Basal Ganglia

Functional Anatomy from Movement to Cognition

Aidine Omidvar, *MD*

Assistant Professor of Neurosurgery

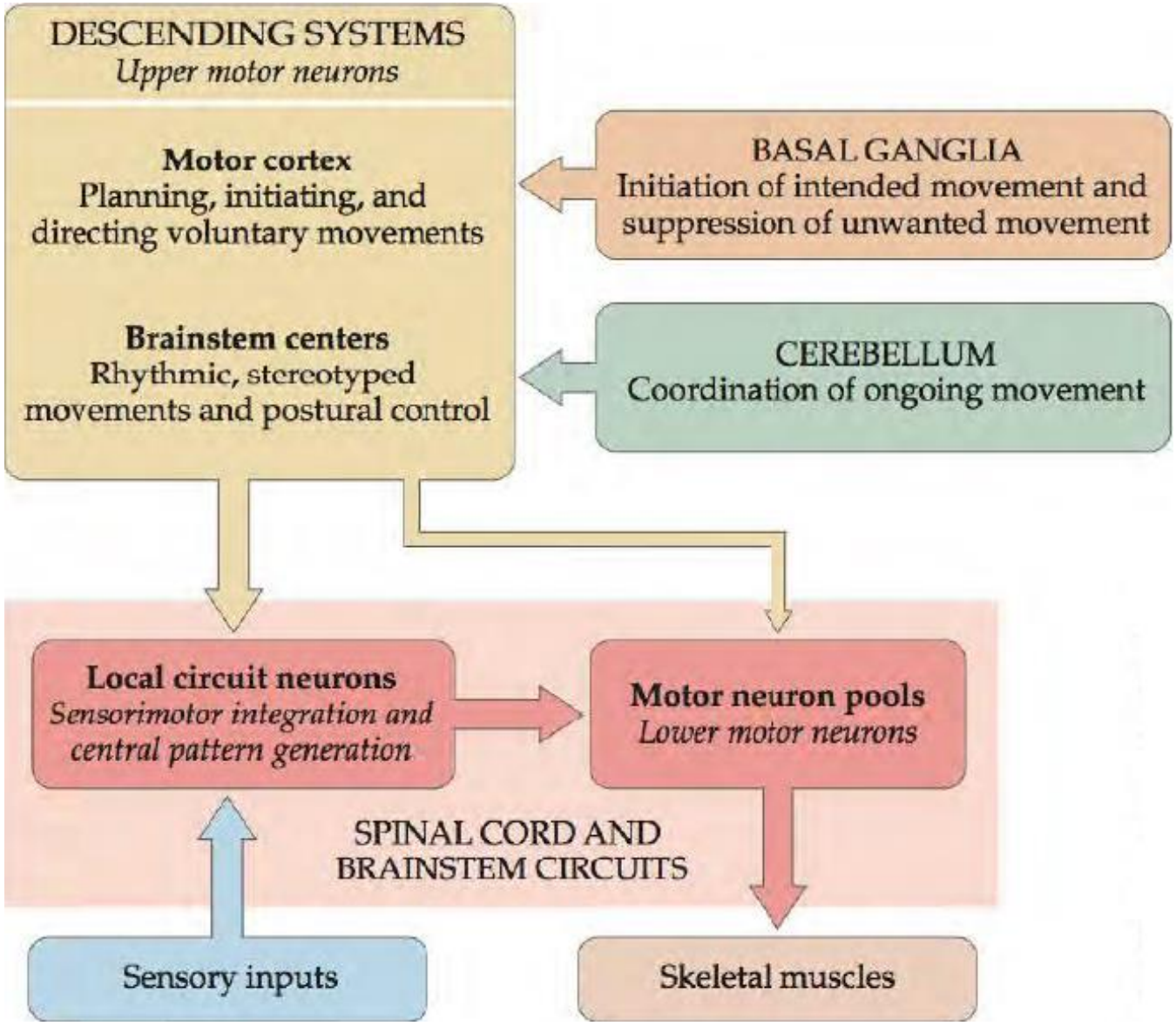
Kashan University of Medical Sciences

NeuroMaPC

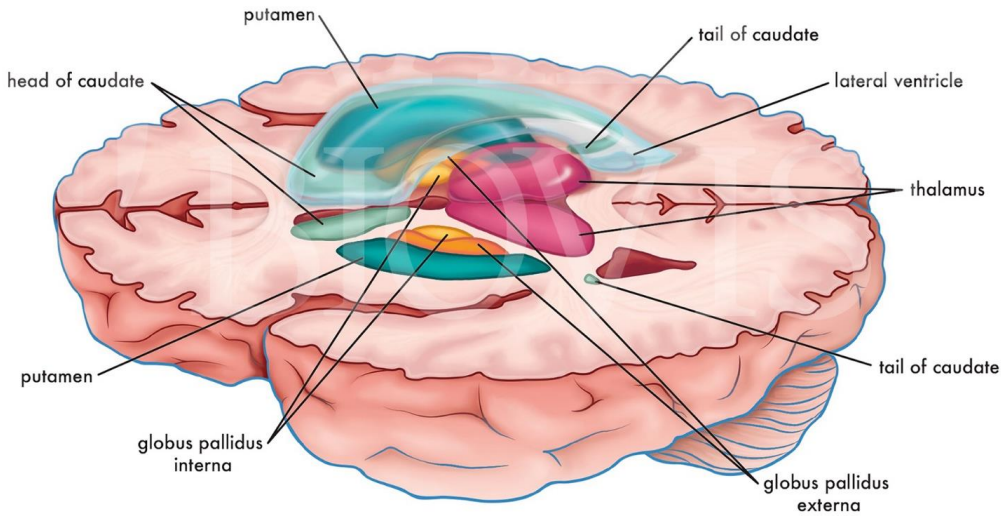
Center for Neuromodulation and Pain

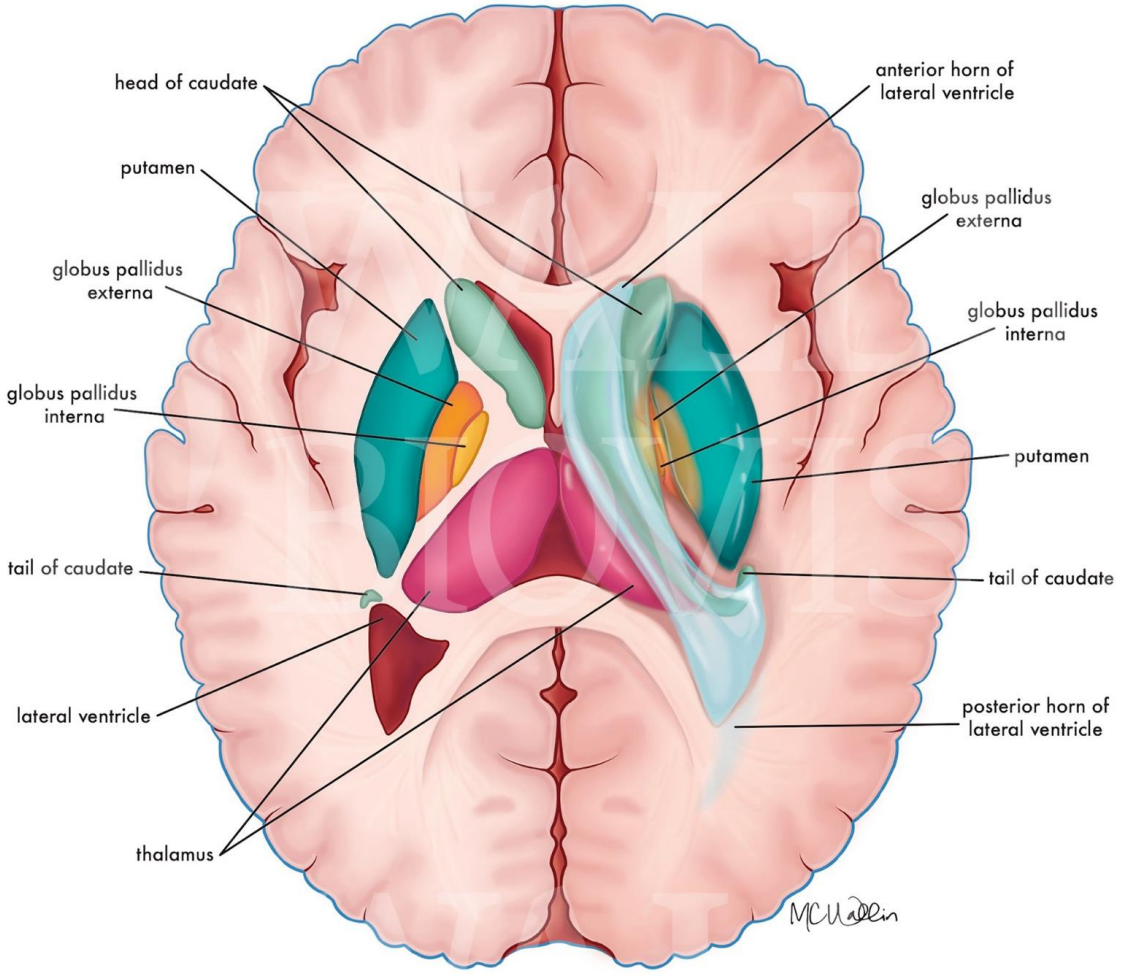
دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کاشان

Neural Centers for Movement



The Basal Ganglia





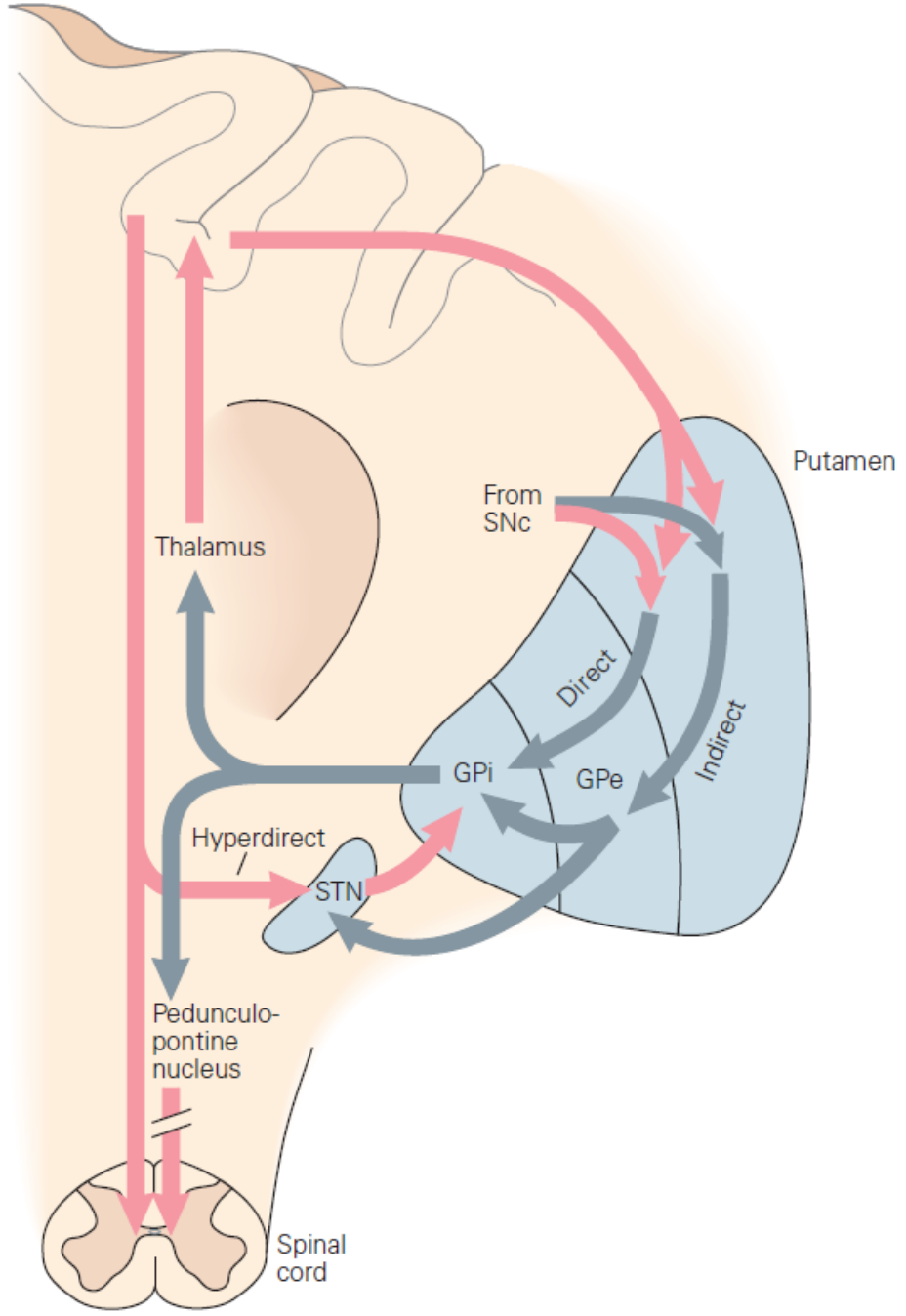
The Basal Ganglia

- **Striatum**
  - **Dorsal** striatum: Caudate n. + Putamen
  - **Ventral** striatum: Nucleus accumbens + Olfactory Tubercle
- **Pallidum**
  - **GPi** and **GPe**
- **Subthalamic nucleus**
- **Substantia nigra**
  - **SNc** (pars compacta) + (VTA and RRF)
  - **SNr** (pars reticulata)

The Basal Ganglia

- **Major functions:**
  - **Modulation of behavior** (based on **desirable outcomes**)
    - **Initiation** of intended movement
    - **Suppression** of unwanted movements
  - **Procedural learning and Habit formation**

The Basal Ganglia Functional Circuitry



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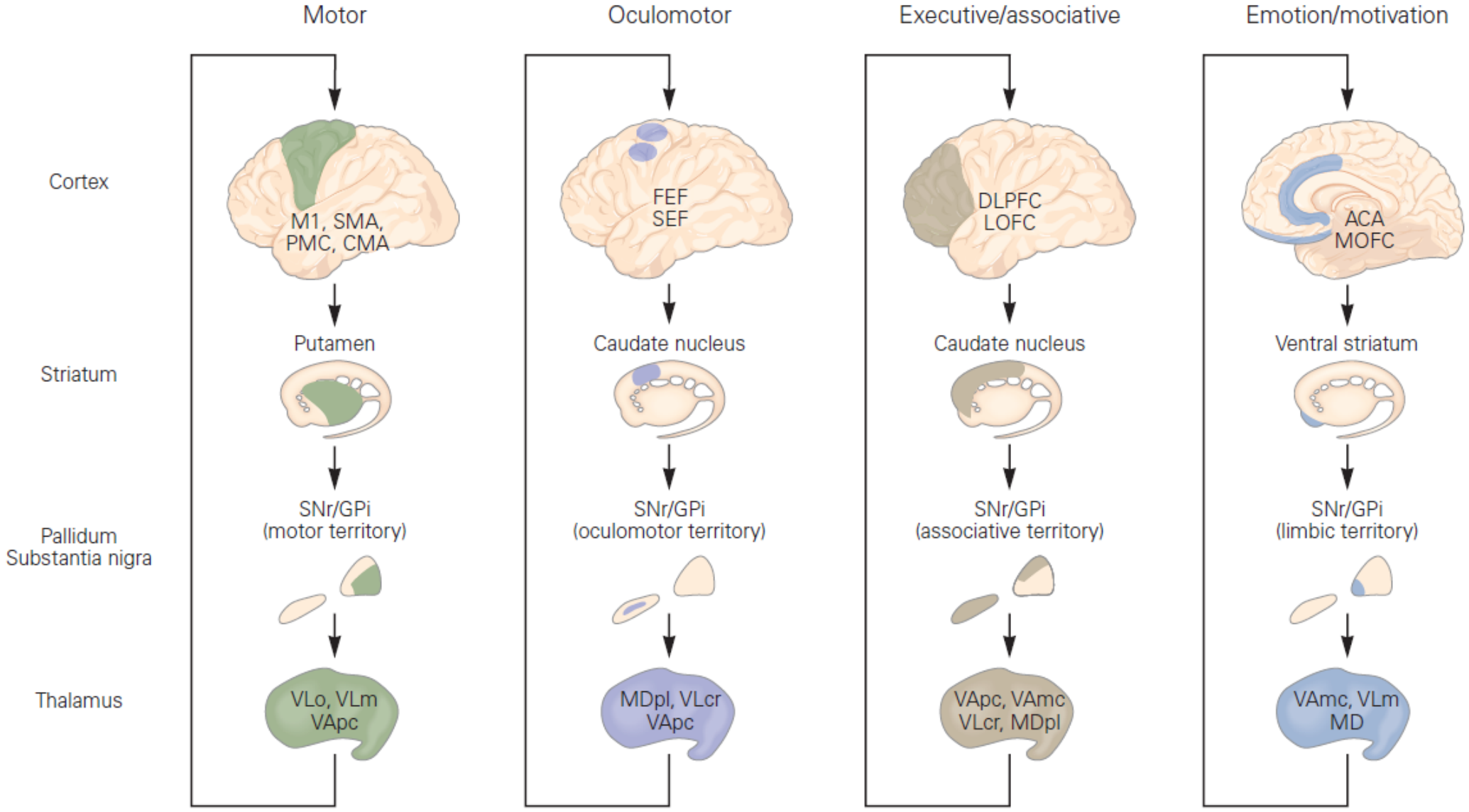

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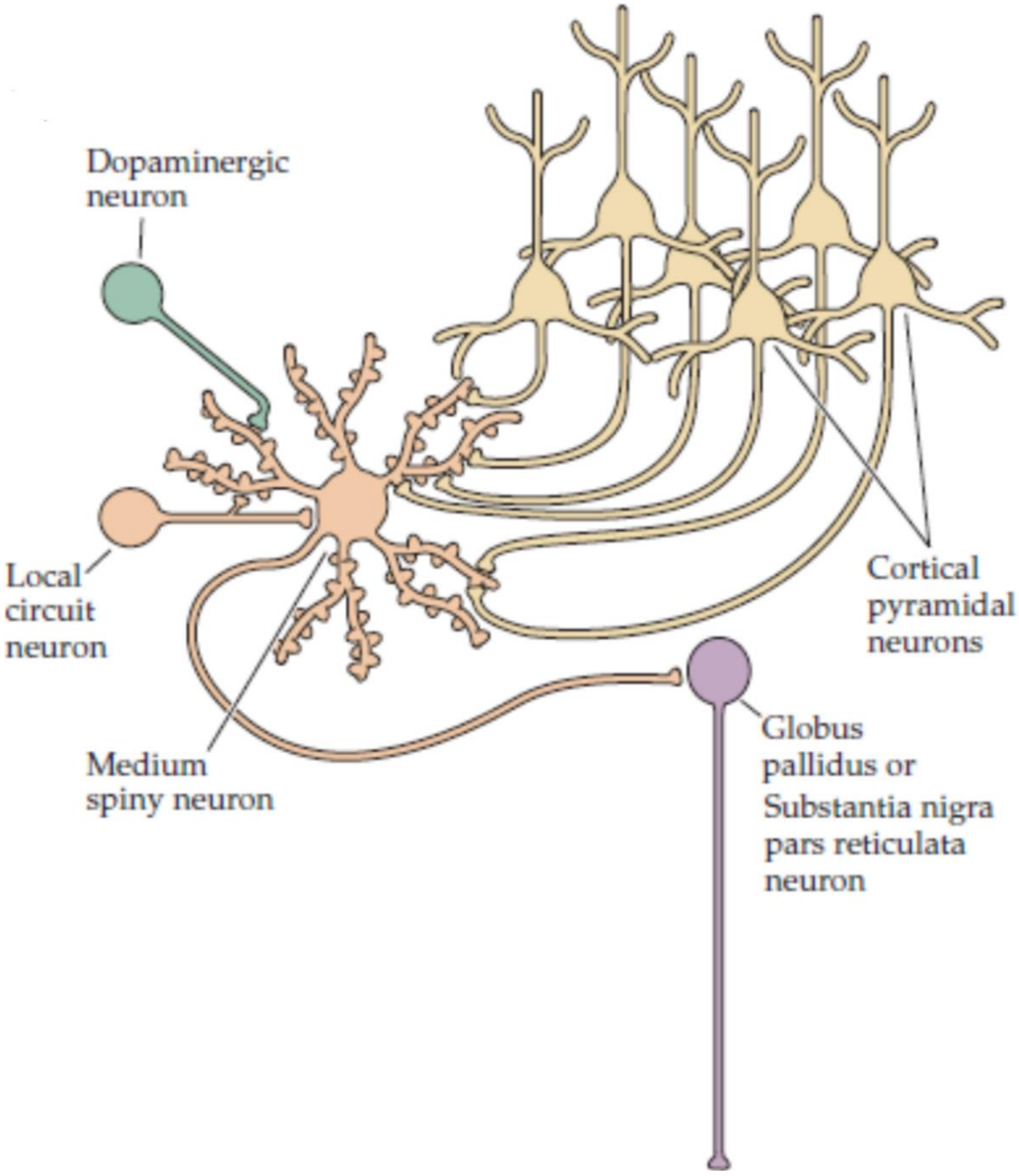
The Striatum

- The **main input structure** of the basal ganglia
- **Cellular organization**
  - Medium spiny neurons (**MSN**) **~** 97%
  - **Interneurons ~** 2-3%
    - Cholinergic
    - GABAergic
    - Thyrosine-hydroxylase (TH)-positive
- **Projections (inputs)** to the striatum
  - Glutamatergic
  - Dopaminergic
  - GABAergic
  - Others…

The Striatum Cellular Organization

- **MSNs**
  - **GABAergic** neurons
  - **Direct** pathway neurons (**D1** rec.)
    - Project to **GPi** and **SNr**
  - **Indirect** pathway neurons (**D2** rec.)
    - Project to **GPe**
- **Interneurons**
  - **Cholinergic**
    - Receive **inputs** from **thalamic** nuclei
    - Dopamine-dependent striatal **plasticity**
  - **GABAergic**
    - **Largest** population of striatal interneurons
    - **Regulate striatal output**
  - **TH-positive**
    - Compensatory mechanisms in the **dopamine depletion states**

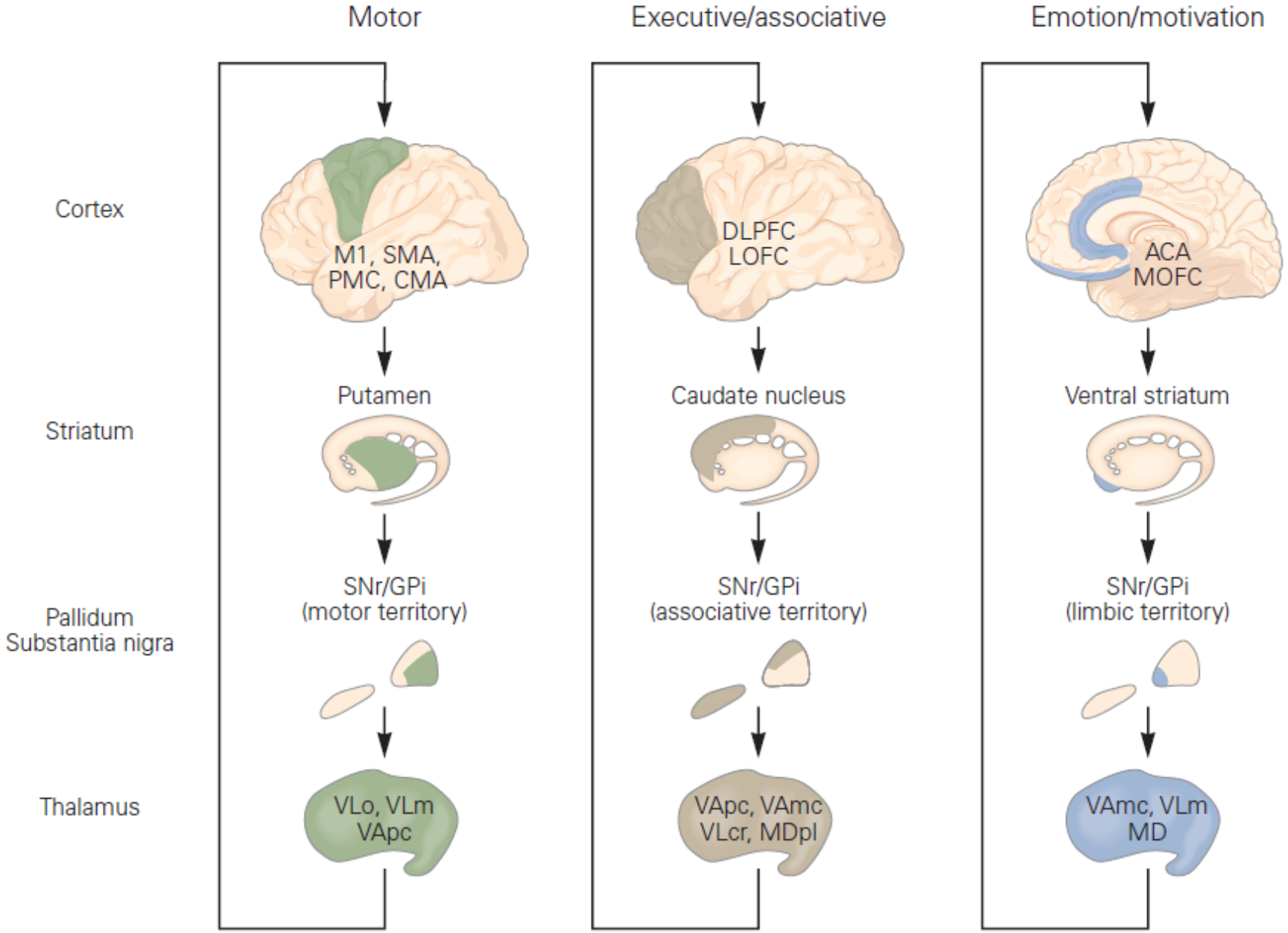
The Striatum MSNs



Glutamatergic Projections to The Striatum

1. Cortico-striatal projections

- Functionally **segregated** projections from cortical areas to the striatum
  - **Motor**
    - From: M1, PMC, SMA and SS
    - To: Post-commissural putamen
  - **Limbic**
    - From: Ant. Cingulate cortex (ACC), MPFC – Amygdala and Hippocampus
    - To: Nuc. Accumbens
  - **Associative/cognitive**
    - From: DLPFC, LOFC - Parietal and Temporal association cortices
    - To: Caudate and pre-commissural putamen


Motor
Executive/associative
Emotion/motivation
Cortex
Striatum
Pallidum
Substantia nigra
Thalamus
M1, SMA,
PMC, CMA
DLPFC
LOFC
ACA
MOFC
Putamen
Caudate nucleus
Ventral striatum
SNr/GPi
(motor territory)
SNr/GPi
(associative territory)
SNr/GPi
(limbic territory)
VLo, VLm
VApc
VApc, VAmc
VLcr, MDpl
VAmc, VLm
MD

Glutamatergic Projections to The Striatum

2. Thalamo-striatal projections

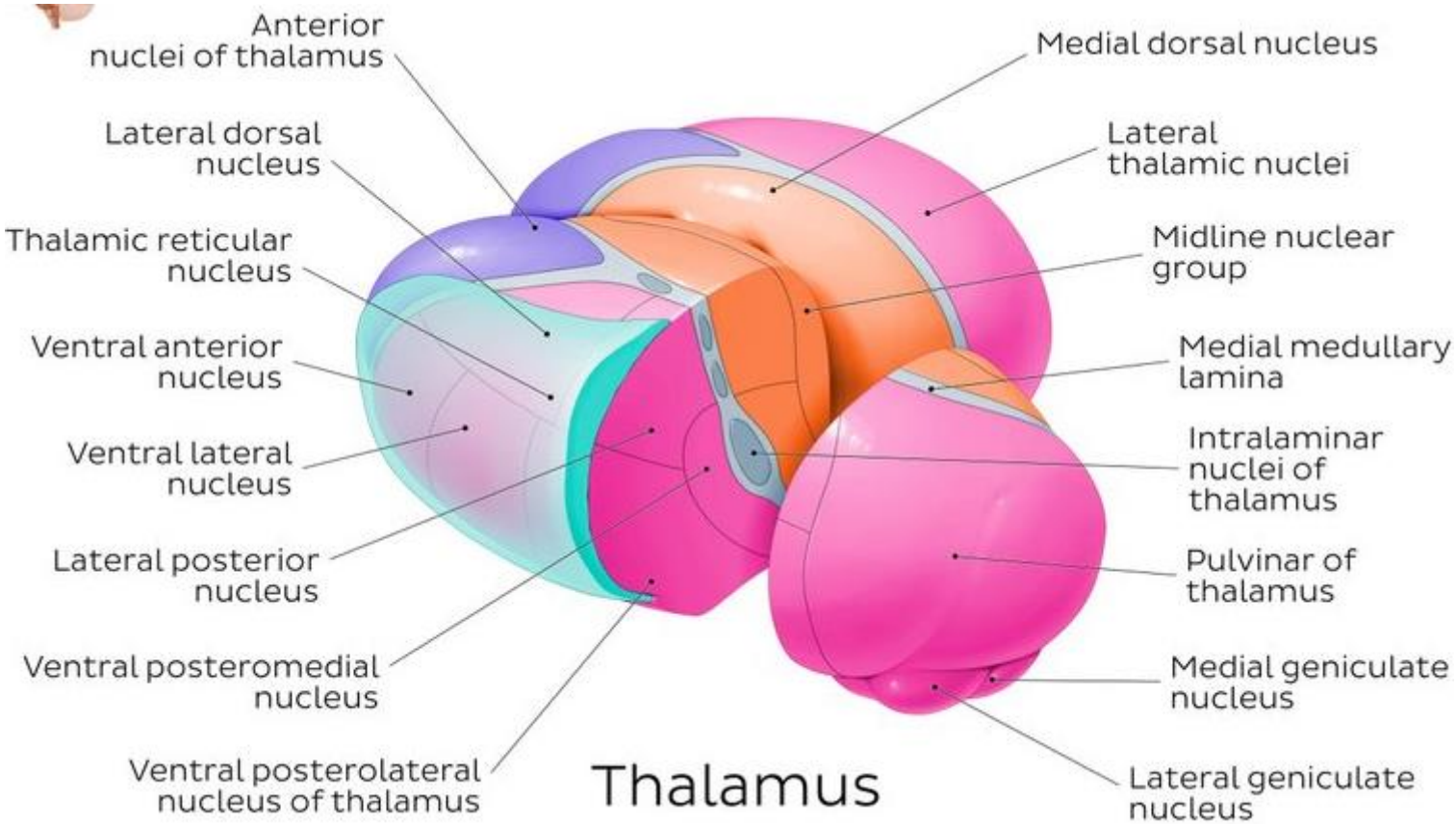
- From: **Intralaminar** nuclei (CM/PF)
- To: **CM** >>> **Sensorimotor** post-commissural putamen

  PF >>> **Limbic** and **Associative** striatum

- Others:
  - **VA** and **VL**

Glutamatergic Projections to The Striatum

- **Thalamic Nuclei**



Glutamatergic Projections to The Striatum

- **Thalamo-striatal projections potential roles**

I. Route of **cerebellar outflow** to the striatum (reciprocal communication)
   - Dentate nucleus to thalamus
   - STN and Pontine nuclei to the cerebellum

II. **Cognition**
   - In **attention-demanding** tasks
   - Infarctions in CM/PF nuclei impairs attention and semantic memory retrieval

Dopaminergic Projections to The Striatum

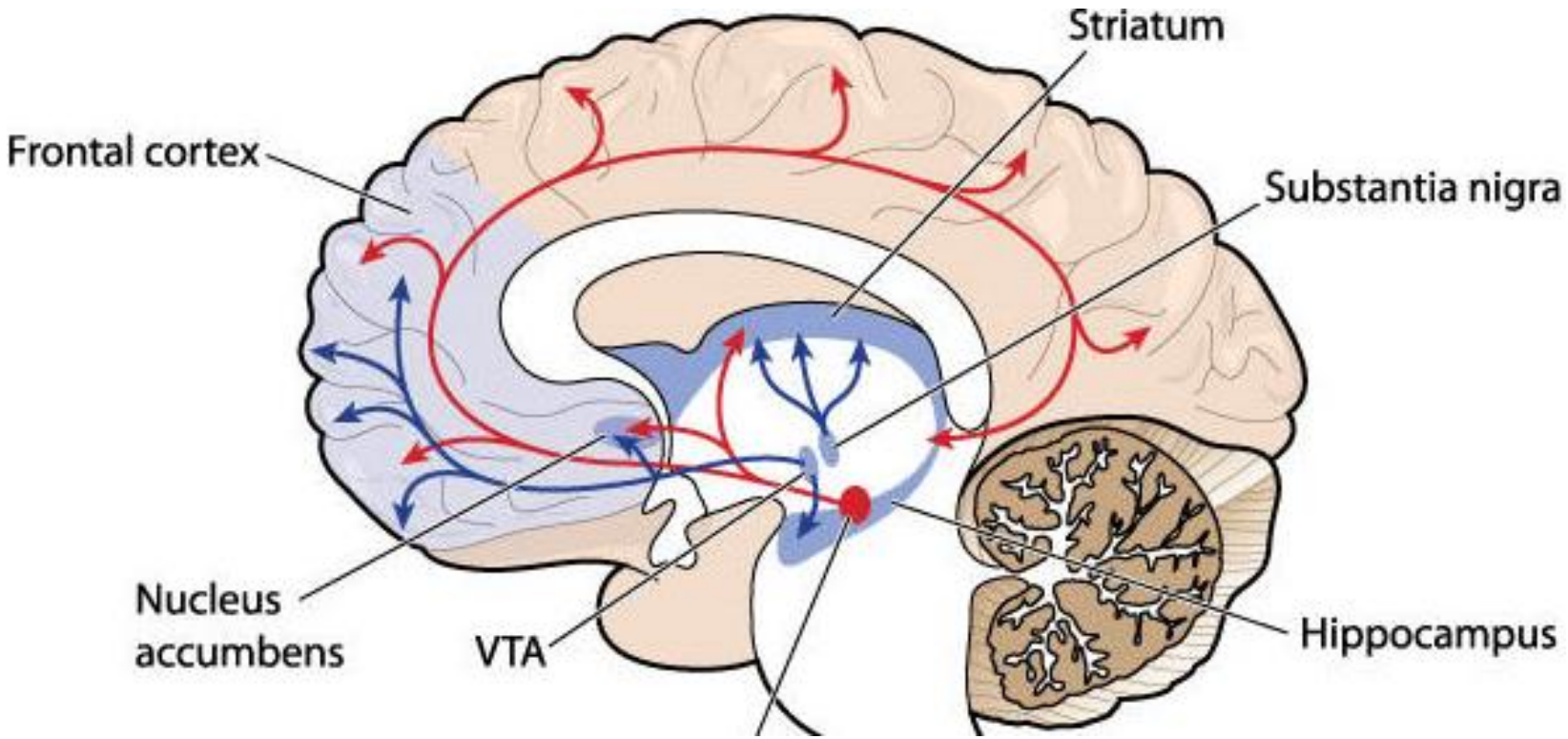
- **Dopaminergic neurons in the ventral midbrain**

I. **Retrorubral field** (RRF; **A8** group)

II. **Substantia nigra pars compacta** (SNc; **A9** group)

III. **Ventral tegmental area** (VTA; **A10** group)

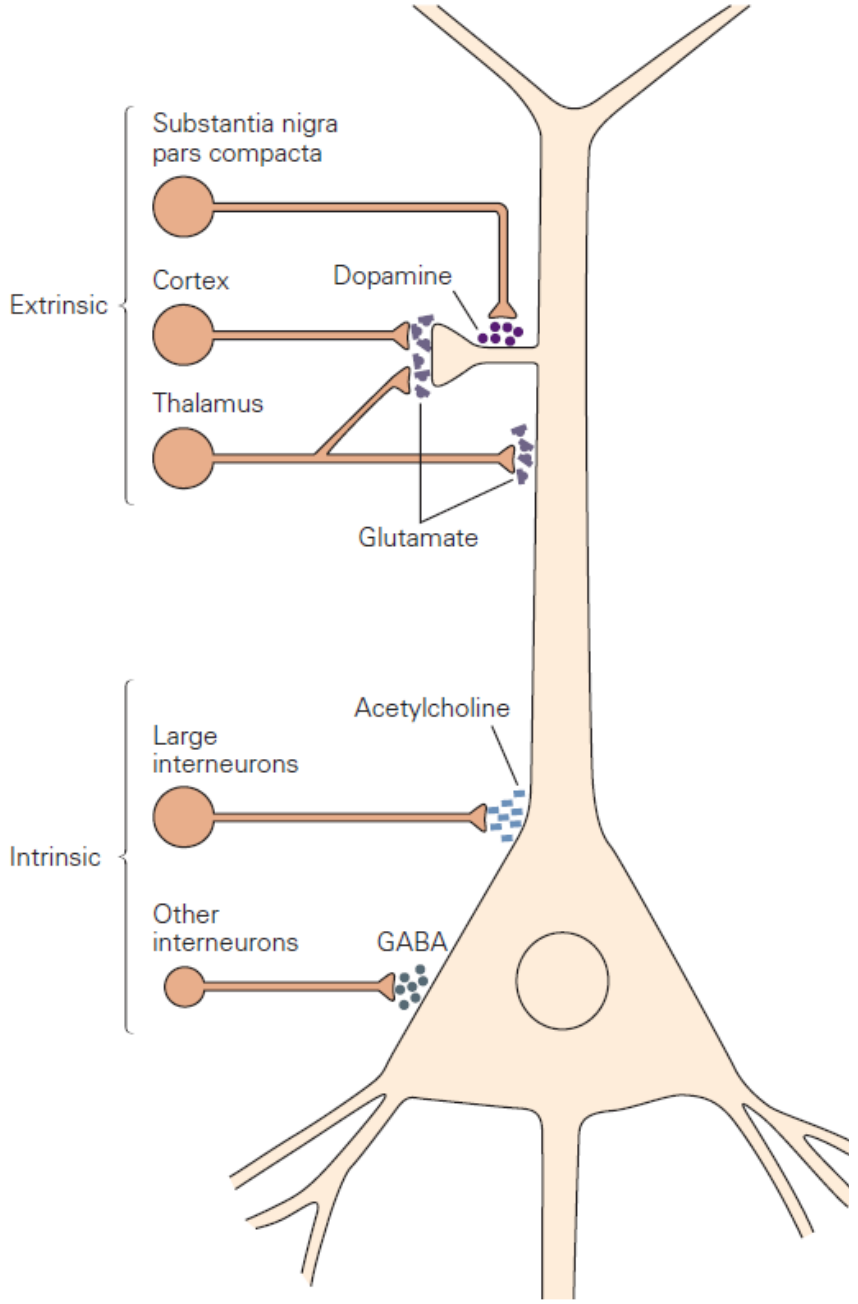
Dopaminergic Projections to The Striatum



Dopaminergic Projections to The Striatum

- **Nigro-striatal dopaminergic projections**
- **Functionally segregated** projections from cortical areas to the striatum
  - **Motor**
    - **SNc-v** >>> Post-commissural putamen
  - **Limbic**
    - **SNc-d and VTA** >>> Nuc. Accumbens
  - **Associative/cognitive**
    - **SNc-v** >>> Caudate n. and Pre-commissural putamen

The Striatum MSNs



Other Projections to The Striatum

- **Pallido-striatal GABA**ergic projections from **GPe**
- **Serotonergic** projections from the **Raphe** nuclei
- **Noradrenergic** projections from the **Locus ceruleus**
- **Histaminergic** projections from the **Hypothalamus**
- **Cholinergic** projections from the **Pontine peduncular nucleus (PPN)**

Basal Ganglia Outputs

- Main output stations
  - **GPi**
  - **SNr**

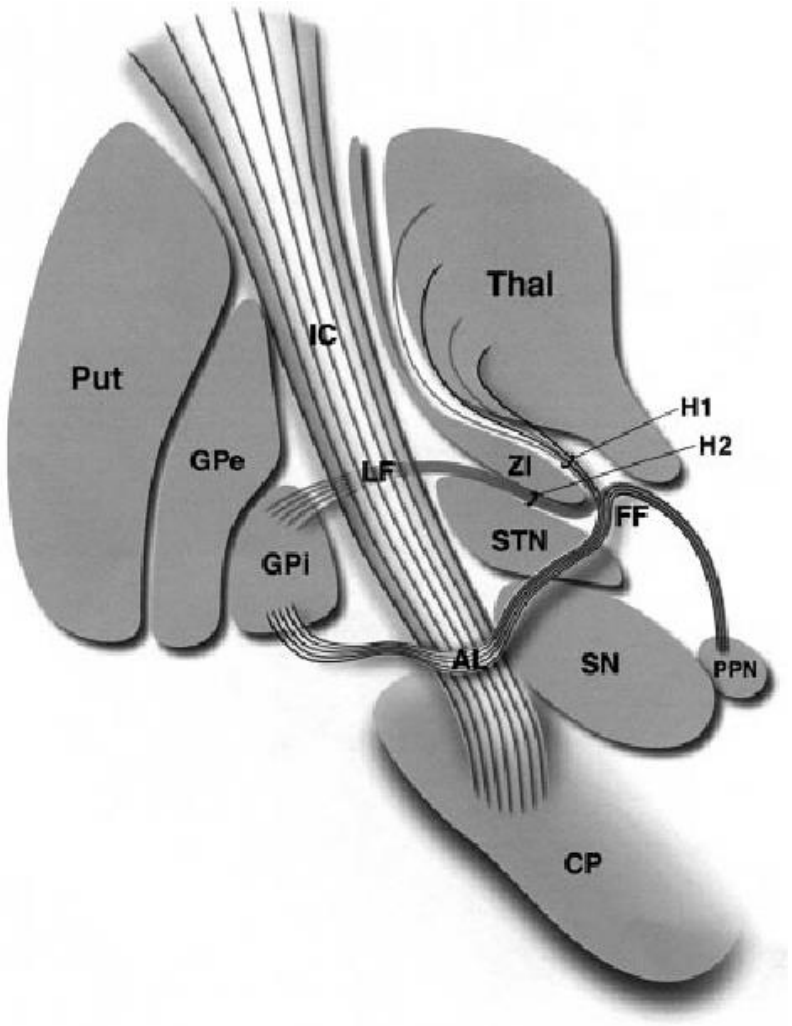
I. Integrate functionally segregated striatal input

II. Massive but functionally segregated GABAergic projections to
  - **Thalamus**
  - Brainstem
  - Reticular targets

Basal Ganglia Outputs

- **Pallidothalamic Projections**

From	To
Sensorimotor GPi	**VL,** Vapc CM
Associative GPi	**VApc** , VL, MD Pf
Limbic GPi	**VApc** ,VLd, MD Pf



Basal Ganglia Outputs

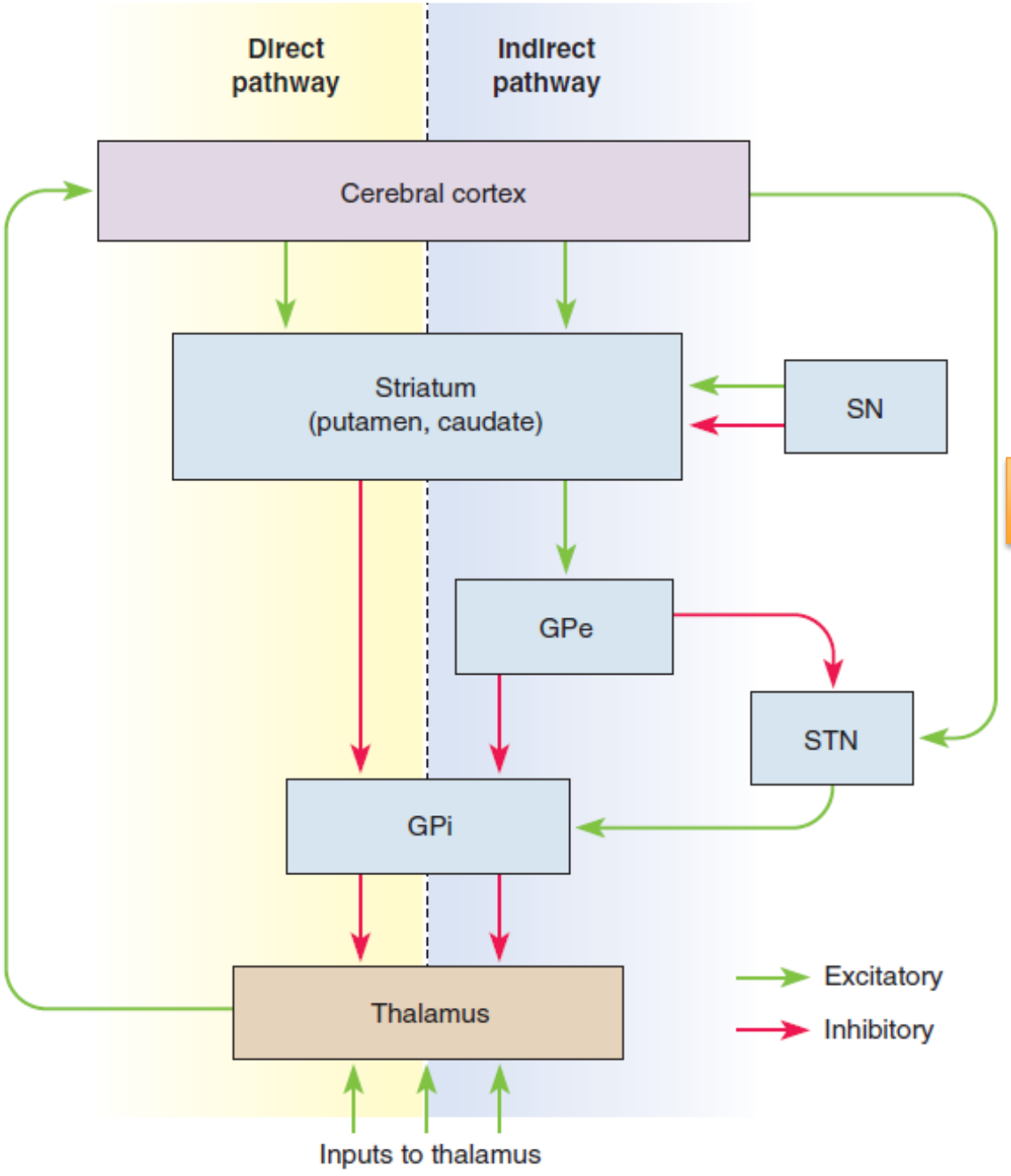
Pallido-thalamic projection vs. **Thalamostriatal projections**

- **Segregated** synapses from axon collaterals of pallidothalamic tract

With

- Thalamostriatal neurons projecting to the striatum

Basal Ganglia Intrinsic Circuitry Organization



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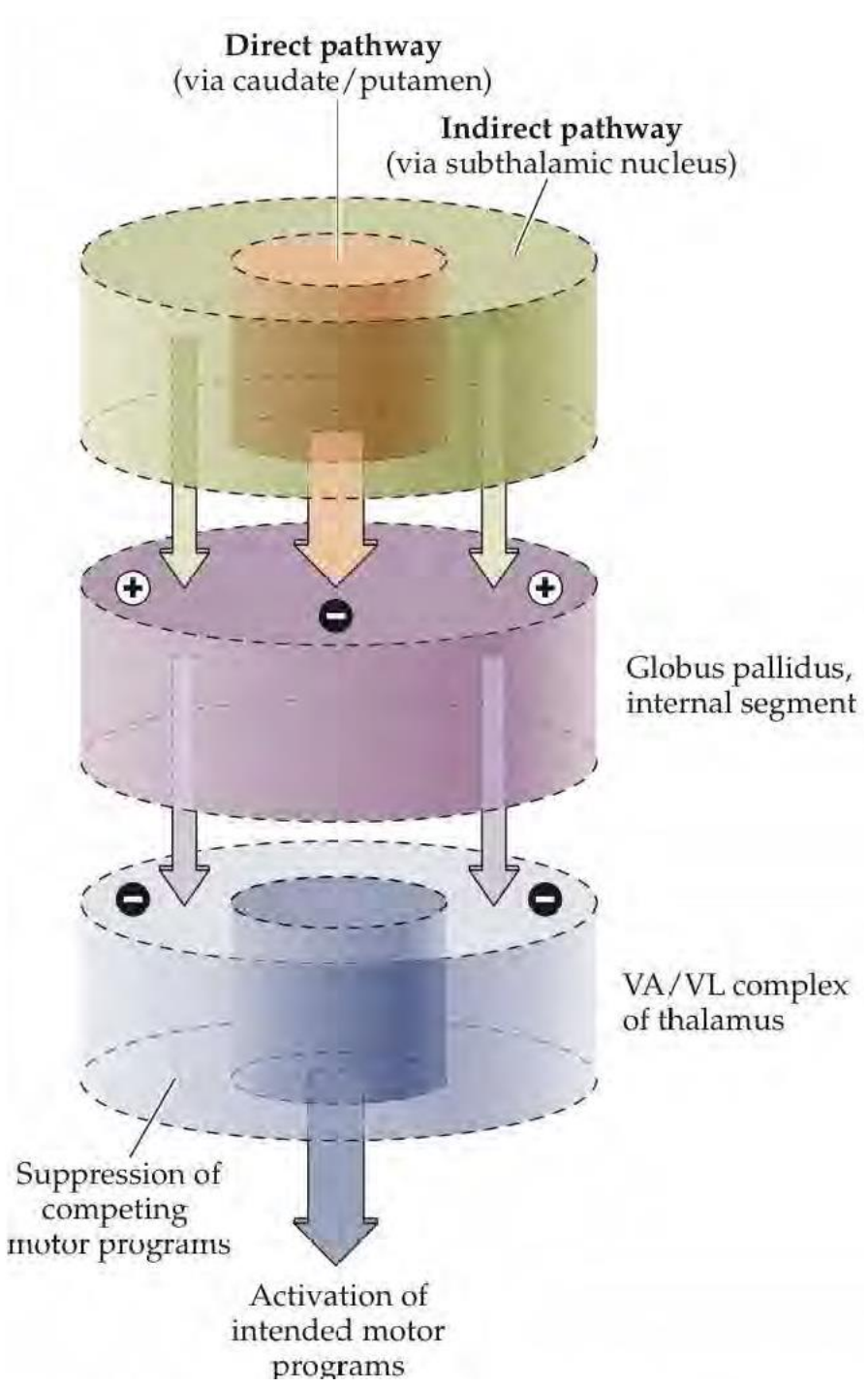
Basal Ganglia Functional Roles

- **“Focused selection” model**
  - **Phasic activation** of the striatal neurons by **cortical projections**
    - **Direct pathway >>> Facilitation of intended movements**
    - **Indirect pathway >>> Suppression of unwanted ones**
      Hyperdirect pathway

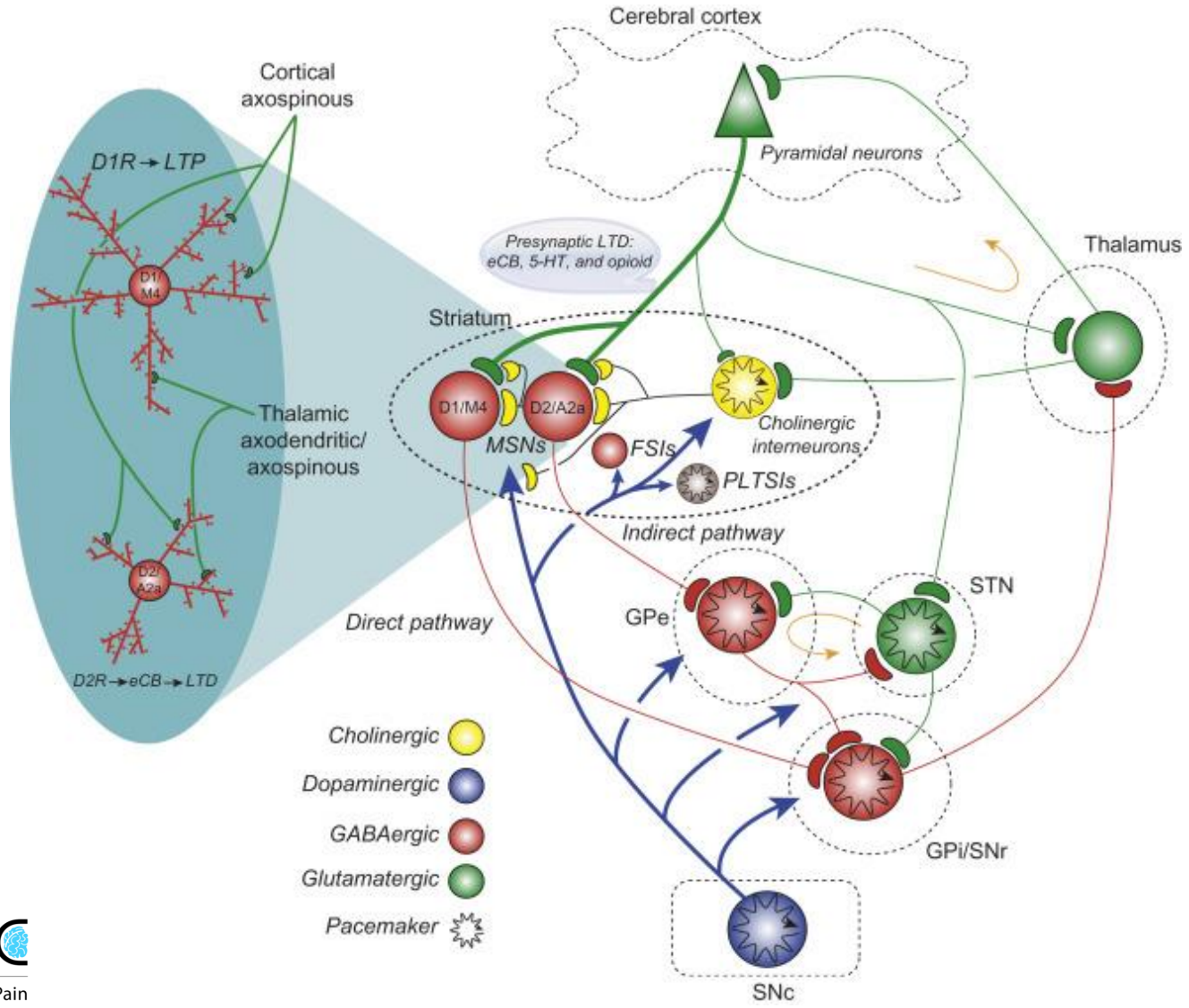
Basal Ganglia Functional Roles



Dopaminergic Projections to The Striatum

- **Nigro-striatal dopaminergic projections roles**
  - **Neuromodulation** of glutamatergic and cholinergic transmissions in the striatum
    - **Pre-synaptically**
    - **Post-synaptically**

Dopaminergic Projections to The Striatum



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Dopaminergic Projections to The Striatum

- **Dopaminergic modulation in Striatal projection neurons**
  - **Acute**
    - **Potentiation** in **dMSNs (via PKA-associated pathway)**
    - **Depression** in **iMSNs (via PKC-associated pathway)**
  - **Long-term**
    - **LTD** in **iMSNs**
    - **LTP** in **dMSNs**

Dopaminergic Projections to The Striatum

- **Dopaminergic modulation in Striatal projection neurons**
  - **Cholinergic interneurons**
    - **Indirect player** in dopamine-dependent modulation
    - **Brief reduction** in **discharge rate** in response to
      - Rewards
      - Reinforcements
      - Noxious and other behaviorally salient stimuli

Dopaminergic vs. Cholinergic projections roles

- **Dopaminergic**
  - Provide information about the behavioral value of the stimuli (Reward)
- **Cholinergic**
  - Inform the MSNs in the striatum about the occurrence of salient stimuli

Cortico-Basal ganglia-Thalamocortical circuit

- **Motor circuit**

  Different cortical regions implicated in different aspects of movement (motor subcircuits)

  - Action **selection** and **initiation** of movement
  - **Preparation** for movement
  - Movement **execution**
  - Control of movement **parameters** (velocity, amplitude, direction, …)
  - **Sequencing** of movement

Cortico-Basal ganglia-Thalamocortical circuit

- **Associative circuits**
  - **DLPFC**
    - **Executive functions** such as
      - Organizing behavioral **responses** to **complex problems**
      - Using **verbal skills** in problem solving
  - **LOFC**
    - **Empathic** behavior
    - **Socially appropriate** behavior

Cortico-Basal ganglia-Thalamocortical circuit

- **Limbic circuits**
  - From **ACC** and **MOFCs**
  - **Motivated** behaviors

Conclusion…

- **Basal ganglia functions:**
  - **Modulation of movements** (based on **desirable outcomes**)
  - **Procedural learning**
  - **Habit formation**

THANK YOU…

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