent processing in basal ganglia pathways. Experimental evidence favors the divergence of cortical inputs to modules in the striatum. Any given module can receive somatotopically matched inputs (labeled F=foot) from different S1 areas (3a, 3b, and 1) and from M1. This divergence can be followed by reconvergence onto sets of basal ganglia output cells in the pallidum. Inputs from the midbrain SN-DA cells modulate this processing, as do local interneurons (small dots) (Gaybiel et al., 1984)

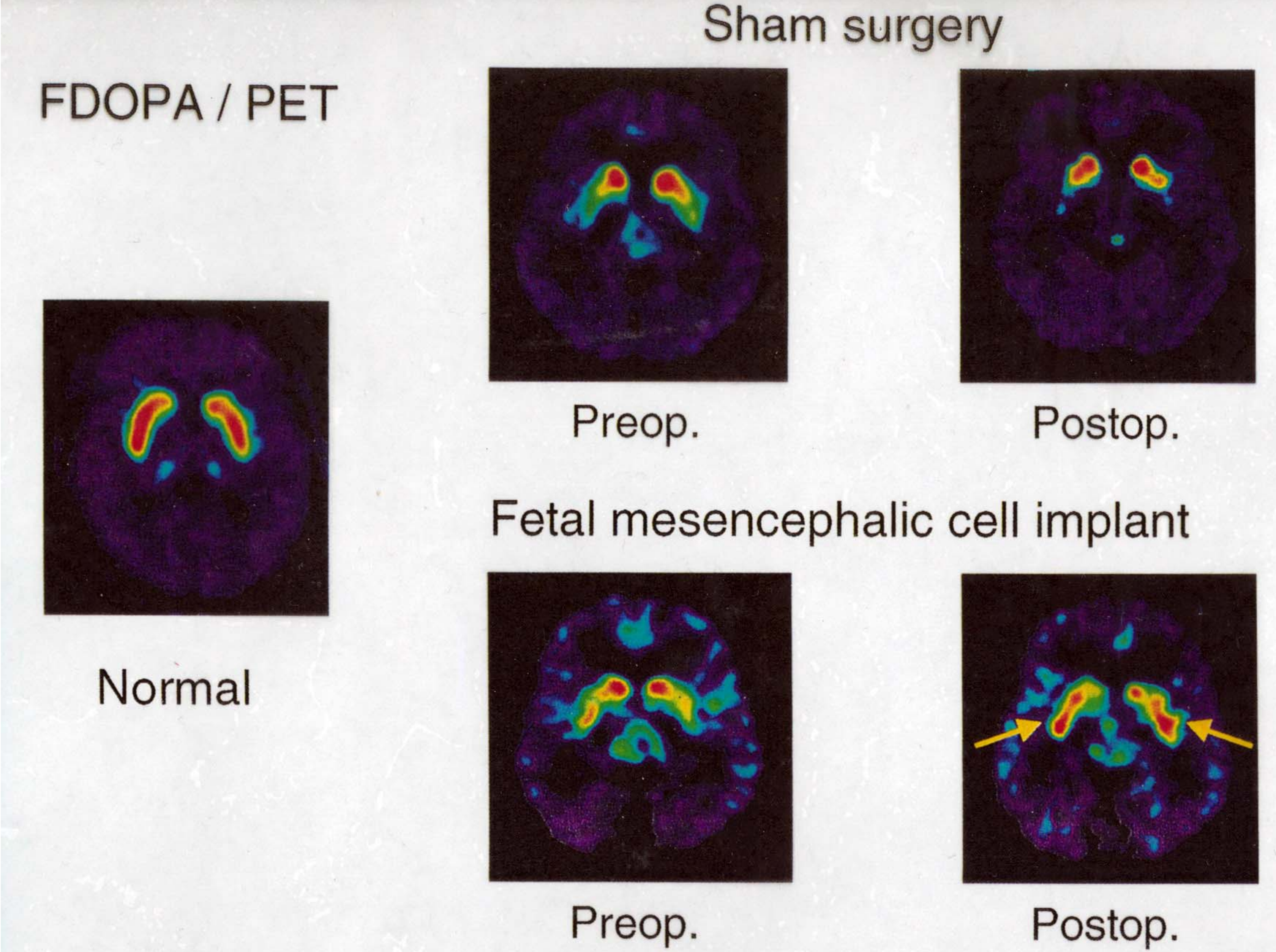
Recording in normal and parkinsonian monkeys



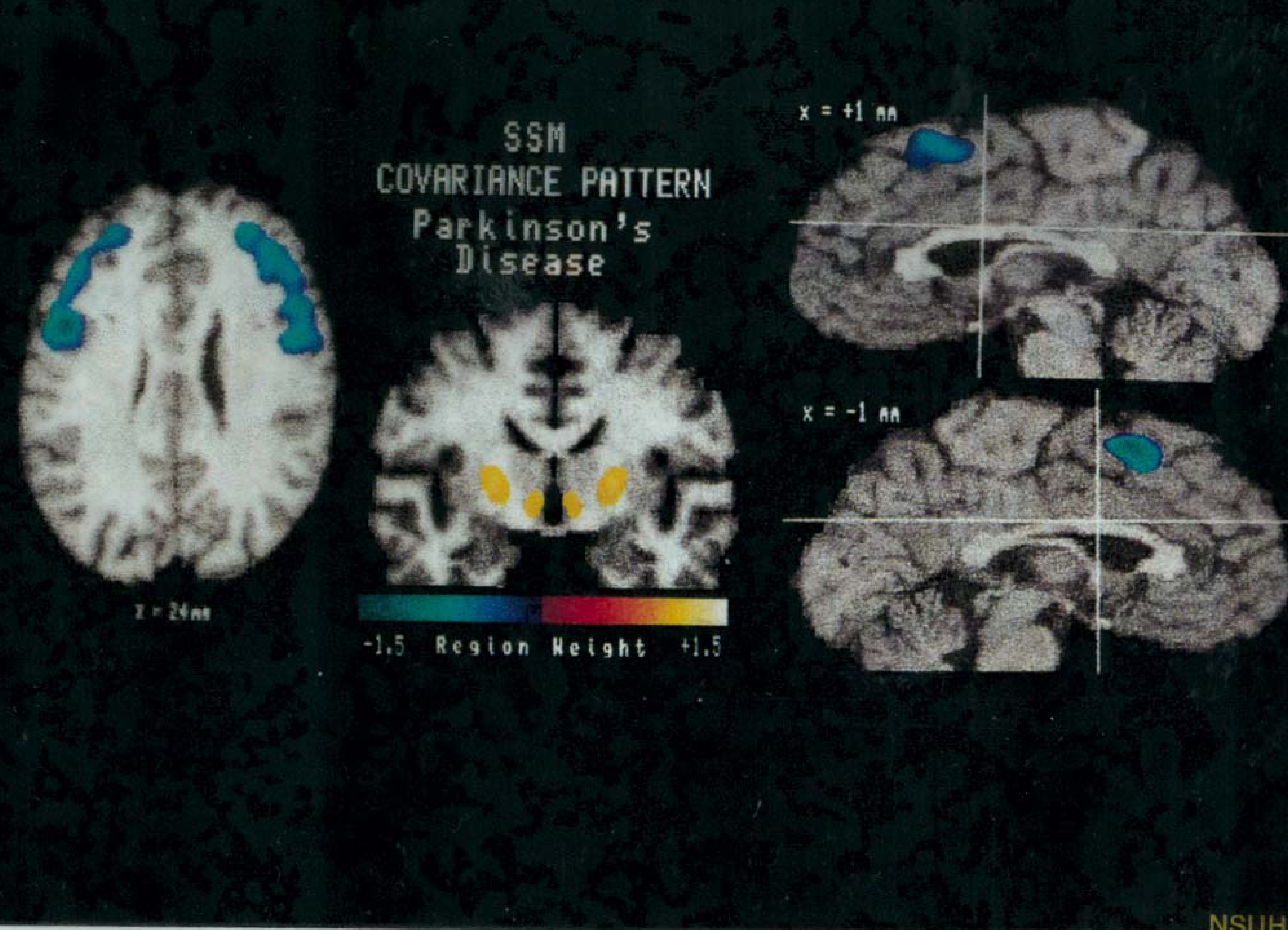
Multiple-electrode recordings in the globus pallidus of normal (A) and parkinsonian (B) monkeys. An example of 2.5 s of the simultaneous output of 3 electrodes. A: The upper two traces are from GPe, the lower one from GPi. B: in MPTP monkey intermittent episodes of synchronous, periodic bursting are seen in about one third of the recorded pallidal neurons, but never in normal monkeys (Bergman et al., 1998)

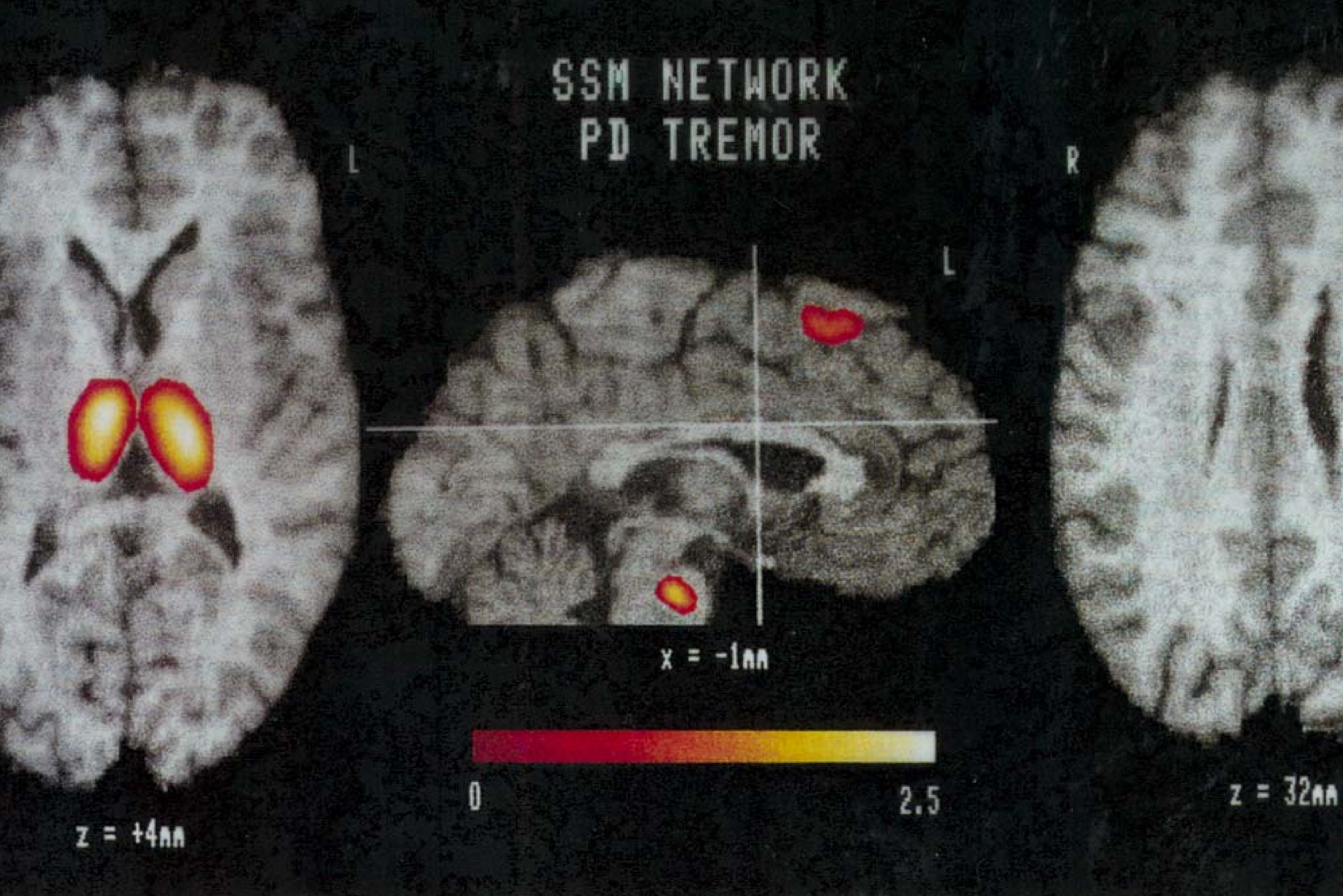


PET images obtained with [18F]FP-B CIT in a normal volunteer (left), in a patient with Hoehn-Yahr sage I, and in a patient with H-Y IIPD



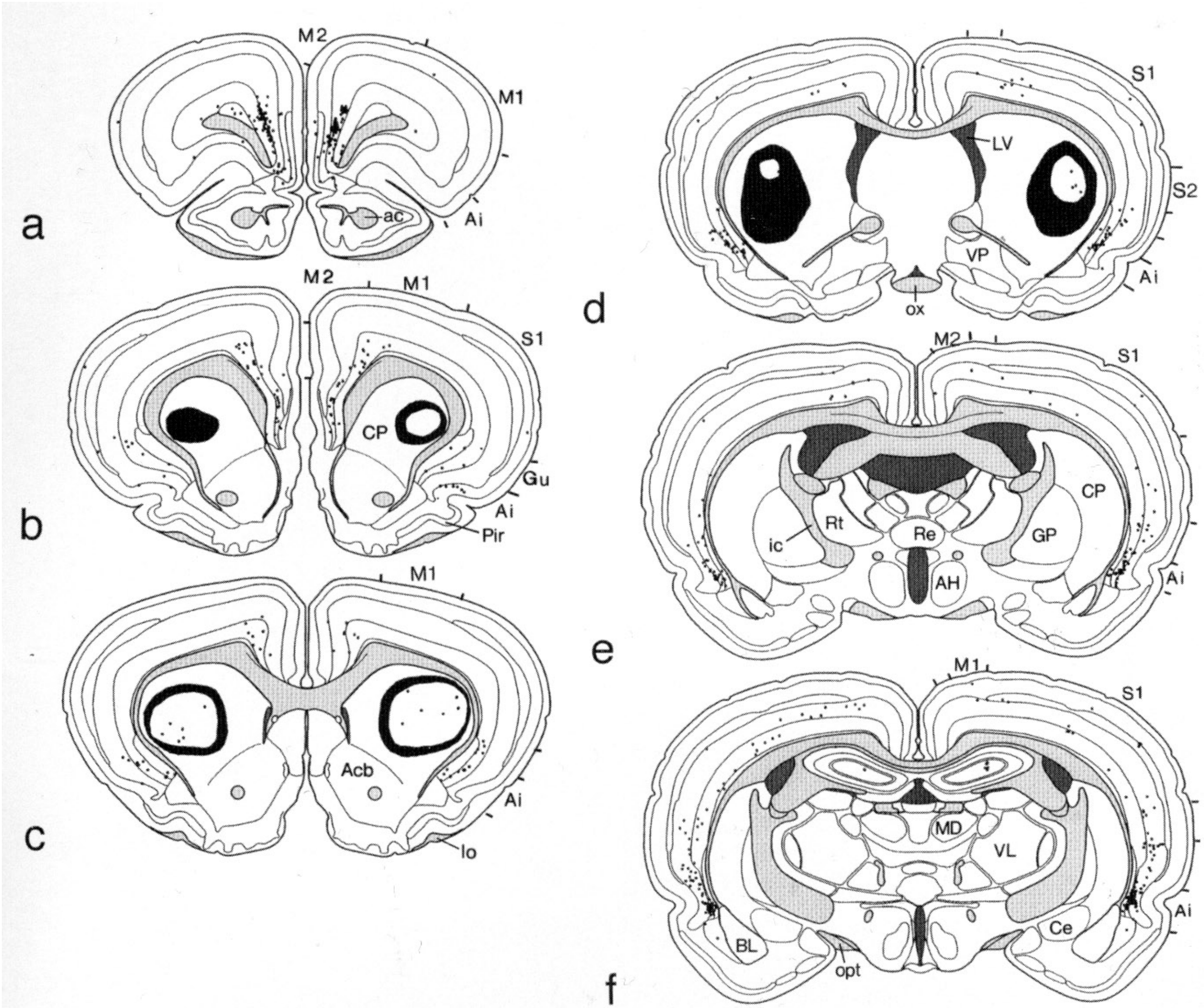
FDOPA/PET images from a normal volunteer (left) and from two patients of a sham and fetal nigral dopamine cell implantation in the putamen for advanced PD treatment. Baseline and 15 – month postoperative scans.


SSM
COVARIANCE PATTERN
Parkinson's
Disease
x = +1 mm
x = -1 mm
x = 24mm
-1.5 Region Weight +1.5
NSUH

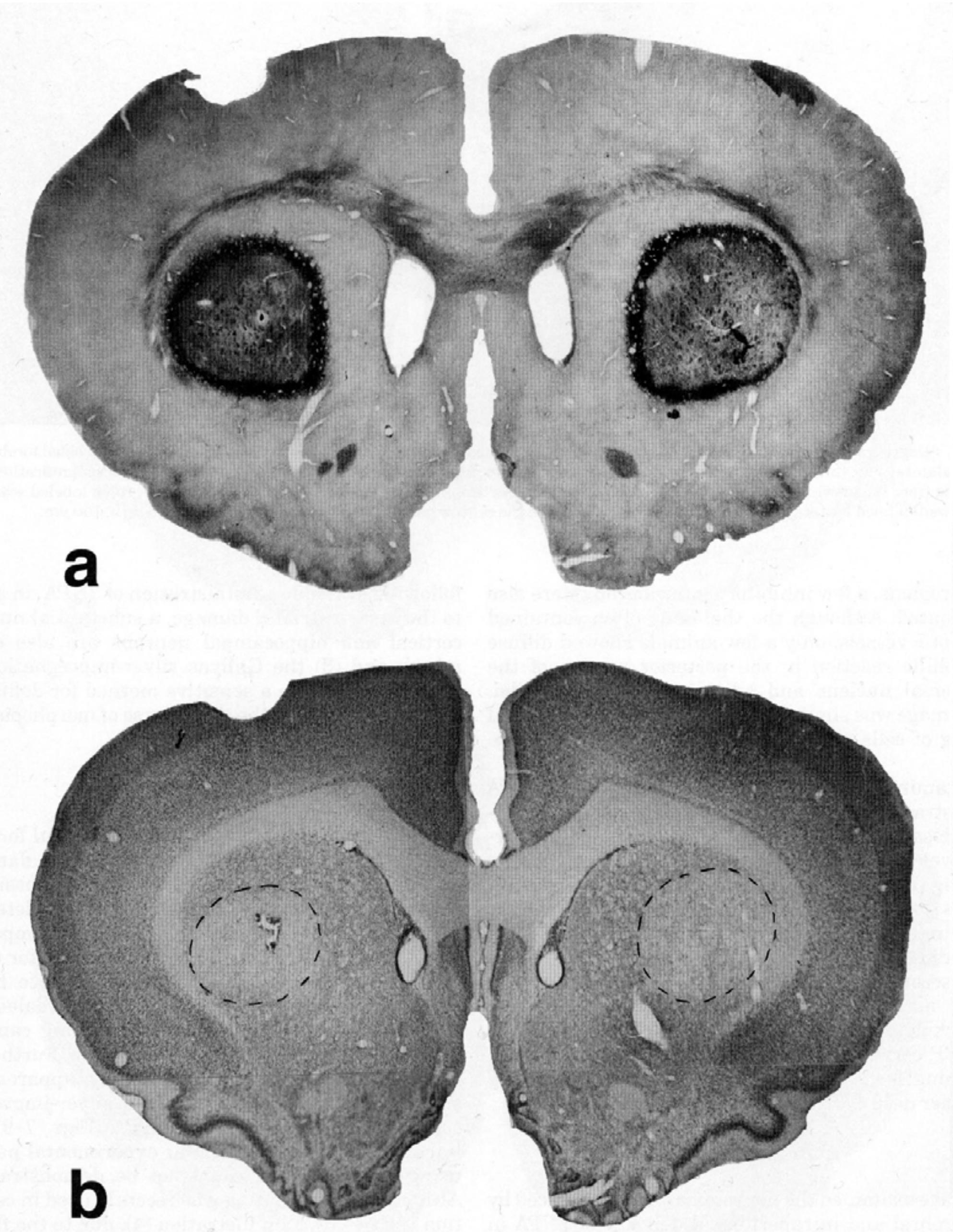


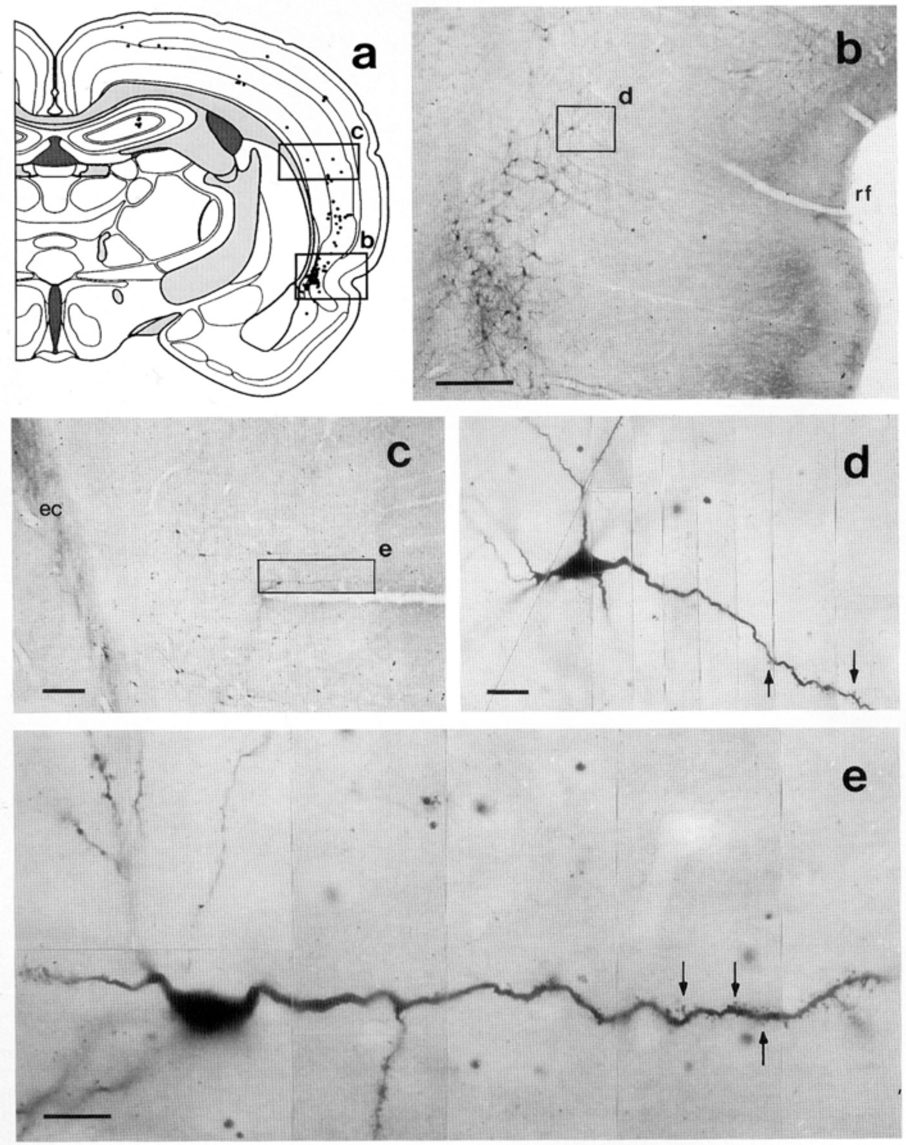
Display of the region weights of the SSM topography associated with parkinsonian tremor, overlaid on a nor
permetabolism (scale) of the thalamus (transverse, left) is associated with covariate metabolic increases in the

HUNTINGTON MODEL IN RODENT USING 3-NPA



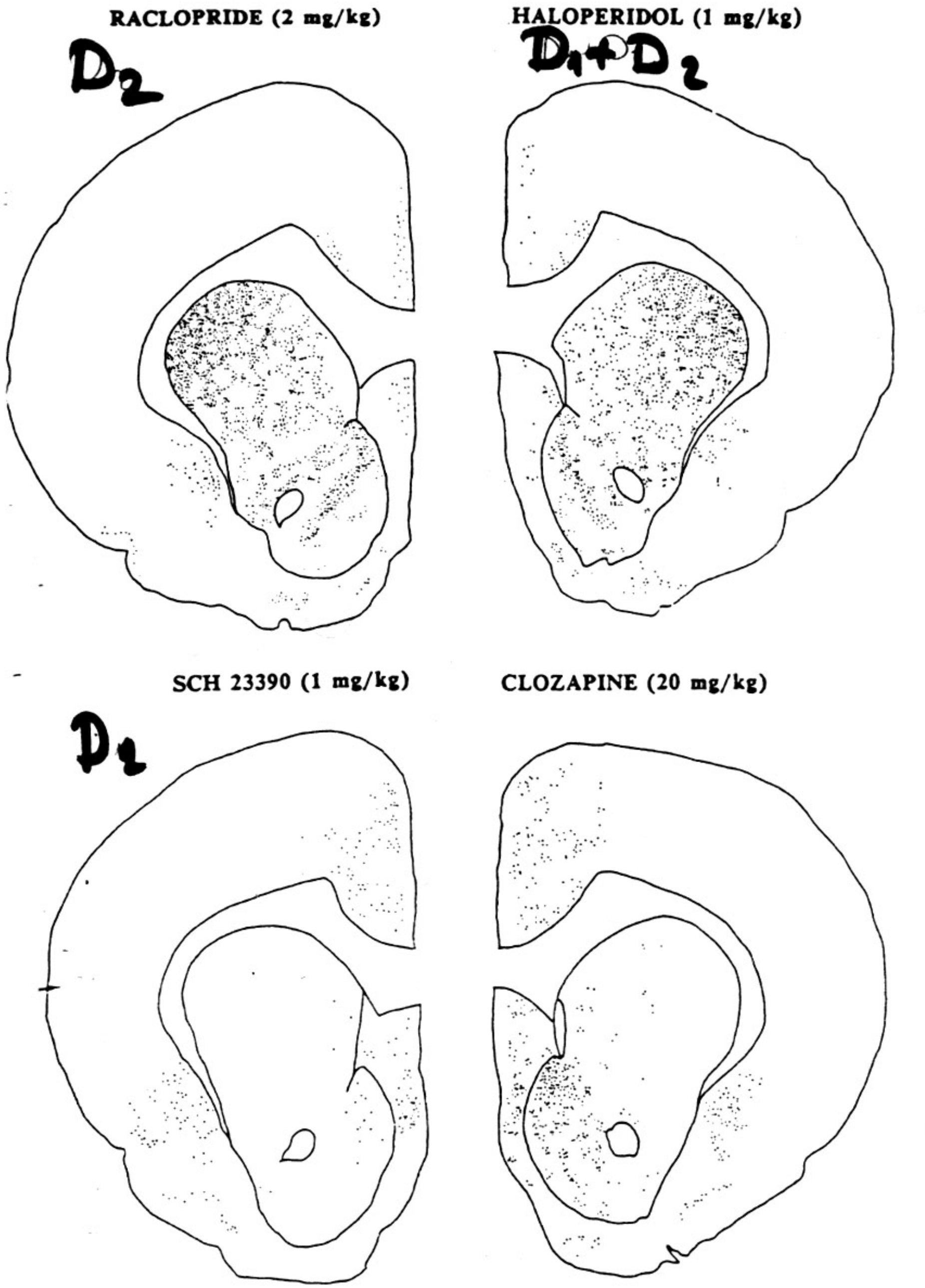
3-NPA induced degeneration in a Huntingon-model in rats. (Miller and Z, 1997)





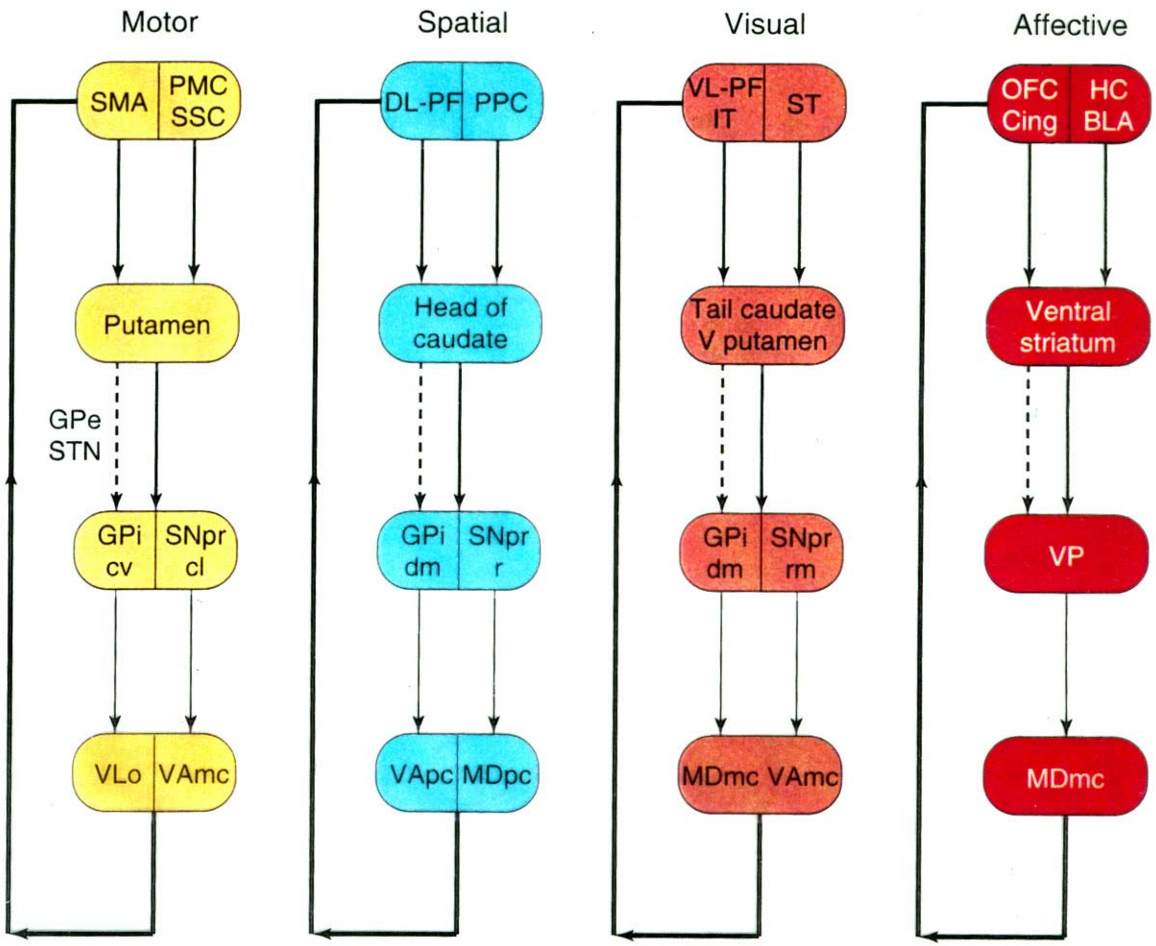
3-NPA induced degeneration in a Huntingon-model in rats. (Miller and Z, 1997)

SITE OF ACTION OF ANTI-SCHIZOPHRENIC DRUGS



Camera lucida drawings representative of the effects of the injection of raclopride, haloperidol, SCH23390 and clozapine on the distribution of Fos-positive neurons in the nucleus accumbens and striatum.

DISEASES AS LESIONS OF THE CORTICO-STRIO-PALLIDO-THALAMIC LOOPS 1.



Corticostriatal loops, modified from the original scheme of Alexander et al. Dashed lines indicate net inhibitory influences of the so-called ‘indirect’ striatal output pathways. (Lawrence et al, 1998)

SMA-supplementary

PMC-premotor

SSC-somatosensory

DL-PFC-dorsolateral PFC

PPC-posteropr parietal

VL-PFC-ventrolateral PFC

ST-superior temporal ctx

IT-inferior temporal

OFC-orbitofrontal

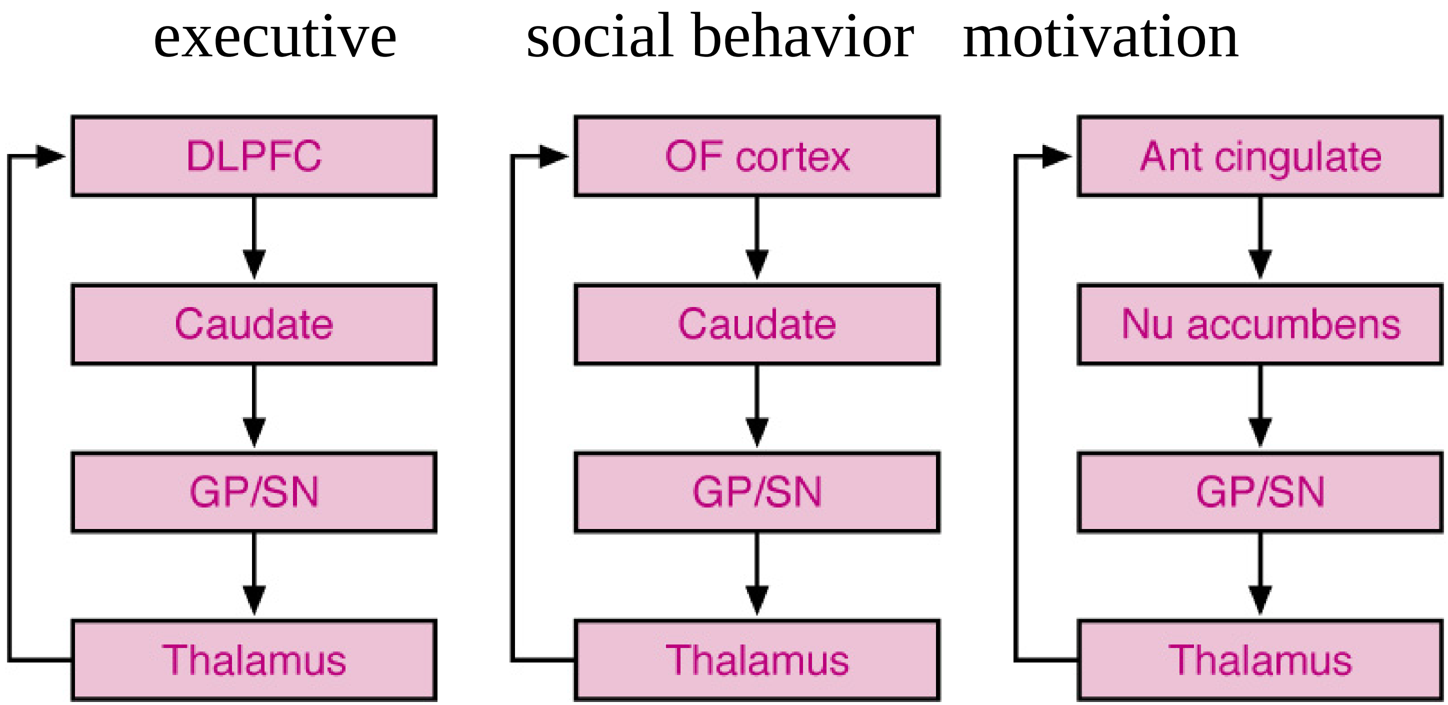
HC-hippocampus

BLA-basolateral amygdala

VP-ventral pallidum

MD-mediodorsal thalamic

DISEASES AS LESIONS OF THE CORTICO-STRIO-PALLIDO-THALAMIC LOOPS 2



Three behaviorally relevant frontal-subcortical circuits.. DLPFC, dorsolateral prefrontal cortex; GP, globus pallidus; SN, substantia nigra; Nu accumbens, nucleus accumbens; Ant cingulate, anterior cingulate; OF, orbitofrontal (from Cummings, 2003.