Neuroscience - The Brain and the Nervous System

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So we started out with evolution, which would ask, how did this behavior of crossing the road evolve over many, many, many millions of years? Why was it adaptive? Why did chickens who crossed the road produce more offspring? All of that. It was studied by old men going around in boats to the Galapagos to see how chickens on different islands crossed the road and then figured out how that happened over millions of years. The next week, we went into molecular genetics.

And there we talked about the actual genes that control this evolution and how it happened. And there we were talking about people thinking about how genes change in the genome over time, how they hop around, if we're thinking about women in corn fields looking at this, and how those individual genes led to evolution. Then the next week, we went into behavior genetics. And this, specifically was asking about what individual genes are accounting for the variation in the ways the chicken crossed the road. So some chickens cross the road really fast. Some of them do it slowly. Some of them don't do it at all. How does the variation in the way that the genomes are structured for these different chickens account for that? So that was behavior genetics. And then on Monday, you heard about ethology, which really talked about studying this behavior in nature. And we talked about the fixed action pattern. And we talked about all the old man in field booths going out into nature to observe that fixed action pattern and talked about the stimulus the chicken would receive, why it would cross the road after that, how it does it, again, looking at that out in nature. And that was ethology. So today, we're going to talk about yet another bucket, yet another way to think about this, which is neuroscience. And neuroscience is going to focus, specifically on this black box that we talked about on Monday where you get the input coming in of some stimulus that makes the chicken cross the road. And neuroscience is about that black box in the middle and why it is that the chicken is doing this. What was going on in the chicken's brain a few milliseconds before it crossed the road? Why is it that the specific cells in the brain are doing this? And how are they doing it? So that's the overall

background of why we're thinking about neuroscience. And the goal for today is really to give you an overview of the brain and the nervous system, get to know some different parts of it not so that you memorize a list of different parts of the brain but so that you get a general overview that different parts of the brain are specialized for different behaviors.

And also, we're going to zoom in a little bit on the actual cells in the brain, how they communicate. Again, not so that you can sit there memorizing lists of different things but that so when it comes up in future lectures, you will have a better understanding of what we're talking about. And just as a caveat before we start, I, as a neuroscientist, think this is the coolest discipline out there, better than all the others. And you'll see I put in a quote from Thomas Edison that says, "The chief function of the body is to carry the brain around," which is a very brain-centric way of thinking about the world. And there are a lot of people who look at neuroscience and think of it that way. Yes, neuroscience has its limitations. Want to put that out there from the beginning. It can be very brain-centric. It can be thinking about how different parts of the brain control different behaviors without considering the bigger evolutionary aspects or any of the other aspects. So it does have its limitations. But I think it's really cool. So that's why I'm going to tell you about it today. So let's start out. You have a brain. Actually, this is my brain. I volunteered for a psych study back in college and got to look at some pictures in a scanner. And they gave me this printout of my brain afterwards. And the brain, I think, is an absolutely amazing, amazing thing. And one thing that people love about the brain is that it starts working and keeps working. But just as a reminder from this quote, "It never stops working until you stand up in front of public to speak." So during this lecture, there may be things that are confusing. If you don't understand them because I'm not explaining them in a way that makes them understandable to you, I've put my email address up there. It's also in the handout.

And it was at the beginning of the presentation. So definitely email me if you have any questions. Or come to see me after class. And I'll be giving this first 45 minutes or so introduction to the brain and the nervous system. Then, Anthony's going to come up afterwards and tell you a little bit more about how neurons communicate with each other. So let's think about the brain and the nervous system. And to give you a really broad overview, the nervous system is divided into two really broad classes, the central nervous system and the peripheral nervous system. And we'll start with the central nervous system, which is what most people think about when they think about neuroscience, which is the brain and spinal cord. So you have this brain sitting up there in your head. You have the spinal cord going down communicating to and from the brain. And this is the central nervous system. And I'm going to go through some different parts of the central nervous system just to give you an idea that there are different parts and that they do different things. Again, don't worry about memorizing them. This is really just to get you familiar with what's going on up there. So if we look at the brain more carefully and look at different parts of the brain, we've got these different parts that people neuroscientists specifically have divided up for us. And if we start at the bottom down there with the brain stem, the brain stem sits at the bottom of the brain at the top of the spinal cord. And it's what ends up relaying the information to and from the spinal cord and to and from the brain. So you have your brain up here doing all the processing, spinal cord down there sending out all the

signals to make you move or to send up sensory information. The brain stem sits in the middle and helps regulate what goes through. Then, you have the cerebellum sitting at the very back of the brain up there. And the cerebellum is a really cool part of the brain. It's really, really wrinkled.

It has lots of different cells packed into it. And what it does is it helps control your motor movement and specifically helps when you have to learn something new. So when you have to learn how to play piano for the first time or when you have to play basketball for the first time, you're going to make mistakes. And what the cerebellum does is it helps correct for those mistakes. So when you are shooting a hoop for the first time and it goes off to the left, then you have to learn, OK, I need to move it over to the right a little bit next time. The cerebellum is what does that. And when I teach this to middle schoolers or high schoolers, one fun thing I do with them is I bring along these specialized classes, which have prisms on them. So when you wear them, it skews your view of the world a few degrees to one side. So if I'm looking, say, at this marker here, when I put on the prisms, it's going to look like it's over here. So I do this to the kids. And the kids look out at the marker, and I tell them to quickly reach for it. They see it over here. So they start out reaching this way thinking that the marker is over there. But what happens over time is that they do this over a few minutes, and eventually they correct for it. So even though their vision is out here, they've corrected for it by moving their arm over here to where the marker is. And that's learning that happens in the cerebellum. Then, the really cool thing is they take off the glasses. And because the cerebellum has taught them that they need to reach to the left of where the visual field is, they look out at this marker. They start reaching over here to try to get it. So the cerebellum corrects for that. And again, after a few minutes, they do that a little bit longer. And they eventually reach for the marker. So that's learning that's happening in the cerebellum, really cool part of the brain. Then above the brain stem and the cerebellum, you have this wrinkled outer layer of the brain called the cortex.

And the cortex we can broadly think of in four different lobes. And again, broad theme for this lecture, different lobes, different parts of the brain are specialized for different functions. So you have the frontal lobe up, as you would expect, at the front of the brain. And the frontal lobe, among many other things, plans your actions and controls your movement. So this is the part of your brain that's going to be sending a lot of connections down through the spinal cord to make you move your arms, move your legs, move the other parts of your body. And that's all happening because of the neurons that are up there in the spinal cord in the frontal lobe. And again, broad theme, different parts of the brain are specialized for different functions. Different parts of the frontal lobe, different parts of that part of the cortex that control movement control different parts of your body. So you've got a part of that frontal cortex that controls your foot and your left foot and your right foot and your left hand and your right hand. And they're all in specific places in the cortex. And they line up the way you would expect them to in the body. So if your foot cortex is down here, then your leg and your knee are going to be up here and then your trunk and then your arms and then the parts of the cortex that control facial movements up at the top. So it's organized according to function. So that's one thing that happens in the frontal lobe. Then, you have behind it the parietal lobe. And right next to the part that controls your movement

in the frontal lobe is the part of the parietal lobe that senses the sensory touch information from the outside world. And again, form follows function. So different parts of the parietal lobe are specialized for different parts of the body, different parts of your touch information. And not only are there different parts of it but the sizes of the cortex that receive that information are also different sizes. So you've got your finger tips that are really sensitive, have lots of nerve endings, have lots of sensory information coming from them.

Your fingertips have a big part of cortex represented in the parietal lobe. So again, different parts, different functions, different sizes. Below the parietal lobe, you have the temporal lobe, which is sitting here next to your temples as you might expect. And the temporal lobe, among other things, receives the auditory information. Your hearing information comes into that part of the cortex. And also, as you'll hear later, deep inside that lobe are the parts of the brain that help for memory formation. So the temporal lobe receives auditory information and also has a really important part for memory formation. Then finally, at the back of the brain, you have the occipital lobe. And all the way at the back of the brain here, this occipital lobe is where you're receiving visual information. So visual information comes into your eyes, travels all the way to the back of the brain to the occipital lobe. And that's where it gets processed. So different parts of the brain are doing different things. And this is just a really broad way of thinking about that. So I'm next going to go over some specific parts of the brain that you're going to hear a lot about in the coming lectures. For now, it's just an introduction. But hopefully, when you hear them again later, you'll be able to say, ah, I remember that. So the limbic system, you're going to hear about again and again and again. It's this series of structures that are underneath the cortex but sort of above the brain stem. And in general, the limbic system controls a lot of things that we associate with emotion, with learning, memory, really important things that an animal has to do to behave. And two structures we're going to hear a lot about time and time again are the hippocampus and the amygdala. So the hippocampus up there in blue is well, the hippocampus word itself means seahorse. And supposedly, when neuroanatomists were looking at this, they thought it looked like a seahorse.

I don't see it, but let me know if you do. And this part of the brain is really important for memory and forming new memories. And the way that scientists first found this out in humans anyway was by a bit of an accident. The hippocampus, they found out, is this place where new memories are made. But they didn't do it by any sort of experimental approach that you would suspect them to. What happened is there was this patient, one of the most famous patients in all of neuroscience, named HM. For privacy reasons, his name up until he died was known just as HM. And this patient had really terrible seizures, really bad epilepsy that could not be controlled and was debilitated by these seizures. So when he was a young man, they tried all sorts of different techniques to try to control these seizures. And in the end, what they had to do was actually figure out where these seizures started in the brain and surgically remove that part. And it turned out that part in this patient included the hippocampus. So they took out the hippocampus on both sides of the brain. And after the surgery, Patient HM didn't have seizures anymore. Great. Wonderful. But what they found out is that this patient afterwards couldn't form any new memories. When he had nurses come in to visit him who visited him every day after the surgery, every time he met them it

was like he was meeting them for the first time. He couldn't store that memory. But the really interesting thing was when they asked him about events from his childhood, he could still remember those. He could remember who the president of the United States was in his childhood. So the memories were stored somewhere else in the brain. But the ability to make the new memories was dependent on the hippocampus. So that's how they discovered by accident that the hippocampus is the part of the brain forming new memories. Another part of the brain you're going to hear about a lot, a lot, a lot is make the amygdala.

And the amygdala are those two yellow almond-shaped things sitting up in the front of the hippocampus. And as you've already heard, these are parts of the brain that are really involved in fear and anxiety. So if you remember the example that Dr. Sapolsky gave on Monday when he was talking about scared sweat versus exercise sweat and how we can actually tell whether we're smelling scared sweat or exercise sweat, one way that they see that difference is when they look at the brains of people who are smelling sweat from a scared person, the amygdala lights up. But when you're smelling sweat that was given off by somebody who was exercising, it doesn't light up as much. So the amygdala's really important for sensing fear. And it's important for forming anxiety as well. So when you look at an angry face or a fearful face, the amygdala will light up. But when you look at a happy face, it won't. So that's the amygdala. You'll hear a lot more about it later, really important part of the brain for fear and anxiety. Other parts of the brain you're sure to hear tons and tons and tons about later on are the hypothalamus and pituitary gland. And these are you can think of them as hormone central. These are the parts of the brain that control how hormones are released to the rest of the body, control a lot of different behaviors. So the hypothalamus sits in the center of the brain right at the very bottom. And the pituitary is underneath it and secretes a lot of those hormones out into the bloodstream. And it's an old joke but one that gets repeated over and over again. You can think of the different types of behaviors that the hypothalamus controls as four Fs. You've got fight. You've got flight. You've got feeding behavior and reproductive behavior. So you've got those four Fs of what the hypothalamus controls. Yes. Now, you get it. Yes. So you're going to hear tons and tons more about this. For now, just know that they sit at the bottom of the brain and help control a lot of these behaviors.

So what else do we have in the nervous system? We've got all these different parts of the brain. But we've also got the spinal cord coming down from the brain. And just like in the brain itself, the spinal cord is specialized. You have parts of the spinal cord that send out information. And you've got parts of the spinal cord that receive the information. So you've got motor nerves. And you've got sensory nerves in different parts of the spinal cord. You've got different parts of the spinal cord, of course, for your arms and your legs, basically what you need to know for now about the spinal cord. You're also going to be hearing a lot more in future lectures about the peripheral nervous system. And the peripheral nervous system has all of the motor nerves and sensory nerves that are outside of the spinal cord. So a lot of the things that sense touch information or heat or anything else out in the periphery are part of the peripheral nervous system. And then, you've also got a whole part of the peripheral nervous system that happens pretty much automatically. You don't have to think

about it. So you've got nerves that are controlling your heartbeat, your digestion, your breathing. And normally, you don't have to think about keeping those going. So those are another part that you'll hear a lot more from Dana later on. So that's really a broad overview of the different parts of the nervous system and what they do. So now, we're going to think a little bit more closely about what's actually inside a brain, what the individual cells are, what they're doing, how they make you behave. And again, this is not a list for you to remember. It's just to let you know that there are different cell types, and they have different functions. And I'm going to tell you first about something that came up while I was looking online and trying to figure out what to say for this lecture. And I realize that it's illegal in seven states to give an introductory neuroscience lecture and not mention the name Santiago Ramon y Cajal.

So Santiago Ramon y Cajal, why is he this god figure in neuroscience? What did he do? So when Santiago Roman y Cajal was doing most of his scientific work at the end of the 1800s, mostly in the 1890s, the general theory about the way the brain worked was that it wasn't individual cells that were performing their functions. Instead, the brain was thought of as this web, this interconnected web of mush, basically, that did all of its computational work to make you behave. People knew that the brain was where behavior started and where it was controlled. But they didn't really know what it was inside the brain that did that. So the prevailing theory was that you had this web. And rather than just take that at face value, Ramon y Cajal decided to experimentally figure out if that was the case. So he found this really cool technique invented by a different guy named Golgi. And this technique allowed him to take small slices of the brain and turn about 1% of the cells in that slice black. We still don't know how it works. But he was able to do it. And then, he drew these really, really detailed pictures of what that looked like in the microscope. And these images are just absolutely gorgeous. There's a whole class of people that when they see these images, tears of joy stream down their face. They fall to their knees weeping, praising the gods of neuroscience. These are the people who become neuroscience graduate students. So these cells and these pictures that he drew showed us that there actually are individual cells in the brain that are doing this work. It's not a complete mess. It's not a complete web. It's actually individual cells. And so he drew out these beautiful pictures of neurons and also all of the other cells that are in the brain. And I have a good friend who studies all of these other cells in the brain that are not the neurons, not the ones that are actually doing the computational work.

And I promised her I'd never give an introductory lecture without mentioning these. So first, I'll start out with those cells. So 90% of the cells in your brain and spinal cord are not actually neurons. They're called glia. And glia basically, by definition is anything in the brain or spinal cord that is not a neuron. And glia, the word, means glue because people saw these cells in there and thought they were just glue sticking the neurons together. But it turns out they actually do a lot more than that. You've got cells called astrocytes, which are these star-shaped cells. And they, in a very general sense, supply nutrients to the neurons and help regulate how they fire. Then, you've also got these cells called oligodendrocytes, or Schwann cells. Again, long names you don't need to memorize. But they wrap around the wires of neurons and make their firing go faster. Then, you've got microglia, which are yet

another glial cell that are in the brain. And they're basically the brain's immune system. They move around the brain. They send out little processes out into parts of the brain to figure out if the brain is getting infected by viruses or bacteria or if there are any dead cells that need to be cleared up. And they do all of that work. So 90% of your brain is actually all of these other cells doing this work. But what they're doing this work for is so that you can have your neurons working. And the neurons are what we're going to focus on for the next 10, 15 minutes or so. And these are the complicated but wonderful computational units of the brain. And in an average human brain, you've got about 100 billion neurons. And each of those has about 10,000 connections to other neurons. And those connections are called synapses. So if you think about that, you've got roughly a quadrillion synapses in your brain, a quadrillion connections between neurons. And just to give you some perspective, the number of stars in the Milky Way, the number of stars that you can see out there in our own galaxy is about 300 billion.

So you've got a quadrillion synapses just sitting there in your brain, which is already more than 1,000 times more than the number of stars that are out there in the Milky Way galaxy. So you've got all of these connections packed in there in their brain doing all of this computational work. So how does it actually work? So here I'm actually going to switch over if I can. Great. So here we're going to talk about the neuron itself and what the different parts of it are, what the different parts of it do, and how it works, how it communicates. So this is a very badly drawn picture of a neuron. But it will give you an idea of what a neuron is and how it functions. So you've got different parts of it. You've got out here, dendrites. And these are what receive the information on a neuron. They get the information from the cell before it and pass it on down into the cell. Down here you've got the soma or the cell body of the neuron. And importantly, you have the nucleus, just like you do in any other cell that has all the DNA in it. And then, there's an important part down here. So you're getting all of this input from the dendrites from the cells before giving you information at the dendrites that goes into the cell. And somehow the cell has to decide whether to pass that information on to the next cell or not. And that happens at this specialized part of the cell called the axon hillock. I guess it's like a hill but not quite as big. So you have the axon hillock there. And then down here, you have the axon, which you can think of as the wire that's sending the information on to the next cell. And then down here, you have the terminal. And this is where the cell will send on information on to the next neuron. So these are the general parts of a neuron that you'll need to think about in terms of how neurons communicate. And information is generally going to flow from dendrites down to the cell body, get summed up at the axon hillock.

The cell will decide whether to fire or not and send that on down to the terminal. So that's a basic overview of a neuron and how those different parts work. So how does it actually work? How does it actually send that signal? And this is just going to give you a really broad overview of how a neuron does this. So if you think about a neuron sitting there in the middle of the brain, there's lots of electrical activity, lots of things going on. Somehow a neuron if it sends a signal has to get heard above all that noise. So the way a neuron solves this problem is it is either on or completely off, completely quiet. It's not a system where you have a continuum, where you have where the cell is kind of on, a little bit more on, a

little bit more on, and then totally on. It's not that way. Because that wouldn't really get heard above all of the noise. So what you have is a cell that's either on or off. And a neuron really wants to make sure that it stays off until it's ready to send a signal. So that's how the neuron stays quiet. And when we talk about that in biology, we talk about the neuron keeping a resting potential, a resting quiet level of activity. So how does a neuron do that? So the way that neurons communicate and the way that they send on electrical signals is going to be through the movement of these chemicals called ions. For those of you who are not science people, just think of them as charged chemicals. We're just going to talk about general ions for today, which are charged atoms. So they can have a positive charge or a negative charge. And we're going to talk about mostly positive charges today. So the neuron has to keep quiet. And the way it does that is by keeping positive charges, positive ions outside of the neurons. So you have all of these positive ions sitting there outside of the neuron. And this is how it stays quiet. Because the flow of these ions is going to be what communicates the signal.

So how does it do that? It keeps these ions out of the cell by using these pumps. So it has pumps that will pump out positive charges from the inside of the cell to the outside of the cell. So by using those pumps, the neuron is keeping all of the positive charges, all of the positive ions mostly on the outside of the cell, rather than on the inside. So that means that the net charge on the inside of the cell is going to be negative. So you've got this imbalance. And this is how the neuron stays quiet, how it make sure that it is not firing. So you've got this cell sitting there trying to figure out if it's going to fire or not. Right now it's quiet. How does the whole process get started to make it fire? So if you have another neuron up here and you'll hear a lot more about this from Anthony sending out a chemical signal, that chemical signal is going to get received at the dendrites. And when that chemical called a neurotransmitter hits a particular receptor out on the dendrite, that receptor is going to open up a channel. And that channel is going to let some of these positive ions in, just like receiving email. It's receiving a signal. So you get these positive ions going into the dendrite. And you get a change in charge. The neuron is now getting more positive on the inside. Before it was really negative. Now, it's getting a little less negative. Another way to say that is it was really polarized before. It had a big negative charge on the inside. And now, it's getting a little bit depolarized. It's getting some positive charge going into it. Great. So you've got a little bit of charge coming in. You've got a little bit of signal. But somehow the neuron has to decide, am I going to fire? Or am I not? It's all or nothing, one or the other. So you get the signal coming in from this dendrite. And you're going to get some positive charge going in, flowing into the neuron. And you'll get a little bit out in the cell body. But from one signal sent, you might not get a lot.

Well, let's say you're getting really, really frequent chemical messages from here, getting lots of positive charge into the cell. Or you're getting several different messages at the same time, getting lots of positive charge into the cell. Then, you can end up with enough positive charge down here at the axon hillock to make the neuron decide to fire. So what is it that makes it decide? There are more channels down here that can open up to let more positive ions in. And the way they make that decision is whether there's enough positive charge. If there's enough positive charge, they open up. And they allow lots more of this positive ion

to go in. And once that happens, it's going to feed forward. Right? You're going to get more positive ion going in. You're going to get more of these channels opening because the positive ions are going in. And it's going to keep going and feed forward. And you're going to get the neuron sending a signal. And the way it does that is it keeps having positive ions go in all the way down the axon, all the way down to the terminal. And then, when you get positive ions going into the terminal, it's going to tell that to go ahead and send a chemical message on to the next cell and start the whole process over again. But the big message from all of this is that this decision that's made here is all or nothing. You've got positive ions that are traveling in. If they don't get to the threshold here, if they don't get enough of them here to make the axon hillock decide to let more of them in, the cell's going to stay quiet. If they do get enough in to reach threshold, then you're going to get lots more pouring in. And the cell's going to fire. There's no turning back. It's going to send the signal down its axon to the terminal. And you're going to get the message sent on. And that's called an action potential. And what happens here is you get all this positive charge going in. You get the cell getting to a really positive level of charge.

And then, somehow it has to stop. So how does it stop? You have a number of other positive ions on the inside. And right after this opens and you get all of these ones pouring in, you can get the cell opening up these other channels to let the positive ions, a different kind of them, flow out. And then, you get restoration of the balance and charge. And remember, you have these pumps that continue to send the positive ions out of the cell. So you get the cell being restored to the quiet state afterwards where it's negative on the inside compared to the outside. So there you have it. You have an all-or-nothing action potential. You have the cell deciding at the axon hillock whether it's going to fire it or not and then sending the message on to the next cell. So that's a really basic understanding of how a neuron fires. Hopefully, that was basic enough that everybody could understand it. You're going to hear more about it later in other lectures. But for now, that should give you a really basic overview of what's going on. So take-home messages from this first part of the lecture, different parts of the brain do different things. As we talked about when we were looking at the brain and spinal cord, you've got the different parts that function for different behaviors. You'll hear a lot more about that in the future as we talk about specific behaviors and what parts of the brain have to do with them. You've also got different cells that are doing different functions within the brain. You've got neurons. You've got glia. You've got different types of neurons as well. You'll hear a lot more about how some neurons send one type of chemical signal, some send another, and how that's going to be really important to different behaviors later on. You also learned that neurons are individual cells making this decision. They're the functional unit of the nervous system, as we learned from Ramon y Cajal. And finally, when they do decide to send that signal, it's an all-or-nothing process.

It's an all-or-nothing action potential that makes the sell send on the message to the next one. So hopefully, if you understood all of that, you have a really basic understanding of neuroscience. We're going to take a five minute break. And then, we'll move on to Anthony's lecture, which will talk more about what actually happens at the synapse as we think about applying this to behavior. Thanks. All right. My name is Anthony. I am a first year biology student, a graduate student in the PhD program. Right now, I'm just wandering from

lab to lab trying to figure out what I want to do research in. Again, like Nathan, there's going to be some topics in here that might confuse you. And if it is confusing, let me know. Stop me. Ask questions. My email is on the handout that you can download from CourseWorks. And after the lecture, I'll actually write it down on the bulletin board right there. But feel free to send me or Nathan an email anytime if you have any questions over the lectures today. I'm going to start by recapping a little bit about what Nathan talked about, the neuron doctrine. So up until the late 1800s, neurons were all thought to be connected by cytoplasm. And really the concept of a neuron as an individual cell, it was difficult to conceptualize. Because all people were really able to observe was this mesh-like network of interconnecting fibers and processes. And it wasn't until the advance of microscopy and staining that people were able to suspect that something else was going on here, that maybe this story was a little bit different. In 1891, a German anatomist named Heinrich Wihelm Gottfried von Waldeyer-Hartz I practiced that proposed what is now referred to as the neuron doctrine, which is basically that this network was made up of individual cells. He wasn't unable to propose this without work done by many others, including Santiago Ramon y Cajal, god of neuroscience. So if you have these separate neurons that are separate cells, if one is to communicate to another, it cannot happen by electrical means only.

If you think about it, if this communication is to happen, it must happen by chemical means. And so before the events at the synapse can really take place, I have to introduce you sort of back up and go back to the action potential, which if you remember, starts here at the axon hillock. So this is where the decision to fire or not fire an action potential will be made. And once the action potential is fired, it will travel along the length of the axon and reach a dead end that is conveniently called the axon terminal. Now, the axon terminal is a structure at the end of the axon that stores large amounts of neurotransmitters. And these neurotransmitters aren't just freely floating or diffusing around inside the cell. They're actually packaged in these discrete quantities in these membranous spherical structures called vesicles. And so you'll see those balls housing these black dots. The balls are the vesicles. And the black dots are the neurotransmitters. OK. So when the axon potential reaches this axon terminal, it will trigger an influx of positive charge, which will then trigger the release of neurotransmitter from these vesicles. So the vesicles will move to the edge of the axon terminal. And they'll dump their neurotransmitter out. So I have to sort of dive into a little bit of terminology here. We try to avoid that with this class. But the signaling neuron is called the presynaptic neuron. The neuron that receives the signal is called the postsynaptic neuron. And the junction at which these two neurons connect and communicate is called the synapse. So once this neuron is bound to the receptor, it can trigger one of two temporal effects. One can be an immediate effect, which is the opening of a channel, which will allow ions to jump in, which Nathan illustrated earlier right here. These ions could either be positively charged or negatively charged. If they're positively charged, they will persuade an action potential to happen if there are enough of these charges.

If it's a negative charge, it might act to dissuade an action potential to be initiated at the axon hillock. So that's the immediate effect. But an effect that might last a little bit longer is when a genomic effect is induced. So a neurotransmitter might be released. And it might

bind to a receptor. And this event might influence the activation of a transcription factor. And this transcription factor might induce the production of more receptor channels that might find its way onto the dendrite here. So if you think about it, if you produce more channels or more receptors, you can make this synapse more responsive to the same amount of neurotransmitter. So that's strengthening the synapse. And you'll hear, definitely, more about that later in future lectures. So not only can a single neuron respond to many different types of neurotransmitters, could be inhibitory, could be excitatory, it is also possible for a single neurotransmitter to have an effect on multiple neuron types located in different areas of the brain with different functions. And so you might ask yourself, how is this possible? So we have like 100 billion neurons in our brain. Why is it that we don't have 100 billion unique neurotransmitters for each brain or sorry, for each neuron? And the concept can be sort of related to the concept of the alphabet. So we only have 26 letters in our alphabet. Yet, we can create an infinite number of messages. The idea of the brain having different functions in different areas, each of these functions are going to be they're going to have different functions because different neural networks, different networks of neurons are going to be responsible for these functions. And they are actually going to, for the most part, have a physical separation between different areas, different neural networks of the brain with different functions. And so it is possible to use a single type of neurotransmitter in many areas of the brain with different functions because of this physical separation.

Sorry. I was opposed to put this slide up. So we call this compartmentalization of the brain, many different functions in many different physical areas. And so because of this redundant use of neurotransmitter, you really don't need more than a few hundred. That's where the current estimate lies. Not all of them have been discovered. Quite a few have been. But there are still a lot out there that have yet to be discovered. And so this brings me to sort of a exercise that we could do to help hammer in certain these properties of a neurotransmitter. Say you are a scientist. And say you are in the business of identifying novel neurotransmitters. And you have this putative molecule. And you want to prove to the scientific community that this molecule is a neurotransmitter. What pieces of evidence might you need to provide to prove that your molecule's a neurotransmitter? First thing that you sort of have to do is you have to sort of ask yourself, well, where are neurotransmitters located? They are just located anywhere in the brain. They're located in specific areas. They're located in the axon terminal. So you have to prove that it localizes in the axon terminal. Another thing that you might want to ask is, what triggers the action of a neurotransmitter? So you're going to also have to demonstrate its release following an action potential. So if you remember, an action potential will hit the axon terminal and through a series of events trigger the release of neurotransmitter. And lastly but this is not good enough. So you have two pieces of evidence so far. But you need one more to make a pretty strong case for why you have a neurotransmitter. And this is you have to ask the question, what is the effect of a neurotransmitter? And so you also have to prove that after a neurotransmitter is released and it binds to the receptor that it induces some sort of influx of charge in the postsynaptic dendrite.

And I just missed another slide. No I didn't. So fortunately for us, a lot of this work identifying neurotransmitters has already been done. And there are a few notable transmitters, neurotransmitters that I kind of want to get you guys familiarized with. And so right now, you don't have to memorize any of the functions that I'm going to talk about. So the whole purpose is to sort of to introduce you to some neurotransmitters so if you hear about them in later lectures, it won't be the first time you hear about them. So one type of neurotransmitter is called dopamine. And it's most commonly associated with the reward system, with pleasure. But dopamine, like many other neurotransmitters, has a very diverse array of functions. It's not just involved in reward or pleasure. And so just a quick recap. How could it have many different functions? Well, if the brain is compartmentalized, if these networks are physically for the most part physically separated, you can have one type of neurotransmitter with an effect in these different areas of the brain. Therefore, one type of neurotransmitter in an organism may have many different functions. And dopamine is no exception to that. You have another type of neurotransmitter called epinephrine. And I know everyone in this room has heard about it in one form or another. Another way to another word for epinephrine is adrenaline. And so adrenaline is involved in the fight or flight response. So if you're Nathan also talked about this earlier if you come across a risky situation or you're feeling threatened you can either fight off and vanquish your foe. Or you can flee, neither of which are bad ideas. And norepinephrine, which you may hear about later on in the course, is pretty much interchangeable with epinephrine. They share a very similar structure. And you don't really need to do much to change epinephrine to norepinephrine and vice versa. So another neurotransmitter that you might hear about later on is serotonin.

And serotonin again, is one of those neurotransmitters that has a lot of functions. And few of them are involved in the regulation of sleep, appetite, and mood. But certainly it's not limited to those. Acetylcholine, I know you'll hear about it on Friday. And so I'll leave that for Friday for you to discover. GABA is and you really can't talk about neurotransmitters without talking about GABA and glutamate. So these are the two most common neurotransmitters in the brain. GABA is the most common inhibitory neurotransmitter. And glutamate is the most common excitatory neurotransmitter. And again, these two have very diverse functions and are involved in many different areas. So I'm going to, for a brief moment, dive into a tangent and tell you about the neuromuscular junction. You cannot have animal behavior in fact, you can't even behave unless you are able to move. And the basis behind movement lies in the muscle, in the contraction of muscles. So what you're going to see here is a similar motif. You're going to see a synapse. You're going to see a neurotransmitter. The synapse is going to occur on the nerve that signals to the muscle. It's going to release the neurotransmitter, which is actually going to be oftentimes acetylcholine. And it's going to bind to receptors in the muscle, which is going to trigger a contraction. And so unlike many neurons in the brain, which respond to multiple different neurotransmitters in general, neuromuscular junctions only use one type. So with that out of the way, I'm sort of going to dive into neuropharmacology. So what is neuropharmacology? It is the external manipulation of synaptic events. Why would people want to manipulate a synaptic event? Well, you can do it for research purposes. You could

manipulate the neurotransmitter or the receptor to figure out more about what their functions are. Or you could do it to correct for disease states. We as humans are very interested in trying to help people who have certain illnesses.

So the general purpose is to increase or decrease the strength of communication across a synapse. So sometimes you can do this by faking out the postsynaptic neuron. You can give it a compound, an artificial compound that's not seen naturally in the body that closely resembles something that is seen naturally in the body. And you'll see a lot of hallucinogenics that utilize this principle. So hallucinogenics, such as mescaline, LSD, and psilocybin, these interact with the serotonin receptors because they have very similar structure to serotonin. And so there are a variety of ways that you can strengthen the synaptic response. One of which is to increase the release of neurotransmitter from the presynaptic neuron. How might you go about doing this? You could increase the synthesis of neurotransmitter. You could force the release you could force the released neurotransmitter to linger in the synapse. And there are a variety of ways to do this. You could block wow, I just skipped something. Oh, don't worry about it. OK. So you can block reuptake or degradation. I can talk about it now. So when a neurotransmitter has done its job, has bound to the receptor, is used up, you can't just leave it in the synapse. You've got to get rid of it somehow. Otherwise, it's going to keep signaling to the receptors. One way to do this is a process called reuptake. This is essentially, the reinsertion of a used up neurotransmitter back into the presynaptic neuron. OK. And so there are a variety of proteins that mediate this process. You can have protein pumps that pump the neurotransmitter back into the presynapse. You can have you're going to have proteins that are required to repackage the neurotransmitters in the vesicles. And you're going to be able to you're going to have to reform these vesicles. And so this is called reuptake. You can also degrade used up neurotransmitters. And when you do so, these degradation products can be detected in certain fluids in your body, such as cerebral spinal fluid or blood or urine.

And so this is important for when you want to detect levels of neurotransmitter when you're trying to diagnose diseases. So right, so you can force the released neurotransmitter to linger in the synapse by blocking either reuptake or degradation. You can increase neurotransmitter receptor activity. So if the receptor on the postsynapse has a certain amount of affinity to the neurotransmitter, if you are able to find some way to make it bind more efficiently to the neurotransmitter, you're able to amplify the neurotransmitter signal and essentially, strengthen that synaptic response. So conversely, if you would like to weaken synaptic response, you could just block any of the processes that are required to release neurotransmitter, that are required for the neurotransmitter to bind to the receptor and trigger this influx of charge in the dendrite. So you can do that by blocking neurotransmitter receptors, blocking neurotransmitter release. You can block, or you can decrease the receptor affinity. So again, we don't really want you to focus on memorizing really the many mechanisms of doing this. If you do need to know it, it will come up later on in the course. But what this really is the whole point of this is to get you thinking about the many ways in which you can manipulate events that take place at the synapse. OK. So there are a lot of ways people can manipulate it. So how would you find out more about some neuropathology? If somebody has something wrong with them and it's going on in their

brain, it's really difficult to make direct measurements of neurotransmitters, or neurotransmitter levels in their brain, especially in a live patient. These measurements are often done in breakdown products, breakdown products of neurotransmitters in the urine, in the blood, or cerebral spinal fluid. And these are often serving as clues. These can often serve as clues. So if you had a patient with Parkinson's and you would like to treat that patient and alleviate that person's symptoms, you might find it pretty difficult.

So Parkinson's- people with Parkinson's have an insufficient or decreased level of dopamine in a certain area of their brain that controls motor movement. And if you were to increase, globally increase, dopamine levels in the brain, you might fix, you might alleviate the symptoms of Parkinson's. But you're going to be increasing it everywhere else that dopamine has an action in, has a function in. And so you might change levels in the mesolimbic pathway from normal to too high and induce symptoms that resemble schizophrenia. And so this really harks back on the theme that we've been trying to tell you that the brain is compartmentalized. It's got different functions in different areas. It can have the same neurotransmitter in these different areas functioning. And if you were to treat some sort of effect that you want to fix, you might see adverse or deleterious side effects in other areas. Yeah, so that's pretty much all I have. So there are a few take home messages and important points. You have to know that this process of axon the process of action potential moving along the axon and how it influences the influx of positive ions at the axon terminal, which will release neurotransmitter. So you have to be familiar with that concept. You have to understand that neurotransmitters after they're used up can be degraded or recycled in a process called reuptake and that degraded products can be detected in blood, urine, and cerebral spinal fluid. You also have to understand this idea, again, of compartmentalization. It's very important. And that pharmacological manipulations, you have to be careful because things could happen that you are not expecting, especially when something is wrong in only one area of the brain. And with that, you guys are free to leave and/or ask questions. We do have one more thing we wanted to show. Oh yes. One of the other TAs in our class last year made an absolutely wonderful video about the synapse and about the synaptic cleft, in particular.

And we wanted to share this with you. HumBio kids, put your books down. Put your books down. And report to the cleft, the synaptic cleft. I'm B Bobby Voltage introducing the Glut-tang Clan. -Check out the synaptic cleft. Thanks to vesicular trafficking, interneuronal signal can be transmitted from electrical to chemical and back again. -Hot and turns to the land of the nerve where firing and wiring will occur and will occur. will occur. Follow me. Neurons gotta be ready to fire at any opportunity. Dendritic input make it hot. Make it hot. Sum it up in the axon hillock. The potential will rise to a constant size. Shape of action potentials ain't no surprise. Snap back to the focus of the rap, tiny little space aka synapse. -Boom. -Voltage sweeps through the end like a broom. Calcium rushes in. Vesicles go boom. -Boom. -Exocytosis so exciting. ACH bonds light it up like lightning. Synapse fanatics gather around. Questions about the story? What? -3, 2. Hmm. Do the transmitters always excite? -No. They can be inhibitory, depending on whether they're the ions of positive charge gone. -Only one synapse? What if there's more? -The hillock will sum it up, like I said before. The synapse is the location for neuron to neuron communication. Remember what Russ Fernald said. -The

mind arises from the brain. -Now listen. -Open. Open. Close. Close. -Check out the synaptic cleft. But thanks to vesicular trafficking -Ion channels. - interneuronal signals can be transmitted from electrical to chemical and back again. -Ion channels. -S to the "ynapse" is where things act like to chemicals that make you relax or collapse. The synapse cleft has receptors that rock to the sympathetic. Ligands by clinics that mimic your chemical condition. That's a small problem for medicine, a hundred trillion synapses. Drugs screaming -Let us in! -The disease is only one part of the brain.

A pill's not a sniper. It's a hand grenade. It'll act wherever there reside effects plus everywhere else come side effects. Don't want to sound like a cynic. We've all got a protein they call nicotinic. It's a receptor that can't tell the diff between ACH and nicotine. -Get a grip. -But nicotine leads to too much binding. ACH receptors get to hiding. Neuromuscular junction, it can't quite function because your receptors went out to lunch. Now, dopamine's on for a prediction. But it's down-regulating, then you're getting addicted. Fixing to kick the habit. We're busting synapses. How tragic. -Synaptic receptors getting abducted. A healthy synapse ain't nothing to mug with.

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