Module:
Biological Foundations of Mental Health

Week 3
Synaptic transmission & neurotransmitter systems

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

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Lecture transcript

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I'm Phil Holland. I'm a lecturer here at King's College London, and I'm primarily interested in headache disorders including migraine, for example. And what we do in our laboratory is we use electrophysiological techniques to record the electrical impulses between nerves and how they communicate with each other. Today, I'm just going to talk over how the normal neurons set up their resting membrane potential and how then they generate and transmit these potentials.

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All cells, including neurons, have this membrane surrounding them, and that's this phospholipid bilayer. This is a hydrophobic layer, so it allows the separation of aqueous ions between the extracellular space and the intracellular space, allowing us to set up these ionic gradients that we're going to discuss.

Now, of course, we need to move ions across these membranes, and for this purpose, we have proteins in the form of pumps, such as the sodium-potassium ATPase on the left, and ion channels, such as the sodium channels and the potassium channels here in grey and purple.

Now, these ion channels can be leak channels. That is, they're open, and they allow ions to passively flux up and down their concentration gradients. Or they can be gated in that they are closed at the resting condition and can respond to an external stimuli, be this electricity in the form of a voltage-gated channel or a neurotransmitter, for example, in the form of a ligand-gated channel, causing this gate to open and allowing these channels to flux ions across the membrane.

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Now, it's important to state that most membranes and neurons have a higher concentration of potassium leak channels, and this is important for setting up the resting membrane potential, as we'll see. In this, ratio is 3 to 1, but this is just representative.

Inside the cell, we have these large, organic anions here in red, and these are negatively charged ions on large proteins. These are locked within the cell, so they can't cross the membrane. And as you can see, this puts a negative charge inside the cell in the intracellular space. This has the effect of drawing positively charged sodium and potassium ions, sodium in the blue and potassium in the green here, towards the extracellular space and repelling slightly negatively charged ions such as chloride ions

here, as can be seen. And that sets up a net positive charge along the extracellular space.

And as we mentioned, there are more potassium leak channels in the membrane. In response to this electrostatic charge, this want for the positive charged ions to be attracted towards the negative ions inside the cell, more potassium will enter the cell, making a higher concentration of potassium inside the cell.

Now of course, some sodium will also enter the cell, but because there are less sodium leak channels, this is relatively fewer than the potassium. And we also have a low concentration of chloride ions within the cell, setting up this ionic gradient across the membrane.

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We have relatively more potassium within the cell, as can be seen here in the green, and relatively fewer on the extracellular space. Again, there's a higher concentration of sodium on the extracellular space compared to the intracellular space.

These sodium-potassium ATP pumps, they act to help maintain this concentration gradient. Of course, I should point out as well that we have a higher concentration of chloride ions outside the cell as opposed to inside the cell.

Obviously, these ionic gradients are established, and the sodium-potassium pump acts to pump ions against these gradients, so it's an energy-dependent mechanism that helps to maintain the high concentration of potassium inside the cell and the lower concentration of potassium outside the cell.

In order to do this, the pump needs energy. This is an energy-dependent mechanism, so it uses adenosine triphosphate and changes this, obviously, to adenosine diphosphate and an organic phosphate molecule. And this energy allows the channel to collect three sodium channels from the intracellular space, as you just saw, and actively pump them to the extracellular space. In turn, two potassium ions are gathered from the extracellular space and pumped to the intracellular space.

This has two mechanisms. This, first of all increases the concentration of sodium in the extracellular space and increases the concentration of potassium in the intracellular space. But also, as three positively charged ions were pumped out of the cell and only two positively charged ions were pumped into the cell, this helps to maintain the net negativity of the intracellular space compared to the extracellular space.

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This is what we can see here. At the resting membrane potential, we have this mix of ions in the outside, largely sodium and chloride and fewer potassium, and on the inside, we have a greater concentration of potassium and fewer sodium and chloride ions. This sets up a gradient across the membrane, and these ions are under two forces.

First of all, they're under the force of the electrostatic force, and that is the charge component. The want for the positive ions to go towards the negative ions, for example, through the leak channels, as we discussed.

But they're also under the force of diffusion. That is that they want to move along their concentration gradients from an area of high concentration to an area of low concentration. So for example, under these conditions for diffusion, potassium would want to leave the cell and go to the extracellular space.

It's important for the action potential, that we'll come to a later section, to see how these electrostatic forces influence the different ions. And for sodium, as you can see here, both the

electrostatic force in red and the force of diffusion want to drive sodium into the cell, so sodium is very potentiated and very ready to drive into the cell should these voltage-gated sodium channels open.

Potassium, on the other hand, has divergent forces. The charge component, the electrostatic component in red, as we discussed, brings potassium into the cell, but the force of diffusion wants to take potassium out of the cell. And for chloride, these are reversed where the charge component wants to repel chloride from the cell, and the force of diffusion wants to attract chloride into the cell.

We have a point called the equilibrium potential, and that is the point for any ion where this net flux across the membrane would be zero, and that would be because the force of the electrostatically charged component and the force of the diffusion would be equal to each other. So under resting conditions, these ions would not move across the membrane potential.

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This is just an example of the relative concentrations of these ions, and what you can see is again highlighting that chloride and sodium are highest outside the cell, and potassium and organic anions here, the big A with the negative, are higher inside the cell. And what the resting membrane potential is, if we were to record, the electrode here on the right hand, side between the extracellular space and the intracellular space, what we're recording is the fact that the intracellular space, due to these ionic gradients, is relatively more negative to the extracellular space. In this case, by around minus 60 to minus 70 millivolts.