PROFESSOR: All right, normally we'd have a quiz today, but we we're so far behind that I decided I'd rather do something through the Stellar site, so we'll try to come up with something by tomorrow.

Also, nobody ever uses the forum section. I don't actually know exactly how it works. I don't know if we talk to each other on that whether everybody can see what everybody puts up or not. Some of you may not like that. But if anybody understands that, talk to me or Andrew about it if you've used it before. Do any of you have a class that uses the forum section? Yeah?

AUDIENCE: Well, I had a class that used the forum. Where we had to post every week to the forum.

PROFESSOR: And did everything you post-- could everybody see it?

AUDIENCE: Yeah, as long as I think-- the professor set the initial settings, or it's just the default, but yeah, it's a public forum. You can post a new topic, and then everyone can read it, and then people can respond. And their messages, if they respond to it, are posted under each individual topic.

PROFESSOR: OK. What I would like about it is if people could ask me questions and then everybody could see what I reply. Because as it's been, a number of you have emailed me, and I answer the emails, but it's nice that everybody can see replies, at least the ones that apply to the whole class. So we need to figure that out.

But anyway, the homework for this week will be something based on study questions that you already have, that have been posted.

All right, we didn't get too far with this topic of diaschisis. It's a difficult one for many

people, but I don't think the basic ideas are really so complicated. To explain it, take a picture like this and imagine a subcortical structure there at the bottom, let's say the spinal cord, and then some higher structure. It could be the neocortex, or it could be something in the brain stem. And it provides excitatory input to the lower structure.

These connections here could be a spinal reflex. So if it was spinal shock, these are the descending connections coming down the cord from the brain. And if we make a lesion and it cuts off all the descending connections, the question is, what happens to this pathway?

Well, we know something about what happens. With the degeneration of those pathways, these cells there become much more difficult to excite because they've lost so much of their excitatory input. You've got to realize that in the brain, cells are getting bombarded with a lot of input, and it takes usually quite a bit of summation-- spatial summation, temporal summation-- in order to get axons to fire their action potentials.

So I've change the color here to indicate some depression of function of these cells after the loss of all these connections. And note that the larger-brained animal is going to lose more connections to these lower structures like the spinal cord than the smaller-brained animal. Which would explain why spinal shock in a frog doesn't last as long as it does in a mammal. And why the loss of function after forebrain removal in a cat is much worse than in a rat. It's a quantitative effect.

Well, there's recovery after that deafferentation-- deafferentation meaning the removal of the input to a structure. There is a recovery. It takes some time, but a lot of it you see in the first two weeks. And then there's a slower recovery that we understand less well after that.

But the two major things that start happening right away are these two, collateral sprouting and denervation supersensitivity. Now, with collateral-- yes?

AUDIENCE: Does the [UNINTELLIGIBLE] in all animals, or in certain animals?

PROFESSOR: In cats and rats, and we assume it's pretty similar. But what we don't know, and the studies haven't been done in enough detail to know, does it happen faster with greater lesions, slower after less deafferentation, or what? There's a limit to the amount of information here. Diaschisis is still-- there are a number of publications on it, but not I would say it's a bit under-studied.

OK, let's just draw in what collateral sprouting is. Near these terminals, and I'm assuming that means connections there with those neurons, we know these cells have lost all these connections. I'm not showing the actual connections. There's a lot of synapses on these cells. The remaining ones, the ones that are still intact, can sprout collaterals. it can happen in the smaller animal here or in the larger animal.

Well, generally the animal that's lost more fibers might feel a little more collateral sprouting. It also may take some time. He's got a lot more to recover. So collateral sprouting in fact is correlated with the recovery of reflex function in the spinal cord.

But there's another thing going on also, and that is, these cells start generating more membrane receptors for the neurotransmitter of those axons that are degenerating. That means they become more sensitive to the neurotransmitter, that neurotransmitter anyway, and often it's the same excitatory neurotransmitter. And so the cells become more sensitive.

How could you test for those things? Well, collateral spouting is not so easy to test for, but it has been done, even with the degeneration tracing methods, but now with injection methods for tracing connections it's a lot easier to follow the sprouting. So we can actually see it with the right anatomical methods, and we can use little micropipettes that spritz out little bits of neurotransmitter, and we can record the response of cells. So we can see the increase of sensitivity of the cells and trace the supersensitivity.

So we have to conclude then when we're dealing with brain lesions, one thing that's certain is you have to know a lot about the anatomy. You're not just subtracting functions when you remove tissue. The quantitative effects of the lesions have to be

considered. You're gonna cause changes in functions of structures a long distance from your lesion if they had long connections.

OK, now let's go back to our overview of function and talk a little bit about these forebrain structures like the corpus striatum. We know from ethology studies that as animals are growing up, they have a lot of inate behavior patterns that appear when the neural structures are mature enough, like walking. We don't actually have to learn to walk. We do learn a lot of details about walking, but we start walking when the spinal cord structures are mature enough to control the walking pattern.

Well, a lot of the inherited behavior patterns, like the components of attack behavior in a cat, have to be linked together in the course the animal's life-- it's development, it's early life-- by learning. And we think probably the corpus striatum is a major structure in accomplishing this, because it's so important in habit formation or procedural learning, sometimes called implicit learning.

We'll talk more about these things later, as indicated by my little asterisk there. And then there are certainly additional issues when we deal with human pathologies of the striatum. We will get to that much later in class. Now, what about the 'tween brain, the diencephalon sitting between the hemispheres. The hemisphere grew out of the diencephalon, really, as did the retinas. Very early in the evolution of the 'tween brain, there were optic inputs. They're probably as primitive, or more primitive, than the factory inputs to the forebrain.

We know that those inputs play a special role in organizing the daily rhythm of activity. Very differing in many different species during day and during night. Some are night active animals, some are day active animals, some are twilight animals. But they also are affected by light levels durying the daytime. I've looked at both of those things in the Syrian hamster.

Let's look at those inputs, where they are-- the hypothalamus and the epithalamus. That's where the connections are made from the light detectors. And I just want to point out that these rhythms indicate that the function of those structures in the tween brain is to modulate the entire system. We're talking about brain states, and

we'll have a small unit on brain states when we deal with motor system, sort of an understudied topic in neuroscience.

So here's the Shmoo 1 brain, and here I show optic inputs, which initially came from eyes that weren't image-forming, like in amphioxus. But with the development of image-forming eyes, this connection to the base of the brain here, and the hypothalamus, was retained. And that's the crucial connection for controlling the daily rhythm of activity, or, I should say, for synchronizing the rhythm of activity with the the cycle of the sun.

But here's the input from the parietal eye. In many species, that is an eye. The top of the head. That has a special function also in controlling circadian rhythms, and it still plays a role even in us, even though it doesn't get the input through an eye in the top of our head anymore, as it does in amphibians and some lizards. But it controls the rhythm of secretion of the melatonin, for example. It gets its visual inputs by a roundabout circuit that originates in this connection with the hypothalamus.

So I think this role of hypothalamus in gating what other systems are doing is very important in the evolution of the diencephalic components, thalamus and subthalamus are the major ones. And we know this kind of gating occurs in major ways. Studies of the connections of hypothalamus indicate pathways whereby this could occur.

And we know from electrophysiological studies, especially of this biting attack behavior in cats-- we have direct evidence for that kind of gating. Because you can record from sensory pathways coming through the thalamus, or you can record in the cortex, where the thalamus projects, and you can alter the animal's motivational state by stimulating the hypothalamus and see the changes in sensory function.

Sometimes they don't know exactly what the changes mean, but they can see the change in activity of cells. And it's my belief that in the evolution of sensory pathways ascending to the endbrain, that function-- that gating function-- may have been a major reason of why these pathways almost always have a synapse in the

thalamus, in the tween brain.

Now, the hypothalamus is the central structure of what we call the limbic system, and we can guess what the limbic system does by some of its connections. Here's the hypothalamus, I show a few red cells there. But note here it's closely connected with systems that get input from olfaction and olfactory structures connect to other areas of the endbrain which then project to the hypothalamus.

And that, we will find out, is one way you can define the limbic system. And why people that say it's just a hodgepodge of unrelated things-- why do we lump it together, why do we call it a system-- I think they're wrong, because I think anatomically we study connections we can define in terms of close connections to the hypothalamus, and that's the way [UNINTELLIGIBLE] defined it.

There was an amazing evolution of major functions that were originally dependent on those olfactory inputs and their projections to the endbrain. These are the two major ones that will come up a number of times later in the class. One is object preferences, identification of the good and bad things. Very important to the earliest evolution of the endbrain. There was also place learning, memory for good and bad places. Initially, I believe, all that was done by olfaction.

So this is my overview of the striatum and the limbic system. I've summarize here some of the major things limbic system does. For example, at first I point out that the struatyn I think initially was a link between olfaction and movement control. And it became very important for all those major systems because of the plasticity that could occur there, allowing the formation of habits and what we call reward-based learning.

And for the limbic system, besides its olfactory inputs, it became very important in visceral control, control of motivational level and emotional expression. Or reward, positive and negative. Initially, the hypothalamus plays a central role in that. And as we mentioned, ability to remember what's good and bad and where such things are.

More generally, it's higher control over what an animal does and when he does it.

But then, of course, higher vertebrates develop more sophisticated, higher control of those kinds of functions with the expansion of non-olfactory cortex, the neocortex.

So we want to talk more about-- introduce that neocortex. And the neocortex is considered by many anatomists an innovation of the mammals. Now, there were predecessors to it, but they really didn't have the elaborate structure of true neocortex that we find in the mammals, even in very simple mammals.

So I want to show you the schematic of the mammalian brain, show you how the neocortex fits in that. Then we'll talk about major ascending and descending connections that are particularly related to neocortex and give you a general review of functions before we go on.

So here's our Shmoo 1 brain and there's this enormous growth of neocortex. The earlier cortex here was mostly limbic, what we now relate to the limbic system, though it included dorsal cortical areas that did get some other sensory inputs that were the predecessors of neocortex.

And this is the Shmoo 2 diagram. This is a mammal. You see the numbers there? Give yourself a little test. This can be a quiz. I won't give it to you right away.

You can blow that up when you look at it, and you should give me the name of all these things. Maybe you can do a lot of that right now. We've talked quite a bit about some of these things.

This you should know is spinal cord. What's this up here? Cerebellum. And below it? Hindbrain. What's in front of the hindbrain? It's all midbrain. What are the bumps here?

AUDIENCE: [INAUDIBLE]

PROFESSOR: Colliculi, OK. Superior and inferior. OK, what are these structures? I've named two structures there in this division.

AUDIENCE: [INAUDIBLE]

PROFESSOR: Thalamus and hypothalamus. And you see the pituitary there attached to the hypothalamus. Now, if we go in front of it, we have this group of structures. What's this out in front?

AUDIENCE: [INAUDIBLE]

PROFESSOR: Olfactory bulbs. And it's connected to this group of structures I've labeled with the number eight, and I said this is number eight too. What are those? All limbic system. All closely connected to the hypothalamus. And the rest here, of course, is neocortex. And there's the picture we saw before, the spinothalamic tract and its root to the neocortex.

So now, I'll show you two major, long pathways associated with neocortex in present-day mammals. One, we sometimes call the neolemniscus because we think, in fact, you just don't find it in non-mammals to any degree, so that's why we can say it's newer.

And then, of course, the major descending connection of the neocortex, the corticospinal tract. And the cortex actually connects to all levels, but that includes spinal cord. So I marked that with a red arrow. Let's follow the dorsal column-medial lemniscal system.

Here comes the input in from the skin. It comes into the brain and ascends without a synapse to the top of the spinal cord. Some anatomists say it terminates in the caudal into the hindbrain. It's a little bit arbitrary now to put it into the spinal cord.

Those cell groups there called the dorsal column nuclei, because these axons are ascending in the dorsal columns of the spinal cord. You take a cross-section of the cord, see those columns of the dorsal side, columns of white matter, heavily myelinated fibers. So it's a rapidly conducting pathway. It conducts more rapidly than spinothalamic tract or spinal reticular pathway.

So the first synapse is right there in the dorsal column nuclei. The axons then cross over right there, and they ascend all the way to the thalamus. And they're terminating in a particular part, a particular cell group, in the thalamus. We call it the

ventrobasal nucleus, and I've named it there. It's actually a part of the ventrobasal nucleus, which is located, as I've shown there, in the thalamus. It's actually in the lateral part of that nucleus, because the medial part gets input from the face.

And then the cells there project up to neocortex. Now, if I just want to name the dorsal column-medial lemniscus pathway, I just have to show those two cells and their axons. That's the dorsal column- medial lemniscus pathway, in contrast with the spinothalamic pathway. All right.

Now, the corticospinal tract. Of course, it starts in the spinal cord, and let's take this cell. Say it's a cell in the motor cortex, a big parametal cell in layer five of the motor cortex. And here comes its axon. I'll just trace the longest axon initially. And it terminates there on an interneuron in the ventral horn of the spinal cord. That would be a common way the corticospinal tract connects.

And notice, it has collaterals on the way. There's on in the corpus striatum, there's one in the thalamus, the more interior part of the thalamus there. Here's a connection in the midbrain. Here's one in the hindbrain or the pons. Many of these axons terminate in the pons, meaning they connect to the cerebellum. Because the pons is a major structure connecting to the cerebellum. And then, through an interneuron it's controlling movement.

I show another line here, and you can trace that also down, it has very similar collateral connections. But this is going more to the sensory side, and it ends up here in the dorsal horn. That's also corticospinal, but now it's connecting to the input side of the cord. Very numerous axons of that nature also. It's coming from a little more caudal, in the cortex from what we call the somatosensory cortex.

OK, now let's look at the same things in this view. First, the dorsal column. Here's our input. Here it comes in, here the axon ascends without a synapse to the dorsal column nuclei. It terminates in the medial most of two nuclei there.

There's a lateral one that gets input from the upper body. This one's coming from the lower body, so it terminates in the more medial one. And then that axon,

remember, decussates in the medial lemniscus, right up to the thalamus, to the ventrobasal nucleus. Same pathway we saw here, but now we're looking at it in top view, so the only difference really is that crossing, the decussation. Decussation means crossing the midline.

We can do the same thing for the corticospinal tract. Take this one, the big parametal cell there. It has a number of collaterals, as we saw before. And now here's where it crosses, right at the caudal end of the hindbrain, before it gets down to its termination in the spinal cord. I have one up there on the other said, likewise. The one that goes to the more dorsal horn. You can trace that down as well.

So that's corticospinal tract. So you can see that this junction here between the spinal cord and hindbrain is a major transition in the way pathways are connecting, because both the medial lemniscus axons are crossing there and the corticospinal tract axons are crossing there.

OK, so what does it do? What's it for? Why do we need a neocortex? We know in evolution there was increasing specialization of the thalamic and the corresponding neocortical areas. One of the things that's very clear, that even in very simple mammals that it's important for, is just sensory and motor acuity. You can make finer movements, you can discriminate more detail if you've got that neocortex.

At least for certain functions. When I say things like that, there's always qualifications. Because an animal with a big midbrain, he's got a lot of acuity for midbrain functions, but not necessarily for learning the difference between two objects. But for midbrain functions like escaping from things and turning towards things, turning towards a novel stimulus.

Now, but it wasn't only learning. They also did affect fixed action patterns. Because the cortex projects to structures in the brain stem concerned with fixed action patterns as well.

For example, I did a study of hamsters and their motor cortex, and found that what seems like a very automatic behavior of seed shelling, that they can do the first time

they ever get a sunflower seed in their life-- they've never learned it-- they can still do better then I can in getting it out of the shell. And I found out that that fine movement of their foot, of their forepaw, in fact does depend on this corticospinal tract.

They also develop greater ability to separate objects from the background stimuli. That's been shown in a few studies. I think more uniquely, what the cortex did, not just quantitatively better, like functions like acuity, but we have an increasing ability to anticipate what we're going to sense and to plan what we're going to do. And that began to appear very early, especially in higher animals, that's quite advanced. So I'm describing that here also.

So I have a little bit of review, just so you know what are the major points we've been talking about, recovery from the diaschisis effects of lesions. So you can go through that. Then these long pathways that evolve with the neocortex. You should study those figures and know the simple pathways I've presented.

And notice some of these terms I've been introducing, when I talk about a projection, I mean a connection of a structure to another structure through an axon. So we talk about the projection of the motor cortex to the spinal cord through the corticospinal tract. It goes through the param--it's sometimes called the parametal tract because of it's shape in the hindbrain.

If I talk about the spinal tectal projection, I mean a projection from spinal cord to the tectum of the midbrain. And we will use terms like that all the way through the class.

So now you've got a very rudimentary outline of brain anatomy. Now we're going to get more involved in learning about the basic structural divisions, and I will introduce, just to keep you interested and to help you learn it, things about evolution and about development along the way.

All right. This is where we were supposed to be able to start today. We're going to talk about development today. We're going to focus mostly on the spinal cord. I want you to remember that as evolution is going on, we don't evolve a cord and

then later evolvee a brain. In the chordates, brain was there in the beginning, but it changed more than the cord. They were all evolving together.

So we'll start with some embryology, the process of what's called neurulation, relation that is the formation of the nervous system in the first place, and follow the early development of the spinal cord. And then, the next class we'll talk more about the adult spinal cord and get to the autonomic nervous system, which we will not finish until the following class, two classes from now.

So these are the developmental steps leading to a nervous system. Starting with the fertilized egg, a clump of cells we call the morula, and then the blastula, a hollow ball of cells. Then gastrulation, where the alimentary tract is formed, and the neurula, where there's the beginning of a nervous system.

Now, that involves particular activities of single cells. And Wolpert has summarized what those activities are. They involve specific contractions, so there are contractual proteins in cells, so they change their shape.

It involves changes in adhesion, which involves particular molecules on the surface in the membranes of cells, where they allow cells to stick together in different ways, and those expressions of cell adhesion molecules can change during development. It involves movement of cells, we'll talk about that for neurons. And it involves, of course, growth. And growth can mean proliferation. It can also mean increasing size of the cells.

So this is one of Wolpert's pictures on following from the egg to the gastrula. Here's the egg and it's divisions. Here it's forming the clump of cells, so it comes to look like a raspberry but it's still just a clump of cells. And then it becomes hollow in the middle, with fluid in the middle. Basically a one cell thick wall, that's the blastula.

And then, look, something starts happening here. Some cells move in. These cells are changing in shape, and the surface there invaginates, as you can see here, due to asymmetric contractions in the cell.

And then something else is going on there. These little extensions called

phyllopodia extend right across the blastula to the other side. And they contain contractile proteins, so they attach to the other side. That involves adhesion, and adhesion molecules. And then they contract and it pulls that part of that membrane right across.

That, by processes I know much less about, it goes here through the organs. So now you have a mouth at one end and anus at the other. And of course it's not functioning in that way, but that's how it begins.

So in gastrulation, you change from this hollow ball shape to a donut shape. And when these cells move inside, they're actually very complex little organisms. It's like you're watching little one-celled animals, because they have all kinds of extensions, adhere in specific ways, and move in specific ways. And Wolpert is just picturing from one study the movement of mesodermal cells that will form a skeleton that could be some of these cells in here.

So now let's talk about neurulation, and how the neural tube forms, that neural tube which we described first when we talked about amphioxus. We'll define what we mean by the neural tube and its formation, the process of neurulation. We'll define the alar and basal plate subdivisions of that tube and the sulcus limitans we'll define also, and the neural crest cells. You'll understand all those terms here in a few minutes.

So to do this, I'm taking sections through the embryo, and there at the top you see the ectoderm, the surface layer. Remember, you have ectoderm, mesoderm, endoderm. The endoderm will form the gut tissues, mesoderm will form muscles and skeleton and the notochord. The ectoderm is at the surface.

Notice something's starting to happen here, right above this mesadermal structure called the notochord. Now, this is true for all the chordates. The cells are thickening. That thickened area is called the neural plate.

And then the cells contract differently at the dorsal and ventral end. They contract more dorsally, and you begin getting an invagination, as I'm showing here. Still one

cell thick, but the invagination now is forming what we call the neural groove. And it's forming all along the embryo. So it's not just a point going in, it's a little groove along the back of the embryo.

And these two edges here come together, and you end up with a tube sort of due to that infolding. And there's a few cells that don't end up in the tube and they don't end up in the ectoderm anymore. Those are called the neural crest. so this is the definition of neurulation, the formation of that neural tube.

And it happens because of an inductive process. There are moleculres here coming from the notochord that are having an influence on those cells overlying it. At a descriptive level, this kind of process was known before induction was known, but Hans Spemann postulated inductive processes from experiments he had done and he turned out to be correct, and they now know what the inducing molecules are.

Molecules are coming up this way, and they begin to influence the more ventral part of this area. The floor plate and the nearby ventral horn. Whereas there are other molecules from the ectoderm here that influence the more dorsal part of the cord. Those are the inductive processes going on.

The inducing-- Spemann did that work and published back in 1924. He did it with a student, Hilde Mangold, who unfortunately died before this was even published. Her original name was Hilde Proscholdt. She died in a kitchen accident when she was only 26. So later, when this work led to a Nobel Prize it was Spemann who got it because Hilde Mangold had been dead for some time.

Later, they discovered this protein called sonic hedgehog diffuses from the notochord to induce formation of the nervous system, also acts as a ventralizing factor influencing the development of motor neurons, for example in the basal plate area. Later, dorsalizing factors were discovered coming from the ectoderm. They turned out to be mainly the bone morphogentic protein, two proteins, BMP4 and 7, that obviously play other roles in bone growth as well as in the formation of the neural tube.

OK, now, this doesn't happen all at once. Here's a picture of human, and you see the neural tube closing here in the middle. It's not closed yet at the rostral end or the caudal end. And there you see the cross section of two different levels. So I want to show you-- it's from class 7 here-- now what I want you to do is I want you to watch up here and here. You'll mostly watch up here, but you'll have plenty of time to glance down at the dorsal view of the embryo, so you'll see the unfolding of the neural tube.

So here the formation of the neural groove is occurring. See there in the dorsal view o the neural groove. And you'll see it close first near were the cross section is taken. And there are the cells that have already gotten outside the ectoderm and the neural tube. Those are the neural crest cells, and watch what happens to those.

The red there is the mesoderm, the primitive mesoderm, forming the muscles. Muscles and skeleton. This part is forming the vertebrae, this is forming muscles. And now they're turning the embryo here, so you look at it from the side and you see the segmentation of the mesoderm now. That's the end of it.

And now you see what's happened to the neural crest cells. There are a bunch of cells here. Those are going to form dorsal root ganglia. These cells here will form the paravertebral ganglia of the synthetic nervous system, part of the autonomic nervous system. But there's some up here, too. Those are forming the melanocytes in the skin.

Now I'm going to show you an actual movie of the xenopus embryo. And we'll show this a number of times, and you actually see the formation of the neural tube and the closure of the neural tube here. At the end of it, it's completely closed. Here's the head end and the tail end. Head end, tail end.

You can look at it on any one of them. It happens pretty fast. It's pretty speeded up. It's an amazing little film clip.

This is just a freeze fracture picture where they've frozen solid an embryo. That's where the neural tube is forming. You still see the neural groove there. Here's the

neural tube. And you see the individual cells, it's still one cell thick. And here you see the membranes. The surface ectoderm, the mesoderm below, and then finally the endoderm. This is all gut cavity here.

And these are pictures of the human just 18 and 20 days after conception. And there you see the neural groove and the beginning of closure. The neural tube here at 22 days.

The neural tube is already closed in the whole middle, but it's not closed yet in the brain area or in the caudal part of the spinal cord area. So just three weeks after conception, it's already very far along. So by four weeks after conception, it's already beyond amphioxus.

So now I've just redrawn these pictures and I'm showing you those neural crest cells. I'm not showing the ones that's on melanocytes, I'm just showing the ones that make up nervous system, and I'm showing some of them are becoming dorsal root ganglion, and then here's the position of the ganglia that make up the sympathetic division of the autonomic nervous system, which we'll be talking about after just a couple more classes.

And if you take a cross section of the tube, you'll notice if you look at the ventricle there, there's sort of an indentation there that allows us to divide the dorsal and the ventral part. The dorsal part we call the alar plate. That's where we found almost all the secondary sensory neurons. And then the basal plate, the more ventral part there, is where we find all the motor neurons and the cord.

Now, of course there's many interneurons in both of those parts of the closing neural tube. And I'm not going to take time here to blow all this up, but it just shows that at different levels of the embryo, those neural crest cells are forming different things. And one of the things they form throughout is the Schwann cells that form the myelin in the peripheral nerves. That's coming from neural crest too.

And way down here, and way up here in the brain, these areas, but not in the central area, we're not getting sympathetic nervous system ganglia forming. We're

getting parasympathetic. Because it has different functions, we keep them separate.

So now we want to talk about proliferation. By that, we mean cell division, increasing numbers of cells. That little neural tube is one cell thick at the beginning, but the cells are dividing, they're proliferating all the time. There's mitoses adjacent to the ventricle. There's two kinds of mitoses, symmetric and asymmetric. Initially it's all symmetric. One cell becomes two, two become four, four become eight and so forth. That's symmetric cell division.

But in asymmetric cell division, one of them stays mitotic but the other one migrates. Those mitoses always happen near the ventricle, so we call the layer of cells by the ventricle the matrix layer or the mother layer. And here's the cell that will undergo mitosis. It's up against the ventricle.

Well, here's what happened just before. It was by the ventricle. Then as the cell body moved along the process, a little further from the ventricle. And then it synthesized its DNA. So now it's got double component DNA. It moves back, comes to the ventricle, and then it starts the mitotic process. And if it's symmetric, showing it's dividing its proteins evenly between the two, they both become stem cells and they both enter this cycle. The mitotic cycle, the to and fro movement of the nucleus.

But later, more and more of them will divide asymmetrically. So the protein distribution's a little different. And we now know what those proteins are that result in the difference. So one of them stays mitotic, the one that's against the ventricle. And the other one becomes post-mitotic, it migrates away from the ventricular surface.