Module:
Biological Foundations of Mental Health

Week 5
Reward, emotion & action

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

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Lecture transcript

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Now we are able to look into another very, very important concept of the basal ganglia. And that is the direct and indirect pathways. Those are pathways that play a crucial role in understanding how the basal ganglia function, and why their dysfunction has such a wide range of disabilities as a consequence. What we are looking at now is the two ways the striatum innovates either the output nuclei or the indirect nuclei.

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So let's first look at the direct pathway. The direct pathway is the direct connection from the striatum to the output nuclei. And as I said before, this is an inhibitory connection. So the direct pathway is the direct connection from the striatum to the GPi/SNr.

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The basal firing rates in the striatum are very low, and dependent upon cortical excitation. That means if the striatum is not activated by excitatory cortical connections, there's not much activity. Hence, its inhibitory connection to the output nuclei is low.

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Under these conditions, striatal firing has little impact on the output nuclei, as you can see here. Remember, the output nuclei show a high rate of tonic firing, which is inhibitory on the thalamus. Now, because the striatum is not activated, its inhibitory connection to the GPi/SNr has no effect.

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Now, phasic cortical excitation drives excitatory discharge in the striatum. Again, you can see that animated by these little bars, which represent action potentials. Now, the cortex has excitatory connections to the striatum. This causes activation of the striatum. Now, because the striatum has an inhibitory connection to the GPi/SNr, it causes a transient inhibition of GPi/SNr firing.

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As a consequence, this activation of the direct pathway promotes action. Why? Because in that phase

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where striatal inhibitory activity inhibits GPi/SNr activity, the output nuclei are not inhibitory on the thalamus. And this can promote action. So let me summarise.

The activation of the direct pathway promotes action. And this is because the striatum has an inhibitory activity on the output nuclei, the GPi/SNr. And because it is inhibitory and the GPi is inhibitory in the thalamus, what you have is a disinhibition of thalamic activity, which thereby promotes action.

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Now let's have a look at the indirect pathway. As mentioned beforehand, we are now looking at the connections from the striatum to the intrinsic nuclei, which is highlighted here. So the striatum has an inhibitory connection to the globus pallidus external segment, with the globus pallidus external segment having an inhibitory connection to the subthalamic nucleus. And the subthalamic nucleus in turn has an excitatory connection to the GPi/SNr, which are the output nuclei.

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Now again let's consider that striatal neurons have low tonic firing rates. Again, dependent upon strong cortical inputs. So without cortical input, the striatum doesn't have much activity. That is, in this case of the indirect pathway, it does not impose inhibitory activity on the GPe.

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Now, GPe neurons are similar to those in the internal segment. They have high tonic firing rates. Keep that in mind. The GPe, the external segment of the globus pallidus, has a high tonic firing rate.

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And because of inhibitory activity of the GPe neurons, the subthalamic nucleus activity is suppressed.

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Firing under these conditions causes high discharge in the output nuclei GPi/SNr because they are anyway tonically active, and they are inhibitory to the thalamus. So because the STN is not able to have excitatory activity to the GPi/SNr, their inhibitory activity is not suppressed.

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Now, what happens to the indirect pathway when we have strong phasic cortical excitation? Focus on the indirect pathway on the left-hand side. You have phasic cortical excitation.

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It now causes a transient inhibition of the external globus pallidus because the striatum has an inhibitory connection on the GPe, and because the GPe shows a high tonic firing rate.

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Now, because the GPe is inhibitory acting on the STN, this leads to the fact that, for a short transient disinhibition of the STN, this can be active, and thereby excite the output nuclei, GPi and SNr.

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Now, in contrast to the direct pathway, this activity of the STN onto the output nuclei increases the

discharge of the GPi and SNr. And because they are inhibitory, this causes a further inhibition of the thalamus and cortex, which causes the suppression of action because of the enhanced suppression of the thalamus.

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So here again you can see a summary of the indirect pathway and the direct pathway. Let's focus first on the left-hand side, the indirect pathway. Phasic cortical activity activates the striatum, which acts inhibitory on the external segment of the globus pallidus.

Now, because the external segment of the globus pallidus normally shows a high tonic rate of discharge, this phasic activity of the striatum causes an inhibition. Now, as you can see, this inhibition of the GPe causes a transient activation of the STN. Why? Because the GPe is inhibitory acting on the STN.

Now, because it has no activity, this inhibitory activity on the STN is released, and the STN itself can fire excitatory to the output nuclei GPi and SNr. Now remember, the GPi and SNr also show a high rate of tonic activity. And because they are inhibitory to the thalamus, this activity of the STN onto those output nuclei causes a further inhibition of the thalamus.

Now, on the right-hand side, you see the direct pathway, where we look again at phasic cortical activity. This phasic cortical activity activates the striatum. Now, because the striatum has an inhibitory connection to the output nuclei, the GPi and SNr, this causes a transient inactivity of the output nuclei. Now, because the output nuclei are inhibitory acting onto the thalamus, this causes a transient inactivity of the inhibition, and thereby action can be facilitated.

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So, once more, you see here a summary of the two major features. The indirect pathway suppresses action, whereas the direct pathway facilitates action. Now, interestingly, recent research has shown that they are both cooperatively active, and regulate motor output. This is very important to memorise.

In old models, it was always thought that motor activity, for example, would rely on direct pathway activity, whereas the indirect pathway was silent, whereas when you had no activity, or stopped an activity, the indirect pathway was active and the direct pathway was silent. This old model is no longer valid. We now know from experiments that I will show you in a minute that it's the cooperative activity of the direct and indirect pathway that regulates adaptive behaviour.

We don't know yet how this works, but we start to have an idea how they together can mediate adaptive behaviour.

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