Module:
Biological Foundations of Mental Health

Week 5
Reward, emotion & action

Topic 2
The structure and function of the Basal Ganglia – part 1 of 5

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Lecture transcript

Slide 1

In the following lecture, we will address the basal ganglia. We will go through anatomy to connectivity and functionality, and then we'll later look at how this function of the basal ganglia relates to specific diseases. We will look at examples of diseases and then we will also look into what the basal ganglia may have to do with free will, and whether their structure is evolutionary conserved.

Slide 2

The basal ganglia are located in the basal forebrain. You can see on the left a picture of a human head, where the basal ganglia are located. And on the right side, you can see the basal ganglia anatomy. We have, on the top left-hand side, the caudate nucleus, and on the right-hand side, the putamen. Those together form the striatum. We then have the globus pallidus, which we will see later, comes as an external and an internal segment. We then have the subthalamic nucleus and the substantia nigra.

Slide 3

Here again, you can see, from a side view, those components, and then the names of those nuclei. Again the striatum, which in primates consist of caudate, putanem, and the ventral striatum, including the nucleus accumbens. We then have the globus pallidus, which consists of the internal and external domains of the globus pallidus. The subthalamic nucleus and the substantia nigra pars reticulata.

Slide 4

Here again on the left-hand side, you see a side-view of the basal ganglia and their location within the brain. And now on the right-hand side, you see a cross-section, like you see when you have post-mortem sections of the human brain. Again, you see the caudate nucleus and the putamen, which together form the striatum. The globus pallidus, the internal and external segment, the substantia nigra, and the subthalamic nucleus.

Slide 5

The connectivity of the basal ganglia. As you can see on the left-hand side, we have, again, the cross-section where we see the parts of the basal ganglia. And on the right-hand side, you see the connectivity through which those parts of the basal ganglia are connected to other parts in the

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brain. At the top, you see that cortical input actually projects directly on the striatum, but also on the subthalamic nucleus. The subthalamic nucleus is connected to the external segment of the globus pallidus as well as to the substantia nigra reticulata and the internal segment of the globus pallidus.

The striatum has direct connections to the substantia nigra reticulata and the globus pallidus internal segment, as well as to the globus pallidus external segment. You can also see what is called the SNC, that is the substantia nigra pars compacta, where dopaminergic connections project onto the striatum. Importantly, as you can see, the SNR and GPI have a projection to the thalamus and they have a projection to the tectum and thereby influence motor programmes.

Slide 6

Here, we see the connectivity of the basal ganglia, but now highlighted are various so-called loops. The connectivity that I just described is repeated several times, and we call them so-called reentrant loops. And they can be categorised because of the functions they are involved in. So we have the sensorimotor loop, we have the associative loop, and the ventral loop. Highlighted are different parts of the cortex, as you can see on the top. And those have connections to various parts of the basal ganglia, such as the putamen, the caudate, the globus pallidus external and internal segments, the substantia nigra, reticulata, and the subthalamic nucleus, and then of course the thalamus, which is a central element as we will see later.

Now if you compare the sensorimotor with the associative loop, you can see that different cortical areas are involved. But also, the different connections among the basal ganglia are involved.

Slide 7

In the next slide now, we look more at the functional connectivity. Again, as you can see on the left-hand side, we have a cross-section of the brain, which highlights the different nuclei of the basal ganglia. And now on the right side, we have a very, very simple scheme of connectivity. At the top, you see the cortex, you see the striatum, you see the two parts of the globus pallidus, the external GPE and the internal segment at GPI. You see the STN, which is the subthalamic nucleus. You also see, together with the GPI, the substantia nigra pars reticulata and you also see the thalamus.

Now what is important are three features. First of all, you see connections that are in green. Those are excitatory connections, that is, they are activating regions that are connected to it. You also see red connections. Those are inhibitory connections. So those activities inhibit the target region. In addition, you can also see that the striatum has two different ways to reach the GPI and SNR, as we will outline in the next slide.

Slide 8

Next slide illustrates the functional connectivity of the basal ganglia, and it's an animated slide where I will guide you through the various parts, their connections, and we will later see why they are important. So again, on the right hand side, you see a cross-section through the brain, with the main parts of the basal ganglia. And on the left-hand side, again, you see the scheme, which highlights the various parts of the basal ganglia, how they are connected with the cortex, with each other, and the thalamus.

Now important is the input nuclei of the basal ganglia are the caudate and to putamen, which together form the striatum. Note the red dots on the right-hand cross-section, the caudate nucleus and the putamen. And on the left-hand side, striatum in the scheme. The intrinsic nuclei are the subthalamic nucleus, STN, and the external segment of the globus pallidus. As you can see, the striatum has an inhibitory reconnection onto the globus pallidus external segment, and the GPE itself has also an inhibitory connection to the STN.

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Next, we look at the output nuclei, which on the right-hand side, you can see with the red dots, is the globus pallidus and a substantia nigra reticulata. On the left-hand side in the scheme, you can see they come together. They are the GPI and the SNR. They receive inhibitory connections from the striatum and excitatory connection from the subthalamic nucleus. This is important. The output nuclei, GPI and SNR, also project inhibitory connections to the thalamus. That is, the basal ganglia nuclei inhibit the thalamus, whereas the thalamus has excitatory connections to the cortex again.

Finally, we have neur0modulatory input to the striatum, which comes from the substantia nigra pars compacta, SNC, which are dopaminergic innovations into the striatum. We will later see why they are important.

Slide 9

Having established the functional connectivity between the parts of the basal ganglia, the cortex, and the thalamus, let me re-emphasize the parallel loops within the basal ganglia that subserve distinct functions.

Remember in a previous slide, we looked at the sensory motor loop, the associative loop, and the ventral loop. Now here again in this scheme, you can see that basically, you can conceptualise these different loops as multiplications of existing connections. But of course, they subserve different functions, which is one of the very important features of the basal ganglia. The multiplication of parallel loops, which are reentrant loops that subserve different functions.

Slide 10

Now in order to understand what the basal ganglia actually do, we shall focus on movement and how this is modulated. Now remember what I told you about the different connections within the basal ganglia. The green ones are the excitatory ones and the red ones are the inhibitory ones. Once again, the cortex has excitatory inputs to the striatum. The striatum has inhibitory connections to the output nuclei, the GPI and SNR, and it also has inhibitory connections to the internal nuclei, the GPE, which itself has inhibitory connection to the STN.

Now what is important is that the output nuclei have inhibitory connections to the thalamus, and it is this output that is important to understand how movement is modulated through disinhibition.

Slide 11

It is highlighted in this slide here, where it is now emphasised the inhibitory connection between GPI and SNR, which are the output nuclei to the thalamus, whereas the thalamus has an excitatory connection to the cortex.

Slide 12

So keep in mind that the output nuclei of the basal ganglia are inhibitory, as emphasised by the red inhibitory connection from GPI SNR to the thalamus.

Slide 13

The output nuclei maintain a high tonic level of discharge, as you can see in this speech circle, where those different lines represent action potentials. So what you can see is a high tonic activity of the output nuclei. Now because they have inhibitory connections to the thalamus, this high tonic activity suppresses the thalamus.

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Slide 14

This high tonic activity of the output nuclei and the inhibitory connection of the thalamus actually keeps the thalamus quiet, and hence, there cannot be any excitatory activity on the cortex, which is the absence of movement.

Slide 15

Now movement modulation occurs through this inhibition of thalamocortical target regions. How is this achieved? As you can see in the illustration, you would need an impaired activity of the output nuclei, which in turn, as you can see in the animation, does disinhibit the thalamus, which then in turn can cause an excitatory activity towards the cortex.

Just look at the speech circles. The tonic activity, the normally tonic activity of the GPI SNR is interrupted in the middle. You don't see these bars, which represent action potentials. That means during this time, the normally inhibitory activity to the thalamus is interrupted, and this is shown in the speech circle for the thalamus. You see all of a sudden in this corresponding time frame, there is activity, which are these bars that represent action potentials. And because the thalamus has an excitatory connection to the cortex, you can see that there is cortical activity. And this is movement modulation through disinhibition.

Slide 16

In the next slide, we can summarise what we have learned so far. So the basal ganglia mediate movement through disinhibition. Key to understand is that the output nuclei of the basal ganglia, the GPI and SNR are inhibitory. They maintain a high tonic level of discharge, thereby suppressing the activity in target regions such as the thalamus. The phasic decrease in firing rate transiently releases the target regions from inhibition. It thereby causes disinhibition, which then can lead to thalamocortical activity, and thereby promote movement.