PROFESSOR: All right, so we'll go through the second part of this class 23, and then we'll get started on the auditory system today.

Now, I had just shown this picture of a very early stage human, seven weeks after conception. And you can see, even though the brain is tiny, you can see how relatively advanced that forebrain is. It's got a huge amount of neocortex, in relative terms. The myelinated part there in the center is thalamus and corpus striatum, and then midbrain and hindbrain behind it. Of course, the cerebellum there at the back is part of hindbrain.

And then this just shows the brain is even relatively smaller than that one. These are done to scale. There is the full-term brain here, the last one, so it's even smaller than that. And yet even at that stage, the human brain is a pretty advanced mammalian brain.

Now, here's that human brain of the mature human, and we have monkey, cat, and rat. So what's happened between these brains that were smooth like that, and the brains with all the gyri and sulci? And one of the most obvious things, besides the fact that it's got all the gyri and the sulci, is the information of that temporal lobe.

So if we take an early brain, and say that this cortex here has expanded relatively more than the rest. And so here's what's happened, it's growing out this way. Now, of course there's no room there in the skull for it to keep growing downward like that, so what happens is it folds up like that.

So it's this part here that's growing relatively more than the rest. It's not that the rest isn't growing, but in relative terms, that posterior part of the hemisphere expands and forms the temporal lobe. So in the rat, this is temporal cortex down here this area, and there isn't very much of it. And we'll see a little more of that in a minute.

So now let's talk about a little bit of the consequences of that. One is changes in the

white matter. We talk about Meyer's Loop which is something that happens, a distortion of the optic radiations that we talked about before. The pathway from genicular bodies up to the visual cortex.

So let's look here at one of Naidu's picture's where he's done a dissection showing the surface of the internal capsule. And in this one, he's shown in the background there-- the corpus callosum-- and he's shown the caudate nucleus here behind the internal capsule fibers. And then back here he's shown the hippocampus.

Now, if we go back to this one I can show you where that hippocampus is in the rat, the smaller brains. It's an in-folding of the dorsal and posterior part of the hemisphere. That's where the hippocampus is located.

Well, when the temporal lobe grows, this shifts down, too, see? So the hippocampus then, in the monkey you will find there, and in the human it's way underneath there in that kind of position. So we call this dorsal hippocampus, this ventral hippocampus. And we'll be talking more about that as we go into the forebrain.

Here now it's taken away those other structures just to show what's happened with the fibers of the internal capsule. And what's happened there is that the visual radiations going up to the visual cortex back here have been pulled into the temporal lobe. And these fibers that get pulled most anteriorally, the part that we call the Meyer's Loop, represent the upper visual fields.

So a person with a temporal lobe injury, a lesion-- say, a gunshot wound or a stroke that affected that part of the temporal lobe-- can suffer an upper visual field defect. Not because of the temporal lobe damage, but because of the damage to the fibers that go up here to the virtual cortex. The upper visual field is located in the lower part of the visual cortex.

Now, what's happening when that whole expansion that we've just been talking about is occurring? One of the things that's happened in the visual system is not just the formation of more and more multi-modal association areas, but more and more visual representations. More and more representations of the retina.

We saw this picture once before, the one on the right here, of these many different representations of the retina in the owl monkey brain. And this is a picture from John Allman where he's just summarizing the mapping of one of those areas, this area here, Area M.

So here he's showing it in more of a close-up of the owl monkey brain. And here he's showing a visual field with the receptive fields mapped for a series of penetrations in Area M. And that's the method used for mapping out these areas.

Well, as the brain has grown in the primates especially, if you plot neocortical surface area-- this is the linear scale down here. Neocortical surface area there on the abscissa, and the number of separate representations on the organ, you can see what's happened. As the brain gets bigger and bigger, you get more and more representations. Now it's true there aren't so many animals up here, but there are enough. Here he's done it in log log scales, and you can see it's a fairly innate method of plotting, it's a fairly linear function.

OK, now where would the human be? This is the rhesus monkey, right up here, the macaque. Humans would be up here, so we would predict that humans should have just a few more. And functional magnetic resonance imaging has been done on humans, but they've not really tried to map out all the visual areas.

Allman, in 2000, put one of the pictures done here in Boston by Roger Tootell that revealed the similarity between human and monkey and mapping, and just a few of the visual field representations near V1. There you see V1, V2, V4, and three other areas, he's got area under T there as well.

OK, now here I have this picture from Striedter, an owl monkey. And then this is also the owl monkey, they've just flattened it out to see more of the buried cortex, the cortex buried in the cell side. And then here you have the rat and hedgehog. Hedgehog is relatively smaller neocortex than the rat.

And you can see in the hedgehog there's not much cortex left after you've mapped out V1, V2, some meta sensory areas, one and two, and the motor cortex, there's

really not a whole lot. OK, this is all olfactory down here.

The rat has a little more left over. Well, what's in those areas? Well, it turns out that the rat does have several more representations of the visual field, there's at least four in the rat. And remember the curve here, because this hemisphere is relatively small, he's going to be way down here near the shrew, if the rat fits that kind of scale.

And this was a study done by Rosa in 1999, who [? quip ?] on a cladogram. a depiction of the areas, because she wanted to show which are the really old ones. It turns out that even in the simplest marsupials, you have a V1 and V2. But in the animal that she was using, they couldn't find [? MT, ?] there wasn't much visual cortex beyond V1 and V2.

In all the others, all the placental mammals, they were able to find at least three-- V1, V2, and MT. Plus varying numbers of others, basically depending on how big the cortex was. The bigger it were, the more representations they had.

So now let's talk about the transcortical connections. We know that V1, for example, has transcortical connections, as well as connections back to the brain stem. It projects the secondary optic radiations go from visual area one-- as well as other visual areas-- back to the thalamus.

They also go a little further, to the midbrain. But then they also go to the V2, and one or two other visual areas. But always nearby areas, they're not long connections. The areas with the long connections we call association [INAUDIBLE].

And I'm going to talk about the projections that go from visual cortex involving some long connections where we know something about important functions. For example, starting with V1, the striate cortex, there are connections to the pre-striate area, it's also called the visual belt cortex. It's a belt of cortex around the first visual area. They talk about auditory belt cortex as well, somatosensory belt of the cortex.

OK, so from this pre-striate area, meaning in front of the striate, you have longer connections originating. So this we call an association area, pre-striate areas. And

it's more than one area, there's several representations of the visual field, it's still unimodal though.

It then projects to a multimodal area. It actually projects to a number of them, I'm only showing one of them. I'm showing the one that goes to the frontal lobes. It goes right past the motor cortex into a pre-motor area called Area 8, and that's the frontal eye fields.

The ventral pre-motor area's another one that has to do with reaching movements that we think is unique to primates. Area 8 you find even in rodents, it controls eye movements. Here's another one that goes from a striate area to the same pre-striate areas. But they also have this more ventral connection that reaches the input temporal cortex.

Now it's still unimodal, the association area here, and it has a particular role in object identification, and we know that from lesion studies. We may not understand the details of object vision from the physiological studies. And Jim DiCarlo spends a lot of time working on that problem here in this department.

And we've had a few talks on it recently. It's a very complicated business. And the details of how object vision occurs, and I think the computational models are just beginning now to be integrated a little better with those studies.

But anyway, lesions within pretemporal cortex wipe out the animal's ability to discriminate complicated patterns and distinguish them. Even though he still has good reaching, the different parts of the visual field, he has his basic visual processes intact.

Humans depend on this kind of pathway, for example, for distinguishing faces of people, and monkeys do the same. We know humans have a particular part of the cortex near the hippocampus, the underside of the [UNINTELLIGIBLE] It's just around the bend there from the pretemporal cortex, involved in the [INAUDIBLE] department face area.

Well, if we look at the outputs then of the frontal eye fields and then we'll do it for the

intertemporal cortex, you see some very clear differences that correspond to their functions. I know this looks a little bit like a bowl of spaghetti, which anatomical diagrams tend to do, but I'm just trying to pick up some principles. And I've noted here that the striate area itself, and these pre-striate areas, have overlapping connections.

This is part of the secondary visual radiations, projections there to the pretectal area and the colliculus, for example. Especially the colliculus, because that's involved in orienting [INAUDIBLE]. Well, if you look at the projections of frontal eye fields, it also projects to those areas involved in orienting, but then just like the striate area, it also projects to corpus striatum, also projects to the subthalamus and the ventral [UNINTELLIGIBLE]

Now to be sure, I've selected the connections-- there are more-- but these are major connections through these areas. Now if you look at the intertemporal cortex, you see something different. Only from the intertemporal, not from Area 8, do you see connections to the amygdala, part of the limbic system in the temporal lobe. I call it a caudal output of the ventral striatum there, a part of the striatum that's pushed back into the temporal lobe.

And the amygdala has strong connections to hypothalamus which defines it as a limbic system area. It also projects directly to ventral pre-frontal areas which then connects to the ventral striatum as well as to the hypothalamus. So very different kinds of projections. And it's the outputs of structures that give you the best clues to their function.

Let's just talk a little bit in theoretical terms about the nature of all these interconnections. If everything were connected to everything else, then if we had just 16 neurons shown in the black there, we'd need 248 axons to get proportional connectivity. Every one of these is connected to every other one. And you don't have to look at these as neurons, you could look at them as columns in the cortex, for example.

Or we could just maintain absolute connectivity, we'll just connect to the nearby

units, cells or columns. And then, of course, we need a lot fewer axons. So what does the brain do? Well, it's a lot closer to this.

If you plot neocortical neuron density number and the amount of white matter-- here's the amount of white matter-- you'll see that as the amount of gray matter goes up in volume, the amount of white matter goes up only a little faster. It's certainly not growing this way, from 12 to 56 to 240. It's not growing like that, white matter is not changing like that. It's changing more like this, and yet we know we have those long connections. So what we call that kind of architecture is small world architecture.

Here you have regular connections to nearby cells that would be absolute connectivity, just as the one on the bottom here. Here you have the connections, not in any regular fashion, they just connect randomly. But we're not going to let axons increase so rapidly, so we're just going to connect them randomly. Or we're going to maintain the nearby connections, they connect to all the nearby units, but then we'll just add randomly a few longer connections. And that we call small world architecture.

And they've plotted the amount of clustering which is what you have in regular connectivity. The moment of separation here plotted as a function of degree of randomness. And you can see that you can reduce the separation in terms of numbers of synapses very markedly without going all the way to complete randomness, and that's what the brain has done.

If you take actual data from the visual system where we have the most information, and take all these different areas in the rhesus monkey-- 30 different areas-- and look at their connections, it fits the predictions of the small world architecture. That's enough said, we're not going to go into more detail than that. But it's a very efficient way to prevent growth of too many axons.

I can say this though, that in the more intelligent animals with a lot more association areas with these long connections, the amount of white matter has grown more than the amount of gray matter, and it's very obvious when you study the brain. But it

doesn't grow at all in the way proportional connectivity would predict.

So now we have time to get at least maybe halfway through the auditory system. Actually, there's two auditory system classes. There's only one chapter, but I combined them when I wrote the book. It took me a lot of editing, and I did eliminate a few things that you'll see.

I may decide later to add some of those back in, but it's always a tussle when you're teaching neuroanatomy, how much you're going to throw at people. Because it just gets overwhelming if you throw too much, too fast.

So auditory system arose as one of the sensory systems of what we call the dorsal lateral placodes. Remember what placodes are? Thickening of the epithelium in the head region that gave rise to primary sensory neurons. So it was one of those systems.

Then I want to ask why it evolved the way it did. Two major kinds of functions. Keeping the animal alive by anti-predator and defensive behaviors, and then major impetus and evolution of the auditory system especially was to improve predation.

And then we're going to look at some detail of the cochlear nuclei and structures that it's connected with. We'll talk about transduction and initial coding in that pathway, and the various channels of conduction. One of my diagrams, I admit, is a little too complex there. But we'll get to that, and I'll go through it with you carefully.

And then two functions that arose as probably the emphasis was on the predatory animals evolved two clearly different ascending pathways. One more involved in localization, the other more involved in pattern detection, which in the auditory system means temporal patterns. And we'll say just a little bit about animals with specialized auditory systems, specialized for echo-location, bird song, or of course, speech in humans.

So the dorsal lateral placodes, they gave rise to multiple sensory cranial nerves, at least eight of them. The sensory categories, besides the eighth nerve system that

we're familiar with for mammals-- auditory and vestibular components of the eighth nerve. It's present in all vertebrate groups.

We have the mechanosensory and electrosensory lateral line receptors distributed in a line along the side of the animal. We find lateral line systems present in the earliest vertebrates. It's absent in terrestrial vertebrates altogether. The electrosensory lateral line system's present in fewer species, they're all aquatic species.

And I'm pointing out here that the lateral line receptors are innervated by up to six separate cranial nerves. We only have one cranial nerve of this system of placodes combined auditory and vestibular nerve. The two branches of the inter-cranial nerve. So now here's a much simplified diagram of the auditory pathways to the endbrain.

Start here in the peripheral ganglia. We call it the spiral ganglia, the eighth nerve. They're bipolar neurons embedded in fibers that run between the inner ear structures and the hindbrain. They reach the hindbrain secondary sensory nuclei which then project directly to the midbrain. But they also project to other cell groups, several of them, in the more ventral part of the hindbrain. So I'm calling those tertiary sensory nuclei.

Both of these then project to the midbrain. And there are projections. They were discovered first in large primates directly from the cochlear nuclei, right to the valves. That would be more like the visual system, the retina to tectum. And retina to thalamus, and from there to the cortex. Because, of course, the thalamic cell groups project to the endbrain. And endbrain structures here include both the auditory cortex and the lateral nucleus of the amygdala.

I've given names here of the midbrain structures. The main one that we talk about the most is the inferior colliculus. If we're not dealing with mammals it's called something else, I've written it there, the torus and the circularis.

And there's other nuclei just below the inferior colliculus. You can think of them as

extra cell groups as part of that system, and just call that the nuclei of that fiber bundle which is called the lateral [? omniscus. ?] So a very simple way to depict what can very easily seem like a pretty complex system.

So why did it evolve as it did? Did it start with anti-predator and defensive behavior?

My favorite anti-predator behavior is shown by a little insect, the moth. When it picks up the cries of a hunting bat, it totally changes its behavior. It dives, and goes very rapidly right into the grass. It's its only way of escaping that bat. Because as long as it keeps flying, the bat's going to catch it. The bat's got very advanced sonar, and can localize them very quickly and catch them.

So that's how the moths have evolved. This particular auditory-triggered anti-predator behavior. And hindbrain circuits for invertebrates, it's been given pretty high priority in evolution.

You take a look at fish and tadpole, we find huge cells that originate in the hindbrain. They get sensory inputs of various sorts. They trigger rapid escape-- the moth, in their cells have very large actions. They descend and trigger the contractions of the body that turn the animal away from the predator.

And we know that amphibian hearing can very rapidly reach the hindbrain. You don't need forebrain, you don't even need midbrain to trigger some of these behaviors. It's a pretty primitive aspect of the auditory system. And these animals don't have the kind of hearing that mammals have at all, but they can detect these vibrations indicating a predator.

We just take a few mammalian examples. There, my favorite is the kangaroo rat, the way it escapes from a rattlesnake attack. How many of you know how the kangaroo rat escapes from a rattlesnake? You might remember.

Remember, the little kangaroo rat hears the rattle. If he's hearing the rattle, he knows he's already within attack range of that rattlesnake very likely. So what does the kangaroo rat do? He doesn't go running away. Because if he starts to run, the rattlesnake attack is very swift, he would probably get killed.

So what does he do? He freezes. He sits there. And then the rattlesnake launches its attack. The open mouth-- let's say this is open mouth of the snake, here's the kangaroo rat. Here comes the rushing movement of the rattlesnake. This movement causes a slight noise because of the air. I mean, it seems like impossible because I think we would have trouble hearing it, but the kangaroo rat is specialized to hear it.

That sound triggers a leap of the kangaroo rat. He leaps up in air, he goes [SNAPS] there the rattlesnake now missing him. The kangaroo rat leaps backwards, does a somersault in the air, lands and runs away. It almost always works, so that's kept the kangaroo rats alive. A nice auditory-triggered escape behavior.

Hamsters respond to novel sounds. I've kept hamsters in semi-natural environments and observed this. Any novel sound-- they've just emerged from their tunnels, and they're starting to forage-- will trigger an alerting.

When they first hear a novel sound, if they're still near their tunnel, you won't even see the details of the movement unless you're filming at high speed. Because hamsters don't seem to move very fast if we keep them as pets, but in fact, in this situation they can move very fast. They're like that, they're in their tunnel. They flee to their tunnel.

So the localization that the hamster has to do isn't localization of the predator, it's localization of his escape route. And how is he doing that? Visually. He needs audition to trigger the fixed action pattern, but then it's guided by his vision. Many small mammals have responses of various sorts like that that have evolved to keep them safe.

We know that rats have an aversion to loud noises. I'm going to show you some information from experiments that are done on the brain mechanisms to show you that, in fact, again does not depend on the forebrain at all. And then we'll talk about learned fear, which does depend on the forebrain. The aversiveness of noise that involves the limbic system.

If you start making lesions of the auditory system, you can ablate this major auditory

structure of the midbrain, the inferior colliculus, the entire auditory cortex. So he's got no audition endbrain at all anymore. You ablate the inferior colliculus, arbitrary intensity thresholds aren't affected. He can still tell the difference of one intensity from another.

If you have a situation where he's doing bar pressing and all that, you can test for this. You can train them to press a lever to turn off the noise if he doesn't like it. And they readily learn to turn it off when it gets too loud. And they don't lose it by ablating the inferior colliculus. If you add the superior colliculus to it, you still don't lose it. Those rats can still discriminate different intensities of sound. If you just have them bar pressing for food, you can test that.

But if the lesion goes more ventrally, and includes the ventral part of the central gray area-- also called the periaqueductal gray, depending on which book you're reading. Central grey area, CGA, is the most common designation. But if you ablate that-- of course, you can't avoid getting a little of the adjacent reticular formation-- then you lose their aversion to loud noises. Even though they can still detect sounds just as well, you've preserved their auditory thresholds. You've eliminated the aversiveness of noise by such a midbrain lesion.

Here's a picture I've used a few times of the midbrain. These are the limbic midbrain areas, the areas closely connected to hypothalamus. This is the central gray around the third ventricle there, I've just marked it in the red.

And here is from a photograph, I've taken a photograph here. I had some damage on the right side I've eliminated here. I want to show here's the superior colliculus of the hamster, a relatively large structure. Here's the aqueduct, the ventricle, going through the midbrain. And it's this slightly darker stained area around the ventricle, you can see the border there very clearly.

This is the third nerve nucleus controlling eye muscles down here. So the central gray is like that, surrounding the ventricle. It's when you make the lesion in the ventral part here which they'll which lose the aversiveness of noise.

We can just say a little bit about learned fear. It's often used in lab studies of learning. There's a special role of a pathway to the amygdala in the endbrain. In two different groups-- I've listed them for you if you're interested in that. LeDoux and Weinberger, they've both studied that, they're both called discoverers of this particular kind of learning.

It depends on the particular pathways to the endbrain. And I've shown you there are pathways from the medial geniculate body that gets that nucleus and cells just surrounding it to get the auditory input of the thalamus. And they project up to the auditory regions of the endbrain.

And what I'm showing here is, if you look at the opossum, the hedgehog and the tree shrew-- and the tree shrew is by no means an advanced mammal in the sense that monkeys and humans are, and apes. All of them have a projection to the lateral amygdala, as well as the neocortex.

Now, I didn't say much about projections to the amygdala when I talked about the visual system. They're not as well known, but I checked and found that yes, there are cells in the lateral poster nucleus that we talked about that project not just to the cortex, but they also project to the amygdala. The lateral nucleus amygdala gets quite a bit of input from the thalus. But the auditory system is more developed.

In fact, in the opossum I've just sketched in there, here's the thalamus and where they put the injections of a tracer. And I've shown in blue here how the axons came out, and then went forward, and then out laterally through the internal capsule. And they reach the amygdala and the neocortex. And in the opossum, the amygdala projection's actually larger than the neocortical projection.

In the hedgehog, the neocortical projection's a little bit larger. In the tree shrew, the neocortical projection is a lot larger. And the rat is like that, but it does have a direct projection to the amygdala. And it's that projection to the amygdala that's involved in learned fear to auditory sounds.

You can train an animal to be afraid of noise. How do you do that? Well, you put

them in a shuttle box where you can shock their feet, and you give a certain sound, and they have to run to the other side of the shuttle box. And to learn that, to learn to be afraid when the certain sound appears like that, they need this projection to the amygdala. Actually, that's a little bit too strong a statement, they can still learn something. But this seems to be the most important pathway, the one directly to the amygdala.

So, next time we're going to talk about the things that were more important to the predators. Needing to identify prey animals, and to localize them in order to be able to grab them.