PROFESSOR: Good afternoon. In the last lecture we talked about the remarkable human brain, and how it empowers our thoughts, or feelings, or desires, or actions in the world, and how we began to understand this remarkable complexity, or at least grasp something of the complexity. How we understand the potential for things like moral character, and judgments. The case of Phineas Gage, to produce language, to speak our feelings and thoughts that's blocked in a patient like Broca's patient, with Broca's aphasia.

We talked about the fact that split brain patients show us not only to the left and right hemispheres of the human brain mediate separate mental abilities, but that they also seem to have almost independent forms of consciousness, or they don't have to be aware of one another. And so my focus today is to say we would learn from very unusual clinical cases. And I'm going to focus today on tools we have to study the typical human brain. And what is it that we can do to understand how your brain-- without having a hemispherectomy or a big stroke-- how does it operate, and what are the principles of human brain function they gave rise to the human mind?

So what are the ways we can learn about the human brain? And one thing we can't do is when animal researchers can do, we can't literally go inside the brain except in very rare clinical situations. I'll talk about them, but it's a rare source of evidence. So there's a million ways in which are trying to understand which part of the brain is which part of the mind, and we talked about the fact that phronology was a big misstep in assigning the functions of mental life to different parts of the brain. And so we hope we can do a bit better than that. And I'm going to review with you today some of the core methods, and there's a number of them studying the human brain. The reason there's a number is none of them are the magic answer. All of them are limited in their own ways, and we sort of need all of them to begin to grasp how your

brain makes your mind.

There's three huge ways in which we now have the human brain organized. Lesions, injuries to the brain, stimulation when you're allowed to stimulate the brain-- rarer, but we'll talk about that. And the most common, the one you see all the time in books and magazines, recording, functional MRI, EEG, methods where we record brain activity, and try to understand how that relates to the life of the human mind. And so we're going to go through these things a little bit and show you how they're applied in some ways that I hope that you'll find interesting. We'll come back to many of these things as we go through the semester, and as we talk about aging, or child development, or personality, or other topics, social cognition. We'll use these tools to understand the brain bases of those kinds of aspects of our mental lives.

So what's a big injury you can have? You can have a stroke, where tissue in the brain no longer receives its vascular supply that it depends on so greatly. And a lot of different things like hypoxia, lack of oxygen, the brain is very sensitive to oxygen. Tumors can grow, you could have degenerative disorders like Alzheimer's, Huntington's, Parkinson's, and others, epilepsy. So there's lots of different ways in which you can end up with brain injury, and ultimately neuronal death.

What's the strength of this form of evidence? Well first of all, it's causal. We've talked about the difference between causal and correlational sources of evidence, causal ones be more powerful for scientific explanation. A certain part of the brain is injured in you no longer can speak, you change your character, you no longer can make memories. We're pretty sure that part of the brain in some way is required, or causal, for that part of your mental life to operate. The deficits you see following brain injuries can be amazing, we talked about Phineas Gage changing his character, unable to produce language, unable to make new memories. We'll talk a little bit about patients with Prosopagnosia, it's a good big word to go home on spring break and if your parents ask what have you learned about, you say Prosopagnosia. That just means a deficit in recognizing faces. Patients with Prosopagnosia will be unable to recognize their own spouse by their face. They'll recognize it by the voice, by the physical movements, but not by their face.

We learn amazing things about the brain that until it happens we didn't know that could happen, what people like to call counterintuitive. So we'll talk later in the course in a couple times about blindsight, patients who say, I see nothing, but their behavior shows some part of their brain sees something.

We'll talk about category specific deficits where patients all of the sudden can no longer name living things, but they can name nonliving things. So you wouldn't have thought of that if you didn't see that. And we get separations in the brain between different things. We talked about the difference between the left hemisphere being important for local features, the right for global. The left thinking in terms of functional things in the world, the right in terms of appearances. We talked about that already. We'll talk about other things, the hippocampus is important for knowing that, knowing a piece of information but the Basal Ganglia is important for learning how to do things, mental skills and physical skills. We'll come back to all of those, it gives us way to organize things.

Much of our most solid understanding of the human brain still comes from the history of neurology and lesions. But what are its limitations? First, brain injuries don't follow anatomical boundaries, they sort of crossover things depending on the injury. So they're not going to selectively damage one part of the brain and not touch an adjacent one they could be doing something different. People can be variable in their response. Nearby systems, if you have two things in the brain that are next door to one another, do quite different things. Injuries are likely to injure them both, and you will have a wrong conclusion about the architecture of the human brain.

When we test a patient and ask them to do things after a brain injury, we don't really test the part of the brain that's not there. We really test a part of the brain that is there, people do the best they can. So there's secondary degeneration to an injury, there's recovery from injury, there's compensation from an injury. When you test a patient with a brain injury, you're testing what the rest of the brain can do in the absence of one of its companions. And finally can offer limited views of normal brain

function. Let me pick one and we'll come back in the course.

We're very interested in variation in people-- individuality-- what's the neurology of individuality? That's very hard to study in lesion cases, because we don't see enough of a lesion. we don't have enough Phineas Gages to ask would that injury look different if you grew up in one culture or another, if you were outgoing versus shy. Those kinds of things are very hard to answer patient by patient. But we can test large groups of people with imaging and ask what's the influence of culture on your brain organization? What's the influence of personality on how your brain's organized? And you'll see later on in the semester evidence about those sorts of things.

So let's go back to Paul Broca, the neurologist who they gave a name to Broca's area, because he sought a patient like this, like [INAUDIBLE]. That this patient had a big injury in this area could no longer speak. And every course you ever take about the brain almost will include a discussion about Broca's area. So I'm going to warp your world in a very narrow way, but maybe a shocking way, and tell you we don't even know how to think about Broca's area once we get more scientific than that. So because this is MIT so we're willing to tell the truth, OK.

So some years later Nina Dronkers said the following thing, she studied a large group of patients who had Broca's aphasia by behavior. That is they had trouble speaking, but the comprehension was pretty good. And then she made maps of their injuries and she overlaid those maps. And she said who has Broca's aphasia, and if you have Broca's aphasia, what's the one part of the brain that every patient with Broca's aphasia has damage to. Because these patients-- what you see on these maps is, some patients have damage here, or here, or here. But you line them all up and you say, what's the one spot that you have to have injured to have Broca's aphasia? And it's not this area that you saw in the picture, it's this area, in yellow, an area called the Precentral Gyrus of the Insula. The Insula is a fascinating, mysterious little structure-- you have one on the left, and one on the right-- that runs along from the temporal lobe, up to the frontal cortex.

Just a couple years ago there was a paper reporting that patients who had stroke in posterior insula instantly gave up smoking, and never wanted to smoke again. There's huge research efforts to help people quit smoking, just because it's such a difficult health problem. Nobody is doing insula lesions to help people stop smoking, OK. But it just stopped the smoking, and their desire to smoke, just like that. This is now more towards the front of the brain, this is not what anybody in a book or a course will tell you is Broca's area, that's out here. But it turns out this is the hot spot, and you could say, well what about the original patient? So kind of creatively Nina Dronkers went back and they did an MRI of the brain of the deceased original Broca's aphasic patient. They still had his brain, they put it in a scanner and they ran a structural MRI. And what they found was sure enough he had damage way inside the exterior limit of this damage, in as well as in white matter that connects to it.

So even now imaging evidence lets us rediscover what is the true basis of your ability to speak, or its vulnerability to injury. And it turns out not to be exactly what Broca thought it was. He saw big lesion and he said, this is the part of matters. It turns out, as far as we understand, it's a slightly different part that he thought was just at the edge and not important. So we can get better even going back to 150 years of imaging a brain, we don't have many of those brains around.

Stimulation, so you like to go in the brain is stimulate. People who do animal work will go in and stimulate a neuron and see what happens. It's rare, you only get into the patient's brain when they have a neurosurgical procedure and they're considering a resection, or removal of tissue. You can also do recordings by putting grids on top of those brains. And Penfield did famous studies for patients with epilepsy, where he would stimulate and map things that contributed a lot to our thinking about the brain. But that's a rare source of evidence, as you can imagine.

Another one that's much more common-- there's one of these devices down the street in building 46-- is Transcranial Magnetic Stimulation, or TMS. So this is one in which people are allowed ethically, and responsibly to give you a virtual lesion for a few moments, if you volunteer to do so. So they put some sort of wire, there's

different configurations, over your head in a targeted location. It generates a magnetic field that passes through the skull and induces a current. And what happens is the current drives lots of neurons to fire. Turns out, this is kind of interesting, if all your neurons are firing at the same moment, in one sense it's as if none of them were, because there's no information.

There's a lot of different ways you could think about that, but for example if on your 300 channel television you had all the channels on simultaneously on the same screen, it wouldn't be very easy to watch, something like that. All the neurons firing pretty much wipes out the function of that area. People do feel a little bit of a physical sensation, if you're prone to epilepsy it's not a good idea to try this, so it does require some careful supervision experimentally. But you can do this with healthy people, and if for example you do it on this side of the motor cortex, people twitch or say they felt somebody touch them. Nobody touched them, but the part of the brain that codes for touch just got turned on. If you put it on the occipital cortex, visual cortex, and you turn on at a certain moment, you could put a word up and word down, and the person will say they saw nothing. You'll make them functionally, cortically blind for a few moments.

People have done experiments like this to suppress activity, to enhance activity, sometimes it makes people even faster, like naming pictures. And it's also been used there's still experimental studies of whether it can be helpful for treatments of neuropsychiatric disorders. It's not invasive, in a sense of you're not going literally inside, you have a causal thing because turning the brain on or off. It's not very well targeted, it can't go into subcortical areas, but it's a very interesting tool.

Let's talk about recording brain structure for a moment. It's really important to separate this concept between recording structure, which is a picture of anatomy, or function, which is a picture of physiology. So there's old ones angiography, and things like that, I'll show you two. Computed Tomography, and MR and a really cool measure called Diffusion Tensor Imaging. And then, dysfunctional measures, and we'll talk about those, EEG, PET, fMRI, MEG.

So here's some different images you can get from the brain. This is a post-mortem brain, this is a cut brain, here's the front, here's the back. If a brain was open in front of you, this is what you would see. So here's an MRI, Magnetic Resonance Imaging, and it's pretty good, and I'll show you some more pictures, in showing you lots of information. Not as good as if you were in there, but pretty good. Here's a CT scan, Computed Tomography. It's not as good, it's more blurry. And this thing that looks really sad, it looks like get your camera to focus, that's actually the quality of the picture that we see that underlies maybe the most widely used tool these days for understanding the human mind and brain, Functional Magnetic Resonance Imaging. It's a very smudgy picture, but it has some really interesting properties.

So here's the kind of thing you go into for an MRI, both structural or functional. Some of you have almost certainly been participants in research or experiments, or studies, stick up your hand if you have. Oh, a lot of you, OK, so you'll speak up on this, is it quiet or noisy? It's super noisy, so you have to have ear plugs in. And this is why people doing experiments with this Functional MRI want to do visual studies, because auditory ones are tricky. So Tyler, your head TA, likes auditory stuff, it's 10 times harder to pull off those experiments. Everybody tries to do visual stuff, so you don't have the noise problem. But you get some beautiful pictures, here's Computed Tomography. And here's an MRI structural scan from the brain, the ventricles, here's Basal Ganglia. With an MRI, beautifully you can see the difference between white and gray matter.

I'm always impressed that the gray matter is just this thin ribbon. Cortex really means bark, it's just like the bark on our tree. And when you look at the brain this way, look at how much white matter there is. Here's your frontal cortex, look at all that white matter and then this thin, cortical mantle, or ribbon, or bark. That's what we think of as the smarts of language, and social planning, and things like that. So that's a structural picture.

And then these two pictures are sort of fun. This is just recorded down the street, we're going to fly through your brain from one ear to the other. And you get amazing resolution, it's not the same thing like being inside the brain. There's things

that you don't see, we know that, but you see a lot. Isn't that cool?

Let's examine what you can see now. Only about 40 years ago, you would have to have a person die to see this. This is a patient with Huntington's disease, we'll come back and talk about that disorder. Here's a healthy person, top of the brain. This is the caudate here, part of the Basal Ganglia. And you could see in a patient who has passed away that part of the brain is completely withered away in Huntington's disease. You would have to wait until person passed away to see something like that. Here's a healthy person top of the brain, again lining the ventricle. This is the caudate. And here in a living Huntington's patients you can see the great withering away. Some of cortex 2 in later stage of disease, but especially in the Basal Ganglia.

Here's a healthy older person, about 70 years of age, top of the brain, bottom of the brain, the ventricle. Here's on the left and right of the hippocampus, the structure we'll talk about, without which you can cannot learn any new fact, or remember any event in your life. So powerful for almost every sense of learning. And look what happens the structure in the same aged patient with Alzheimer's disease. It's virtually gone, it's greatly weathered. You see it's much wider here, because the tissue's greatly shrunk in the Alzheimer's patient. So we can see these kinds of changes in living people, for both research purposes and clinical purposes.

Here's one that's more cheerful, and more reflecting your experience. Here are studies of brain changes from age four to 21. So they follow a large number of people at NIH from age four to 21. And what this shows is this color coding is the thickness of the cortex. And you might imagine that as you get older, and smarter and go through grade school, and middle school, and high school, and MIT college, and as you head towards grad school, your brain will get thicker, and thicker with cortex. It's exactly the opposite.

Ever since you were about five years old, you've been shedding neurons by the millions, and connections among them by the trillions. And you're still going to do that until your probably about 22 or 23. Then you peak, and you decline and

become faculty members. But that's really interesting, we'll come back to this, that what happens as your brain get smart, experienced, knowledgeable, all the differences between you now, if you're 17, 18, 19, 20, and when you were four, it all goes with your cortex getting thinner. And we'll come back to that and how people think about that, but let's see if I can get this next movie to run.

There's also an ordering-- and we'll come back this but I want to show you this movie. So the more blue you are, the thinner you are, the more advanced you are in terms of ultimate young adult development. Here's visual cortex, vision coming in. This is Somatomotor Cortex, how you feel, your body, and how you move yourself. And what you see is, as you go from age four to 21, the blue spreads, that spreading is your brain maturing in higher thought areas. So we're going to review your life on average right now, here you go. And now you're ready to graduate. It's kind of an amazing story of fantastic brain changes that move you from what you could do and not do at four, to what you can do and not do at age 21. And we couldn't see these things, we couldn't begin to see these things, until just a few years ago in any scientific sense. All these things are like miraculous sources of information.

So let's pick another thing, and we'll tie it to school work. Here's the structure we said, the hippocampus. So important for the formation of new memories on an everyday basis, everything that's important and that you learn. So here's a fun study they took, and as you hear it, think about its scientific limitation, but it's fun as students to think about. They looked at students in medical school in Germany. They looked at the measure of an anatomic thickness of the hippocampus before and after they studied like crazy for a huge exam over some number of periods. This is the difference between the two, and what they're showing you is that as you study, your hippocampus got thicker as you crammed for your test. So will there be a day where instead of having to give you tests we could just measure the thickness of your hippocampus to know how much you studied, and you could just zoom in and out of a scanner, I don't know. But one cool thing about it is it's showing you that we can see structural changes not just on a giant scale from when you're four to 21, but from some number of months of experience, we can see a physical

change in your brain. Now that's trivial for animal researchers, they can show amazing things in seconds, but you see the human brain physically changing.

So let's take a look at another one, slightly more controlled, we'll look at two more examples. London taxi cab drivers. If you've travelled in various cities, and have gone in various taxis, you may have had better or worse experiences whether the taxi driver knows where he or she is going exactly. London is famous for having a very high code, taxi drivers have to take big exams to get their official taxi license, they create a very demanding thing. And when they ask this in the hippocampus if you learn lots of routes, if you know tons of routes in London, what happens to the hippocampus as it's memorizing all these special routes? And what they saw, that taxi drivers had bigger hippocampi, and the longer they drove, the bigger it was.

So is this a causal or correlational source of evidence? It's correlational right? So let's start with this, they have bigger hippocampi, and now maybe that's simply because, what? Maybe somebody who has an awesome hippocampus is ready to go to be a taxi driver. Maybe they pass the test, and the one who got lost all the time, and was driving to the wrong airport and stuff, small hippocampus, never became a taxi driver. So the size of the hippocampus is the cause of your success, not the consequence. Because the longer you drove, the bigger it got, that kind of goes with that.

But you could do a causal experiment this way. They taught people to juggle three balls, they practiced every day for three months. Three months juggling every day. What you see in yellow are parts of the brain-- that's a statistical map-- parts of the brain that significantly got thicker in three months of practice. So they could compare directly before and after, it's a causal experiment. And these are areas that are involved in the visual motion, and it makes sense that areas involved in visual motion would somehow change. But the fact that we can see three months of experience change the structure of your brain, it's kind of remarkable in they way that we can measure and scientifically scrutinize.

You might be curious if you did three months of this and you were a pretty good

juggler, you're impressing your friends at parties, your brain scan is different. What do you think happened-- they followed these people up-- after the juggling requirements stopped? They kind of stop, most of the people, they were too busy. They would show off here and there, but that was it. They measured their brain's again about six months later, and this change was gone. It came in, and it went out with the activity, it's activity dependent. So depending on what you do, you could think about every activity you do-- mental and physical that you do-- is constantly slightly changing your brain. And if you do a lot of it, you're fundamentally changing it like in these individuals. But if you stop doing it you go right back to where you were, because you're going to be doing something else.

And another fun measure that's kind of beautiful and intriguing is Diffusion Tensor Imaging. Now every [INAUDIBLE] we talked about so far has been gray matter of the brain, the neurons and then the circuits they form. We're going to turn to white matter, which is the myelinated axons that are the super conducting highways of the brain. And what Diffusion Tensor Imaging does, it shows you something about the organization of that white matter, measuring directly the movement of water at very, very tiny distances.

This is a cross-section of a myelinated nerve fiber. Those are the fibers that are covered with white matter that have to go some distance. And the myelin protects the quality and speed of that signal through your brain. And you could see at the level of, if you're a tiny, tiny drop of water, or smaller than that, this is a pretty big bump in the road. So imagine you're a little drop of water moving a little bit, and you bump up against the myelin, you go oh, can't go that way, and you go back this way, and you go with the flow. You go parallel with a myelin, it's hard to cross it at that microscopic scale.

But we can measure that movement in areas where it's highly constrained, and that's a property of the water. Here cerebral spinal fluid, things can go anywhere. Here's where there's a lot of white matter, and the water tends to flow along parallel with the white matter, just for physical reasons it can't cross it over. And here for example, is a statistical map comparing this measure of white matter organization

between adults, who either in their childhood had a diagnosis of dyslexia, reading was difficult for these individuals. Or people who typical reading development, where you learned to read and wasn't particularly difficult.

And you can see that in this area around the Temporal Parietal Cortex, there's a significant difference. But we can do one more thing. These are reading scores this way, this is the measure of the white matter organization from the Diffusion Tensor Imaging. Each of these as an individual person now. So the open dots are the people who had typical reading development. The filled dots are the people who had poor development, and you can see it's pretty continuous. Even in the people with the open circles who never had a problem, the better they read, the more the organization is here.

So this is not just the difference between good and bad readers, it's a difference between really good readers, and medium readers, and poor readers, right, continuous. So now, cause or effect? Were those of you who at three, who had awesome myelin, were you going, reading's a snap. I love this stuff, where's *War and Peace*, mom? Or, were you like the jugglers, and you were reading a lot, and you were exercising this part of the brain, and altered its physical structure. And the answer is we don't know. How could we know? How could we know? If you were scientists and were given a pot of money to do this, how could you know? Well--yeah?

AUDIENCE: Track the entire lives of multiple people.

PROFESSOR: Yeah, do a longitudinal study and start like, before people read. And you could see is it different then? Are we born to be big readers, or by being big readers do we alter the architecture our brain. What's the effort, and what's the talent, or what's the predisposition at birth, and what's the time you put in creating this part. We don't know that yet, but we have a place to look at that. And then you can create these kinds of beautiful pictures, and I'll say a word about this.

So this is an individual person's white matter organization. So we could take this picture of you, or anybody you know who wants to go in a scanner. And what's color

coded here in blue are fibers that are running up or down, we can't tell with the fibers which direction they're going, but we can tell other orientations. Up and down, left and right in red, up and down in blue, and green is front to back. Pretty cool, huh? I can tell you that I'll say a word about this. Should we do that again? I like it, but I work in this area. This is fantastic, this is an individual person's white matter organization. As information is flowing around in your mind, here's the paths that it's flowing around in as you just do anything that's interesting in your feelings or thoughts or anything. It's fantastic.

I can tell you that the algorithms that are used to create these maps, there's some debate about the better ones. So the last steps of this are a bit debated, and a bit depending on how cool you are as a visual engineer. But there's a lot of things that's right about Diffusion Tensor Imaging, there's a lot of things that are right about it. Function, so most of all we're interested in structure, not just for itself, but how is it makes your mind do the things you could do. And when we think about different functional measures that are available to neuroscientists or psychologists, we often think in two dimensions, Spatial Resolution, and Temporal Resolution. How precise are we where we are, and what's the time scale that we're measuring in, milliseconds, are we averaging over many seconds, many hours. We know mental operations, roughly speaking, occur at the millisecond level, or maybe 10 milliseconds. There's no answer to that, but we know lots of things happen that fast in the mind.

So if you look at this here you can see that, for example, if you're in animal work, looking at size, you can get down to the Synapse or the Dendrite. We can't touch that in humans, we can't touch that cellular stuff. And it's not until we get up to here, which is like big patches of the brain, that we can state things about people. That's why it's always going to be fundamental in neuroscience to link the human work to the animal work, because we can't get to the neurons or anything like that in a person almost ever. That has to come from animal work, where you can do invasive work. So we have to look at a pretty big patches of the human brain.

How about time? Well, we can get down to milliseconds in time in the human brain.

Functional things like PET and MRI are here and in the order of multiple seconds, I'll come back to this. But you can see all these things have strengths. Now you don't always want to be down to a single synapse, it's not clear that we would understand much of the organization of the brain at the level of the synapse. There's things happening in the synapse, but a thing like knowledge, or love, or something like that probably we can't study at the level of the synapse. Effectively, yet. Bigger units are probably more interpretable.

So here's a fun one, EEG's, Electroencephalography. So they put on your head some sort of a cap with electrodes, and they measure changes in electrical activity that are being picked up through the skull. And you're picking up huge changes in hundreds of thousands of neurons, but you're able to do it millisecond by millisecond at the speed of thought. The same electrical signal for EEG and ERP, that evoke response potentials, with EEG you just watch it over time. So you can see these different rhythms that go with a person in coma, or in deep sleep, asleep, drowsy, relaxed. You can see these characteristic rhythms that people can measure.

If you do an experiment, you can time lock these moment by moment to some stimulus or task you give the person. So here we're going to time lock these, and then you get a thing like this that says, here's a response, maybe the first moment after I see a word, a second moment after I see a word or something like that. So you can time lock large electrical responses in the brain. And you get some studies like this, and we'll come back to this, but here's a fun one in language for example. You read a sentence like, It was his first day at work, OK that's the baseline condition in purple, not a particularly exciting sentence. Although, your first day at work is actually pretty interesting-- but to read the sentence. How about this one: He spread the warm bread with socks. You go, Socks? I'm shocked, that makes no sense at all. What happens as you read it, here's in broken blue line, you go wow, and that's called the N400. But that's kind of cool, that's 400 milliseconds after you saw that word you said, I get it's socks but it doesn't make sense. So you're violating semantics.

And then they have to do a control experiment. And a lot of psychology, in a course like this, we can't devote enough time to this. But I can tell you high quality research in psychology is high quality thoughtfulness like in any other field. You could say, well maybe it's not the word "socks" that's bothering you, maybe just because it's odd, just like a weirded out signal, it's a weirded out signal. So they do this, She put on her high-heeled shoes, but they put shoes in big print that you didn't expect. So now you're weirded out, but it makes sense. So what happens in your mind, you a very different response here. So here the meaning is wrong, here the size is wrong. And see you can read a person's mind in this sense, millisecond by millisecond as they understand something like a sentence. You can do it with babies, which is pretty cute, and incredibly exciting too.

So we can measure to the milliseconds. Lots of people can take doing it, it's relatively inexpensive. Why don't we just run around and do that? And we do that at MIT, and lots of places do this too. Well, Spatial Resolution is really problematic, we don't know where in the brain the signals are really coming from. We know where the electrode is on the head, but that's picking up a lot of stuff below it, we don't know where the brain is coming from. The way I think about it a little bit, imagine you went to a football game, and you were on the outside of the stadium, and you heard big cheering on the side that you knew was MIT. You might think something good happened to MIT, then you hear big cheering on the side where CalTech team is sitting, and there's fans, it'd be the usual Rose Bowl. You might figure something good happened at CalTech, but you don't really know exactly what happened, and exactly where it happened. So we don't know where the signals are coming from in a very precise way.

There's another method that's sort of very intriguing too, and we're just installing it at MIT, and you could be amongst the first generation of participants, if you so choose to be. This is called Magnetoencephalography, active neurons produce small magnetic fields. You can use a superconducting quantum device to measure this tiny, tiny change to the magnetic field, they're secondary to the neurons firing. These signals are problematic to measure because they're estimated to be 100 million times smaller than the earth's magnetic field. And all these measures we

have in human brain function, all of them, the signal is terrible compared to the noise, it's terrible compared to the noise. And MEG might be the worst, there's a number of places that installed MEG, and had to take it out because the local traffic on the road was too big relative to the difference between the earth's magnetic field in the signal they get. Signal to noise is terrible in every noninvasive human brain measure we have. But you get something beautiful.

Now, any mental thought we have of any interest of any kind, we pretty much understand to be the property not of a single part of the brain doing its thing, but a remarkable concert, different parts of your brain playing or interacting with one another. It's a symphony orchestra doing anything interesting in the human mind, and MEG can show that beautifully. So here's an individual's structural MRI that's been inflated, they've sort of blown it out like a balloon so it's sort of easy to look at.

And what you're going to see now from Dale & Halgren in an MEG measurement millisecond by millisecond of what your brain does, roughly speaking, when you read a single word, OK here we go. See, back and forth, back and forth, and there's all this interaction feeding forward from when you see it, feeding being backward from parts of your brain that say, I think I know what it is, let's double check. Back and forth, back and forth. Let me do it one more time, because I think it's just so cool.

Anything interesting that your brain does is an incredibly complicated millisecond by millisecond interaction between large scale brain networks. So here we go again, reading a single word, arrives in the back of the brain, front's thinking about back, front, back, front, back front. We read the word. It's just amazing, and MEG is one of the better measures for us to see this time based way in which your mind accomplishes things. The strengths are it has great temporal resolution, noninvasive, Spatial Resolution is it maybe better than EEG, or perhaps better, not as good as a fMRI, we'll come to that. And it only can measure neurons in the cortex that are parallel to the skull, so we can't see lots of things like support local structures like the hippocampus.

So now we're moving to the measures that you most often see, but these other ones all help us a lot. And they are all derived from the following things. Sadly, for PET or fMRI, the most widely used studies to understand how your mind works, we can't interrogate the neurons to compute your mind, we can't, they're off bounds to us. The other measures you just saw are based on neurons. What we have to do is we have to look for gossipy neighbors, that is the vasculature that surrounds and supports the neurons that compute the mind. And we know the neurons require oxygen and glucose, metabolically to do their work, the cellular life. And the brain area's active, there's increased blood flow, and increased energy supplies that come to that. So it's all the sort of inference by the secondary consequence of neurons doing their business.

So the brain is about 3 and 1/2 pounds, it's about 2% of your total body mass. So it has a tenfold, 20% extra demand of body oxygen, your brain cries out for oxygen at every moment. So 2% of your body, but 20% of the oxygen demand. And it's so sensitive that only 10 minutes of loss of oxygen can often cause irreversible brain damage, especially in structures like the hippocampus.

The first discovery that blood changes that are going with brain changes, blood changes that are the sort of the echoes, if you will, a secondary consequence, is low tech character current machines. This is work from Angelo Mosso in the late 1880's, and he saw a patient who had a unusual sort of malformation, so he had almost no skull here. And he put on it something that measured the pressure there, and he also measured-- and what's shown here in red is this pressure as a control thing, that's pretty clever-- pulses of blood in the forearm, so those are in blue. That's the control, that's not just blood everywhere.

And what he did is, the guy's still sitting there, nothing happening, and he noticed that when the church bells rang nearby, boom, this device picked up increased pressure over this part of the head. That's pretty cool, it has to be blood, it's not neurons, OK, it's blood. But now he has the signature of mental life in your brain, the blood consequence of a thought, which is I hear the Church. They asked the guy, does it have to be something that you hear, he says, did you make your

prayers today, your Ave Maria? Again nothing happening peripherally, but boom, as he gives his answer, a change in blood pressure there. Or do math problem, boom, a change there. So all of the sudden, blood changes of a part of the brain become the witness to that part of the brain supporting the mental operations to do that task.

And here's a PET study, the first weighted Positron Emission Tomography, which is basically used to measure local brain activity by looking at the consequences of photons disintegrating as they're measured in this sort of a device. And here's the way they use this task to discover which parts to map the neural organization of the human mind.

So I need somebody who's willing to do a task at their seat, and it's just going to be reading words, or coming up with words. OK, thanks. Here you go, ready? Look at that, in our field we call that fixation, you're just looking, OK, just looking. Alright, good job. Ready for something else? Alright, now just look at these things, OK, you see the words? The technical word is reading. Alright, now imagine we did one more thing with you-- and actually if you were in a PET scanner here's what would happen. If in a PET scanner, you'd be sitting down there like that, there'd be a physician in their lab coat like this.

There'd be physicist in the basement making up some sort of a tracer they're going to inject into you every round of this. Because that's what they need to sort of track this, and it comes up an elevator, and people take turns running down the hall with it, because it has a pretty short half-life. The shortness of its half-life is what makes you able to do these multiple measures. This is a pretty big deal process, and in fact the one or two PET sessions I ever attended, you would rotate who would run down the field with the radioactive substance, so you would share the radioactive substance.

So now you've done that, and you feel like, I'm doing pretty good. So now they come and they say, are you ready for another injection? They have a catheter running into your arm, and they inject you again, here comes the radioactive stuff, the oxygen. And now they ask you to read the words aloud presented one at a time,

why don't you just read aloud one at a time, go ahead.

AUDIENCE: Rose, cat, apple, pen, plane.

PROFESSOR: OK, and they say thank you very much, and we're going to do one more injection if that's OK with you, of radioactive substance. And now we're going to ask you to do one thing, and this is harder, as you see each word tell us a verb that describes what you might do with that object, or what a person might do, so go ahead, for rose tell us.

AUDIENCE: Smell, pet, eat, write, fly.

PROFESSOR: Perfect. Yeah, I can tell you that in the experiment they present a lot of these, and a lot of subjects after while just go use, use, use, use, hold, hold, hold, hold. But you did a good job, OK. This is just looking at something, this is looking at a word, which is reading. Now don't forget, we're the only species that ever read, reading has been around in our culture only for about 700 years on any scale, and reading is an incredible thing to work correctly. And you saw the whole brain flicker to get it right. But now you're going to say the word in the next condition, so you're not just looking at the word, but you're also saying it. And now finally you're not only saying a word and looking at it, but you are thinking about it to come up with smell, or pet.

So they say, what we're going to do is we're going to do a hierarchy of your mind, just looking, reading, reading and talking, reading and talking and thinking. And by comparing those different conditions, we'll subtract them against each other, and pull out the part of your mind that sees a word, that speaks a word, and that thinks about a word, and we'll separate those out in the brain. So basically the subtraction method. So when we compare looking at fixation versus looking at words, we'll see what part of your brain discovers that it's a word, knows how to read words, looking at words versus repeating them. We'll discover the basis of speech, speaking a word versus coming up with the verb, thinking about stuff, their meaning, and coming up with an answer.

So again the idea is if you're saying something like pet for the cat, you're doing all

these things. Or you might just be reading it aloud, and we'll subtract them. In both these conditions, here you saw a word and read it, here you saw a word and came up and produced a verb, you subtract these two and you end up with a statistical image like this. This is not a raw image of blood, all these you ever see those are statistics of the areas that differed by some statistical criterion between one condition and another. They're all statistics, they're not blood, or raw blood, that underlies it, but what you see is a statistic, and here's the statistic. Now in both of these cases, you saw the word. In this case you simply read it, in this case you read it in your head and you came up with a verb. But why don't we see anything back here? Why don't we see the seeing of the word, even though the seeing occurred in those conditions? Why isn't it visible in this brain picture? Because it's been subtracted out.

So always in these brain imaging experiments, for reasons I'm about to tell you, we almost always have to do some kind of subtraction. And I'll tell you why, but that subtraction is very big. Because what you subtract out, that's the heart of the experiment, and your decision about what's a legitimate subtraction. And the reason we have to do it is this, look at these two things. Here's one condition, and here's the other condition. Do you see that they look pretty similar? Again, signal to noise. Your brain is busy all the time, now we ask you to do something and see the difference.

And the difference is very tiny by the way we measure it. It's not tiny mentally, it's not tiny in terms of the consequences for civilization in the world. It's tiny because of the weird way we have to measure it. I can tell you that if I've put on an optimal checkerboard, the psychophysicists have said, this turns on your visual cortex. I'll get about a 3% to 5% change in your brain signal. If you wave your arm, I can get 3% to 5% signal change in your cortex here. If I ask you to do everything in between seeing something and moving your lips or hand, everything about thought, emotion, memory, desire, motivation, everything that's big in our life will get something like that one tenth of 1% of the signal change. One tenth of 1% of the signal change. Yeah, Tyler's like yeah, that means you have to test a lot of subjects, and work 40 years on your Ph.D.

So we have to do that subtraction, because if we just take a picture of what's going on in your head, it's so much that we can't tell what's going on at all. And if we have you do something that's pretty big, like seeing like a really provocative picture, we'll just get one tenth of 1% of the signal change. So we have to do the subtraction to have a hint. And then we do one other weird thing, we don't have to but we often do it. We want to average people to make some general statement about humanity, as far as we can do it, based on the 10 MIT students we test. So we scrunch everybody's brain into common space, everybody's brain's a little bit different, like their bodies are a little bit different. We scrunch everybody to line them all up so we have a common physical space. So by the time you see this picture, it's a statistic on an average of people in most cases, but you get an amazing story.

Which up until these pictures-- about the late 1980s, it was unimaginable that you could go inside a living person's brain, and see what it is that allows you to hear a word in auditory cortex, to see a word in visual cortex, to move your mouth to speak, or to think, what's the verb that goes with that word? Unimaginable at your-- OK, now I have to do the quick math, but you'll help me out-- what year were you born in? '82? '92? I know, at my age it all blends. '92? OK, so just a year or two before you were born-- this was 5 years before you were-- unimaginable that you could see such a picture.

When I was a graduate student at Harvard, and the people at Washington St. Louis University-- who did the first of these-- did an incredible service to the field. Here we saw, oh my gosh, it was like landing on the moon. Going inside the human brain, and knowing which part of the brain endows us with human capacities.

Now, we can be appreciative or we can be skeptical scientists, and we can say this, let's pick this one. Let's compare seeing a word like "board," versus seeing a fixation. We do that subtraction, and that's seeing a word. Just by common sense, what's wrong with this comparison? It's OK it's not terrible. How can you control it better? To understand what this part of the brain is really doing? I heard something? Well partly it's a meaningful word, versus something that doesn't mean

anything to a plus. But what else could you say is different between them? Yeah? [INAUDIBLE]

GUEST SPEAKER: [INAUDIBLE]

PROFESSOR: In this case, oh my gosh, yes, and I'll come back to that, but let me not do that one for the moment, because that's a giant story which I can't fit in today. Yes your mind can be all over the place. So that's definitely the case, so that's a good one. Yeah?

GUEST SPEAKER: You could replace the plus, which is like really small, with [INAUDIBLE]

PROFESSOR: Yeah, that's perfect, OK that's the way I was going-- the other one's great too, two great comments. Yeah you could say like, maybe this is a part of your brain it goes with five things, or something this big versus this big. No you go, that's not so interesting, the part of your brain that looks at something this big, versus this big. But that's just as legitimate a conclusion here. How about this, five different things, versus only this. There's a lot of different ways in which you could say, what is the mental operation that I've discovered in the human brain and mind, it all comes down to the comparison.

So here's what they did to try to do a better job. They showed you a more complicated thing that doesn't mean anything. A bunch of letters that you can't pronounce, a bunch of letters that you can pronounce, but it's not a real word, and here's the real world itself. So if you want to say, what do you think this part of the mind is doing? What part the mind does this part of the brain allow to happen in humans, and only humans on this planet? And every word you ever read only happens because this part of the brain does what it does.

What is that part of the brain doing? Is it just simply responding too complicated things, five of them? No, not much, a little bit, but not much. How about letters, letters are pretty interesting, but there can't be a word by English, you can't pronounce this. Not too interested? A word, a set of letters you've never seen together before, but you can pronounce by the rules of English. Boom. That's what I do, says this part of the brain, that's what I do. I say, I see something, and it's

possibly a word and I can say it by the rules of English. And by the way, if it's a word I've done before, I do that too. I'm pretty flexible, I can do new words, I can do words I've known before. It matches what you see with language, that's reading. Only our species can take our visual system, and the language you learn as a child, and put them together, and allow our civilization to read. And this is a part of the brain where those roads meet.

And by the way, we talked about local and global, the forest and the trees. And consistent with what we talked about the split brain patients, looking at global stuff right hemisphere, if you're looking at local stuff, left hemisphere. So we like it when the information we have from split-brain patients, or stroke patients aligns with healthy people doing a task as they typically do. Because then we sort of believe there's something right about that.

So PET, pretty good spatial resolution, I mean, depends what you mean by good. My neuroscience colleagues dismiss everything we ever do as sort of pathetically imprecise. But 5 to 10 millimeters, not as good as fMRI. The temporal resolution is very poor we can only take one picture that lasts about a minute, and averages everything across that. You have to inject people with radioactive stuff, and it's correlational. But it has one other thing that's really, really interesting, Positron Emission Tomography. Because you're injecting a radioactive label, you can create different kinds of labels that go to different parts of the brain. So here's Parkinson's disease, which involves damage the Substantia nigra, and the Basal Ganglia. Here's a healthy persons Substantia nigra, and here's a person with Parkinson's disease, where these cells have died away. Typically, at least 80% of these have to die before a person shows Parkinson's disease symptoms clinically.

Here's an injection of radioactive stuff using PET that binds to Dopamine receiving neurons. And you can see that in the living Parkinson's patient, this tremendous reduction in these receptors waiting for Dopamine. In a living patient specifically Dopamine receptors. So that's a disease. Here's why video games are taking over the world. Oh no, not yet. We can do one more thing. We can track the disease from a typical person, to a person with moderate Parkinson's disease or severe.

Within the disease, we can see differences.

But here's why video games are taking over the world, because if we take a healthy person, young adults, give them this kind of Dopamine binding tracer, and have them play a video game, two things happen. A, the parts of your brain that are involved in reward, Dopamine, is the strongest to reward neurotransmitter that we know. Things go crazy, and what this graph is showing you is the better you do, the more rewarded you are. This is why you will go for the next level, because to get that dopamine fix, you got to keep going. And we think these reward mechanisms underlie everything, in many ways they relate to everything. Why do you do whatever you do, because at some level, in some way, you find it rewarding. And the data is very compelling that way.

The last method I'll talk about is functional MRI, and it's the one that's most widely visible. So you sit in a scanner, stimula are presented to you to perform a task. We do a lot of stuff in our lab with children, we show them how the frog would do it. For those of you who've done a functional MRI experiment, because there were so many hands that were put up. Do any of you want to say a word about your experience doing that? What was it like, easy, huge fun, recommend, no, not so much fun. It will vary a little bit. We said noisy. Some people find it claustrophobic.

GUEST SPEAKER: I dont know, I didn't really do anything. I just had to sit there for a really long time and not move.

PROFESSOR: Oh, so they didn't ask you to do a task, maybe.

GUEST SPEAKER: Well, for a big part of it, I was watching a movie.

PROFESSOR: So for the student they were watching a movie not doing anything,

GUEST SPEAKER: [INAUDIBLE]

PROFESSOR: You were doing yes or no clicks. So that would be typical functional MRI kind of experiment, some of them are more obnoxious, some are less, some are funny, some are not as funny. Any other experiences? Was it comfortable, not so

comfortable, medium. Anybody else want to share? No, OK. OK.

So how does this work? Functional MRI takes advantage of MRI but it focuses on hemoglobin, the stuff that carries oxygen in your blood. And it rests on the fact that after oxygen has been extracted it's more sensitive to the magnetic field than oxygenated hemoglobin. So it's like this. Here's basically capillaries and veins, arteries and veins. And as you go through the capillary bed, the smallest vessels, neurons are extracting oxygen to support their physical life. What happens when this part of the brain gets active, is that more oxygen is extracted to support the active neurons. So we call this BOLD effect, blood oxygen level dependent. So we're measuring the change in blood, changes the ratio of oxygenated to deoxygenated hemoglobins, that changes the magnetic field as we measure it. And that's what we directly measure, not the neurons.

So if the neurons are using up oxygen, why does the BOLD signal increase, why does this ratio go up? Because intuitively you'd think it would go down, because oxygen is being extracted at a higher rate. If you look at oxygen being extracted, right after something happens, 10 seconds, there's an initial dip of oxygen. That's the neurons extracting oxygen to replenish themselves from their activity, their activity has been to give your mind its life. Then what happens is there's this vast oversupply for much longer time. Intuitively, it's as if we said it's so important to metabolically support the neurons that make up our minds, that if some areas demanding a lot of blood, we send over way too much extra as soon as we can, from a distance to make sure everything's OK. And because our measurement is so sad, we almost can never measure this initial dip. We almost always measure the sustained oversupply of oxygen to that part of the brain.

So you could say it's such a house of cards. The oversupply of the blood going to a part of the brain changes the balance of oxygenated to deoxygenated hemoglobin that changes the magnetic property. And that's how we try to figure out what that part of the brain is doing for your mind. But it works pretty well in some cases. Decent Spatial Resolution, no injection, you can zoom in a scanner and do a lot of different things. Modest Temporal Resolution, because it's not milliseconds, it's

always on the order of seconds, that's correlational, not causal.

But you get some amazing results, I'm just going to present to you two or three. So here's one, a thing we're very interested about humans is empathy. How much we understand and feel other people's happiness, or sadness, or pain. So the "observation or imagination of another person in a particular emotional state automatically activates a representation of that state in the observer," empathy. And how do we understand how another person feels, and we think that's a big thing in how we relate to one another as humans.

So Tania Singer did the following experiment, we talked about this before a little bit, embodied cognition. That we understand others out there by the feelings we know within us. We don't know their feelings, but we know our feelings inside us. So here's what she did, she brought in pairs of people who were friends, or romantic partners. And she either had them get some pain, it was a shock, within ethical boundaries, but not pleasant, that's the pain. Or, you got to watch through a video camera, while you're being imaged, your partner getting the shock.

So think about somebody you care about and think about them getting something painful, and how you would feel at that moment. And they asked in the brain, what's similar and dissimilar, and we'll focus on what's similar right now, between feeling pain yourself, and observing pain in somebody you care about, emphasizing with the pain you see them having. And what they found is two areas, something of an Anterior Cingulate, and something in the Insula, which we talked about before, where there was a lot of overlap. So this phrase, I'm feeling your pain, in your brain when you feel for somebody else's pain in this physical sense, you turn on some of the same brain areas as when you feel physical pain directly. It's as if the basis to imagine another person's feelings is the feelings you know so well yourself. And this is literally shown now by the brain imaging. It could've been a story, a metaphor, an argument, this is scientific evidence that supports that likelihood.

So we're going to expend it in a slightly fun way. There's been a lot of study in neuroeconomics thinking about how we think about, for example, things like trust.

So one game, and there's a number of them, is called the ultimatum game. And many people probably know this, but let me remind you of this. This version of it has two players, a proposer, and a responder. And what they do is they give to proposer a certain amount of money, and the proposer is allowed to make an offer to the responder. If the responder says, No, nobody gets any money. Usually people offered about 50%, so let's make this concrete just for a moment. Can I pick you for a second? You can decline. Imagine if Tyler came over to me and give me $10, and I said, how would you feel if I gave you five and I kept five. What do you think? Might you go for It?

GUEST SPEAKER: Yeah, sure.

PROFESSOR: I mean, you go, I'm $5 dollars ahead, you're $5 ahead, Tyler won't eat this month because graduate student stipends are modest, but it's a zero sum game in the end. So now Tyler comes over hands me 10 more dollars, and I offer you one. What's your first feeling assuming that I wasn't your teacher grading you? He saw me get ten, I say here's one. What's your feeling? Think about it just for--

GUEST SPEAKER: You'd feel kind of cheated.

PROFESSOR: --yeah. You don't have to, by purely economic perspective, would you be ahead by taking that dollar? Yeah. A dollar's a dollar, $2 is $2, but people have a sense of fairness. Even to their own detriment, if you offer $2 and lower. Even knowing that you're just ruining $1 or two you would've gotten for nothing, except saying yes, people half the time will say no. It's like, you are so unfair-- you were saying to me, I would never say this to you-- you are so unfair, that we're going to take us both down, rather than you have the pleasure of the $8. OK It's so unfair, that my sense of fairness is disturbed.

It's an interesting way to think about it, imagine a friend of yours is handed $10, and they offer you half, and if you say no, nobody gets anything, so it's a trust game. They had the people in the scanner playing this game with two people they saw on a video monitor. The two people they're playing with are set up. The person in the scanner is the real participant, the people out there they see, are confederates,

they're play actors. And one is a fair person, here's $5, thank you, here's $5, thank you. Here's $6, oh, you're awesome, we can get along, And then there's an unfair player, here's $1. And you go, why is this guy a jerk? How about $2? And after a while, you go the fair player was very decent, this unfair player-- who you believe is part of the experiment, but is a set up-- and you're just thinking, why is this person such a jerk? They're constantly getting $10, and constantly giving me one or two. No, no, no thank you.

Now, you get a shock, and you see these two strangers, one of whom was a wonderful, fair player, and one of whom was an absurdly unfair player. You see them get a shock. And they had both men and women in the scanner watching these things happen. And here's what happened, and it's kind of funny, but you know. For the women they had overlap again between the parts of the brain to turn on in here in the insula, when they got a shock, and when either the fair player got a shock, or the unfair player. They felt bad for both by this measure. Look at the men in the study. I feel bad if the fair guy gets it, but this part of the brain's like, yeah, give it to 'em, can you push up the voltage?

It just came out this way, whether it would work that way under all circumstances, all ages, all societies, other groups of men and women, don't know. But in this sample in the United Kingdom, the men had no empathy. It's worse than that, it's worse than they had no empathy, let me show you this. If they asked to indicate their desire for revenge against-- this is a behavioral response-- their desire for revenge against the bad player. I don't think they pursued the unfair player down the street, but just that feeling. And the women said, a little bit, the men said yes, if only I could take down this person, that would be great.

And here's the amazing thing, we'll come back to the structure called a nucleus accumbens. It sits in the bottom of the Basal Ganglia. It's the structure that in the human brain is most identified with reward and pleasure, most identified with reward and pleasure by fMRI imaging. Look at the nucleus accumbens when the unfair player gets zapped. The women, nothing much, the men boom, big reward. Revenge is rewarding in their brain. No sympathy, and lots of revenge satisfaction

for the unfair player. Now you can decide on your own life who this applies to or not, but it's sort of fun to explore these different things. How we form ideas about empathy, trust, whether they are in a society we grow up in. Somewhat different on average men and women, huge ranges within men huge ranges within women. So it's a sort of fun thing to explore.

Let me end with something that's much more difficult and disturbing, but another place where imaging is giving us insights that you could not imagined having some time ago. So this is a very difficult case, I don't know if any of you gone through it, I don't wish it for you. Some of you probably have, and many of you will at sometime in your life, when you have to make an end of life decision. And amongst the most famous of these cases was Terry Schiavo. Now I don't know that name even rings a bell for you, but it got very, very famous amongst these kinds of cases. So she had a cardiac arrest, she had took a lot of diet pills, and that may have contributed. In February 25, 1990, she went into a coma, and then a vegetative state. So a vegetative state is when a person seems to be kind of awake, but when you talk with them, they're not very aware, they're not responsive, they're not noticing, they're not talking. But their eyes are open, and they're awake, their eyes are not closed, so that's what she is. And they put in her a feeding tube, because without that she wouldn't live, she couldn't eat and feed herself.

It was a heartbreaking difference of opinion between her husband and her parents. Her husband petitioned some years later, actually eight years later, to remove the feeding tube and let her pass away. The parents opposed that, they said that's not her wishes, she would want to keep on going with the feeding tube. The husband said no, I don't believe that's her wishes. So you have this very tragic confrontation between the parents who loved her, and the husband who presumably loved her having different ideas about what to do with her, whether to end her life or not. So finally her tube was removed, but then the parents went to court, and a judge reversed it, and they put the tube back.

She became, sadly, kind of back and forth, living nonliving, on judicial decisions. Her case became particularly famous, for a bunch of reasons, and it went back and forth

from court, to court. Moving up in the state courts, and there were several US Supreme Court decisions about whether to remove the tube, or keep the tube in. And it's a tragic thing, it's a tragic choice between the parents and the husband. It got to the US Congress, in the US Senate. President Bush signed a bill to keep her alive. Everybody got involved, with various opinions, finally the Supreme Court made a series of decisions. It was disconnected in 2005, and she died in March 31 of that year. So tragic difficult decision, and a tragic family situation that became kind of a political, and judicial football.

So what's going on in the mind of somebody like this, and how could we even begin to interpret it for a person who can't speak for themselves and can't respond. So let me tell you about a different case, we don't know her case. So, again a vegetative state is one where you appear to be awake, but there's no sign of awareness. Eyes are open, but the person's not talking or responding to anything in their environment. So here's a different woman, 23 years old, in 2005 she had a road traffic accident, severe traumatic brain injury.

Five months later she's un-responsive, but she has preserved sleep-wake, like she's waking up going to sleep, waking up going to sleep. Eyes open, but un-responsive in every other way. They put her into an fMRI scanner, as well as healthy comparison people, and they have them do to mental imagery tasks. they read instructions to her. But you go into scanner, and you're told to imagine two different things. Playing tennis, so imagine in your mind's eye you playing tennis for a moment, imagine that. Or imagine visiting all the rooms of your house starting with your front door, in the house that you are living in now, or where you grew up. Imagine those two things in your mind.

First of all, just a pure cognitive neuroscience level, and we'll come back to that, imagination is a really interesting thing. And it turns out when we imagine things, again we use the parts of our brain that does them, imagination is perception run backwards. We can see imagination in the human brain. And depending on what you're imagining, you use the same systems that you see with. If you imagine something you're looking at, it will turn on your visual system, it's even more specific

than that. So let's first look at what happens with the controls. When they imagine they're playing tennis, they turn on the supplementary motor area, that's a part of your brain that plans your physical movements.

You're not moving, but you're thinking about it, this is imagination of movement. When you plan a movement., you turn that on. When you go around your house, you turn on spatial areas that are in the parahippocampal cortex, and similar areas, parietal cortex, and parahippocampal cortex. They're turned on if we show you a movie where you're moving around in spaces. If you see spaces, you turn those on, if you imagine spaces, you turn them on. So imagination in the brain is perception run backwards, or physical action run backwards, you're not actually doing it. But look at this patient who got in the scanner, who was non responsive, you read her the instructions, and see what she does, and look at her brain. Asked to imagine tennis, asked to imagine the rooms in her house. It looks just like that.

What does that mean, just in a common sense, what does that mean? Did she understand the instruction, at some level yes, she wouldn't turn on those parts of the brain if she didn't understand the instruction, she imagines the thing you ask her to instruct. So this guy on the front page of the *New York Times* said fMRI could tell you the internal mental life of a person could no longer speak, or communicate with any other way.

Now it's turned out since then, that when they put in other patients into the scanner, most of them don't show this pattern. So it's not that every patient in a vegetative state this is full of mental life like this person. And a deeper way, we don't really understand what this mental life is like. We don't know whether she simply understands some things, but doesn't have feelings, or plans, or desires, or whether she has those too. We don't understand really the full range of mental life, but we know that she can understand an instruction, and her brain follows through with it. Most patients, it turns out, don't look like that in vegetative states.

So again, brain imaging has taken us inside the mind of somebody who cannot communicate for themselves and let us say something about what it is that's going

on in that mind.

In conclusion, we've talked about different ways of learning about the brain, different methods to record structure and function that vary in their temporal and spatial acuity. And incredibly different ways in which we can understand the organization in time and space of how the brain supports the human mind.