STRUCTURE AND CIRCUITS OF THE BASAL GANGLIA

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Basal ganglia

- **Nucleus caudatus, putamen, globus pallidus (pallidum externum, pallidum internum), nc.subthalamicus, substantia nigra (compacta, reticulata).**

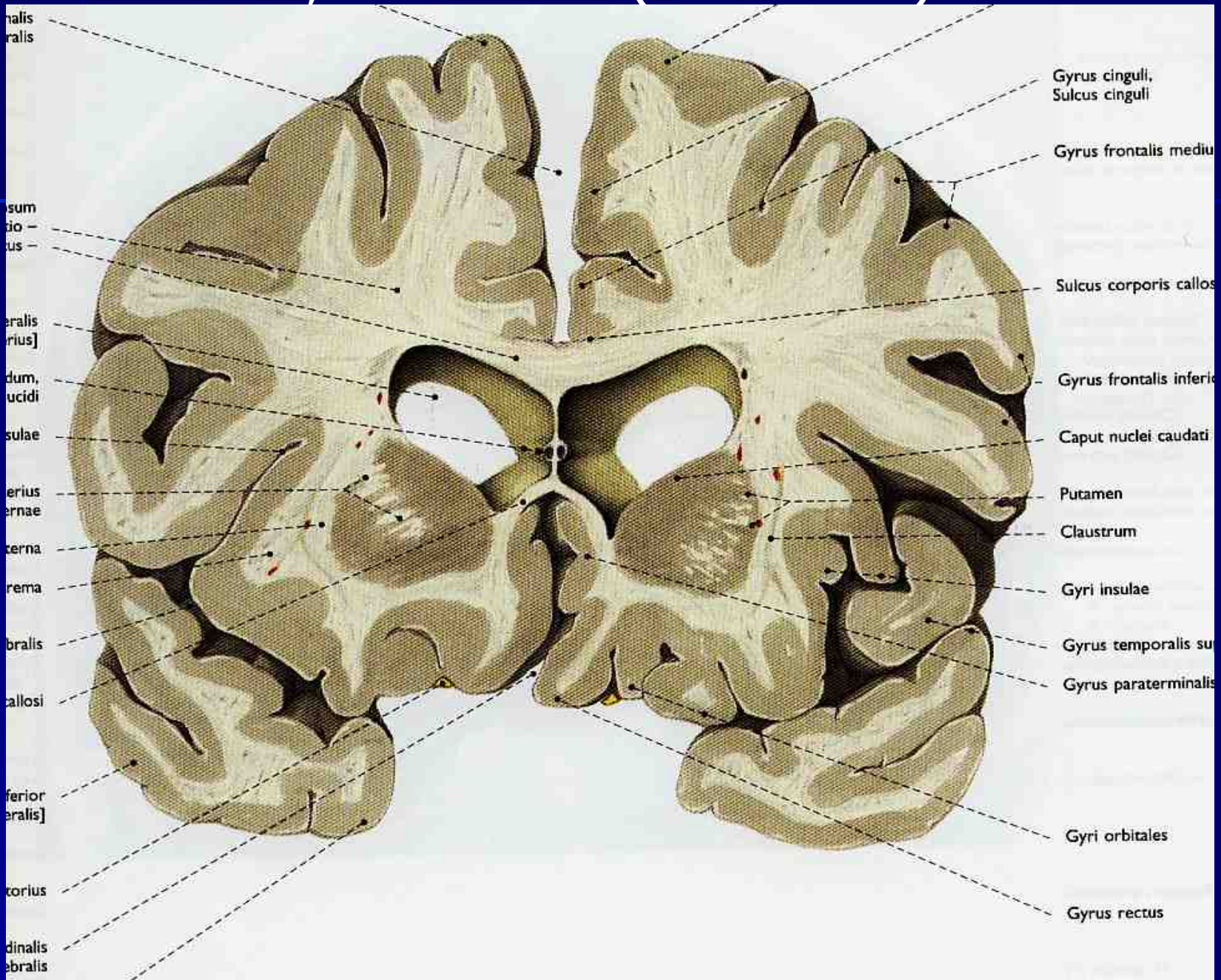
- **amygdala, claustrum**

- Nucleus caudatus + putamen = striatum
- Putamen+ globus pallidus (pallidum externum, pallidum internum) = nucleus lentiformis

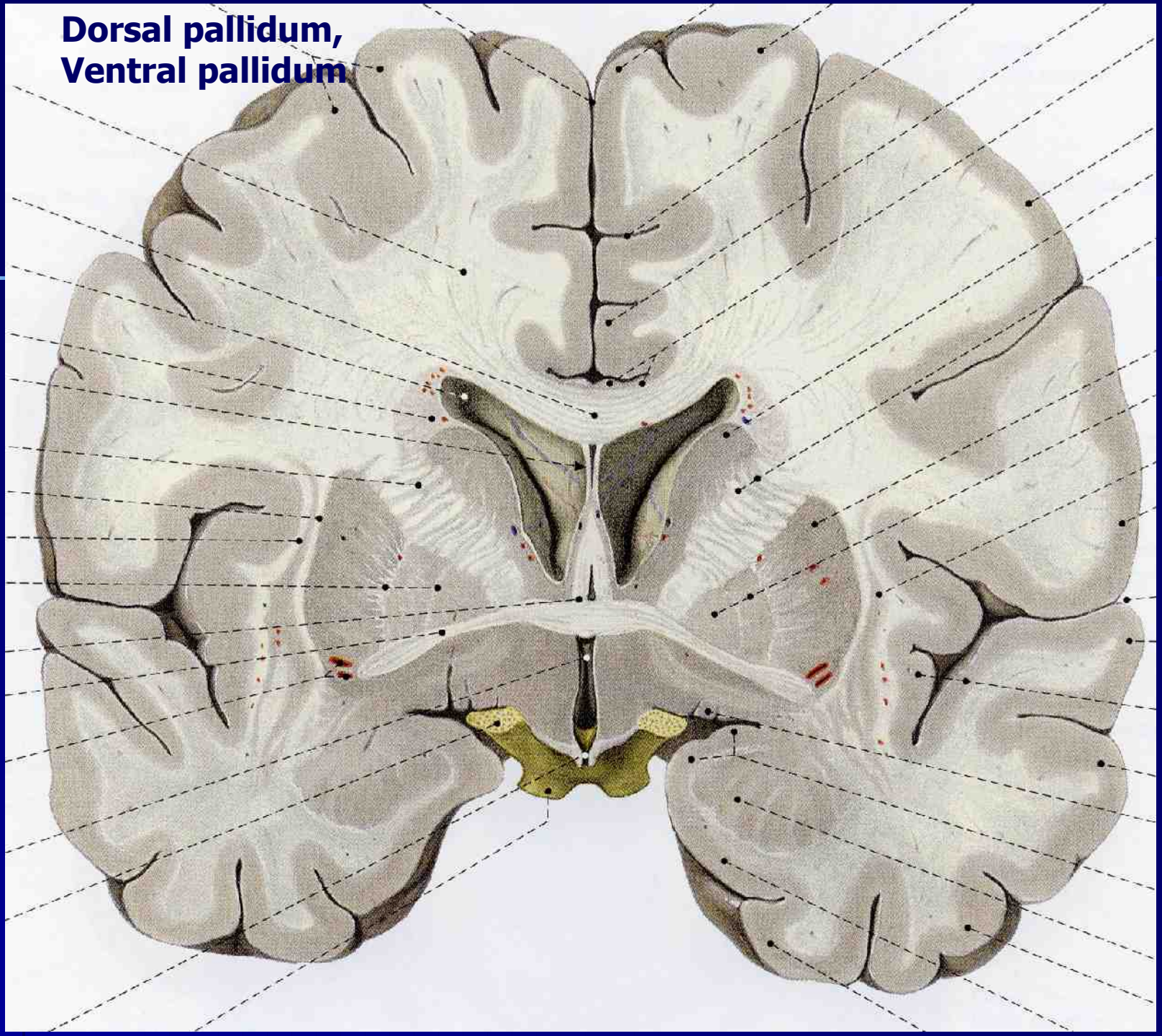
- Amygdala (limbic system)
- Claustrum

Topography of the basal ganglia

Dorsal striatum, Ventral striatum (nc. Accumbens)

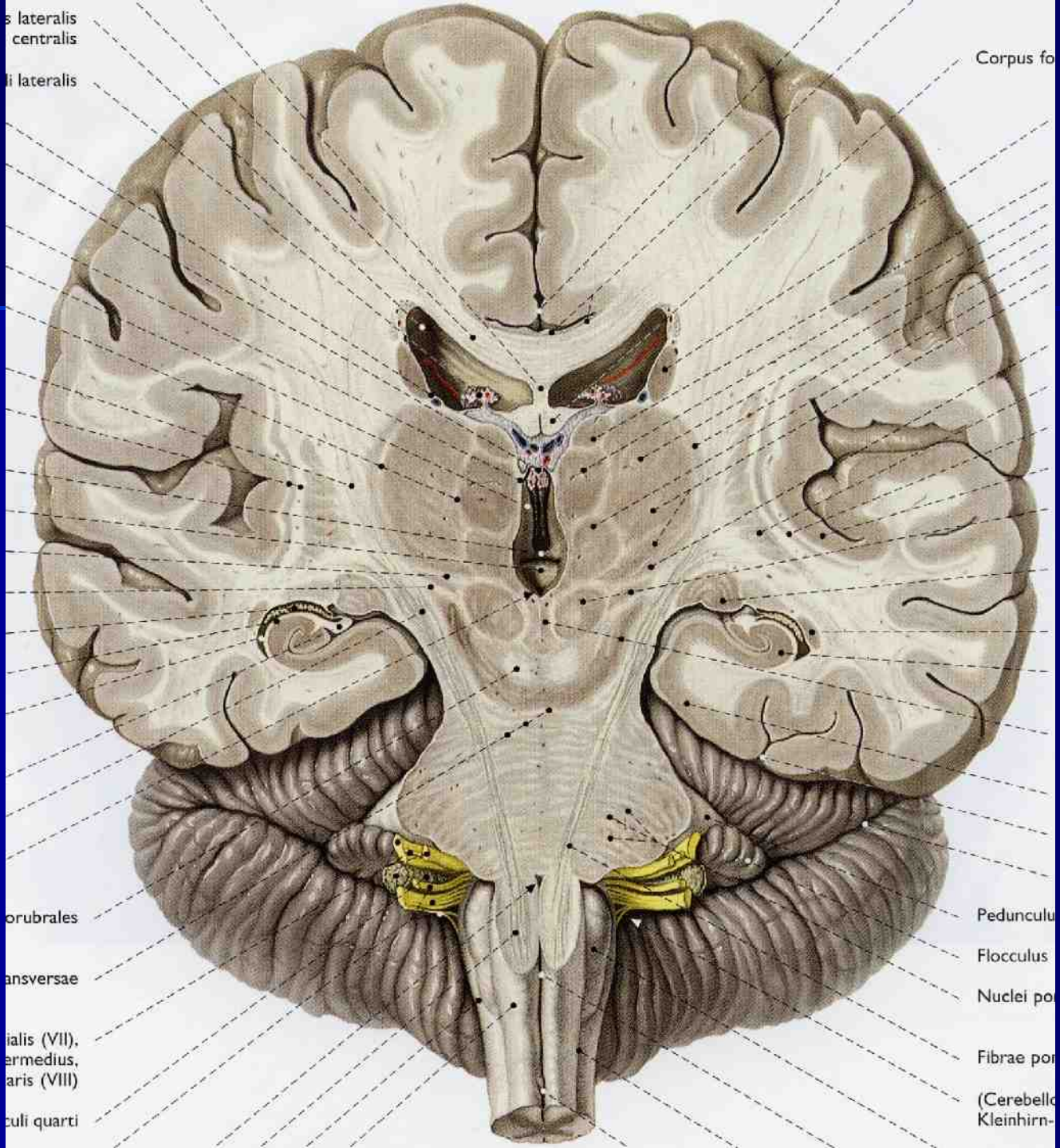


Dorsal pallidum,
Ventral pallidum



Striatum dorsale a striatum ventrale

- Striatum ventrale = nc. accumbens and adjoining part of the nc. caudatus a putamen
- 22 % volume of striatum
- Reward centrum
- Striatum ventrale – significantly activated in the process of addictive behavior (alkohol, nikotin, drogy, gambles, sex)
- Projections from orbitofrontal and cingular cortex and from limbic system (hippocampus, amygdala)


s lateralis
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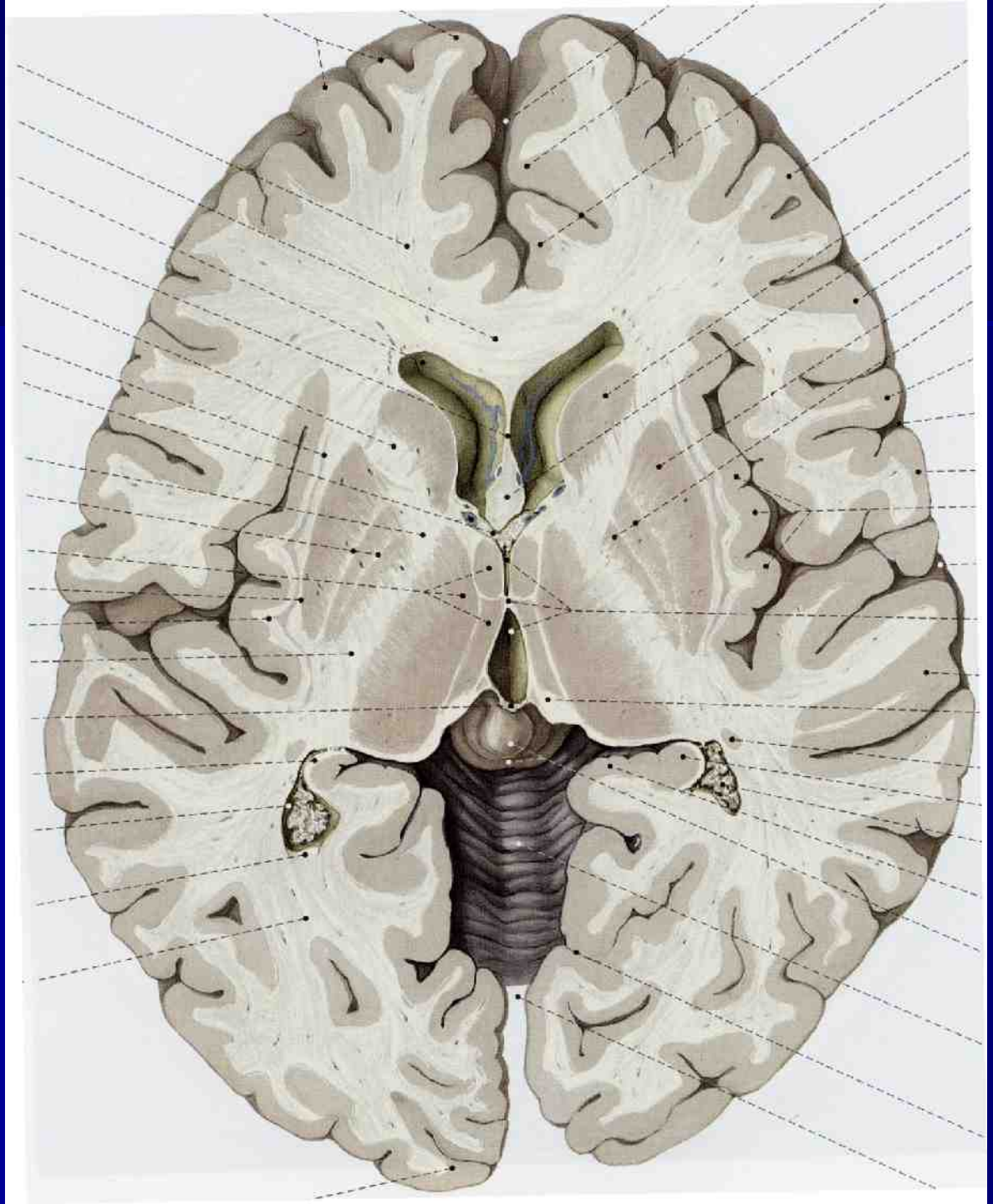
ialis (VII),
ermedius,
aris (VIII)
culi quarti
Pedunculu
Flocculus
Nuclei po
Fibrae po
(Cerebello
Kleinhirn-



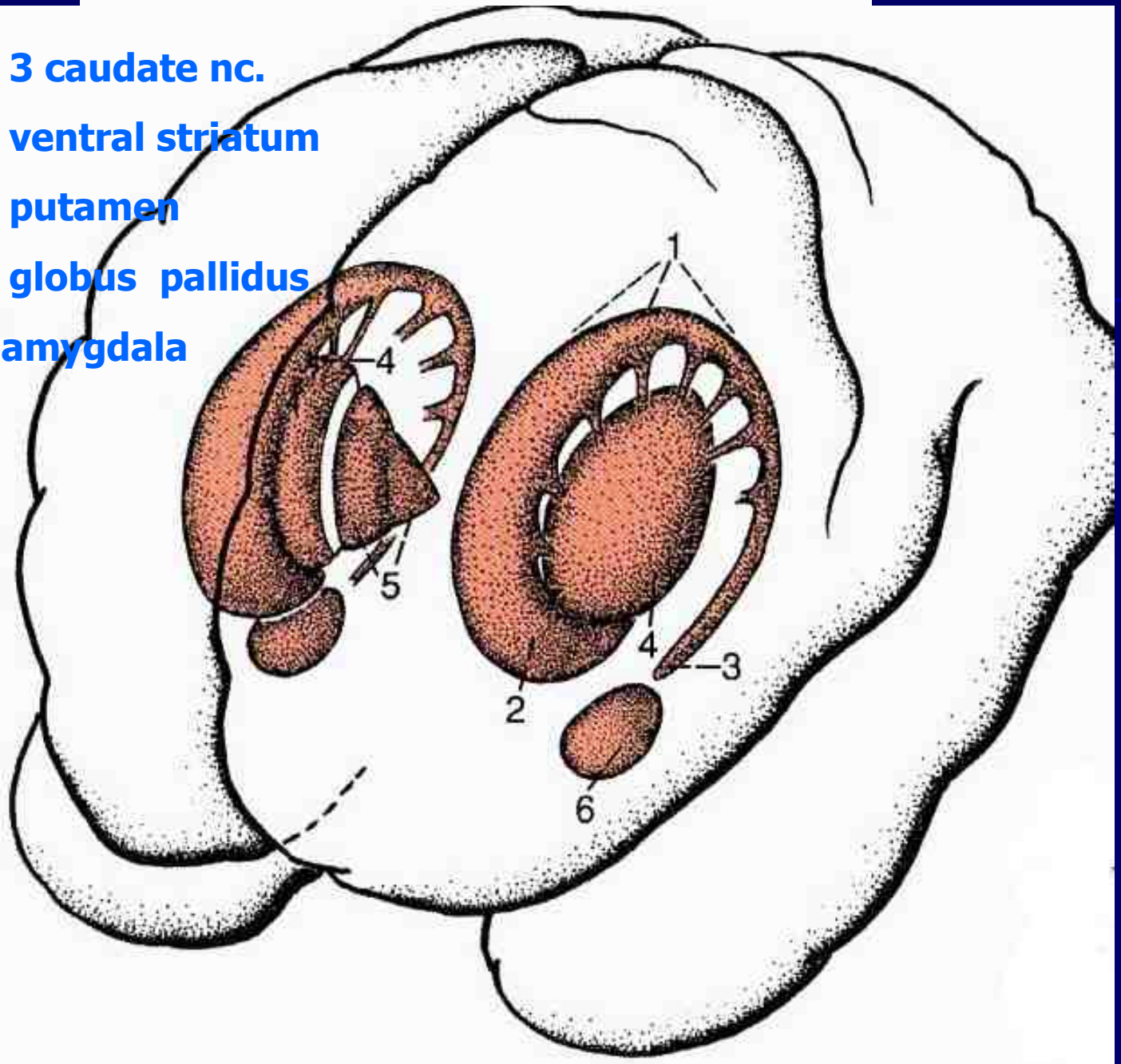
1 – 3 caudate nc.

2 – ventral striatum

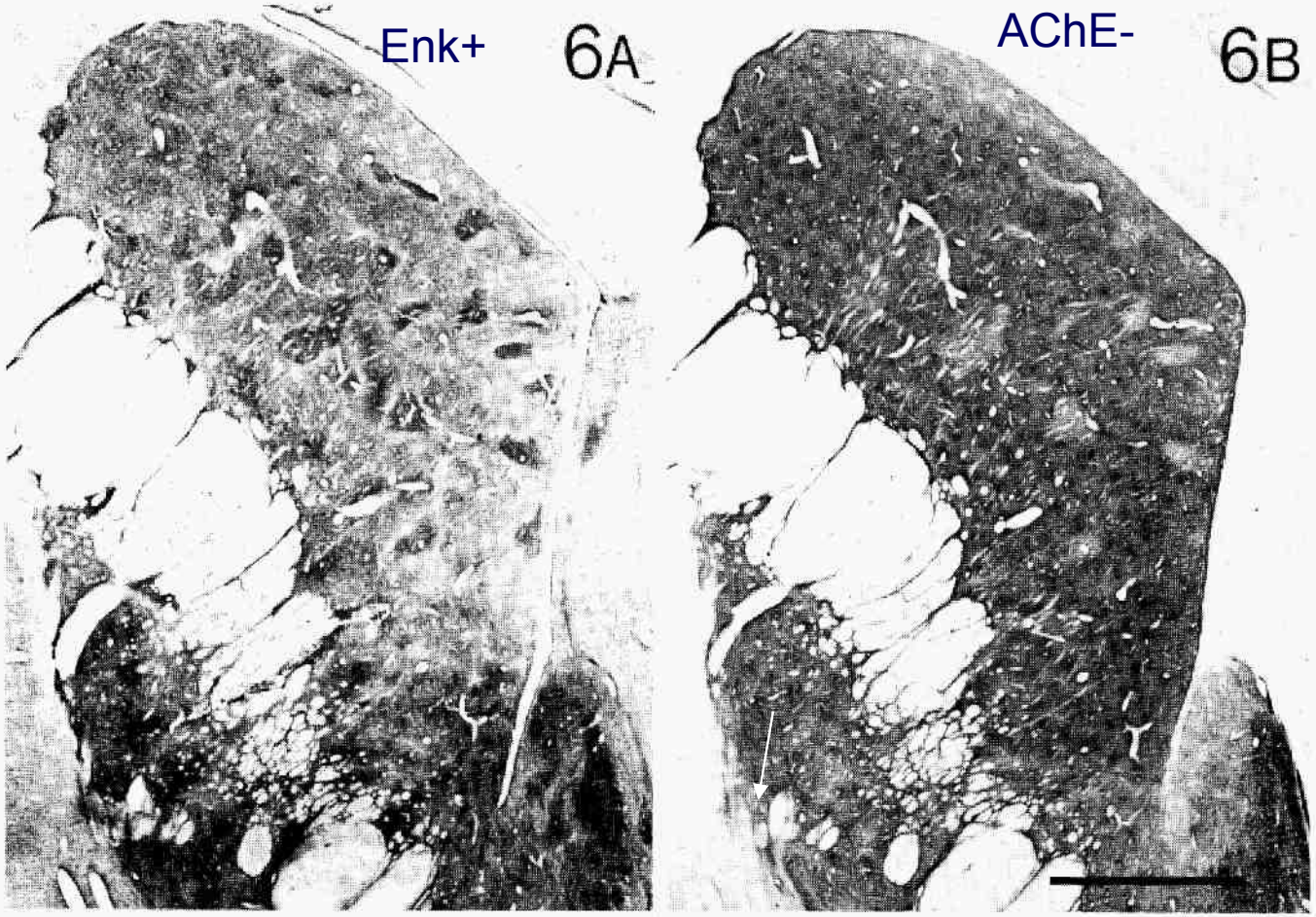
4 – putamen

5 – globus pallidus

6 - amygdala



Striatal compartments – matrix, striosomes



FIGS 4–6. Three pairs of sections from 3 different brains illustrating the alignment of enkephalin-rich (A) acetylcholinesterase-poor (B) zones visible in serially adjoining sections through the caudate nucleus. Fig. 4: case CP-4L; Fig. 5: case CP-3X; Fig. 6: case CP-7. Arrows in Fig. 5 point to an elaborate figure in the enkephalin stain and its cholinesterase-poor correspondent. Arrows in Fig. 6 mark one of a set of enkephalin patches in the putamen and matching zones of low-cholinesterase activity. Note the richly figured nucleus accumbens in Fig. 6A. Bar in Fig. 6 denotes 2 mm; scale the same for all 6 photographs.

Striatal neurons

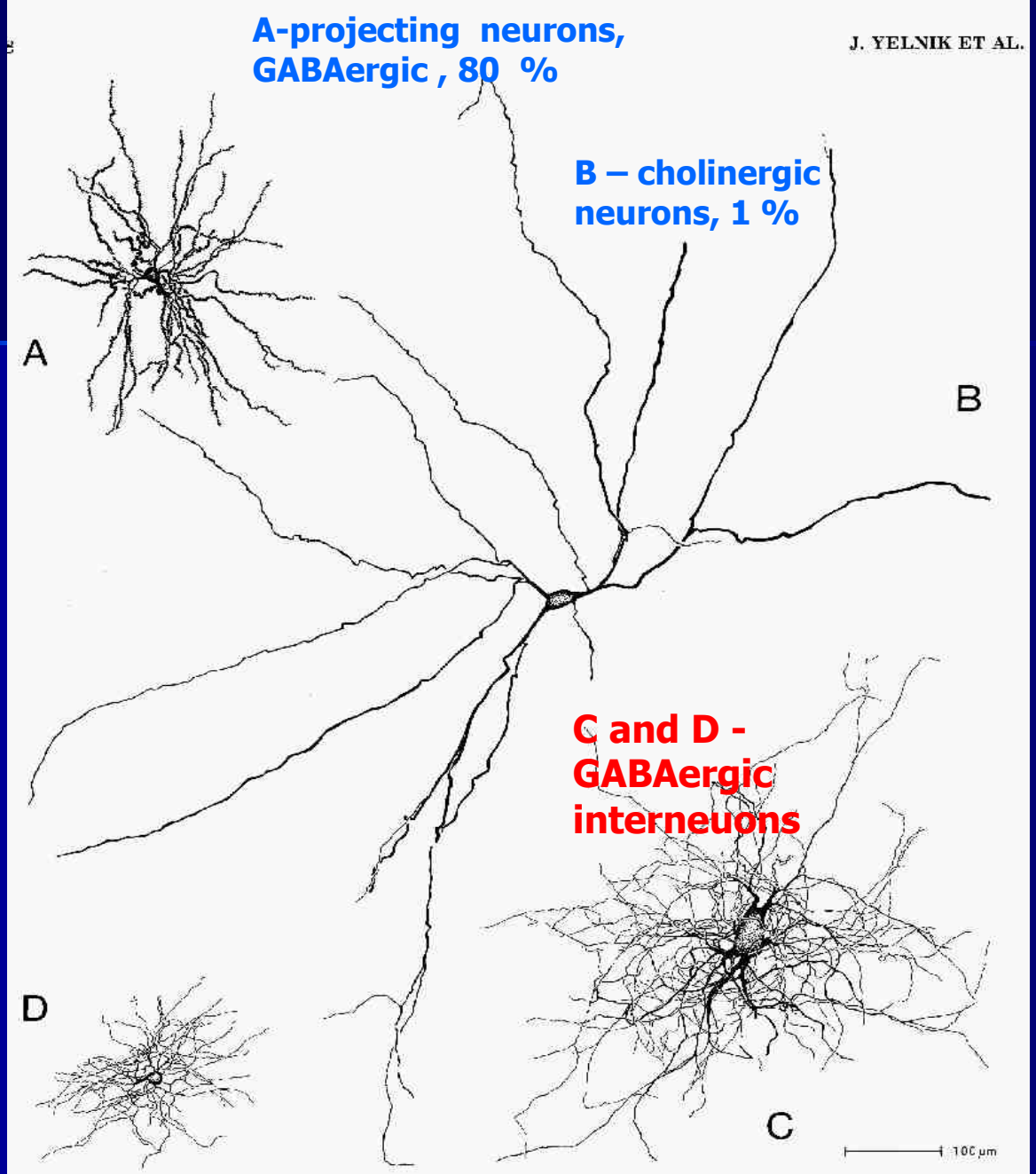
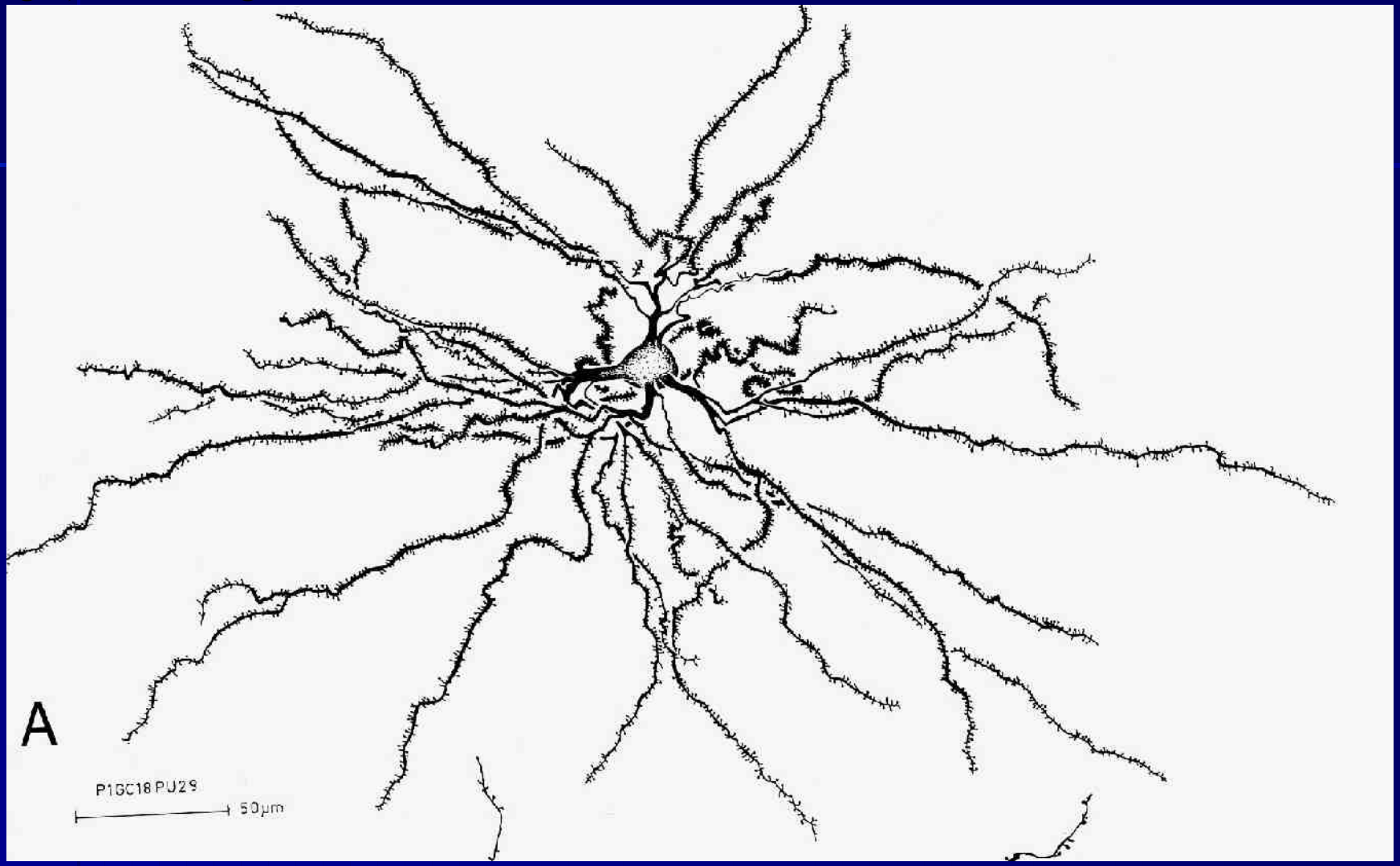


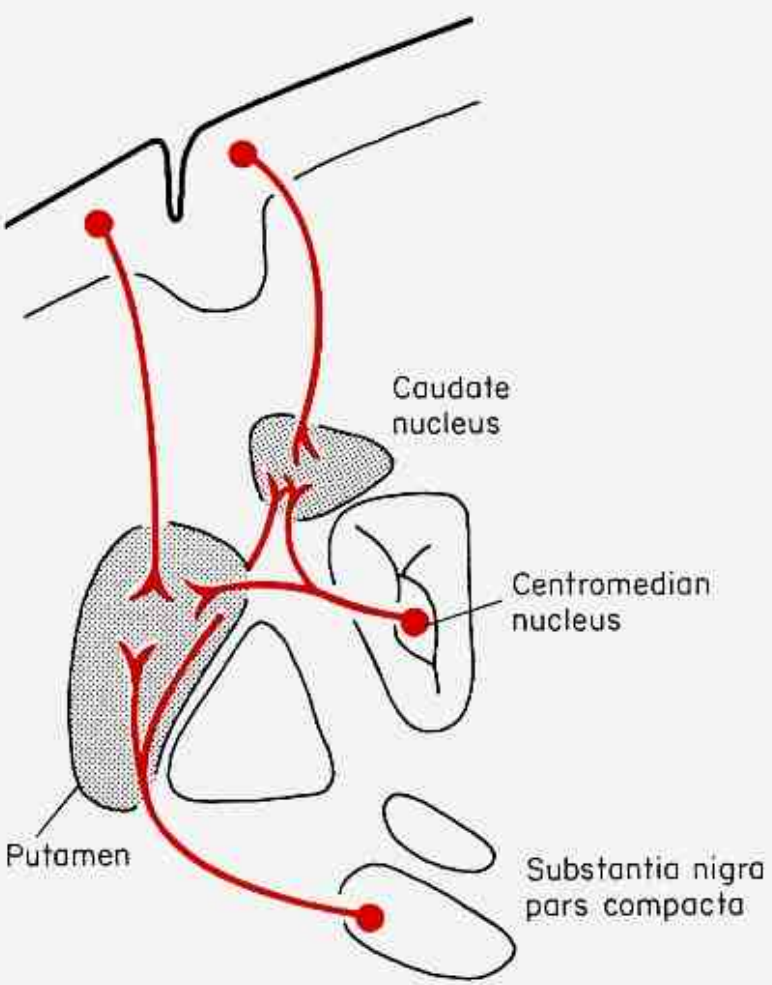
Fig. 3. Camera lucida drawings of the four neuronal species of the imate striatum: spiny neuron (**A**), leptodendritic neuron (**B**), spidery uron (**C**), and microneuron (**D**). Golgi method. All arborizations, constructed from serial sections, are illustrated at the same magnification. Note that the leptodendritic neuron has extremely long dendrites with several thin axonlike distal processes and that its cell-body size is intermediate between that of spiny neuron and that of spidery neuron.

Medium spiny neurons, projecting neurons (globus pallidus, substantia nigra), GABAergic, 80 %



STRIATUM - afferent connections

cortex, thalamus, amygdala, substantia nigra (p. compacta, Dopamin), rapheal nuclei (serotonin)



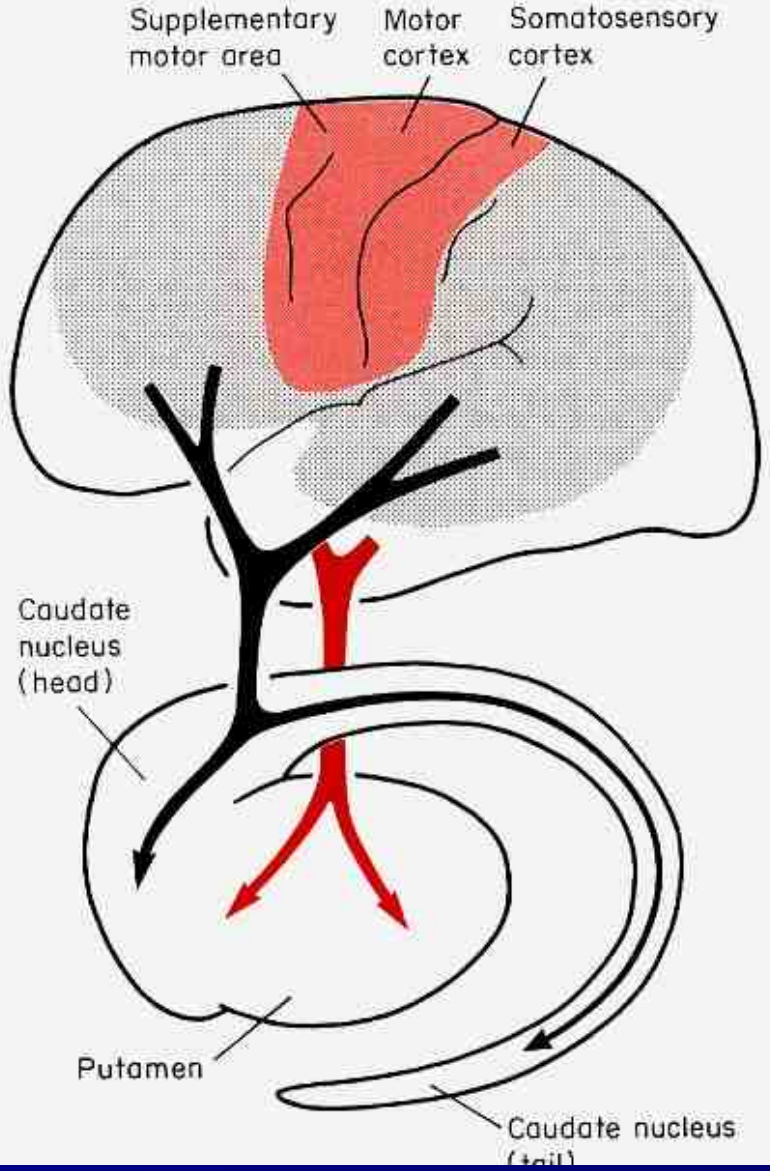


Fig. 10.4. *The main efferent connections of the striatum.*

PM area 6
M I area 4

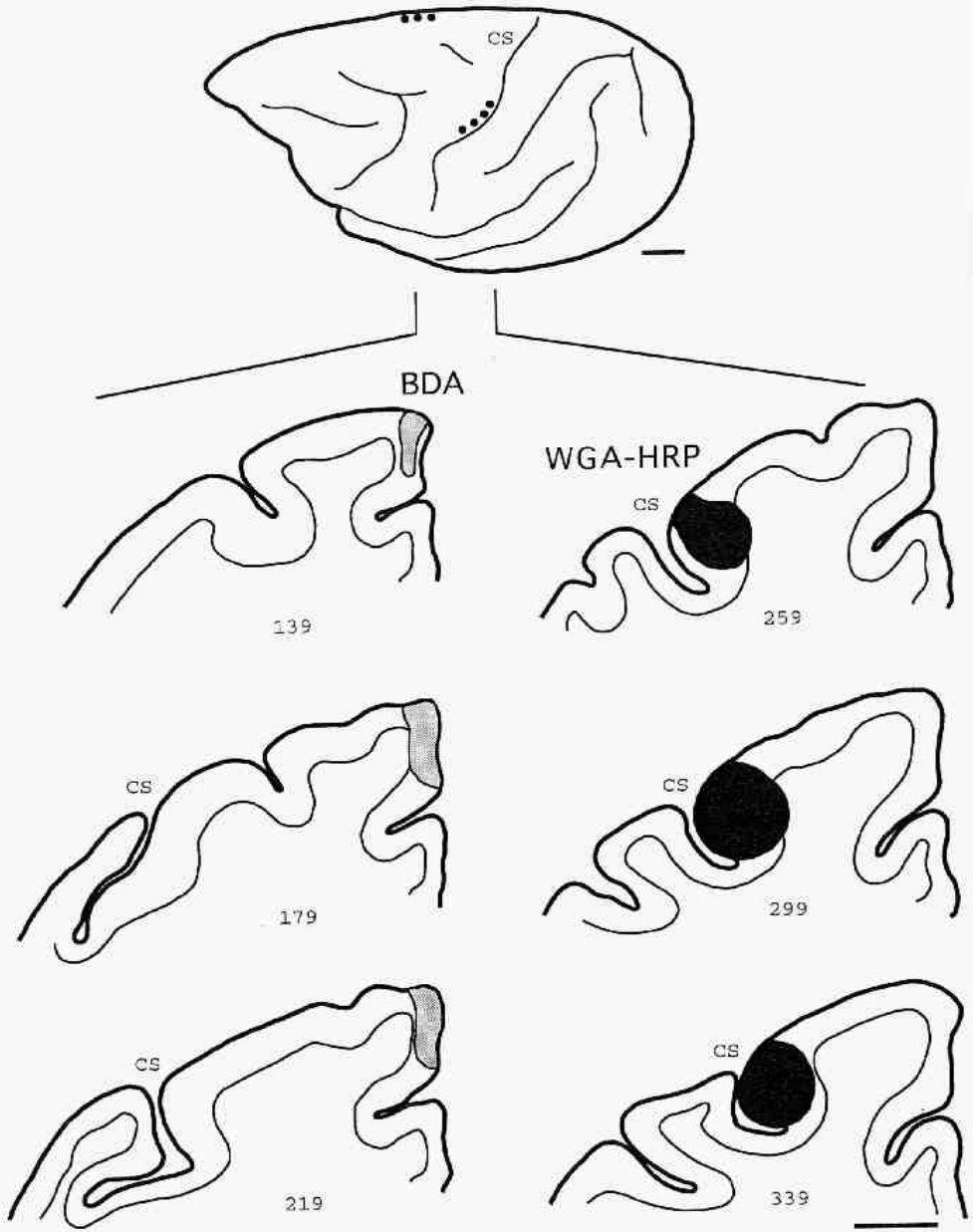


Fig. 3. Coronal sections demonstrating diffusion of the injected tracers, BDA (stippled areas) and WGA-HRP (filled areas), in the SMA and MI of monkey O at six rostrocaudal levels along with serial section numbers. A dorsolateral view of the hemisphere at the top shows penetration sites for the injections. Scale bar = 5 mm.

Anterograde intraaxonal transport

Cortex – – striatum

PM + M I - putamen

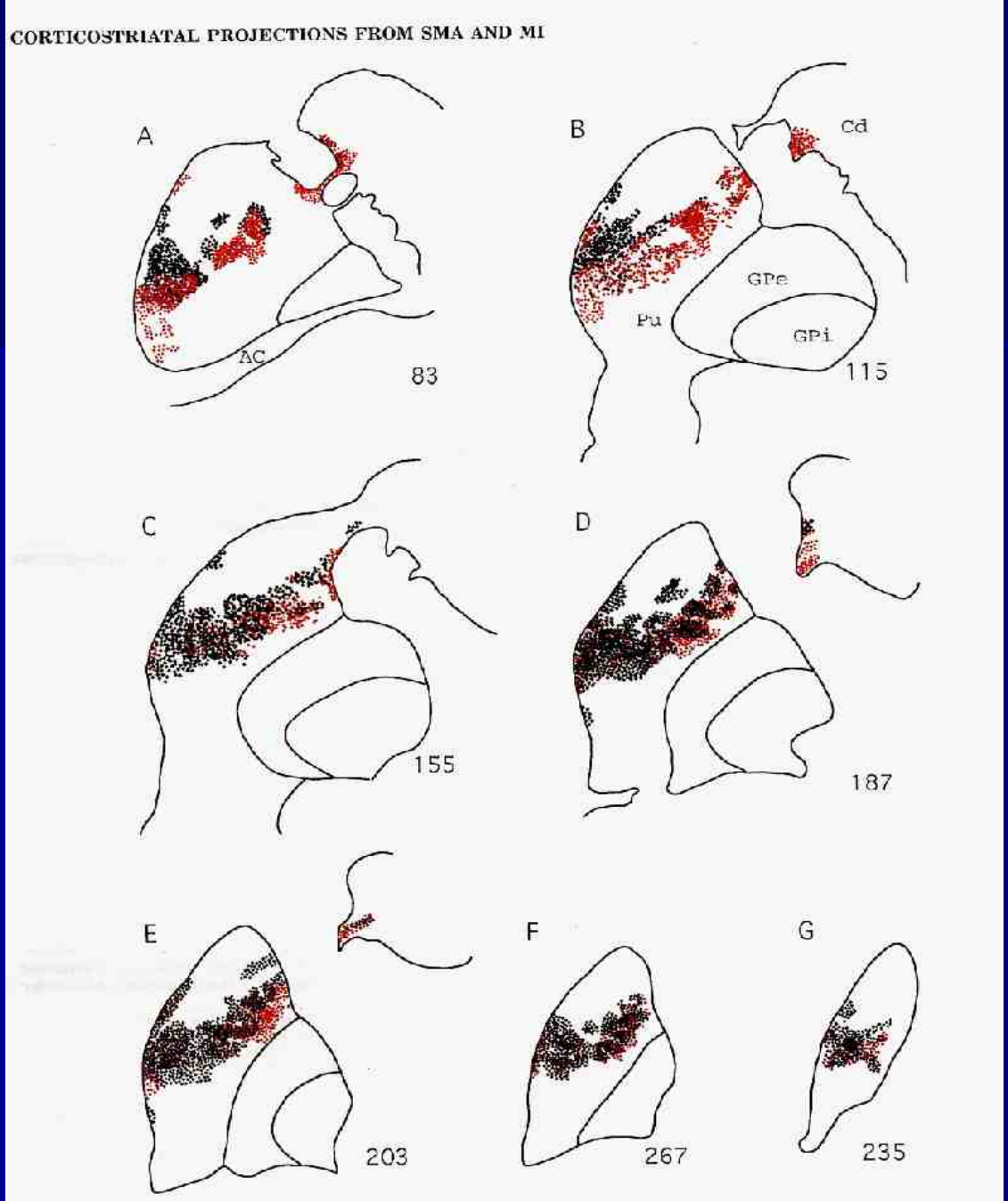
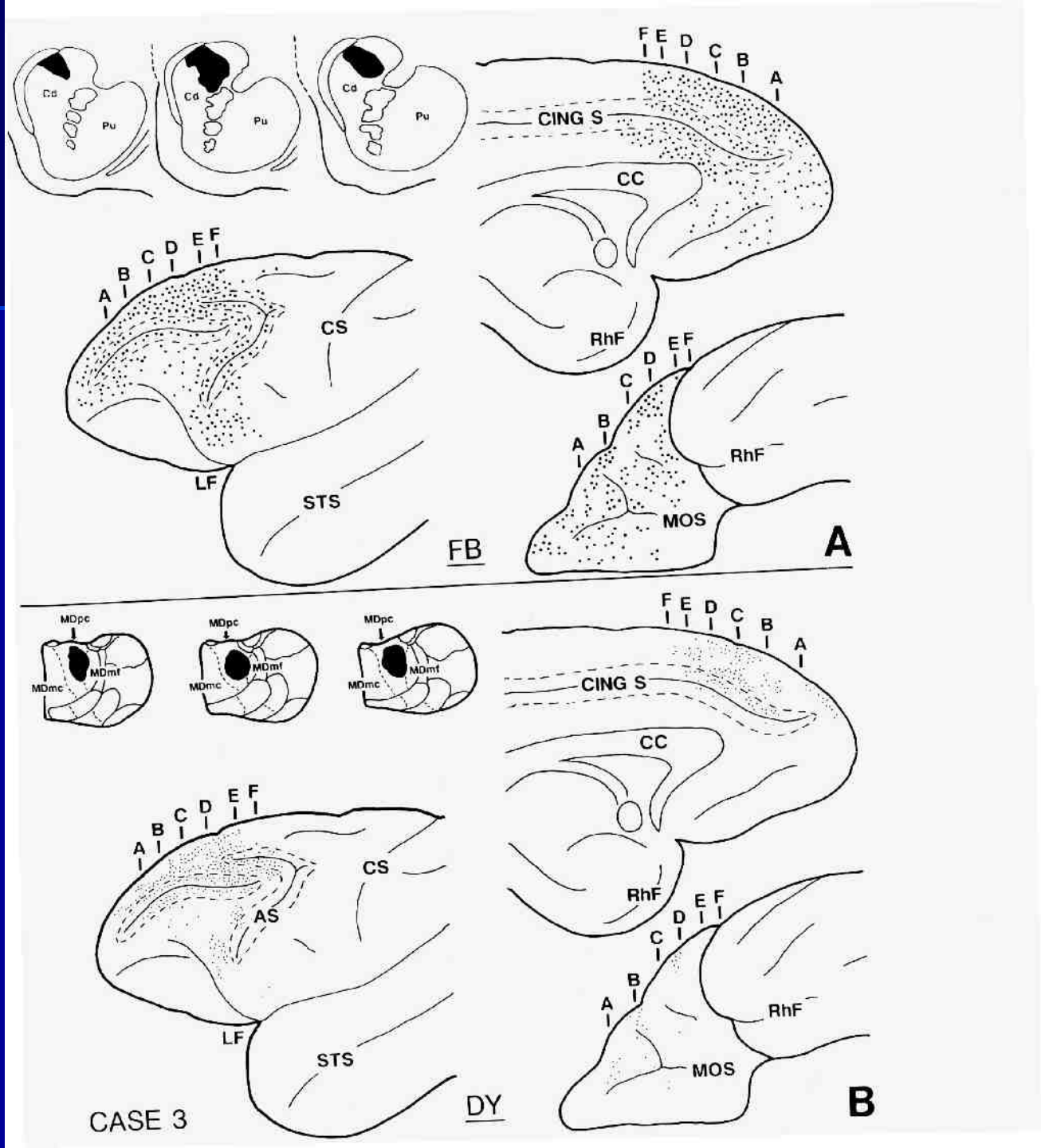


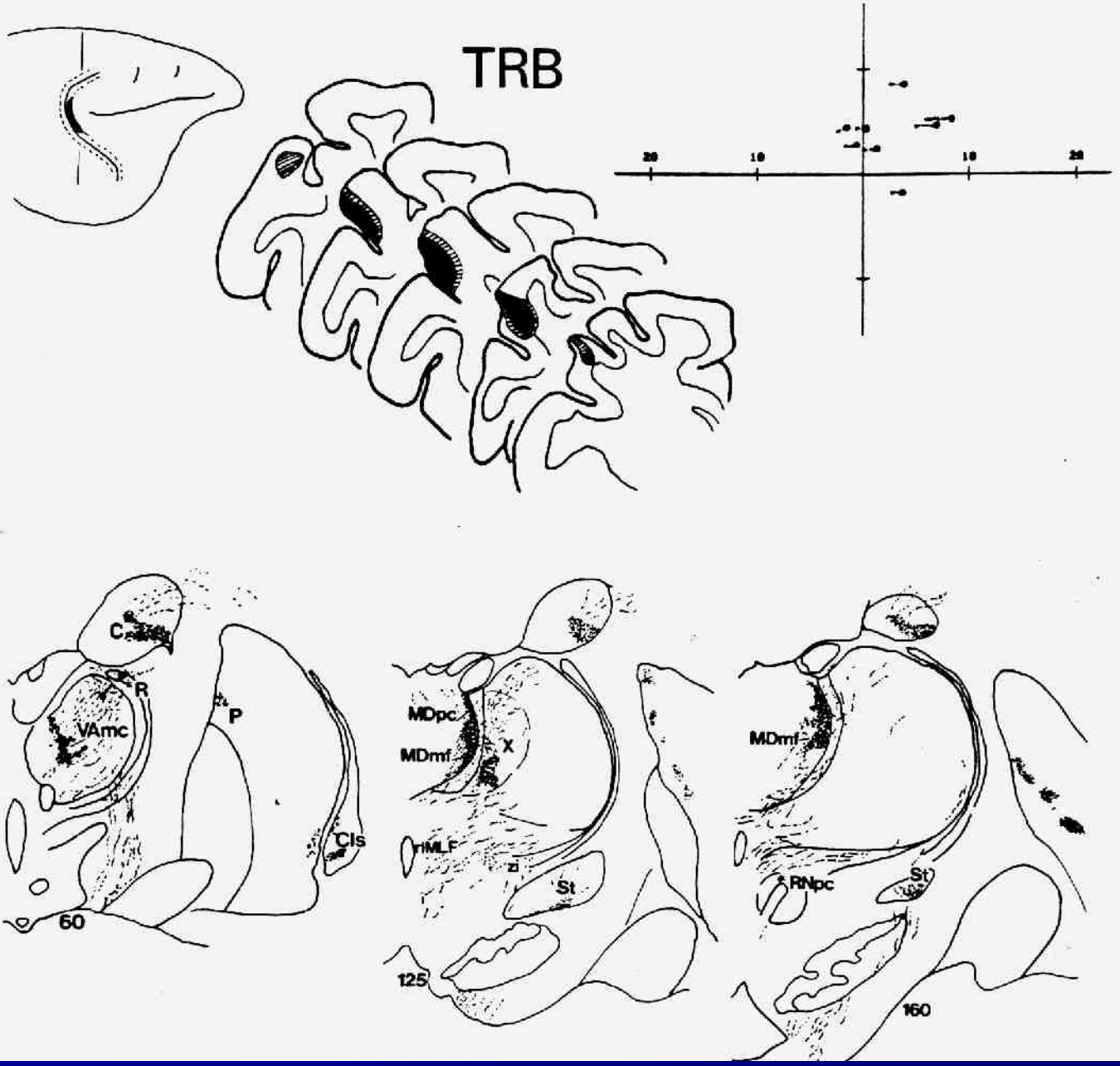
Fig. 7. Coronal maps showing distributions of presumed afferent terminal fields from the forelimb area of the SMA (red dots) and the MI (black dots) in the striatum of monkey O at six anterior to posterior levels. Note that the two distributions considerably overlap. Scale bar = 2 mm.

Retrograde Intraaxonal Transport

Assoc. Cortex-

Nc. caudatus

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Assoc. Cortex – nc. caudatus

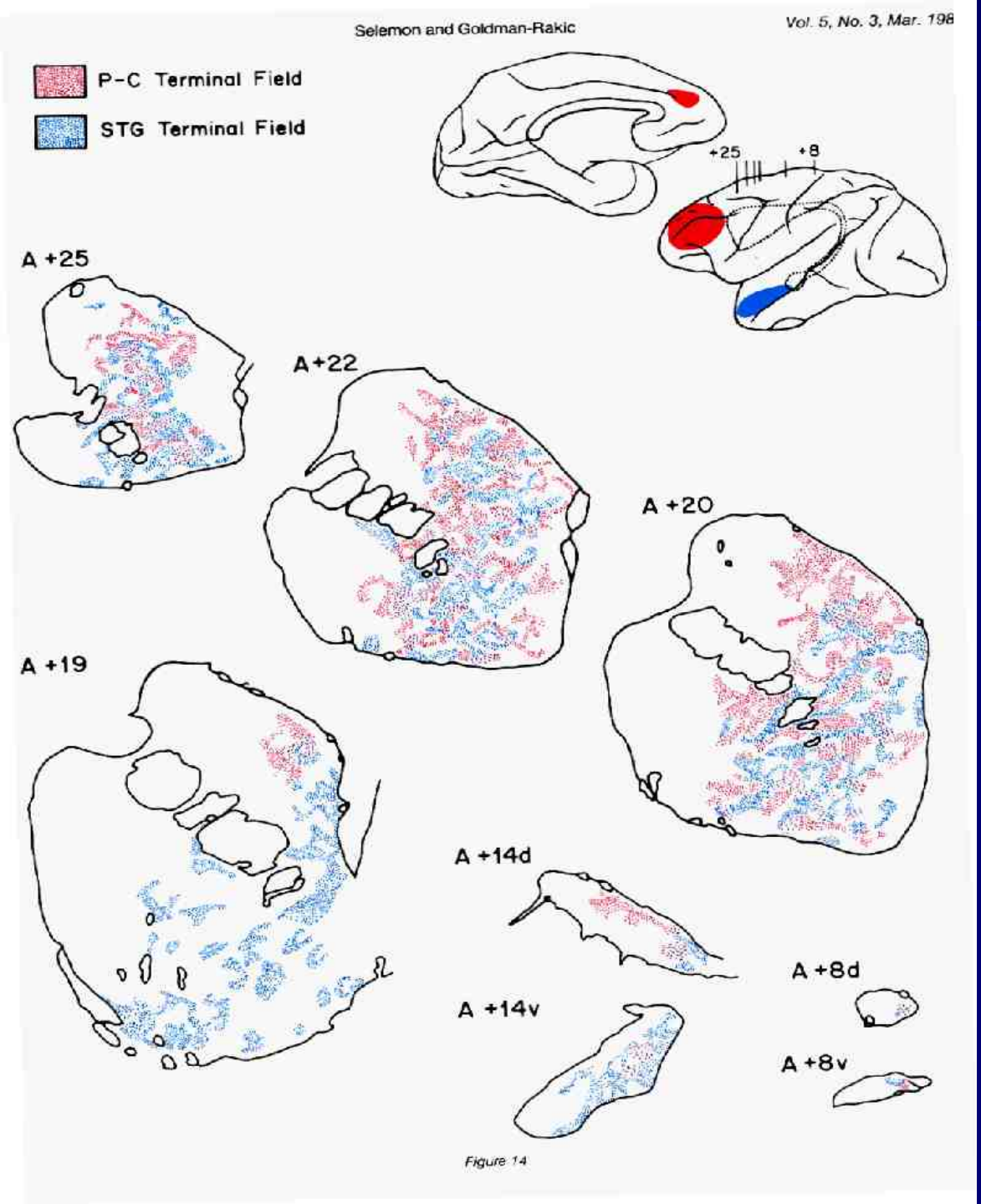
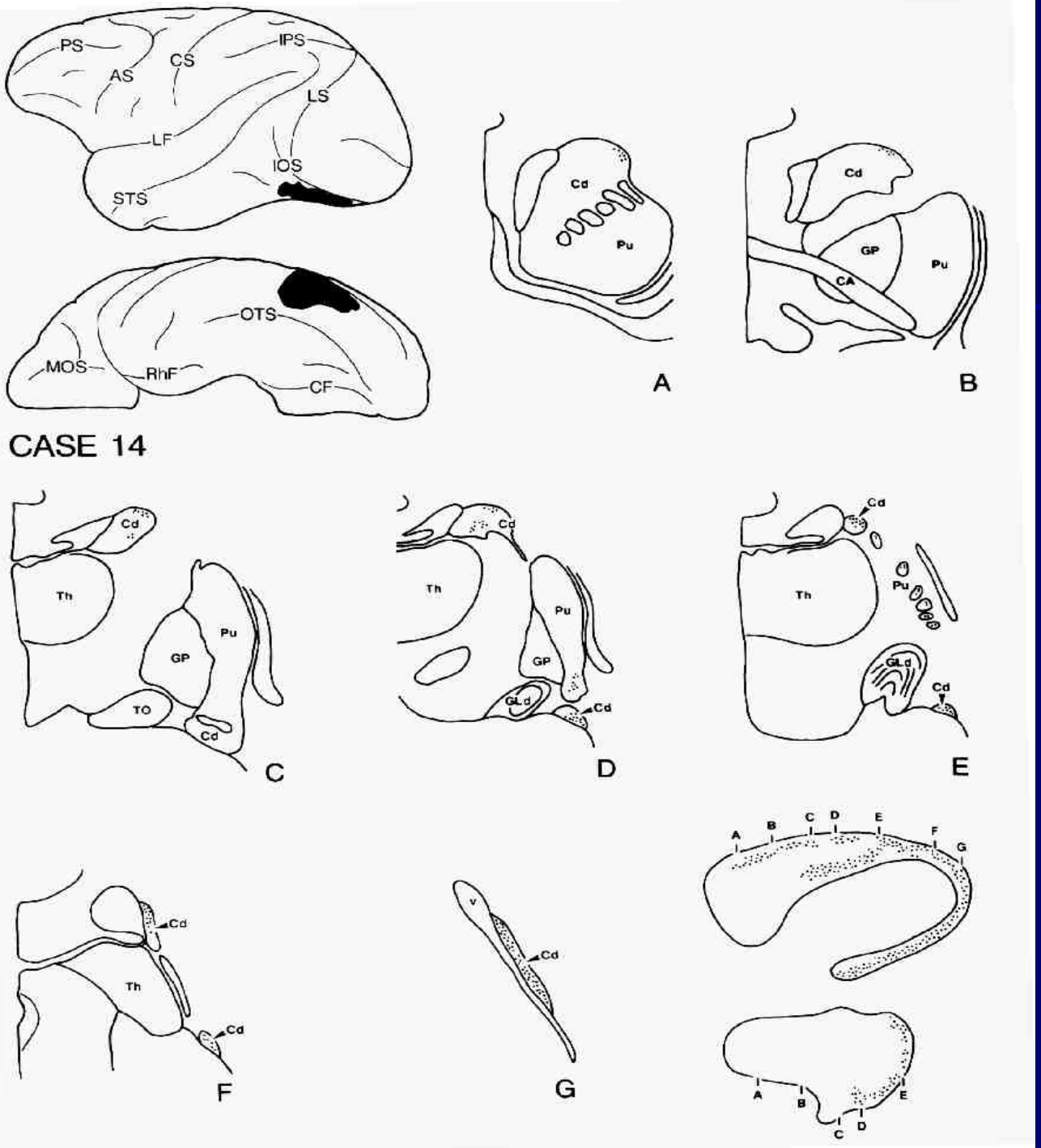


Figure 14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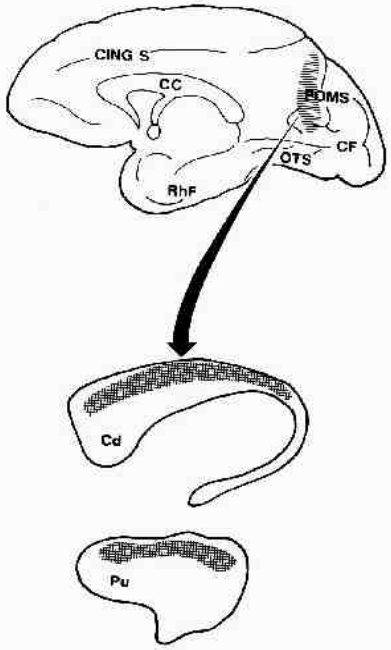
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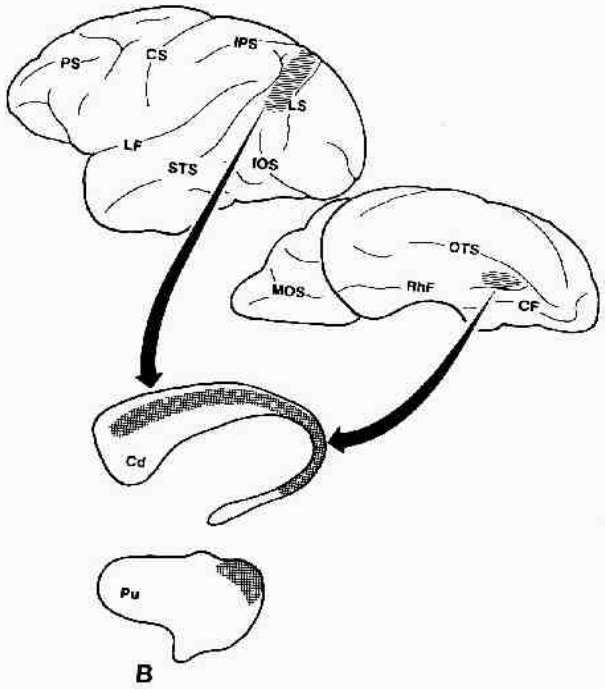
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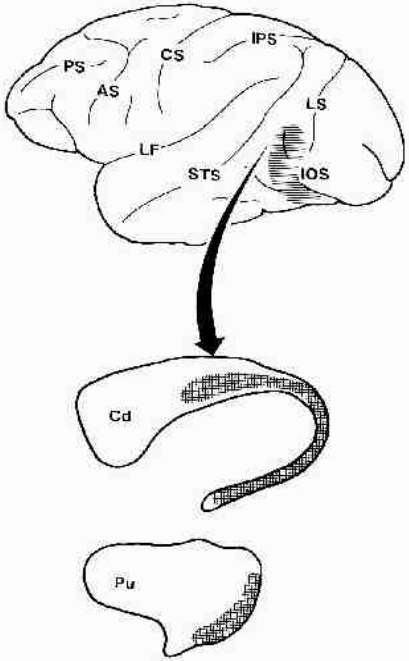
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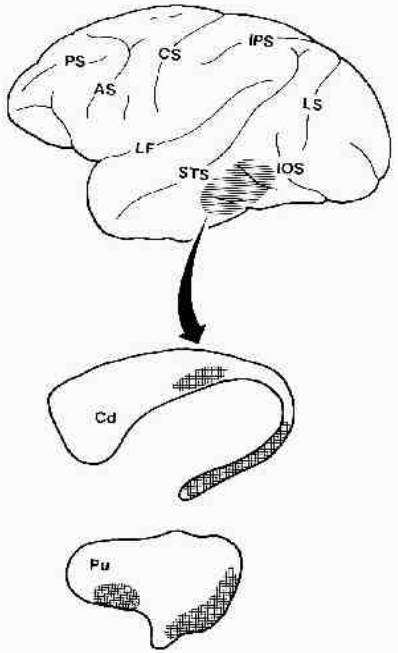
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Amygdalo – striatal projections

Amygdala-

Projects to

the Ventral striatum

(Nc. Accumbens)

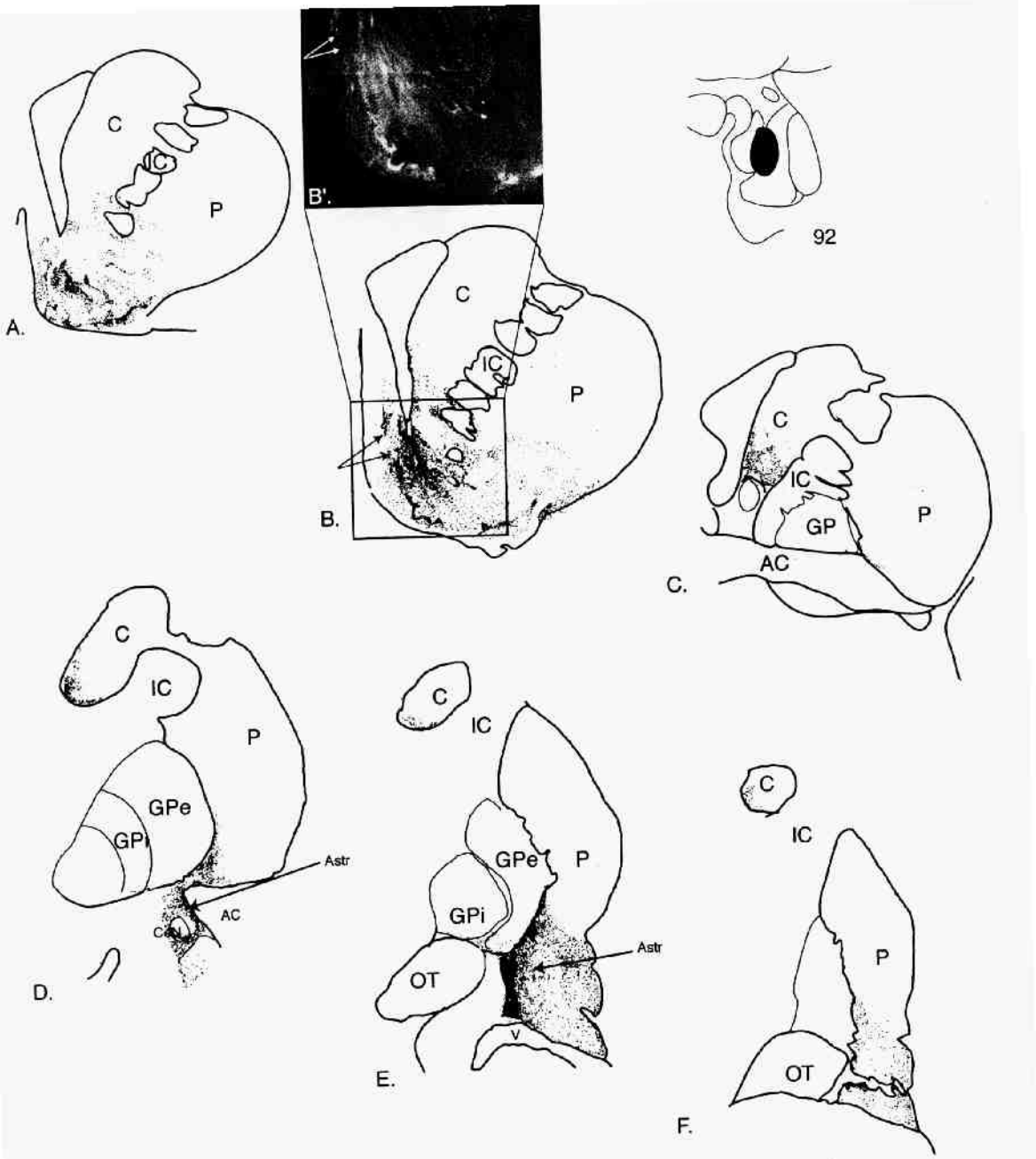


Fig. 7. (A–F) Distribution of anterogradely labeled fibers in the striatum after a tritiated amino acid injection encompassing the Bi, ABmc, and ABpc. Labeled fibers are heterogeneously distributed from the rostral to the caudal striatum. A portion of the dorsomedial shell has a relatively decreased number of labeled fibers compared to the surrounding shell, as depicted in the dark field photomicrograph (B, B', arrows). Dense labeling in (E) represents labeling in fiber tracts.

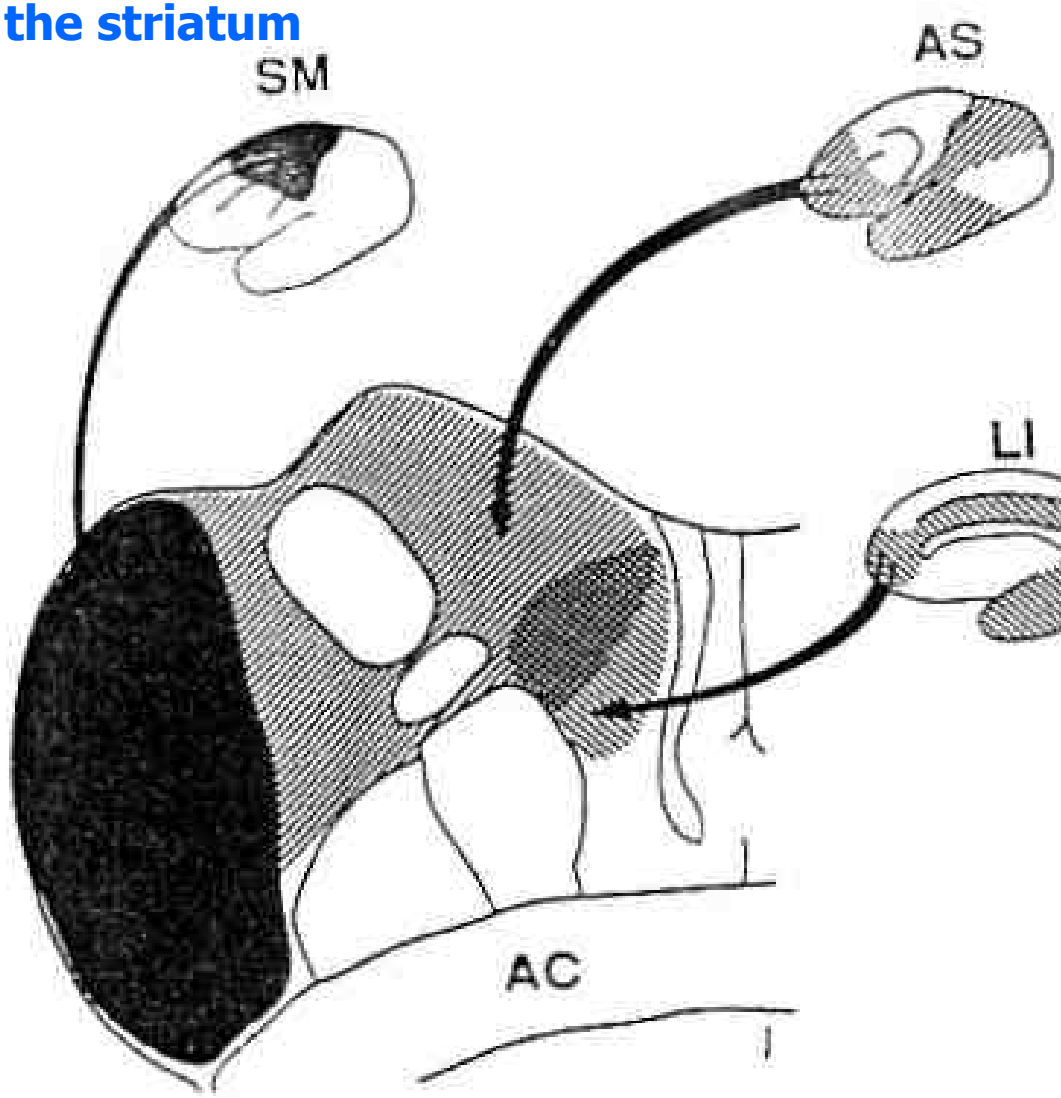
Parahippocampal gyrus and orbitofrontal cortex -

Hippocampal formation –

project to the ventral striatum

Cortico – striatal projections - summary

Functionally different sectors of the striatum



Limbic structures

Distribution of corticostriatal neurons in cortical layers

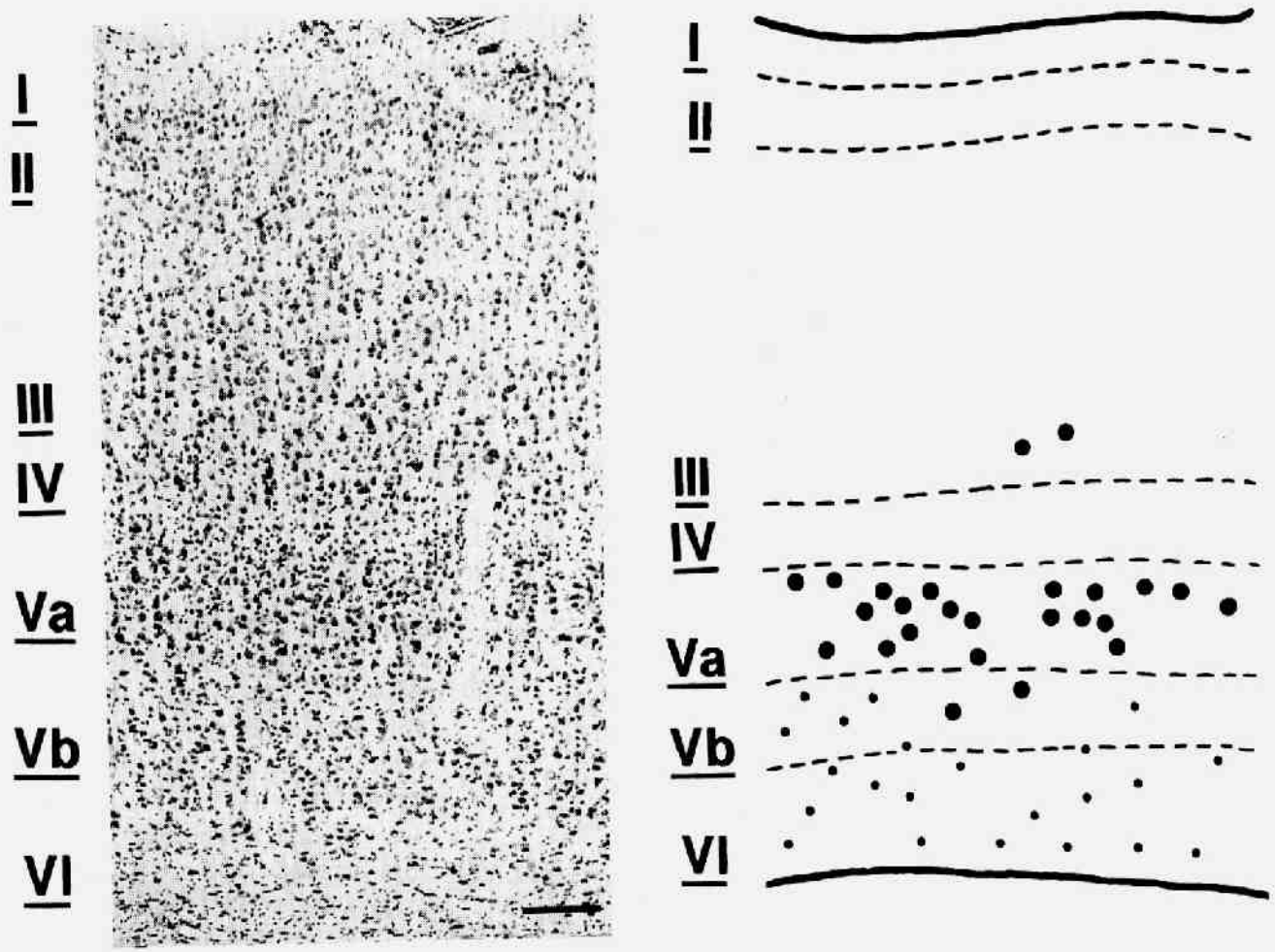


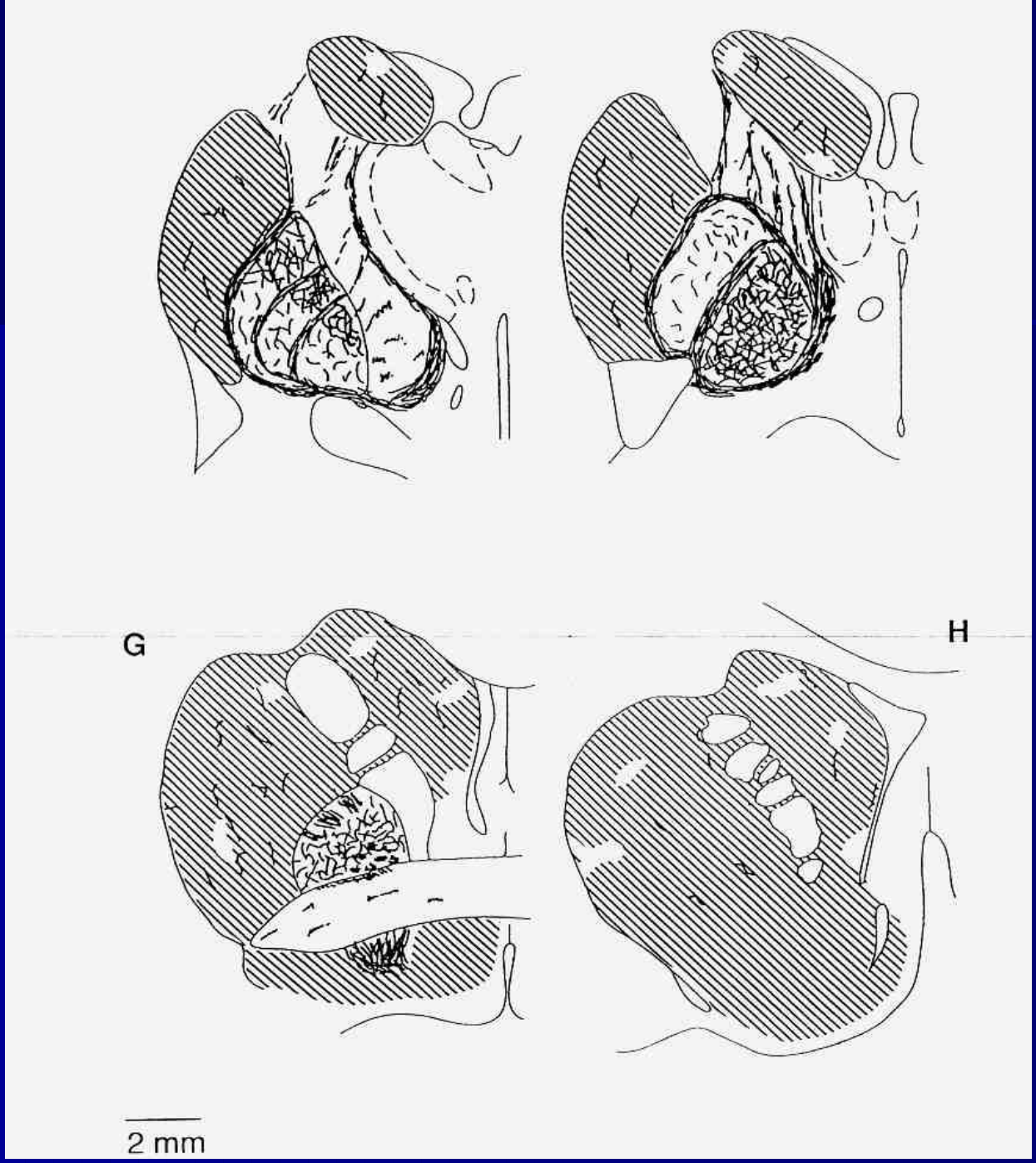
Fig. 7 On the *left* is a photomicrograph of a Nissl-stained section from area 10 in case 2. On the *right* is a diagrammatic representation of the cortical laminae in the same area depicting the distribution of fast blue-labeled (corticostriatal, *large dots*) and diamidinc yellow-labeled (corticothalamic, *small dots*) neurons. *Scale bar* 150 μm

Large dots – striatum

Small dots - thalamus

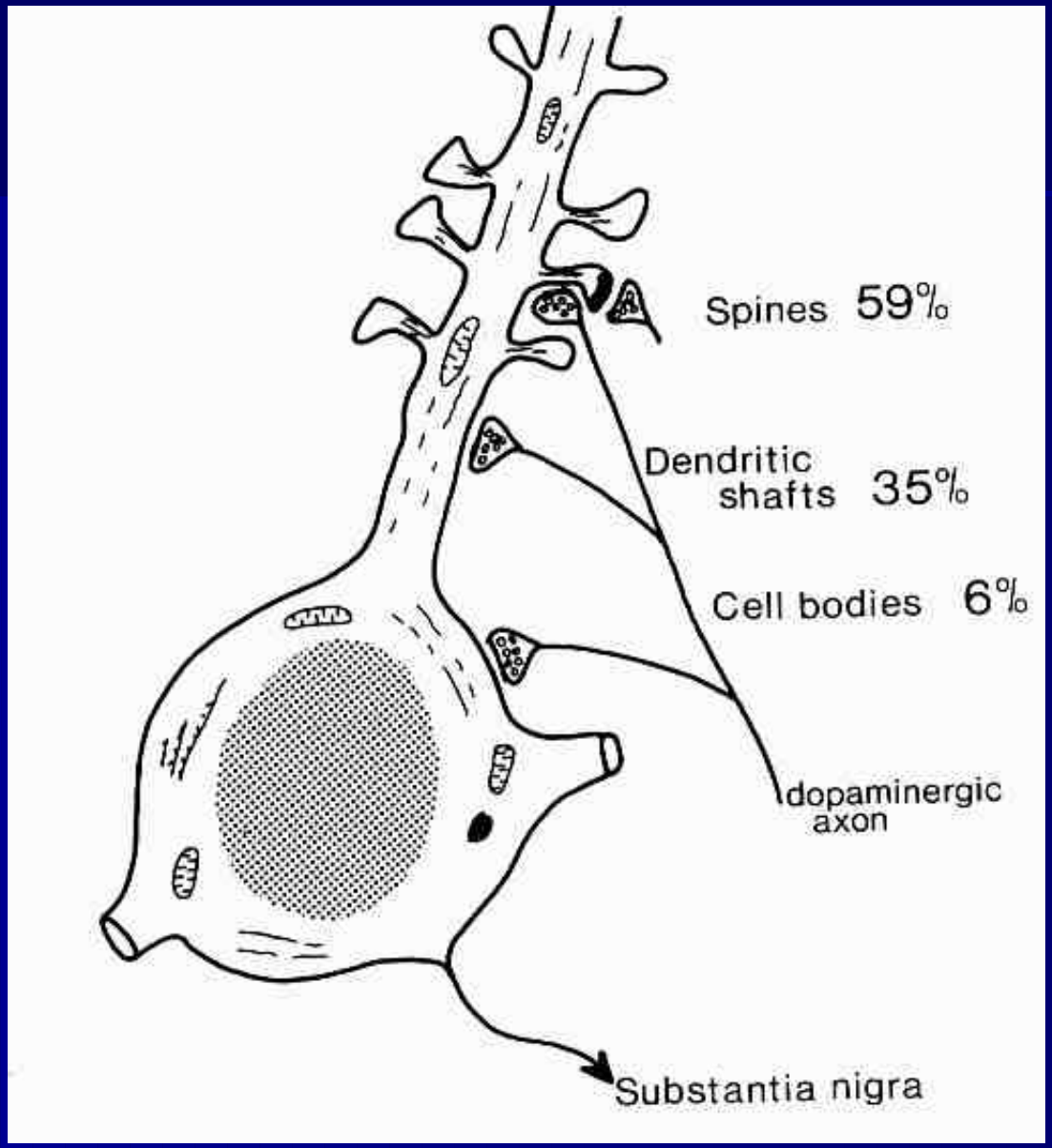
Nigro-striatal projections

Dopaminergic



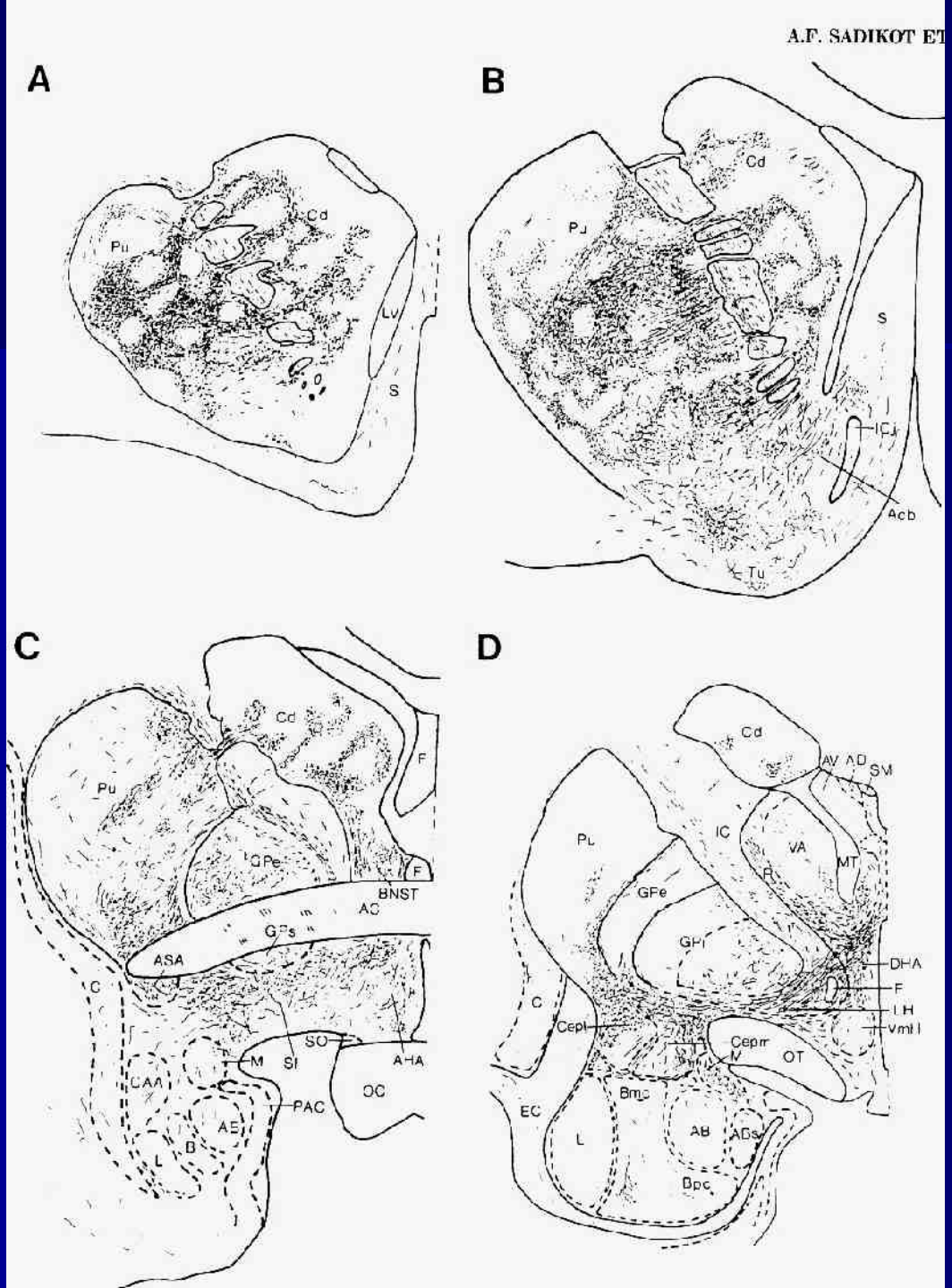
Distribution of dopaminergic terminals (SNc) on MSNeurons

Dopamin – usnadňuje přenos na kortiko-striatických synapsích



Raphe nuclei –

Striatum /pallidum



SEROTONIN

THALAMOSTRIATAL PROJECTION

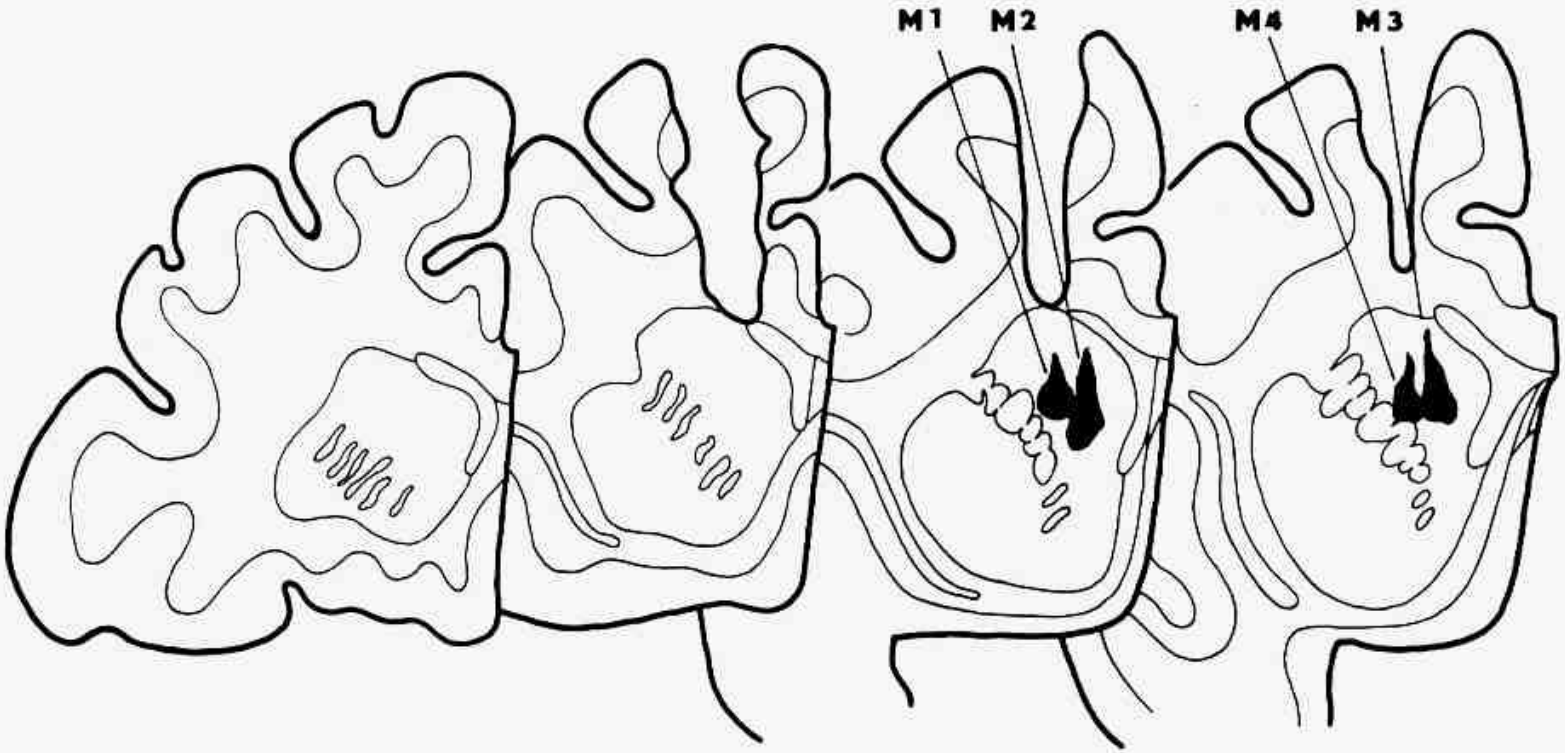


Fig. 1. The locations of injection sites in the caudate nucleus (semi-schematically). Black area designates the dense injection site zones in monkeys M – 1, M – 2, M – 3 and M – 4.

THALAMIC NEURONS PROJECTING TO THE STRIATUM (CAUDATE NUCLEUS)

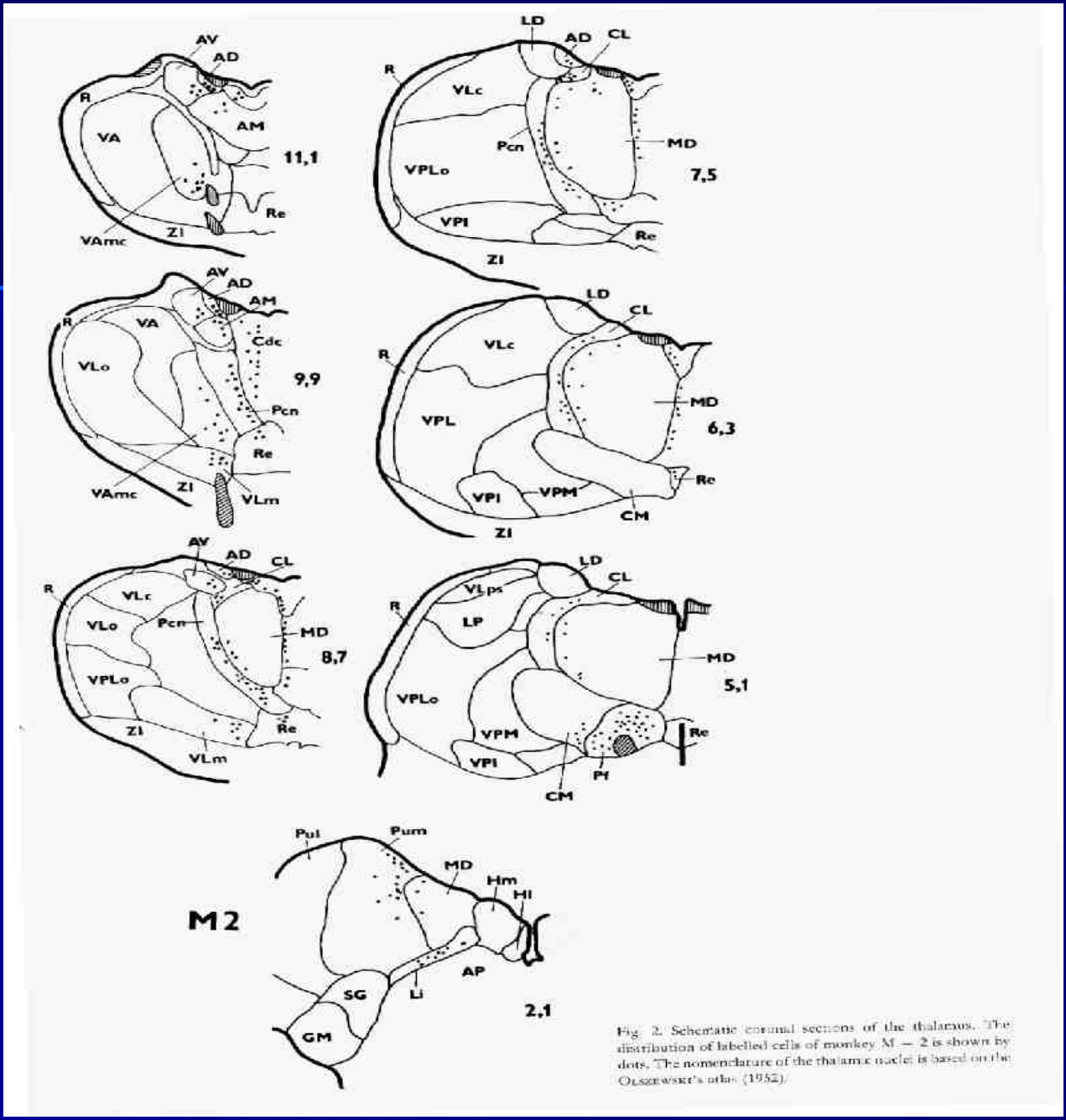


Fig. 2. Schematic coronal sections of the thalamus. The distribution of labelled cells of monkey M — 2 is shown by dots. The nomenclature of the thalamic nuclei is based on the Olszewski's atlas (1952).

VAmc

MD

IL (PF)

Pulvinar

DORSAL STRIATUM - efferent connections

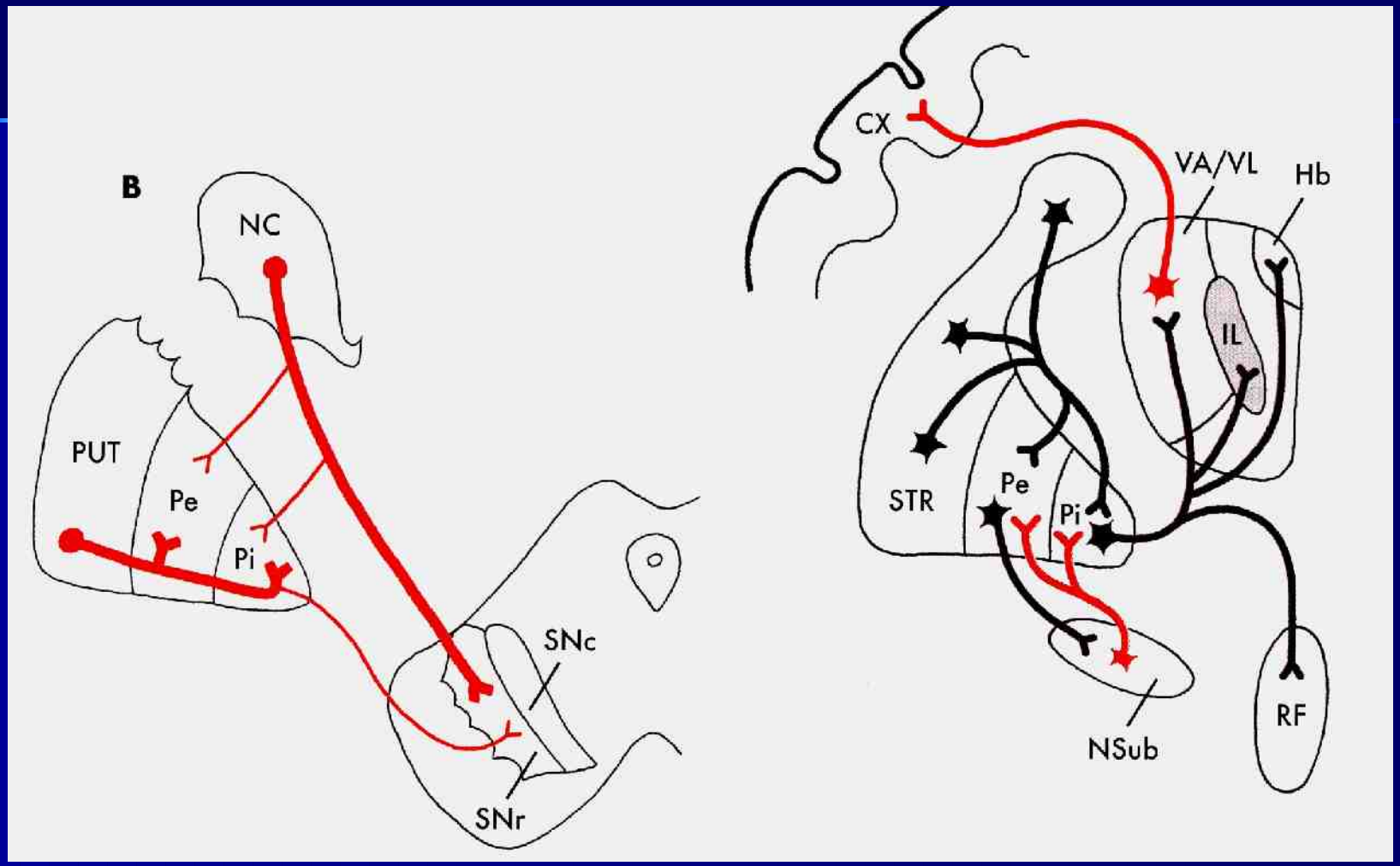
globus pallidus **(GPe,GPi),**

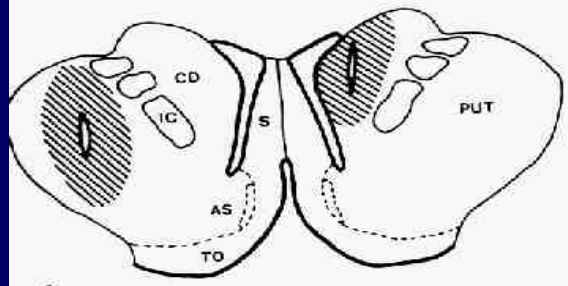
subst. nigra **(p. reticulata)**

Putamen – globus pallidus
Caudate nucleus – subst. nigra (pars reticulata)

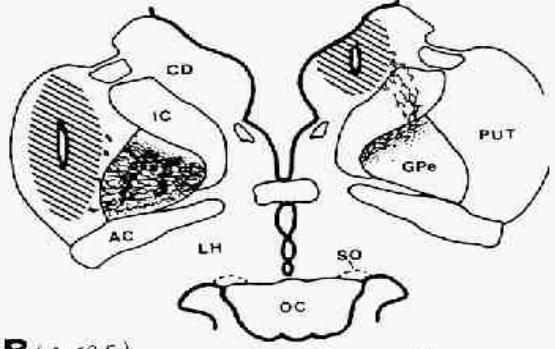
Striatal efferents

Pallidal afferents and efferents

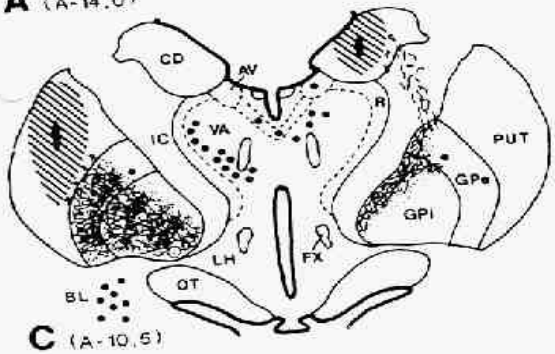




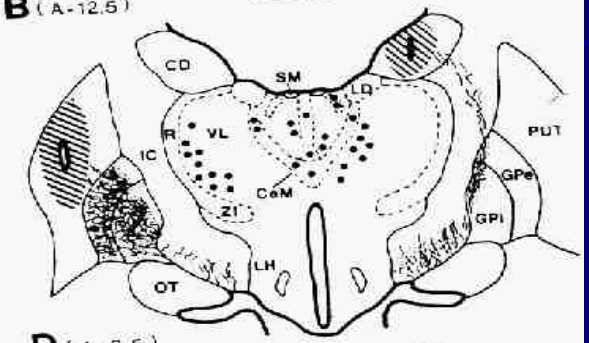
A (A-14.0)



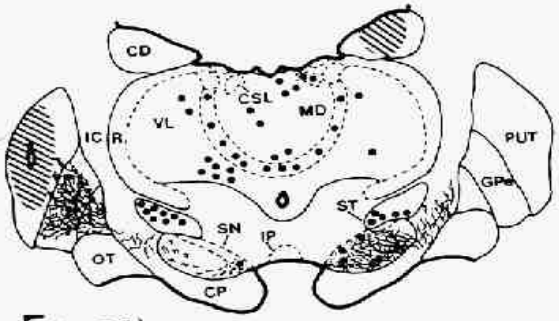
B (A-12.5)



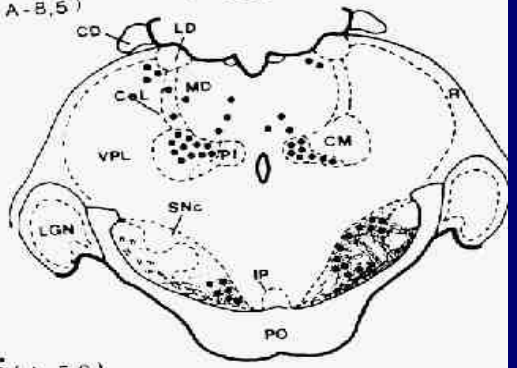
C (A-10.5)



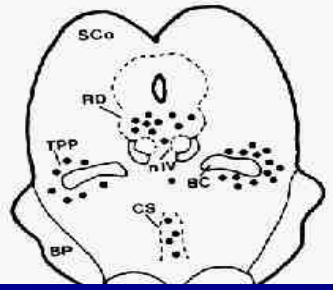
D (A-8.5)

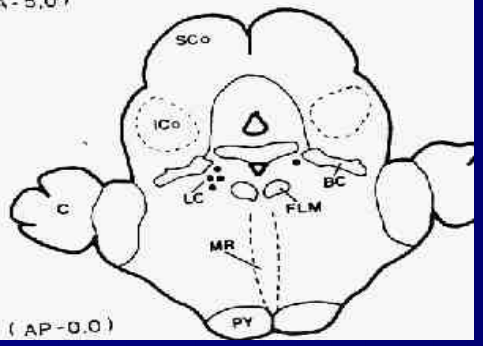


E (A-7.5)



F (A-5.0)





H (AP-0.0)

Striato-nigral projections

Putamen –

s. Nigra

weak proj.

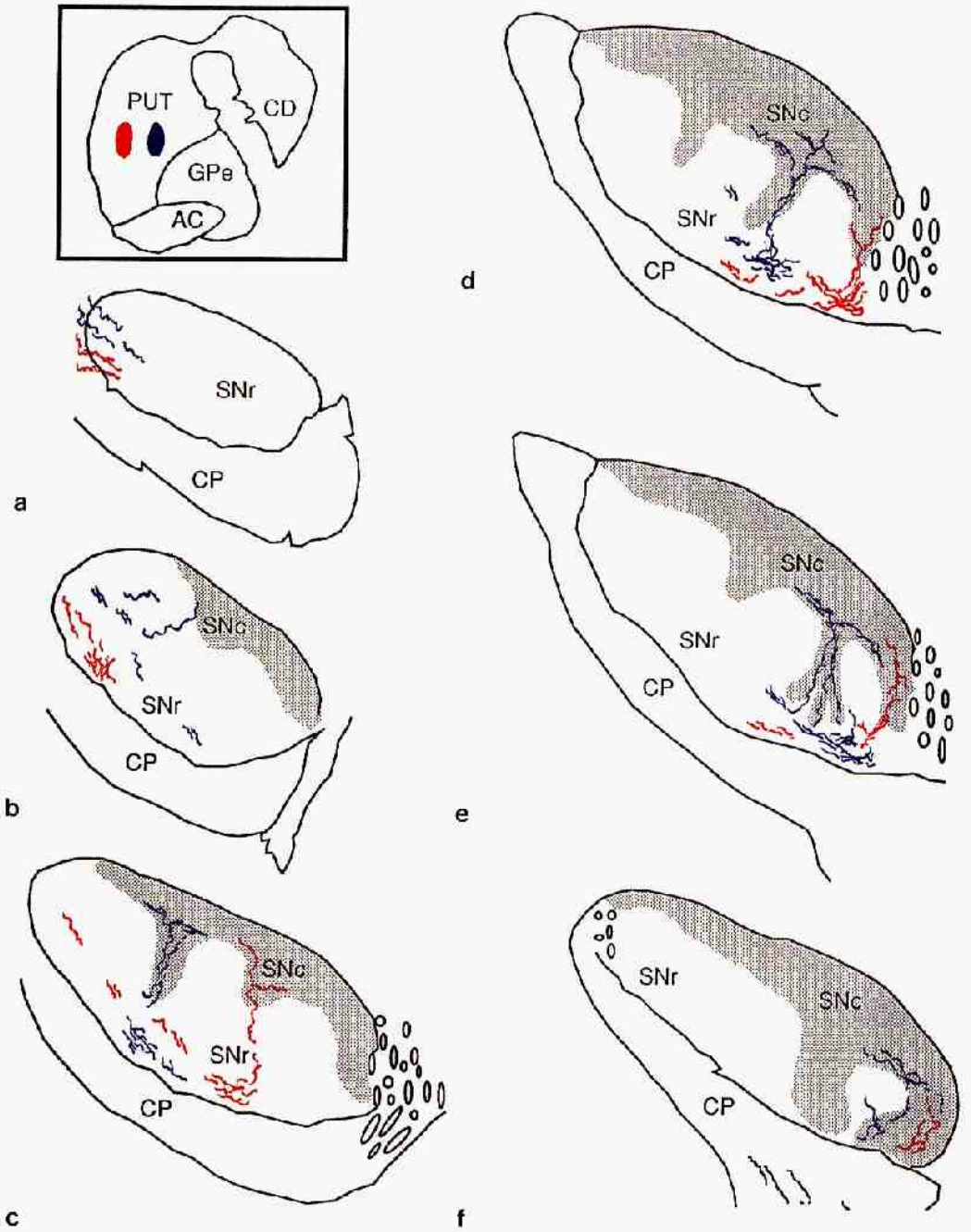


Fig. 5. a–f: Drawings of transverse sections through the substantia nigra showing the distribution of anterogradely labeled fibers (sinuous lines) following PHA-L and biocytin injections in the putamen (inset). See Figure 4 for color code and Figure 1 for abbreviations.

Caudate nc. – subst. Nigra

Strong projection

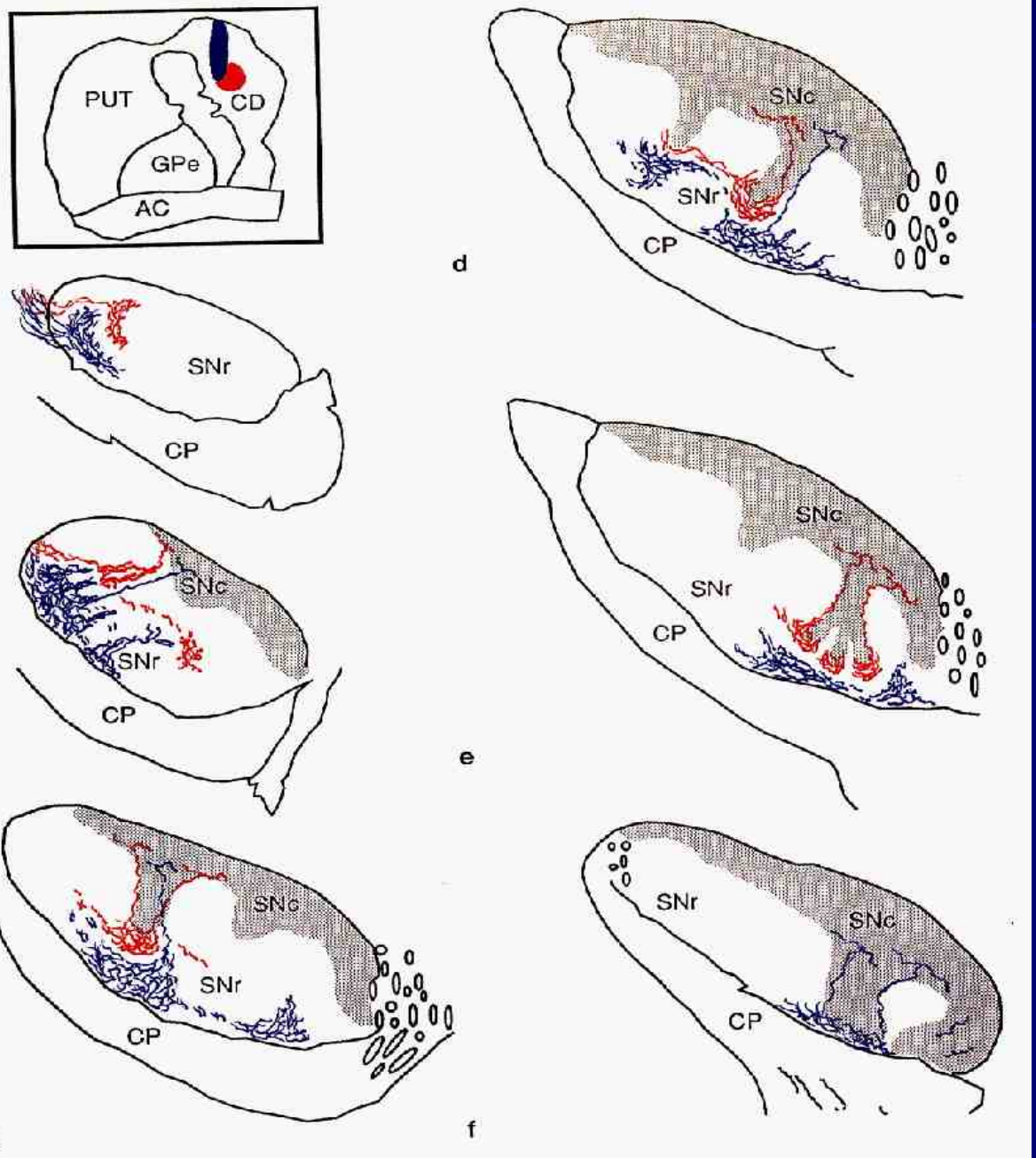


Fig. 4. **a–f:** Drawings of transverse sections through the substantia nigra showing the distribution of anterogradely labeled fibers (sinuous lines) following PHA-L and biocytin injections in the caudate nucleus. The location and maximal extent of the injection sites are indicated in the inset and the PHA-L- and biocytin-labeled profiles are illustrated in blue and red, respectively. The substantia nigra drawings are displayed in a rostrocaudal order, and the extent of the pars compacta, as determined by tyrosine-hydroxylase immunohistochemistry, is indicated by the shaded areas.

GLOBUS PALLIDUS

afferent connections:

Striatum (Pe, Pi), Nc.subthalamicus (Pe, Pi)

efferent connnections :

Pallidum externum - Nc. Subthalamicus

Pallidum internum -

Thalamus (VA, IL,Hb), Reticular formation

Projections rfrom the subthalamic nucleus to the pallidum

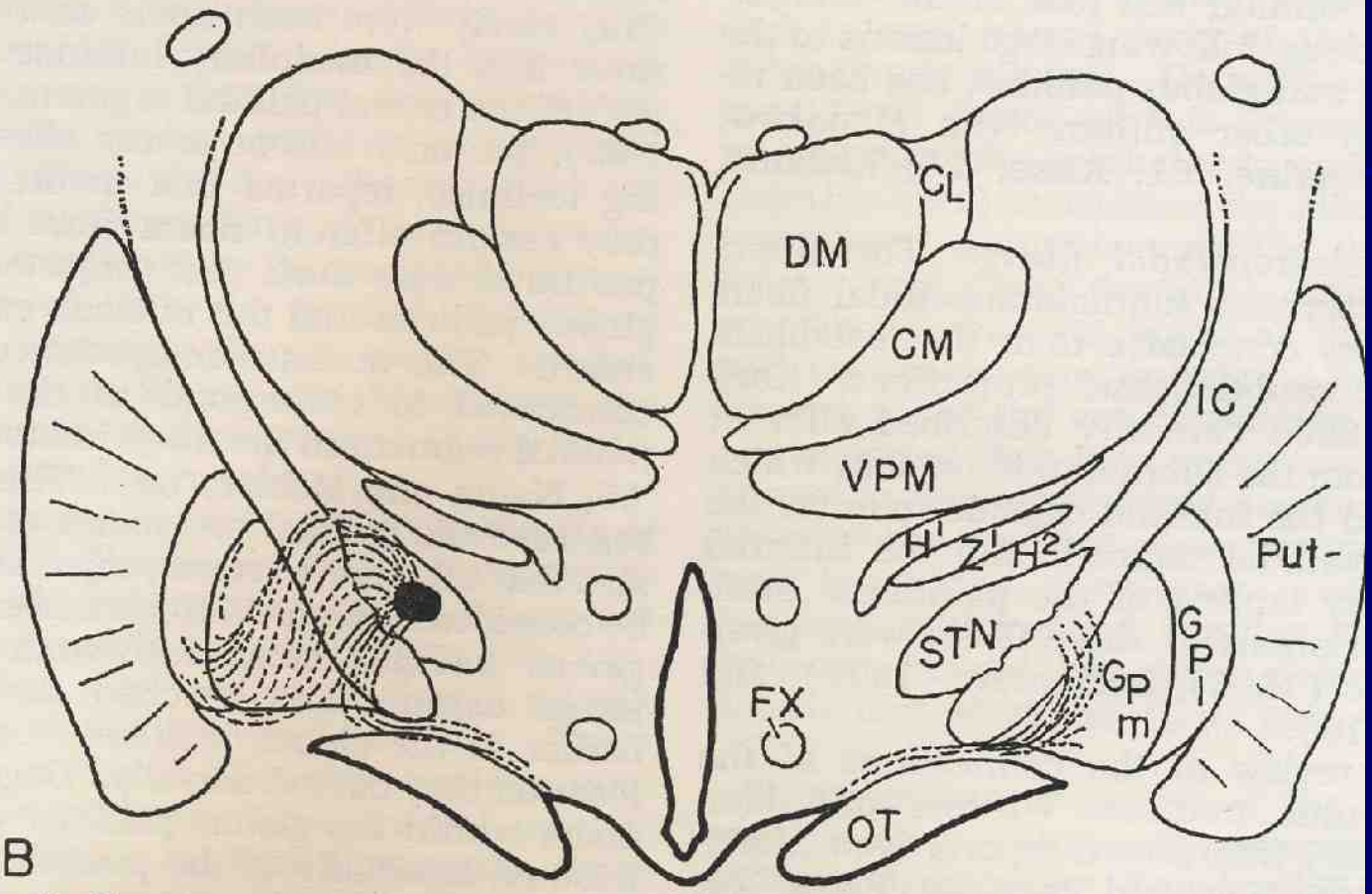
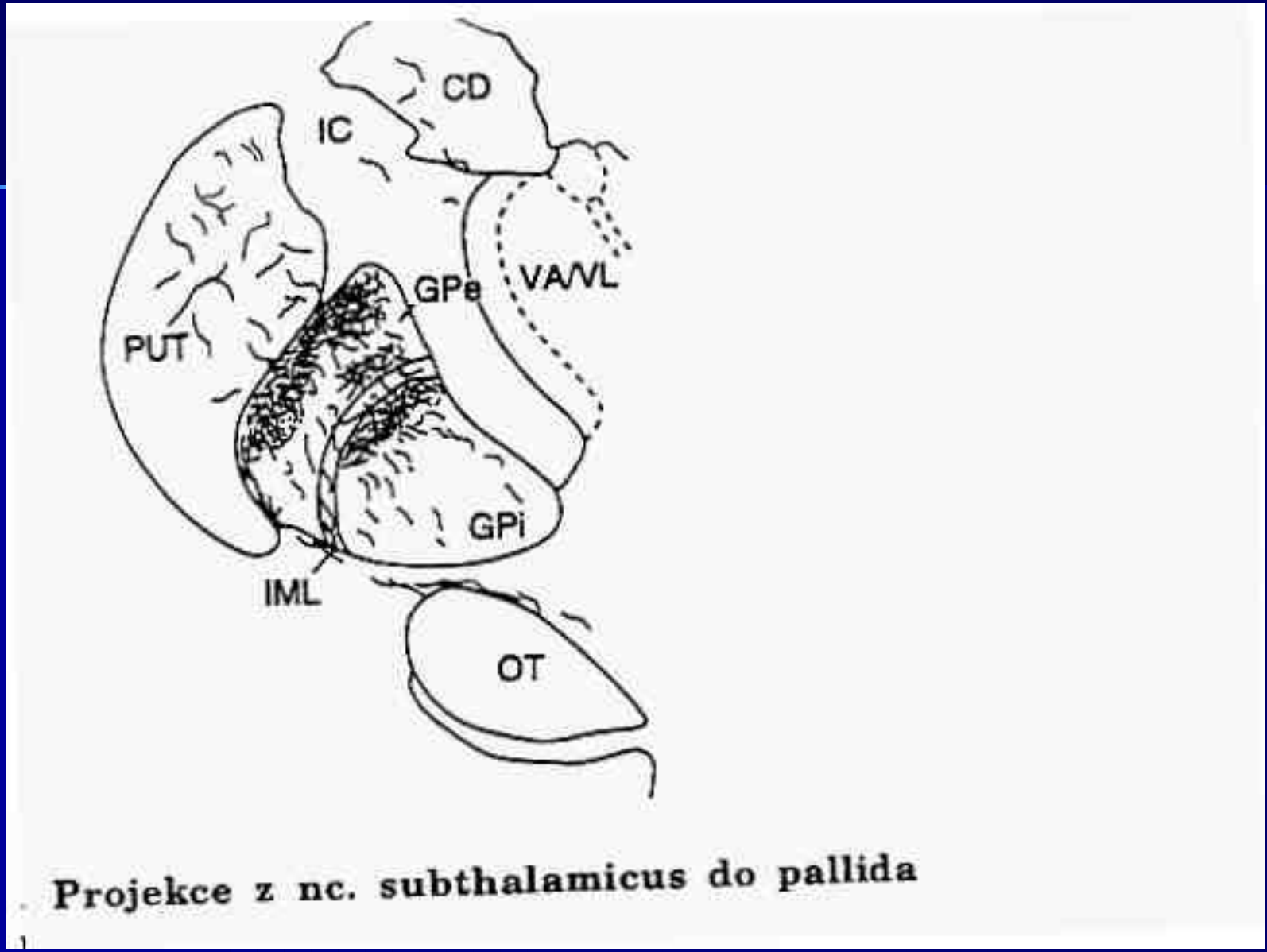


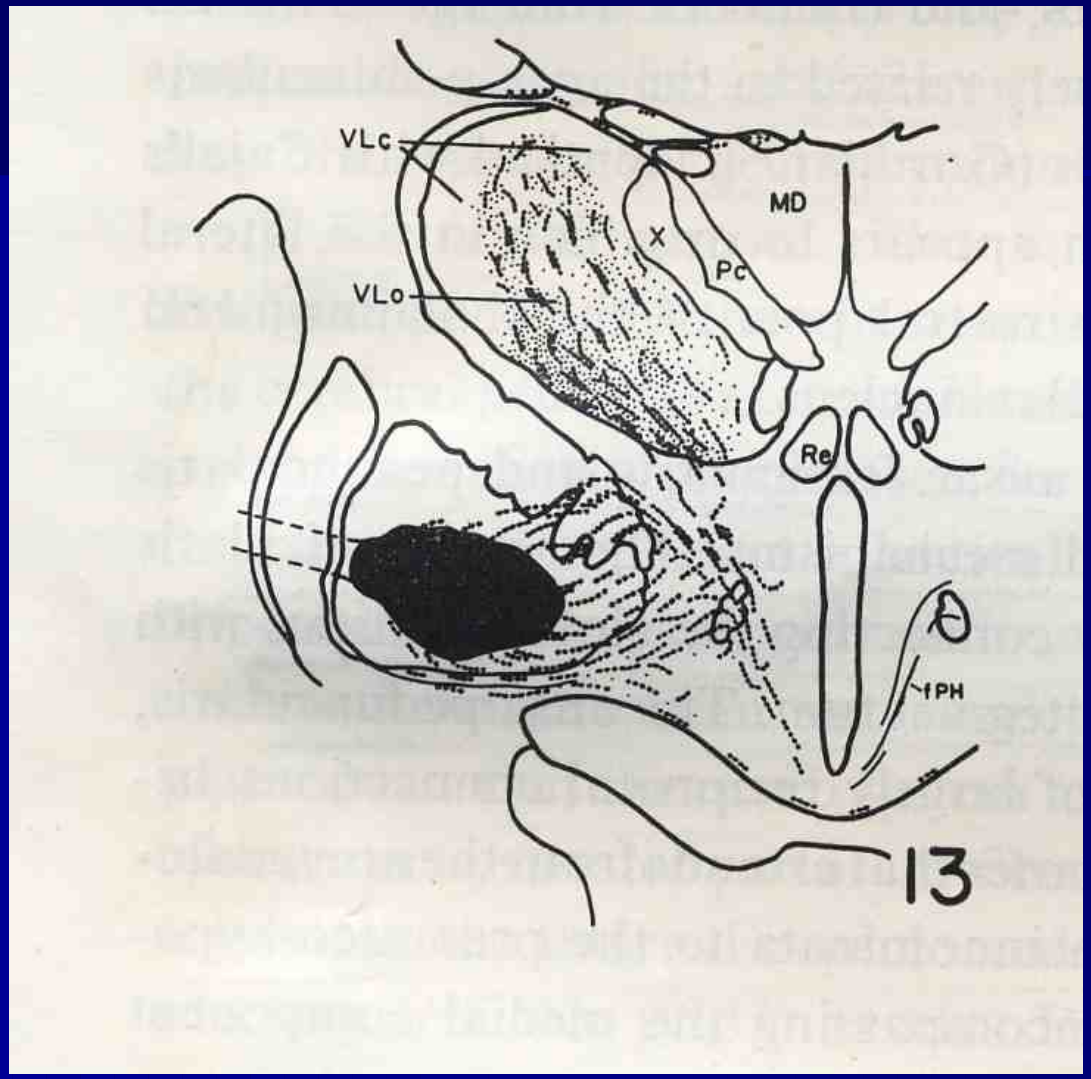
Fig. 2 Drawings of transverse sections of the brain to show the distribution of de eration considered to arise from a lesion in the subthalamic nucleus (B). The princ degeneration traverses the internal capsule to be distributed to the medial pallidal segm (A, B). Some of these fibers enter both the internal and external medullary laminae the pallidum. A small number of subthalamic efferent fibers enter the dorsal suprao decussation, cross to the opposite side, and enter the contralateral globus pallidus (A,

Projections from the Subthalamic nucleus to the globus pallidus (excitatory, glutamatergic)



Projekce z nc. subthalamicus do pallida

Pallidum internum projects to the thalamus ! (W.J.H.Nauta and W.R. Mehler 1966)



Circuit of the basal ganglia

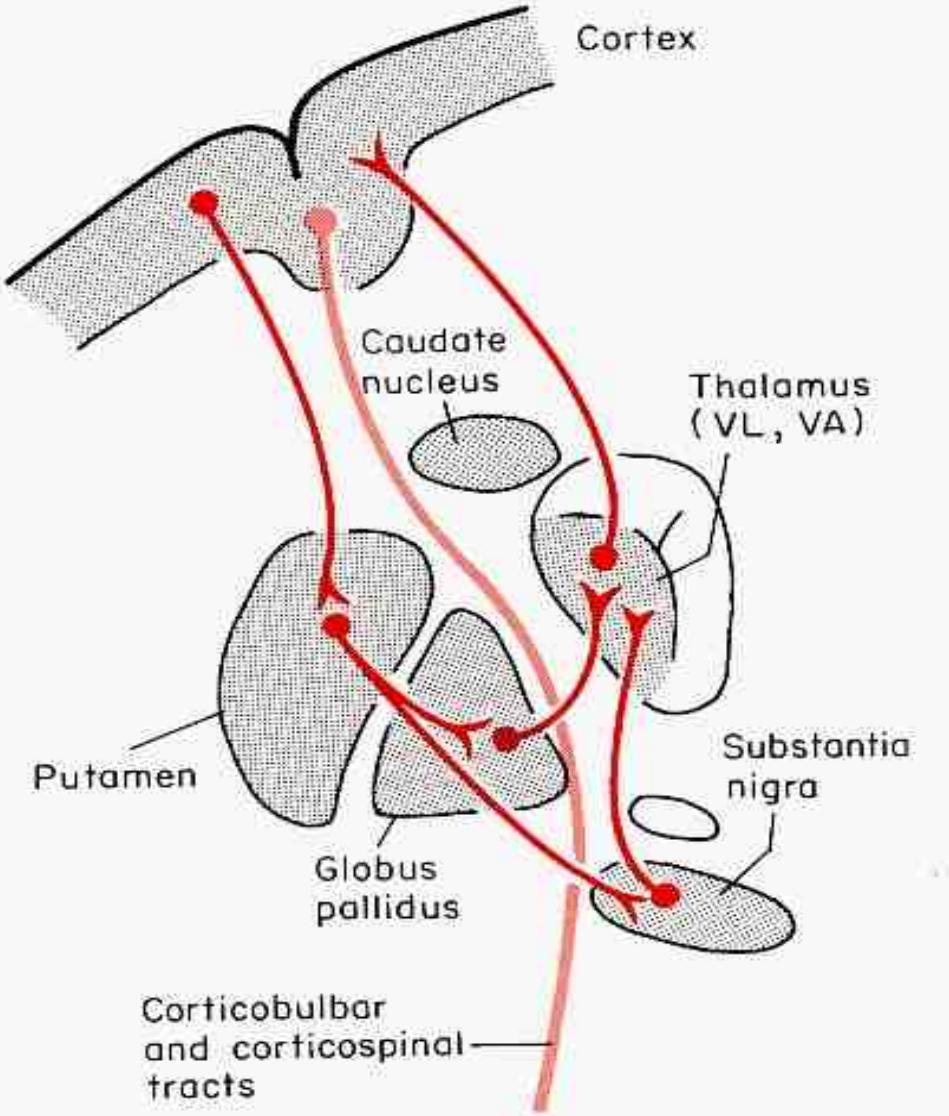


Fig. 10.3. *Main connections of the basal ganglia.* Note the pathway from the cortex, through the basal ganglia, and back to the cortex via the thalamus.

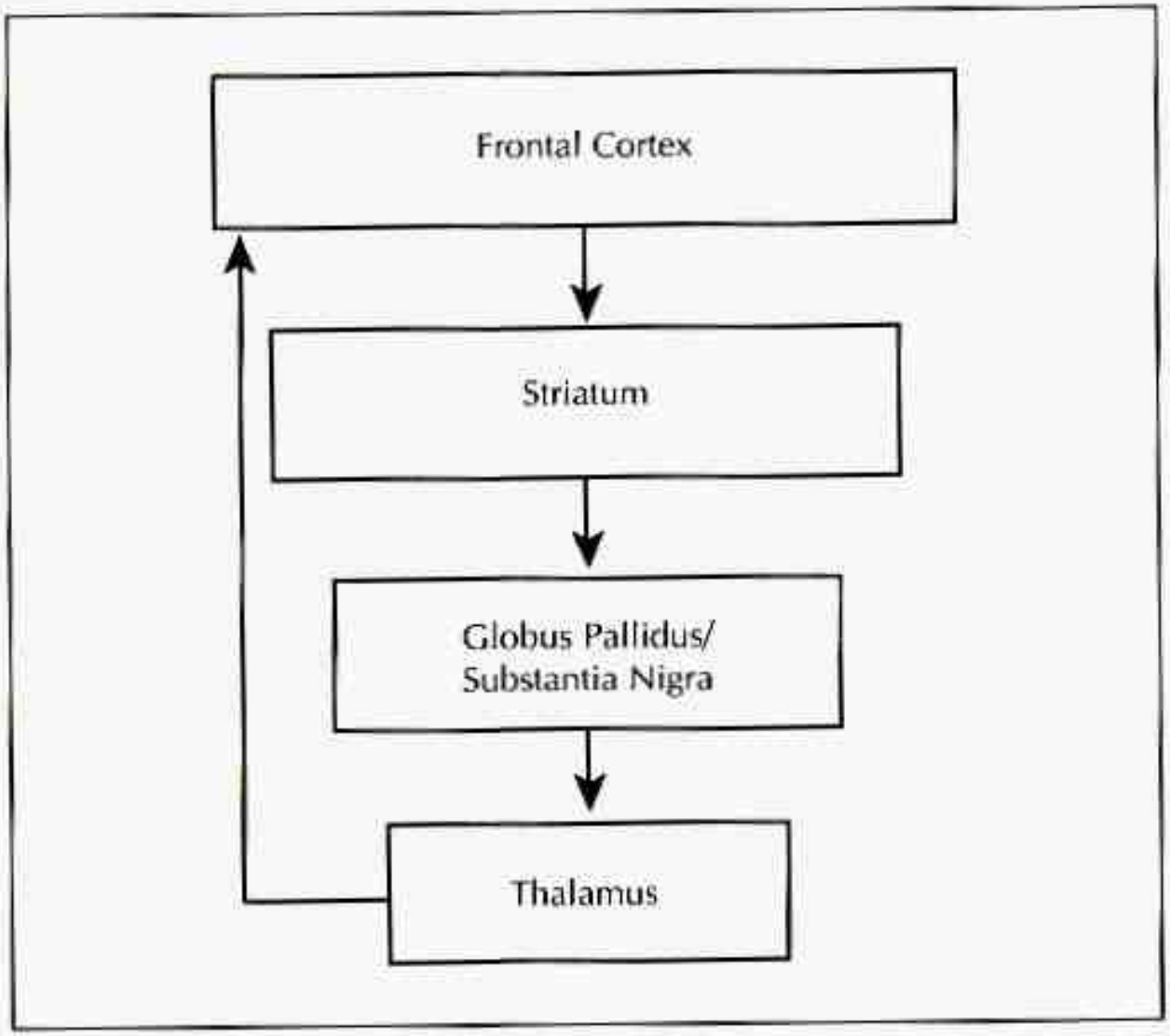
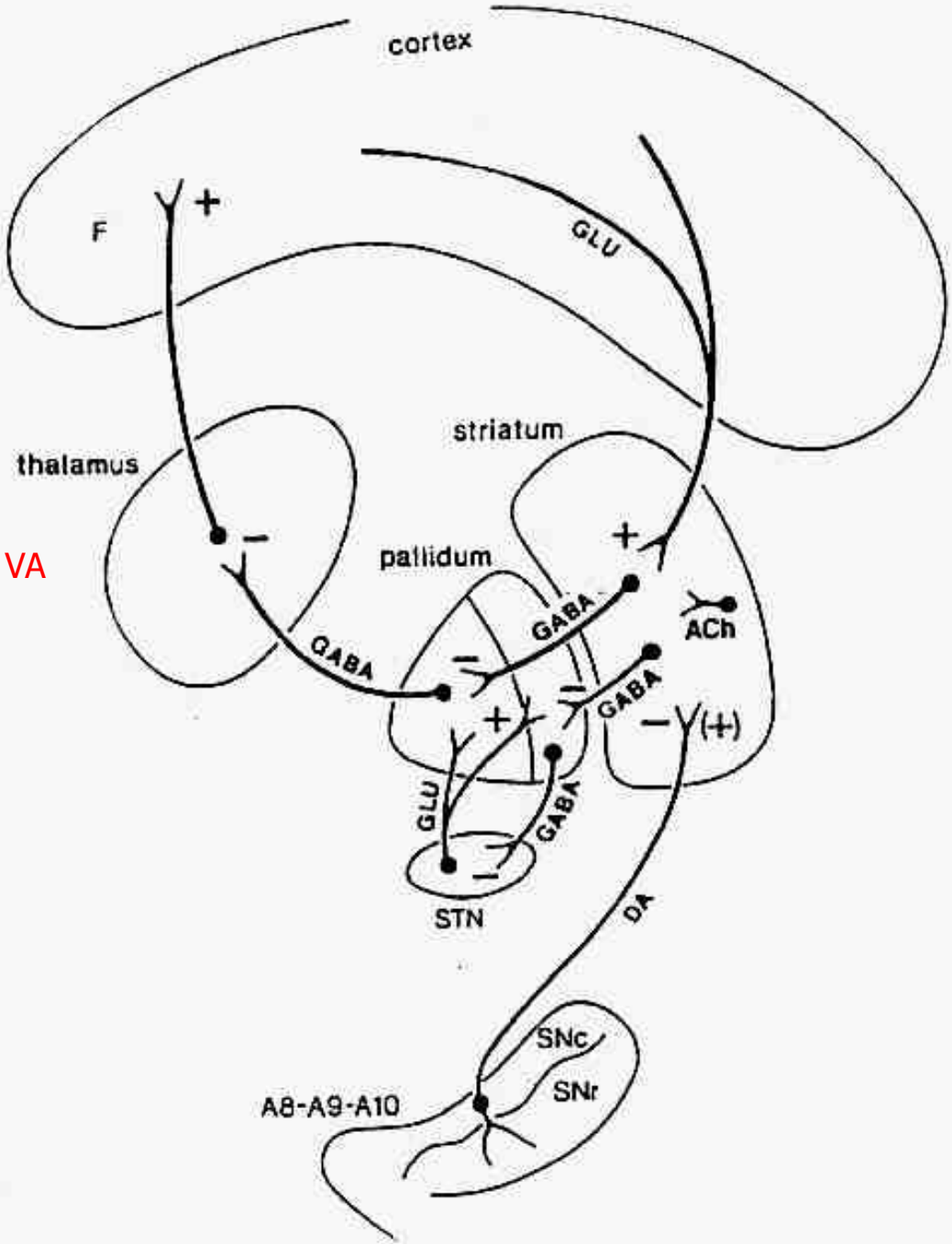


Fig 1.—*General organization of the frontal-subcortical circuits.*

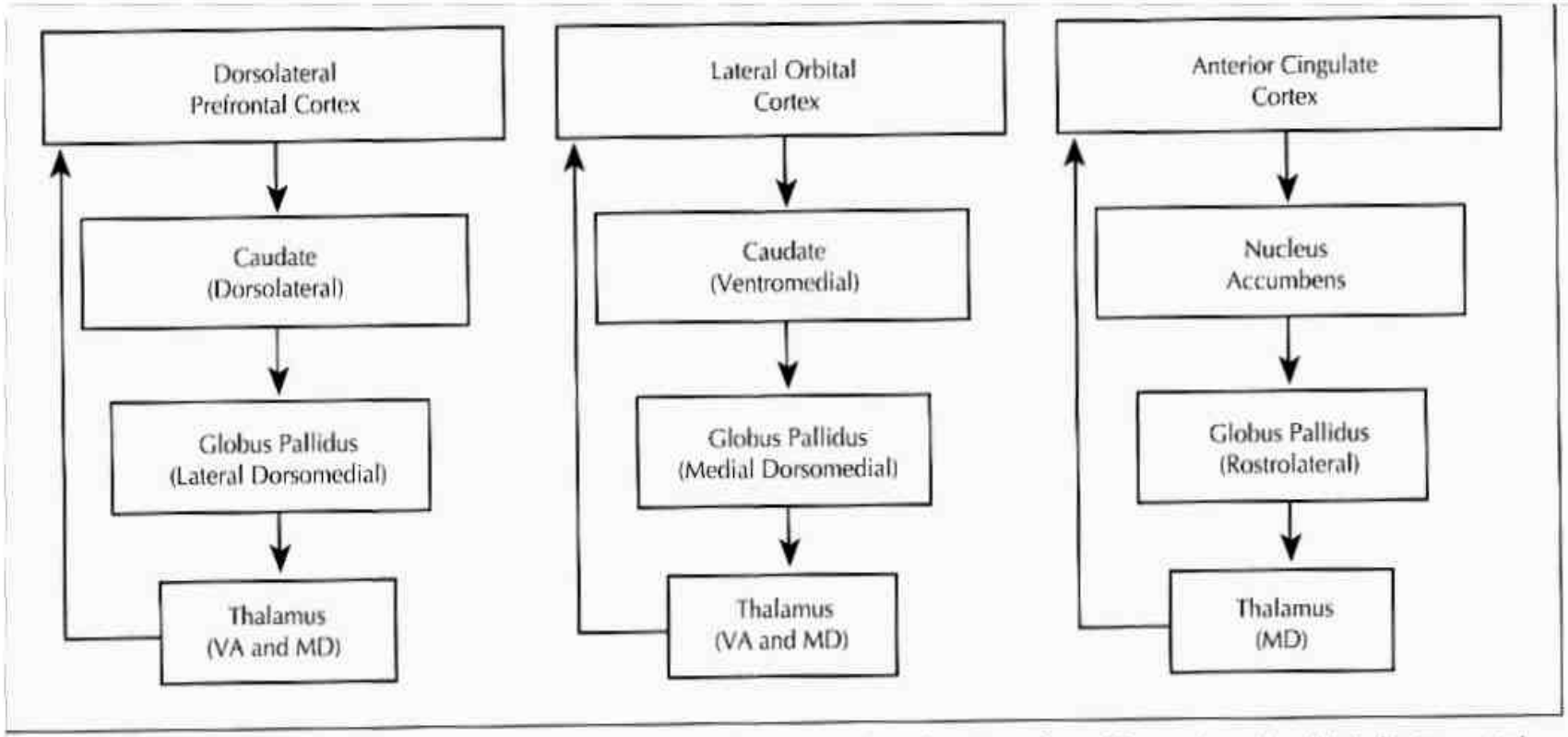
CIRCUIT OF THE BASAL GANGLIA (Nauta – Mehler 1966)

CORTEX-STRIATUM – PALLIDUM – THALAMUS (VA) - CORTEX



Prefrontal circuits

Limbic circuit



ig 2.—Organization of the three frontal-subcortical circuits in which lesions produce alterations of cognition and emotion. VA indicates ventral an-erior; MD, medial dorsal. The indirect circuits and connections of the substantia nigra and the subthalamic nucleus are not shown.

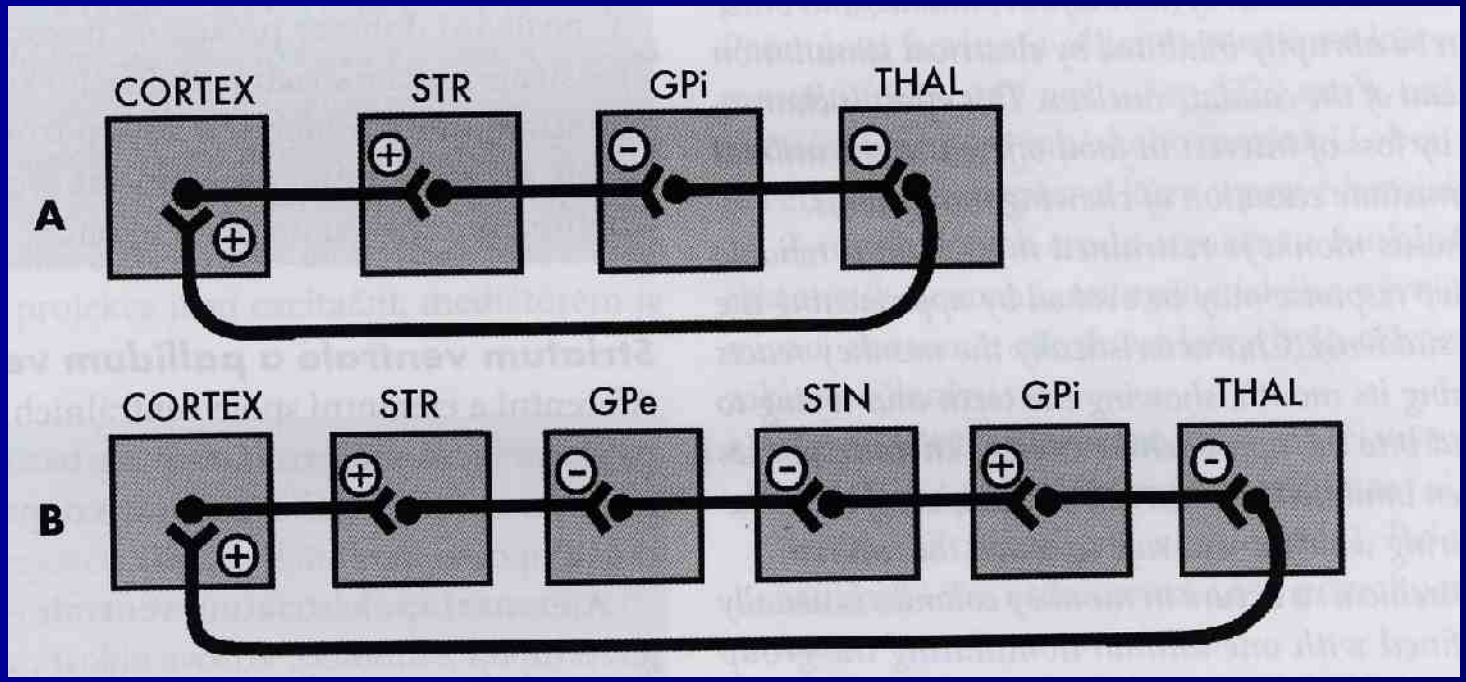
CIRCUIT OF BASAL GANGLIA (Nauta –Mehler circuit, 1966)

OKRUH BAZÁLNÍCH GANGLIÍ

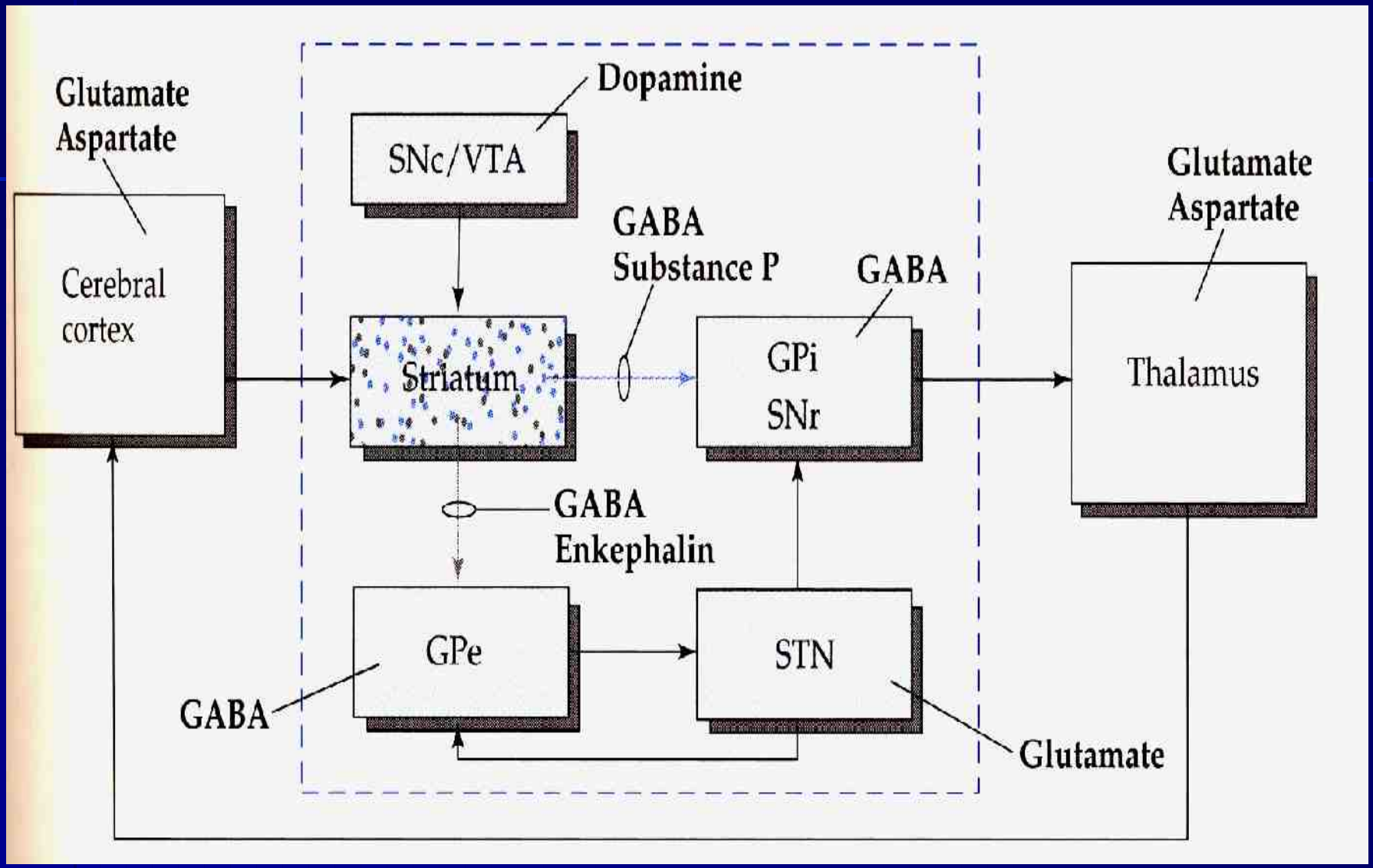
Neocortex – striatum – globus pallidus – thalamus (VA) – neocortex – cortical projections to the brain stem and to the spinal cord

A = direct pathway – stimulates motor activities (P-substance, dynorphin)

B = indirect pathway – depression of motor activity (Enkefalin)



Circuit of basal ganglia - Direct and indirect pathway



Direct and indirect pathways of basal ganglia

- **Direct pathway :**
- cortex …(+) striatum … (-) pallidum internum/subst. nigra … (-) thalamus … (+) cortex (increases the activity of the thalamus and the excitation of cerebral cortex = increased motor activity)

- **Indirect pathway :**
- cortex … (+) striatum … (-) pallidum externum … (-) subthalamic nc. … (+) pallidum internum … (-) thalamus … (+) cortex (decreases activity of the thalamus and the excitation of cerebral cortex = decreased motor activity)

Circuits of the ventral striatum (nc. accumbens) and ventral pallidum

- Ventral striatum
  - **Afferent connections**
  - **Limbic cortex**
  - **VTA (medial part of the SNc - dopamine)**
  - **Efferent connections**
  - **Ventral pallidum**
  - **Substantia nigra**
- Ventral pallidum
  - **Afferent connections**
  - Ventral striatum
  - **Efferent connections**
  - **Thalamus (MD)**

Syndroms of the basal ganglia I.

- Hypokinesia
- Akinesia – impairment in the iniciation of movement
- Bradykinesia – reduction in velocity and amplitude
- Parkinson disease (tremor at rest, flexed posture, paucity of limb and facial movements)
- Decrease in production of Dopamine
- Loss of dopaminergic neurons within **substantia nigra** (pars compacta).
- L-Dopa will cross BBB (after amination in brain is converted to Dopamin

Syndroms of the basal ganglia II.

- Hyperkinesia
- **Choreiform movements** – irregular dancelike movements of the limbs and in facial muscles – loss of striatal medium spiny neurons, decrease in the size of the striatum, gliosis – **Huntington disease (major affective psychiatric disorders, partly hereditary)**

- **Hemiballism – uncontrolled (dangerous) flingting movements of limbs – vascular lesion in the subthalamic nucleus**

Different role for striatal dopamine

- **Low levels of dopamine** = strong inhibitory output of the BG to the thalamocortical system (paucity of movements, cognitive, emotional behavior, Parkinson disease)

- **High levels of dopamine** = low activity of the inhibitory output of the BG to the thalamocortical system (a facilitation of movements and cognitive/ behavioral acts

- **Dopaminergic neurons (SNc**) show phasic activations following the encounter the animal with novel stimuli particularly with presentation of primary reward. Such activation leads to a spatially release of dopamine

- Dopamine release enable or facilitate the output of a particular population of striatal neurons (to the GP and SNr)

Function of the striatum – inhibition ?

The normal interest of monkeys in bananas and other food can be abruptly inhibited by electrical stimulation of the head of the caudate nucleus. This effect is characterized by loss of interest in food offered to the animal and immediate cessation of chewing movements.

In rhesus monkeys restrained in a chair, a reliable aggressive response may be evoked by approaching the animal suddenly. Characteristically the monkey reacts by opening its mouth, showing the teeth and trying to grab and bite the approaching object. These responses have been inhibited by electrical stimulation of the striatum, during which it was safe to touch the animal.

Hierarchical structure in monkey colonies is usually well defined with one animal dominating the group and the ranking order of the others determined by their social relations. In one of our experiments programmmed stimulation of the caudate nucleus in the boss monkey initially produced only slight relaxation of his body. After 6 – 8 minutes, the other animals began to circulate more freely in proximity to the boss and crowding fearlessly around him. During caudate stimulation, the boss showed no territoriality or aggressive behavior and his top ranking position was lost. About 12 minutes after the end of stimulation, however, the boss resumed his aggressive behavior, recovering both territoriality and colony rank.

José M.R. Delgado : Inhibitory functions in the neostriatum. 1979.

- Stimulace a poškození globus pallidus

LESIONS AND STIMULATIONS OF THE STRIATUM (an inhibitory structure)

- LESIONS – hyperactivity
- drive to run forward, regardless of obstacles (without to avoid the obstacle)
- stereotyped approaching and following of persons, objects
- Tremor
- Choreic - like movements

- STIMULATIONS –
- hypoactivity
- Arrest of voluntary movements and speech
- Short confussion and amnesia
- Sleep – like effect
- Rejecting of food
- Inhibition of agressive behavior

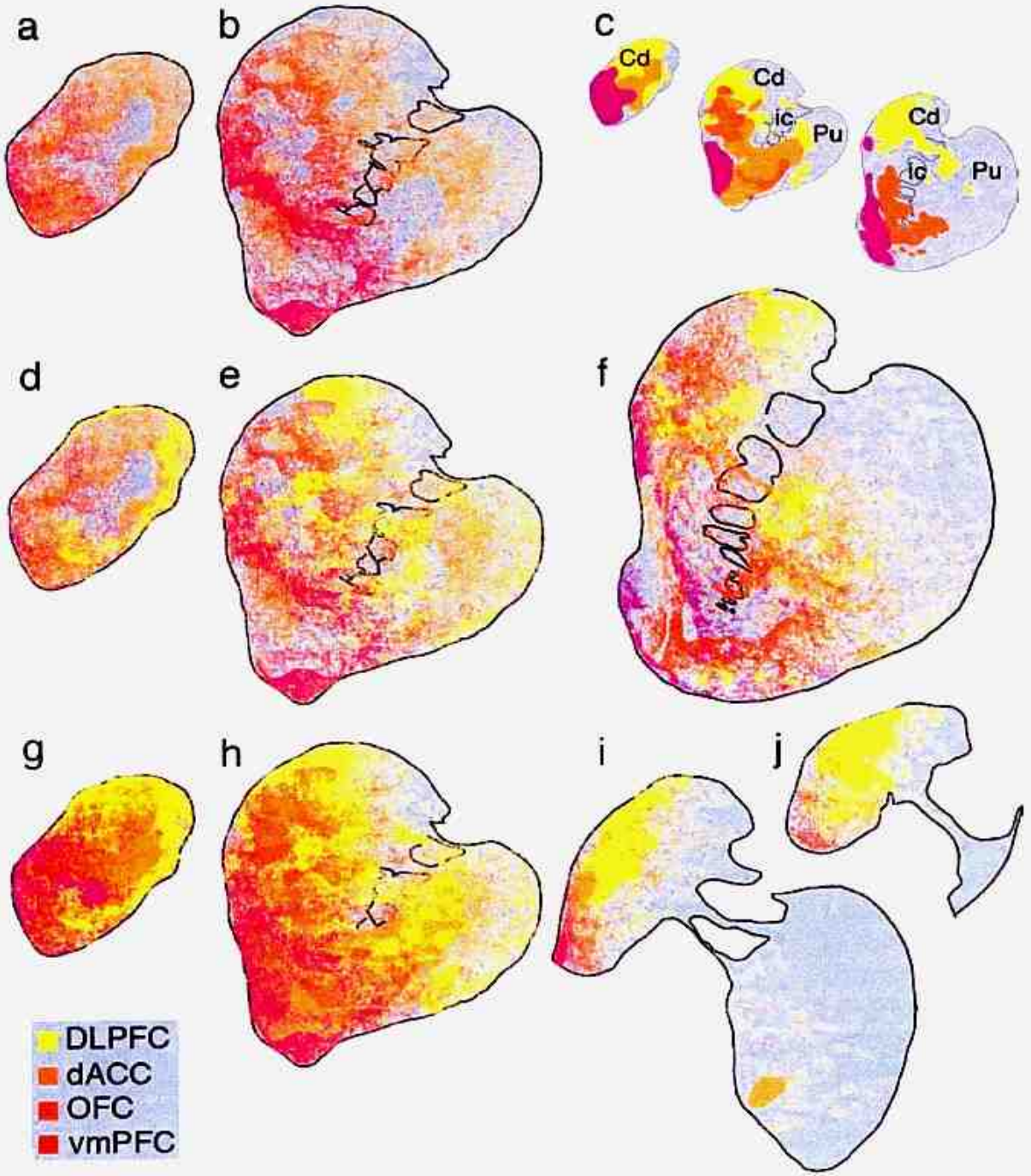
Functions of the striatum

- THE DORSAL STRIATUM
- The selection of motor and behavioral processes appropriate for a particular context
- The release of desired and the supression of unwanted movements
- *Important for stimulus – response behavior*

- THE VENTRAL STRIATUM (nc. Accumbens)
- The learning and execution of reward-related movements and activities. The ventral striatum is activated in reward situations.
- Reward= smoking, alcohol, drugs, sex, economic reward

The reward related striatum

Red and purple colour



Haber et al. 2006

Thank you

The dorsal striatum and the ventral striatum

- The ventral striatum = nucleus accumbens and adjacent caudate nucleus and putamen
- The reward- related striatum is defined also by projections from orbitofrontal and anterior cingular cortex and by projections from limbic structures (hippocampus, amygdala)
- 22 % of the striatum
- The nc. accumbens may play an important role in behaviors related to addiction (alcohol, nicotine, drugs)

[illegible] lower vertebrates.

The basal ganglia are here considered to be a crucial element in the process of selecting different motor programs, particularly the striatum, with its wide input from the cerebral cortex and thalamus and its high threshold for being switched from a down state to the transmitting up state (requiring appropriate dopamine tone). Subpopulations of neurons in the striatum deter-

Circuits of the ventral striatum and pallidum II

- Limbic cortex, amygdala –
- Ventral striatum -
- Ventral pallidum / subst. Nigra -
- Thalamus (mediodorsal nc.) –
- Prefrontal cortex

- Circuit might be crucial for the learning and executionof reward – related behavior

5. Conclusions

On the basis of PET activation data currently available it is possible to come to the following tentative conclusions about the role of the basal ganglia:

(a) It seems unlikely that the basal ganglia play a primary role in determining basic parameters of movement.

(b) The basal ganglia are not directly involved in motor skill acquisition or in promoting automaticity of movement. The cerebellum is the subcortical structure most likely to be involved in these processes.

(c) As the basal ganglia are not differentially activated by performance of complex sequences of movements compared with stereotyped actions, facilitation of sequential movement is unlikely to be their primary purpose.

(d) The basal ganglia do not appear to be directly involved in decisions regarding direction or timing of movement. They are, however, equivalently activated during imagination and performance of actions which suggests that they play a role in movement preparation and execution. This role could conceivably be to monitor and optimise the pattern of muscular activity employed by a limb to reach its target most efficiently once a motor decision is taken.

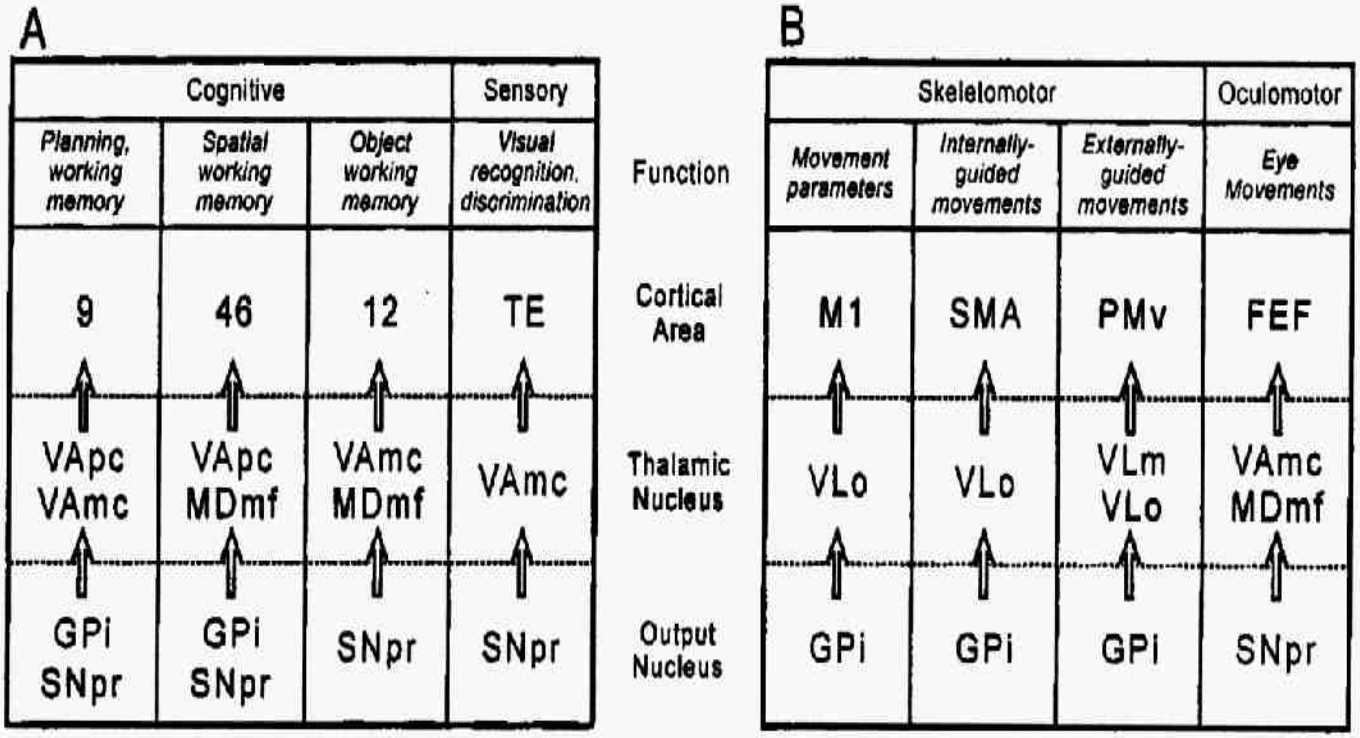
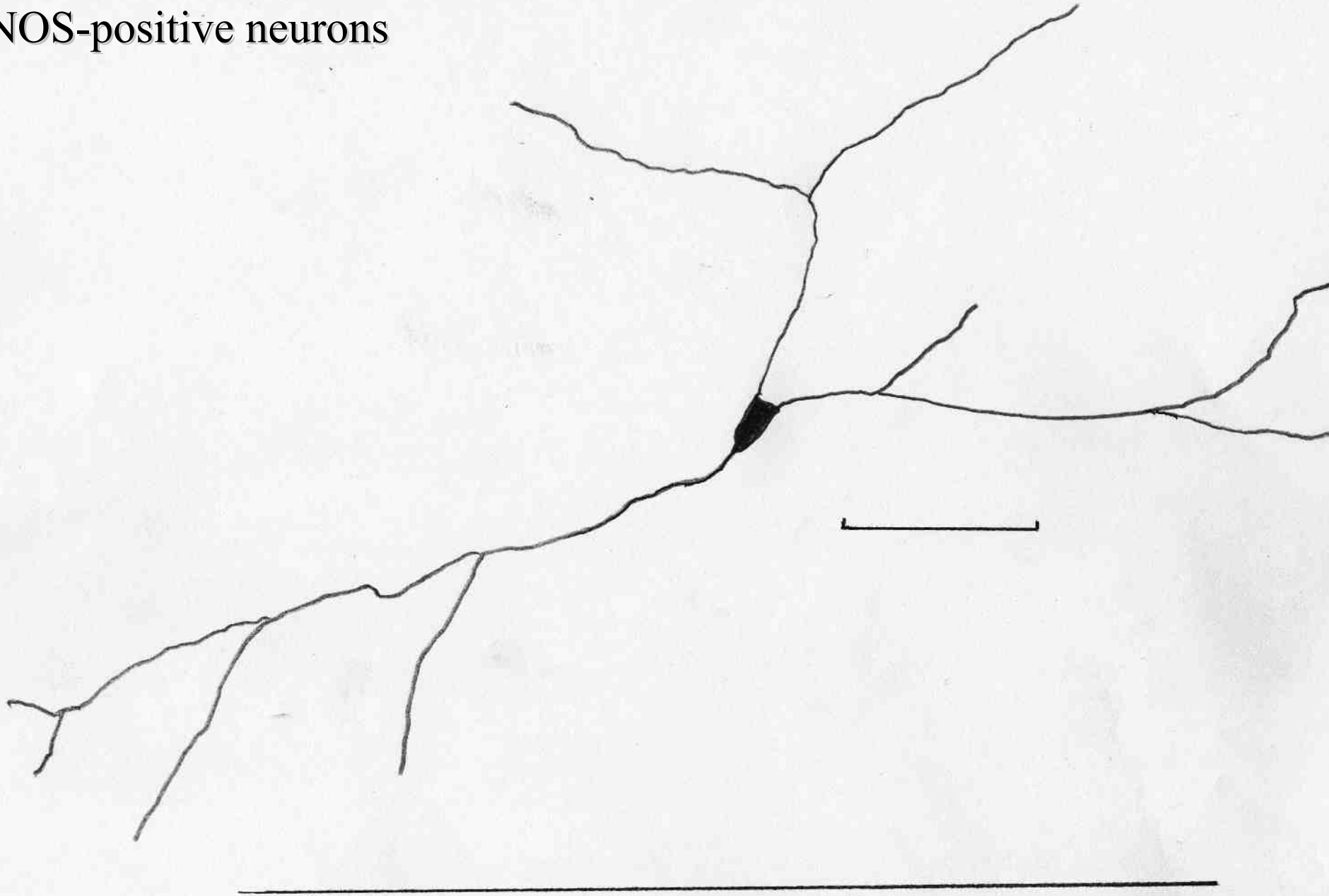


FIG. 4. Nonmotor (A) and motor (B) output channels. The basal ganglia project to a diverse set of cortical areas via the thalamus. These projections form anatomically and functionally distinct output channels. Thalamic abbreviations according to Olszewski (1952).

NOS-positive neurons



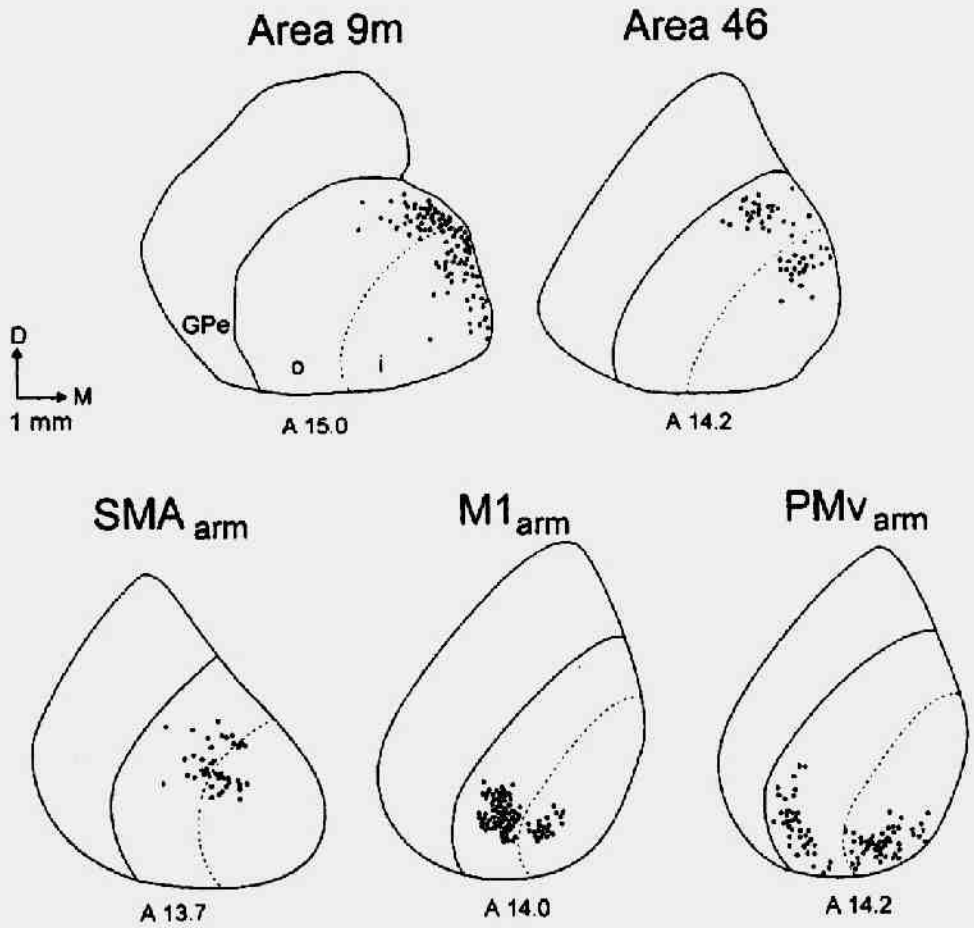


FIG. 2. Pallidal projections to motor and nonmotor cortical areas. Injections of HSV1 into portions of M1, PMv, SMA, and areas 46 and 9 all labeled neurons in GPi. Representative coronal sections through the globus pallidus of animals that received these injections are shown. The sections display labeled neurons found on one to three adjacent sections. GPe, external segment of globus pallidus; o, outer portion of the internal segment of globus pallidus; i, inner portion of the internal segment of globus pallidus.

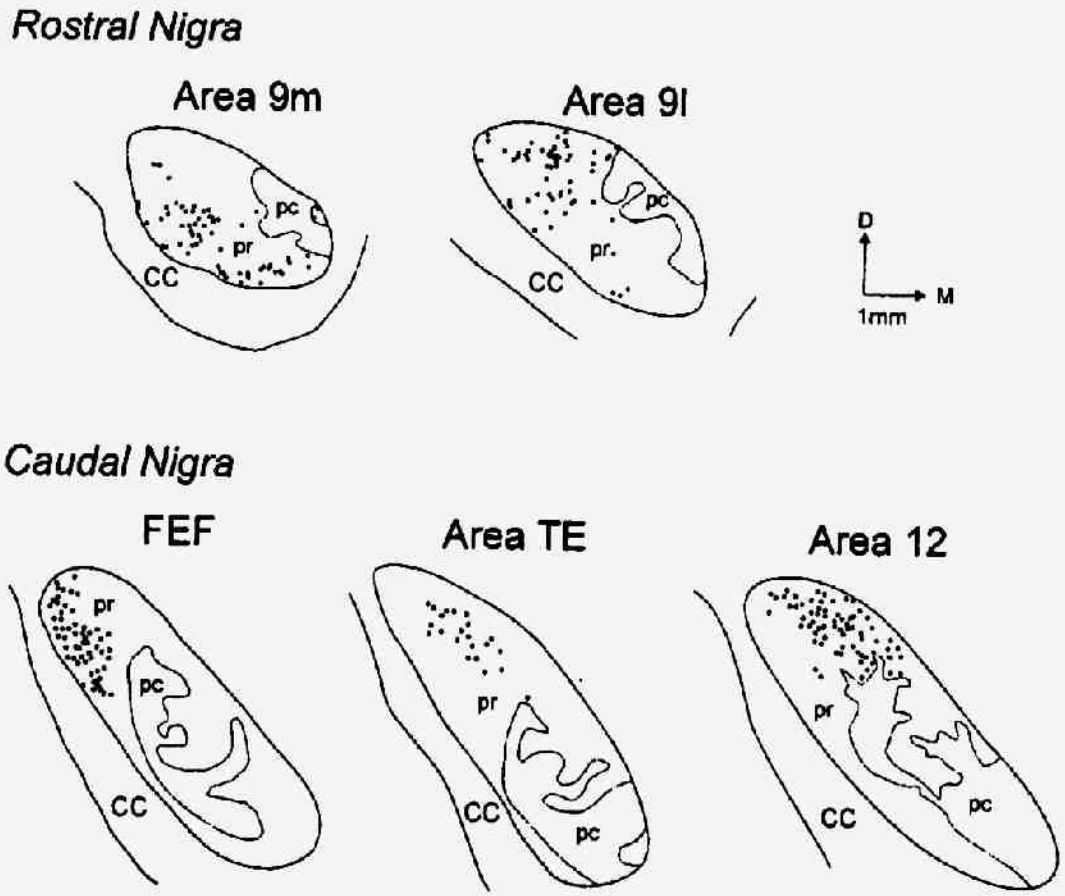


FIG. 3. Nigral projections to motor and nonmotor cortical areas. Injections of HSV1 into portions of area 9, area 12, the FEF, and area TE all labeled neurons in SNpr. The conventions for this figure are the same as those for Fig. 2. CC, crus cerebri; pc, pars compacta; pr, pars reticulata.

In conclusion, recent anatomical observations have challenged the view that basal ganglia output is solely concerned with motor control. It is now apparent that multiple cortical areas are the target of basal ganglia output, including not only the primary motor cortex, but also at least 9 other cortical areas, including subdivisions of premotor, oculomotor, prefrontal, and inferotemporal cortex. The basal ganglia output to individual cortical areas appears to originate from distinct clusters of neurons in the nigra or pallidum. This output is directed through specific regions of the thalamus to distinct

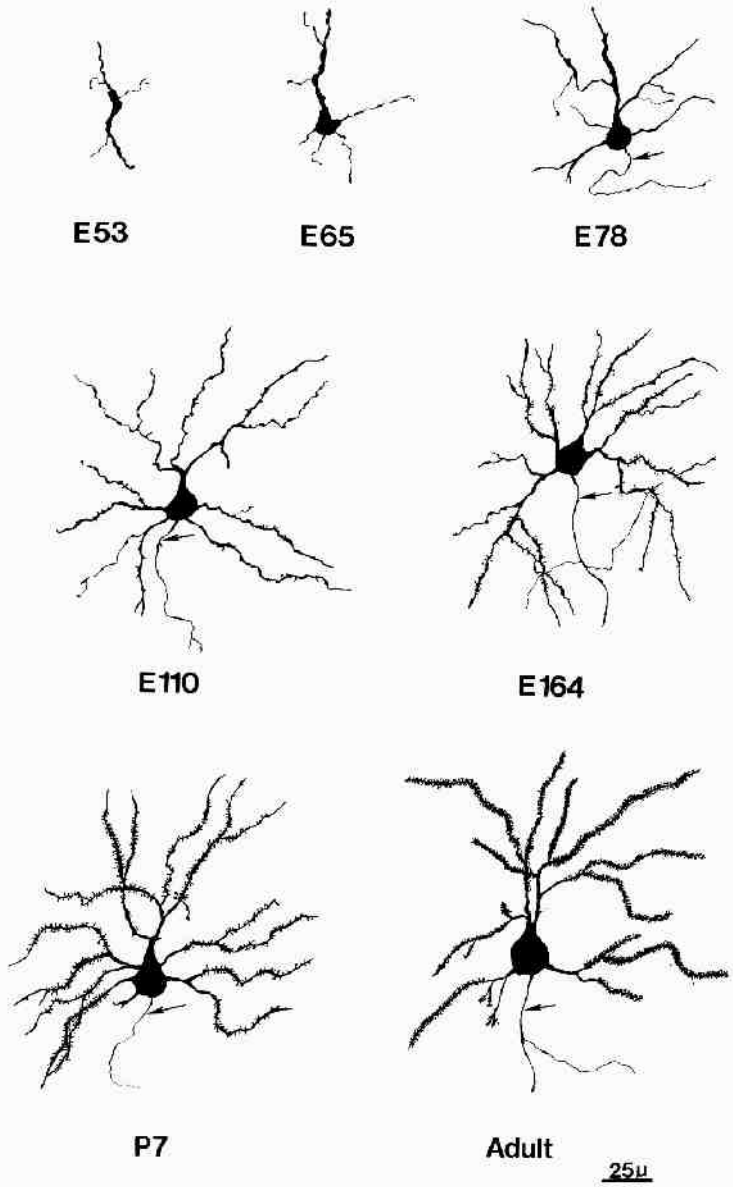


Fig. 1. Camera lucida drawings of the typical neostriatal spiny type I neurons impregnated with the Golgi method at selected embryonic (*E*) and postnatal (*P*) ages. The arrows indicate the position of the axon as it leaves the cell body. In situ, cells have random orientations, but to facilitate comparisons all neurons in this drawing are arbitrarily orientated so that their axon leaves the bottom of the perikaryon

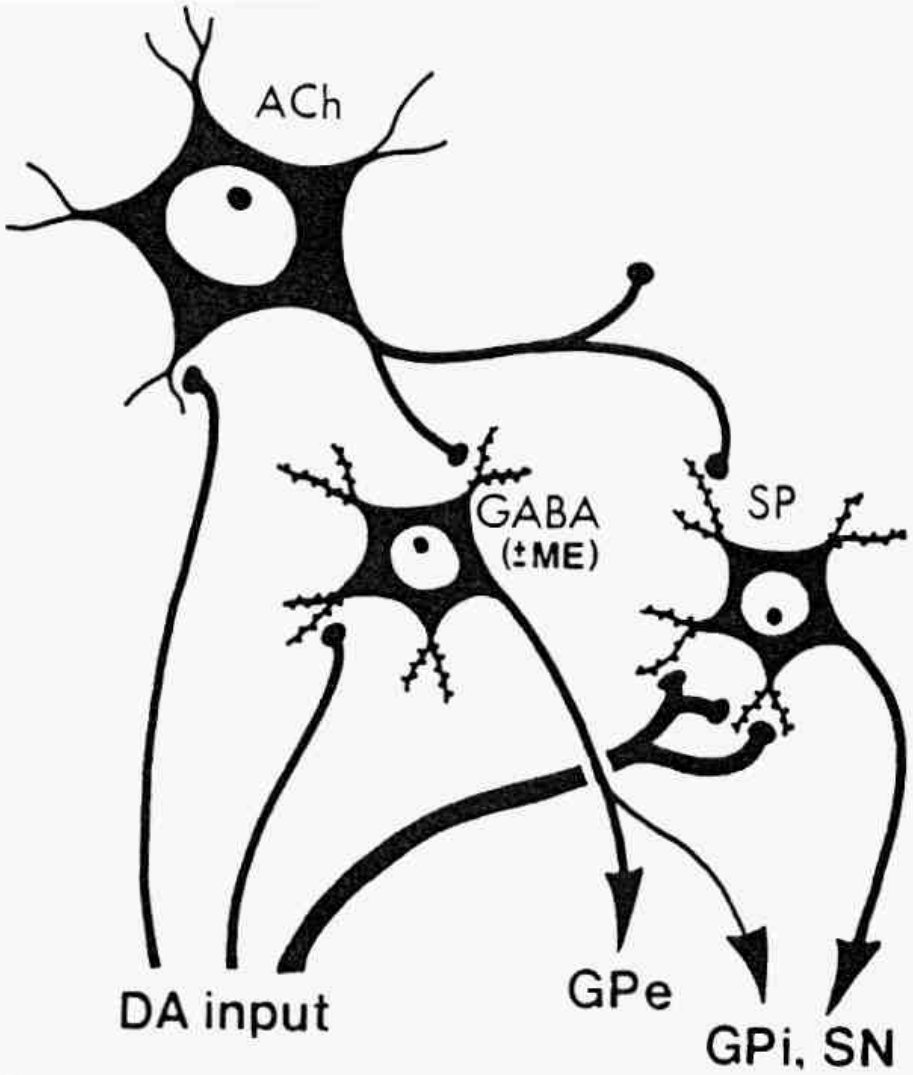


Fig. 9. A schematic representation of the dopaminergic innervation of striatal neurons by nigral axons based on the present and other observations. The heavier nigrostriatal line indicates a preferential input to the SP striatal cells. See text for discussion.

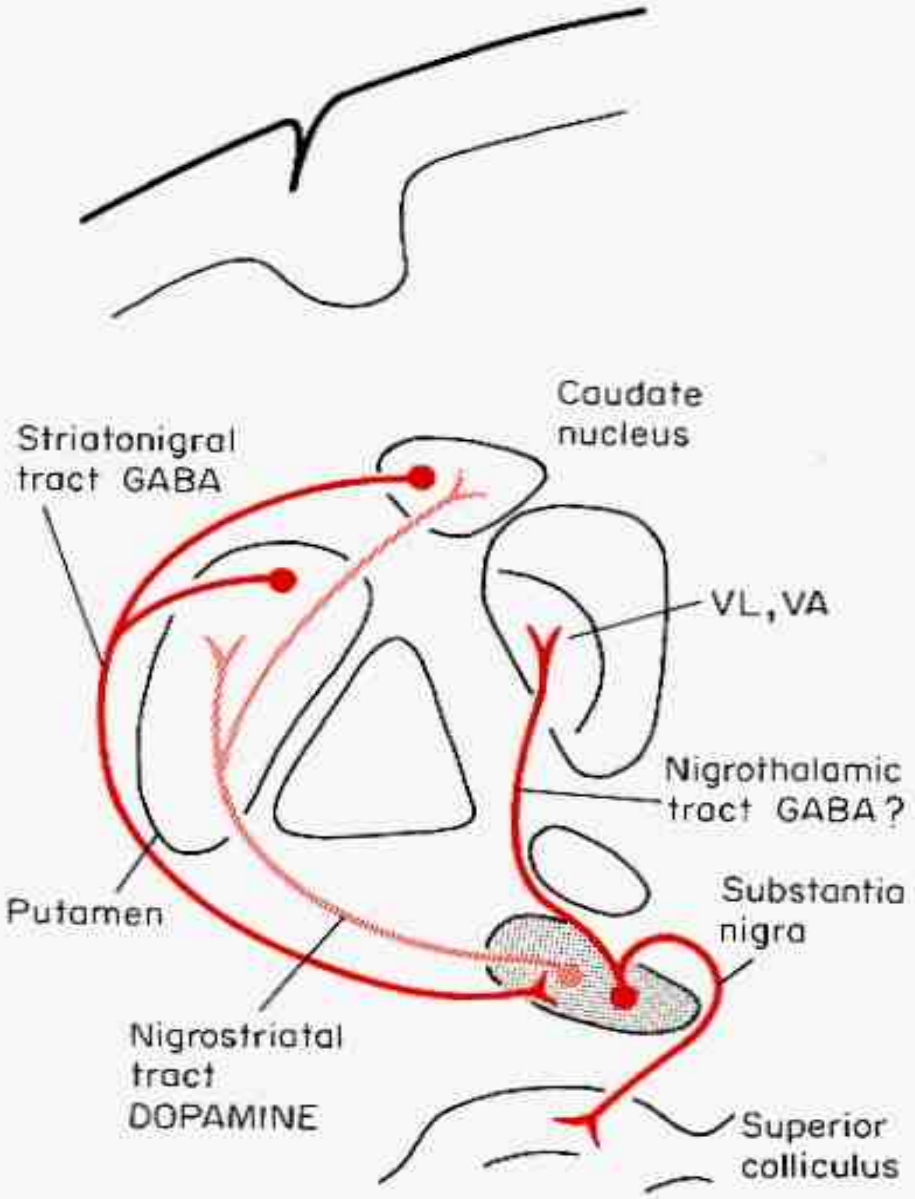
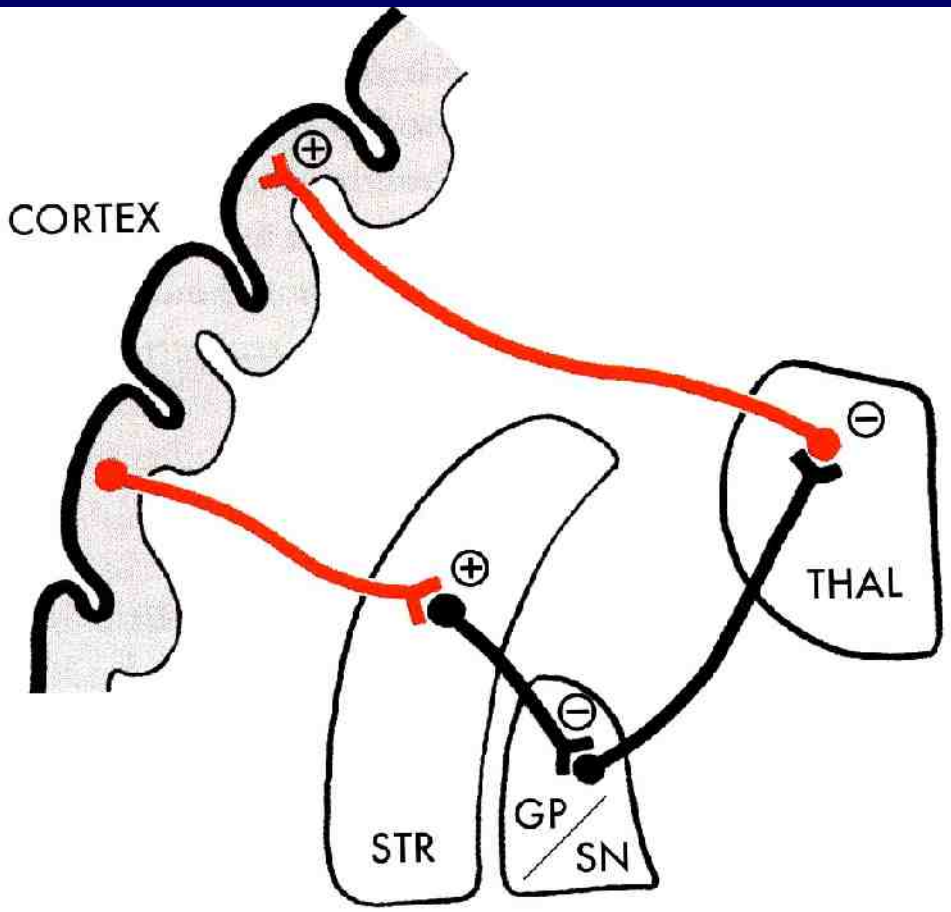


Fig. 10.6. *Main connections of the substantia nigra* (see also Fig. 10.10).

Circuit of the basal ganglia



Obr. 105. Okruh bazálních ganglií (okruh Nautův a Mehlerův). CORTEX = mozková kůra (neocortex), GP = globus pallidus, SN = substantia nigra, STR = striatum, THAL = thalamus. + = excitační synapse, – = inhibiční synapse. Upraveno podle W. J. H. Nauty a W. R. Mehlera (1966)