PROFESSOR: Can somebody tell me what the homeobox genes are? They're often called Hox genes. What are they code for? Transcription factors. And if you delete certain Hox genes or change their position, you can get abnormalities in the segmentation of the body. Some of that has been done with flies. They can produce a fly, for example, with legs coming out his head or something like that.

And it's interesting that of rearrangement on the chromosome that the position of the gene and the sequence of genes on the chromosome, it's always consistent right across the species. As we saw last time this slide of a mouse showing the expression of three different genes. They were doing immunostaining of the antibodies for the proteins of those genes.

And here, this is actually not-- it's mesodermal expression. But these genes are expressed in nervous system and other body tissues. But you see each on of them, each of these transcription factors has a rostral limit for its expression, less precise than the caudal side. But now, if you look at the hindbrain, during development at a certain period, you see this pattern appearing. The segmentation is visible in the bulges of the hindbrain. We call them rhombomeres. Mere for for the section or segment. Rhombo, of course, for the rhombencephalon. These are segmentation of rhombencephalon.

When you look at the expression of transcription factors, including many of the Hox genes, they have an interesting pattern. And here's a little cartoon of the rhombomeres of the hindbrain from rostral here on the left, the caudal on the right. And if you look at the pattern of gene expression this way, it looks like a bar code. It's interesting that some of them are expressed in like one rhombomere, and then

they're not expressed in the next one. Then they are expressed in the next one down line. And that's true of a number of them. You see here, they skipped two. This one's in one and two, not in three. Then these two are both present the fourth, and they're present again in the sixth, and one of them's also in the seventh.

So that's true about of a number of different genes. And this is just one experiment showing an effect of these genes. Here you are seeing what you saw on the previous slide, expression of these particular Hox genes. There's two that have that more limited expression in certain segments and not others.

If you take stem cells, basically the precursor cells from the embryo, and infect them in another embryo, if you do it before those rhombomeres form, you can inject them near a boundary and they spread right across that boundary. Because the boundary i before those genes are expressed, it doesn't have the reality it does later. Because after the rhombomeres appear, you inject those cells and they don't move over the boundary.

Of course, the genes must be doing other things, too. We know that there's developmental differences. The motor neurons didn't originate in a particular rhombomere, just innervate a particular part of the mesoderm corresponding to the branchial arches of the embryo.

So now, this entire class is about the hindbrain and the cranial nerves of the hindbrain. We've talked a bit about hindbrain specializations already in chapter six, but we'll talk a little more about hindbrain specializations today. So first, back to the columns of the secondary sensory neurons and the motor neurons, and compare the hindbrain with spinal cord.

This is probably the third time I've presented it. I want you to start to remember it. In this case, I'm trying here for the spinal cord. This is based on a figure of [INAUDIBLE], where I've added the colors. There are sensory and motor columns, but also I've colored in the visceral column, prepangliotic motor neurons of the sympathetic system.

And then, in the hindbrain, I've used to red color for the visceral sensory and the visceral motor neurons. Visceral sensory gets input from the entire gut. They do have sensory fibers that come in through dorsal roots, but they reach this nucleaus in the hindbrain. The rostral part of the nucleus is the [INAUDIBLE] nucleus, getting input from the seventh, ninth, and [INAUDIBLE] cranial nerves.

But here, just across the boundary between [INAUDIBLE] and basal plates, you have this motor column. That's this very long column with the big dorsal motor nucleus of the vagus nerve. And you'll note here, here there's just two roots; the dorsal root and ventral root at each segment. That's not true in the hindbrain. Here, the sensory fibers are coming in in two different positions. This is where the input is saved from the auditory and vestibular senses would come in.

Whereas the somatosensory input from the face comes in a little further ventrally, the trigeminal And then you have-- so these are sensory nerves, but the fifth actually has a motor component, too. It has a motor nucleus. It's just on the other side of this boundary. it's the matiscatory nucleus for chewing movements. It goes out. It joins the sensory fibers of fifth nerve. I don't show it here.

And then you have mixed nerves-- the seventh, ninth, and tenth primarily, where you have a mixture of sensory fibers and motor fibers. So no [INAUDIBLE] roots at all. But then you have somatic motor column controlling eye movements and controlling tongue movements, that just contain the motor neuron axons.

I want to now go through cranial nerves a little bit. And then we'll talk about hindbrain some more, naming cell groups, looking at fibers, going through the cord and fibers of those cranial nerves. First of all, what is a sensory placode? Remember how the secondary sensory neurons of the spinal cord originate from neural crest cells. The secondary sensory neurons of the cranial nerves don't just originate in neural crest in the head region, they also originate from sensory placodes.

What is a placode? There's several of them. They contribute to the [INAUDIBLE] nerves, in addition, in the vestibular sense. The olfactory neurons originate in a

placode. It's just a piece of the ectodermal tissue, the surface tissue, that is neurogenic. It gives rise to, among other things, to neurons. So they don't-- all those secondary sensory cells don't come from the [INAUDIBLE] crest.

And then we want to know about the cranial nerves and their number. I have a table in the book. You start studying that table because I'm going to give you some time, but we're going to memorize all the cranial nerves and a few things about them. I'll give you more instruction about that, but I want you to start paying attention to that because when I say seventh nerve, I expect you to know what it is. If I say twelfth nerve, you should know what it is. Now you probably don't, but just start learning it, and over time, pretty much the numbers and the names mean the same thing to you.

After all, you need to know the number and the name and a little bit about the function. [INAUDIBLE], sensory, or motor. So these placodes, so a little more about them. First of all, the dorsal lateral placodes include the trigeminal placode. There's two main portions, a thalmic and the [INAUDIBLE] mandibular portions. They give rise to the secondary sensory cells of the trigeminal ganglia, that make up the trigeminal, the axons of those cells, those neurons, give rise to trigeminal nerve, fifth cranial nerve.

And then the otic placode, another one of the dorsal lateral placodes. They're named according to position in the embryo. That gives rise to vistibular and auditory segment of sensory cells, those ganglian cells that outside the central nervous system. And then, as I already mentioned, the olfactory placode gives rise to the olfactory [INAUDIBLE]. Remember, the primary sensory neurons are right in epithelial. That is a specialized region, [INAUDIBLE] region of the ectoderm that gives rise to them.

There's also, I don't stress this, but there's an epibranchial, sometimes called epipharyngeal placode that gives rise to some of the ganglia cells of nerves seven, nine and 10, but those are more complicated because the neural crest also contributes to them.

So let's talk about these cranial nerves. The 12 cranial nerves is actually not a full description at all. Even humans have more than that, especially in the embryo. So why is it so traditional to name just 12? It's because it is pretty adequate to describe the adult brain. There's a table in the Bulter and [INAUDIBLE] book that lists 25 different cranial nerves. Some of them are found only in certain groups of vertebrates.

We've mentioned a few times here the lateral line nerves, there's up to six of them in animals, say with [INAUDIBLE] reception. There's also mechanical lateral line organs, mechanosensory organs. But most vertebrates don't have those. But some of our cranial nerves in mammals, the facial or the glassopharyngeal or the vagus nerve. There's actually two distinct parts. The nerve forms the fibers of those two components are together in many vertebrates and in humans.

So the tradition is to name just 12 for human. We know they're very tiny nerves, but we don't know much about the function. It is certainly accounts for all of the things that are well known and well studied in the vertebrates. So we just learn 12.

So let's take now a look at all the hindbrain of an adult mammal, and look at the locations of cell groups, look at those columns of secondary sensory neurons and motor neurons, and also where the axons are that are passing through. We're going to look at figure 10 [INAUDIBLE] in the book. It's a slice through the adult caudal hindbrain. That is the part of the hindbrain we call the medulla or medulla oblongata, the elongation of the spinal cord, not-- below the cerebellar region, the prompting region.

First of all, what are the sensory modalities that you know about from that caudal hindbrain region? I mentioned them a number of times already. I've even mentioned them in this lecture. Auditory, vestibular, what about somatosensory? Of course, that's a hindbrain nerve, too, the trigeminal. That starts in the rostral hindbrain, but you still see it in the caudal hindbrain because of the very long descending nucleus of that system. And in addition, you have visceral sensory. And we include in that the taste sense. All of that's represented.

I know you can answer this one. Which cranial nerves carry somatosensory input from the face into the brain? You should by now know the number and the name of that nerve. What is it? Trigeminal nerve, the fifth nerve, fifth nerve. Sp we want to look-- first of all, where are the primary sensory neurons, like every dorsal root, every cranial nerve, [INAUDIBLE] sensory fibers? The answer to this question is always the same.

Where are the cell bodies? In a-- what's the word? Not nucleus, if you're outside the CNS, what's it called? A ganglion, right. So it's in the trigeminal ganglia. It's a big ganglion. It's on either side of the hypothalamus, but it has nothing to do with the hypothalamus. It just happens to be there at the base of the brain. That's because the nerves are coming in from the head region, from the face, and they're coming in under the [INAUDIBLE], and they enter the rostral part of the hindbrain. They actually penetrate through the rostral pontine region, below the cerebellum.

So where are the secondary sensory neurons? Well, they're in the hindbrain, and they've got to be in this region here, in that column. So let's look now at the adult hindbrain here. This is where those trigeminal nerve cells are. We see them in that position every section of the hindbrain, in the rostral portion, where the cerebellum distorts the whole picture so much. And we'll take a look at that maybe in the class.

And it just continues, because axons form follow this area right here. A lot of axons come in from the rostrum. You only see them penetrating varied [INAUDIBLE]. Sp this would have to be a section of the embryonic brain, to actually be coming in at this point.

So what else can we ask there? We've already answered. Here's where you see the special senses coming in, vestibular, auditory. And that's exactly the position, at the very caudal end, when you're entering the spinal cord. That's where the dorsal column nuclei are. But the dorsal column nuclei are really in the very rostrum end of the spinal cord. Some people still call that hindbrain.

Here's where the motor axons come out. So all the eye muscles are controlled by neurons like this. There's only one that doesn't exit that way, the fourth nerve, the

trochlear nucleus, but otherwise, it's the same as all the others. And then the nuclei controlling the tongue, hypoglossal. So that's very much [INAUDIBLE] ventral view.

But look at the axons now going through. I show them all here. The descending pathway's, here is the sort of pyramidal shape of the pyramidal tract coming from the cortex, corticospinal accents, pyramidal tract, right at the base. They always run on either outside when you're looking in at a sheep brain. If you turn it over and look at the ventral side, you'll see these grooves. They're little grooves on the midline. The basilar artery might be there if it hasn't been pulled away.

But then you'll see a little bit of an indentation and the edge of the pyramidal tract. And this will have a slightly whitish appearance because of the myelin. And then right above it, you see the sensory fibers coming from the spinal cord and from the dorsal column nuclei. Dorsal column nuclei give rise to the medial lemniscus.

So, if is this is the medial lemniscus here on the right side, where are the cells that give rise to those medial lemniscus stem cells? Remember, dorsal column, medial lemniscus, those two names should be starting to link in your mind. Dorsal column, medial lemniscus [INAUDIBLE]. So where would the cells be? They would be at the top of the spinal cord in the dorsal column nuclei, but on the other side because there's a [INAUDIBLE] the hindbrain. You drew that out in your homework.

And then we have-- I drew the descending pathways on the left here. And I'm showing you where, for example, the tectospinal axons are, axons from the vestibular nucleus. I'll also follow those axons from the cerebellum. Now if you imagine that the brainstem is transparent, and you want to see where each of these groups of nuclei are, study this. And this, I used color coding to see them.

So I've shown the sensory cell groups here. This figure is based on [INAUDIBLE]. And the motor group's on the left. So that's where you see the cochlear nuclei. And a little below the cochlear nucleus and a little more medial, you see the vestibular nuclei, fairly large nuclei. There's actually four separate nuclei. We just lump them together and call them the vestibular nuclei.

Cochlear nuclei, there's two main-- two or three depending on how you divide it up. We just call them the cochlear nuclei here. And then trigeminal-- see there is the principal nucleus. But here's the axons that come in way up here. They keep going all the way down into the top of the spinal cord. They go a little further than this picture shows. That's all secondary sensory cells representing inputs coming at the face.

And then, and what is the remaining one? Well, it's a red color. It's got to be this'll visceral [INAUDIBLE]. It has a particular name because of its appearance in [INAUDIBLE]. It's called the nucleus of the solitary tract. Because the tract that does standout, even in [INAUDIBLE] can be seen. Right next to it, solitary tract. Many taste fibers in that track as well as visceral sensory fibers coming in from cranial nerves, cranial nerve 10, primarily but also from seven and nine.

And then the various motor neuron groups are shown here. It includes some that weren't in the other picture because they're very small nuclei. They're part of that visceral motor cell group column that controls salivation.

Now those kinds of figures, this one and this one, don't memorize them. Use them for reference if you forget, and you're reading something about these nuclei, you want to remember where they were, look back at chapter 10 and look up where they are. And notice, they go all the way up in to the midbrain. I mentioned that one in red there, the [INAUDIBLE] nucleus. Remember what it controls? The pupils, pupillary cells. Not the blink of the eye, but just the pupils of the eye, the iris. And then the oculomotor nuclei, the third and fourth, and then one more down here, the sixth, controlling different directions of eye movement.

So we want to look more at these trigeminal nuclei. But I want to say a little-- go back to this topic about the evolution of the system. Because these pathways really terminated with pretty important factors that influenced the evolution of the hindbrain and also more rostral structures. So first of all, where's the information go when it comes in the trigeminal nerve? There should be local reflexes.

I just mentioned eye blink. That' a reflex that depends on input coming in to the

trigeminal nerve. It could come from the cornea, from there, it will cause an eye blink. It could be a touch of the eyelashes or a touch of the face. But it also could just be visual input. We're concerned with this somatosensory input. There's got to be a pathway for the eye blink, so look at that. I mentioned that it could be considered a [INAUDIBLE] pattern. There's actually a drive associated with it. You blink your eyes periodically. It's very important in keeping the cornea lubricated.

And then we have the lemniscal pathways. Remember the lemniscal pathways in the spinal cord. There was a spinoreticular pathway. There were spinal [INAUDIBLE] tract, and then the dorsal column the the lemniscus system. There must equivalent systems here for the trigeminal system.

But first, let's go through this hypothesis, the [INAUDIBLE] of the axons to the midbrain and forebrain evolved with or after the evolution of the cross retinal projection to the tween brain and midbrain, and that led to cross projections in the trigeminal system as well, and even the auditory system has been affected by that. So, in fact, the entire midbrain and forebrain in the sensory world is represented side opposite to where brain representation is, but not in the hindbrain and spinal cord.

So what is the most ancient descending pathway from secondary sensory neurons to the trigeminal system? What did I just call it? What was the oldest one from the spinal cord? Can you say it louder than that?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Spinal reticular. So what do we call it here in the hindbrain? Trigeminal reticular. And then you should be able to at least give a quick description of the hypothesis for how somatosensory and [INAUDIBLE] pathways evolved to become predominantly crossed. The simplest possible way the hypothesis is that it was to increase the speed of the escape movements.

So let's go through that in a little more detail. First of all, in these little diagrams, I've sketched spinal reticular and trigeminal reticular pathways. Mostly it's lateral

pathways, but a few axons, spinal and even brain levels have reached the other side. And then, here, I show the same. I leave the spinal reticular and I add to it, here in black, the trigeminal reticular, axons that [INAUDIBLE] this.

[INAUDIBLE] the very caudal forebrain. I don't show that here because there's so few of them. But I show them mainly in the midbrain and hindbrain, going into the reticular formation, and a few of the axons going to the other side. That's all you have in the most primitive vertebrates. That's the somatosensory pathway. There

In all the more advanced creatures you end up with these crossed pathways. I just have a few drawings to illustrate that. We'll start with this one. These are the basis for those figures. So what I'm showing here is, first of all, here's the trigeminal input. And here I show spinal reticular pathways and note, a few of them are getting to the other side. Most of them are [INAUDIBLE].

Here's the retinal, primitive retinal input, the most ancient pathway, coming into the hypothalamus. And even in modern mammals, that pathway goes pretty much equal to the two sides. In the hamster where I've studied it with several different methods, I can't discriminate the quantity in the two sides. It's a bilateral projection. It's a little nucleus and it sits above the optic chiasm. And the fibers go mainly to the suprachiasmatic nucleus, but they also spread outside it and go to the adjacent areas.

So the question is, why with further evolution, do they end up mainly crossed? Here's what the animal had to do if it's going to get away from something coming here from the right side. It causes a shadow affecting the lateral eye. It could be touching the animal or causing water currents. So you get a trigeminal as visual input. What we want to do is turn away and swim like hell. OK The turning away was critical, and people have generally ignored this in studying it.

They studied the, what they call a startle response or rapid swimming, but they forget they don't want to swim right towards the attacking animal. They want to turn. So I think the speed of that was very important. That's my own hypothesis. So the

result was, to get turning, you need to contract muscles on the left for input coming into the right. So you've got to reach motor neurons on the left.

And if you're doing that with forebrain input, put in the case of the visual system, there were no long pathways going all the way down the spinal cord or even the hindbrain. They did [INAUDIBLE] in the midbrain. They went directly to hindbrain and spinal cord. So that I'm showing in red. So the most rapid pathway to get there was a cross pathway. Even saving a very small fraction of a second can make the difference between living and dying. Yes?

AUDIENCE: [INAUDIBLE]?

PROFESSOR: There are. Again, for hindbrain and spinal cord, they don't cross. And what's critical here is what's in the hindbrain and the spinal cord. So the midbrain pathway that reaches those, is uncrossed. And that's very clear, even in modern mammals.

So this is the behavior. These are the pathways that had to evolve ti get that very rapid response. The question is then, how did that evolve afterwards? And I'll just go through that quickly here. We know-- this just says what I've already gone through. We know that the projections of the midbrain surface became typographically organized. With topographic input, first of all, it could add a little bit of directionality to that escape response. I'm not sure just how important that would have been. But one thing's very clear, that once you have a topographic projection, it become useful for a lot of things besides just rapid escape.

When you look at escape responses in animals, the direction they turn in doesn't differ that much. It generally is away from the animal, but it doesn't vary that much. But if you want to find food, turn toward something that's not dangerous or [INAUDIBLE] approach another fish. Then, of course, the topography becomes critical.

And for that, again, the most efficient was you've got to contract the muscles on the opposite side. Instead of doing this, you want to orient towards something if it's not dangerous. You're going to have to contract the muscles on the other side. So that

led to the evolution. This is from our earlier class where I show the input to the surface in midbrain. Here is the ipsilateral descending pathway, controlling locomotion. Here, then, is the cross pathway controlling turning [INAUDIBLE].

That's the tectospinal [INAUDIBLE]. It only reaches the rostrum-most part of of the spinal cord in the animals that I know about and it's been studied a number of different animals. So you end up with a cross pathway from the tectum and an uncrossed pathway with very different functions.

And once this visual pathway became crossed, the somatosensory pathways and even auditory that also gave information about the space around the head, had to match it. Otherwise, there was a mismatch between somatosensory and visual, and between auditory and visual. And that's exactly what happened in evolution. And that is how all the senses, midbrain and forebrain, became represented on the opposite side.

AUDIENCE: [INAUDIBLE]?

PROFESSOR: Yes, it is. So that is simply arguing for the importance of visual system very clearly. There is some variation when we look across species, that some species have projections that are more bilateral in the forebrain. But they're more specialized species. I'm talking about sort of the main line that led to modern mammals. But there is some variation. And I don't know of any review that's gone through. I know individual studies that show some of these odd pathways. But most of the vertebrates have the kind of pathways I'm talking about. In the very ancient ones, this is what you have. Well, the most ancient ones don't even have spinal [INAUDIBLE] tract crossed yet. They just have spinal reticular.

There's a lot more study that could be done, especially on those primitive animals, to look for more evidence of this. And animals like amphioxus, you don't see any. We don't know much. There's just little pigmented areas. They would respond to shadows. There were animals after amphioxus, before the hagfish and the sea lampreys though, but we only have fossil records. [INAUDIBLE] did appear long, long before the hagfish and lampreys.

AUDIENCE: [INAUDIBLE]?

PROFESSOR: You have to talk louder.

AUDIENCE: [INAUDIBLE]?

PROFESSOR: Good question. [INAUDIBLE].

Let's see what else. I want to say a little more about the trigeminal system. In this picture, I'm showing where they are in the embryo. And then here they are in the hindbrain again. And here, I've just shown the trigeminal, left the others out .

But I've included the facial motor nucleus because I want to show the simplest pathways for the eye blink, going directly from interneurons here in the trigeminal nucleus, going to either, by way of interneurons, or to this neuron directly to the facial motor nucleus, causing the eye blink. I assume that some of the pathways are probably direct because it's very important functionally for that to be a rapid movement. It's a little bit like the escape response. It's protective. It's preserving the eyes, so it's very rapid.

Now I want you to be able to contrast the trigeminal nerve and the trigeminal lemniscus. Think of the meaning of each of those terms, trigeminal nerve, primary sensory cell axons. These are the axons themselves in trigeminal ganglia. Then what is the trigeminal lemniscus? What is the secondary sensory axons, exactly. Just like from the spinal cord. But now we're talking about pathways that originate in the hindbrain.

This looks complicated only because I added some other nuclei here and a bunch of words. But I can very simply show you what I'm talking about. Here's the trigeminal ganglion, sitting, remember, below the brain in humans. Here's its three branches, opthalmic, maxillary, and mandibular branches of trigeminal nerve. There the cell bodies are in that ganglion. And here the axon comes in and terminates in the trigeminal nuclei. Sometimes it's called the brainstem trigeminal complex.

They're just secondary sensory cells of the trigeminal nuclei. principal nucleus at the top and then the descending nucleus. They're all getting direct input from those primary sensory axons. Now the cells here, they're not performing reflex, like that eye blink reflex, they may be sending an axon across the midline and descending in the lemniscus. That's the trigeminal lemniscus.

We can't separate the spinal, [INAUDIBLE] in the spinal cord, we had the spinal [INAUDIBLE] in the dorsal column [INAUDIBLE] lemniscus. There are axons in different sides. Obviously, the ones from come up here are going to reach this [INAUDIBLE] cortex a lot more rapidly. They're more like the dorsal column system and meet in the medial lemniscus. Whereas the ones down here, including pain input, that goes down into the spinal cord. Those pathways to the brain are slower, more like the spinothalamic tract.

But they're all called the trigeminal lemniscus. You can see them. They simply join the medial lemniscus and the spinothalamic tract axon as they cross there through the midbrain into the caudal thalamus terminate in the ventral posterior nucleus, where the cells then project the [INAUDIBLE] somatosensory cortex, very much like the spinal cord.

I'm leaving out the spinal reticular here, just showing these more recently evolved pathways that are so important in getting to the forebrain. And I already mentioned this is where the pain in the foot goes. And this enlarges a little bit. Here you see the crossing. These are trigeminal [INAUDIBLE] axons. Notice here in the ventral basal or ventral posterior nucleus, those two names mean the something thing.

I'm showing green here. I omit the lateral most part. Why? Because the ventral posterior nucleus gets input from the body surface, too, from the spinal cord. This one goes out here. The body is topographically represented in that nucleus. Caudal parts of the body are here, the more medial parts here, the very medial most is input from the tongue and is the taste area there, the most medial part of that nucleus.

And I describe there what you're seeing at each level. We talked about [INAUDIBLE]

I just mentioned here the masticatory nucleus of feeding. And we talk about these specializations before, except this one I didn't have the picture. Amy mentioned this star nosed mole. And notice, here's that specialized organ. But here is proportionally how it's represented in the neocortex. All this is, is the [INAUDIBLE]. If they distort the picture according to how much brain is taken up by representing--

AUDIENCE: [INAUDIBLE].

PROFESSOR: I didn't actually plan to copy the figure from the paper, the most recent paper that mapped this [INAUDIBLE] cortex. That was done by John [INAUDIBLE]. Amy found the paper, but I didn't pull the figure out yet.

And then, the trigeminal system representing whiskers-- so here it shows the face. And then it shows the barrel fields in cortex. But here they are in the thalamus. We don't call them barrels. We call them barelliods. And down in the brainstem, you call them barrelettes. Just cute names to represent the fact that you can actually see these little clumps of cells for each whisker in the hindbrain, in the thalamus, and in the cortex.

We've seen this in the cortex. I wanted to show you a few more of the axons. This is from a frontal section, where each little puff of axons there labeled with [INAUDIBLE], It which diffuses through the axons even in a fixed brain. And you can see the little puffs, one puff per whisker. And here they are cut tangentially. We see the axons, the barrels. The cells will be mainly in the dark areas there. Here they are in acetylcholinesterase, and here they are in cytochrome c. You just keep seeing them with these various methods.

And then we talked about distortions. Why don't we do the distortions. We've already seen these. But I want to talk about the distortions from the incredible development of the cerebellum, which is particularly prominent in animals with [INAUDIBLE], manual dexterity, dexterity of other body movements. So we'll look at it for human and go through some of these terms. So we're going to end right there, and we'll come right back here next time.