Basal Ganglia Physiology

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Normally, there is balance between systems:

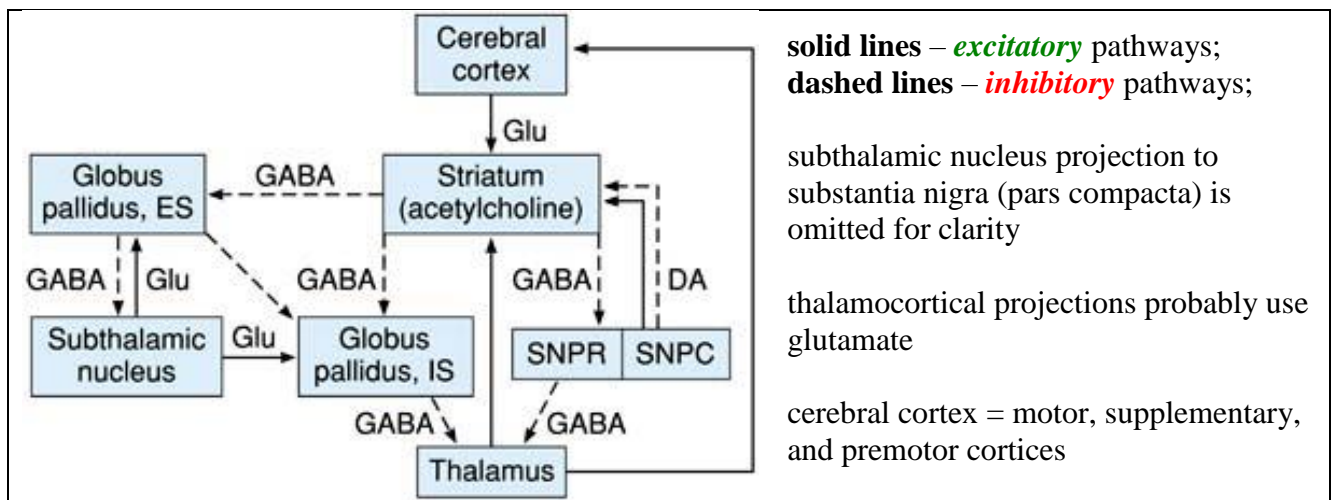**CHOLINERGIC** (*excitatory*) – **INTRASTRIATAL**.

- there are two types of cholinergic receptors in basal ganglial structures - *nicotinic* and *muscarinic* (interneurons within striatum are primarily muscarinic, but nicotinic receptors also populate striatum as well as other basal nuclei).

GLUTAMATERGIC (*excitatory*) – **everywhere excitation** is needed, except intrastriatal.

DOPAMINERGIC (*inhibitory* via D_2 receptors; *excitatory* via D_1 receptors) – **NIGROSTRIATAL**.

GABAERGIC (*inhibitory*) – **everywhere inhibition** is needed (e.g. striatonigral, striatopallidal), except nigrostriatal.

> Striatum inhibits pallidum!

solid lines – *excitatory* pathways;
dashed lines – *inhibitory* pathways;

subthalamic nucleus projection to substantia nigra (pars compacta) is omitted for clarity

thalamocortical projections probably use glutamate

cerebral cortex = motor, supplementary, and premotor cortices

black arrows – *excitation*;
speckled arrows - *inhibition*.

GP_i = globus pallidus internal segment;
GP_e = globus pallidus external segment;
STN = subthalamic nucleus;
SNr = pars reticularis of substantia nigra;
SNc = pars compacta of substantia nigra;
thal = thalamus.
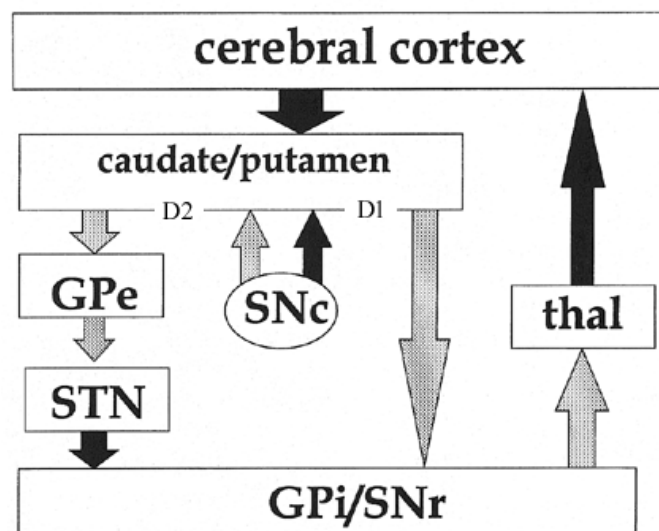
Note two primary pathways from STRIATUM to INTERNAL PALLIDUS + SUBST. NIGRA RETICULATA:

> **"direct" pathway** (*inhibitory*) - flows monosynaptically to GP_i
> **"indirect" pathway** (in sum *excitatory*) - has intermediate synapses in GP_e and subthalamic nucleus.

N.B. subthalamic nucleus regulates output of basal ganglia to thalamus!

- direct and indirect pathways balance one another physiologically.
- tonic dopaminergic input (from SUBST. NIGRA COMPACTA on striatum) *activates* **direct pathway** neurons that express **D_1 receptors** and *inhibits* **indirect pathway** neurons that express **D_2 receptors**.

Afferents to basal nuclei:
- **cortical** afferents to caudate/putamen are somatotopically organized and *excitatory* (GLUTAMATE).
  > *limbic system* provides major input to striosomes, whereas *neocortical areas* primarily project to matrix of striatum.
- **brain stem** input is primarily *inhibitory* from pars compacta substantia nigra (DOPAMINE).

Efferents from basal nuclei:
- emanate primarily from GP_i and pars reticulata substantia nigra.
- tonic *inhibitory* influence passes to thalamic nuclei (i.e. various influences on GP_i provide phasic modulation of tonic inhibition on thalamus).
- final part - *excitatory* thalamocortical projections.

SUBTHALAMIC NUCLEUS (CORPUS LUYSI)

TOPOGRAPHY

- oval shaped.
- lies on inner surface of peduncular portion of internal capsule.
- caudally, medial part of nucleus overlies rostral portion of substantia nigra.

NEUROTRANSMITTERS

- dominant **neurotransmitter** - glutamate - powerful excitatory effects on target structures (STN has been suggested to be major driving force and central feature of basal ganglia circuitry)

  N.B. classically STN was thought be GABAergic and inhibitory!

CONNECTIONS

1) *primary motor cortex* - major input to STN; arises from layer V; primarily collaterals of axons terminating elsewhere (STN is pivotal nucleus through which cortex influences output of basal ganglia*); STN has no efferent projections to cortex.

   *cortex is thought to drive basal ganglia circuitry, not only through its classic input to striatum but also through STN!

2) *globus pallidus pars externa (GPe)* – heavy inhibitory afferents to STN; STN projects excitatory input to all parts of greater pallidal complex

3) *substantia nigra pars reticulata (SNr)* – receives excitatory input from STN.

4) *pedunculopontine tegmental nucleus (PPN)* - reciprocal excitatory projections.

INACTIVATION

Hemiballismus (series of violent chorea-like movements) –

OVEREXCITATION

PD symptoms (akinesia, rigidity, and tremor).

- in PD patients DBS of STN alleviates parkinsonian symptoms

BIBLIOGRAPHY for ch. "Basal Nuclei" → follow this LINK >>