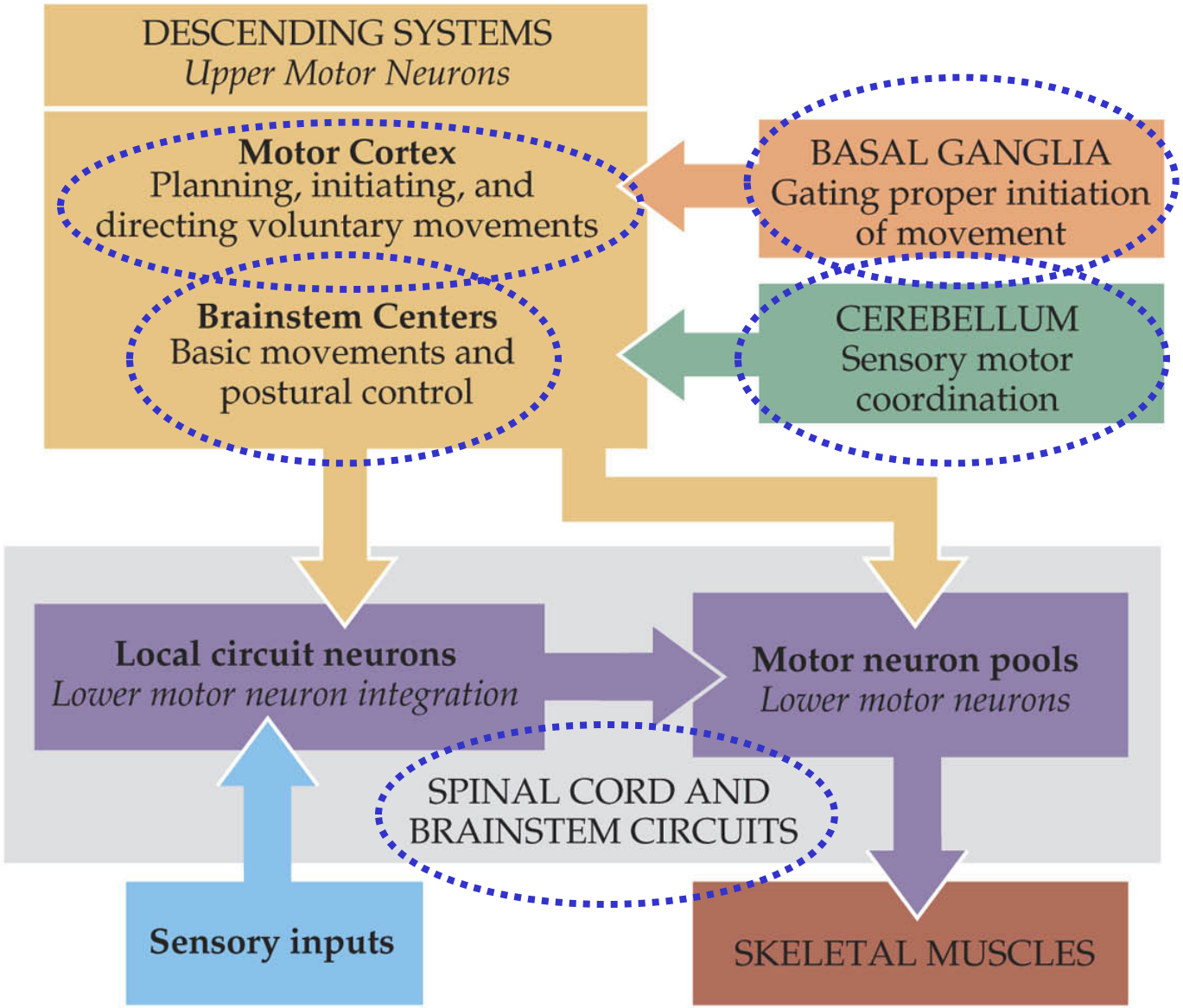
Neural structures involved in the control of movement



NEUROSCIENCE, Third Edition, **Figure 15.1**

Basal Ganglia

Key take-home messages:

- Components of the basal ganglia

- Function of the basal ganglia

- Functional circuitry of the basal ganglia
  e.g., direct and indirect pathways, transmitters

- Circuitry involved in movement disorders discussed

Basal Ganglia

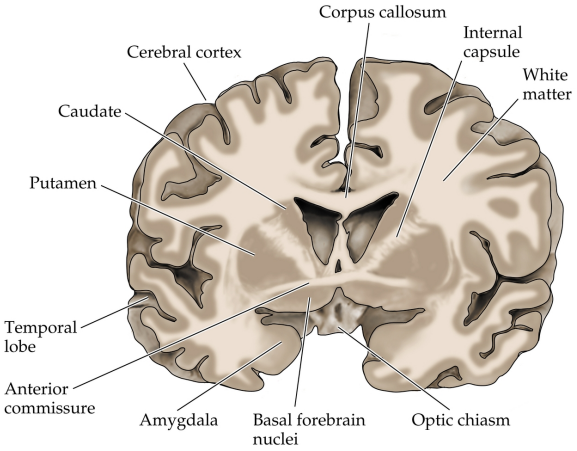
1. Neostriatum
   - Caudate nucleus
   - Putamen
   - Ventral striatum (nucleus accumbens)
2. Paleostriatum
   - Globus pallidus external segment (GPe)
   - Globus pallidus internal segment (GPi)
3. Substantia Nigra
   - Pars compacta (SNc)
   - Pars reticulata (SNr)
4. Subthalamic nucleus (STN)

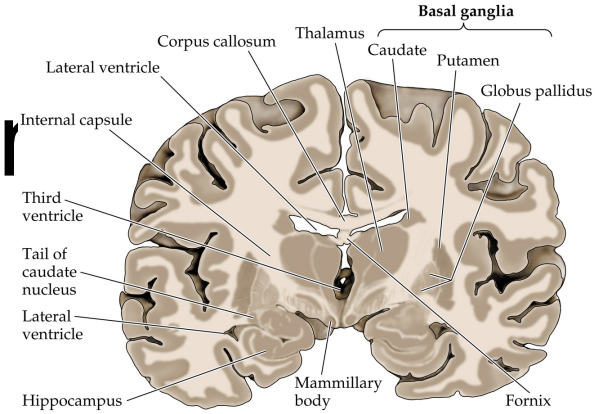
What do the basal ganglia do?

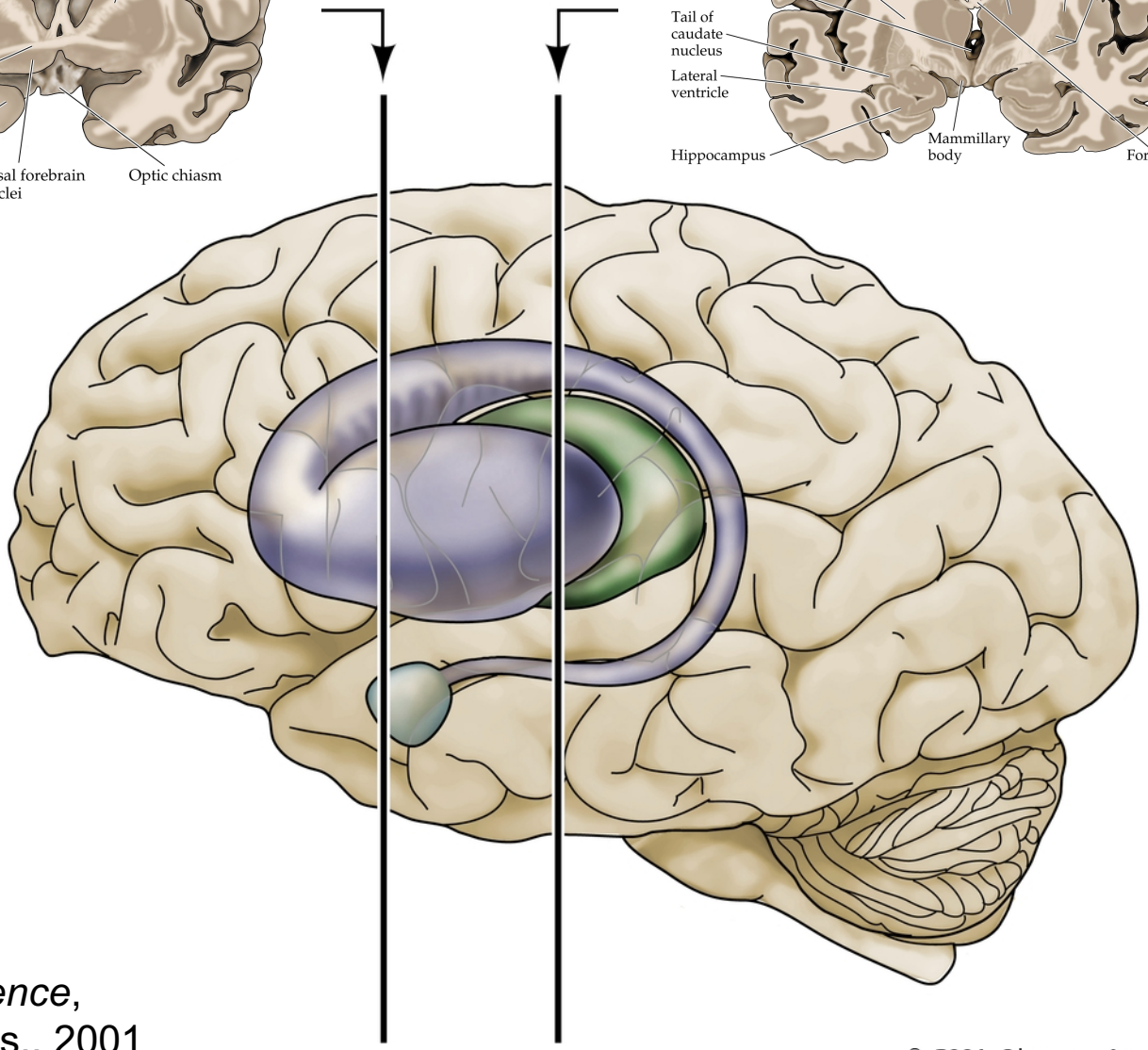
Basal ganglia are involved in generation of *goal-directed voluntary movements*:

- Motor learning
- Motor pattern selection

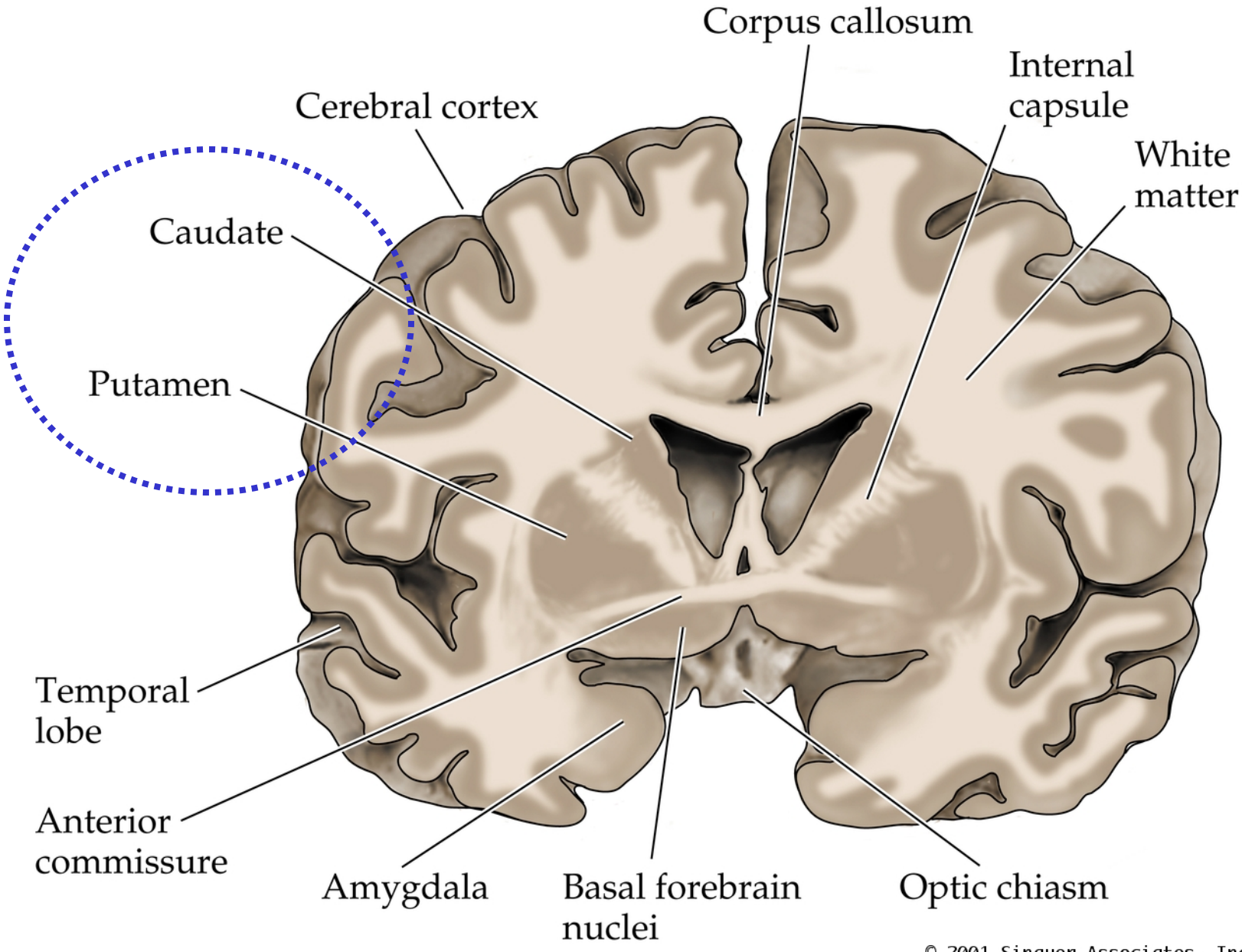
on in hur

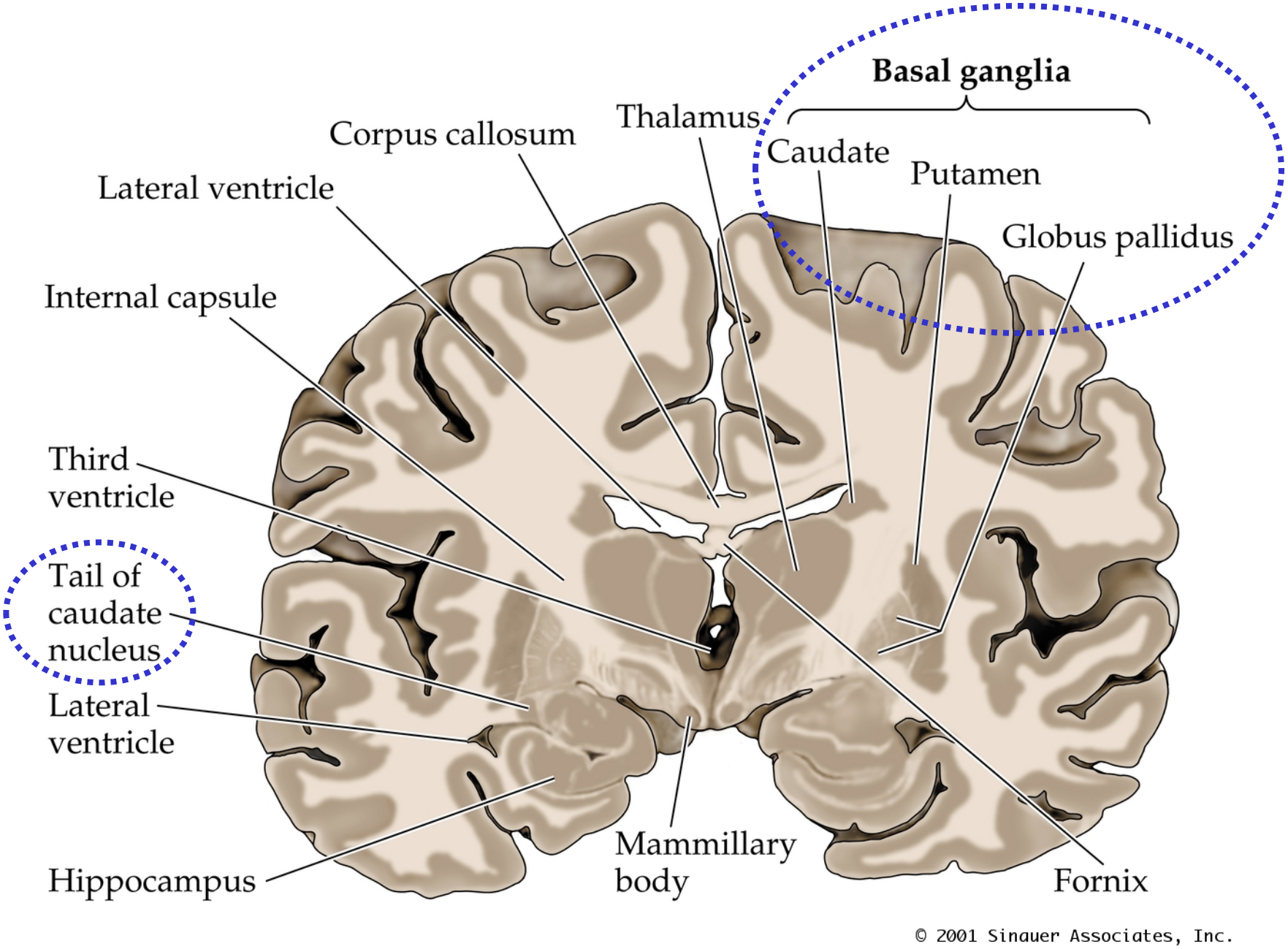


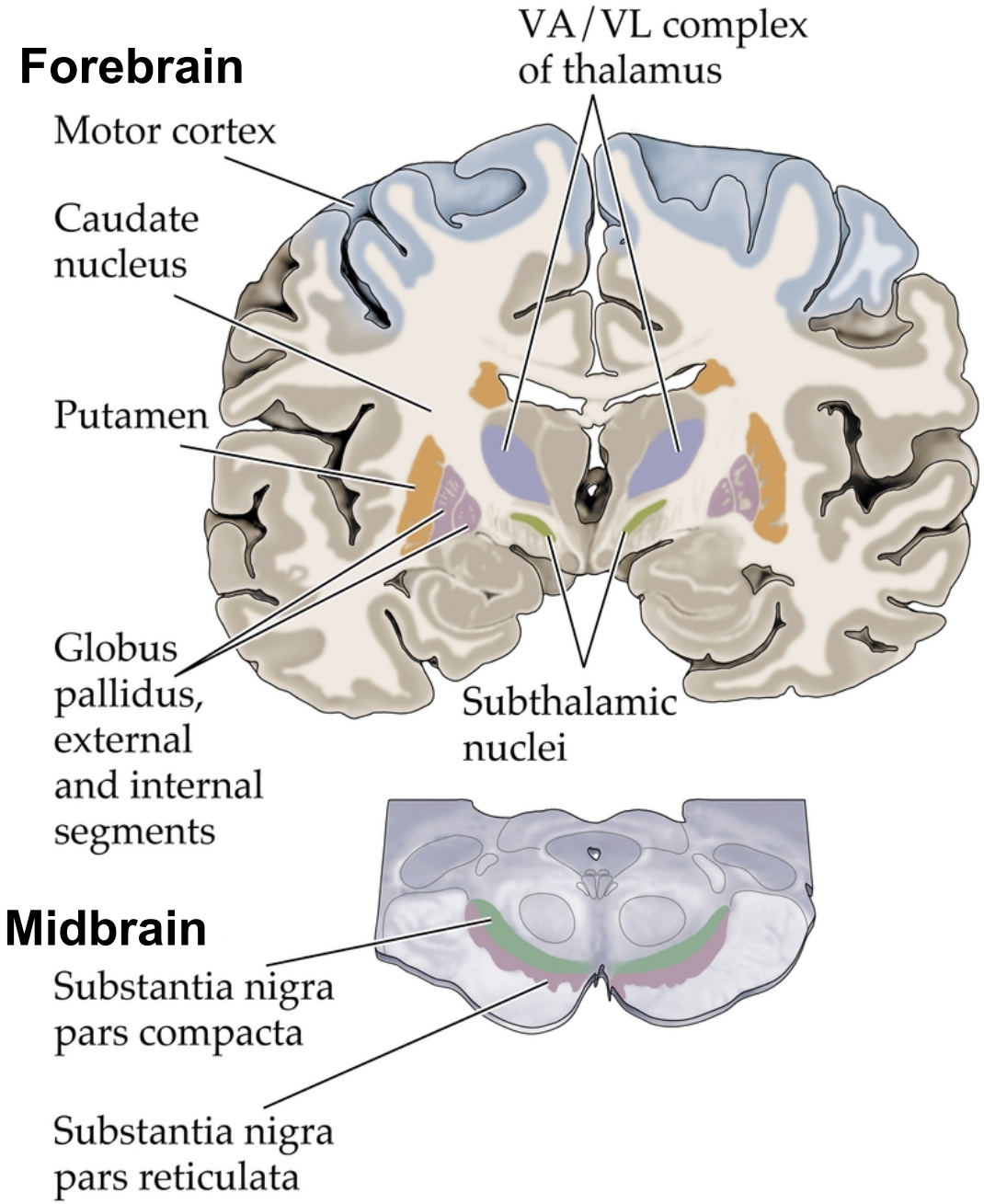


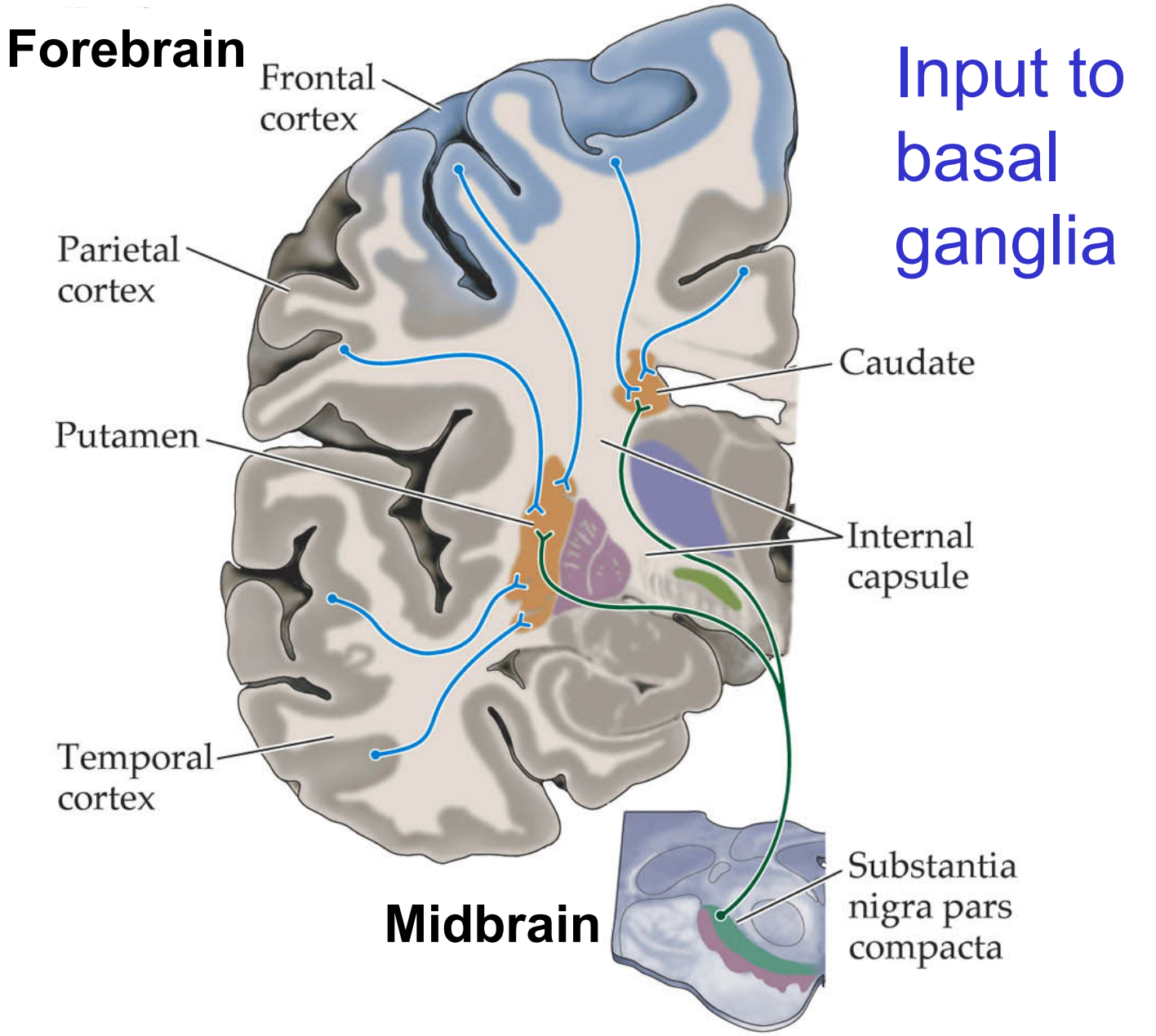


From *Neuroscience*,
Purves et al. eds., 2001





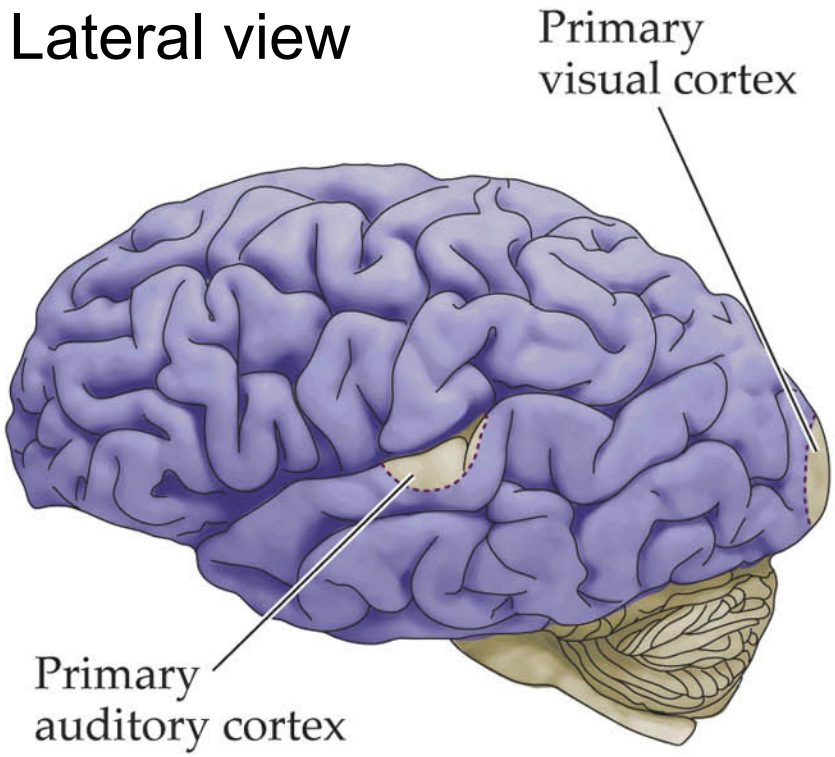




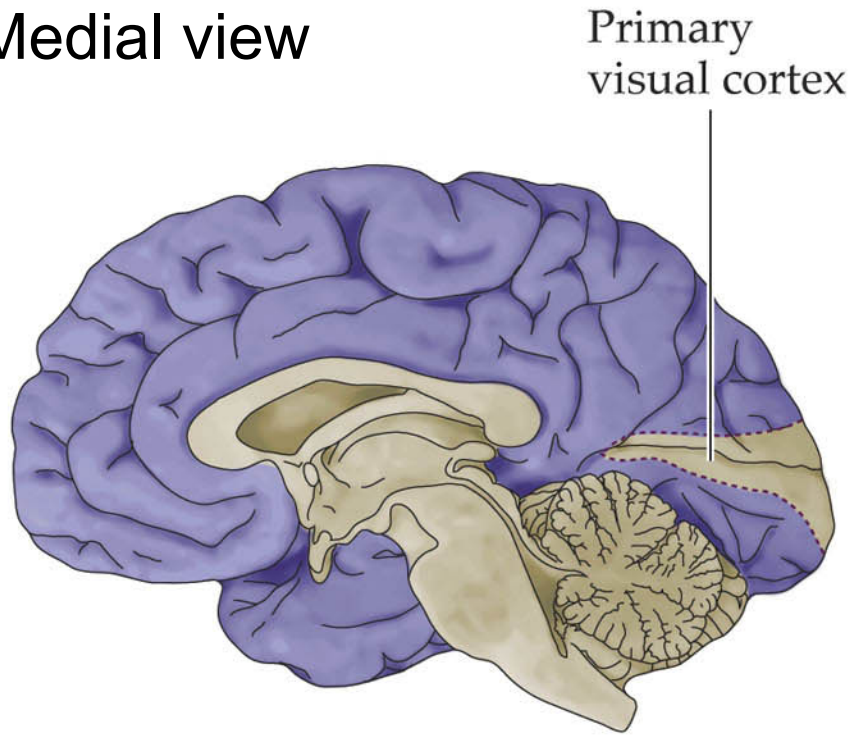
Input to basal ganglia

Regions of cortical input to the basal ganglia (blue)

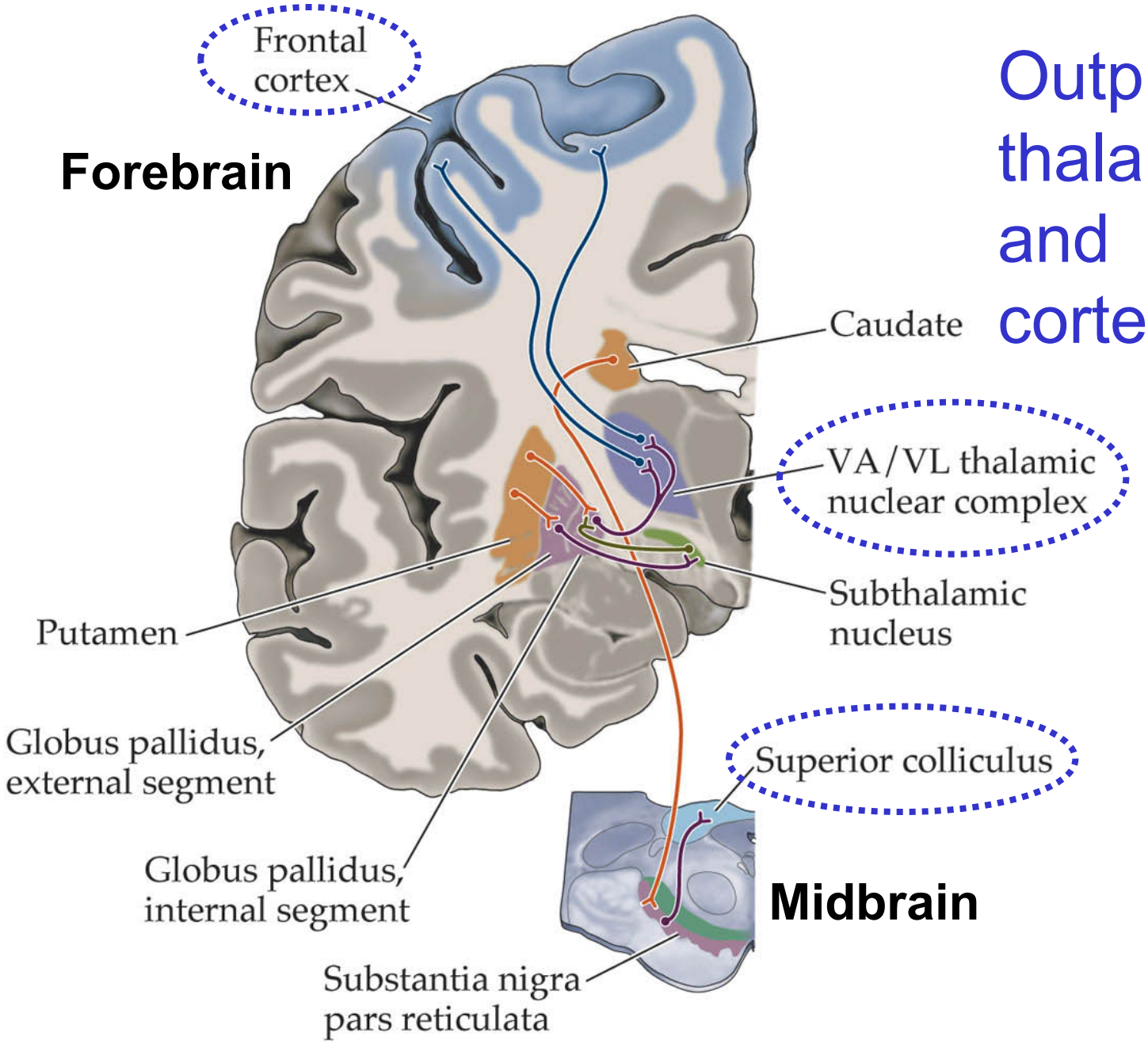
Lateral view



Medial view

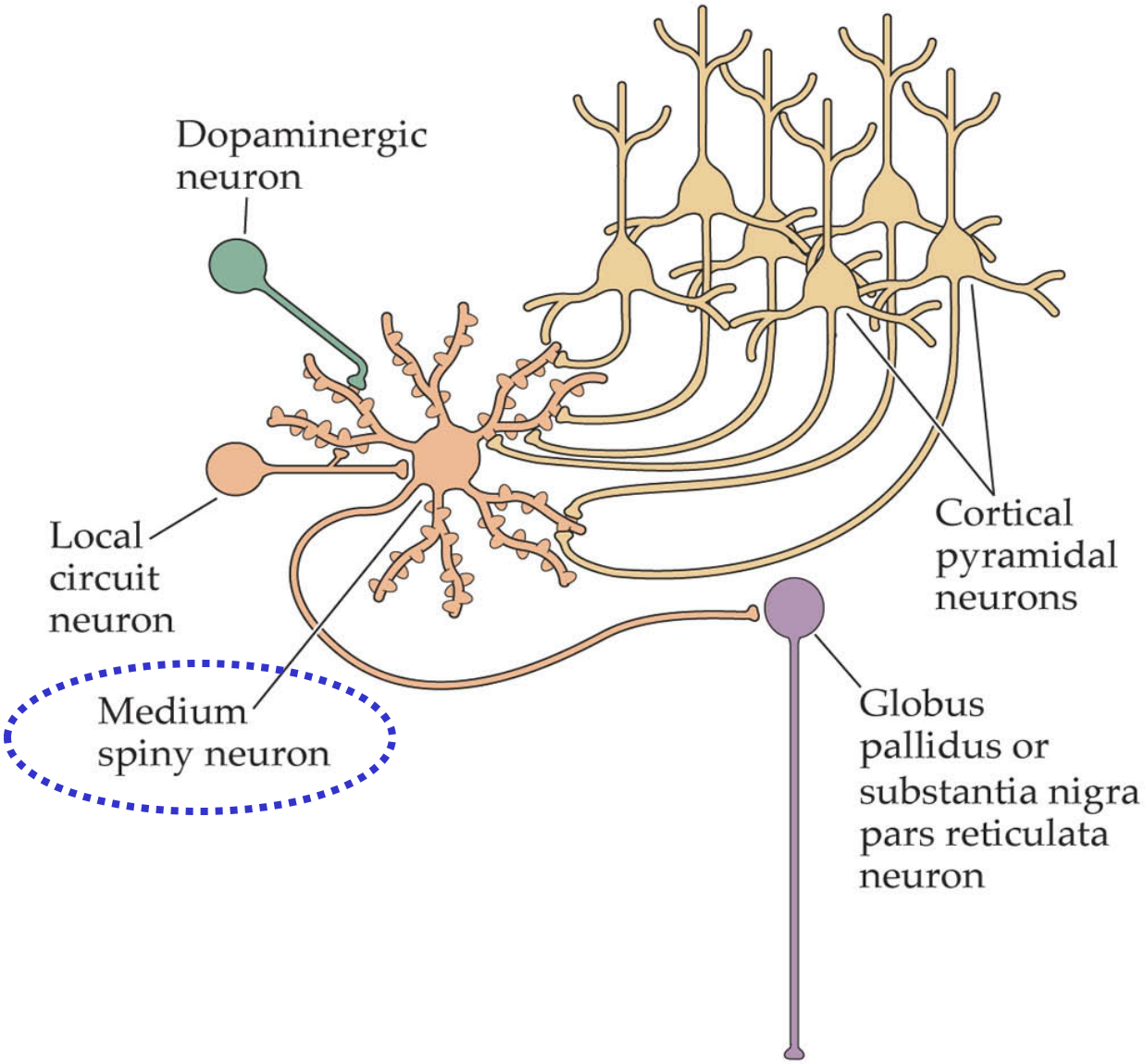


Output to thalamus and cortex

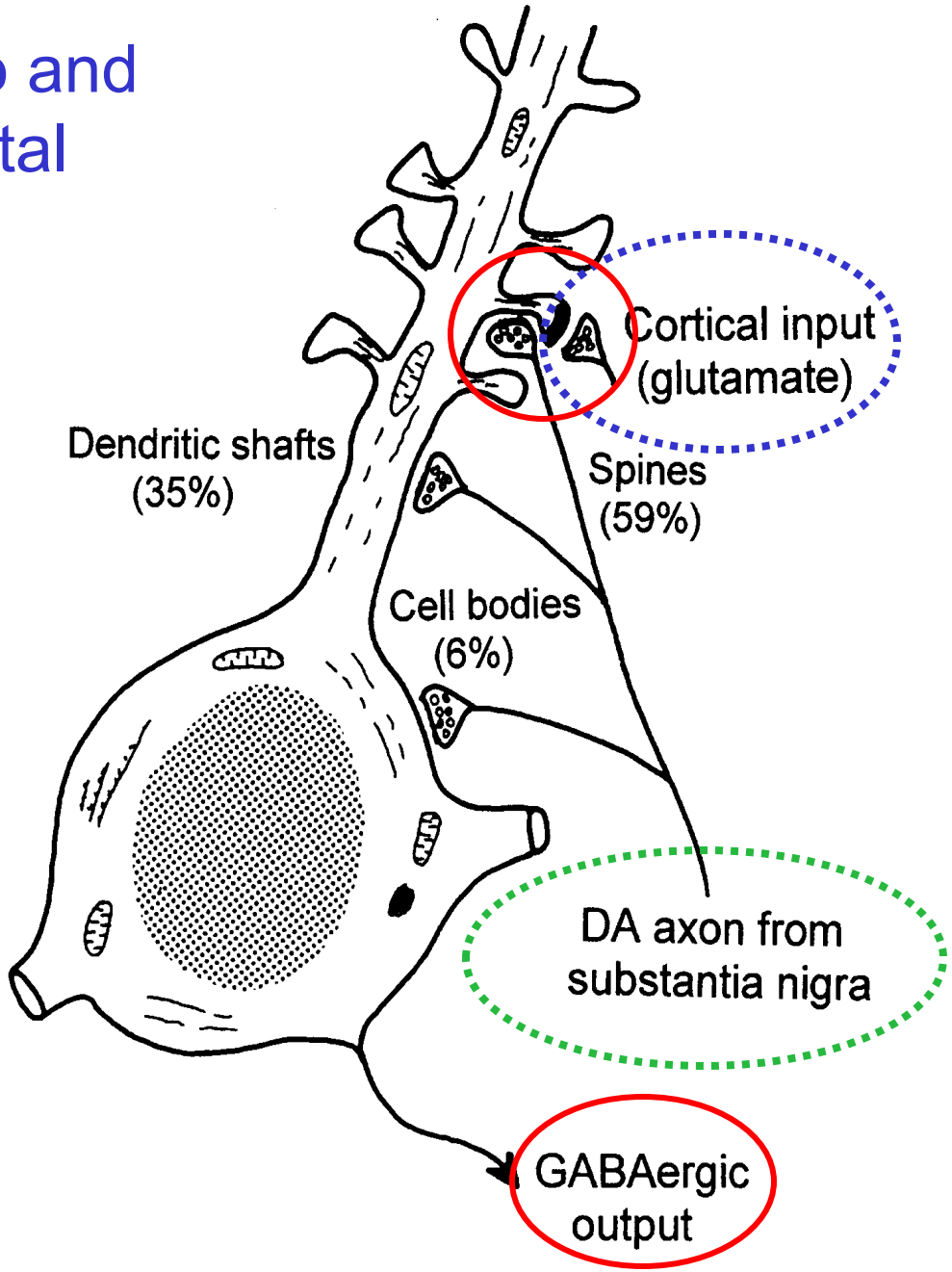


NEUROSCIENCE, Third Edition, **Figure 17.5 (Part 2)** © 2004 Sinauer Associates, Inc.

Neurons of the basal ganglia

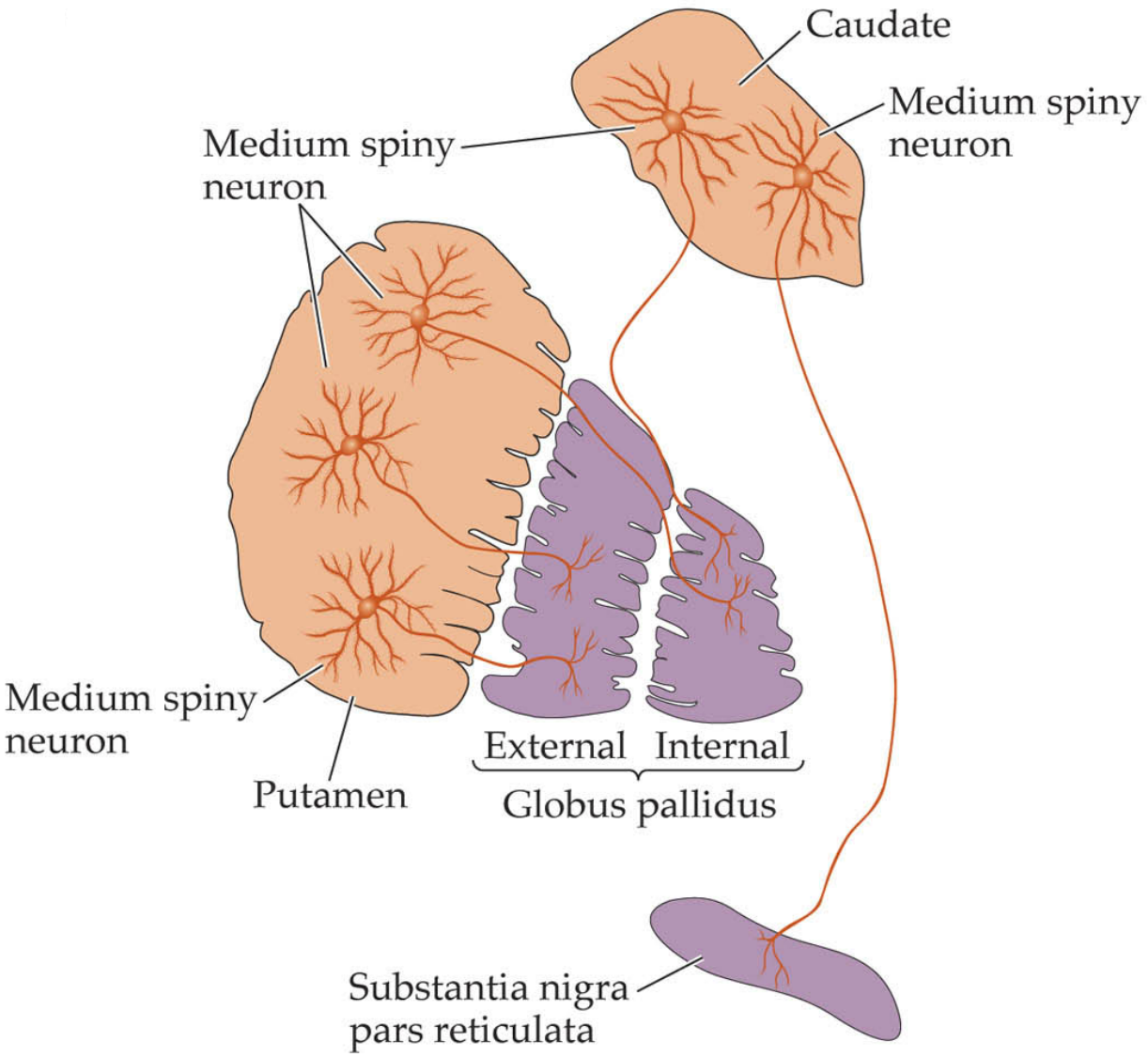


Synaptic input to and output from striatal medium spiny neurons



Smith and Bolam 1990

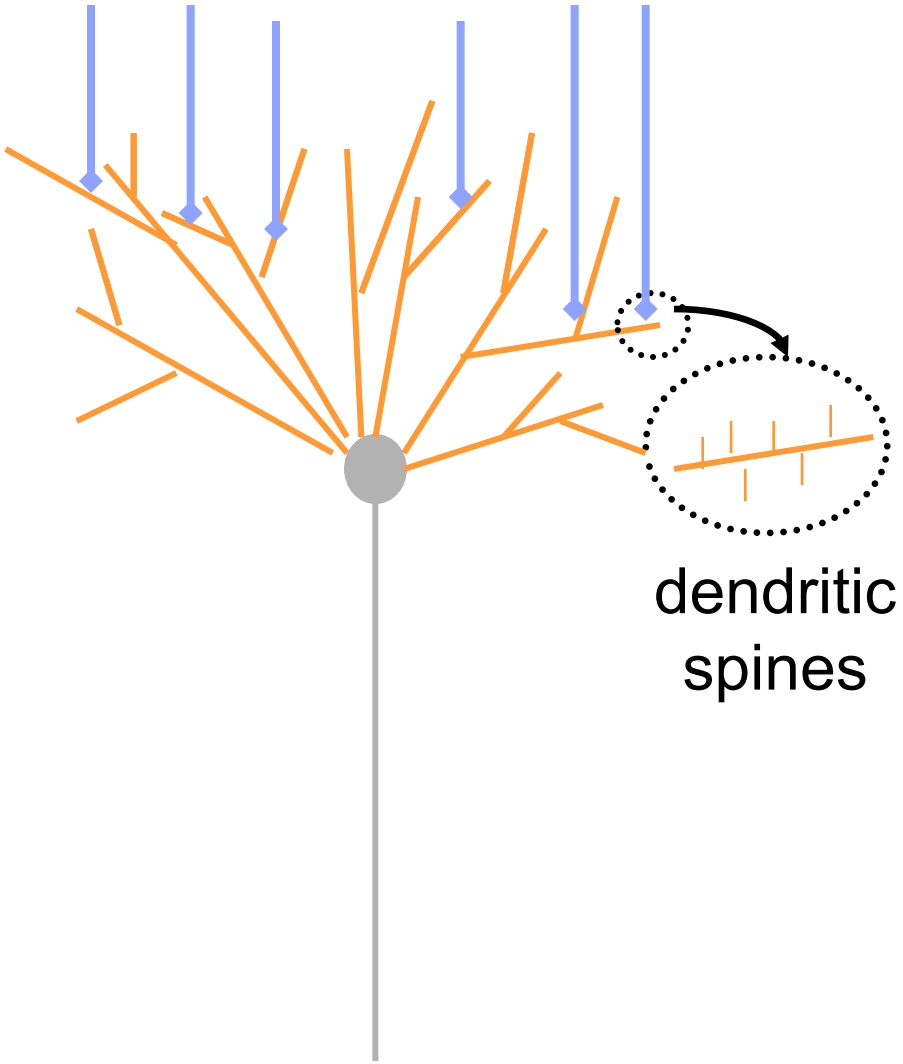
Medium spiny neuron projections



Basal ganglia loops

Convergence

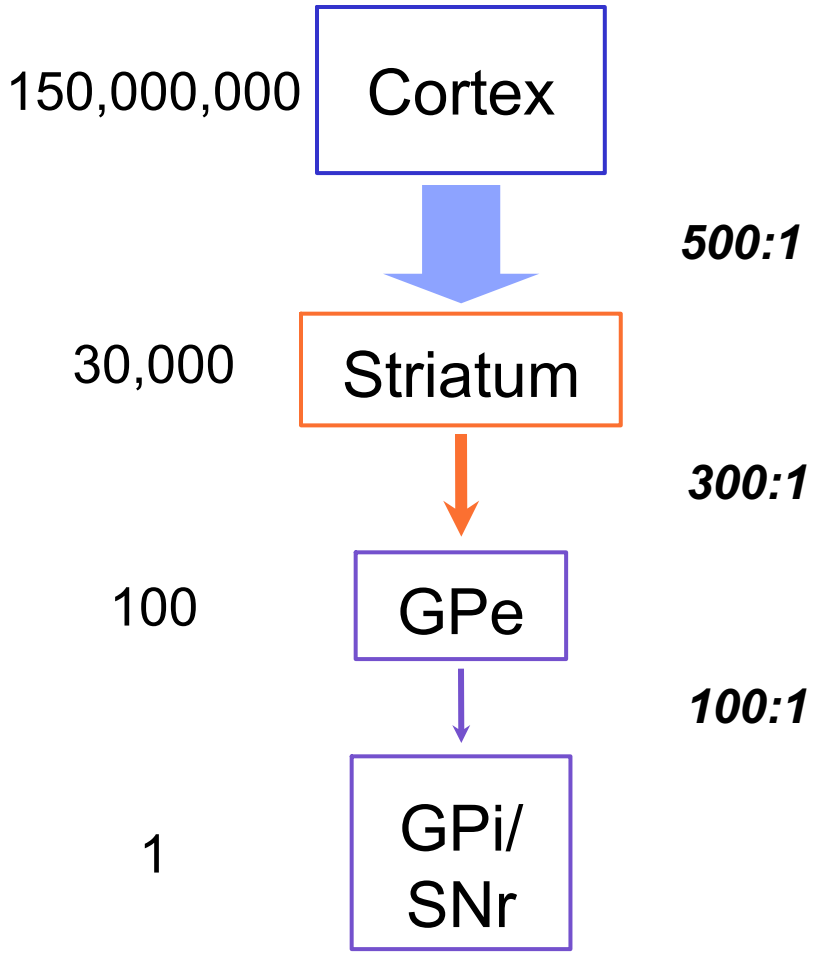
– large dendritic trees of striatal output neurons (medium spiny neurons)



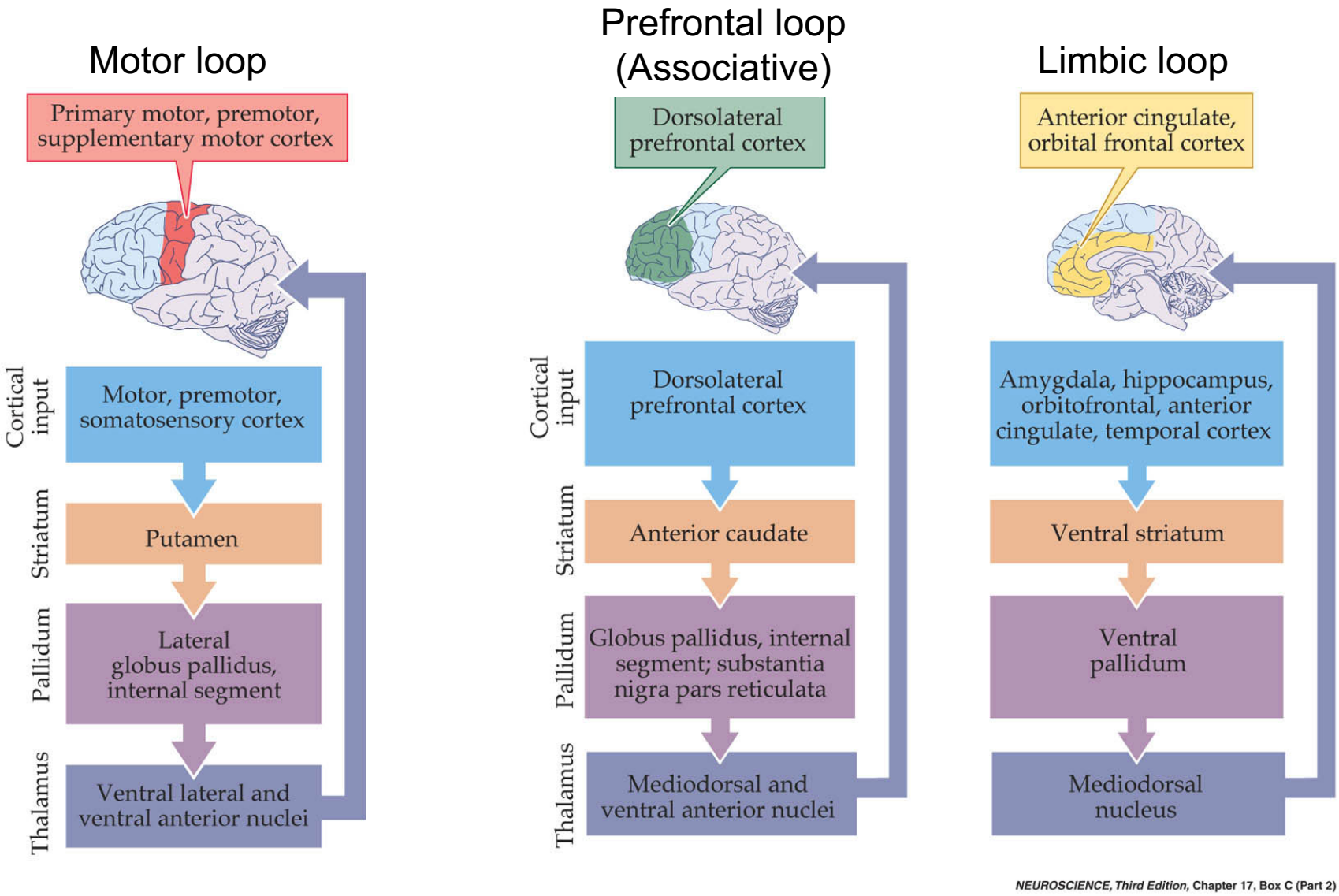
Basal ganglia loops

Convergence

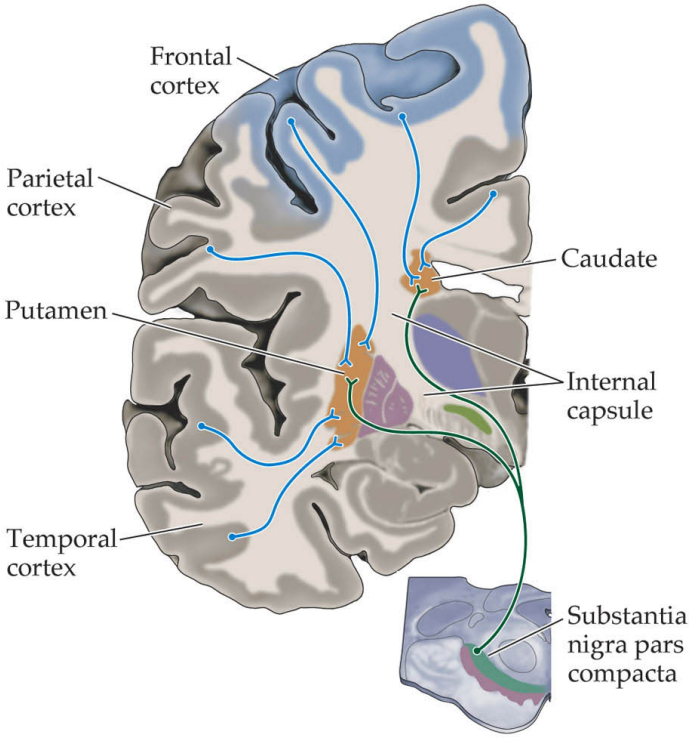
- large dendritic trees
- decreasing cell number



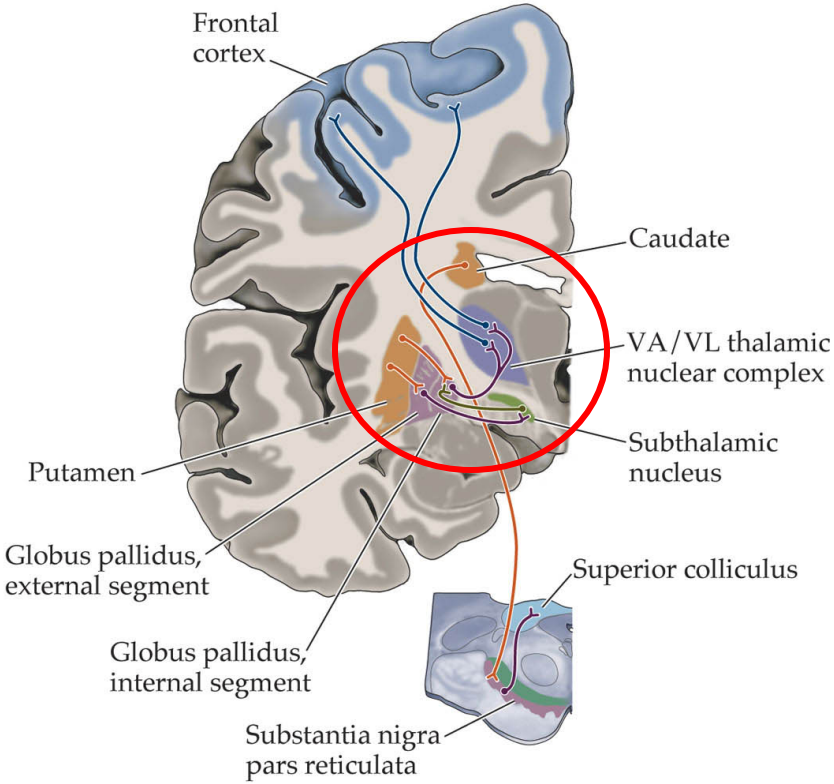
Basal ganglia loops – motor and non-motor

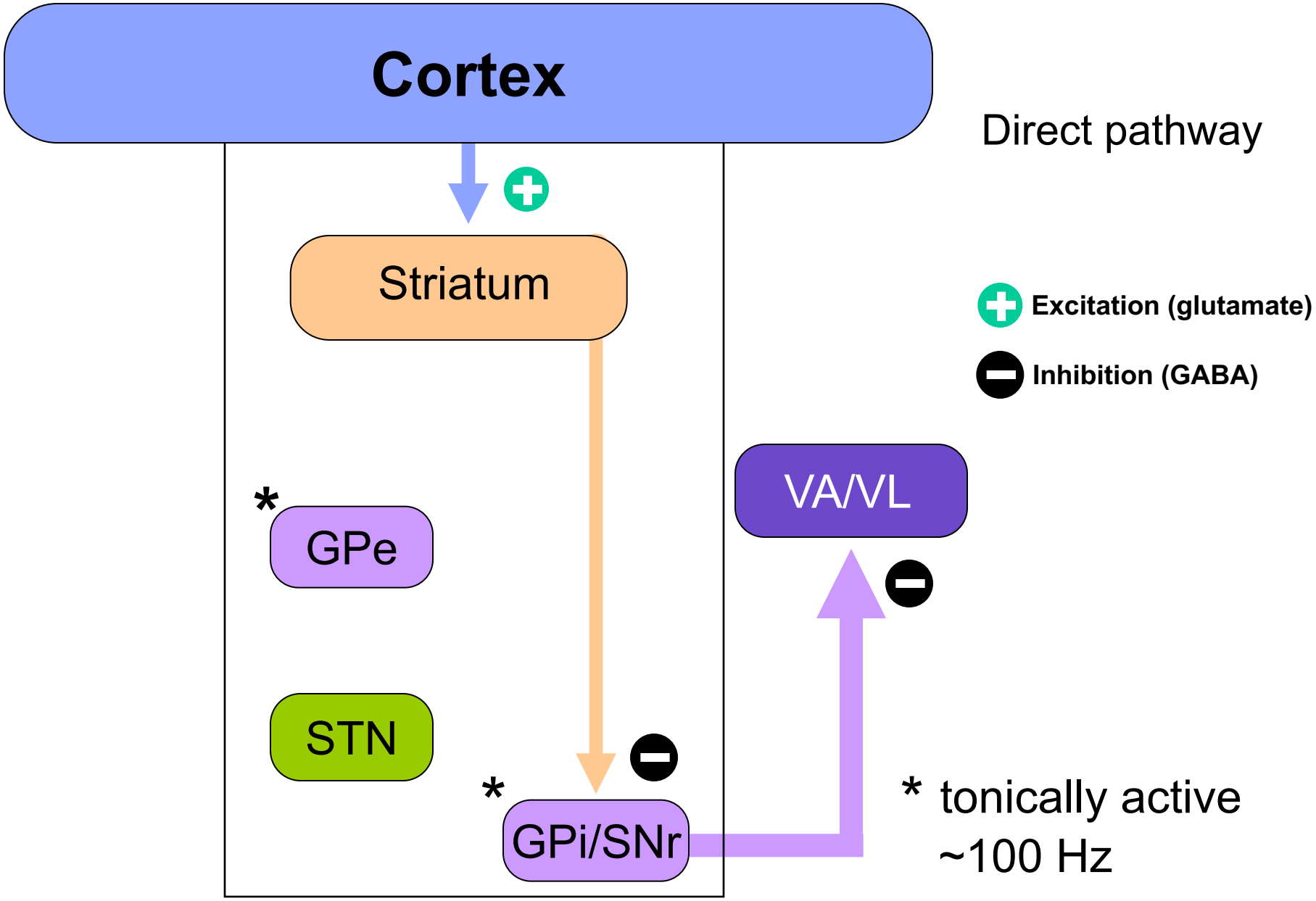


Input

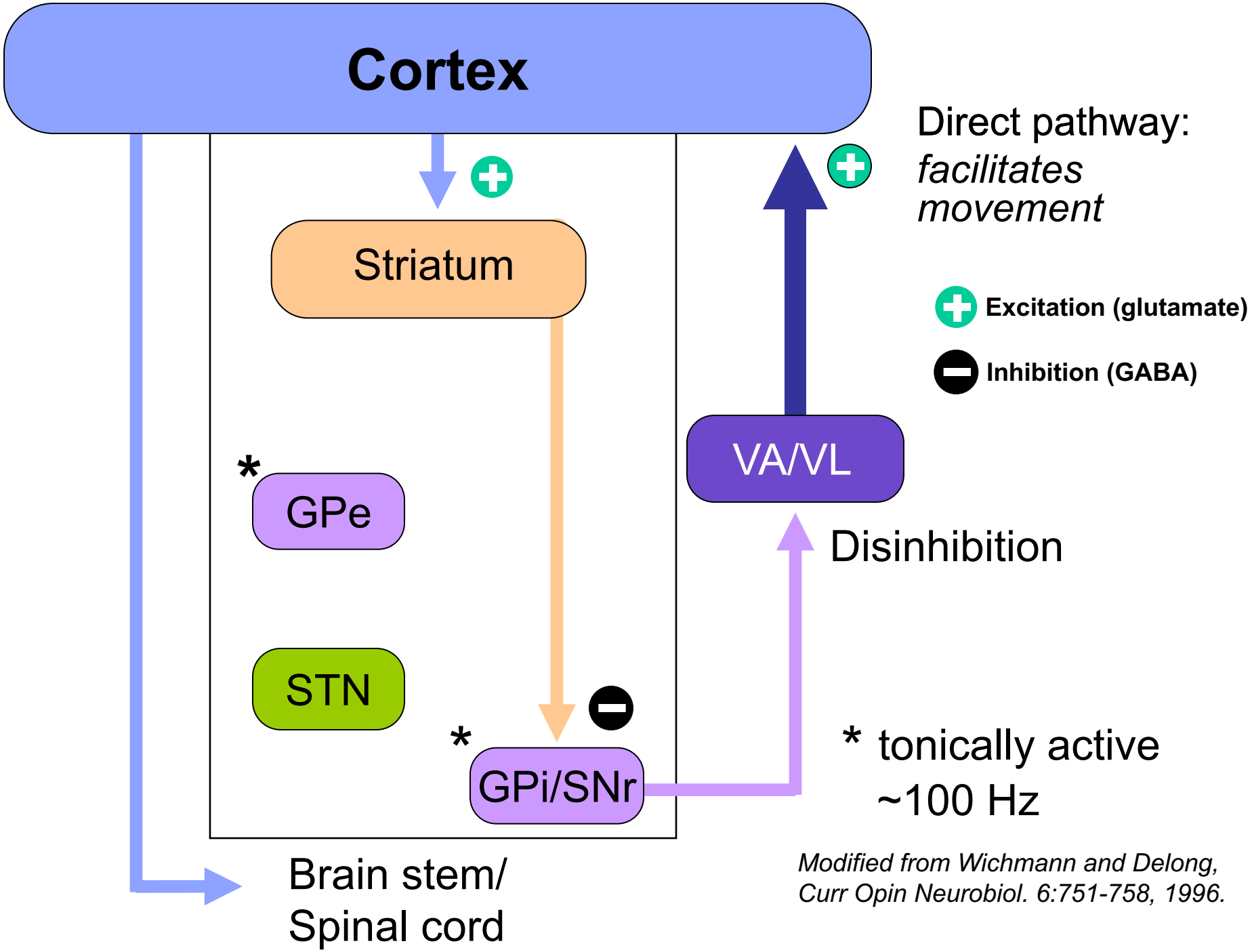


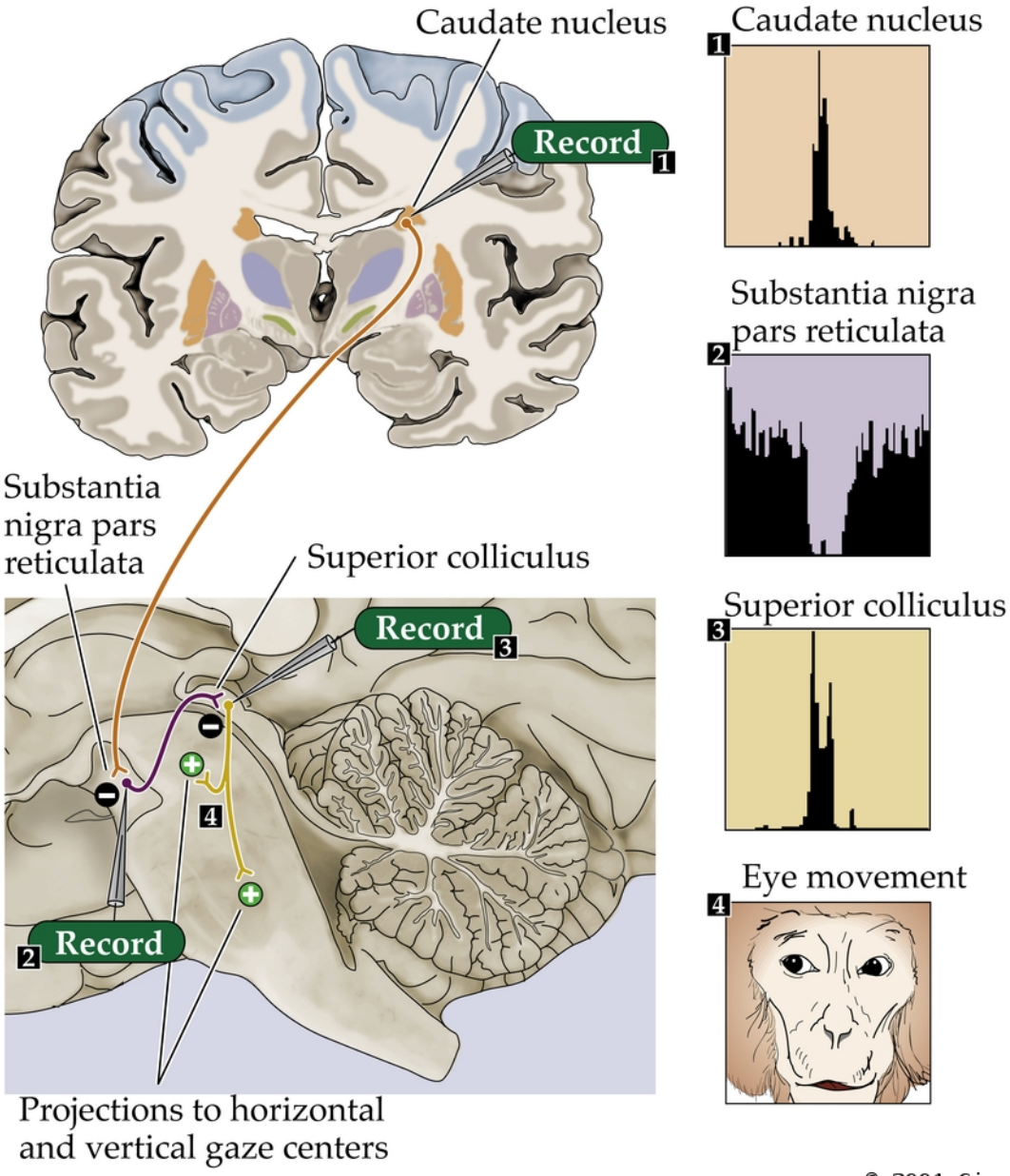
Output and internal circuitry



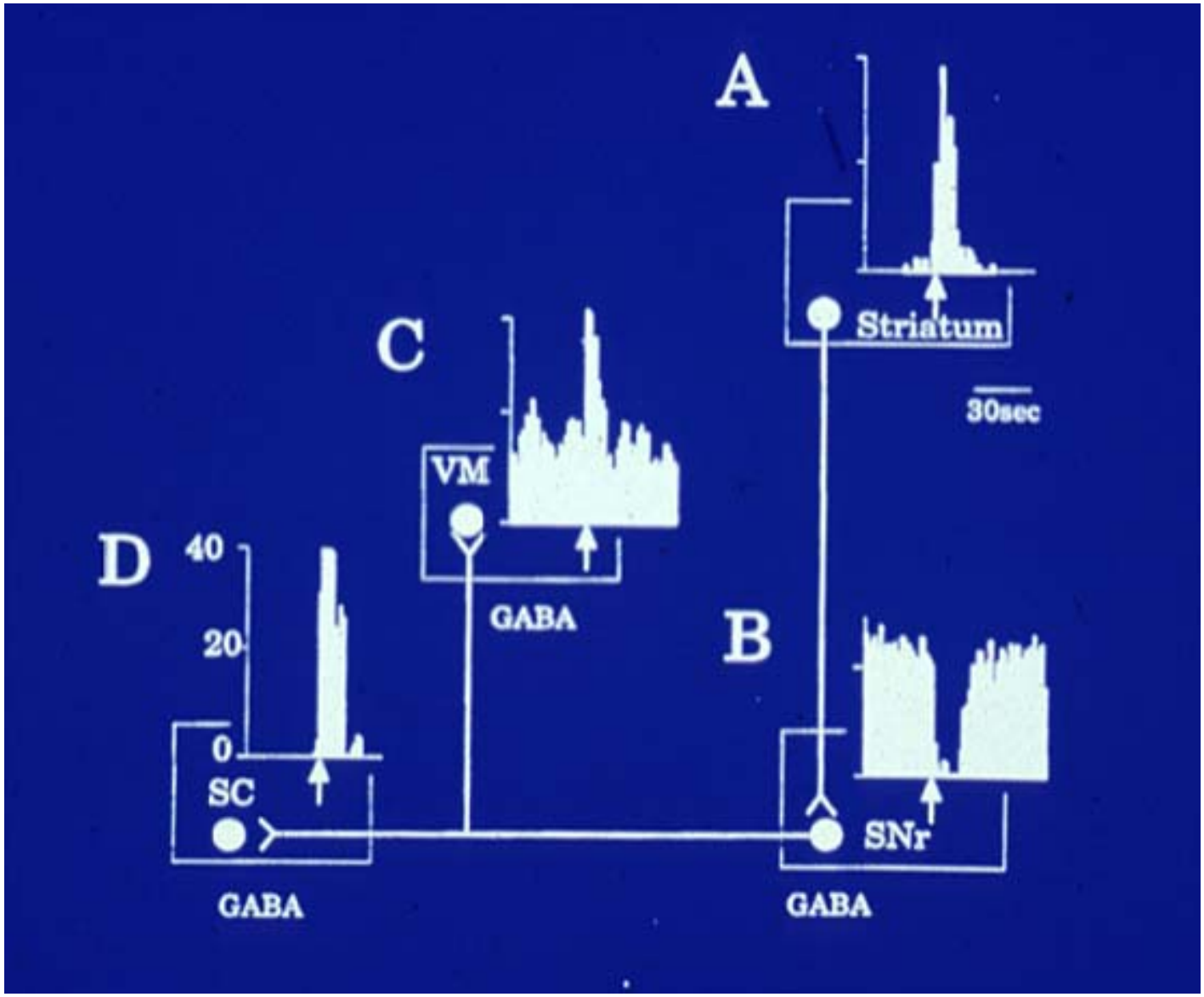


Modified from Wichmann and Delong, Curr Opin Neurobiol. 6:751-758, 1996.

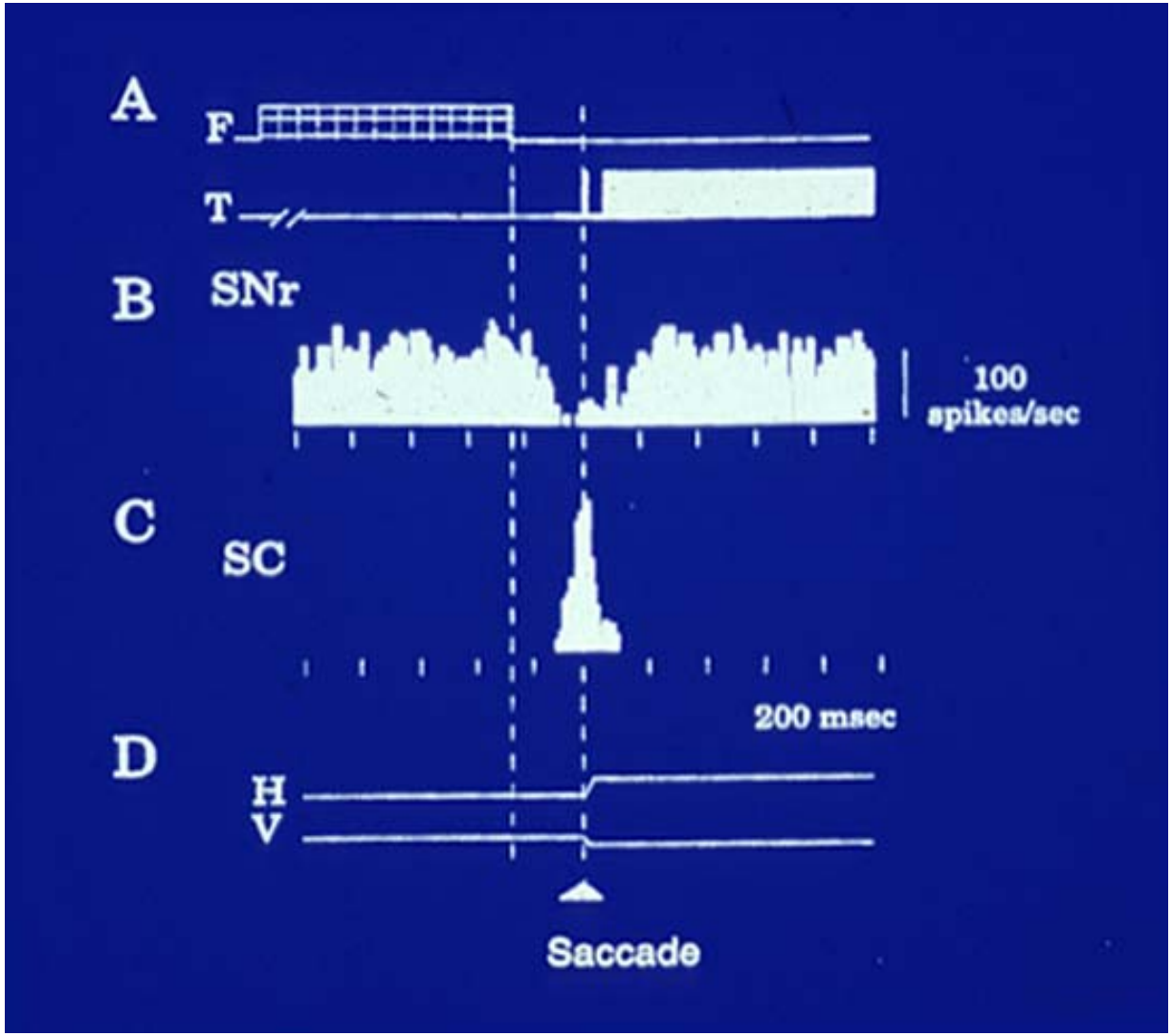

Cortex
Striatum
GPe
STN
GPi/SNr
VA/VL
Brain stem/
Spinal cord
Direct pathway:
facilitates
movement
Excitation (glutamate)
Inhibition (GABA)
Disinhibition
* tonically active
~100 Hz
Modified from Wichmann and Delong,
Curr Opin Neurobiol. 6:751-758, 1996.

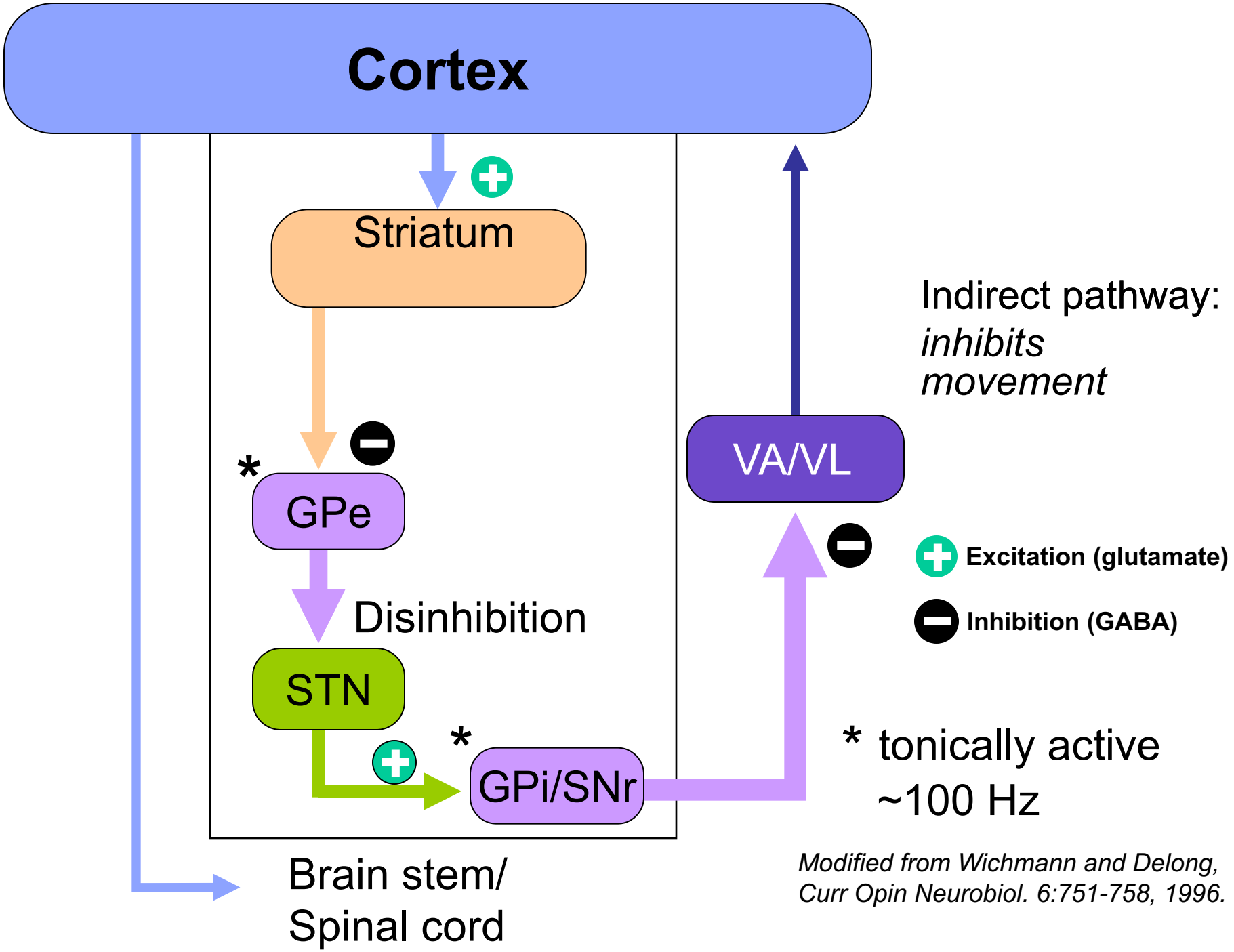


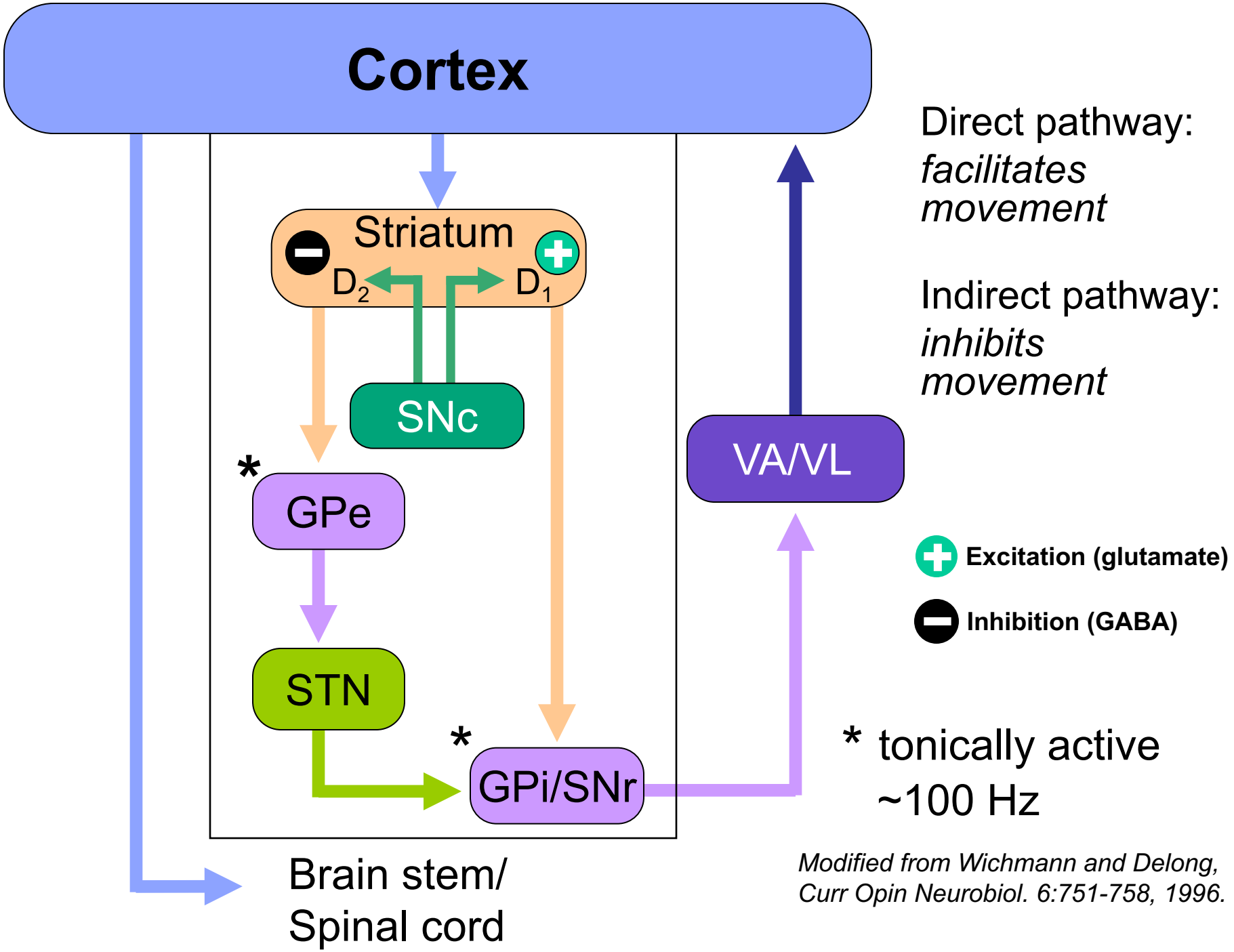
Patterns of activity when glutamate is applied in striatum



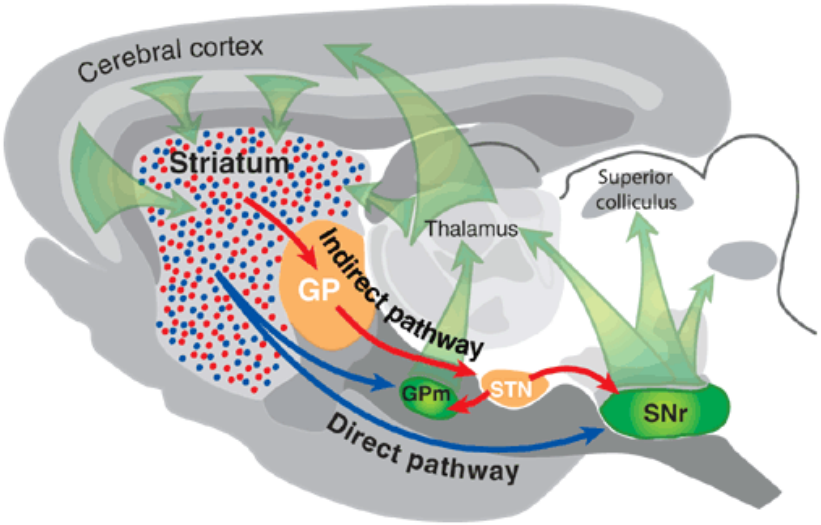
Patterns of activity during motor behavior

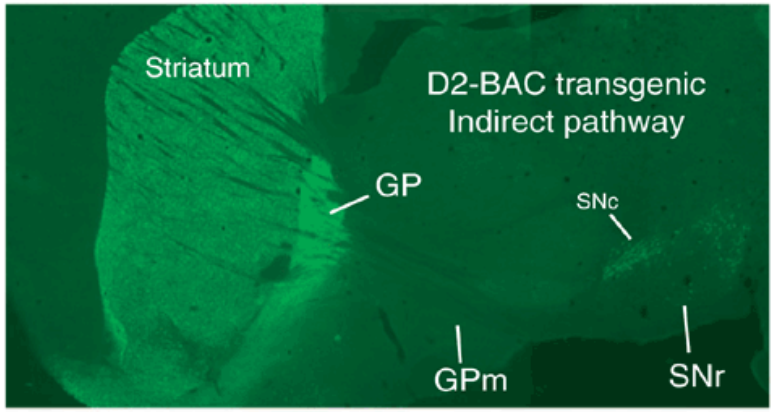


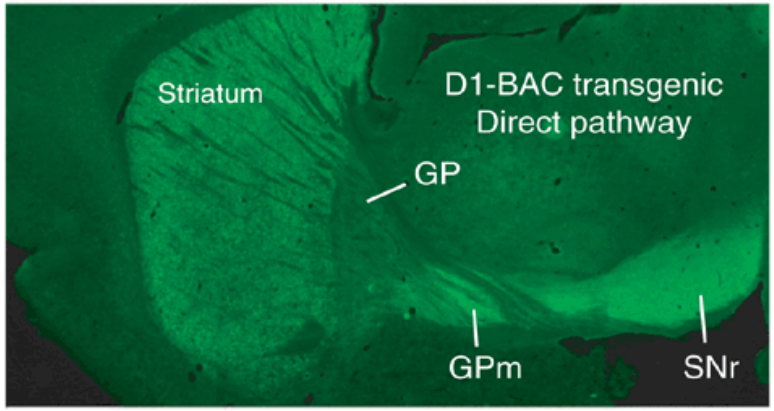

Cortex
Striatum
GPe
Disinhibition
STN
GPi/SNr
VA/VL
Brain stem/
Spinal cord
Indirect pathway:
inhibits
movement
Excitation (glutamate)
Inhibition (GABA)
* tonically active
~100 Hz
Modified from Wichmann and Delong,
Curr Opin Neurobiol. 6:751-758, 1996.


Cortex
Striatum
D2
D1
SNc
GPe
*
STN
GPi/SNr
*
VA/VL
Brain stem/
Spinal cord
Direct pathway:
facilitates
movement
Indirect pathway:
inhibits
movement
Excitation (glutamate)
Inhibition (GABA)
* tonically active
~100 Hz
Modified from Wichmann and Delong,
Curr Opin Neurobiol. 6:751-758, 1996.

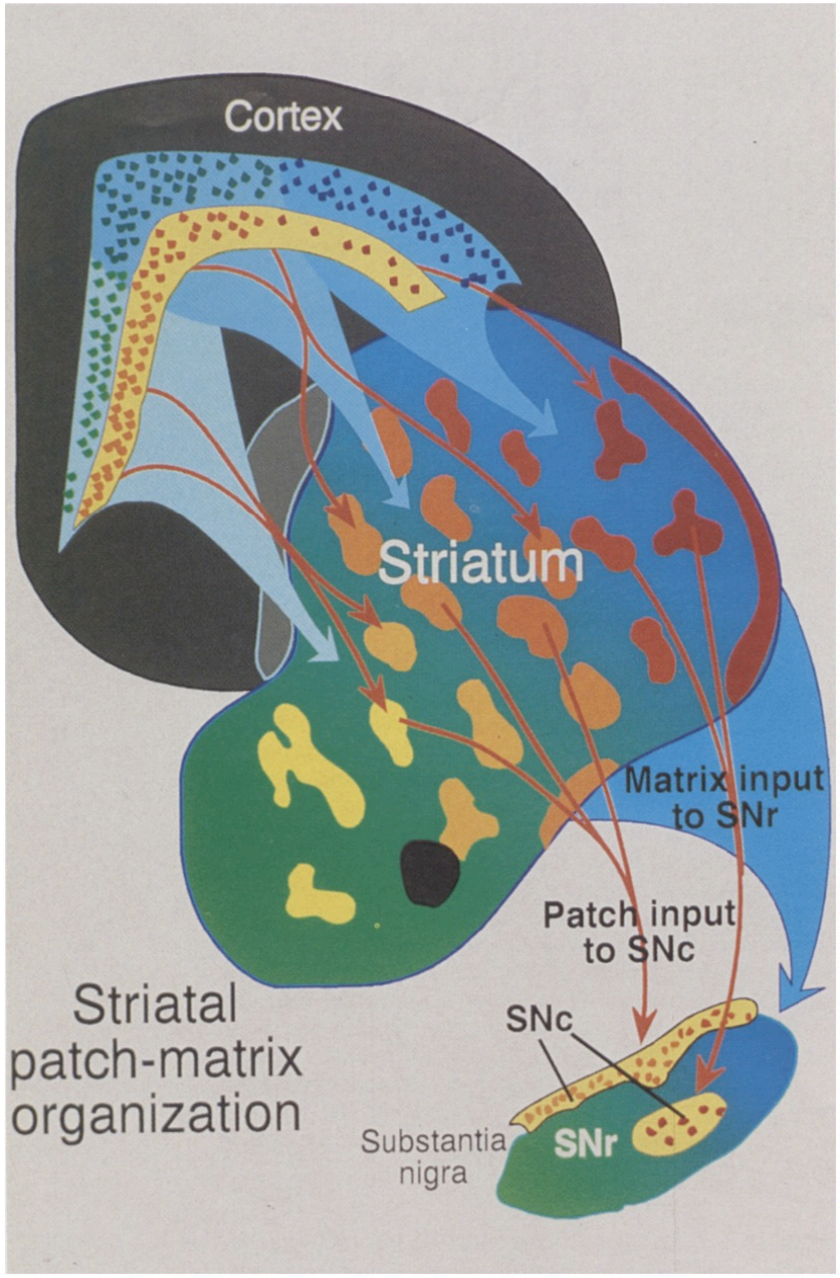
Direct and indirect pathways in mouse brain







Gerfen *Nat. Neurosci.* 2006



Patch-matrix compartmental organization of corticostriatal and striatonigral pathways

Corticostriatal neurons deep in layer V provide -> patches

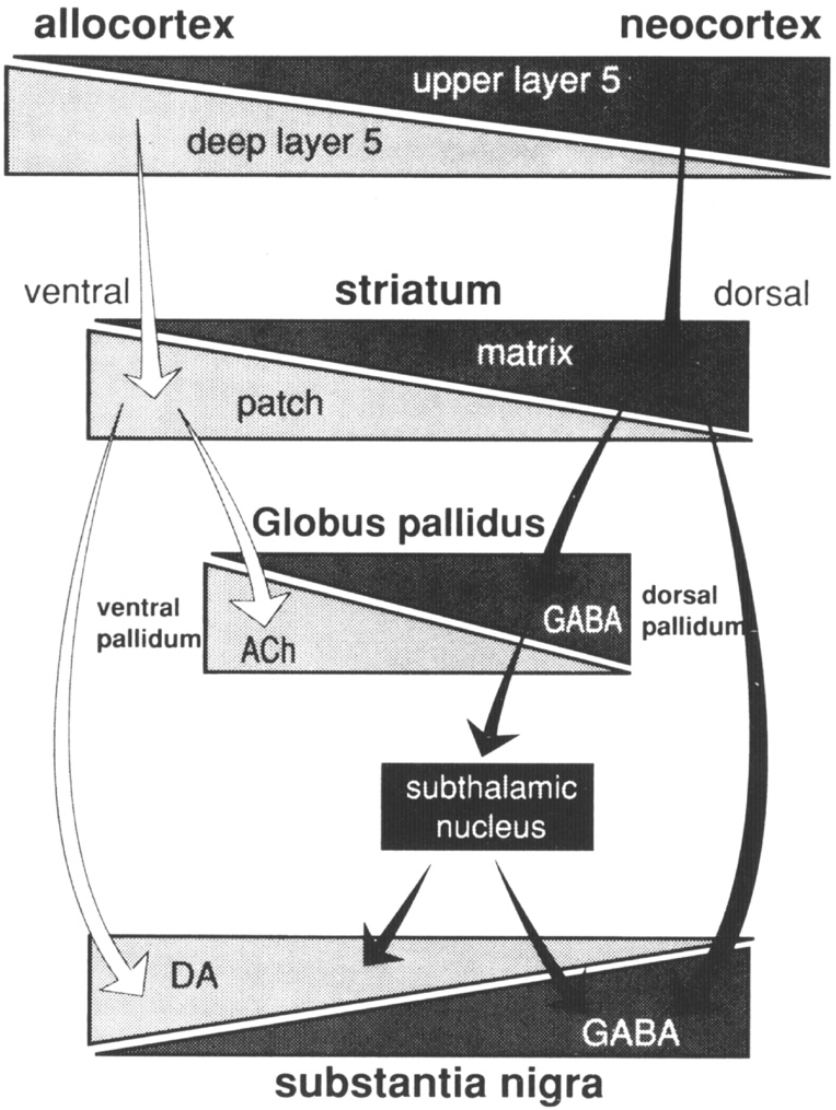
Superficial layer V neurons -> matrix.

Patch MSNs -> DAergic neurons in SNc

Matrix MSNs -> GABAergic neurons in SNr

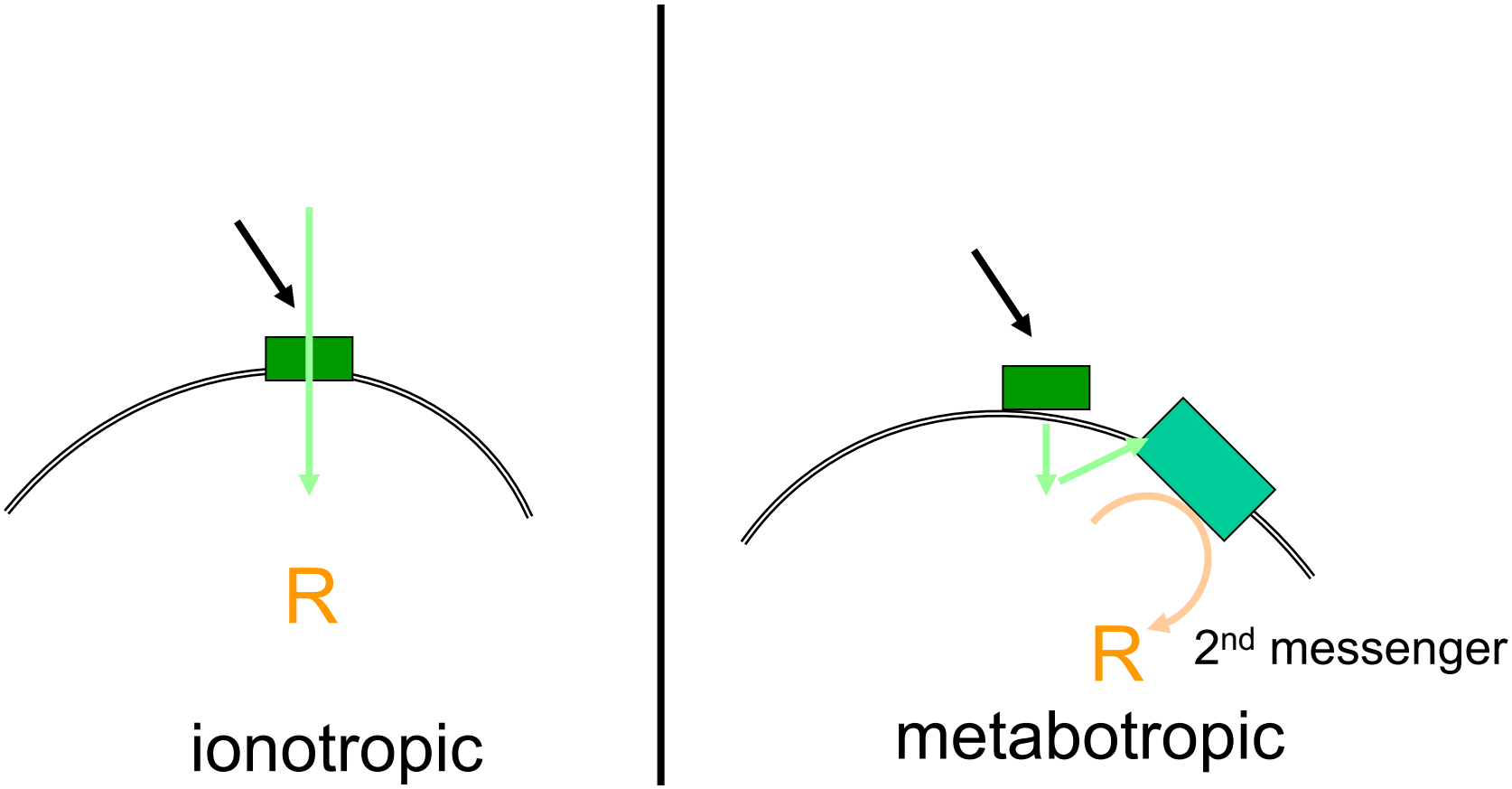
Gerfen *TINS* 1992

Patch-matrix organization of corticostriatal and striatonigral pathways

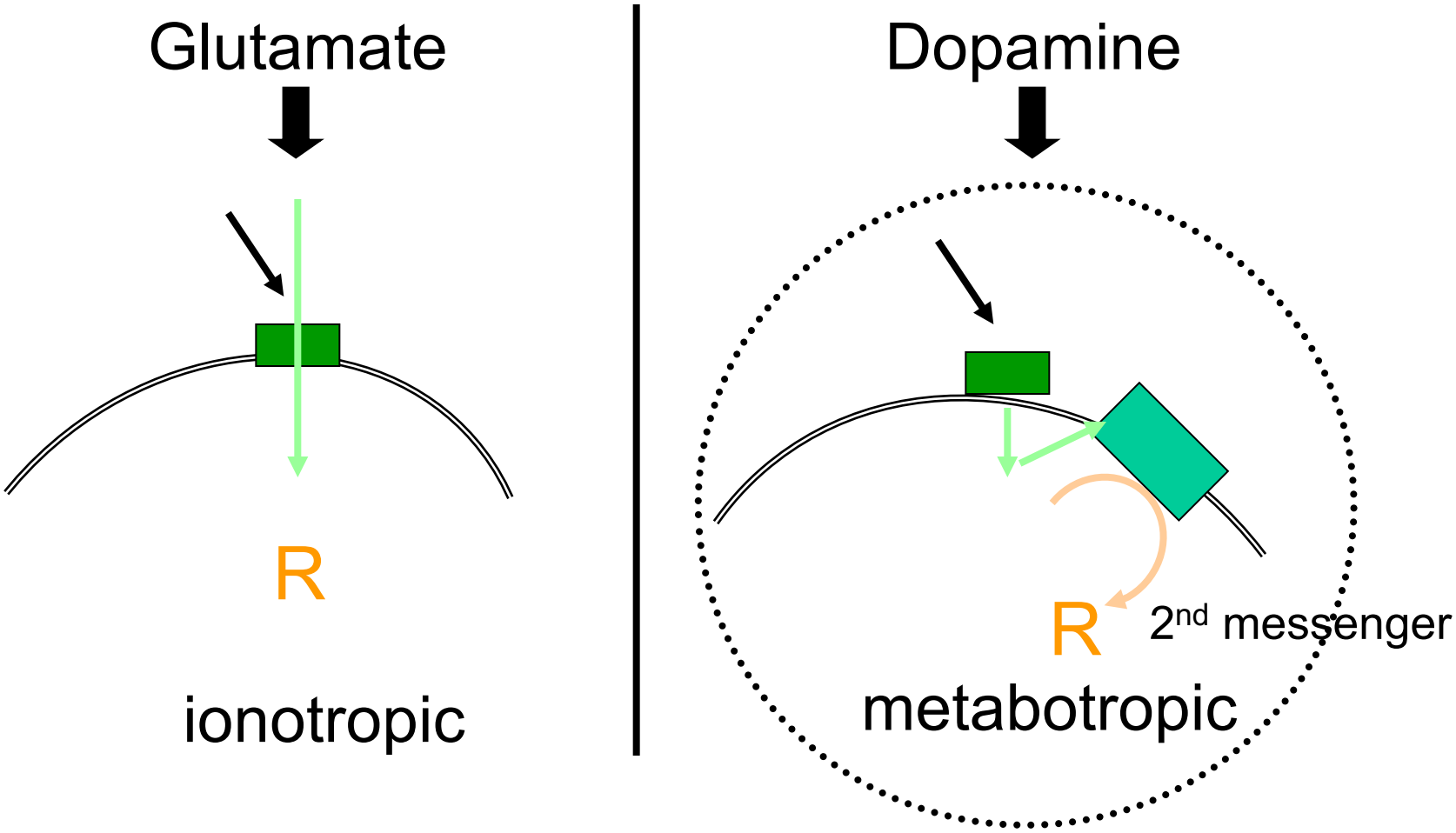


Gerfen *TINS* 1992

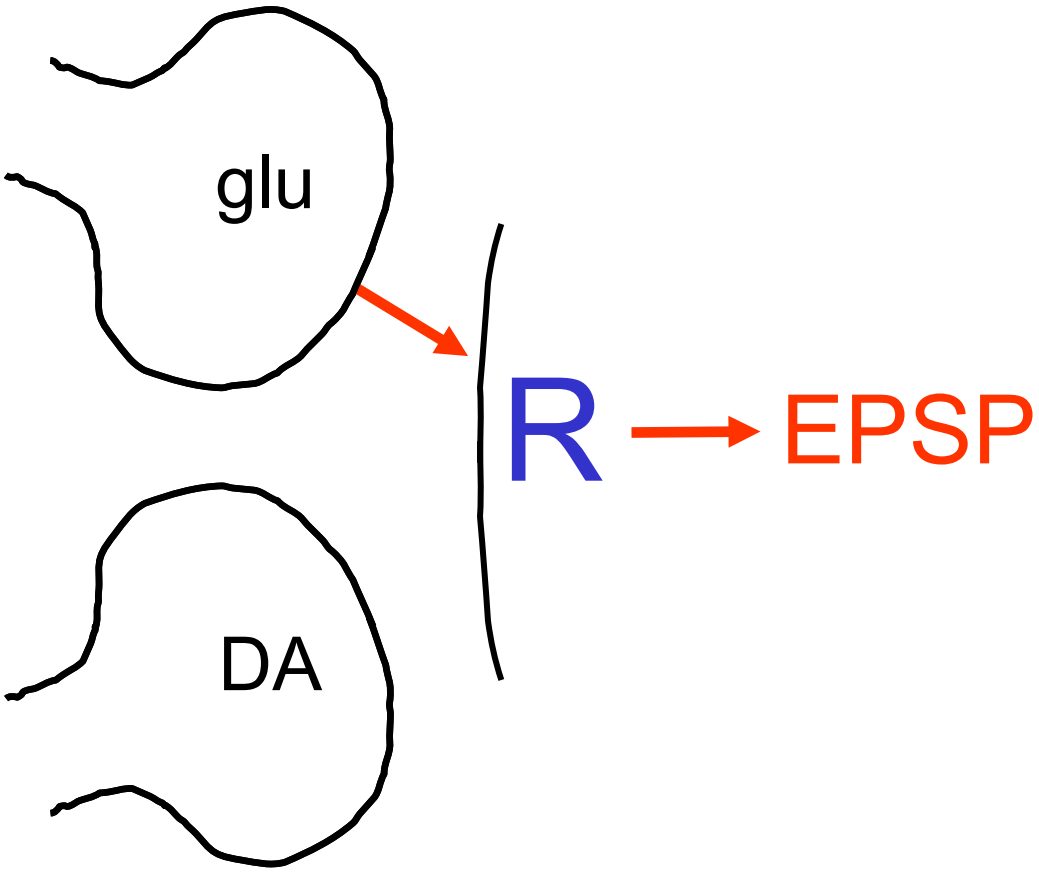
Ionotropic *versus* metabotropic



Ionotropic *versus* metabotropic

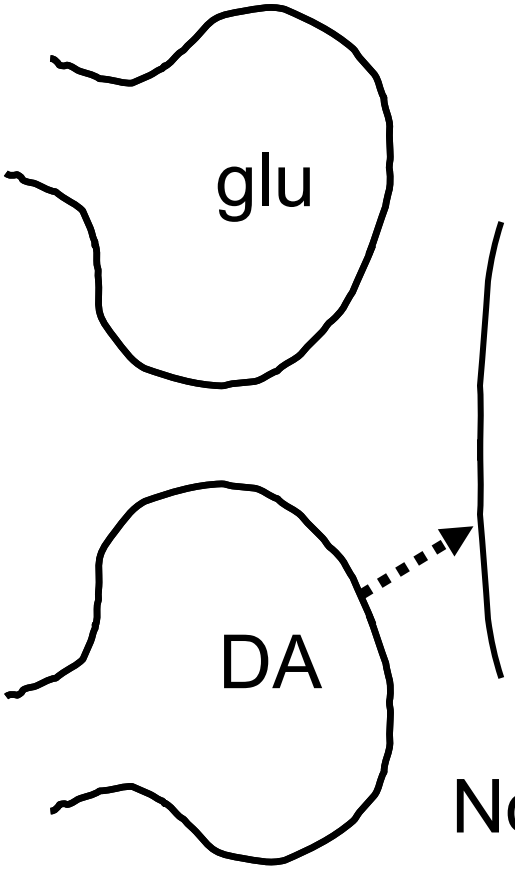


Direct transmission *vs.* modulation



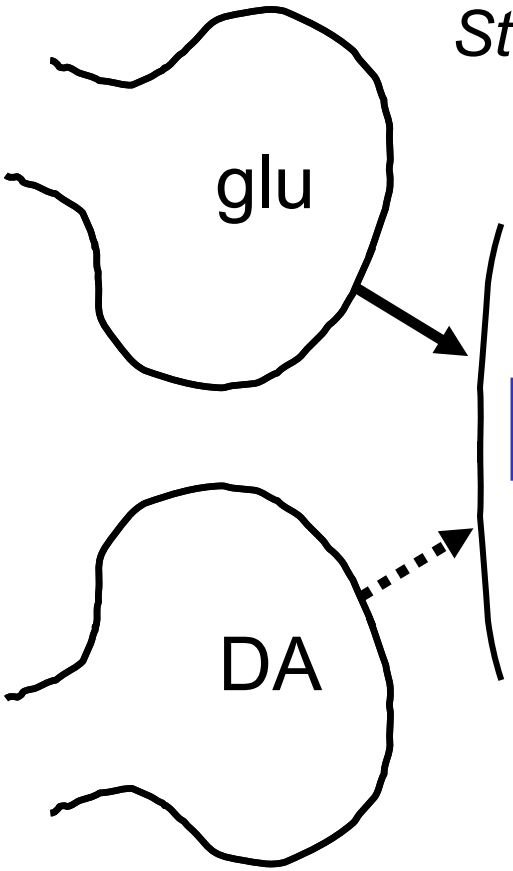
Direct transmission

Direct transmission *vs.* modulation



No direct effect of DA

Direct transmission *vs.* modulation



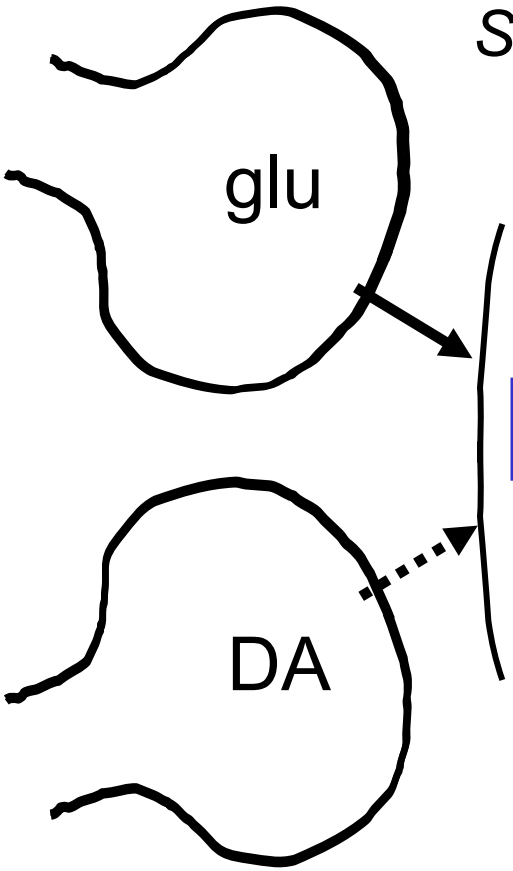
Striatal medium spiny neuron

enhanced
or diminished
response

D1-Rs in the direct pathway:
1) increase GluR phosphorylation
2) alters ionic conductances
to amplify cortical input

Modulation

Direct transmission *vs.* modulation



Striatal medium spiny neuron

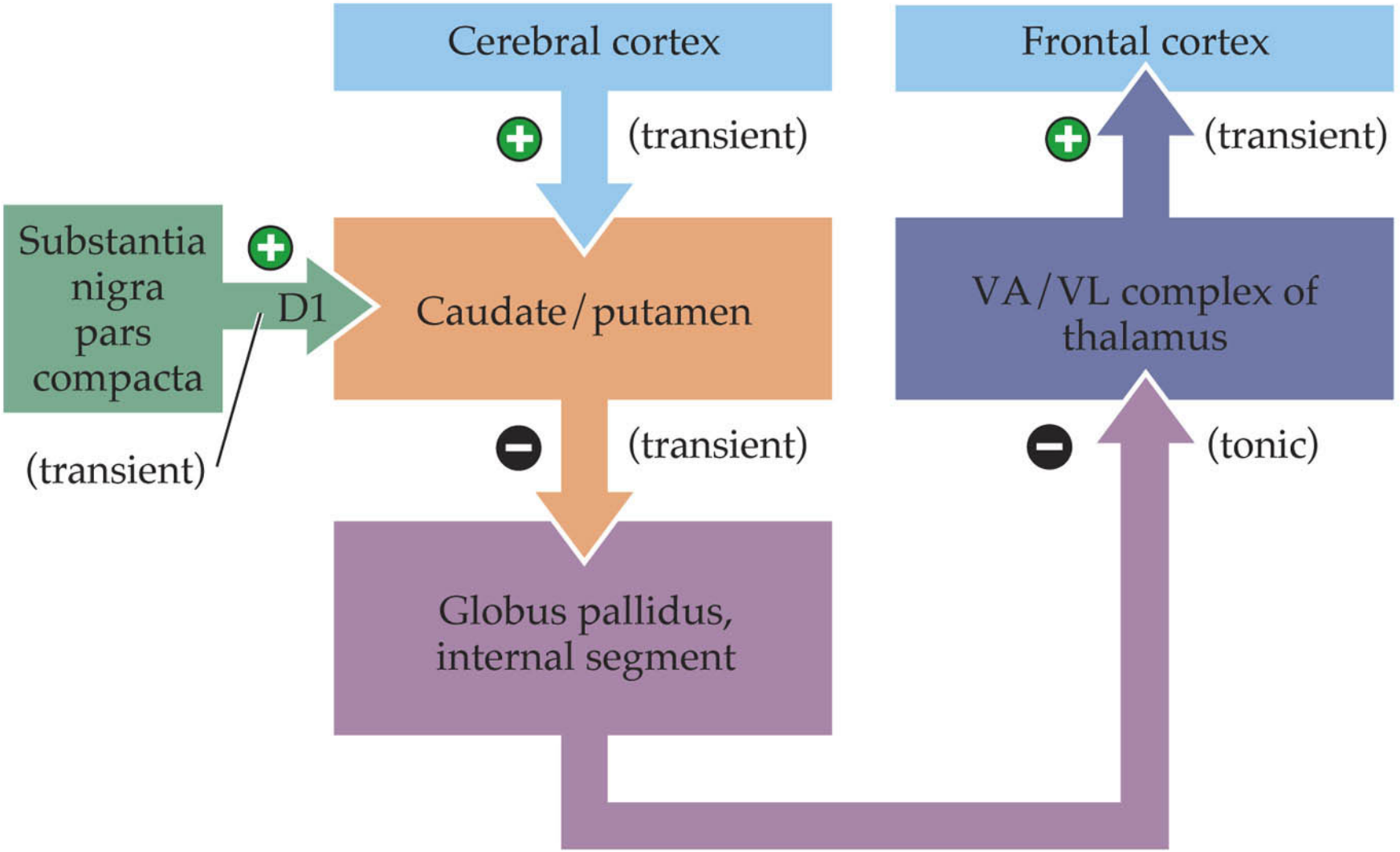
R

enhanced
or ***diminished***
response

D2-Rs in the indirect pathway:
1) increase GluR phosphorylation
2) alters ionic conductances
to dampen cortical input

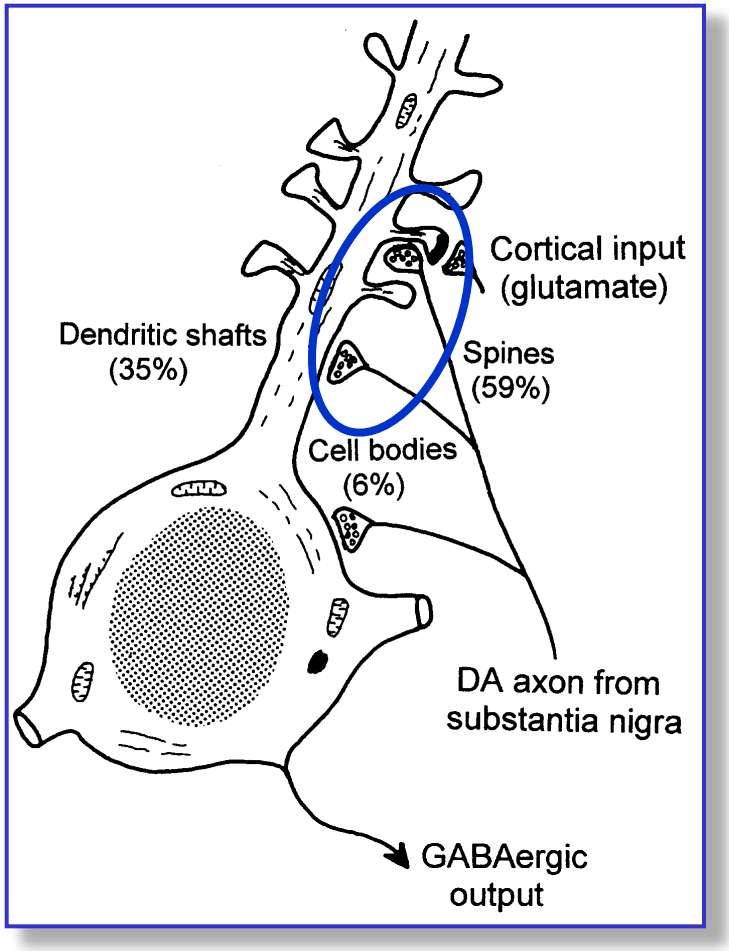
Modulation

Direct pathway



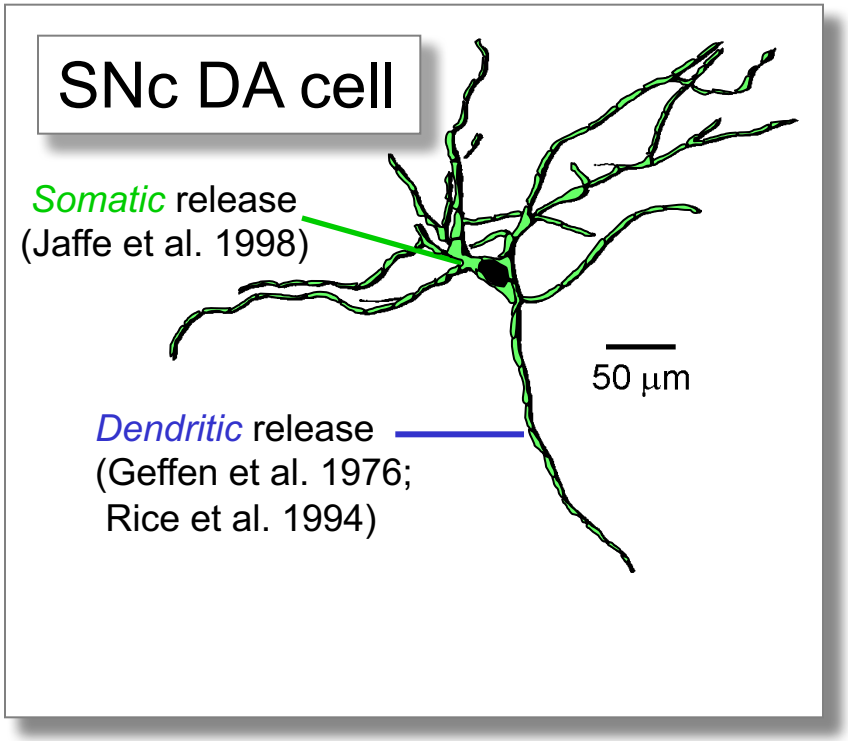
Release of DA in substantia nigra, as well as in striatum is required for control of movement by the basal ganglia

Synaptic DA release in striatum

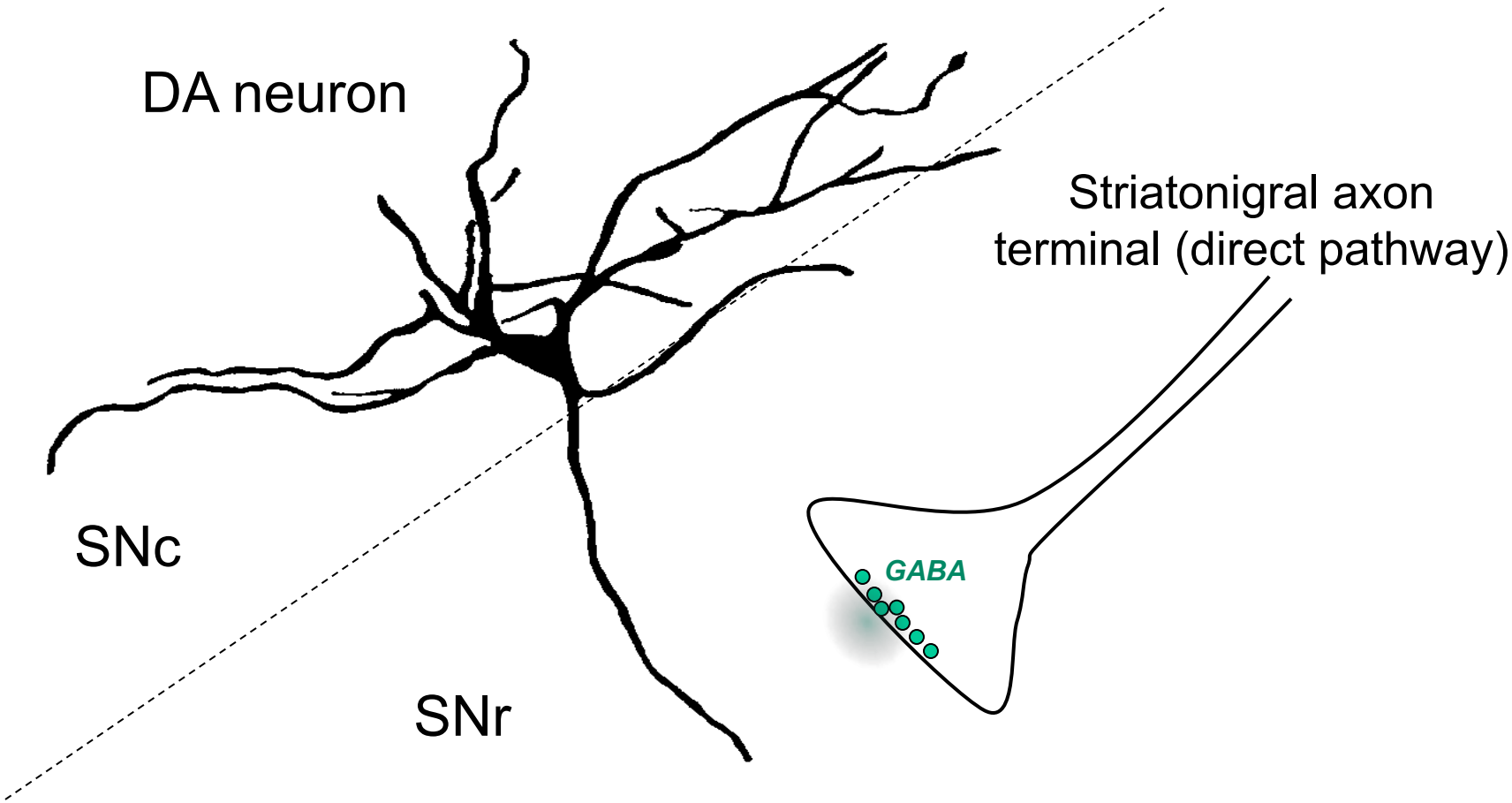


Smith and Bolam 1990

Somatodendritic DA release in SNc

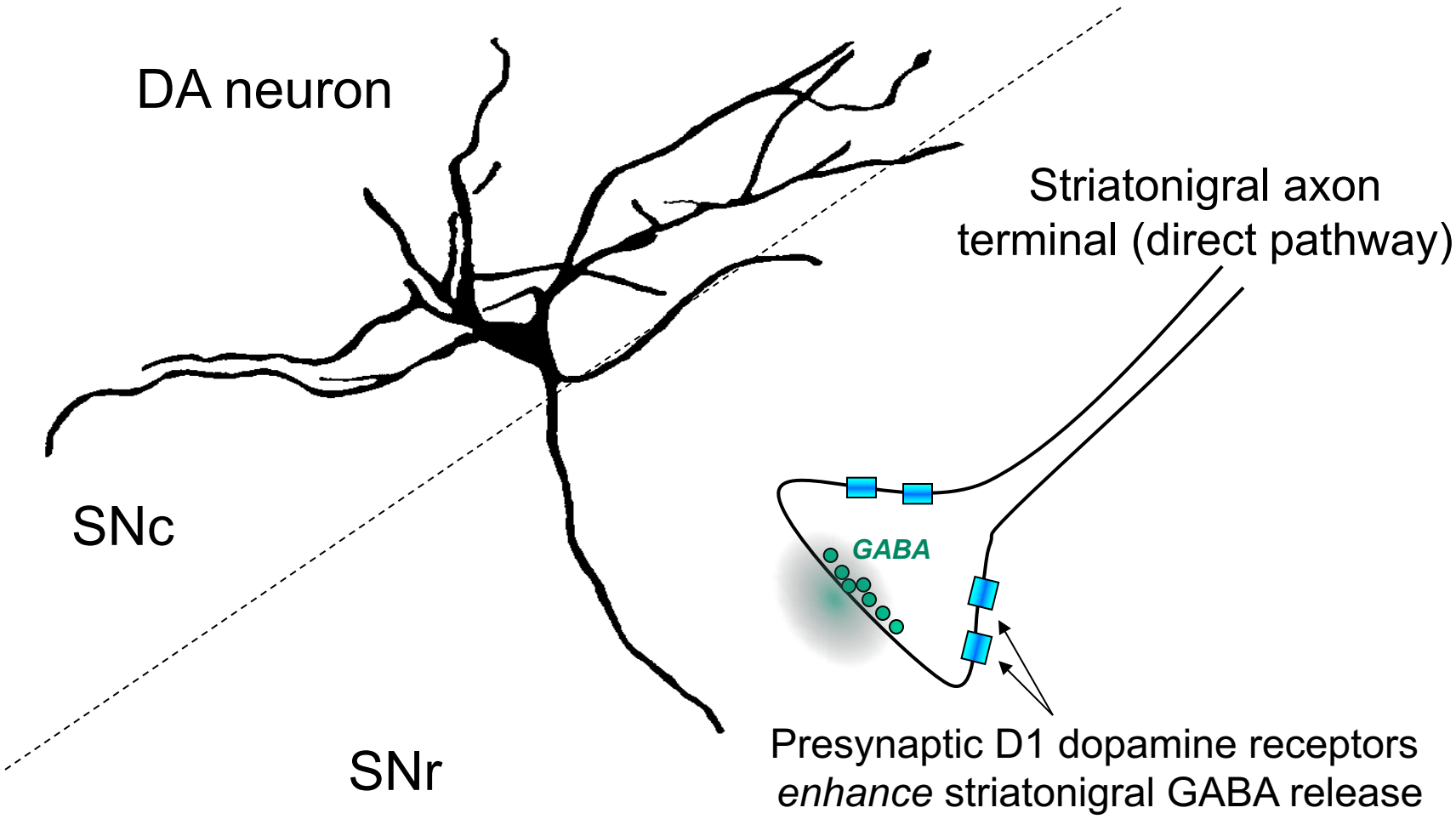


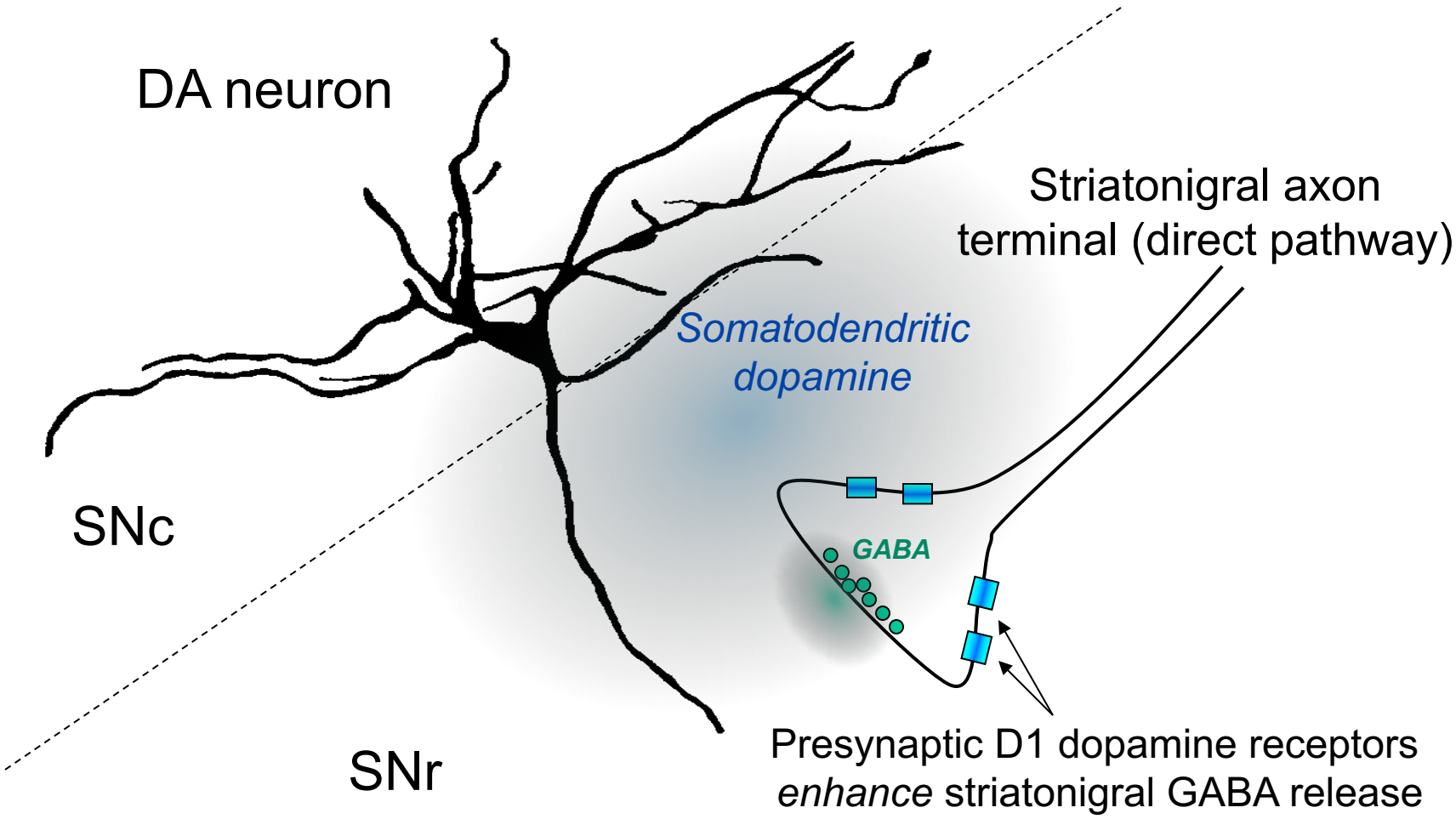
modified from Fallon et al. 1978



SNr output neurons

(GABAergic, tonically active, project to thalamus)
are inhibited by the direct, striatonigral pathway,
leading to ***disinhibition*** of the thalamus and ***facilitation of movement***

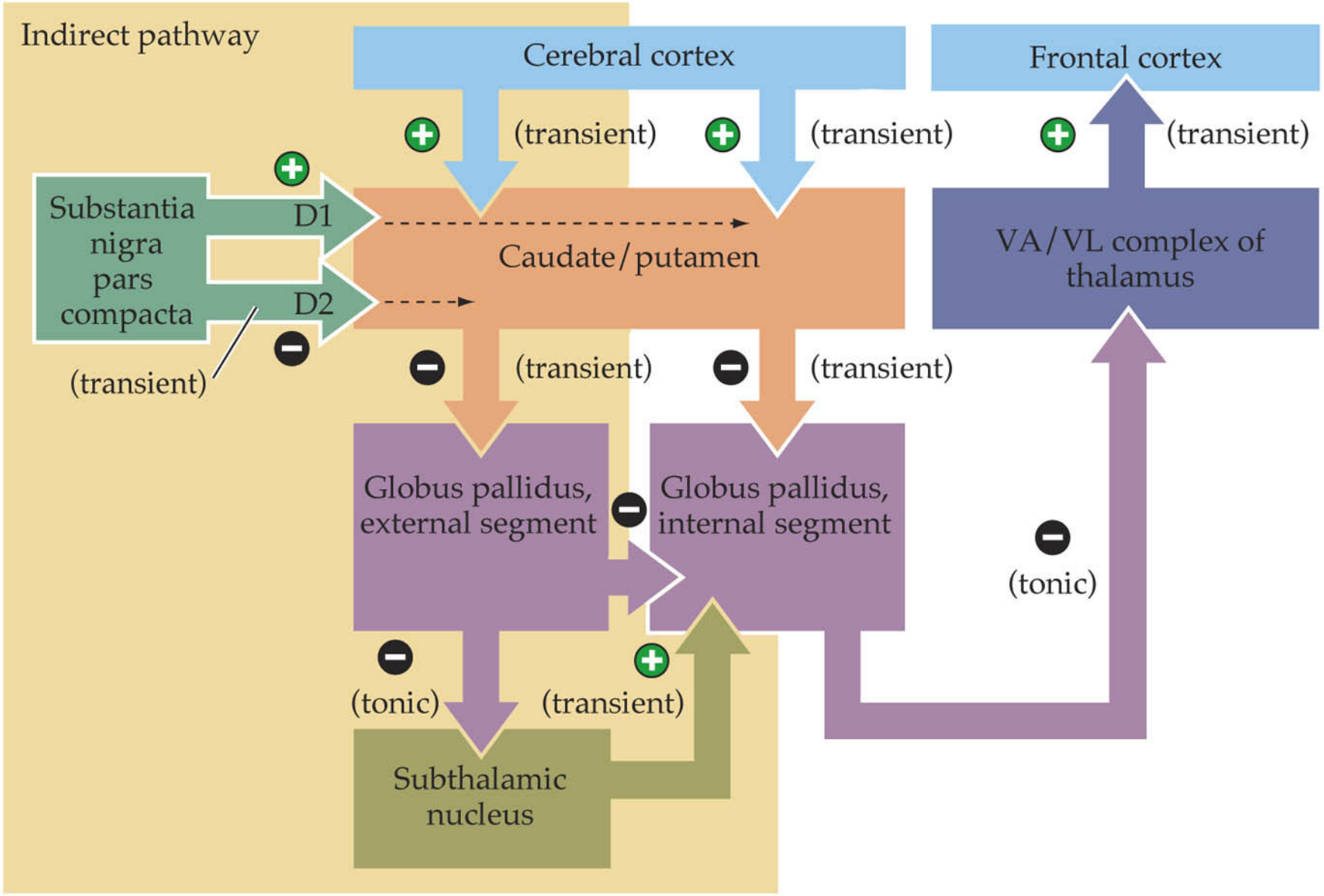

DA neuron
Striatonigral axon terminal (direct pathway)
SNc
GABA
SNr
Presynaptic D1 dopamine receptors
enhance striatonigral GABA release



Somatodendritic DA release, therefore, *enhances* the effect of the direct striatonigral pathway to facilitate movement


TEDx CCS
x = independently organized TED event

Direct and indirect pathways



Motor behavior is determined by the balance between direct/indirect striatal outputs

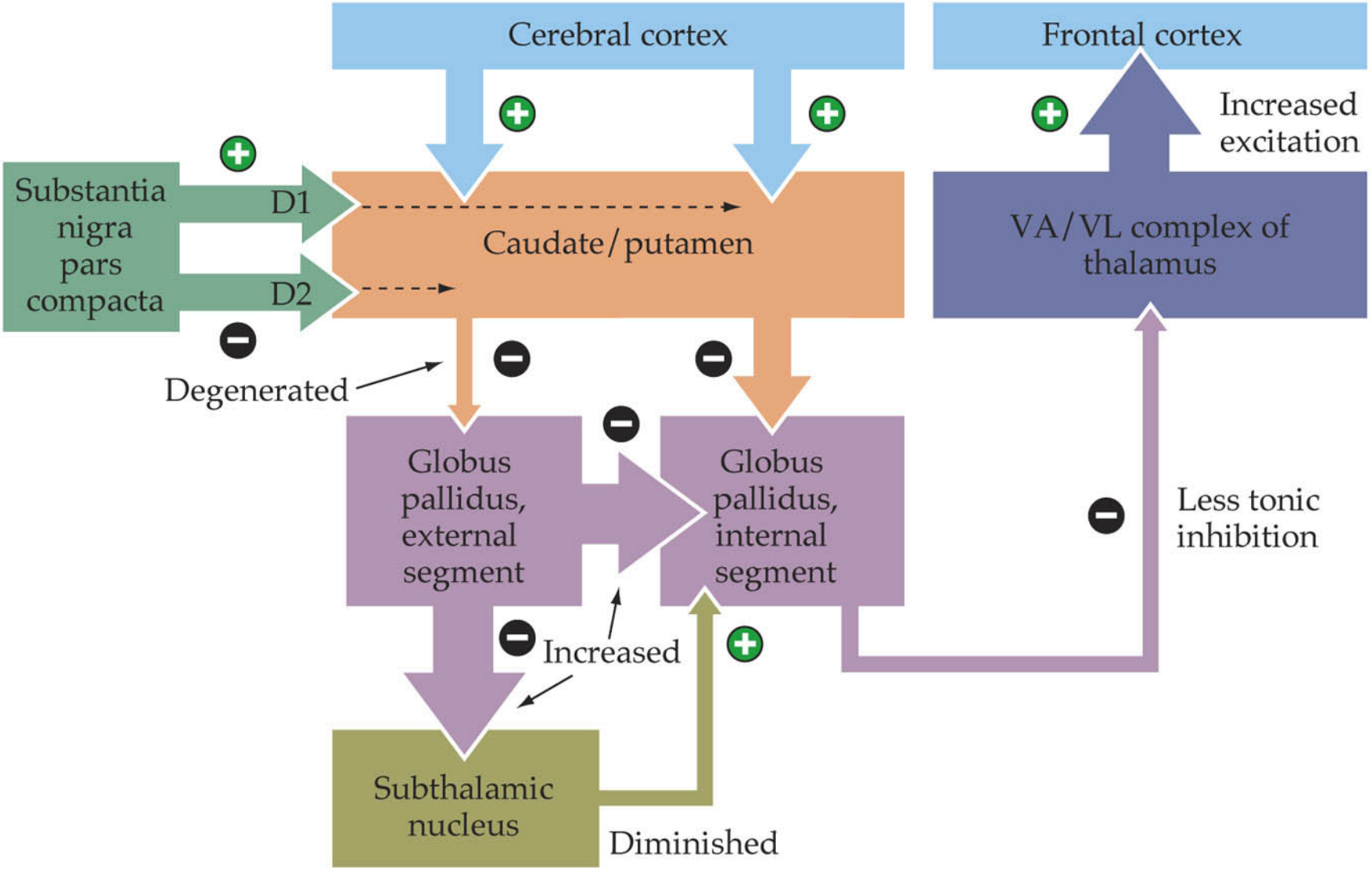
Hypokinetic disorders

- **insufficient direct** pathway output
- **excess indirect** pathway output

Hyperkinetic disorders

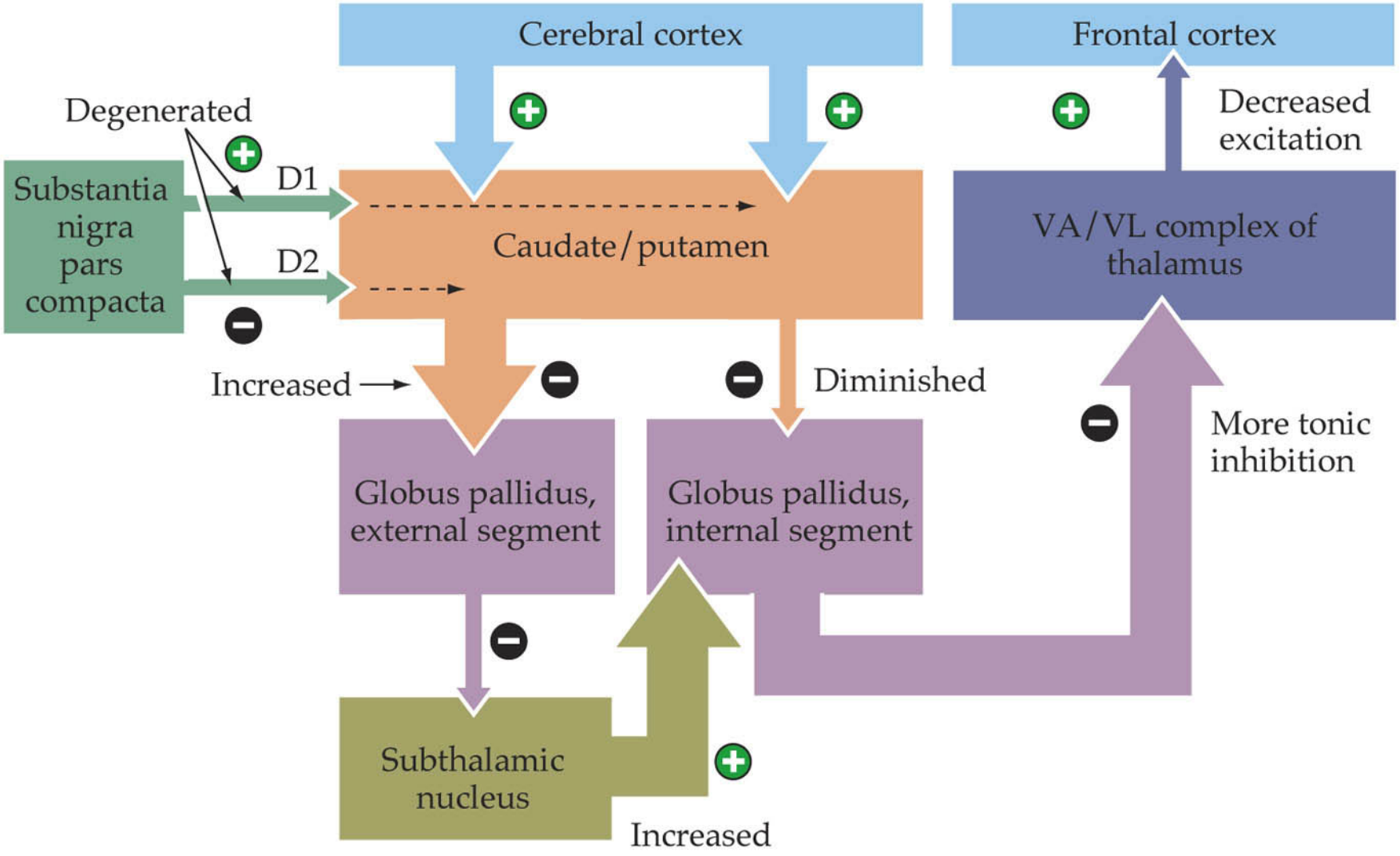
- **excess direct** pathway output
- **insufficient indirect** pathway output

Huntington's disease



NEUROSCIENCE, Third Edition, Figure 17.10 (Part 2)

Parkinson's disease



Parkinson's disease

Michael J. Fox

Muhammad Ali

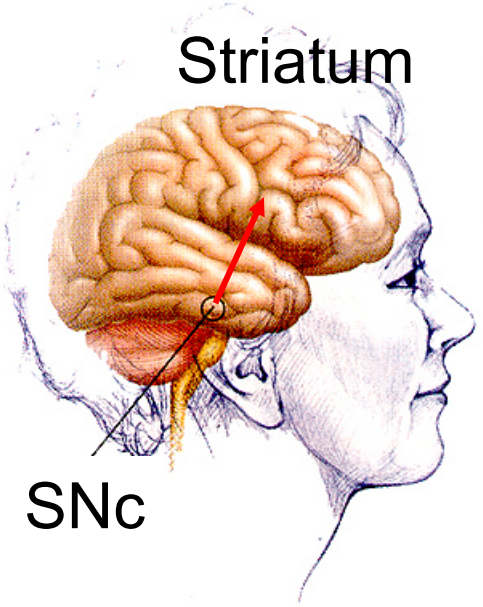
Pope John Paul II

Janet Reno

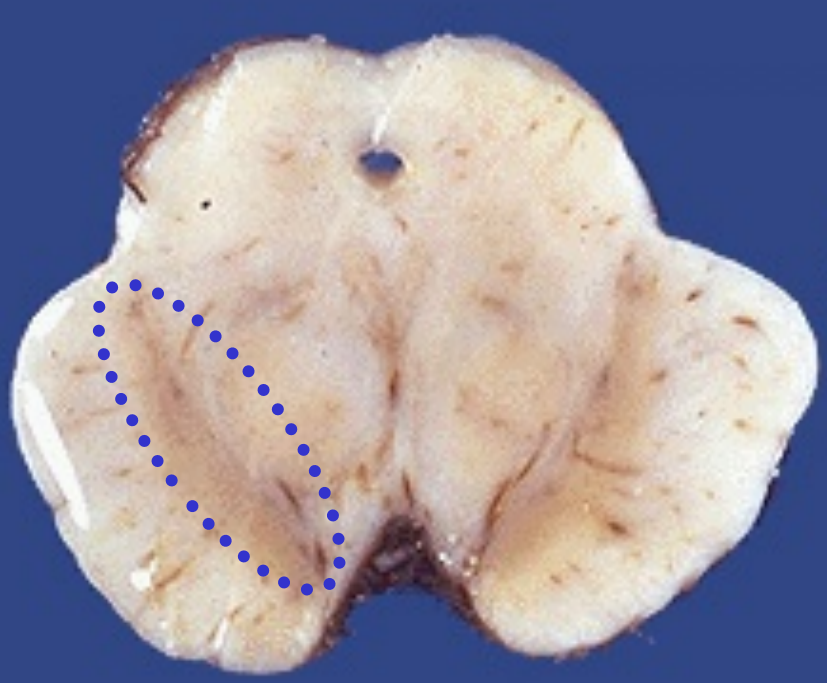
Katherine Hepburn

Pathophysiology

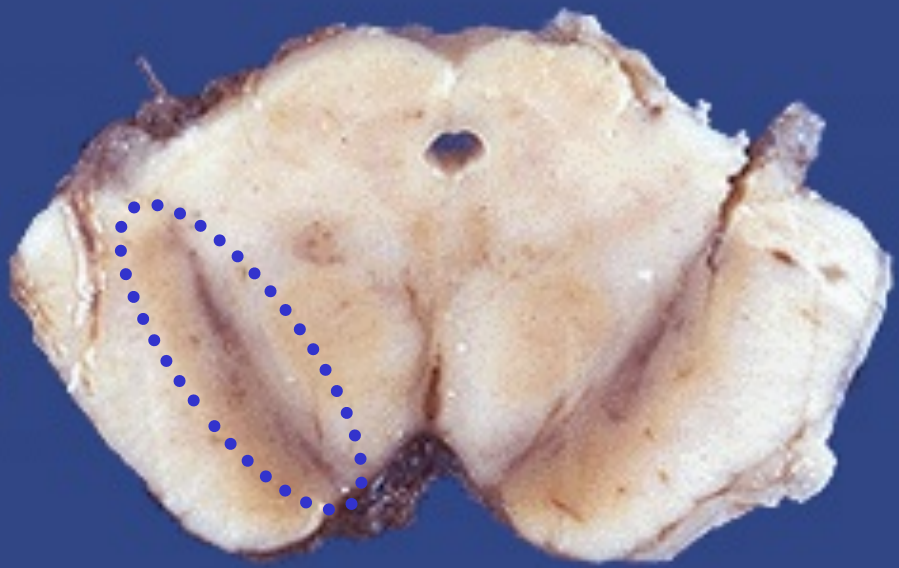
Primary: loss of nigrostriatal DA projection



Human midbrain



Parkinson's disease



Normal