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[INTERPOSING VOICES]

AUDIENCE: I don't know. Everybody's getting it. I am working. I'm trying. [GROANS] Is there any scan [INAUDIBLE] that let's you see their own activity?

ABBY NOYCE: Activity? Sure, an fMRI or an EEG is going to you activity. But if you want to think about how many neurons are there, then what you want is small slices of brain on a microscope slide and a good microscope. Which should tell you something about what kind of subjects you can use for that study.

AUDIENCE: Not humans.

ABBY NOYCE: Not humans.

AUDIENCE: Rats. [INAUDIBLE] Humans with no identity.

ABBY NOYCE: Humans who have donated their brains to science is the exception to that, but they're hard to get your hands on. There are very few of those on the grand scale of things.

[INTERPOSING VOICES]

AUDIENCE: It would have to die. It would have to. Well, it wouldn't have to. [INAUDIBLE]

ABBY NOYCE: There are ways of euthanizing animals so that you don't affect what you want to measure.

AUDIENCE: OK, so we're going to kill it humanely.

ABBY NOYCE: Yeah. "Euthanasia," "sacrifice" are both terms that you would see used for that.

[INTERPOSING VOICES]

ABBY NOYCE: Is there any way you can measure what?

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: Like the presence of neurotransmitter?

AUDIENCE: Yeah.

ABBY NOYCE: Yup. It usually involves synthesizing a molecule that will both bind to the neurotransmitter that you want and then will also bind to some kind of dye, and then use the dye. So there's some cytochemistry involved. But yeah, you can do that.

AUDIENCE: OK.

AUDIENCE: Do we have to do all of those things or just one?

ABBY NOYCE: Just one.

AUDIENCE: Oh, OK.

ABBY NOYCE: You guys feel pretty confident that you've come up with a scenario with some rats?

AUDIENCE: Wait, I have a question. This is not hypothetical [? anymore. ?] If there are more synapses, right? Do more neurons mean more likely to have an action potential? If, for example, you have one synapse and [INAUDIBLE] one synapse in here, then that [INAUDIBLE] fire or not fire? If there are more synapses, does it affect more?

ABBY NOYCE: Well, so what you're likely to see in that case-- remember, you're not going to see more neurons, but you might see this one presynaptic neuron and one postsynaptic neuron, but then there'd be three or four synapses going between them, the axon terminals branching out at the end. It's synapsing in four different places and releasing transmitter in four different places, changing the postsynaptic potential in four different places.

AUDIENCE: Oh, OK. So there'd be more postsynaptic neurons with [INAUDIBLE]

ABBY NOYCE: Or even one postsynaptic neuron would be more strongly affected by having more connections with the presynaptic neuron.

AUDIENCE: Oh. [INAUDIBLE]

ABBY NOYCE: But also you might also see them branching out onto other [? nods. ?] You just tend to see more connection would be what you might expect to see.

AUDIENCE: OK, so it would be stronger than action potentials?

ABBY NOYCE: Action potentials are all or nothing. You know that.

AUDIENCE: Oh.

[INTERPOSING VOICES]

ABBY NOYCE: How are you guys doing?

AUDIENCE: We're thinking.

ABBY NOYCE: Still thinking? How to measure the brain. What about the brain would you like to measure?

AUDIENCE: We want to learn what changes.

AUDIENCE: How old do they have to be?

AUDIENCE: So [INAUDIBLE] a maze, and there's a marked right path and a left path.

ABBY NOYCE: OK.

AUDIENCE: The right path has cheese. [INAUDIBLE]

[INTERPOSING VOICES]

ABBY NOYCE: To turn away from the smell.

[INTERPOSING VOICES]

ABBY NOYCE: OK. So what kind of changes do you think-- what kind of changes do you want to look for?

[INTERPOSING VOICES]

ABBY NOYCE: Olfactory?

[INTERPOSING VOICES]

ABBY NOYCE: Maybe, but remember, it's still going to detect the cheese smell just as well as ever, where it's got to do-- where it's making doing something different isn't in how it's perceiving it. Where is it making a change?

[INTERPOSING VOICES]

ABBY NOYCE: It's a decision and it's a decision about what?

AUDIENCE: Motor.

ABBY NOYCE: That's where I would suspect you'd see changes, would be in the connection between that olfactory information coming in and the motor coordinating areas, in a purely hypothetical sense.

[INTERPOSING VOICES]

ABBY NOYCE: You ladies sound finished. We can close the blinds. Maybe. Can we close the blinds? Nope. Is there a wand? There it is. Better?

AUDIENCE: Yeah.

ABBY NOYCE: All right. So what did we come up with? Who would like to share an experiment design that they thought about? Sure. All right. Show me your awesome.

AUDIENCE: So.

ABBY NOYCE: So.

AUDIENCE: So we have monkeys that [INAUDIBLE]. And [INAUDIBLE] for five years--

ABBY NOYCE: OK.

AUDIENCE: And then we have different shapes, like recognition. We showed them-- you know the things where you have the silhouette of something, and they give you a [? wholestock ?] pile of random shapes and you're supposed to move them around?

ABBY NOYCE: Like tangrams?

AUDIENCE: Tangrams. Yeah, those. We would arrange them from easy, medium, hard.

AUDIENCE: And see if the monkeys are able to do it properly.

ABBY NOYCE: OK.

AUDIENCE: And we'd try to do it basically. Yeah, and then we'd have to sacrifice them and look at their brains.

ABBY NOYCE: All right. So you're training monkeys to solve tangram puzzles.

AUDIENCE: Yeah. And then we'd have one monkey that hasn't done anything. He'd just be in the house [? sitting ?] there. The control group.

ABBY NOYCE: The control monkey, or the control group. Do you have multiple levels of your independent-- what's your independent variable, kids?

AUDIENCE: Oh. Independent variable?

ABBY NOYCE: The thing that you, the experimenter, are manipulating.

AUDIENCE: The level of difficulty for the tangrams.

ABBY NOYCE: All right, so you're operationally defining learning as how hard the tangrams they have to solve are.

AUDIENCE: And their ability to do it.

ABBY NOYCE: And their performance. OK. And your dependent variable is? What are you measuring to--

AUDIENCE: The neurons.

ABBY NOYCE: The neurons. And what kind of neurons are you going to measure?

AUDIENCE: [INAUDIBLE]

AUDIENCE: The brain.

ABBY NOYCE: What kind of changes do you want to look for?

AUDIENCE: Big changes.

[LAUGHTER]

ABBY NOYCE: Do you want to look for changes in neurotransmitter? Changes in synapses?

AUDIENCE: We basically compare them to the control monkey, who has nothing going on in the slide.

ABBY NOYCE: OK.

AUDIENCE: And look at all the differences.

ABBY NOYCE: So you're looking for all kinds of differences. You're going to run a bajillion analyzes on these brains? All right. Who else wants to share?

AUDIENCE: They do.

ABBY NOYCE: Zechariah.

AUDIENCE: So we're going to take a sample of hamsters.

AUDIENCE: Sample?

ABBY NOYCE: A core sample? No. OK, so you're going to have a group of hamsters.

AUDIENCE: A sample. You know, a sample from the population.

AUDIENCE: Your [? thing's ?] on hamsters. You make them sound like food.

[LAUGHTER]

ABBY NOYCE: It's OK. Take a deep breath. Keep going. We're going to have a group of hamsters that is not every hamster in the entire universe. Check. What are you going to do with them?

AUDIENCE: We're going to put them [INAUDIBLE] [? in a ?] maze.

ABBY NOYCE: What kind of maze?

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: Like a T-maze. OK.

AUDIENCE: There are two of them and one of them has to smell cheese.

ABBY NOYCE: I need to diagram this.

AUDIENCE: That's definitely a T.

ABBY NOYCE: It's a T-maze. It could be a Y-maze, too, but you're more likely to see T-mazes because they take up less space. If you want to run these off at angles, they get longer and then they're hard to put on the table. All right, hamster.

AUDIENCE: Is that a cow?

ABBY NOYCE: It does not look like a cow. All right, we have a hamster and a T-maze.

AUDIENCE: On the left side there will be a tray set filled with cheese. On the right side, there will be cheese with a scent, a scent but no scent.

AUDIENCE: Scentless. Cheese with no smell.

ABBY NOYCE: All right. We have scentless cheese and we have a cheese aroma.

AUDIENCE: Cheese flavored something.

ABBY NOYCE: This is my smelly thing of cheese. It's like a pod of cheese. Anyway, all right, cheese and no cheese. And what does the hamster have to learn to do?

AUDIENCE: The hamster has to learn to turn away from its natural sense to turn towards the cheese-- the smell of the cheese. And it will turn it's back on the smell and then find the real cheese.

ABBY NOYCE: The hamster has to go that way. OK. So you're training the hamster to ignore the olfactory information coming in. What's your independent variable?

AUDIENCE: Well, we can make the maze harder. Say, instead of two different choices, three or four. Those would be our levels.

ABBY NOYCE: That's one possibility. An easier one would be to have a bunch of hamsters that you don't teach to run through this maze, and then you have a control group. And remember that having one experimental group and one control group counts as two levels of your independent variable. And for a nice, big, vague change--

AUDIENCE: Our control group-- looking at the brains of the hamsters before they learned how, and then we're going to-- our dependent variable is the amount of change in the pathway between the senses, olfactory.

ABBY NOYCE: OK.

AUDIENCE: And then the motors.

ABBY NOYCE: What methodology are you going to use to look at these hamster's brains?

AUDIENCE: Slice them up.

ABBY NOYCE: And then you're going to have them run the maze?

AUDIENCE: That was nice. There's so many. [INAUDIBLE]

ABBY NOYCE: Slice them up is a perfectly adequate way of doing this. It's perhaps not the most professional way of wording it. But the flaw here is that, how are you going to measure, if you want to do this-- ladies-- if you want to do this-- within samples group, where you have the same subjects both as your control and the experimental group, you need to figure out a way of measuring them when they're in the control condition.

AUDIENCE: Oh.

[INTERPOSING VOICES]

ABBY NOYCE: And most of the things that we're interested in, even if you-- some of them, there are ways of measuring in vivo, in a living organism, but not on a scale that is probably useful for this, especially when we're talking about hamster brains, which are probably all of about that big. So I think you want an experimental and a control group so that you can slice up brains from both. What's your dependent variable?

AUDIENCE: The amount of change in the synapse and change in the [INAUDIBLE]

ABBY NOYCE: You have a change in what pathway?

AUDIENCE: From the olfactory sensors to the motor that would control its movement.

ABBY NOYCE: OK. And what operational definition? What operational definition of that change are you going to use? What kinds of changes are you looking for? I'll take input from anyone else who is in on this project. What kind of changes would you look for in that pathway?

AUDIENCE: For synapse?

ABBY NOYCE: Sure. Changes in number of synapses.

AUDIENCE: Yeah, and [INAUDIBLE]

ABBY NOYCE: Yup. So changes in synapse arrangements, or changes in number of synapses, you probably would look for by taking very thin slices of hamster brain, drop it on a microscope, hire some poor slogging undergraduate to sit there and count synapses.

AUDIENCE: That's horrible.

ABBY NOYCE: Yeah. I can vouch for that one. It's not as bad as it sounds, but it's definitely not fun and exciting. And compare. Are there more synapses in the slides that came from the learning group than the control group? Cool. Good. Who else would like to discuss an experiment they came up with?

AUDIENCE: Our experiment's awesome.

ABBY NOYCE: You guys sounded pretty excited about it, I don't know. All right, so you have the hypothesis that learning involves physiological changes in the brain. How are you going to study this?

AUDIENCE: All right, so we're going to take some rats and--

ABBY NOYCE: Some rats.

AUDIENCE: A large sample of rats. And we're going to split them up into two groups, and one group, we're going to teach them. They're going to be our control group. And we're just going to use the knives and cut up their brains [INAUDIBLE]

ABBY NOYCE: OK.

AUDIENCE: And the other group, we're going to teach them how to push a button. I don't know, move the button [INAUDIBLE] walk over to it and then push it, instead of having it right in front of them, pushing it. And then we're going to, after we've run this, also these are [INAUDIBLE]

ABBY NOYCE: All right. So it sounds like your independent variable is the amount of learning they're doing, and your dependent variable then is what?

AUDIENCE: The amount of neuron activity.

AUDIENCE: Yeah, OK. the amount of neuron activity. And you'd measure that after you cut up their brains. You look at the number of synapses. Is that what [INAUDIBLE] Yeah, I think so.

ABBY NOYCE: You're going to measure the number of synapses?

AUDIENCE: And then compare it. Kind of like theirs.

ABBY NOYCE: That's OK.

AUDIENCE: But with a different animal.

ABBY NOYCE: Helen and Oshu?

AUDIENCE: [? Sashi. ?]

ABBY NOYCE: [? Sashi. ?]

AUDIENCE: We're going to use bats.

ABBY NOYCE: Oh, lab rats are sweeties. Well, except for the one who bit me once, but.

AUDIENCE: So the independent will be the amount of [INAUDIBLE].

ABBY NOYCE: Mhm.

AUDIENCE: Yeah, I guess. And then we'd have different levels of these. [INAUDIBLE] difficult control group. [INAUDIBLE] there will be an easy maze and then a medium maze and then a super hard maze. [INAUDIBLE]

AUDIENCE: [INAUDIBLE] number and the mazes and synapses. So you slice up the brains and look at it under a microscope and look at the changes.

ABBY NOYCE: Cool. Good. Excellent. And what would you expect to find if your hypothesis was true?

AUDIENCE: More synapses.

ABBY NOYCE: More synapses. And if your hypothesis was wrong, what would you expect to find?

AUDIENCE: No change.

ABBY NOYCE: No change. Good. Cool. Jessica, did you want to share? I know we're kind of dropping you in in the middle here. OK. Your call.

So moving right along, we've thought a little bit about how you would find these things out. Let's take a look at how some people who actually do this found this out. And the original classic study on this is from the '60s. And these guys, I think, were afraid that they wouldn't find big enough differences in most of the scenarios that you guys have proposed.

So they split things, critters, into three groups. They had standard laboratory living conditions. The standard condition, where you've got three animals in a little cave. They've got food-- little

cage-- they've got food, they've got water.

And they wanted to compare this to both an isolated condition, where animals were living on their own, and then this enriched condition, where they had a big cage. Think of the big ferret cages you see at the pet store sometimes with ramps and ladders and wheels and things to climb on, and things, little bells hanging that they could play with, all sorts of toys and other stimulus objects, and a large group of animals all interacting.

And the theory here is that learning is going on even when you're not deliberately being trained on a task. Just by walking around and interacting with your world, you're learning stuff. We talked yesterday about this latent learning idea, where animals that weren't actually being rewarded for running a maze still seemed to be learning something about it's layout. You'll see the same thing with little kids who are just playing house, playing kitchen. They're playing with all of this stuff and they're, by doing it, exploring and learning about their world.

So the idea here is that by changing what living conditions these animals are in, they're changing the amount of informal, not really structured or goal-driven, but how much changes in their environment are leading to informal learning. So they were all littermates. They'd be littermates of the same genders. They take all the boy rats from a letter and split them out evenly among conditions. An over-simplified version of what's going on there. And there's also other neurons modulating that circuit that are saying, hey look, there's nothing dangerous. We don't actually need to contract that gill reflex muscle.

This is what seems to be working in something like Pavlovian conditioning, where if every time that tuning fork gets rung, then these salivary control neurons start going. Then a connection between the two of them would start to form, which is assuming a really simplified understanding of what that neural circuit actually probably looks like, but the key underlying idea is valid.

Neurons that fire together wire together, which isn't actually Hebbs' formulation of it. But it's catchy and easy to remember, so everybody says it. So remember, what's happening here is it's not just if one neuron is-- if the first neuron in the chain is often excited. It's if the first neuron in the chain is excited and it's successful at exciting the second neuron, then you're going to see this kind of strengthening in synapses.

You guys might remember when we talked about vision two weeks ago, back in the day. One of the things we discussed was that in very young kittens-- remember, a lot of visual work has

been done in cats-- in very young kittens, you'll see that most of the neurons in primary visual cortex don't have a strong preference for one eye or the other. They'll take input from both. And then as the visual system develops to adulthood, each of these cells will usually develop a preference for the left eye or the right eye.

And you can think of this as being if input from the left or the right eye is slightly more effective than the other one at exciting this neuron in primary visual cortex, then that synapse will just get strengthened in relative to it, this other synapse will become much less strong. So you'll see cells develop these very strong preferences from relatively weak initial set states.

Five minute break, and be quick. And actually five minutes because we have a big chunk of, what's happening in these synapses, anyway, to get through.

AUDIENCE: What determines whether your eyes are stronger or more dominant?

ABBY NOYCE: For an individual neuron, you mean? So you have a primary visual cortex, right? And we talked last two weeks ago about how cells in there respond to different things, but most of them respond preferentially to edges in the left eye or edges in the right eye. As far as anyone can tell, if you are normal and you have decent input from both eyes, then they're set up kind of at random, but one or the other will have slightly stronger input in the beginning.

And then because that synapse is already stronger, then that synapse is going to be more effective at exciting the cell than a synapse coming in from the other eye. And then so it'll get strengthened by this Hebbian process, and then it'll become stronger and, yeah.

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: That's how it was originally thought about, although-- can you not ladies today? Draw on that one. Here.

AUDIENCE: I think she's just rolling them.

ABBY NOYCE: Are you just rolling them or are you drawing?

AUDIENCE: Just rolling.

ABBY NOYCE: You can roll them. I don't know, sometimes I come in and there's graffiti all over my chalkboard.

AUDIENCE: I don't do that. That's all Jen.

ABBY NOYCE: Yeah, yeah. Whatever.

[INTERPOSING VOICES]

ABBY NOYCE: How are you doing, Jessica? You hanging in there? Let me know if you're like, oh my God, what is she talking about? Because I know you're coming in halfway through, so.

[SIDE CONVERSATIONS]

ABBY NOYCE: I need you guys back in here in two minutes.

AUDIENCE: What?

ABBY NOYCE: Two minutes.

[SIDE CONVERSATIONS]

ABBY NOYCE: OK, kids, class time. Class, we will have class. You should be in here. Thank you, gentlemen. If one of you could get the window on your way in, please. All right. So discussing a process. We've been talking about this kind of Donald Hebb's idea of what sorts of changes you would see in the nervous system if you've got this kind of to instantiate learning in a synapse.

And in the '70s, people started identifying a process that seems to be one way that this could happen. It's called long-term potentiation. So long-term, we know what that means. And potentiation, meaning that it makes a synapse stronger. It causes the postsynaptic cell to be more responsive to action potentials in the presynaptic cell. And it was discovered in rabbit hippocampuses is in the '70s, although at this point, it's been documented in invertebrates and aplysia, and just every kind of little mammal that somebody studies. It's been documented in human samples, all sorts of stuff.

So long-term potentiation is definitely something that happens. Whether it is the one thing underlying memory is still a bit open, but it definitely seems to be at least part of the process. So slidey board. All right. So we have a synapse, synapse going up. So here's our presynaptic and our postsynaptic cells.

And just for review, let's talk about so what happens when an action potential comes along

down the axon of the presynaptic cell? What happens?

AUDIENCE: Calcium.

ABBY NOYCE: Calcium. So there's a voltage-gated calcium channel. So calcium goes in. And what does calcium do?

AUDIENCE: [INAUDIBLE] receptor [INAUDIBLE] bone.

ABBY NOYCE: Right. So the neurotransmitter that's in the axon terminal is inside these little vesicles, these little like pouches of membrane material. And the calcium binds to that and causes these vesicles to do what? Somebody--

AUDIENCE: Binds to the membrane.

ABBY NOYCE: Binds to the membrane. So this vesicle actually ends up cutting down and binding to the membrane and opens up. And when the vesicle binds to the membrane, the neurotransmitter gets released into the synapse. Excellent. And neurotransmitter in the synapse does what? Binds to?

AUDIENCE: Receptors.

ABBY NOYCE: Receptors on the postsynaptic cell.

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: Right. So [? biased ?] receptors on the postsynaptic cell causes one of a variety of changes, depending on what kind of receptor and what kind of neurotransmitter we're considering at this synapse. And then, shortly afterwards, it gets cleaned up, either by an enzyme that comes along and breaks it down, or by a re-uptake transmitter that vacuums it back up into the presynaptic cell. So it all gets cleared out of the synapse.

All right, good. So when we're talking about long-term potentiation, we're talking about glutamatergic synapses, synapses where glutamate is the neurotransmitter. And it requires two different kinds of cellular receptors.

So backing up a step. So long-term potentiation refers to a particular kind of change that you'll see at a synapse, in terms of how responsive it is to the previous cell. So the classic demonstration of this is if we stick an electrode in the presynaptic cell and we just keep

stimulating it electrically, like maybe a pulse a second, and about an action potential a second. Then you'll see the cell causing excitatory postsynaptic potentials, because it's glutamate and glutamate is an excitatory neurotransmitter.

And they'll all be about the same size, very steady, and will cause a steady stream small excitatory postsynaptic potentials. And if we then go from this slow and steady stimulation of the presynaptic cell and stimulate it much more so that it just starts suddenly firing off action potentials as fast as it can go, about a thousand a second, that upper limit-- this is called a tetanus, this sudden burst of action potentials all at once.

So if we do that for a couple of seconds and then go back to our previous slow and steady stimulation, what we'll see is that after the synapses had that tetanus, that set of really fast action potentials coming in, which has presumably caused enough changes in that secondary cell to cause it to fire, then what you'll see is that action potentials that come in now will cause larger postsynaptic potentials. It will cause a bigger change in the membrane potential of the postsynaptic cell. That is long-term potentiation. That's this difference in how big of an effect the presynaptic cell has on the postsynaptic cell.

So how does it do it? Well, we know we're working with glutamate. Glutamate has two main receptor types that are involved here. Glutamate has a bunch, but we'll talk about these two. AMPA receptors are sodium channels, primarily. So they're an ionotropic receptor. When the glutamate binds to an AMPA receptor, the AMPA receptor opens up and is a sodium channel.

NMDA receptors are both sodium and calcium channels, but there's a catch. An NMDA receptor-- here's our cell membrane-- looks about like this, right? We'll think of it as looking like most of our receptor proteins. But it has a little magnesium ion that hangs out, blocking its channel. Magnesium, Mg2+, a little magnesium ion. So unless that magnesium ion gets gotten rid of in some way, no matter how much glutamate binds to this NMDA receptor, calcium can't get in.

So the NMDA receptor needs to have the cell depolarized past a certain point. This magnesium ion is held here because the inside of the cell is more negative than the outside of the cell, that resting potential. So there's an electrostatic force holding that magnesium ion there, and it's not until the cell gets depolarized to a certain point that it pops out. It gets pushed out and then calcium and sodium can go in. So NMDA receptors depend both on the neurotransmitter, on glutamate, and on a significant voltage change at the synapse.

We've come along. We've had our glutamate released into the synapse here after an actual potential comes from this presynaptic cell. And the glutamate-- here's our AMPA receptor. The glutamate binds to an AMPA receptor, and sodium can flow into the postsynaptic cell. That's a positive ion coming in. Is that an excitatory or an inhibitory change? Excitatory, right. It's making the membrane less polarized. It's moving it towards that firing threshold.

Now, what happens is if there's only the occasional impulse coming in from this presynaptic cell? Then the potential along the membrane here doesn't change a whole lot. The cell gets excited, but it doesn't get excited enough to fire on its own or anything like that. It's not unless you get a whole bunch of action potentials at once so that there's a whole bunch of sodium flowing in and the cell can really depolarize, that that magnesium ion on the NMDA receptors pops out.

So eventually, once the cell gets depolarized to about minus 35 millivolts. Notice that's even further than the firing threshold. This only happens when you have lots of excitatory input coming into a cell. So the NMDA receptors then finally open up and you get both calcium and sodium coming in through your NMDA receptors.

So sodium is an excitatory ion flowing in. It's making the second cell more likely to fire. Calcium, though, is also excitatory, but we know that calcium does a lot of really interesting stuff. Mostly, calcium tends to act to activate other proteins in the cell and cause them to go off and do a whole cascade of interesting things.

So in this case, NMDA receptors are acting like both an ionotropic, because they've got ions coming in, but they're also acting like a metabotropic receptor in that they're causing these long-term changes. So what this calcium does is calcium comes in and it binds to a bunch of protein kinases, protein kinase A, protein kinase C, CAM kinase.

Kinases have that -ase ending on them, so they're an enzyme, right? So they're cells, they're proteins, that encourage a reaction of some sort. Kinases phosphorylate other things. They stick phosphate groups onto other molecules. And they all do different things. CAMK here does a couple of things.

One of the things that CAMK does is it goes back up to those AMPA receptors and it phosphorylates those. Sticks a phosphate group onto that AMPA receptor, and that makes the AMPA receptors stay open longer. Every time that they get opened by the glutamate, those receptors open up. They stay opened longer. More sodium can come into the cell. And so the

excitatory effect of that receptor being activated is increased.

So one of the ways that the NMDA receptor, letting the calcium in, strengthens the synapse is by phosphorylating the AMPA receptors so that they, in turn, can allow more sodium in every time that a glutamate bonds to them. CAMK also moves up the neuron to other AMPA receptors that are not on the membrane yet but have been produced by the neuron and are hanging out.

And it goes and gets these AMPA receptors and it brings them up to the membrane. So it encourages the movement of more AMPA receptors from the interior of the cell to the membrane. So it's not only increasing the effectiveness of this receptor, it's actually causing them to be more of them sitting there waiting to soak up neurotransmitter.

And the other thing that all of these kinases seem to do is that they seem to all be involved in phosphorylating a protein called CREB, which is this Cyclic AMP Responsive Element Binding protein. Question?

AUDIENCE: No.

ABBY NOYCE: OK. So the Cyclic AMP Responsive Element Binding protein, when it's phosphorylated, when these other proteins come along and stick a phosphate group onto it, it moves down, actually, into the nucleus of the cell and binds to specific regions of the cell's DNA, particularly the cyclic AMP responsive elements of the DNA, which is why it's called the Cyclic AMP Responsive Element Binding protein.

And so it binds to specific regions of the cell's DNA and it promotes transcription of the genes that are next to those regions, so it's modulating which proteins are actually formed. You'll remember from Bio that you've got your DNA to RNA to protein model of how cells work, the central dogma of molecular biology. Nod if you've heard this before. Yes. Right.

So by going down here and binding to the DNA, this CREB protein can cause it can control the rates of transcription of some of these genes. So it's controlling how fast the cell builds these particular proteins. And this is where this starts getting kind of vague. What genes? What proteins? I don't know. I think people do know, at this point, what some of them are. We know there's more than 100 regions in