CNS

Doctor 2021

Physiology

Modified (15)

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Neurophysiology

Basal nuclei

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Ganglion refers to a collection of neuronal cell bodies in the PNS.

Basal nuclei

Nucleus vs ganglion

Nucleus refers to a collection of neuronal cell bodies inside the CNS , although some literature (as the reference the doctor instructed this lecture on) still refer to this collection as ganglion, please skip any misnomer you might face while reading .

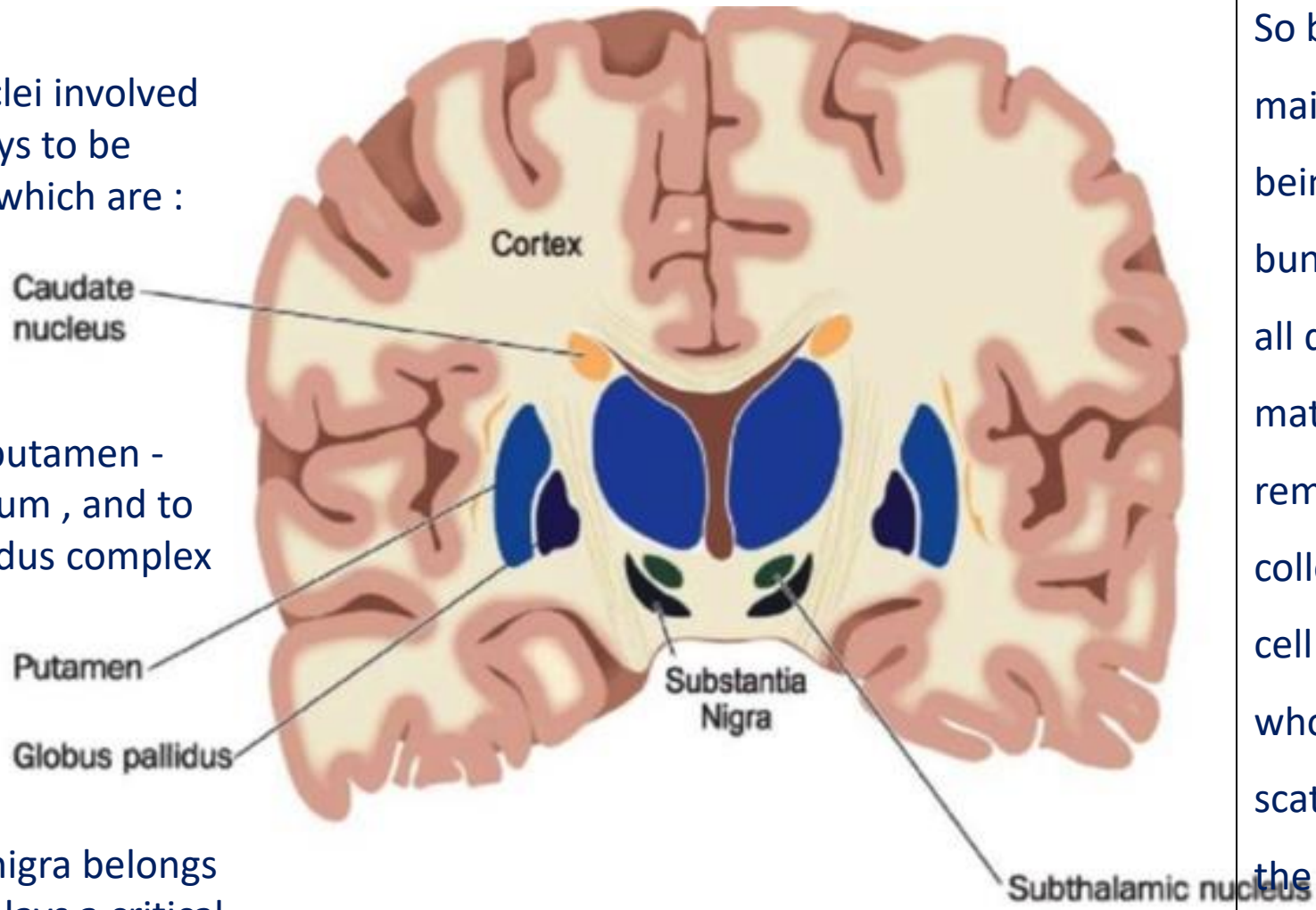
- Mainly, The basal nuclei along with higher cerebral centers help plan and control complex patterns of muscle movement like determination of what entities ,and specific sequence of motor units to contract, and what responsible motor fibers to be fired to accomplish this appropriate motor behavior , as well as carrying out the fine coordination of movement.
- They control relative intensities of the separate movements, directions of movements, and sequencing of multiple successive and parallel movements to achieve specific complicated motor goals.

We concern the basal nuclei involved in the physiologic pathways to be discussed in the lecture , which are :
1- Putamen
2- Caudate
3-Globus Palllidus

Collectively , we refer to putamen - caudate complex as striatum , and to the Putamen-Globus Pallidus complex as lentiform structure .

4-subthalamic nuclei
5-Substantia nigra

Anatomically, substantia nigra belongs to midbrain , however it plays a critical role in the physiologic pathways carried out by basal nuclei , so functionally it can be considered as basal structure



So basal nuclei are mainly characterized by being gathered as bundles, surrounded in all directions by white matter, unlike the remaining brain collections of neuronal cell bodies in cortex , whose bodies are widely scattered, displaced to the periphery , related to the white mater only internally .

MR Spectroscopy Findings of the Basal Ganglia in Bipolar Disorders: a Systematic Review. June 2018Current Psychiatry Reviews 14(2). Hanjing Emily Wu et al.

Basal nuclei interpret motor decisions provided by pre motor and prefrontal areas , and consequently prioritize some , and reject others and even modify the pattern of some. However to perform their control role , basal nuclei need to receive an input of the cortical motor plans and send back the control signals of final plan, this requires the basal nuclei to be in direct contact with the pre motor and pre frontal cortex and related cortical areas to perform the final controlled, motor outcome ,this connection is bridged by means of neural circuits linking in between .

Motor plans consult the basal nuclei before being applied by primary motor areas sending signals to the involved motor units ☺ .

- the basal nuclei receive most of their input signals from the cerebral cortex and also return almost all their output signals back to the cortex.

- Almost all motor corticospinal and sensory nerve fibers connecting the cerebral cortex and spinal cord pass through the space that lies between the caudate nucleus and the putamen: the internal capsule of the brain. An intimate association between the basal nuclei and the corticospinal system for motor control.

The first neural circuit connecting cerebral cortex to basal nuclei is the putamen circuit

Putamen circuit

- One of the principal roles of the basal ganglia in motor control is to function in association with the corticospinal system to control complex patterns of **m**otor activity.

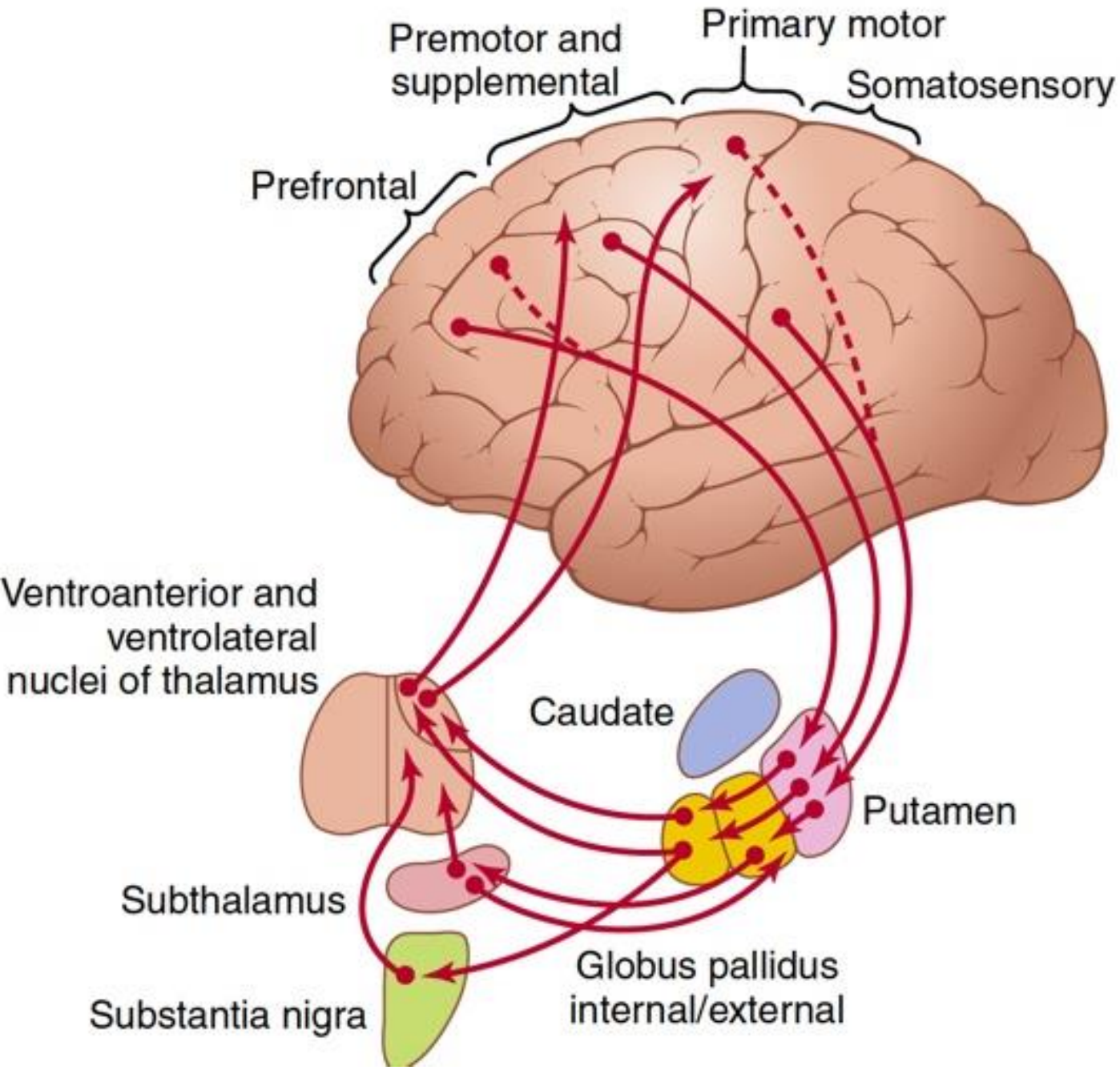
So what would be such complex level of coordination¿

Imagine annoying tickles by insect moving on your face while sipping hot soup , integrating the external stimuli , pre motor areas would plan irrational simultaneous 2 motor activities, of sipping and pushing the insect away, definitely this would harm your face , therefore these two motor decisions go through putamen circuit, where the basal nuclei send back the :

-Approval , prioritization to premotor plan of holding the spoon, by means of excitatory signals to the responsible planning cortical motor fibers , after integrating the input signal of such plan in the direct pathway.

-Disapproval to the plan of washing the insect away by means of inhibitory signals after the interpretation this plan in indirect tract .

Further details are to be discussed in the coming slides ☺



The adjacent figure shows pathways and linkages involved within the putamen circuit .

As all neural circuits, Putamen circuit starts and returns back to the cortex passing through the following basal structures : putamen- Globus pallidus (interna and externa) – subthalamus- substantia nigra – ventroanterior and ventrolateral thalamic nuclei.

-Internal and external globus pallidus differ slightly in their functions .
-Caudate nucleus has a close relation with ventricles , it has a C-shape 3D structure , it appears circular in the adjacent structure due to the cross section, it is examined through.

Putamen circuit

Putamen circuit has distinctive cortical input and output .

- the putamen circuit has its inputs mainly from the parts of the brain adjacent to the primary motor cortex, pre motor ,supplementary, pre frontal areas but not much from the primary motor cortex itself , as stated before Putamen circuit controls motor activity on the complex level , that's why it concerns integrating only planning areas of motor cortex. Primary areas only perform the outcomes of the circuit .Moreover Putamen circuit receives an input from somatosensory area.
- This wide input aids in enabling the basal nuclei to process the best consultation and prioritization of motor plans with regard to the whole status of body, and decide which plans should be prioritized ,accomplished and approved which plans to be diminished .

- inputs complete all the way through basal nuclei, to the ventroanterior and ventrolateral thalamic motor nuclei .
- Then outputs of the circuit do go mainly back to the primary motor cortex or closely associated premotor and supplementary cortex to perform the final controlled plan on the related motor units, through the thalamus , the only relying pathway between basal nuclei and motor cortex.

- Till reaching the thalamus ,Putamen circuit involves two pathways , the direct and indirect , which differ in the basal nuclei to pass through , and therefore their resultant control signals are completely different .
- The direct pathway passes through putamen → Globus Palladis Interna. → Motor thalamic nuclei.
- The indirect pathway passes through putamen → Globus pallidus Externa → Sub thalamus → Globus palladis interna

- Neuronal-transmitted signals in between basal nuclei in the circuit are all inhibitory, in which GABA neurotransmitter is critical , except for the sub thalamic → Globus palladis interna signal.
- For example, Putamen → Globus pallidus interna

Globus pallidus interna → thalamic motor nuclei

are inhibitory signals in which GABA is released .

Back to the direct pathway

putamen -ve→ Globus Palladis interna -ve→ motor thalamic nuclei.

Notice that the inhibitory "putamen to the Globus palladis interna" signal suppresses the inhibitory effect of the subsequent signal from "Globus palladis interna to the thalamic nuclei "

Ultimately the inhibitory effect of basal nuclei on thalamus is diminished , and motor thalamic nuclei can perform their excitatory glutamate-mediated output on the planning motor fibers which sent this input , and the basal approval is confirmed towards the premotor and primary cortical areas .

Therefore; the net effect of direct pathway is said to be excitatory ; in which motor plans are approved and the related skeletal excitation-contraction coupling takes place .

- On contrast , on the indirect pathway ,
- The indirect pathway passes through putamen. -ve → Globus pallidus external -ve → → Sub thalamic +ve → Globus pallidus interna -ve → motor thalamic nuclei .

- initially “putamen to Globus pallidus externa “ inhibitory signal suppresses the inhibitory “globus pallidus externa to sub thalamic”signal .

- Soon after, the sub thalamic nucleus is excited to perform its extraordinary basal excitatory effect on the inhibitory” Globus pallidus interna” , this collectively allows the inhibitory signal of “Globus pallidus interna to thalamus” to take place .
- And the thalamus is inhibited from producing its excitatory effect on the motor plan , and the basal rejection is confirmed , no skeletal excitation-contraction coupling is there .

- That’s why the indirect putamen pathway is said to be inhibitory , it shunts the signal to the sub thalamic nuclei to re-obtain the inhibitory basal effect .

After analyzing the general input to the neural circuit, signals of appropriate motor activities are transmitted to be integrated in the direct pathway to be excited and fired , whereas the inappropriate activities are turned off through

Direct vs indirect pathway

- There are two distinct pathways that process signals through the basal ganglia: the direct pathway and the indirect pathway.

- These two pathways have opposite net effects on thalamic target structures.

- Excitation of the direct pathway has the net effect of exciting thalamic neurons (which in turn make excitatory connections onto cortical neurons).

Direct vs indirect pathway

- Excitation of the indirect pathway has the net effect of inhibiting thalamic neurons (rendering them unable to excite motor cortex neurons).

- The normal functioning of the basal ganglia apparently involves a proper balance between the activity of these two pathways.

https://nba.uth.tmc.edu/neuroscience/m/s3/chapter04.html

Nigrostriatal projection

- An important pathway in the modulation of the direct and indirect pathways is the dopaminergic(dopamine releasing) nigrostriatal projection from the substantia nigra pars compacta to the striatum (again to the putamen).
- Nigrostriatal projection has two separate effects on both direct and indirect pathways within the putamen circuit due to selective transcription of Dopamine receptors between direct and indirect motor putamen areas .
- Direct pathway striatal neurons have D1 dopamine receptors, which depolarize the putamen cell in response to dopamine.
- In contrast, indirect pathway striatal neurons have D2 dopamine receptors, which hyperpolarize the cell in response to dopamine.

https://nba.uth.tmc.edu/neuroscience/m/s3/chapter04.html

Nigrostriatal projection

Nigrostriatal projection generally has excitatory effect on both direct and indirect signals of motor plans .

- The nigrostriatal pathway thus has the dual effect of exciting the direct pathway (D1-mediated depolarization of direct putamen areas enforces the net excitatory effect of the pathway) while simultaneously inhibiting the indirect pathway (D2 mediated hyperpolarization of indirect putamen areas weakens the net inhibitory effect of the indirect pathway, this in turn excites the thalamic motor outcomes about indirect motor plans)
- Because of this dual effect, excitation of the nigrostriatal pathway has the net effect of exciting cortex by two routes, by exciting the direct pathway (which itself has a net excitatory effect on cortex) and inhibiting the indirect pathway (thereby disinhibiting the net inhibitory effect of the indirect pathway on cortex).

https://nba.uth.tmc.edu/neuroscience/m/s3/chapter04.html

Nigrostriatal projection

- The loss – degeneration- of these dopamine neurons and consequent impairment of – direct and indirect-excitatory dopamenergic signals on different levels in Parkinson's disease causes the poverty of movement , as inhibitory indirect signals will override , that characterizes this disease, as the balance between direct pathway excitation of cortex and indirect pathway inhibition of cortex is tipped in favor of the indirect inhibitory pathway, with a subsequent pathological global inhibition of motor cortex areas, therefore, Parkinson's patients suffer from problematic initiation, along with slowing of movement.

https://nba.uth.tmc.edu/neuroscience/m/s3/chapter04.html

Globus pallidus

- lesions in the globus pallidus frequently lead to spontaneous and often continuous writhing movements of a hand, an arm, the neck, or the face. These movements are called **athetosis**.
- The following video illustrates what is athetosis from doctor
- https://youtu.be/JrnUf2dI27s?si=byuiugwUyWbrUhy-

Subthalamus

- A lesion in the subthalamus often leads to sudden flailing movements of an entire limb, a condition called **hemiballismus**.

- The following video illustrates what is hemiballismus
- https://youtu.be/ivWSFiIDiLw

Putamen

- Multiple small lesions in the putamen lead to flicking movements in the hands, face, and other parts of the body, called **chorea**.
- Chorea has several types the generalized form , as in the adjacent case, may involve upper,lower limbs along with trunk in involuntary movement .
- The following video illustrates what is chorea

  https://youtu.be/nEXu0hMcAek

Substantia nigra

- Lesions of the substantia nigra lead to the common and extremely severe disease of rigidity, akinesia, and tremors known as **Parkinson's disease**
- **PD Will be discussed later in this lecture**

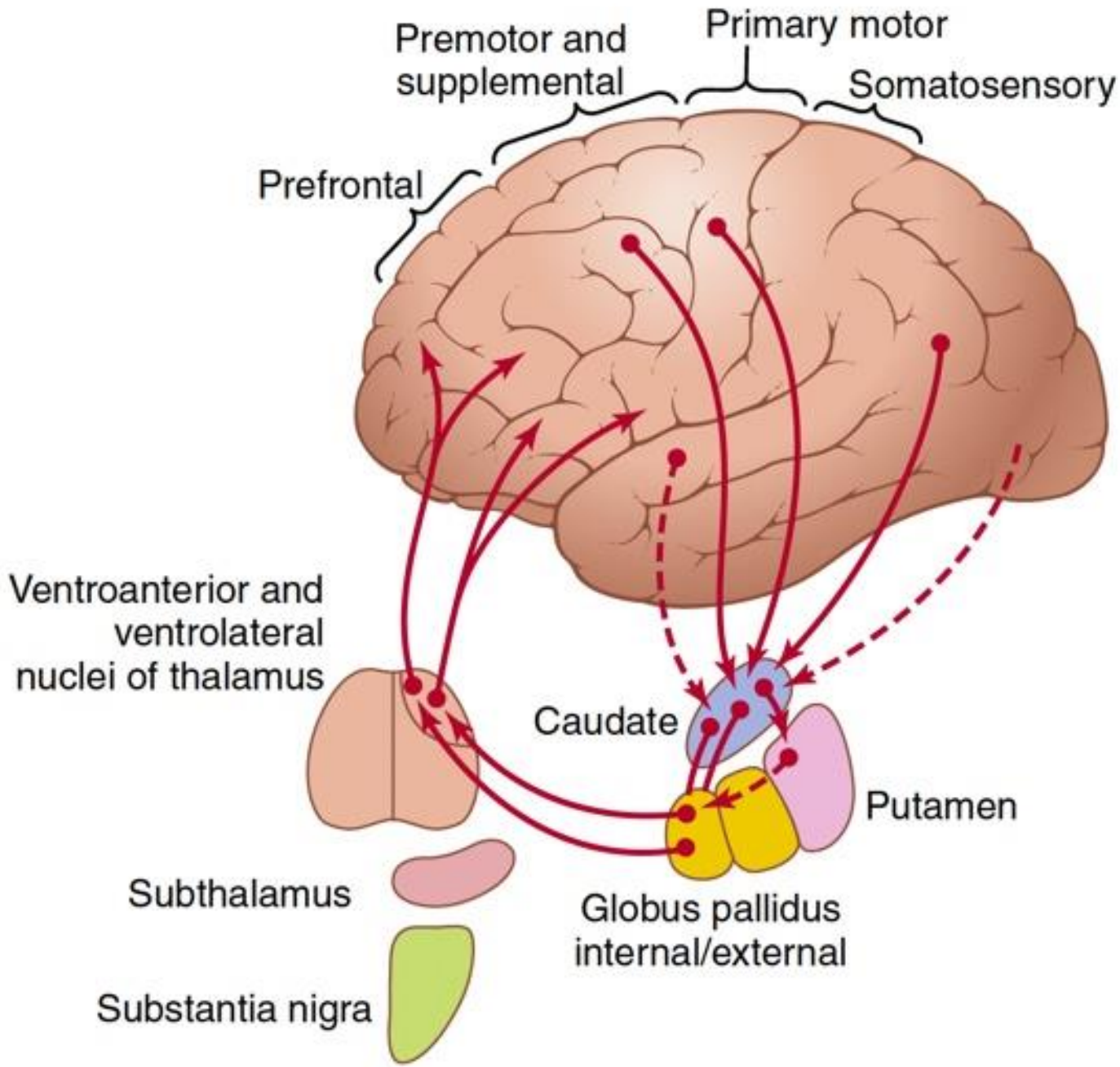
The second major neural circuit linking the cortex to basal nuclei is the caudate circuit

The caudate circuit

This circuit controls motor activities on the level of cognitive reasons behind , and takes decision of cognitive actions to undertake.

- The term cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory.

- Most of our motor actions occur as a consequence of thoughts generated in the mind, a process called cognitive control of motor activity.
- The caudate nucleus plays a major role in this cognitive control of motor activity.


Premotor and supplemental
Primary motor
Somatosensory
Prefrontal
Ventroanterior and ventrolateral nuclei of thalamus
Caudate
Putamen
Subthalamus
Globus pallidus internal/external
Substantia nigra

The caudate circuit

- the caudate nucleus extends into all lobes of the cerebrum.

- the caudate nucleus receives large amounts of its input from the association areas of the cerebral cortex overlying the caudate nucleus, almost all parts(lobes)of the cerebral cortex, mainly areas that also integrate the different types of sensory and motor information into usable thought patterns. To have sufficient hints for consultation of the appropriate motor activity with the most reasonable cognitive backgrounds.

The caudate circuit

Passing through Striatum, Caudate nuclei , plans in the caudate circuit reach Globus Pallidus interna before continuing to the thalamus, the only relying station toward the prefrontal cortical area which specializes in cognition-based motor decision making .

- Almost none of the returning signals passing directly to the primary motor cortex, instead, thalamus serves as the only relying station towards.

- Instead, the returning signals go to the accessory motor regions in the premotor and supplementary motor areas that are concerned with building sequential patterns of movement lasting 5 seconds or more instead of exciting individual muscle movements.

The caudate circuit

- cognitive control of motor activity determines subconsciously, and within seconds, which patterns of movement will be used together to achieve a complex goal that might itself last for many seconds, through caudate circuit, basal nuclei sort and preview the suggested cognition-based plans , prioritize the suitable based on large general base of incomes .

Furthermore, through caudate circuit, basal nuclei use the large base of cognitive input to do: timing and scaling .

Timing and scaling of movement

- Two important capabilities of the brain in controlling movement are to
- (1) determine how rapidly the movement is to be performed (timing)

Like when you speed your writing in the last 5 minutes of exam.

- (2) control how large the movement will be.(scaling)

Like when your written letters become random along with speeding in the same condition.

Or when children learn how to arrange their writings in more neat patterns, and are more enabled to write letters in their reasonable sizes .

- In patients with severe lesions of the basal ganglia, these timing and scaling functions are poor.

Posterior parietal cortex

- the basal ganglia do not function alone; rather, they function in close association with the cerebral cortex.

- One especially important cortical area to collaborate with the basal nuclei is the posterior parietal cortex, which is the locus of the spatial coordinates of objects or of body parts . for motor control of all parts of the body, as well as for the relationship of the body and its parts to all its surroundings.

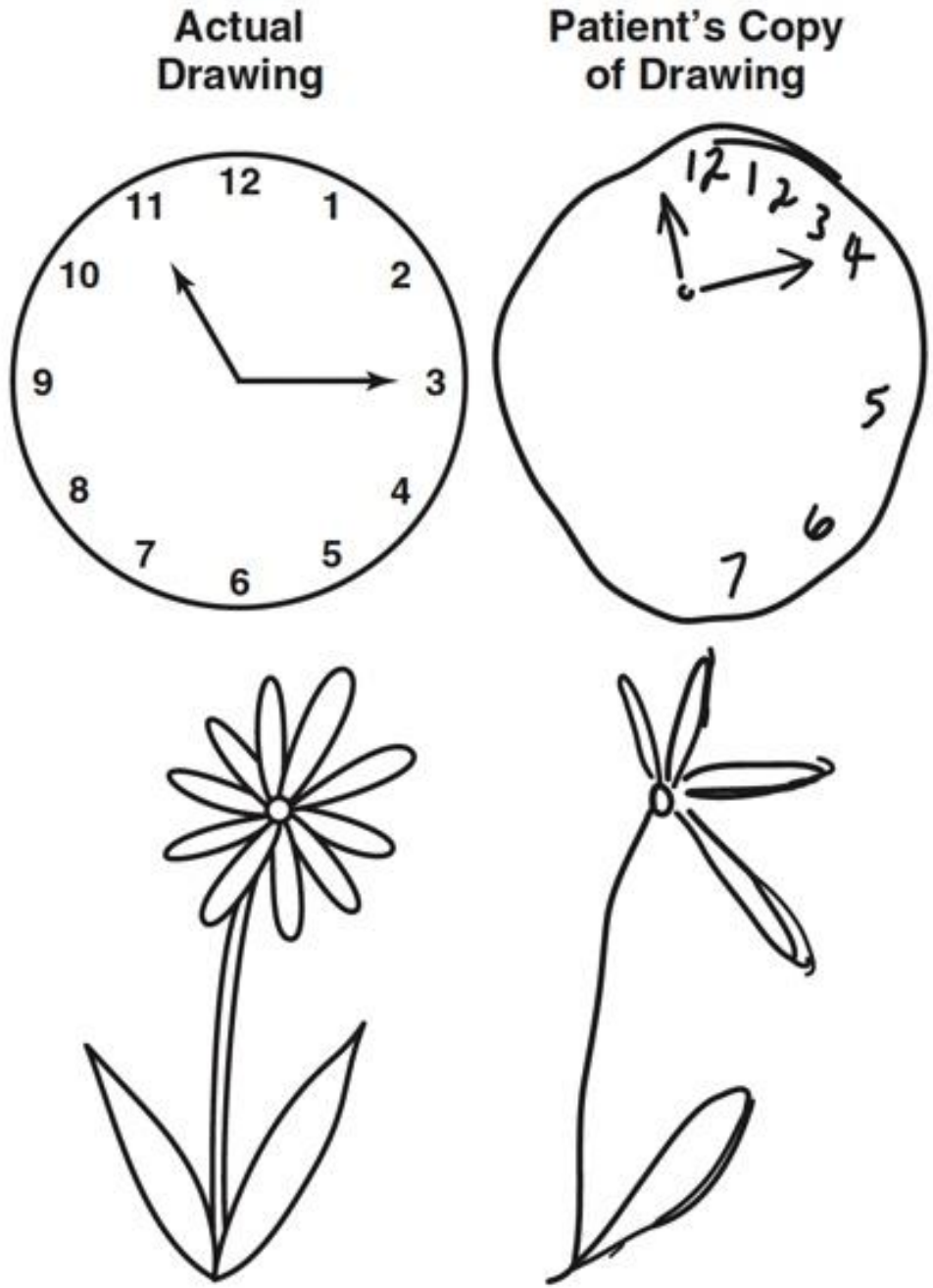
Posterior parietal cortex

- Damage to this area does not produce simple deficits of sensory perception, such as loss of tactile sensation, blindness, or deafness.

- Instead, lesions of the posterior parietal cortex produce an inability to spatially perceive objects or body parts accurately through normally functioning sensory mechanisms, a condition called **agnosia**.

Posterior parietal cortex

- Such patients suffer from kind of neglect syndrome , in which patients can’t perceive the spatial dimensions of one side(right or left) , they deal completely with only one side of the world and consequently have poor (or even no) interaction with the other half of objects, bodily movements, all kinds of stimuli and fields of perception on the opposite side, they simply forget this side would exist, and aren’t aware of this defect, it’s this functioning spatial half they believe the world is.
- Also, such a person will always try to avoid using his or her left arm, left hand, or other portions of his or her left body for the performance of tasks; the person may not even wash this side of the body (personal **neglect** syndrome), almost not knowing that these parts of the body exist.


Actual Drawing
Patient's Copy of Drawing
12
1
2
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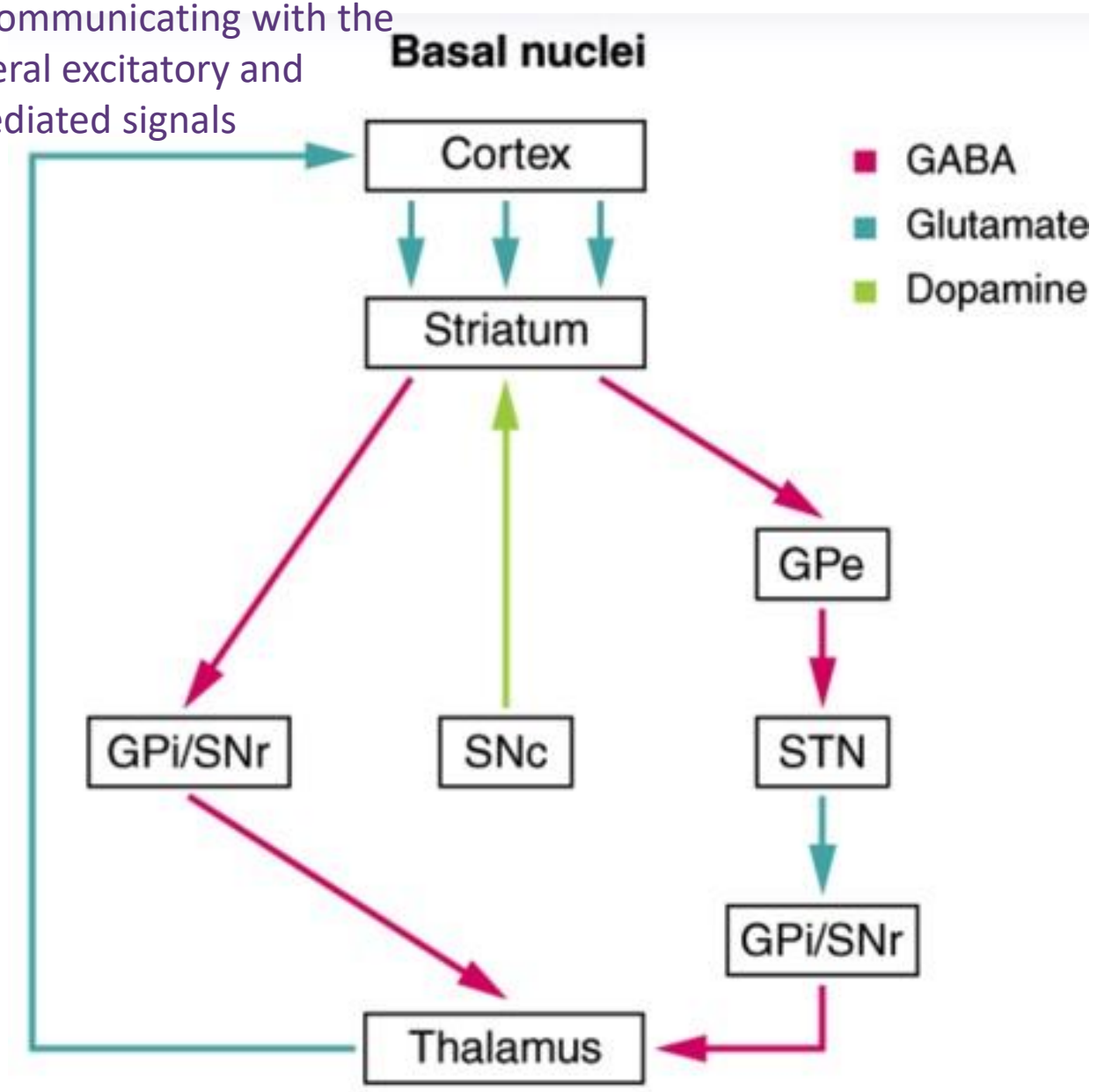
11

So in between basal nuclei or communicating with the surrounding structures are several excitatory and inhibitory neurotransmitter-mediated signals

Substantia nigra controls basal nuclei through inhibitory dopamine

"Thalamic to Cortical" signal is always excitatory by means of glutamate.



main inhibitory

excitatory

inhibitory

GABA is the main inhibitory neurotransmitter between basal nuclei , except for the excitatory signal from "Subthalamus to Globus pallidus interna" , that is mediated through Glutamate.

https://www.nursinghero.com/study-guides/garrettcollege-ap1/the-central-nervous-system

Diseases affecting the basal nuclei:

1 Parkinson's disease

Rigidity (increase in the muscle tone)because there is a relationship between basal nuclei and the reticular formation(reticulospinal pathway)

https://stanfordmedicine25.stanford.edu/the25/parkinsondisease.html

Symptoms of PD:

*MOTOR(mentioned in the figure)
*cognitive symptoms(Memory loss, dementia, depression and behavioral).

Critical thinking :
This is disease of substantia nigra
Part of basal nuclei which makes us expect motor symptoms only
But in reality, basal nuclei are involved in other functions (Intellectual function, learning ,..) and may be Psychiatric function involved in basal nuclei and neurotransmitters .

[2] Huntington's disease

- Huntington disease is an inherited(Autosomal Dominant) disorder in which the [1]caudate nucleus and [2]putamen degenerate, with loss of neurons that normally release GABA or acetylcholine.
- A key sign of HD is chorea, in which rapid, jerky movements occur involuntarily limbs and without purpose.
- Progressive mental deterioration also occurs.
- Symptoms of HD often do not appear until age 30 or 40. Death occurs 10 to 20 years after symptoms first appear.

3 Tourette syndrome

- characterized by involuntary body movements (motor tics) and the use of inappropriate or unnecessary sounds or words (vocal tics).
- Although the cause is unknown, research suggests that this disorder involves a dysfunction of the cognitive neural circuits between the basal nuclei and the prefrontal cortex.

Psychiatric disorders

- Some psychiatric disorders, such as schizophrenia and obsessive compulsive disorder, are thought to involve dysfunction of the behavioral neural circuits between the basal nuclei and the limbic system.

Function of the basal nuclei:

1) Initiation of movements
2) Suppression of unwanted movements
3) Regulation of muscle tone (association reticulospinal tracts)
4) Regulation of nonmotor processes

Initiation of movements

- The basal nuclei play a major role in initiating movements.
- Neurons of the basal nuclei receive input from sensory, association, and motor areas of the cerebral cortex.
- Output from the basal nuclei is sent by way of the thalamus to the premotor area, which in turn communicates with upper motor neurons in the primary motor area, then activate the corticospinal and corticobulbar tracts to promote movement.

Suppression of unwanted movements

- The basal nuclei suppress unwanted movements by tonically inhibiting the neurons of the thalamus that affect the activity of the upper motor neurons in the motor cortex.
- When a particular movement is desired, the inhibition of thalamic neurons by the basal nuclei is removed, which allows the thalamic neurons to activate the appropriate upper motor neurons in the motor cortex.

Regulation of muscle tone

- Neurons of the basal nuclei send action potentials into the reticular formation that reduce muscle tone via the medial and lateral reticulospinal tracts.

- Damage or destruction of some basal nuclei connections causes a generalized increase in muscle tone.

Regulation of nonmotor processes

- The basal nuclei influence several nonmotor aspects of cortical function, including sensory, limbic, cognitive, and linguistic functions.
- For example, the basal nuclei help initiate and terminate some cognitive processes, such as attention, memory, and planning.
- In addition, the basal nuclei may act with the limbic system to regulate emotional behaviors.

Thank you