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**PROFESSOR:** All right. Listen, I didn't much like the way things went in the last class. And the reason, it's because of the way I had planned it. By having a quiz not on the chapter we're covering in a day, you're always going to spend your time reviewing for the quiz, and you're not going to read-- or at least, you won't all read the chapter for today. So it's not a very good way to do it.

I asked you to read chapter 12, I believe, for today. You all should do that if you want to get the maximum out of the class. So this is what I would like to change. There's a number-- I talked to some of the students, and I talked to Caitlin. I would like to have a quiz every class, but only one, occasionally two questions. One idea would be to have one fairly easy question on the new chapter, just to make sure you've read it and get you to read it. But I also could have a question on the previous class that you should be able to answer if you've come to the class and gone over the slides afterwards that I post online.

Students also suggested perhaps some worksheets that you can work on. Any suggested I give some of my pictures, but don't label them. You label them-- something a little more active that you can do, trace in certain pathways, for example. It's a good way to learn it, if you're actively doing it and not just always passive.

So I think it's a good idea and I think we should do more of that. I welcome your suggestions for other things. So why don't you-- we'll do a practice quiz right now of this nature, so you know what it could be like. Take out a piece of paper, and I will put them on the screen. I will not grade them. You will grade them afterwards, OK?

Practice quiz. The first one is actually from the last-- from the midbrain class, and

the second one is from today's class. Today's chapter, I should say.

So Caitlin, I just went over with them a little bit what we were talking about, how to change the class a little bit. Designed really just to promote your learning.

OK. You ready to grade them? OK, the three types of multipurpose movements can be controlled by midbrain structures. I'm not even asking you what the midbrain structures are. I'm just asking you about the function level, which is quite important in this class. I always try to relate function to structure.

But the three types we talked about are locomotion, midbrain locomotor area, the second one was orienting movements-- you could say turning movements or turning of head and eyes, but just orienting movements is a good way to summarize it, used for many different motivations-- and the third is grasping-- you could say reaching and grasping, but grasping the most basic part of it.

All right, so that was from last time. Now, what are the two largest subdivisions of the diencephalon? It's already come up several times, but it was a particular part of this chapter for today. I'm just wanting you to say thalamus and hypothalamus.

Now, there are two other divisions. And according to gene data, there's actually several more. But that's because you can subdivide the hypothalamus into several divisions.

This is a practice quiz, OK? So they wrote out the answers. You have just barely time now to look at them, but you're grading them yourself.

[SIDE CONVERSATION]

All right, so what are the two other subdivisions? I could have asked you, what are the four main subdivisions? The epithalamus and subthalamus, right. One above the thalamus, the other below the thalamus. And that's how they're named-- epi for above, sub for below.

So there's a little bit to finish up from last time, and I'd like to do that first. This is

where we ended, pointing out that both the midbrain and the tweenbrain can be divided into two major functional regions. They're not just functional. Functional divisions correspond to the dominant type of connection these areas get-- the limbic and the somatic regions.

And you can see what they include. In the midbrain, central gray area and ventral tegmental area. And these will come up repeatedly now in the class. Similarly, the somatic regions, which are basically everything else here, includes at this level, the superior colliculus. More caudally, it would be the inferior colliculus, and what we call the midbrain tegmentum below it, going all the way down to the base here, substantia nigra and the axons of the cerebral peduncles there coming from the cortex.

Now, if you follow those two regions forward-- and you could do that just by connections, you could trace connections from either the central gray or the ventral tegmental area, and you would see that in the tweenbrain, they divide and they go up to the top, the epithalamus, and in through the hypothalamus. And if you labeled cells in the hypothalamus or epithalamus and trace connections from there, you would find that they go largely to those areas of the midbrain, the caudal projections. Of course, they go rostrally too.

All right. So, a few more questions about these somatic regions, this section of the midbrain. The first one is, there are motor neurons located in the midbrain. What movements do those motor neurons control? I haven't talked much about them, but I have mentioned them a few times, when we talked about cranial nerves, because it gives rise to the third nerve, third cranial nerve.

There they are. I put the label in red here, ocular motor nuclei, the third nerve nucleus. Now, the fourth nerve nucleus is also in the midbrain, so you could have answered that too. It's another ocular motor nucleus, but it's called the trochlear nucleus. It controls a different eye muscle. The ocular motor nuclei concerned with lateral eye movements, the trochlear for the twisting of the eye.

And at the base of the midbrain, you find this fiber bundle that's hugely different in

different species. So what's that fiber bundle? It's at the very bottom. There's an enlarged picture of the midbrain. It's this bundle. We call it the cerebral peduncle. What does it contain? All the fibers-- go ahead. Sorry?

**AUDIENCE:** [INAUDIBLE].

**PROFESSOR:** Always from the cortex, always going down. So they're efferents from the cortex. And where do they go? Spinal cord, and where else? The corticospinal.

But remember, we keep talking about another main projection that ends in the hindbrain. Well, they go to a lot of places in the hindbrain too. But there's one in the rostral hindbrain that's particularly important, because it's going to the cerebellum. To get to the cerebellum, what does it have to terminate? Where does it go? Does it go directly to the cerebellar cortex? No, it goes to the pons, the gray matter of the pons, the corticopontine axons.

So then there was one here-- the last question is a more difficult one. Another pathway that actually occurs-- oh, here's the one I meant to show you. This shows the peduncle in three different animals that I've just sketched. A rodent like a mouse, or a hamster or rat, would be like that one at the top. This would be a hamster. The rat, the mouse, superior colliculus, just slightly smaller. Otherwise, proportionately it's very similar to this.

But look at human, look at the biggest difference. The huge cerebral peduncle, and also corticopontine fibers, because of the very large neocortex in humans. So any animal with very large neocortex is going to have a pretty large cerebral peduncle too. But humans, it's relatively the largest.

And then there's a treeshrew. We used to think the treeshrew was a primitive primate. It turned out, because of the position of the corticospinal fibers, we realized it wasn't a primate, because in primates, the cortical fibers followed the lateral columns into the cord. But in the treeshrew, they're at the base of the dorsal columns, just like in the rat, or in insectivores.

So it eats insects, among other things, it was classified as an insectivore-- very

much, though, like a squirrel, a rodent. What characterizes it is that very large superior colliculus, so large that we could call it an optic lobe, just like we call it an optical lobe in the predatory fish, for example, or in birds, because they have so many important movements, particularly orienting movements, that depend on the midbrain. Their innate kind of learning is just short term. So that's the treeshrew. And there's the corticospinal tract. It's not that they don't have a decent size cortex, but the midbrain is much larger than in these other animals.

Now, the last question then about pathway that goes forward from the cerebellum. I drew these in here on this picture that we're showing with the red circles, the locomotor areas. So there's the midbrain locomotor area, defined by electrical stimulation.

And then I've sketched-- the BC means brachium conjunctivum-- not something you're likely to remember very well right now. But the axons from cerebellum don't just go down to the spinal cord in the hindbrain to affect movement. The kind of timing coordination, the movements that they do, is also important for endbrain functions for the neocortex. So to get there, it goes through the midbrain. The fibers cross over, because remember, hindbrain is uncrossed.

So when it gets into the midbrain and forebrain, they're crossed. So they cross here-- big bundle of axons in the caudal part of the midbrain.

**AUDIENCE:** [INAUDIBLE].

**PROFESSOR:** Sorry, ascending. Yeah, they're coming out of the cerebellum just behind this level, and now they're crossing over. And they're going to go to the red nucleus and then forward into the more anterior parts of the ventral nucleus of the thalamus. The posterior parts of that ventral nucleus, remember, gets somatosensory. But the more rostral parts get their input from cerebellum and from corpus striatum, and it goes to the motor areas of the cortex.

All right. So that's the brachium conjunctivum. I'd like you to begin to hear these things and learn about it. We will come back to it later. But we won't be talking in

great detail about the cerebellar pathways because we don't know enough about them.

I'm going to say here a little more about these long axons. This is a-- let's just look at this picture of the midbrain and talk about the long axons. Well, some of the long axons come in and just terminate there in the midbrain, like the optic tracts. I have those at the top here. You see some indicating that they're terminating there in the superficial tectum.

But what about the ones going through? Well, all those pathways from the spinal cord that carry somatosensory information, to get to the thalamus and subthalamus, especially the thalamus, they have to go through the midbrain. And there, these green axons form in this C-shaped region that includes, at this level, medial lemniscus down here and trigeminal lemniscus, and then spinothalamic tract.

And the spinothalamic includes a spinotectal component. In other words, many of them don't make it to the thalamus. They terminate in the superior colliculus or tectum. But they don't terminate up in the surface layers like the renal fibers do. They terminate just where I'm showing you here, in the deeper layers of the tectum. It's the tectum-- so important for orientating, you would expect it to get multiple inputs, and it does-- visual, somatosensory, and auditory.

The auditory fibers, many of them pass through. They're way out here at the edge in this bundle. It's called the arm of the inferior colliculus, brachium of the inferior colliculus. Brachium means arms. But some of them-- I don't show it here, but some of them terminate right in the middle there. So you have visual, then auditory, then somatosensory.

And in those deeper layers where the somatosensory input comes in, the output neurons are all multi-modal, almost all. They're getting input from various modalities, but all controlling the same kind of movements. So they converge on the cells like this, that give rise to the tectospinal tract. Most of them are getting converging inputs from the different modalities.

All right. What have I indicated in red there? In these pictures, I'm always using red for the limbic related things. That's pathways carrying limbic-type information. The ascending ones are mostly viscerosensory. They're coming in from the hindbrain, and they're traveling into the central gray but also they go all the way into the hypothalamus by that route. They also come through the ventral tegmental area, and they continue on to the hypothalamus also. I didn't show those here.

And what are the other ones passing through? What about fibers in the other direction? Well, I've shown them in the blue dots. Almost all those axons are just passing through from the neocortex to the pons and to the hindbrain and spinal cord.

So that's just summarized verbally here. I mentioned cerebellum, but I didn't show those on that next picture.

All right. So another question, what two major instigators of action are discussed in this chapter on the midbrain? One involves sensory motor pathways. What are the actions we were talking about here?

First quiz question, sensory motor pathways for orienting movements, or for locomotor movements, or for reaching movements. For reaching, the somatosensory pathways are dominant in most animals. For turning movements, it varies. Usually somatosensory is the most dominant because that means something's very close to you. But visual, of course, is very important too, and also auditory.

All right. But I say there's two major instigators of action. All those sensory motor things I'm just classifying as the one type. What's the other type? What makes an animal start to move, to do one thing rather than another thing? Not just the sensory stimuli bombarding its senses at the moment.

Motivation, yes. So the limbic areas there, best seen in this picture, the reddish areas there. And there is motivational control from the midbrain, although it's really dominated by the forebrain components of the limbic system, which these areas get

input from. Hypothalamus and the connections of the endbrain that connect to the hypothalamus. So that's what I mean by the two instigators of action.

And I just made a note there where you in the book actually say this. And I usually include old slides. Some of you might find them useful, but we don't need to go through them in the class. Because I want to talk a bit about the forebrain now and the comparative studies that have given us some idea about the evolution of the forebrain.

These are the major topics, the major subdivisions, with an overview of the tweenbrain or diencephalon. This is basically the quiz question-- thalamus and hypothalamus are the dominant regions, and then subthalamus and epithalamus are the two other major regions of the tweenbrain.

Then we'll talk about two pathways originating in the endbrain that actually correspond to this subdivision. It has a reality of the organization of axons in the brain. And then I'll say a little bit about evolution of the forebrain, especially from genetic data.

All right. That's question two, the two largest subdivisions of the diencephalon. That was the quiz question. And then two additional ones. But there's another question before that-- what are the ganglionic eminences of the developing endbrain? I don't think we've used that term before. It's a term from embryology, the ganglionic eminences.

They actually disappear with development. So that means they must be what? They're big collections of dividing cells. Oh, and I forgot to bring the book on my shelf. I wanted to show you actual pictures so you see what they look like. I'll try to remember that next time.

OK, so here is a cross-section. Notice a huge ventricles that's very far anterior. It's through the endbrain. There's no diencephalic structures here. And you see in the outline by the little dash lines there, the separation of the dividing cells, the ventricular layer of cells, cells undergoing mitosis, and the cells where axons are

present and cells that are post-migratory, they've already migrated into this region. So just like in the spinal cord, you have cell division happening mainly near the ventricles.

So if these areas are so big, they can't all be going to the striatum. The striatum isn't the biggest structure of the endbrain. And yet there they are, just where the striatum would be in an adult. So large that they get this special name, because at the more anterior levels, they can be divided and form these two main bumps. We call it the lateral and medial ganglionic eminence.

And then there's a little region-- at least in mammals it's small-- that could be called part of the lateral ganglionic eminence, but it's often given a special name because it's right at the angle there between the subpallial region and the pallium. The lateral ventricular angle region-- that's a particularly interesting region because some of those cells move up into the cortex with development.

This just shows you where that section was taken. And talks about endbrain evolution always involve some discussion on where these cells go, because they don't do the same things in mammals and non-mammals. So we will talk about that today.

Now, some of the evidence on that have come from gene expression data, homeobox gene expression in particular. This was one of the earliest studies of that nature. They just studied two genes-- these two, EMX1 and DLX1, and there's several related genes that they've also studied later. But in this study, they were looking at frog, turtle, chick, and mouse.

And EMX1, they found, was expressed in the areas that became neocortex, also hippocampal cortex, also olfactory cortex. This whole pallial region expressed that gene. And if they looked at the corresponding area in the chick, they found it was a thick region that included parts of the brain that actually were labeled striatum in the early studies. If they looked at a turtle, you'll see the region included, and then a frog.

And if they looked at the one labeled green here, DLX1, you'll see it's labeling the striatum. Now, this is showing the adult. But of course the gene expression data, what's important is what's expressed very early. So this is the striatum, but that gene is expressed also all the way down to the base, and also the medial area, the area we call the septum. So the basal forebrain, the septum, and the corpus striatum are all included.

But then there are regions that don't express either one. And notice how different they are. It includes this area in the turtle and in the chick that we call the dorsal ventricular ridge. Whereas in mammal, the only corresponding area in this initial study that they found was the amygdala of the mouse, the amygdala and the claustrum, which is near the amygdala-- and some studies have even included it with the amygdala-- and part of the septum here.

All right. So we'll come back to that kind of study later. I want to talk about major features of these forebrain structures. And then we'll pause just to review what I consider some of the important concepts we've been covering in the class so far.

But first, here's the embryonic mammal stretched out, hemispheres pushed apart. And these are what the sections look like, the one that includes the diencephalon. And there you have the cerebral hemispheres up above, and then here, the more anterior picture. So first, four regions of diencephalon, thalamus and hypothalamus, subthalamus and epithalamus.

You know the relationships, visceral. We call them limbic because they're related to the limbic or fringe structures of the hemispheres. We'll talk about pathways related now to these two divisions. Now, that hypothalamus and epithalamus on the one hand, thalamus and subthalamus on the other. Limbic and somatic. So there's that picture we saw earlier.

It's this question now I want to deal with. The division of pallial and subpallial regions of the endbrains, this division into somatic and limbic, supported by evidence of two pathways followed by their output axons. And you find these two pathways not just in mammals but in all the other vertebrates you can find, at least in development,

but usually right into adulthood these two kinds of pathways.

So let's go through these. First of all, this pathway, these are pathways coming from neocortex. We'll just color it in there. We'll use blue for the somatic. And these axons are going to and coming from the thalamus and also the subthalamus, coming from subthalamus. But we associate the most with this bundle of axons. This is the bundle we're talking about here. It's called embryologically the lateral forebrain bundle. And we'll talk about all the fiber components of the lateral forebrain bundle now in a minute.

And then, the medial forebrain bundle is here. This bundle here is the fornix coming from the hippocampus, but it includes all these fibers that come in and out of the hypothalamus. It also includes a bundle right here coming in and out of the epithalamus. And of course it's on both sides. So that's the medial forebrain bundle, and as you can expect, it's in a more medial position when we look at the endbrain, or here at this level, the more caudal forebrain. But remember, it includes both the epithalamic and hypothalamic components.

So here's the more anterior picture. You see the same bundles. so now, the medial forebrain bundle is down here. And on the left side, I'm showing where the axons are coming from.

**AUDIENCE:** The medial forebrain-- because you had some at the top and the bottom-- they both end up projecting to where you're showing the medial forebrain now because you have some at the top? So both of those come together?

**PROFESSOR:** Yes. That's right. These axons here are going both up here and down here. Think of it that way. When they came into the thalamus, they were together. But then one goes over the top, one stays below. One below goes to the hypothalamus. The one above goes to the epithalamus. And it has a special name, the stria medullaris. And that's what this is called. This is the stria medullaris.

So here's the medial forebrain bundle. And see where the axons are coming from? They're coming from the ventral parts of the striatum. They're coming from olfactory

regions. So ventral striatum and olfactory regions-- but also, there's the medial pallidum. This is the position of the hippocampus. In most mammals, it's very tiny at this level, mostly it's larger, more caudally. But it's definitely hippocampus.

And the larger hippocampus in most mammals gives rise to a pathway that goes forward, goes right through this region and then down, joining the medial forebrain bundle. And then these axons, many of them coming out of the hemisphere there as I show on the left here. I show them coming from neocortex, many different regions of neocortex. They're going into the lateral forebrain bundle. They're coming also from the output structures of the corpus striatum.

When I talk about striatum here, I'm going to lump together at this point the output structures which are called the globus pallidus. We'll just include them as part of the striatum, because they are very closely tied to the striatum.

All right. So this just gives all this in words. It's giving you the origin of these two pathways. Now, this is a picture of the lateral forebrain bundle. Now you'll see it's really a lot of words that you're very familiar with already. It includes fibers coming from the neocortex, the white matter of the neocortex. And then they come down through the striatum. And when they come down through the striatum, we call them internal capsule. They're capsulated by the corpus striatum.

They're joined by fibers from the striatum. It's all part of this somatic system. So here they are at the tweenbrain level. You'll see them up there in the white matter of the cortex, and now the peduncle is coursing along the side of the tweenbrain. That's the cerebral peduncle. That's simply the same axons right here, coursing along the side of the tweenbrain.

Then they keep going. They go on that big bundle at the base of the midbrain. So I show that in the embryonic midbrain here, in this section. Then they keep going. They get to the pons. They course through the middle of the pons. And they emerge from the caudal end of the pons and keep going. There they are at the base of the hindbrain. There, they get a different name. Now we call them the pyramidal tract.

Same axons, just changing names because of the way they look at different levels and where they are. They reach the caudal end of the hindbrain and they decussate. You can say, well, why didn't they decussate as they entered the hindbrain? Well, they don't. That's all I can say. They don't decussate until later.

There they decussate in all the vertebrates, they cross over, and in the primates, they travel in the lateral columns. When we studied spinal cord, I showed that big bundle in the lateral columns of the spinal cord. That's where the corticospinal axons are. We just call them corticospinal axons after that decussation. We stop calling them pyramidal tract, although some anatomy books might say this is the pyramidal tract. Strictly speaking, they're only called pyramidal tract at the base of the hindbrain when they have that pyramidal shape. If they're a rodent, they're in the ventral part of the dorsal columns.

OK. So there I have the different names given for the very same axons of the lateral forebrain bundle at all these different levels. They're all descending. Now, since you brought that up, remember here at these rostral levels, the internal capsule fibers, that's a two-way street, because many fibers come from the thalamus. They're going up into the cortex.

They are part of the internal capsule, and they are part of the white matter of the cortex. They are part of the lateral forebrain bundle there. But here, we're just dealing with the ones going down. And once we're past the diencephalon, almost all of the axons in that bundle are descending all the way down into the spinal cord.

OK. Now the other system, the limbic system, we just review here. Not showing the details. The axons tend to be a little different. They're much shorter connections. So we will never be able to follow pathways like this for the limbic system. With a few exceptions, the hypothalamus in many species has evolved a few long connections to the spinal cord. For example, the one controlling urination goes directly into the spinal cord.

All right. So this is just reviewing what we already said for these two systems. So this

division into somatic and limbic, you see, is supported by the neuroanatomy very strongly. So here's another question about these pathways. What is a striking difference in the outputs from the neocortex on the one hand and the corpus striatum on the other? If you had to answer that, I put you on the spot and say, give me a quick answer to that, something really simple, can you guess?

**AUDIENCE:** [INAUDIBLE] directly to it?

**PROFESSOR:** Directly?

**AUDIENCE:** So the neocortex goes like directly to the [INAUDIBLE]?

**PROFESSOR:** Longer axons. Where do the longer axons from the cortex go? Spinal cord. Some of them go to motor neurons. Corpus striatum doesn't do that. Pathways from corpus striatum don't make it past the midbrain. And the neocortex is involved in both of those systems. I separated somatic and limbic here, but here's the way I summarize it.

Here's the somatic on the left. There's the limbic on the right. So you see here, the limbic system connections are shorter. They don't make it past the brain stem. In fact, I could have been even more specific. I'd say they don't make it past the midbrain. Whereas the neocortex goes into the spinal cord.

The other difference, of course, is the neocortex is related to limbic structures as much as to somatic structures. And what about the striatum? Well, here, I've been a little unfair because I've just lumped the limbic parts of the striatum and called them limbic structures, just to simplify the diagram.

The better diagrams is this one. It looks more complex because limbic system structures are shorter. So you're going to have more of them. Strongly connected to hypothalamus, strongly connected to other limbic structures that aren't striatal. Most of the connections that are large are going in and out of the hypothalamus, but there are a few that go into the brain stem, especially to those structures in the midbrain. That's how now to define the limbic midbrain structures.

He made lesions in the limbic endbrain structures like the amygdala and hippocampus. And he said, the fibers not only go to the hypothalamus, they go beyond the hypothalamus into these medial midbrain structures, the central gray area and the ventral tegmental area. So that's how we define them.

All right. So this is for your review. Read them, and make sure you understand these various things. Just listing major things we've gone through in the class. It's a good review when you're preparing for your midterm, which unfortunately occurs all too soon. So that's why I put these in here. It's a good point to review.

What we're going to do next time, we will start by talking about segmentation. That's what a neuromere is. So what would a prosomere be? Remember, in the hindbrain what neuromeres were called? Rhombomeres, right. The midbrain only has one or two, the mesomere. There is an isthmus segment too. Some people would say that's midbrain. Other people would say, well, it's between the midbrain and the hindbrain. I would say it's midbrain. It's caudal midbrain.

But then, when you go forward, prosomeres. Remember, prosencephalon-- it means the endbrain and tweenbrain together, both prosencephalic, forebrain. So they're the forebrain segments. The segments of the diencephalon were initially defined just structurally. You can make them out in careful studies, especially with fiber connections, in early development. And you see, epithalamus, thalamus, subthalamus, and hypothalamus. The structural studies initially just indicated those four.

And interesting enough, they're caudal to rostral. We think of them as dorsal to ventral, but that's just because of the way the neuraxis bends around during development. So anyway, we'll talk about this the beginning of the last class. This shows those divisions as they've been made largely from gene expression data. But you can see the interpretation has changed. It's changed from this at the top to this down here, because the gene expression data are pretty complex. And people get slightly different results, and they put more emphasis sometimes on one gene versus another.

So it's changed a bit, and it's the most argument-- they used to think that the entire endbrain here developed out of just one or two neuromeres. With the tweenbrain now, that's not so accepted. It appears to develop quite largely separately. So we'll go through that. And then we'll talk a little bit more about the meaning of that gene expression data.

So we'll come back to these questions. I won't go through these in class unless you can't figure them out. You please bring it up or post questions of the forum. And also, if you think because of the changes I'd like to make I'm going to give you a quiz at the beginning of every class. If it's a question on the reading for that day, I will try to make it a fairly easy question that you'll be able to answer if you've read the chapter carefully, but I won't expect you to get every detail.

And sometimes I will be including a question on the previous class, just like today, the little practice quiz you had today. So we won't take a full 10 minutes at all-- just a few minutes at the beginning of the class, and then I'll go ahead with the discussion.

But if you have any issues about this or you can make suggestions about what kind of worksheets you would like, just post it for me on the forum, and I will listen, and Caitlin will listen. We'll try to come up with something. We can bring you worksheets that you can work on. You suggested this the other day, and I think it's a good idea.