Module:
Biological Foundations of Mental Health

Week 3
Synaptic transmission & neurotransmitter systems

Topic 1
Action potentials and synaptic transmission – part 5 of 5

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Lecture transcript

Slide 3

We've seen in our previous sections now how the dendrites in the cell body aim to create the incoming signals, how the action potential is generated at the axon initial segment, and how this is transmitted along the length of the axon. And in this section, we're going to focus now on how this signal, then, is transmitted between axon to axon. We're going to focus on neurotransmitter release, so chemical synapses in this section, but it's important to note that electrical synapses also exist, and you can read further in those if you wish.

Slide 4

We're going to focus now on this very small region here between the two neurons, known as the synaptic cleft, and to do this, we have a presynaptic zone here in blue in the top.

In the membrane, we have voltage-gated channels, but in this case, now, we're focusing on voltage-gated calcium channels. We should mention, much like sodium, calcium has a much higher concentration in the extracellular space than the intracellular space, so calcium wants to come into the cell.

We also have mitochondria here in yellow, because of course, there's an energy-dependent component to it here. We have vesicles, the circles, and within these vesicles, we have neurotransmitters, the little dots, and these are stored here in the presynaptic terminal, waiting for them to be triggered and release to happen across the synaptic cleft.

In response to an incoming action potential that invades the terminal field, the voltage-gated calcium channels are now opened. They trigger. Calcium can flood into the cell, and via a calcium-dependent mechanism, the vesicles are now moved to the membranes, so this process called exocytosis. They're moved toward the extracellular membrane of the neuron where they fuse with that membrane, and there are a number of proteins involved in this process, such as SNAP25 and SNARE, and you can read up those further if you wish. This allows the membrane to fuse with the extracellular space and allows the neurotransmitter to be released into the synaptic cleft. This neurotransmitter will then diffuse across this very small gap where it can act as a ligand to trigger the ligand-gated ion channel, for example, on the postsynaptic cell.

So if this was a neurotransmitter that was triggering a ligand-gated sodium channel, for example, it would open the channel, allowing sodium to flood into the postsynaptic cell. If you think back to a previous section, this would induce an excitatory postsynaptic potential, so it would excite the cell.

But equally, this neurotransmitter release could cause chloride influx because there's a chloride ion channel, and it could be inhibitory. So this is this integration component that we spoke about previously.

Slide 5

The neurotransmitter, of course, has been released, and it's having its effect on the postsynaptic cell, but there has to be a mechanism for controlling that and what happens here. This mechanism really is a stimulus-dependent system, so the postsynaptic neuron doesn't just want to know that my presynaptic partner fired. He wants to know what's the relative intensity of the signal. That's important for how the signal was transmitted.

Experimentally, if we record-- so these arrows are recording electrodes, shall we say, and we're recording the graded potential that's coming into the cell body. We're recording what's happening at the axon initial segment triggering zone, and we're going to record the action potentials from this axon.

In the first example, what we can see is that the graded potential, in this case, is minus 40 millivolts, so we'll all agree that's above the minus is 55 millivolts threshold that we've been using here. That allows the triggering of an action potential here at the axon initial segment, and we can record these action potentials along the axon. These will invade the terminal field and result in the release of neurotransmitter from the presynaptic neuron based on the mechanisms we've just discussed.

Now in the second scenario, a larger graded potential, which reaches the triggering zone in the axon initial segment with a higher threshold will induce more in action potentials as seen here by multiple action potentials in the top graph. This will invade the presynaptic terminal. Because it's voltage-dependent, or stimulus-dependent calcium channels, more of these calcium channels will be opened.

Therefore, more calcium will flow into the cell. We will get more exocytosis of neurotransmitter, and therefore more neurotransmitter into the synaptic cleft to signal to the postsynaptic neuron. So we have the stimulus-dependence component where the postsynaptic neuron can sense both the activation, but also the level of activation, of its presynaptic partner.

Slide 6

Now of course, once these neurotransmitters are released, we have to have a mechanism by which we can control this. We can't just have them acting continuously. There are a number of mechanisms by which the neurotransmitters can be removed.

The primary mechanism is actually reuptake into the presynaptic cell. So the presynaptic terminal will reuptake the neurotransmitters and recycle them back into vesicles to use again. But they can also be taken up by support glial cells, for example, astrocytes here on the grey on the left hand side. This is a very energy efficient mechanism by which they can recycle these neurotransmitters.

Alternatively, on the postsynaptic membrane, there are mechanisms by which these neurotransmitters can be degraded. They can be broken down, and then, of course, the products are taken away into the bloodstream and then expelled.

The final mechanism is just the act of simple diffusion. These neurotransmitters will diffuse away from the synaptic cleft and can be taken off into the bloodstream, and taken away from the region. But as I mentioned, the presynaptic reuptake of these neurotransmitters is the primary mechanism and the most effective mechanism.

In the context of mood disorders, this is actually a very important target. So for example, the antidepressant selective serotonin reuptake inhibitors, they actually act to prevent this reuptake of the serotonin.

So if you imagine, now, the serotonin is released. It's having its effect in the postsynaptic cell. These drugs now block its reuptake, so they potentiate the effect of your normal release. They don't have an artificial effect and increase the level of serotonin, but what they do is they potentiate your own endogenous, internal response, and that's the mechanism by which they have their antidepressant effects. So this scenario here where we can potentiate or change the effect of the presynaptic talking to the postsynaptic neuron is very important in the context of mood disorders.

Slide 7

Just by way of review, I think it's important to look at this in animated perspective. What we have here is we have, again, this incoming action potential, which is triggering a voltage change at the presynaptic terminal. This is opening the voltage-gated calcium channels, and calcium - positively charged calcium - is flooding into the cell.

This triggers vesicle like cytosis, so these vesicles move towards the cell membrane. They then fuse with the membrane and release the neurotransmitter across the synapse. This activates, as you saw there, the local postsynaptic ion channels and allows, in this case, sodium flux into the postsynaptic dendrite.

What you see here, now, is this excitatory postsynaptic potential because sodium has a depolarising effect. But equally, this could have been hyperpolarising effect had the ion channel on the surface of the postsynaptic neuron been fluxing chloride ions, for example.