Neurobiology

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Lecture 4.4: Properties of chemical synapses

Hi everyone, welcome back to Neurobiology. In the last video we looked at the structure of chemical synapses. We saw how neurotransmitters are released, how they are received by the postsynaptic receptors and how they are recycled back. We also looked at the postsynaptic potentials that are generated as a result of this activity. Now in this video we will see what are the various advantages of having chemical synapses that are made possible by this kind of organization. We will also look at various kinds of neurotransmitters that are used by various nervous systems and finally we will see the two main classes of postsynaptic receptors that are present in neurons.

So arguably chemical synapses are more complex than electrical synapses in their organization. They involve many more steps and require many more types of proteins to be formed and they also add a delay in the communication time between the action potential in the first neuron and the postsynaptic potential in the second neuron. So there must be some very good reasons why the brain still uses chemical synapses. The one major reason is that there is an amplification factor in chemical synapses.

By that we mean that if there is one action potential in the presynaptic neuron that can cause release of hundreds of vesicles, each of which can contain thousands of neurotransmitters and they can activate large number of receptors on the postsynaptic side. So how much change do we see on the postsynaptic side in response to one action potential can depend on all these factors, how many vesicles there were and how many receptors there are and that provides a tunable amplification factor for the synapse. So some synapses are strong, they have lots of receptors and lots of vesicles and that can result in generation of large postsynaptic potentials in response to a single action potential whereas some synapses are weak in which the postsynaptic potentials are very small on the order of microvolts. And in fact this strength of a synapse is not always constant, it can be changed with experience. And in fact this is one of the ways in which experiences or memories are stored in our brain, that the synapses between specific neurons get modified, they become stronger or weaker with experience and that is how our memories are stored.

The next advantage of chemical synapses is that they provide a flexibility in terms of various neurotransmitters and their receptors. So a single postsynaptic neuron can receive input from multiple presynaptic neurons and if it is using different kinds of receptors at these different synapses then it can have different effects in response to action potentials in these presynaptic neurons. So it can have an excitatory synapse with some neuron and it can have an inhibitory synapse with some other neuron. So all that flexibility is provided by chemical synapses. A third advantage is filtering and by that we mean that neurotransmitters are released only when there is an action potential in the presynaptic neuron.

So if there is some weak activity in the presynaptic neuron that does not generate an action potential, then it would not cause any release of neurotransmitter. And that is good because it allows removal of noise from the system. So if there is some spontaneous noisy activity that changes the membrane potential of the presynaptic neuron, it will not get communicated to the postsynaptic neuron. It also makes the communication between the two neurons nonlinear. In the case of electrical synapses, whatever effect there is in the first neuron, we will see a proportional effect in the second neuron.

But here because there is thresholding, this effect on the second neuron is nonlinear. And what that means is that we now have a circuit of neurons with nonlinear communication between them. And from theoretical studies, we know that nonlinear circuits can perform a wider array of functions than linear circuits. So it increases the range of functions that the neural circuits can perform. Let's look at some of the common neurotransmitters here.

The most common excitatory neurotransmitter in the brain is called glutamate. It's a small molecule. It is actually the anion of glutamic acid, which is a common amino acid present in all organisms. Almost 90% of the synapses in human brain use glutamate as a neurotransmitter. The most common inhibitory neurotransmitter is called gamma-amino-butyric acid or GABA in short.

GABA is also a small molecule with a simple structure like this. We have already seen acetylcholine in earlier videos. It is also a common neurotransmitter. And in vertebrates, it is commonly found in the motor neurons. So the synapses between the motor neurons and muscles include acetylcholine as a neurotransmitter.

But in simpler organisms like insects, acetylcholine is also a very common neurotransmitter present in the brain. There are some types of neurotransmitters that are called neuromodulators because they are involved in large-scale modulation of the brain activity. So these neurotransmitters carry information about the global state of the person. For example, dopamine

is thought to be involved in reward processing. So if you eat a chocolate or you win a lottery, then the dopaminergic neurons in your brain are likely to be active.

Similarly, serotonin or adrenaline, they also convey global information about the state of the person, the mood of the person or the state of arousal, etc. It is already known that our actions and our perceptions can change depending on the state of the body. So if we are feeling happy versus sad, or if we are feeling awake versus sleepy, that can have a profound impact on how we perceive things or how we act. And these kinds of effects can be modulated by these neurotransmitters. And the way they are able to do it is that the neurons that release these neuromodulators, these are generally widely branching neurons that go to many parts of the brain.

So they can affect processing in large parts of the brain. And this is not a complete list. There are many more neurotransmitters that are present, but these are the more common ones. The reason for having multiple neurotransmitters is that it adds to the flexibility. So it allows a postsynaptic neuron to receive input from different neurons in different ways.

And it can also modulate the synaptic strengths of the synapses independently. So a neuron can strengthen the glutamatergic input while weakening the GABAergic input. Or it can be affected by say dopamine, but not by serotonin. So depending on the function of the neurons, they can receive different kinds of inputs and they can modulate these inputs as per experience in different ways. Neurotransmitters bind to the receptors and cause opening of ion channels.

Now there are many types of receptors that are present on the neurons, but broadly they can be classified into two categories, depending on whether they open the ion channels directly or indirectly. The first category that results in the opening of ion channels directly is known as ionotropic receptors. These are basically ligand gated ion channels to which the neurotransmitters bind. So the neurotransmitters serve the role of ligands. They bind to specific pockets on these receptor proteins.

And in the middle of the protein, there is a pore which can open when the binding happens. So this binding causes a change in the confirmation of the protein and results in opening of the pore and then ions can pass through. So these receptors function both as receptors as well as channels. The second class of receptors that open the channels indirectly are known as metabotropic receptors. And they often belong to a class of proteins known as G protein-coupled receptors.

Now this class of protein is actually a very large class of proteins that includes receptors for various types of ligands, including neurotransmitters. And these receptors are just the receptors, so they do not have an ion channel present inside them. The neurotransmitter binds to the receptor that causes a change in the confirmation of the receptor protein and that results in

activation of some interacting proteins. In the case of G protein-coupled receptors, these are G proteins. When these G proteins are activated, they can go and bind to additional effector proteins such as adenyl cyclase.

And these effector proteins in turn result in activation of secondary messengers, such as cyclic AMP inside the neuron. These secondary messengers can then go and bind to ligand-grated ion channels that are present elsewhere on the membrane. So in this case, when cyclic AMP would bind to this ion channel, that would cause the opening of channels here and the ions can pass. So we have a somewhat more complicated system in the case of metabotropic receptors. The binding of the neurotransmitter and the opening of the channel is separated by a couple of layers in between.

So in terms of speed, obviously the ionotropic receptors would be faster because the binding of the neurotransmitter and opening of the channel is happening at the same location. Whereas here, there are a couple of layers in between. But one advantage of G protein-coupled receptors is that they allow a fine control over how many ion channels open in response to the binding of neurotransmitters. Because these intermediate levels can be regulated by the cellular machinery. And as we have discussed earlier, that one of the ways in which our memories or experiences are stored is by regulating the synaptic strength.

So eventually how many ion channels open in response to the synaptic communication, that is an important determining factor. And the metabotropic receptors allow a finer control of that. The same neurotransmitter can have multiple types of receptors. And this is particularly true for glutamate, which is the most common neurotransmitter. So glutamate has both ionotropic receptors and metabotropic receptors.

The ionotropic receptors can be classified into three main classes, NMDA receptors, AMPA receptors and Kainate receptors. And metabotropic receptors belong to the GPCR family of receptors. All these three ionotropic receptors NMDA, AMPA and Kainate are basically cation channels. So they are permeable to both potassium and sodium. And because they are permeable to both, their equilibrium potential is somewhere in between the equilibrium potential of these two ions.

So their permeabilities are such that their equilibrium potential is around 0 millivolt. And because the neurons are typically at a resting membrane potential of around minus 60 or minus 65, these channels have an excitatory effect on the neurons. And therefore glutamate is commonly called an excitatory neurotransmitter. Similarly for GABA, there are different types of receptors. There are ionotropic receptors as well as metabotropic receptors.

The ionotropic receptor for GABA is known as $GABA_A$ receptor and it opens a chloride channel. So this is basically a GABA-gated chloride channel. And the metabotropic receptor for GABA is known as $GABA_B$ receptor. And this receptor results in indirect activation of a potassium channel. And because the equilibrium potential of chloride ions is minus 70 millivolts and potassium ions is even lower, and these values are lower than the resting membrane potential, these channels have an inhibitory effect on the neuron.

So if the resting membrane potential is minus 65 and these channels are opened, then they would take the membrane potential towards minus 70 so they will be inhibitory. But if for some reason the neuron happens to be at minus 75 millivolt resting membrane potential, then this same channel can have an excitatory effect because it would try to take the membrane potential from minus 75 to minus 70 millivolt. So GABA can also function as an excitatory neurotransmitter in certain cases. But for most neurons whose membrane potentials are above minus 70, GABA through $GABA_A$ receptor will have an inhibitory effect. And similarly through $GABA_B$ receptor, it would also have an inhibitory effect.