

**GERALD**

OK, We were doing this last time. Let me just review it, the correlation centers in the midbrain and its motor outputs, and then we'll get the species comparisons, which I started with last time. OK, when you think of midbrain, we should always think of the midbrain tectum, superior and inferior colliculi.

**SCHNEIDER:**

The superior colliculus is the more complex structure because it gets multi-modal inputs. Visual inputs occupy the upper layers, and then the auditory and somatosensory inputs come in the deeper layers. They're all concerned with orientation and escape from predators.

We think of it usually in terms of orientation, but that's just because scientists have studied that more than the anti-predator things. It's also got major modulators. It was one of the-- in terms of evolution, it was an early output of the corpus striatum, a major one, that came into the midbrain and affects the colliculus.

OK, we're going to talk about the-- we'll look at this again, the origins of these two pathways. If you look here, and this is all the superior colliculus. All of these upper layers, it goes down to about where you see the arrow, seeing spinothalamic tract, OK? Those are the deeper layers.

And some anatomists actually include at least the upper part of the central gray as part of the superior colliculus. But most anatomists not do that. They are connected, though. Central gray is more of the limbic system structure, but it does influence the deeper layers of the colliculus.

What I'm showing here is that there are large neurons in the colliculus-- not at the very bottom of it but very large neurons that give rise to output fibers that affect head and eye movements. And they do that by way of a couple of pathways. The major one for orienting movements is a cross pathway called the tectospinal tract.

You can see the axon going here entering a tract that travels immediately on the opposite side. There are other pathways that descend for control of other kinds of movements. The other pathway I'm pointing out is a very different kind of output, one concerned with limb movements.

This is the red nucleus because in a human brain dissection, it has a red pigment. And there's two structures in the midbrain that have some pigment in human brain-- the one down here, the substantia nigra, related to the corpus striatum, and the red nucleus. And it has-- the red nucleus has an axon that also crosses over, goes to a more lateral position, and descends through the lateral hindbrain, reaches the spinal cord.

OK let's just go through some species comparisons that'll help you remember the midbrain. That's really an exercise in topology because these are huge size distortions. But all the basic structures are there in these different species.

But the outline of the midbrain just looks very different. Here's a human. How's that different from that little rodent we're looking at? Here's an outline based more on rodent that's commonly used in anatomy.

Just look at the relative size of these fibers at the base here, the cerebral peduncle. These are axons coming from the forebrain mostly from the neocortex. Going for the spinal cord and also to the pontine gray to influence the cerebellum.

OK, now look at the human. The obvious thing here is this huge cerebral peduncle. And that's going to be true in any species with a large neocortex. Anything related to the neocortex is going to be big too.

And these are axons coming from the cortex, contains all of the corticospinal axons, axons from cortex to hindbrain, as well axons from cortex to the pons, which is pre-cerebellar. The superior colliculus up here looks relatively small. It's not really smaller than it is in a rodent. It's actually a little bigger in absolute terms.

The red nucleus is in a fibrous stain. It would be much clearer in a cell stain, but it's right here. And you see a lot of axons. Those are axons actually coming from a nucleus right here.

Again, the cells aren't staying here, but we see their axons. It's the oculomotor nucleus, and their axons go right out at the base here. That's the rostral-most group of motor neurons going to striated muscles, controlling the lateral rectus muscle of the eyes.

This is actual size down here. But of course, that would be true only in the original printed version that I got this from. OK, now I have not drawn these to relative scale, but I've shown a rodent like a hamster or a rat.

This would be most like the hamster, human, and treeshrew. We've already pointed out the huge cerebral peduncle of humans. Look at the colliculus now.

In relative terms, if you just look at the upper half of the midbrain, human is not so different from rodent. But look at the treeshrew and the squirrel would be similar. The distortion here is this huge development of the optic tectum, the visual layers of the midbrain tectum, whereas in relative terms the cerebral peduncle is much smaller.

It's actually not smaller than in the rodent. It's just the way I've drawn it here. This midbrain would be a lot bigger than this midbrain here.

OK, now let's talk about the long axons going through. We talked about that the behind brain. We should be able to find all these things.

I put pontine in red there because on your handout, it probably says corticospinal, right? I think it was missed-- I did a correction there. Usually, when I put something in red, that's what it's for.

So we've already pointed out where those axons are in the cerebral peduncle. So those are long axons going through the midbrain. So now let's find the spinothalamic tract.

Let's find the medial meniscus, trigeminal meniscus, the ascending fibers There's the spinothalamic tract. In fact, many of those axons come in and terminate in the superior colliculus. But many of them go to central to it on their way into the lateral part of the ventral posterior nucleus, whereas the medial meniscus fibers here are further down or medially, and the most medial ones there would be trigeminal lemniscus, representing the face.

And I summarized that here. They're going to terminate most medially in the ventral nucleus. OK.

So we went rushing through the midbrain because we really want to get to the forebrain. And to try to help you to simplify a little bit, I'm pointing out here that we can think of both midbrain and forebrain in terms of two types of regions, one somatic and one limbic.

Somatic means connected to somatic sensory and motor systems. And by somatic sensory systems, I mean all the sensory systems except the ones coming from the viscera. So they include vision, audition, somatic sensation, except for visceral. Olfactory, we would include with limbic.

Connected to the autonomic nervous system and closely associated with the limbic forebrain-- basically, always associated with hypothalamus. So let's first look at the midbrain. And the limbic structures, then, are the central gray there except for the oculomotor nuclei there and then this area, which we call the ventral tegmental area where the dopamine containing neurons that are always activated when we feel pleasure, when we get rewarded.

Those are the limbic regions in the midbrain. And they're closely connected with this part of the forebrain, the hypothalamus. I just color it on one side there. They're also connected with the epithalamus up here.

Those are the limbic structures-- so the 'tween brain, OK? So now we're entering the forebrain. And that is the continuity I want you to understand. The continuity between the limbic midbrain area, named that way by [INAUDIBLE] after he had studied the connections, was able to extend the limbic system concept into the midbrain as well as in explaining how it gives an anatomical definition of limbic forebrain and brain structures.

So when we get into the far brain, we're going to go over the general picture subdivisions. We'll review several times how the hypothalamus and epithalamus are related to limbic structures. We just outlined those.

And the thalamus and subthalamus together are related to somatic sensory motor systems. And then I'm going to talk about the two major pathways coming out. We've already talked about one of them a lot, OK the corticospinal cortex to hindbrain. That's all called the lateral forebrain bundle.

And then there's a medial one related to the limbic system. So let's just take a look at all that. So here's our cross sections.

We've seen this figure a number of times before. Now we're at this rostral level, the level of end brain and 'tween brain. And you should get familiar with these cross sections, the general shape.

You see them enough, eventually you'll be able to try them in your sleep. I'm going to use red here commonly to mark the limbic system and blue for the somatic system. The hypothalamus in the diencephalon, or 'tween brain, and the epithalamus we can group with the hypothalamus, though we know most about the hypothalamus, is the area that gets visceral inputs.

It's connected with the limbic midbrain areas. And in the inbrain, the structures closely connected the hypothalamus we group together, and we call them the limbic system-- limbic system, OK? But it's really called limbic not because of that.

It's called limbic because of where it's located in the hemispheres. It's located at the limbus of the hemispheres, the fringes. Question.

**AUDIENCE:** [INAUDIBLE].

**GERALD SCHNEIDER:** Visceral inputs-- what are visceral inputs? Coming from the guts, OK? Coming from the intestinal tract, coming from other organs that we associate with the viscera, sexual organs, connected with gland tissue of various sorts of the endocrine system.

OK, so now the somatic part of the diencephalon, thalamus, and subthalamus. The somatic inputs from the lemniscal pathways-- we've followed mainly somatosensory so far into the ventral nucleus. But it also gets connections from the midbrain tectum and tegmentum. Tegmentum is somatic parts of the membrane, major inputs, probably in evolution appeared earlier than the more direct visual pathways to the diencephalon.

We had these camel's head, the connection from the midbrain tectum into the dorsal thalamus. And that was the route to the corpus striatum before there was much neocortex. So all I've done here is add to the diagram we looked at before.

But now I'm adding the somatic regions, including in the midbrain here, the whole what we call the midbrain reticular formation, which I've marked there. But then you should include the optic tectum. And also related to the somatic system is this structure, which gets output from the corpus striatum and has major connections to the thalamus, to the corpus striatum, and also to the membrane tectum. It's all part of the somatic system.

OK so now let's talk about the major outputs. These are the cross sections now of the end brain and 'tween brain that we're going to use. They're similar to cross-sections in rodents that are commonly used in anatomy, but it's also like embryonic human. Before the neocortex is grown so huge, you would have cross-sections that are not so dissimilar to this.

OK, so what we're going to talk about now is the lateral forebrain bundle and the medial forebrain bundle in the next few slides. First of all, the lateral forebrain bundle, these are the axons coming from neocortex, and here they are entering the cerebral peduncle. They've all come from the cortex which is out there, OK, surrounding there.

Remember, the hemispheres sort of balloon out if you imagine the neural tube like a balloon here, and it develops a couple of the weaknesses up anteriorly, and it balloons out. That's how the hemispheres form out of the rostral end, OK? You can see that right there.

Let's look in the upper left here. There you see the neural tube. And here you see it ballooning out, forming these two hemispheres. OK, so the lateral forebrain bundle are the axons coming out of the endbrain and going caudally.

Now there are axons going in the opposite direction too, and I show that to-- if you look at this neuron I'm coloring green, that would be axons going in the opposite direction. But the lateral forebrain bundles on the output side are all those corticospinal axons. And then the medial forebrain bundle is coming from the limbic end brain structures. And it's going through and connecting with the hypothalamus.

And it goes through the lateral hypothalamus on both sides, of course. That's called the medial forebrain bundle. And in your anatomical textbooks now, the term lateral forebrain bundle is not used very much. They always talk about the cerebral-- they use all these different terms that all mean the same group of fibers. It's very confusing.

The embryologists had the right idea. They classified them more broadly. Much easier to learn.

But the term medial forebrain bundle is still pretty commonly used. But even then, we mostly hear about the big bundle right there coming from the hippocampus, the fornix fibers. But the hippocampal fibers are just one of the many groups of fibers coming out of the limbic end brain structures coming down to the hypothalamus.

They all connect to hypothalamus, all these limbic end brain structures. And then there's some of them, the longer fibers, go right on into the midbrain, limbic midbrain areas-- central gray area and the ventral tegmental area. Very few of them go caudal to the midbrain.

It fits the pattern of the early shrew brain without neocortex. The midbrain was the link between the forebrain and the motor system controlled by the hindbrain and spinal cord. It's with the arrival of neocortex that the midbrain starts to be bypassed.

OK, so if we go just anterior, I'm showing here there are those accents of the medial forebrain bundle. And on the other side here, I'm showing you where they're coming from. They're coming from this cortex, which is olfactory cortex.

And they're entering that bundle, OK? They're also coming from those structures at the fringes of the hemisphere. And you'll find them at all levels of the hemisphere. You'll find the limbic cortex and also subcortical regions-- for example, this one.

Here's one from hippocampus. It's also entering the medial forebrain bundle. So both cortical and subcortical structures enter that.

There are some structures here in the ventral part of the corpus striatum we call the ventral striatum that also contribute to the medial forebrain bundle. The larger part of the striatum does what you're seeing here, sending fibers into the lateral forebrain bundle. But most of the little forebrain bundle is made up of axons like these coming from neocortex. And that's by far the bigger of these two bundles in the higher mammals because of the large size of the hemispheres.

I'm pointing out here some of where those things come from. Besides the pyramidal tract is the big one in human, but it also goes to the subthalamus, midbrain, reticular formation, optic tectum. Other-- also the auditory tectum.

So it goes to midbrain structures and thalamic structures in addition to the hindbrain and reticular-- and the spinal cord. Pyramidal tract always means axons going to spinal cord or hindbrain because pyramidal tract is named in the hindbrain level. When it's further up, it's got different names. So that's very confusing to students too.

So we'll go over that a little bit. But first of all, just the summary of these two major bundles-- lateral forebrain bundle, outputs of the corpus striatum, and then from the neocortex. So it starts in the neocortical white matter, and then it comes down through the corpus striatum, where we call it the internal capsule. And then it becomes cerebral peduncle, and then it becomes pyramidal tract.

So we'll look at a picture of that next. This is the summary of medial forebrain bundle coming from off the-- just as I showed in the picture-- olfactory cortex, limbic cortex, subcortical limbic system structures like the amygdala and basal forebrain. You'll encounter this in your dissection, especially the basal forebrain. Remember how the forebrain form.

So in this picture, we're still in hemispheres here. But when this becomes-- Using too small a pen here. OK, when this becomes joined, it'll be continuous across the bottom.

So there's no hemispheres there. That's basal forebrain. As you follow, basal forebrain caudally, you're in hypothalamus, OK?

So here you're looking-- in the upper left here, you're looking at the hemispheres. If I had cut that section a little further down, we wouldn't see hemispheres. We would just see the continuous neural tube below where the hemispheres have ballooned out.

That's the basal forebrain. I'm trying to give you some spatial idea of what the brain is like here. It'll become more clear to you when we see more cross sections.

And then-- so then it goes through lateral hypothalamic area and limbic midbrain areas as we pointed out. OK, now let's take another look at the lateral forebrain bundle. Here I've put it in orange, and I'm doing it this way to try to help you with something that's very confusing to students reading anatomy because they don't realize these are all the same group of axons.

It's all lateral forebrain bundle mostly coming from neocortex. And I'm showing if you just look here in the left, we're seeing them originate mostly in the hemispheres, also in the corpus striatum. It's sort of not a very fair way to represent corpus striatum, and it comes more as a bulging out of the neural tube at the further down.

But anyway, those are the two origins of those axons. And then they come through the internal capsule. And then they're along the side of the twin brain here. And that's where we start calling them cerebral peduncle.

We keep calling them, and here they are over here. Then they go through the midbrain, through the hindbrain as pyramidal tracts. Then they cross over the decussation of the pyramidal tract. Then they go through the lateral column in the cord.

OK, so here we are. Do it again. Here we are in this cross section of the end brain.

And there they are coming out of the neocortex, forming the white matter of the hemispheres. And then they come down through the corpus striatum. That's where we call them internal capsule, OK?

Internal capsule here. I'm sorry. I did this because I had numbered the sections starting A, B, A with the spinal cord, B, c and so forth going in that direction. I did that.

I should have put them in same order here. And here I started with the spinal cord. We're going to have to start at the bottom here. So in the end brain, we call them internal capsule. But first, it's the critical white matter, OK?

So there, it's in the cortical white matter. Then it becomes the internal capsule coming down through the corpus striatum. Now at this level, we're still seeing them as white matter of the hemisphere.

But to get down here, of course, they had to go through internal capsule. And they had to go-- the ones from the caudal hemisphere had to run forward and then out through the internal capsule in order to get into the cerebral peduncle.

So now here, we're all on the side of the twin brain. And all those axons are all on the side here. They're called cerebral peduncle, the brain's little feet.

And here at the base the midbrain-- remember, it's those fibers at the base of the midbrain that had become so huge in humans when we saw that cross-section in the midbrain. So here they are in the embryonic membrane. Still called cerebral peduncle there.

Then it goes through the pons, the rostral hindbrain level here. And what emerges from the pons, they're right there, the very bottom. And that's where they're called pyramidal tract because of the pyramidal shape in the cross section.

Same axons. Of course, there's fewer because we've lost a huge number of them that went to the pons because they're going to the cerebellum and a few of them in the midbrain too. But now we have left-- as we come out of the pons, we have left all the ones going to hindbrain and spinal cord.

OK, so the ones that don't terminate behind brain-- and a lot of times, it's just branches that terminate there-- they cross over, most of them. A few of them stay uncrossed depending on the human family you're in. Most of them cross over and all of us, and then they cross, in humans, in the lateral columns seen there in the embryonic spinal cord section.

So that's the lateral forebrain bundle. It's got so many anatomical terms we describe it with. But there's just because they give different words at different levels of the nervous system. And you're going to have to get used to that.

Anatomists get bored, you know? So we've got to think of these nice terms for everything. And sometimes we think of three or four terms for the same thing. We'll name them after the person that described them, and then we'll name them for what they look like and a few other-- and sometimes different anatomists give them different words.

OK, so we've already done this. But remember here, for the limbic regions in the twin brain, the medial forebrain bundle is lateral. But all of the hypothalamus is limbic system.

It's just that the long axons that we call medial forebrain bundle coming from the limbic end brain are traveling at the lateral part here. And some of them have come up here too. And this we did before too.

I'm just outlining the limbic areas here. And then here, I'm showing the entire limbic system as seen in this cross section of the embryonic end brain where the outputs collect here in the medial forebrain bundle. But they originate-- we come to the neocortex here and go to the very edges.

We come to the limbic system here. And we come to the limbic system here. so the neocortex is involved in both systems. What I want you to look at here-- I hate purple. Well, too late.

The neocortex-- I want to show you that it's involved in both systems. Nothing escapes the [INAUDIBLE] the neocortex in evolution. It was a big change.

And its outputs here go to limbic structures which then connect to hypothalamus, a few of them right down into the brain stem. The larger connections are to the striatum, first of all, which then has outputs to the brain stem and in humans even larger outputs into the thalamus and right back to neocortex.

But then the neocortex goes, remember, to every level of inner axis midbrain, hindbrain, and spinal cord. Now what that-- this is putting the emphasis on the larger part of the striatum, OK, related to the somatic system. In recent years, we found out that there's a ventral striatum too that's more related to the limbic system. It's very critical in habit formation.

Probably it's the most primitive part of the corpus stratum in evolution. In my view of evolution, it's evolved before the somatic structures did. It was really part of the olfactory output.

And of course, if habit formation is so critical, then we've got to have reward and punishment mechanisms involving roles of ascending pathways involving reward from taste and also punishment from pain systems. And we find those. Anatomists have outlined those kinds of connections.

So I don't expect you to learn all of this, but it's actually a very simplified summary picture now of how the neocortex is related to these two systems. And here we have simply added the ventral striatum. So all of this is subcortical striatum.

The ventral part of the striatum is related to the limbic system. The rest of it is related only to the somatic system. And then I'm pointing out here the note that here, the neocortex in its limbic type connections has no connections to brain stem and spinal cord.

They don't go directly. But for the somatic system, they do. Now they used to point out that the neocortex is very weakly related to the limbic system.

Now we know that there are more association connections than he knew about, and they're probably very important in our learning. And I've shown them here as interconnections within the end brain, within the end brain structures. A little bit to the twin brain, and I'm showing here a weak connection, a little dashed line here, of neocortex to hypothalamus.

Our orbital prefrontal cortex, the cortex just above your eyes, does have some connections to the hypothalamus. That's probably the only direct control we have over our basic instincts to switch suddenly to behavioral terms. But the other connections that I show here all can be found, and there are connections between ventral and dorsal striatum here that we know less about. If we knew more about them, we'd probably understand learning a lot better, OK?