PROFESSOR: I decided against giving you any kind of quiz today, because I put those questions up pretty late. And some of you are studying on a schedule that might not have fitted my schedule for this week. But we're working on worksheets that will be full-page things like this, and where I've-- basically on something like this, I've taken out the identification, so you have to fill them in. Or we might ask you to draw a pathway on a diagram like this-- these major pathways that we want you to learn.

So Caitlin and I'll come up with questions. And we'll do some of that partly homework, I think, and maybe a quiz, but we'll decide just when. We want you to have a chance to work with it for a while before it gets thrown at you in an exam. And that way, in the exam, it's just a test to see whether you can remember what you did.

All right, let's finish talking about axonal plasticity. First of all, we hadn't finished talking about regeneration at all. I just introduced it a little bit last time.

So what's the answer to this? What happens to regeneration of central nervous system axons in mammals that changes it with development? Basically, you cut axons early enough in the developmental period-- at least in the systems that have been examined, the optic tract, and the lateral olfactory tract, and corticospinal tract. And these systems will all regrow if you do the lesion early.

And if you're a frog or a fish, it'll still regrow even when you do it later in life. But not mammals-- in mammals, there seems to be a pretty early cut-off. There are a few exceptions. There's a few systems that have a lot more growth-- vigor of growth-- that is retained right into adulthood, although that doesn't mean they'll cross an actual gap, but they'll find some way to get around, like the norepinephrine-containing axons.

But that's what this slide summarizes. So I want to talk about methods now that have been used to get that regeneration later in life. This is a topic that I've done research on for a number of years. And I still collaborate on some of this research with Rutledge Ellis-Behnke, who comes here in January to give a little neuroanatomy class in IAP. So some of you have met him.

All right, so this is what we've been doing. We've use peripheral nerve bridges. Why would you do that? It was discovered a while back-- yeah, you wanted to answer?

AUDIENCE: [INAUDIBLE] actually do regenerate [INAUDIBLE]

PROFESSOR: Exactly, that's exactly right. The idea was very simple. You cut a nerve in the arm, and it will regenerate, or in the leg. OK?

Unless the axons just get outside their usual track-- so they have no guidance-- then sometimes, they just won't find their way back to their normal termination point. But the idea was, since axons will grow in peripheral nerves, but they won't grow in the CNS after a certain age, maybe if you put some peripheral nerves into the CNS, maybe the central nervous system axons would grow. Maybe there's inhibitory factors in the CNS. And separate investigations of that have found exactly that-- there's a lot of factors in the central nervous system, in the mature central nervous system, that inhibit axon growth. So one way to get around it is to use peripheral nerve bridges over lesions in the CNS.

This has been tried in just a few labs. It's not easy to do this kind of surgery. The details make a huge difference.

And after meeting some of the failures that weren't complete failures-- they were only partial failures-- I decided to give it a try myself in this at MIT, working with several students including Rutledge. And we found that we could get quite a bit of regeneration. We started with cutting the optic nerve right behind the eye and connecting a long piece of peripheral nerve from the leg, right to that stump.

Now, these are central nervous system axon coming from the retina. They had to go 17 millimeters, all the way to the midbrain tectum. We wanted to put them there, because we knew the function of the tectum in controlling orienting movements, so we could test for the functional return.

The problem with that was it took a really long time to get the regeneration. Almost every lab that had tried it gave up many months before I gave up. I kept doing other experiments, but returning to these animals and testing them some more.

And I had about given up when students told me they just couldn't see anything. I decided before we get rid of these animals, I'm going to try it, look myself, and see. And I saw something really remarkable in an animal where we had put the nerve in the mid brain.

We had led it from the eye to the midbrain. But we put it on the wrong side. So if we got any functional return, they would turn in the wrong direction.

And I started seeing wrong direction turning. That was the first animal where we succeeded in getting a peripheral nerve to work. I'll show you that animal in a video.

And then how we've used shorter bridges to improve the percentage of animals and the speed of return-- percentage of animals where we get success, and the speed at which it happens. So I'll show you all that. And then we'll talk about using new materials that seem to act like extracellular matrix.

They support axon growth, and let me get to that in a minute. They also inhibit scar formation. We've worked with a few other things, like genetic transfections.

I want to show you the two methods where we've been most successful. This is how we start. We just transect. On at least one side, we transect the optic tract as it comes into the midbrain tectum.

If you test such animals behaviorally, they cannot orient in the opposite side-- the visual field on the opposite side. So it's a very good model to look for functional return. So this is, then, the method of the shorter bridges.

Instead of putting it all the way from the eye, they don't have so far to grow if we can get them to grow in on the side towards the retina, and get them to grow across the lesion where they've been transected, and grow into the tectum on the opposite side. It's very tricky. I'm happy to discuss the details. Obviously, for this to be used in neurosurgery, these details can make a lot of difference.

All right. I was able to put up to three bridges like this across a single transection. This distance here is only about two and a half millimeters-- the width here. So it's not very big.

But the pieces of peripheral nerve proportionately are about the way you see them there. We take-- these are branches of the sciatic from the leg. The animal is impaired a little bit without the nerve we take out, but he gets along pretty well. There's enough redundancy in the innervation of the periphery so we don't render them functionless.

All right, so what I'm going to do here, put on the PowerPoint where I can show you these video clips most easily. These are the slides we've seen already. OK, this is, first of all, an animal leg with that last lesion where made the lesion, put the little bridges across several of them. OK.

So here he is. Just to give you an idea-- a method of testing them. They can't see much at all of that white wire. There's a white background surrounding them normally. You don't see it here, but when we're testing them, we have them surrounded with a white background. We can put that wire in over the barrier, and about all they see is that black ball.

And this animal's fairly old. He's been kept a long time just to see how far he would recover. So he's a little slow when he turns, but he's obviously able to turn, whereas he didn't before the regeneration occurred.

Now this one is the very first animal. We did the surgery when he was 12 weeks old, cut the nerve behind the eye. And then we led the implanted peripheral nerve all the way from behind the eye to the tectum on the same side-- so it was the wrong side. And we eliminated the other eye. So he was blind unless he got-- these were the first animals we were testing.

Now, I actually put several of the sequences together. So you see it three times. Note the stimulus come in, stimulating this right eye. And see what he does. He turns to the left.

Every time he catches that stimulus, he turns in the wrong direction. And that was the first success with that method we had. There's no way it can be any other explanation.

There's no auditory cue, olfactory cue. People will make up all kinds of things to explain away your behavior. And I appreciate that from scientists. They want to make sure you're really seeing what you're claiming. So this was a perfect control for that.

OK, this case shows what that-- when you label the axons. Here's a piece of the peripheral nerve bridge. It shriveled quite a bit, but axons are growing through it. And you can see all of these labeled fibers in the tectum have regenerated.

Because the tectum was completely denervated before this, the only way to get in is through those nerve bridges. And quite a few of them did grow in. Here's another-- the one that live five and a half months after the surgery. And you can see quite a few axons coming in, and terminating not throughout the tectum, in this case, but in the tectum right near were the implant was put in.

OK, the other method uses a self-assembling peptide, usually a sequence of 16 amino acids that are-- there's usually only four different amino acids. But they're put together in a certain sequence in a good protein lab. So they're synthesized peptides.

They have unique property that they assemble into a kind of gel when they contact a salt solution. So it looks like a little vial of water when we use it in the surgery. And we can put it into a pipette.

And we put it right into the gap. If this is a deep lesion in the middle of the tectum, that's how we started the experiments. We put it right in that gap.

OK, now without putting anything in, this is what you end up with-- just gaps in the tissue. So the axons are way up here. They will not grow all the way down and around, unless it's a baby animal Then they will, but in an adult, they never do. So they just come up to that barrier and stop, if we label them.

But here's what we first noticed about this material-- the tissue seems to heal itself. The gap disappears. This is not the gap over here. This is a distortion due to the-- after the surgery. The cut is here. You can see the bright fluorescence of the red blood cells there to indicate that.

OK, so this is the model. This shows the pathway we're testing. The pathway from the eye crosses at the optic chiasm and reaches the superior colliculus, which represents the entire-- on the right, represents the entire left visual field.

And the crossed pathway from there-- the tectospinal tract that controls turning movements-- so it controls turning to the left. And the same for the other side. So then what we do is we make the lesion, for example, like that.

So there's the tectum. And you can see it. And during surgery, it looks like this, though, of course we never get this wide view. You get the view through a tiny, little window.

But you get so-- if you're a good surgeon, you learn to recognize all the landmarks. And you can expose it. And you can see these landmarks. We make the cut right there. And we've been pretty successful at putting it where we want.

And here shows some histology, where we put a fluorescent label in the axons. There the red cell-- these are blood cells. And you can see where the gap was.

And you see quite a few axons-- the green the axons-- in that, among those red cells. OK, and if we do a histology with parasagittal sections, the cut was right here. And this is pre-tectal termination here.

Here's the superior colliculus. It's a little thinner than normal here near the lesion, but you see the axons growing right across and re-innervating the superior colliculus-- not at full density. They don't all regrow, but enough of them regrow that you can get function.

OK, so I'm going to start here by showing you an animal that has no right eye. This is the control. And you can see it's very simple.

He doesn't respond at all on the right. We're staying away from the whiskers. We're basically up above him a little bit. As soon as we move far enough across the midline, he turns.

This is an animal, now, who's been rewarded many times for turning. He simply won't turn unless he sees it, or you touch the whiskers, either one. And that's always a control.

Like this animal, we stimulate many times by stimulating the whiskers on the right side. Then he does turn right. So we show that he's perfectly capable of the motor response. So now here's the one where we had the self-assembling peptide in the cut that transacted the break in the superior colliculus. And then we put that bridge over the break in the superior colliculus.

And you can see, again he's fairly old. And he is not making a quick, wide turn, the way a normal young animal would do. But he is turning. And he keeps turning until he gets to the seed. All right.

AUDIENCE: So the hamster [INAUDIBLE], it's all in the [INAUDIBLE]?

PROFESSOR: They don't orient without visual input into the superior colliculus. Some of it does come from the visual cortex. But in a hamster, you can take the visual cortex out completely, and he will still orient, as long as he's got that retinal projection to the superior colliculus. That's what makes it such a nice animal for this.

Animals with a somewhat smaller tectum depend more on other things. Did you want to-- oh, sorry.

AUDIENCE: What's the life expectancy of a laboratory hamster?

PROFESSOR: Yeah, very good question. They live anywhere from about nine months up to a year and half. The oldest I've ever had was about two years and three months. No, in fact, I've had one at home live three years.

But in the laboratory, they usually don't make it much beyond two years. And even that's unusual. We don't know why that difference. Nobody's ever studied it. But people with pets have often told me they have hamsters live longer.

I think it's because their parents replace them, and the kid doesn't know, because they all look alike.

AUDIENCE: Pet rats also live longer than laboratory rats.

PROFESSOR: You think that's true? See, that's an--

AUDIENCE: [INAUDIBLE] live a really long time, turned completely gray.

PROFESSOR: Whoa. See, it's an interesting thing. People-- scientists simply haven't paid attention to that phenomenon. I think it would be an interesting thing to try to figure that out.

AUDIENCE: Is there a reason-- I'm curious-- why you chose a hamster [INAUDIBLE]?

PROFESSOR: Yes, I did because hamsters are cuter.

[LAUGHTER]

No, I did because-- for several reasons. One is, the behavior is easier to study. They show all this visually guided behavior.

It's very difficult to see in rats and mice. I've done it with the rats and mice, but it's harder. With the hamsters-- and also, hamsters are stupider.

And that is a big advantage. You don't want them learning all the time. And you know what? You want really fixed action patterns. And that's what the hamster's doing for us. He's very predictable.

They learn, too. I've tested their learning, visual discrimination. Sorry?

AUDIENCE: Are ferrets smarter than hamsters?

PROFESSOR: Oh, yeah.

AUDIENCE: A lot of people like ferrets.

PROFESSOR: Yeah, ferrets are good. The ferret gives you the advantage of a large cortex. And the other thing where the ferret fits, also, is that hamsters are born in a very immature state.

They're born less than 16 days-- they are born on the 16th day after conception. You know, the nearest to that among the laboratory animals is 21 days, or 23 days for mice and rats. So the hamster is much more immature than those animals.

So the optic tract is just starting to grow into the tectum when they're born. And the critical projection to the tectum appears later-- all postnatal. So those are some of the advantages.

OK, so you can read this. Rutledge summarized the whole problem of getting central nervous system generation as a series of problems. Preserve-- keeping cells from dying-- if they're missing the tips of their axons, they no longer are innervating their target. Many cells will just gradually shrivel up and even die.

So you've got to keep them alive. You've got to give them a permissive environment. There's a lot of inhibitory factors in adult tissue.

And in some cases, you have to promote their growth. Sometimes, like I told you, that not all the axons are growing. We were able to get enough of them to grow to get good function, but all of them won't. In some systems, you can get none of them to grow. You need to use growth factors, and perhaps even genetic transfections to get them to grow.

AUDIENCE: Do they remyelinate?

PROFESSOR: And then there's-- they do have to myelinate. That's another problem. But generally, it takes a long time for all this recovery to occur.

And even after we can label the regeneration in the tectum, we don't see function right away. One of the reasons might be plasticity. The places they terminate on in the tectum have been occupied by other axons.

The proper ones, when they come in, often have to compete for axons that have taken over the synaptic space. And in studies of non-mammals, that's been examined, and they find out that they are able to compete. They will basically push out the ones that are there. But in any case, however that's happening in the mammal, we're getting it to work in the colliculus.

All right, well, I want to get started talking about the motor system today. This just summarizes where we are in the class right now. We've looked at all the levels of the CNS.

I want to go through specific functional systems. We start with the motor system. And I'll talk a little bit-- it won't be very long-- about brain state control before we get into sensory systems. And then after sensory systems, we have quite a bit of study of the limbic system, the corpus striatum, and finally, the neocortex.

So I start by considering the evolution of motor control, with these questions that you see-- three major questions. And to study organization of that system, I want to begin with the motor neurons. Because that's what's essential. If you don't reach the motor neurons, you don't get any movement at all.

So we'll see how the motor neurons are organized. And then we'll see what connects to those motor neurons. We've already done a little bit, just to talk about the simple reflex function.

So the first questions are simply a review of things we've talked about before. The general purpose movements that are used for many different purposes, and what are the three types of movements we talked about already? We were talking about the midbrain, remember? Yeah.

AUDIENCE: Locomotion, orienting and [? resting. ?]

PROFESSOR: That's right, locomotion, orienting movements, which means turning towards the source of a stimulus, usually, and grasping it. That can be by mouth or by the limbs. OK, and then I said before a neocortex evolved, the midbrain had evolved structures for controlling those three types of movement.

So can you think of the structure in the midbrain we talked about for each of them? First--

AUDIENCE: [INAUDIBLE]

PROFESSOR: The locomotion, the midbrain locomotor region or area. And there are other locomotor areas, but that's the one in the midbrain that seems to be almost always involved in locomotion. OK, now for orienting, we know that the tectum in the majority of vertebrates is the dominant structure for orienting. It doesn't mean it was the first.

And then for grasping, well, it depends on the kind of grasping, doesn't it? What animals-- we probably-- earliest vertebrates probably didn't have limbs at all, so you had to get oral grasping. How do you get that?

Well, what controls opening of the mouth and shutting the mouth? It's the trigeminal system. And there's a motor component there that's involved in jaw control.

And there are pathways to that system from the optic tectum, OK? But then to get grasping with limbs in tetrapods, there is a nucleus there in the midbrain.

AUDIENCE: The red nucleus.

PROFESSOR: The red nucleus, or nucleus ruber, in Latin. There's only one issue there, though, that's a bit of a problem. I said tetrapods, animals with limbs.

Then why is it that, at least the more advanced fish have them, too? The fact is, we don't fully understand the red nucleus. It may not have evolved initially for control of limbs.

But then, again, fish have fins, of course. They can be used, but not really for grasping, except for the rare fish that use their tail as a means of-- as a weapon to kill prey and slap them out of the water and so forth. There are fish like that. Yes.

AUDIENCE: [INAUDIBLE] fish that essentially [INAUDIBLE]

PROFESSOR: Well, that's right. Yeah, you see it moving in that direction. But then, you'd have to postulate that all the advanced fish developed the red nucleus, and then went back to having no limbs later. And it seems very unlikely that that is true.

So OK, these are what we just talked about. And these are the specific pathways involved with those three kinds of movements. We've talked about all of them.

We know there are descending pathways from the midbrain locomotor area. How have they been studied? It's very difficult to define precisely that area anatomically. It involves a number of structures.

AUDIENCE: [INAUDIBLE].

PROFESSOR: So they use electrophysiology. They use electrical stimulation, where, with very low amounts of current, they can elicit locomotion. And it's in one region there, the caudal midbrain.

We'll talk about some of those components later. Some of them have horrendous names like nucleus tegmenti pedunculopontine pars compacta is a big part of it. And it gets a direct projection from the striatum.

And then you have the tectospinal tract. We've talked about that. It's not the same as that pathway that controls the skate movements. Here we're talking about turning movements.

The skate movements are part of the locomotor system. That ipsolateral pathway from the tectum goes to the midbrain locomotor area, and other locomotor areas, too, to control rapid locomotion. And then you have the rubrospinal tract from the red nucleus, nucleus ruber, another crossed pathway for controlling the limbs.

And then I mentioned for oral grasping, the separate pathways involved in that. And they, of course, are the main pathways for grasping in most fish. So here's that picture of the midbrain, just to remind you where these pathways are.

There are deep neurons in the superior colliculus that get input from the more superficial layers. They get input from what's stimulating the superficial layers. These axons are coming from the retina. What are the other axons coming in there-- non-visual inputs?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Somatosensory and auditory, right. And there are actually maps of auditory space, and somatosensory space, especially in animals with whiskers. OK, but anyway, you get a convergence of input on these deep neurons, the output neurons, that send an axon down across the midline. And they descend right near the midline on the opposite side, the tectospinal tract.

We call it tectospinal. Like a lot of pathways, we name a pathway after its longest axons. The longest ones reach the cervical spinal cord. The others terminate in hindbrain, because the pathways for orienting movements include a lot of postural adjustments. A lot of that is done in the reticular formation of the hindbrain and involves various movements in the spinal cord. All right.

You remember this statement from before. I talked about the midbrain being the connecting link between the forebrain and motor systems, early on before the neocortex evolved and got so big. And generally, the bigger a structure is, the more connected it is. And the neocortex, when it got large, bypassed that midbrain for many of its functions. That's not true in animals without this very large endbrain.

And then I mentioned the visceral nervous system. And various motivation states are also represented in the midbrain, OK? It's not all done by hypothalamus.

And what are the areas in the midbrain? That central gray right around the ventricle, and then more ventrally, the midline areas, the ventral tegmental area-- site of many dopamine pathways. And there are studies that show that, even without the hypothalamus, you can elicit various actions triggered by motivational states from that midbrain area, including sexual behavior, including attack behavior in predators. All right.

So what sensory systems are evolved? Well, we've just been mentioning this. But look at-- this is one of your questions there.

I asked what two sensory modalities most strongly shaped the evolution of the forebrain, which then influences the midbrain? Olfaction, and the second one, vision-- these are the two forebrain cranial nerves. Actually there are others, but these are the largest ones.

There's a terminal nerve. There's an [? epiphyseal ?] nerve, another where visual input can come in. But the ones that are prominent in modern mammals are those two-- olfaction and the retinal projections.

So we talked a little bit about these things-- olfaction and vision-- and their links to these motor systems in the midbrain. And then there are other inputs, too, that come in there that also affect movement-- gustatory input, somatosensory, and auditory inputs. And we know-- I've just mentioned here-- these are also important.

What is the diencephalic structure often involved in the initiation of locomotion-- much more than that midbrain structure? Can't hear you.

AUDIENCE: The hypothalamus.

PROFESSOR: Hypothalamus is the best answer. Now, there is a specific area in the hypothalamus. We've mentioned the hypothalamic locomotor area. But the hypothalamus in general is the best answer.

What about the gaits of locomotion? Where's that control? Where are the organized circuits that control walking, trotting, rapid running, or galloping, if you're a four-legged animal? And many more animals are four-legged, of course, than are two-legged.

AUDIENCE: [INAUDIBLE].

PROFESSOR: Sorry?

AUDIENCE: The brainstem.

PROFESSOR: The brainstem is, no doubt, involved. But in fact, the gates are controlled further down in the spinal cord. So let's talk a little more about-- I use Larry Swanson's way to conceptualize it initially. And then I show how the forebrain [INAUDIBLE].

This is his hierarchy. He has, at the bottom here, the pools of motor neurons in the spinal cord. And of course, there's some of them in the hindbrain, too-- just not for locomotion that involves the legs. So it's mostly spinal. But many other behaviors are controlled by hindbrain, too.

So the motor neurons at the bottom, and connected to those motor neurons are many interneurons of the brain and spinal cord. We call them the central pattern generators. Those would be things like the gaits of locomotion.

It's built in. It's an innate pattern of wiring. Grooming movements would be something like that, too, controlled by, mainly, hindbrain and spinal cord. Many of them, again, are spinal cord, generating the innate patterns of movement.

But above them, like in the midbrain, you have the central pattern initiators-- in Swanson's terminology-- like the midbrain locomotor area. And above that, the pattern controllers, the forebrain levels of control, that are usually involved in animals initiating these movements, OK?

So this is what I did. This is in your book. And here it just shows some of the network generating these patterns of activation of the flexors and extensors of the limbs, controlling various movement patterns. And then this would be midbrain level, like the midbrain locomotor region, if we're just talking about locomotor behavior here.

And then this would be hypothalamus. This is where you get the input from what we call drive states, the motivational states. And then I show, with evolution, how first olfaction as the endbrain began to expand-- remember, that was how the forebrain began-- how the endbrain began, anyway, with olfaction, which projected to the most primitive parts of the corpus striatum, which then projected right into the hypothalamus.

And also, as it grew, it started projecting directly to the midbrain as well. So in all modern mammals now, you have those two kinds of projections, just controlling locomotion. And then second, you other inputs besides olfaction.

Remember, that was the second major factor involved in the expansion of the endbrain. Other inputs came into the forebrain through the diencephalon, through the older parts of the thalamus, which went to corpus striatum. Those other inputs then went to cortex as well, and a newer part of the thalamus evolved. So I put it third here, because it was this neocortex that expanded the most.

Which again, projected the corpus striatum, also to the medial pallium here, involving the two kinds of learning-- habit formation and learning of place. But notice the big change here with neocortex when it comes to locomotion. Projections to the midbrain locomotor region, yes, but also projections directly to the spinal cord. That was a big change with the expansion of the pallium as the neothalamus and cortex evolved, and that structure began to enlarge.

All right, so this just discusses these pattern controllers and initiators of the midbrain and caudal hypothalamus. And I should mention here that there's subthalamic locomotor areas, too. Some people just lump them together, but the localization by the physiologists indicates that they're probably separate.

And the subthalamic structures and their involvement in these things, including locomotion and even things like feeding, is less studied. We usually focus on the hypothalamus. And yet I think the subthalamus is very important in brain evolution, too.

But this is just the-- I have a question in there-- discuss the types of connections that the early forebrain could have used to influence the general purpose movements of the midbrain in those first questions. And so here I show the midbrain locomotor area. Here I show the hypothalamic locomotor region, and I show pathways from the olfactory bones.

There are a few more direct connections in many fish. I show how the polysynaptic pathways were probably more common. They came into both of these locomotor regions. And some of them took a different route through the epithalamus, which then also projected into the midbrain.

All right, and these are the-- did I show you this before-- just the maps of these locomotor regions by electrophysiologists? And then we know that locomotion is influenced by a lot of other kinds of inputs. Maintaining balance of the body during standing or locomotion depends on multiple pathways, some of them from the reticular formation of the hindbrain.

But there's two other really important descending pathways. Do you know what they are besides reticulospinal? They're mainly concerned with controlling the body axis and what we call whole-body movements like locomotion. Locomotion involves a lot more than legs. It involves your whole body.

AUDIENCE: Vestibulospinal.

PROFESSOR: Vestibulospinal, exactly-- so reticulospinal, vestibulospinal, and remember a structure that coordinates the timing when multiple systems are involved in controlling the same movement-- cerebellum. So we usually don't call it the cerebellospinal. It's OK with me if you want to call it that, but it gets the name of the structure in the cerebellum that gives rise to it, the nucleus fastigii.

So we'll just wait and see the pictures of it. So this just talks about what we just said. And this is the picture.

Based on pictures of-- this is the picture of [? Nauta ?] where he shows the position. I've emphasized it here-- the position of the vestibular nuclei in the top view and the side view, the vestibular nuclei near the dorsal part of the hindbrain there, at the same level as the cochlear nuclei, so just hovering near the lateral edge of the cerebellum here. You have that vestibular input coming in through the eighth nerve.

And the cerebellum developed as a vestibular structure, as far as we can tell. This is-- I used a different figure in the book, but it's really very similar. This one is from [? Rodahl ?].

The most primitive part of the cerebellum is here, the floccular nodular lobe-- the flocculus out here, the nodulus near the midline. And things near the midline in the cerebellum control the body axis, as does the vestibular system. Out in the hemispheres, it's very different. The hemispheres are mostly concerned with the distal muscles of the limbs.

And here on a sagittal section, they show the position of those vestibular structures. But this one shows that the vestibular system-- primary sensory neurons of the vestibular system-- project into the cerebellum. And they do so an interesting way, because no other system does this.

They go directly to the cerebellar cortex. So here's a little diagram. You see the vestibular nerve. These are primary sensory neurons in the vestibular system.

You see them coming into the vestibular nuclei. But they also go up into the cerebellum. And the cerebellum normally projects to these various deep nuclei-- below the cerebellar cortex. But in the case of the vestibular system, it projects directly to the vestibular nuclei.

And there you see a very simplified view. There's actually four different vestibular nuclei. They don't show that here, but this is, again, the [? Rodahl ?] book, where he shows the origin of the vestibulospinal tract.

And there's also another set of axons going in the opposite direction, connecting to the motor neurons controlling eye muscles. There's a very close tie between vestibular system, cerebellum, and eye movements, and head movements. And there's a whole group of axons running between these nuclei interconnected with reticular formation, vestibular nuclei, and cerebellum, always coordinating the eye and the head and turning movements. They're so important for animals to get around.

All right, you don't need to learn this, but I wanted to emphasize this nucleus. That's the nucleus that projects directly to the spinal cord. It's heavily connected with the vestibular system as well.

OK, so we'll come back there next time. And we'll start by going over orienting a little more in order to finish this introduction to the motor system. I didn't expect to finish this today. But what follows is a little easier.

So you've got-- I've posted all the things here for you to read. So please continue with that reading. And we'll give you something on Wednesday. If we're going to give it a little bit as a quiz, we'll let you know. I'm not sure we'll do that, but we'll get that done as soon as we can.