GERALD SCHNEIDER: This is class 31, which is listed on the syllabus for today's date. I'm sticking with the numbers on the syllabus-- we took one class out of order, the one Neville gave, that was class 29.

OK, at the end of the last hour, we were talking about the Kluver-Bucy syndrome, due to large temporal lobe removals in monkeys. And I said that the visual parts of that syndrome were due to the inferior temporal neocortex, the inferior convolution of the temporal lobe in the monkey. And if you make lesions of just that area, just inferior temporal neocortex, you get only visual effects.

If you don't go too deep, that is. If you go very deep, you might get some of the optic radiations coming from the geniculate body and cause an upper field defect. But otherwise, you don't get field defects-- that is, don't get a scotoma-- you don't get a blind area.

But they have problems. They have problems with the more complicated shapes and patterns.

Now, that area gets its inputs, visual inputs, in three different ways. And this is really true for most cortical areas. OK, they get transcortical input. In this case, it's coming from the striate cortex, but not directly-- it goes from striate to the juxtrastriate areas, areas near striate cortex, which are also association areas, the secondary areas. And then it goes from there to these tertiary areas, like inferior temporal cortex.

And we think that's the main way-- the main visual inputs come that way. But there's also subcortical inputs, it's connected to this, the lateral thalamus-- the part of the lateral thalamus that's become very enlarged in the higher primates. It's so big, it looks like a big pillow in the back of the thalamus-- we call it the pulvinar, which is a word that means pillow.

The pulvinar nucleus of the thalamus. And the pulvinar does get some input from the superior colliculus. So it does get some visual input that we think that parts of it may not get this kind of extrinsic input at all. It might get it only from the cortex.

Then, in addition, there's a third kind of input that comes from the opposite side of the brain. Now, why would it need that? Well, there's multiple reasons why you might want to talk-- one side of the brain might want to talk to the other part. Maybe sometimes, your right hand doesn't know what your left hand is doing, and it's literally true in some cases.

But usually, because of inputs across the corpus callosum, there is communication between the two sides. And in this case, there are receptive fields if you record. From the neurons in the temporal cortex, you find receptive fields that are not limited to just one half of the visual field.

So if they're not limited to the side, the visual field half of the striate cortex that's providing their input, and the only way they could get the input would be from the opposite side. And that's what happens-- the receptive fields generally include the fovea, and they're very large.

Those inputs, also some of them go through the anterior commissure, which is just like the corpus callosum, except that it connects olfactory areas in addition, but it connects the temporal lobes on the two sides.

Now, besides these very large receptive fields include the fovea, they also have very interesting response properties that correspond to the behavioral findings of the lesions. They respond best to very complex shapes-- I'm not going to go through all of them. I'd like to look at this textbook page. If you've not read that, take a look at this, I've listed it for you.

And they summarize some of the work on inferior temporal cortex unit recording. Since that time, there have been other findings-- they find some units there that will respond specifically to monkey faces or to monkey hands.

What I want to do is focus now on the lesion effects, because this is a very important type of study that applies to humans, OK? I want you to think about this-- this is a series of three lesions. I make a striate cortex lesion on one side, what would that do, by itself? Saying to make a lesion of the left striate cortex-- what would happen to the monkey?

Big scotoma, right? Big blind area. Where? Right half the visual field. The would go right through the fixation point, which would be the center of the fovea and the retina.

And then they make an inferior temporal cortex lesion on the opposite side. What does that do? Well, actually, it doesn't do very much-- these monkeys behave pretty well. Unless they make a third lesion, posterior part of the corpus callosum. Then suddenly, the monkey acts like he's got a bilateral inferior temporal cortex lesion.

So what's going on? You see, we're disconnecting the visual cortex from the inferior temporal cortex. Let's just look at that.

Here's the basic anatomy of transcortical connections that you need to know to understand what I've just said. So in the back here, there, you see the dot, that's striate cortex. A lot of striate cortex is exposed on the surface of the monkey brain. In human, very little-- most of it's buried in [? this whole side. ?]

And that cortex connects to adjoining cortex. It connects to this belt of cortex-- we call the juxtastriate areas. And that's been known for a long time, but now we also know that there are actually multiple representations of the visual world in these adjoining cortical areas.

Well, this is meant to represent the inferior temporal cortex, and it gets its inputs from this belt of cortex around area 17. And then, the callosal connections go between-- mostly between the juxtastriate areas. Now, there are some inferior temporal cortex connections, mostly through the anterior commissure, so coming over there.

But the main one is the one between these areas. So now here are those lesions. Lesion one, first lesion, striate cortex on one side. And these are actual studies-- that's funny, maybe I put it in later. I was going to tell you who did this.

These are studies of Mischkin-- he's an investigator, very well known investigator at the National Institutes of Health in Washington, at the laboratories they have. There OK, so his group made lesions of the striate on one side, and that caused the hemianopia. We call it lack of vision in one half the visual field.

And then he made the inferior temporal cortex lesion on the opposite side. But you can see here, why didn't the animal show much defect there? Because input coming into the right striate cortex can still get to the opposite inferior temporal cortex. But see, most of it is going to go across the callosum there, the posture into the callosum.

Knowing that anatomy, then, he made a third lesion just severing the posterior part of the corpus callosum. And that was the lesion that caused the drastic defects.

Now, I want you to think about humans. Pretend that that's a human brain. What do we have in the left hemisphere of the temporal lobe of the human brain that's different from the right hemisphere? Speech areas, right? In order to understand written or spoken language, humans need this cortex-- the temporal lobe association cortex, OK, in this region.

OK, now let's say we have a person that has this kind of lesion. There was a patient of Norman Geshman's, a neurologist, a very well-known neurologist in Boston-- he's not alive anymore, but he was the first modern neurologist, behavioral neurologist, to make clear the nature of disconnection syndromes. And I'm going to describe now a disconnection syndrome in humans.

OK, a person that had an infarct-- a vascular lesion-- that destroyed the visual cortex on the left, but because of the distribution of the artery that was blocked, she also suffered-- the lesion spread to the caudal end or splenium of the corpus callosum, OK. So that was her lesion.

She could not read at all after this lesion. Now, why? She still got her right visual cortex, she's got her right temporal lobe and the connections to it. The problem was, that there was no way for the information to get from striate cortex now to the speech system in the left hemisphere. So she had a disconnection between the mechanisms of speech and her vision.

So you see a human being can be literally carved into parts with brain damage. It's best known in the case of callosal split brain people that have the entire callosal section. But this was the first case in modern times of a clear effect of the corpus callosum.

If you show her a word, she could not write it with the right hand, but she could with the left. We have a neurologist here in the front row, so OK. Very good question.

OK, I am just going to mention to you here that there is another pathway-- let's draw that monkey hemisphere here. The one we had on the previous slide.

And here's striate cortex. There is another pathway that starts here in striate cortex, goes to these areas adjoining. And then, rather than going into inferior temporal cortex like that, goes like this across to the prefrontal cortex in front of the central fissure into the prefrontal areas-- in an area we call the frontal eye fields. Because we know, if you stimulate there, you get eye movements.

And it's been found it's important for more than just eye movements. They found, now you'll see in the books, they talk about the ventral stream going from visual cortex into the temporal lobe, and the dorsal stream, going into the frontal cortex directly. And they find that pattern and shape discriminations are influenced by the ventral stream-- the ability for a person or a monkey to identify objects-- which we know the striate cortex is very important for.

But to do that, you need your association areas, as well. Whereas, this more dorsal pathway is important in spatial orientation.

So when we see larger objects, and judge their orientation, their location, and so forth, we're using the dorsal pathway. Now, that seems strange, doesn't it? We can identify things without being able to make out their spatial arrangement. But that's exactly how vision is divided up.

So that's how the work that was started with the hamster work, and then later rat work, with subcortical and cortical lesions, it led to this division of function within the human hemisphere.

All right, now, let's say a little more about the subcortical areas. Lesions of superior colliculus. I'll talk about the adult hamster and rat first. But then I'm going to say what happens when you make those lesions in babies, because the effects are not the same. And then we'll say a little bit at the end about a few other species.

Remember the two visual systems diagram-- I said that if you just undercut the colliculus or ablate it, you get this loss of visual orienting movements. They don't turn accurately anymore. You show them things that they want, because they're hungry, and they want to turn-- or they love sunflower seeds, they love sunflower seeds even if they're not hungry, why is that?

Because they're hamsters, they're hoarders. They put it in their cheek pouches and save it for later. That's one reason we like to work with hamsters. Don't have to make them hungry.

They just sit there when you show them things, and you would swear they're blind. And when I first saw this, I thought they were blind. I thought, gosh, they discovered an animal that doesn't fit the classic descriptions of Kluver and Lashley at all, because he's blind without a midbrain-- without the midbrain tectum. He's got his visual cortex, you see.

This is the animals with just the colliculus lesion. But in fact, they do see patterns, they just can't orient to them. You say, well, how can you tell? He can't tell you, the hamster can't talk to you. So how do you know he can see patterns?

Well, we can give him a problem where he's put on a little apparatus and he has to approach two doorways. And one doorway's unlocked and one door was locked. And we always locked the doorway with the vertical stripes. And leave the door open with the horizontal stripes. And then we varied the position trying to fool the animal, so you can't just learn to go right or left.

And these animals can solve that problem. But the way they do it is they don't sit back from them and make an orienting movement, and then go to the correct one. Instead, they always follow the same path, and they stop in front of each door and then make a choice, yes or no. And they go to the next door, yes or no.

When they're learning, sometimes they say no to both of them, and then they go all the way back to the start and start over again. Do it again. Whereas a normal animal is orienting from a distance.

And I noticed these things. And I knew they had problems with orienting. So as long as I counted it correct, or counted it wrong, only if they pushed on the wrong door-- actually pushed on it, not just if they approached it-- then they could do well. If I counted the errors differently, made them orient at a distance to the correct door, then they would fail.

So I found out that the response you require of an animal makes a huge difference in these tests. Just like the person-- if you require them to tell you in words what something is, but they've got a disconnection from their speech areas, they can't do it. But if you give them another kind of test, then they can do it. Use reaching movements that are connected to the visual areas.

Now, that's not always done. And modern neurologists still make that kind of mistake and they still misinterpret things if they don't realize that this kind of disconnection can occur. So what's happened here is that the orienting mechanisms are disconnected from the visual input.

So they can't orient. But they can solve the pattern of discrimination. And remember, the animals without the visual cortex are the opposite-- they can orient fine, but they can't solve pattern discrimination problems.

I found later that those lesions also caused the loss of anti-predator behavior. So these animals-- these little animals are preyed upon animals, and if there's a hawk overhead approaching the animal, they will orient-- usually, they freeze. That's their orienting movement, they freeze when they see that hawk.

And the hawk flies towards them anyway. When he's approaching, the stimulus is getting larger in his visual field, then they run like hell. And often, they'll run right towards the hawk. The reason is, the hawk will then overfly them and miss.

So that's anti-predator behavior, freezing and running. And that also is very dependent on the superior colliculus. And that was found in the hamsters first, and then also in rats. Most of these things have been found in both of those species.

OK, then, I got interested in early brain lesions because the literature on humans-- and there was some on a cat-- that showed that sometimes early lesions have much less effect. And this, I began to wonder, what sense did that make? If you can make the same lesion early in life, and it doesn't cause the same defects, maybe we're not thinking properly about what these structures do.

But I also knew that maybe something's changing in the brain after you make an early lesion. And I had begun working with Professor Vallenauto here at MIT learning neuroanatomy. I wanted to see if, in fact, we were changing the anatomy of the brain.

And that is what I found. I would make early lesions-- I would get some sparing of orienting movements. But then I found out there was a reason for that-- they developed connections that didn't exist in the normal animal.

Let me go through some of that with some pictures. On the left here is a picture of the adult hamster brain, it's still in the skull there. These are tear glands. Here's the olfactory bulbs in front, the right and left hemisphere.

Here, you see the midbrain not fully covered by the hemisphere. And there's the cerebellum and hindbrain.

Well, here's the brain of a newborn animal. Note that the hemispheres are much tinier, because a lot of their development is postnatal. Cellular migrations are still happening. Remember, we talked about migration in the ventricular layer, up to the cortical layers. And in development, that's still going on. There's a lot of development to do.

And here, the entire midbrain is exposed under a very thin bone-- I removed the bone here. Here, 2/3 of it is covered, 2/3 or more. Here it's exposed. And the cerebellum is hardly developed at all. Most of the development of the cerebellum is postnatal in these animals.

Well I learned that I could make a lesion of the superior colliculus here-- I could ablate it, in fact, soon after birth, just by applying heat to that curdled cartilage like skull. And I could destroy the underlying tissue with heat without ever opening the skull. So it's actually much easier to make lesions in the baby than it is in the adult.

I also made lesions of the visual cortex in the posterior part of the hemisphere up here.

OK, now this summarizes some of the things that were happening. Here on the left is a diagram of the optic tract, just showing a group of fibers here coming through the chiasm, terminating in the two geniculate bodies. Here's the dorsal geniculate that projects to the striate cortex. Here, it's going over the pretectal area, the longest axons are terminating in the superior colliculus.

I'm also showing that the superior colliculus projects to the lateral thalamus, and to the one part of the geniculate body-- actually, now we know it projects to both parts of the geniculate body, but more heavily in that ventral part.

OK, so now I remove the whole retinal terminal area in the colliculus-- just ablate it. So now what do the axons do? They grow in. They're actually still forming terminations at the time I do this.

What happens is that they regrow, but now their target area is missing. Some of them terminate there anyway-- they terminate in deeper layers. Not as many of them can terminate-- as many fewer terminations, but some of them do terminate there.

But they also sprout connections, new connections, back in the thalamus. In those mainly in the two areas that have lost their normal input from the colliculus. But this you would call collateral sprouting. Here, you would call it regeneration-- these axons have regrown, they've been severed by the early lesion. But you also get collateral sprouting.

OK, so now, we've got three abnormal terminations. Here they are-- here, here, and here. I found that this one here is the one that's important for orienting movements, the sparing of orienting movements.

Well, this is just what I got through telling you. And if we look at a section-- now I'm showing you a section of an animal where I did that lesion on only one side. So on the left here, you see what the normal hamster brain looks like in frontal section. Here's neocortex up here, there's the pial surface, here's the white matter down here-- there you see it over here. And pial surface here, the white matter here.

There's the ventricle, not as pretty-- don't really see a fluid space there, but there is a little fluid in it. Hippocampus would be beginning right there-- you don't see most of it in this section. OK, so now, here's the midbrain. There's the aqueduct, the ventricle of the midbrain. There's the central gray.

And here's the colliculus-- it goes all the way from the midline, clear over to here, the superficial layer. On the right, it's just missing-- you don't see a big scar, you don't see inflammatory reaction. It just looks like the animal has a congenital absence of the colliculus.

And that's characteristic of many early lesions that's been noted by some neuropathologist in humans, also. When they look at babies that have had some destruction real early, they'll show this lack of gliosis. That's more characteristic of older animals. In fact, when these lesions are made, these animals simply don't have the same kind of glial structures.

OK, so what I found was that there are optic tract axons coming in over the surface-- normally, they would be way up here, and they would be terminating in the superficial layers. There are some that terminate right here.

But if I've made the lesion on only one side, some of them actually sneak across the midline, and grow into the superficial layers on the wrong side. And I got very interested in that kind of connection.

Let me show you what these brain stems look like if we just do a dissection. This is a normal hamster brainstem, and let me explain it to you here. There's a millimeter grid there in the background-- give you an idea how big it is.

OK, so what's that up there? Olfactory bulbs. What's way at the [INAUDIBLE] [? limb ?] here? Behind the midbrain, it's all hindbrain. Well, I've removed the cerebellum.

Some of you remember your sheep brain, the sections, I pulled off the cerebellum there-- that's the cerebellum peduncle there. Here's the inferior colliculi, here's the superior colliculi. There's the optic tract-- I've adjusted the light here, so it shows the optic tract pretty well.

There's the medial ledge of it, the lateral edges out here. This is the medial geniculate body. OK, but where's the cortex? I pulled it off.

And the internal capsule fibers come up through this structure-- which is the corpus striatum. And you can see where I've broken them off there all along there, and there's little bundles all through here. And there's a little bit of cortex, prefrontal cortex that I've spared. This is the septal region here, part of the limbic system.

Now, let's see what happens if, at birth, I've applied heat to the right side here-- I've ablated that right tectum. Look over there. It's just missing. The colliculus on the left, you can see in my drawing there, too, has moved over a little bit past the midline, because there's a big gap there.

And you also see a bundle. Those are axons of the optic tract, not finding termination sites in the damaged region that have grown right to the wrong side, right over the midline to the wrong side.

As soon as I saw that, of course, I realized that that predicts-- if I was right about the colliculus being so important for orienting movements-- these guys should show some abnormal behavior. And I began testing for that, and they did. This spells out that prediction very clearly.

I've shown here the eyes, the optic nerve and tract. I've shown where the hemispheres would be, all the optic tract goes under the hemisphere. And then, I've just moved the tectum back a little bit, the roof of the midbrain, to show how the connections are made from eye to the tectum on the opposite-- mostly on the opposite side.

These animals have eyes that look 60 degrees out to the side, so there's not very much binocular overlap. There is a little. And they do have a small ipsilateral connection also, but it's pretty small.

So I'm showing here the main optic connections. The connection from the left eye goes to the right superior colliculus, primarily. And that colliculus has a descending cross pathway that causes turning to the left.

Now, there are some ipsilateral descending fibers, too-- primarily the ones concerned with the anti-predator behavior.

So here's the prediction now-- if we get a tract, if we take out an eye, and ablate the right tectum, I should be able to make this projection very large. I've removed all the competition now from the right eye. So now, the left eye is going to go to both collicula. And the fibers going to the wrong side here should be turning to the right, even though the eye here is looking at the left visual field.

So the ones-- axons that are crossing the midbrain, normally will terminate only a little bit of the medial side. But if I remove the eye that normally goes there, their competition is removed and they spread. You get that large, re-crossing connection.

Let's just-- I want to show what this actually looks like. This is an animal where I created that kind of connection in adulthood by getting regeneration-- it's exactly the same kind of thing.

I have rerun this three times-- I'll show it to you several times. Now, this is what's happening. There's the stimulus, there's a sunflower seed on that, actually, that they've learned. And he's got an eye, in this case, on the right-- you can do it on left or right. In this case, I have the right eye projecting to the wrong side.

So here's the stimulus. And if you watch carefully, you'll see that he's responding by turning to the left. And we run through it-- we repeated it a few times, so you can see it. See?

He's turning away from it instead of towards it. Now, he will not do that unless he's rewarded. He quickly loses that if he's never rewarded. So before I ever started this, I realized that I had to reward them no matter what they did. It was very hard to teach MIT students to do that.

But see, I wasn't trained at MIT, originally, so I was able to do it. I just made myself. I just had to put everything else out of my mind-- whenever this animal does, if it looks like a response, it's following the stimulus, I'm going to reward him.

He turned down, upside down, somersaults, anything, I'm going to reward it. And what happened was, they began making these movements. Initially, I saw-- I also saw animals that were not making the movements. But then, when there'd be some distractor, something to make them a little emotional, some strange sound out in the hallway, or something, then suddenly they would do this.

So then, I began rewarding it. And I was able to make it very strong. And then, I did it with control animals, too, and found out that they never do the same thing. You can teach a normal animal to turn in the wrong direction, but not like this. They will always make their first movement towards the stimulus.

And then, they learn. It's like they stop and say, oh, yeah, it's over there. I got to turn the wrong direction. But that's not what these guys are doing.

I can get rid of that only if I-- oops-- I can go back to the other-- back to the tablet here. I can't use that program to show the video clips, that's why I have to go to PowerPoint.

This shows an anatomical experiment where I've-- you see in the dark, this is a degeneration stain. Which you can also do this with NHRP tracing, or colored toxin tracing. In this case, this was an early study I did with regeneration. You see the missing colliculus on the right, it's dramatically reduced in size.

And you see a pretty large projection-- the dark things there, degenerating axon terminals. You also see axons crossing the midline there and going to the medial side. All-- if I looked at the projection of the opposite eye, the right eye, it went to here and just stopped short. It never went to the entire tectum, because there was a competition between the two eyes.

And then I found that if I simply remove that competition, this would spread-- I could get the whole colliculus on the wrong side to be innervated by the wrong eye. And I found that I could get rid of that abnormal behavior, by if I could open that skull and just make a little lesion of that mid-- that bundle that you saw in the picture. So I could do psycho surgery and correct the behavior.

Now, if you do this colliculus lesion in the cat or the monkey, the adult, you see some sparing of orienting movements, particularly in the central part of the field. But then it was discovered by Peter Shillers and company upstairs that if you add the lesion of the frontal eye fields-- remember that area that gets this trans-cortical connection, the dorsal stream-- of the dorsal stream going from striate to juxtastriate, to frontal eye fields.

If they had that in addition to the tectal lesion, they were much more severely deficient, showed little orienting at all. And that's true both the cat and the monkey.

It's been done also in these animals with very large superior colliculus-- tree shrew and frog, tree shrew and squirrel are the mammals that have the very large optic tectum or superior colliculus. And you do get rid of orienting to the small food objects.

But they discovered another thing-- and initially with frogs, and then later, there was a claim that it's true for the tree shrew, also-- that in fact, they can't orient to little objects in the field, but they will step around barriers. They had some ability to orient, as if these were controlled by a different system.

So this man, David Engel, working in Boston, did a very interesting experiment on that. He took some frogs, ablated the colliculus on one of the optic tectum-- they don't call it colliculus in the frog-- ablated the optic tectum on the right side. Well, the frog shows regeneration, unlike the mammal-- I had to do these lesions very early in the mammal to get this.

But he got the regenerating axons to grow to the wrong tectum. But he had not damaged the pretectal areas and [? thelamic ?] areas. He found that when they oriented towards a fly or a worm in the visual field, they turn in the wrong direction. But let's say we put a fence in front of them, here.

And here's the frog back here. And we're showing him a worm on a stick here, and we'll show it behind that barrier. Here's what he does-- he will sidestep, go over here accurately-- he knows which way to turn to get around that barrier. But when he orients towards the worm, he turns in the wrong direction.

So he's got two visual systems, too-- one for the barriers, stationary barriers, and one for the small stimuli, moving stimuli, that indicate food to him. And the claim was that the tree shrew could negotiate a maze where he had to respond to stationary doorways. He could find his way through the doorways, but he still couldn't orient if he didn't have the tectum.

It apparently depends on the pretectal area, and they have found units there that do respond to such barriers. These studies were done by Engel here in Boston, and by York Peter Ewert-- or Ewert he's usually called in America, and he's in Germany.

OK, now, the optic tract projects to other areas, too. And it's at the end of the class, so I'll have to keep you in suspense about that until next time.