CENTRAL NERVOUS SYSTEM

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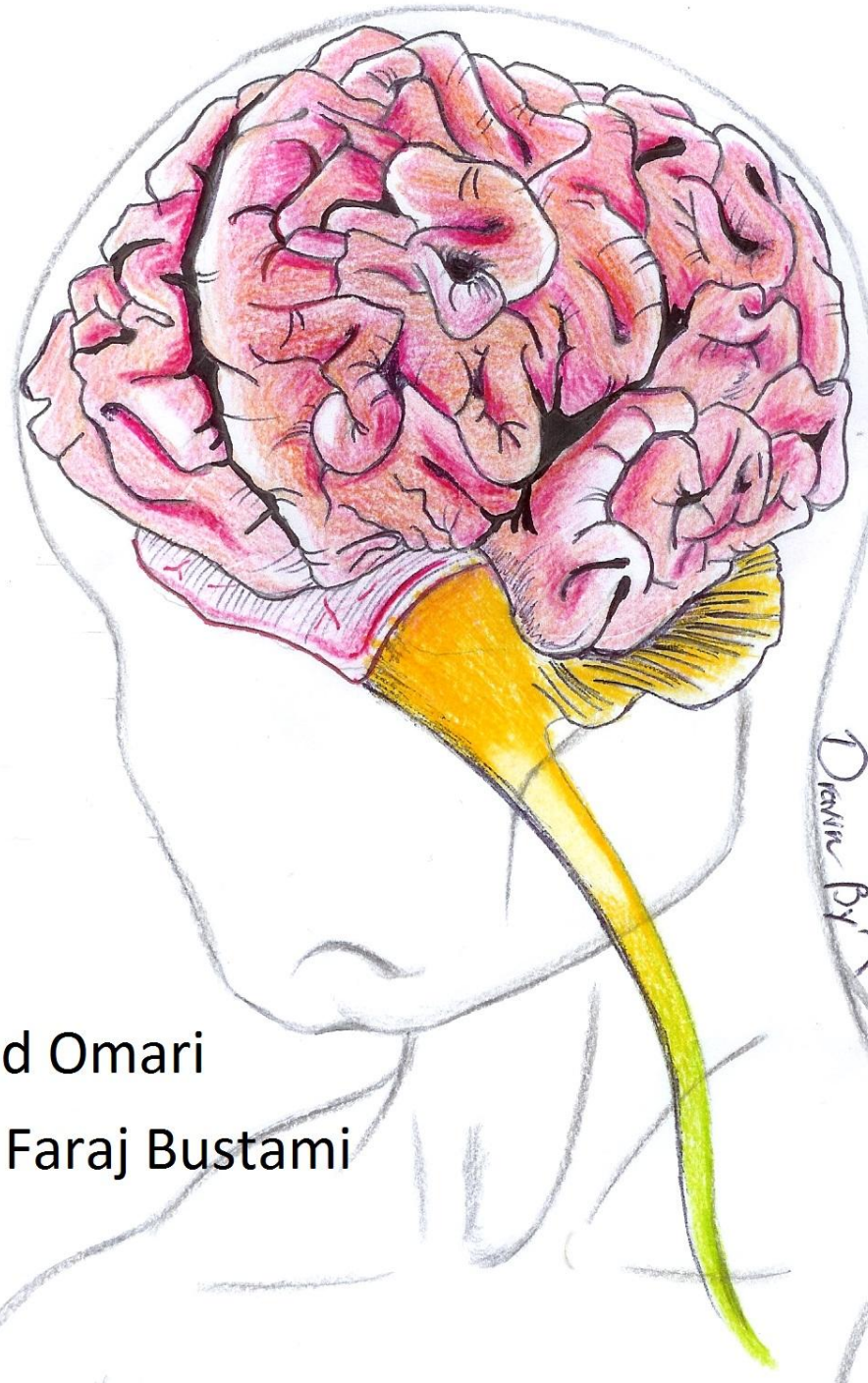

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The Basal Ganglia

Hello, I rearranged some information in the record because the doctor kept jumping from one topic to the other, but the rearrangement makes it easier to understand, I hope. Good luck!

Regarding the Cerebellum:

On the inferior surface of the cerebellum there's a tonsil. If there's herniation in medulla, the tonsil would go out and compress the medulla, causing an increase in intravenous pressure and compressing the blood supply of the medulla. This leads in increased pressure in the medulla and thus vital centers in the medulla would fail to function leading to Respiratory failure.

The Basal Ganglia:

The basal ganglia normally acts through reciprocal connection with the Cerebral Cortex i.e it receives input from the Cortex and then sends its output to it as well (like the Cerebellum)

The Corpus Striatum in the Basal Ganglia includes the Caudate Nucleus, Putamen and Globus Pallidus. The Globus Pallidus and the Putamen together are called the Lentiform Nucleus, thus, the basal ganglia is almost mainly the Caudate Nucleus (Head, body, and tail) and the Lentiform Nucleus. There's also another part of the Basal Ganglia which is the Amygdaloid Nucleus; it is present in the temporal lobe near the inferior horn and is functionally related to the limbic system. The final part of the Basal Ganglia is the Claustrum which has unknown connections and functions.

The Globus Pallidus has two parts; external (GPE) and internal (GPI). Note that these two parts have different connections and functions.

The Corpus Striatum itself is divided into two parts:

1) The Neostriatum (normally called "striatum") which includes the Putamen (Part of Lentiform Nucleus) and the Caudate (Part of Caudate Nucleus). This is where the input from the Cerebral Cortex reaches the Basal Ganglia.
2) The Paleostriatum (normally called "pallidum") which includes the Globus Pallidus. The Globus Pallidus Internus is where the output of the Basal Ganglia leaves to the Cerebral Cortex.

The Basal Ganglia also has some other nuclei outside of it which are functionally related to it. The first nucleus is the Substantia Nigra which is part of the midbrain and the mesencephalon, it has dorsal and ventral parts; the dorsal part is called Pars Compacta (Releases Dopamine), and the ventral part is called Pars Reticulata (Same functions and connections as the GPI).

The second nucleus related to the Basal Ganglia is the Subthalamic Nucleus which is part of the diencephalon.

In order for the commands of the Cerebral Cortex to be accurate, it has to be under the control of the Cerebellum and the Basal Ganglia i.e in order for the movement initiated by Areas 4 and 6 to be accurate and precise; we need help from the Cerebellum and the Basal Ganglia.

Recall that the Cerebellum receives unconscious proprioception from joints and muscles, vestibular information from the inner ear, and information about the external environment, after processing these information it sends its output to the Cerebral Cortex. If a patient has a lesion in the cerebellum, his movements will be disturbed (Cerebellar Ataxia= Loss of coordination).

As for the Basal Ganglia, it controls the decision to move, the direction and amplitude of movement. It also has to do with the expression of emotions (Limbic System).

Disturbances in the Basal Ganglia lead to either Parkinson disease or Chorea i.e dyskinesia. On the other hand, disturbances in the Cerebellum, as we said earlier, lead to Ataxia.

In Parkinson's disease:

1) Bradykinesia; slow movement.

2) Hesitant movement.
3) Increased Tone.

In Chorea:

1) Hyperkinesia.
2) Involuntary spontaneous movement.

NOTE: In diseases related to the Basal Ganglia there is NO paralysis or paresis, there's only disturbed movement. (Same for Cerebellar diseases)

Normal Pathway of the Basal Ganglia:

Excitatory impulses from certain parts of the Cerebral Cortex (PMA, SMA, Association, and Sensory) will reach the Striatum (Putamen and Caudate) through Glutamate. The neurons at the end of the Striatum release GABA, which is an inhibitory neurotransmitter, to the Pallidum, especially GPI. GPI normally sends inhibitory signals to the Thalamus (GPI always has TONIC inhibition on the Thalamus). The Thalamus sends signals to the Cerebral Cortex.

The inhibitory signals from GPI to the Thalamus are called the Pallido-thalamic tract.

The inhibitory signals from Striatum to GPI are called the Strio-pallidal tract.

Disinhibition mechanism: Striatum is inhibiting the GPI which normally functions to inhibit the Thalamus, thus the Thalamus has no inhibition. (Two successive inhibitions = disinhibition)

This entire pathway is called Cortico-striato-pallido-thalamo-cortical tract.

Anatomically, there are two pathways from the Globus Pallidus to the Thalamus which are Ansa Lenticularis and Lenticular Fasiculus, both combine to form the Thalamic Fasiculus which sends signals to VA and VL nuclei in the Thalamus.

The doctor again emphasizes on the importance of the disinhibition mechanism.

Relation of the Basal Ganglia to the Limbic System:

Nucleus Accumbens forms from the union of the VENTRAL parts of the Putamen and the Caudate. This nucleus belongs anatomically to the Basal Ganglia while it belongs to the Limbic system functionally. It is involved in the regulation of motivation, emotion, behavior and the motor control of facial expression (Functions of the Limbic system).

The doctor noted again that the striatum receives excitation from the Cerebral Cortex, while it sends inhibition to the Globus Pallidus.

Affects on GPI from different parts:

1) The doctor noted again that the GPI alone sends tonic inhibition to the Thalamus, while in the entire pathway signaling (i.e when it receives inhibition from Striatum through GABA), the Thalamus is disinhibited and thus, activated.
2) The Subthalamic nucleus sends excitatory signals to the GPI, thus it increases the GPI's tonic inhibition on the Thalamus.

The Direct and Indirect Pathways:

We have two different signaling pathways from the Cortex to the Striatum to the GPI which are:

1) The Direct Pathway:
   It begins in the Cortex which sends excitatory input to the Striatum (mainly putamen), the Striatum then sends inhibitory signals to the GPI, the GPI, as we said, normally sends inhibitory signals to the Thalamus, so when this pathway is activated we get DISINHIBITION of the Thalamus. When the thalamus is released from inhibition, it sends signals to the cortex facilitating essential movement.

2) The Indirect Pathway:
   It begins in the Cortex which sends excitatory input to the Striatum through DIFFERENT neurons than those used in the Direct Pathway. The Striatum (mainly putamen) sends inhibitory signals to GPE, and the GPE normally

sends inhibition to the Subthalamic nucleus. The Subthalamic nucleus, as we said, is normally excitatory to the GPI, thus, when this pathway is activated we get DISINHIBITION of the SUBTHALAMIC nucleus (GPE inhibits it, but it is inhibited by the striatum), which then excites the GPI to send tonic inhibition to the Thalamus. When the Thalamus is inhibited, the Cerebral Cortex is also inhibited since it's not receiving any signals from the Thalamus, thus unneeded movement is limited.

Note: Another signaling pathway to the Striatum is from Substantia Nigra through release of its Dopamine. Dopamine is excitatory to the DIRECT pathway and inhibitory to the INDIRECT pathway.

Basal Ganglia Diseases:

1) Parkinson's Disease:

Pathogenesis: Loss of Dopamine.
-Regarding the Direct Pathway: This causes decreased excitation on the Striatum which normally sends inhibitory signals to GPI, so the GPI's inhibition would be decreased, which increases its function in inhibiting the Thalamus through VA and VL, thus there would be less signaling to the Cortex due to the excess inhibition to the Thalamus which decreases movement and slows it down. (No Paralysis, only slow movement)
-Regarding the Indirect Pathway: This causes decreased inhibition on the Striatum which normally sends inhibitory signals to the GPE, so the GPE's inhibition would be INCREASED due to increased inhibitory signals from the Striatum, causing the GPE to send less inhibitory signals to the Subthalamic nucleus. The Subthalamic nucleus is excitatory to the GPI, so when it receives less inhibition from GPE, it will over excite the GPI (making it also OVERACTIVE) when in turn it sends more tonic inhibition to the Thalamus.
So the hallmark in this disease is the OVERACTIVE GPI.

Clinical Picture:
-Bradykinesa (Slow movement)
-Akinesia (Hesitant to move)

-Rigidity:
A comparison between spasticity and rigidity: Spasticity is a sign of an upper motor neuron lesion or stroke and it affects flexors of the upper limb and extensors of the lower limb (Antigravity muscles). It's associated with hyperreflexia, positive Babinski sign, & Clonus. While Rigidity has bidirectional effects on both extensors and flexors, this is often referred to as Cog-wheel rigidity.
The cause of rigidity: Overactive GPI sends other inhibitory signals to a part of the midbrain called Midbrain Extrapyramidal Area(MEA). This area normally sends inhibition to the pontine reticulospinal tract and the rubrospinal tract. So inhibition of the MEA would stop its inhibition on the mentioned tracts (Disinhibition) resulting in hyperactive alpha and gamma which leads to hyperactive stretch reflex resulting in increased tone.
Regarding the hyperactive Rubrospinal tract, it increases the tone mainly in the distal flexors and little in the extensors.
-Difficulty in initiation, continuation, and termination of movement.
- Tremor: This Tremor is present at rest and disappears upon movement, unlike the cerebellar tremor which is only present when you intentionally move a muscle.

Cholinergic interneuron role in Parkinson's disease:
The Striatum's main cells are GABAergic neurons which are inhibitory; next to it lays a cholinergic interneuron. The Cholinergic neuron receives inhibition from Dopamine. If there's loss of Dopamine, the cholinergic interneuron would be excited and it will send excitatory signals to the GABAergic neurons which cause over activation of the indirect pathway leading to overactive GPI and therefore, they increase the symptoms of Parkinson's disease.

Treatment:
The treatment for Parkinson's disease is only SYMPTOMATIC treatment and NOT curative.
1) You give the patient L-Dopa which can cross the Blood Brain Barrier; the remaining cells of the degenerating Substania Nigra would convert it into Dopamine. Note that the Substantia Nigra doesn't stop degenerating,

so the remaining cells which used to convert L-Dopa to Dopamine eventually die as well and this symptomatic treatment would be no longer effective.

2) The Anticholinergic drugs are most effective against tremor for unknown reasons. For example, Amantadine is used to increase Dopamine secretion and to inhibit Acetylcholine.
3) Surgical removal of the overactive GPI through a puncture in the lateral fissure.
   If you insert a needle in the lateral fissure you pass through Insula>Putamen>GPE>GPI>Internal Capsule>Thalamus

Chemical changes in a patient with this disease:
Decreased Dopamine Acetylcholine ratio (Dp/Ach).

2) Chorea:

In children: as a complication of Rheumatic fever (Rheumatic Chorea)
In adults: Huntington Chorea, and is normally associated with dementia.

Pathogenesis: Loss of GABAergic neurons in the indirect pathway which normally inhibit GPE, thus, GPE would inhibit and suppress the Subthalamic nucleus in a way that it can no longer excite the GPI to inhibit the Thalamus. As a result, the GPI would be UNDERACTIVE and there would be no inhibition on the Thalamus, causing it to send more signals to the cortex than it should, and the cortex would be hyperactive resulting in involuntary spontaneous movement.
<u>So the hallmark in this disease is UNDERACTIVE GPI</u>

Note: in both of these diseases, the upper motor neurons and the lower motor neurons are perfectly normal.

SO the Basal Ganglia only prevents undesirable movement and its damage results in DYSKINESIA only and NOT paralysis. It also causes Hypertonia and tremor for reasons which will be discussed later on (Parkinson's).

Major Differences between the two diseases that the doctor kept repeating forever:

1) In Parkinson Disease there is OVERACTIVE GPI and EXCITED Subthalamic Nucleus.
2) In Chorea there is UNDERACTIVE GPI and SUPRESSED Subthalamic Nucleus.

One last note: The Basal Ganglia saves movement programs specifically in the Striatum. These stores save up every move you've ever learned since you were a kid.

The End

Rand Omari