>> Tonight, it is a pleasure to welcome Dr. Christopher deCharms, a neurologist who reads minds. With his company, Omneuron, he has developed real-time functional magnetic resonance imaging, a technology that enables researchers and experimental subjects to visualize active regions of the brain while the subject is performing specific activities in responding to external stimuli, all in real time. Well, monitoring their own neurological activity, subjects can be trained to change their brain's response. A goal of this work is to provide biofeedback to subjects so that they can control their cravings for addictive substances, manage their perceptions of pain, and develop the ways their brains respond to various stimuli thoughtfully and actively. Dr. deCharms received his B.A. from Brown University and earned his Ph.D. in Neuroscience from the University of California at San Francisco. The work you hear tonight was initiated while he was at the Keck Center for Integrative Neuroscience. This work has received a claim in the New York Times, the MIT Technology Review. It has been highlighted on BBC Radio, NPR, Fox News, and it has been published in several prestigious scientific journals including science, nature, and the proceedings of the National Academy of Sciences. This talk should be stimulating but please be careful what you think because someone may be watching.

[Laughter]

>> I wanna tell you a little bit about our first speaker in the fall before we get started. Our first speaker is scheduled for September 8th, and it's Dr. Matthew Crawford. He received a Ph.D. in Political Philosophy from the University of Chicago and he owns a motorcycle repair shop and is the author of the book Shop Class as Soulcraft: An Inquiry into the Value of Work. If you would like to hear rather than see what he is thinking, please join us in September 8th. For more information about the Caroline Werner Gannet Series, you can visit our website at cwgp.org and you can get information there about past and future speakers. There you will find links to additional information about all of our speakers including links to WXXI interviews and announcements regarding next year's speakers. Now, please help me welcome Dr. Christopher deCharms as he tells us to imagine your own brain with real-time fMRI while seeing you're imagining. Imagine that.

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[Laughter]

[Applause]

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>> Thanks so much. Introduced--introduction suitable for Paris Hilton, it sounded like with all the media. So it's great to be here and thanks very much to the organizers, especially to Mary Lynn Broe for making this possible. And it's great for me to have the opportunity to talk to you about something that I'm really passionate about. I'm gonna go back to my childhood to start. I remember when I was very young, I saw a film. Some of you may have seen it as well. It was terrifying to me at the time. Let's see. I don't seem to have a pointer on here. Uh-oh. The video is always the toughest part. There we go. That was a film about what it would take to go inside the human body and, ultimately, inside the human brain. It was at the time a conceptualization that may have originated from our quest for going within. So you may remember Fantastic Voyage. You take the spaceship, you shrink it down, you inject it into the bloodstream. It's terribly dangerous especially if you're the guest star. You don't want to be Raquel Welch in this feature. She gets coated in white blood cells in the vasculature. It's, you know, it's all very alarming. And I think it speaks to a fundamental human desire for exploration and exploration within. I live personally on the very western coast of the very western part of the very western state of the western edge of western exploration from Europe. I look out of my window while I'm having coffee in the

morning and see the Pacific Ocean which is where European western expansion essentially stopped. And our generation does not have a frontier to look outward to and try to explore in the way that many previous generations had. So, where might we go to explore? Well, I'd suggest one possibility is when we run out of terrestrial places to explore, we can start to explore the sea. This is a set of images that I took of a mom humped back in her calf in Polynesia a few months back. And I think it's worth noting that we have better clarity on the surface of Mars than we have on the surface of our own oceans right here on this planet. And so I think over the coming generations, maybe the second most interesting area of new exploration is gonna be to try to understand the oceans. I think that people are familiar with this one. Another thing that people think about a lot is taking our exploration off this planet and going into outer space asking what we'll find when we colonize new worlds. And this, I think, also has the potential to be the second most interesting area of human exploration over the coming generations because when we get there, who knows what life we might find. We may go to Mars, discover crazy new creatures. This one is actually in Tanzania. But what I wanna ask you to think about today, maybe even to experience, is the possibility of taking exploration inward and the possibility that the technologies that are now afforded to us are gonna allow us to explore what makes us who we are, allow us to explore the entire universe, which, of course, comes from within us and is all formed in our own experiences and I'm gonna tell you about technologies that are allowing us to do that today. So, where might we go? Well, these are some of the things that are created in your nervous system. These are some of the parts of who you are that reside in an organ between your ears largely and in its social context and societal context. So I'm gonna ask you to think about and consider what the possibilities are for exploration here, what it might be like if you could explore these things. Explore yourself. Explore what it would be to be you when these things are able to change and whether that might be the most fundamental kind of exploration we as species are gonna be making over the next coming generations that we're just starting to make today. If we can control our brain and its performance, what cannot be accomplished? Which of the diseases that plague about a third of our society, our society of humanity, would we not have the potential, the diseases of the brain, to treat in fundamentally new ways? These are diseases that impact almost everyone in this room through a close friend or family member as you know. The brain is fundamentally an organ of plasticity and change. That's why we have a nervous system so that we can evolve not only on an evolutionary timescale but on a human lifetime scale so that we can make new choices, learn new things, and become fundamentally different people tomorrow than we are today. That's the reason to have a nervous system. It's also the opportunity to change the one that we're born with, to be different people tomorrow than we are today. I want to show you an example of that. This is an example that I got on a bus kiosk on the way to one of these lectures. I absolutely loved it. It's from Business Week. I haven't seen the control group but I love the image. So for anybody who hasn't seen this image before, I'm going to permanently change your brain with it. As you look at this image, if you haven't seen it before, what do you see? Probably some modeled patterns. For anybody who's not seen this image, do you see anything jump out at you? Raise your hand if you see something jumping out. So a good number of people are getting it, but most, it looks like, are still not. Keep looking at it. If you haven't seen it before, try to see the image in this image. I'll show it to you in a moment. This is an example of your brain changing. Here is the image. It's a Dalmatian dog. You can also see some other features of the scene where the dog is sitting. I hope everybody can see now the head, the leg, the form of the dog. And the amazing thing, which has been well studied, is if I now go back to this

image, the dog is quite easy to see. So if I can get a raise of hands again. How many people now see it? Essentially, everybody, and the amazing thing is that if I show you this same image again in 20 years, and this has been studied in some detail, you will see it. Your nervous system has been fundamentally changed by this single trial learning. That's the promise of being able to change what your brain can do. It can change who you are. It changed what your experiences are. This is a simple example but I'm going to talk about the variety of things that reside within your brain and a series of evolving technologies including, ultimately, our own that I think are going to revolutionize the kinds of plasticity that we can produce and the kinds of people that we can fundamentally become.
^M00:10:10
>> In prior generations, there was a process of going out and exploring, of cartography. This is an early map of the world, of our physical environment, at a time when people didn't have good ideas about the borders. Things were pretty murky and the early explorers were out looking. They tried to find what was there. They tried to figure out what was possible on this planet. There's a new cartography that's been happening, and that's the cartography of this organ. The brain is about 2 percent of your body mass. It actually takes up about 20 percent of your body's energy to make your reality. In concert with your body, the rest of your nervous system and the society in which you live, this organ produces the entirety of everything you will every experience. Now, fortunately, this organ, about the size of a large grapefruit, fundamentally made of flesh, some people eat them both. How is that possible? How is it that possible that a piece of physical flesh like a grapefruit allows you to open your eyes and see this talk and understand what I'm saying, I hope? How is that possible? Well, the cartography of today is going into this organ and trying to understand how it's organized. Increasingly, it is hopefully color coded and numbered with the brain areas that perform different functions. Now, it may have been that the brain was a big complex organ where there is no rhyme or reason to where functions took place, but we've discovered increasingly over the 20th century that, in fact, there is a quite systematic set of maps and representations in the brain. No two people have the same brain. But just like most human faces share a lot of common features, generally, eyes, nose, and mouth in the same place, the brain is also like that. It's more similar across people than it is different. And so we can ask what functions happen in what areas. So vision for the most part takes part--place back here in the back of your head, movement and touch happens up here, hearing and receptive language, higher cognition, and there's an ongoing movement to try to increasingly accurately map how this structure works. Here's an example of receptive language from Groucho Marx. How do we understand this sentence? Turns out we use an area here largely in concert with others but an area that is dedicated to receptive language and understanding what it means. This is known because back in the 20th century and even the 19th, gunshot wounds were increasingly discovered in soldiers to produce language deficits when they hit this area of the brain. That was the state of the art at that time. Similarly, there's a part of the brain that's mapped for productive language. When you want to say this sentence, this is a part of your brain that is actively engaged. And the principle that I'm trying to lay out is that there is a systematic mapping of the way that the hardware that is your brain works. So the fundamental unit of hardware in the nervous system, as you probably know is the neuron. Here's an actual neuron. Here's a diagrammatic neuron. How do these little master widgets actually function? I'm gonna take you through a little bit of the logic there. One of the fundamental features of neurons is, of course, they represent, they transmit, and they transform information. In this case, this is

a neuron in the hand that takes information about tactile sensation. It transmits it up the arm into the spinal cord and into the brain. And the way these neurons are organized is very systematic. Neighboring parts of the skin are represented at neighboring parts of the brain just like a physical map of the world. California is always next to Nevada on the map because it's next to Nevada in the world. Similarly, neurons that have receptive fields that are next to each other on the finger are going to be connected to mapped locations that are next door to one another in the brain and this is true for tactile sensation. There's an entire map of your physical body. In fact, there are multiple maps of your physical body. It's also true of visual area. This area and that area in my visual field are adjacent to each other in my visual cortex. Also true of the auditory system. Different pitches on the piano are mapped next door to each other. This is a fundamental principle that allows us to understand the nervous system. This is what the map looks like. You can see its origin in evolution. This is where the different regions are co-localized and they form what's called a homunculus of sensation about here, one on each side of your brain. And, interestingly, as many of you probably know, these different brain regions represent different parts of the physical body and they don't do it in direct proportion to the size of the body. There's very little neural hardware that's dedicated to the center of your back. Why? Because you don't spend very much time or very much interest on receiving sensation from the center of your back. However, your fingertips and your tongue and lips receive a large amount of tactile information and, therefore, the system has evolved to dedicate the most processing power to those areas and this changes throughout your lifetime. As you choose what you do today, be careful who you listen to because your brain is listening as well. Your brain is changing. Your brain is reallocating its hardware resources to optimize the tasks that you're performing. If you use your fingers even more as a pianist, your brain will be correspondingly rewired. Again, this allows the possibility to be a different person tomorrow than you are today. This is an example of a topology of many visual areas, in this case in the primate, a monkey. The idea here is that visual input comes in obviously through your eyes. Starts out here in the thalamus, makes its way up to the primary visual cortex. This is neurons that are sensitive to very exquisite tiny details of visual information. It propagates its way up through this very complex hierarchy of multiple brain maps. Each one of these areas is a separate map of the visual world that represents different kinds of features. These neurons, for example, represent the color in your visual world. These neurons represent motion. Some of the neurons farther up here allow you to do things like allocate attention and intention and change where you want to look and what it is that you're therefore going to see. So, again, a fundamental principle for understanding the nervous system is that neurons have individual features that they represent in combination with distributed codes of many other neurons and that those features can become increasingly complex and thereby allow you to understand the reality in which you live, and these are changeable. So the question that gets a lot of airtime recently is whether consciousness can ever understand itself. I would put forward that this is a question much like a question from the 19th century about life. Where is the elan vital? Can we ever understand life? I would put forward that in another hundred years this question will have been subjected to the same kind of rigorous mechanistic analysis that life has been subjected to over the last century and, increasingly, will seem unrelevant because we will have come to understand what makes our own consciousness, what makes our own experience, and been able to learn how to change it. How does the brain represent information? Well, there are many theories but there are several codes that I think are increasingly clear. One is what's called intensity

coding. Like I told you when the neuron that responds to your fingertip is touched, the more you touch your fingertip, the more coding there is. More intense stimulus will produce a greater number of action potentials, a greater code in that neuron. There's also the question of where the signal is. This is spatial coding. I told you that the codes are mapped in space. That means when one part of the map is active, there is a signal that corresponds to that part of the physical body that's being touched, visual space that's being activated, auditory space, and even much more complex spaces. There are also more complex codes like temporal coding regarding how and what the nature of the signal in the nervous system might be. These are all derived from the fundamental unit of neuro coding which is for a single neuron, essentially, an all or nothing action potential code in most cases. It's essentially a binary signal. Another fundamental principle is that neurons look for features in particular ways. So I said that neurons look for features, how do they do it? Well, these are some neurons that are looking for contrast between a central region and a surrounding region. You can see if this surrounding region is inhibiting the center, then this is a neuron that's looking for an edge in space. If you line a whole series of these up, you'd get a detector for an edge, for a line. This is a neuron that responds quickly and then fades away. It's looking for an edge in time like when I say "pa", this neuron is gonna be responsive to the initial P sound.
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>> This neuron is gonna be responsive to the sustained vowel. So this is the way that the neurons are constructing your own virtual reality, if you will, simulation of the environment as well as your own conceptualization of what that environment means to you. As you know, this electrical code is fundamentally transmitted between the neurons using chemical bridges between the cells. One neuron releases a chemical within milliseconds or less, activates a downstream neuron and that's how these signals are propagated and of course, all of pharmacology and the drugs that have been the revolution of the 20th century act by replicating this process or enhancing it through that neurochemistry that most of you have probably learned about in high school and college biology. It's worth remembering that a hundred micrograms of many neurotransmitter related substances can completely change who you are. It can give you an experience of yourself unlike any other experience that you might have. It can change what it means to be you, what you care about, how you act, how you interact with other people. So, I just wanted to throw this one in because this is the one thing that people who aren't brain scientists know about the brain and that's that you only use about 10 percent of your brain. So where did that idea come from? It's a greatest red herring in all of neuroscience. That's like saying you only use 10 percent of your body. Where is the other 90 percent? I'm not sure, you know, I may not be using my full body to its fullest potential. In fact, I'm quite sure that I'm not but in a similar way there is not 90 percent of your brain sitting around waiting to be used. You're using all of it. You may not be using it to its fullest potential and that's part of what we're gonna talk about, but it's not sitting vacant. The place where this originated was some work by Lashley and associates in the '50s where they removed tissue from rats and then showed that the rats could still perform this very, very simple task and did in fact discovered that the brain is highly redundant and the rats can perform this task with large amounts of their brain absent. However, if you're not a 1950s rat trying to navigate this maze, I think it's a fair bet that you're using most of your brain, if not all of it. Sleep is an 8-hour mystery. What is it that we do there? Fundamental to life for most of us, not all of us actually. But what is it that's taking place during this 8-hour mystery? I wanted to start out with this introduction of

some of the fundamental concepts of the brain for those that may not be neuroscientists and now I wanna take us on a fantastic voyage into our own brain. So, I'm gonna ask everybody to stand up and we're gonna see what this thing can do. I'm gonna ask you to look inside yourself. We're gonna use introspection, the oldest piece of neuro technology, the oldest way for trying to understand what the brain is about. So, look around you. Get yourself comfortable so that you feel like you're, you know where you are. And now I'm gonna ask you all to close your eyes. No cheating. And to really start to notice something that you typically take for granted and that's what this brain of yours does for you and in fact, even what this concept of you that you have right in this moment is. So, I'm gonna be quiet for a moment and I'm gonna ask you to just talk to yourself. Say some things. Listen to yourself talk inside your own mind.
^M00:24:06
[Silence]
^M00:24:12
>> Where on earth is that coming from? Where is the you that's making the decision about what it is that you want to say? Where in this machine does that process start? The decision to know what to think about or what to say, where does that come from? Now, I'm gonna ask you to think about one of those not so positive thoughts first. I won't do this for too long. Don't worry. But think about one of those things that maybe somebody said to you that that made you feel badly or one of those things that you might have said to yourself that you wished were not true, an error that you made. Think about that for just a moment and let the feelings that you have in your body and your thoughts, let them come forward for a moment. Let yourself feel frustration it may right now. Let yourself feel whatever your emotional tone is. Where does that come from? Now, let's go on the other direction and look at the reaction of positive imagination. So, if you're a sports person or aspiring athlete, think about the sport that you like to play or would like to play. If you like to play basketball, imagine the turnaround slam dunk. If you like to play tennis, imagine the overhead smash. Really try to imagine yourself performing this. Feel it in your body. Imagine it happening. If you like to dance or aspire to be a dancer, imagine yourself dancing around the stage. Feel your body doing these things. How is this possible? How is it possible that your nervous system allows you to have this movie going on inside and what is your emotional tone now? How does it change? Do you feel the difference? Now, take your arms and move them in front of you in space. Feel proprioception happen. Feel the extent to which without your eyes open you can tell where your arms are. You can move them around. You can feel how they move. You can imagine where they are in space. You have a very detailed model of the entire room around you. Try to think about where I am on the stage relative to you. Try to think about the stage, the colors that you see. See if you can remember the people that are in front of you. Try to think about how far you are from the aisle. Think of the incredibly detailed model that you are creating in your mind of the world in which you live. These are only some of the things that the nervous system is of course doing for you all the time but we don't normally think about. Now, I'm gonna show you one of the miracles that the nervous system provides for you every morning when you wake up. When I ask you to, but not quite yet, I want you to really pay attention to what happens when you plug the screen back in and open your eyes. Really notice what takes place in the incredible glory that is our conscious experience of vision. Everybody ready? Open your eyes. Did anybody get a [inaudible]? Every morning I wake up and I try to see the world that way and remember the miracle that we can look out and see. Thanks. Let everybody sit down. I wanted to do that because we so often take for granted

what the nervous system is to us, what our brain provides and what the opportunities are if and when we are able to change its possibilities. That is the next section of the talk, which is the promise of neuro technology and fundamentally exploring and being able to change the world within us. There is a tremendous societal reason for this enterprise. This is the number of individuals afflicted by many of the major diseases of the nervous system. Many of these diseases like, for example, anxiety impacts about a third of individuals, third of the people in this room over the course of a lifetime. That means clinical anxiety sufficient to seek treatment. The nervous system is a precious organ to us but one that suffers many problems that can be devastating to a person and tragically often are. This is the U.S. economic burden of these diseases. As a comparison, the entire U.S. automotive market is about 300 billion dollars. These are huge societal impacts. Global pharmaceuticals, one of the leading 20th century modes of treatment that were developed, a huge industry. A large percentage of the population is of course aging and many of these diseases do as we know grow with age. So what are the technologies that would allow us to try to interface with the nervous system? Well, there are many and I've divided them into those for recording from the nervous system, broadly speaking, reading and those for writing. On the reading side, we can try to do this electrically and this has been the historical approach recording from single neurons, from arrays of neurons, we're using EEG from outside of the head. Increasingly, there are optical imaging methods which have the advantage that photons aren't destructive to the tissue that they're trying to record from.
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>> Unfortunately, the brain is very challenging which is why unlike many other organs, we have very limited information that allows us to diagnose and treat it. It is protected by a big hard box, by the blood-brain barrier. The structures are small. Neurons are microns in size, extremely fragile, almost gelatinous. The whole thing is shaking around on a scale hundreds of times larger than the individual elements. It's very difficult to record and I'd say, by the way, that that's one of the reasons that optical images are so promising for the future is that they are inherently nondestructive. There is also the question of writing into this system. Increasingly, I think, the 21st century is going to see more and more applications of deep brain stimulation and I will show some of those, trying to change what's happening in the brain by directly writing electrical signals into it as well as noninvasive methods. Some from today are transcranial magnetic stimulation and people are working with direct current stimulation as well. These are some of the technologies that are in use today. This is the bionic ear that you may remember from science fiction of a half generation ago. Today, more than 100,000 people have received real cochlear implants. These aren't hearing aids, this is a device that takes sound and directly stimulates the nervous system to restore hearing and in cases where this is successful, people may be able to understand, for example, speech over the phone, somebody who would otherwise have been profoundly deaf. So this is an example of a technology. Actually, my mentor Mike Merzenich was fundamental in developing for taking the interface of the nervous system and deriving fundamental benefit to human health. This is the example of deep brain stimulation. In this case, an electrode is implanted into the brain of a person. They wear around a device that is implanted, a device similar to a pacemaker. Wires run up and connect to device and that allows you, crudely today, but nonetheless, it allows you to directly stimulate areas of the brain and change their functions. So what does this do? You just saw an example for yourself of what the nervous system provides for you. What can happen if you

change its function? I've got a couple of patient videos to show you some examples.
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[Film Clip]
^M00:32:44
>> This is the kind of devastation you see from nervous system disease.
>> Two months ago, I had an operation on my brain on which they inserted two electrodes. The result has been complete healing regarding my dyskinesia.
>> Here is another example.
^M00:33:07
[Silence]
^M00:33:13
[Film Clip]
^M00:33:19
>> Before, he just use the device to turn the stimulator off magnetically. [Background film] This is what this person would otherwise be living with.
^M00:33:29
[Film Clip]
^M00:33:49
>> Now unfortunately, this kind of almost miracle cures certainly don't work for everyone. We're at the very early stages of trying to get these kinds of technologies to work. We're really just learning but I think that they point out the promise of being able to change what the nervous system does and how it functions. Another example that is being developed today is stimulation of the vagus nerve that is being used in severe epilepsy and depression, it's in trials. Another is robotic radiosurgery. For example, using this thing developed originally from an automotive robot, in fact, to deliver radiation to the brain to try to, today, destroy tumor tissue and potentially in the future, destroy unhealthy brain tissue, although that's still highly experimental at this point. There are also technologies for allowing precise navigation in the surgical suite because the brain is a very complex structure, allowing surgeons to remove the structures that they need and to spare critically the tissue that they are trying to avoid. There is a growing movement that I think we are going to be seeing over the coming decades and we already see products coming to market for directly targeting neuroplasticity through training so there are more conventional tools like broadly speaking, educational software. There are intermediate tools for remediating diseases like language learning impairment. Increasingly, there are games for things like trying to reverse aging and I think there is a whole category that is just getting developed to try to use neuroplasticity to change the processes that cause disease and to change the problems that result when disease takes hold in an individual, to see if the process of plasticity can be used in a positive way to reverse these changes. Again, we are very early in this process but I think it shows tremendous promise. So those are technologies that are largely already on the market. I'm gonna tell you now about some investigational technologies and then move into some of our own. So transcranial magnetic stimulation is a technology for using magnets outside of the head to stimulate neural structures inside of the head. This is a technology that has important clinical potential. Its primary challenge is that the spatial localization is quite poor and it's only today possible to stimulate, broadly speaking, surface structures for the most part. An area that people have longed to produce is a direct analog to the cochlear implant for vision which is to say a retinal implant. This is an area that there has been a great deal of working to try to directly implant or in some way stimulate the structures of the retina in the case of disease. There is also the question of trying to restore function in patients who don't have normal

connections to their periphery, for example, who've lost motor control and I'm gonna show you a video of a technology called BrainGate that's a technology for restoring motor function in humans. There's only been a very limited number of uses of this kind of technology and this is one example in a human.
>> Matthew Nagle was paralyzed from the neck down after being stabbed several years ago, but technology gave him hope. He was one of four testing BrainGate, a new technology where a chip is implanted in the brain that picks up electrical impulses. A computer then interprets those impulses as actions. The chip is implanted just beneath the patient's skull and is only a few millimeters square. Here is Matthew playing a computer game. He is not using a mouse or a joystick, rather he is thinking of where to move the dot. All thoughts are electrical impulses and after extensive research and testing, a computer has been trained to decode those impulses and create the corresponding actions.
>> Now close it.
>> Now close, nice, open [inaudible].
>> This is Matthew completing another task where he is controlling the green dot with his thoughts and trying to follow the red dot. At Boston's Museum of Science, BrainGate's creator talk about the technology and what he hopes it can do.
>> Actually, I'm going to talk about the technology. Again, my point isn't that this is available for primetime today. We're at the very early stages of this but I think that what we're going to see and the vision that I'm trying to impart is a vision where we are able to interface the nervous system and what this is going to make possible increasingly for successive generations in the way that exploring the earth has made possible things that they would have not found, that previous generations wouldn't have been able to even dream of. Lately, this is even becoming a pop culture. There are a number of EEG-based game technologies for trying to control computer games using EEG. I think it's worth pointing out that there are some real problems regarding the relative signal quality from this kind of technology but it's certainly something people are enjoying and having fun playing with. This is a real world prototype nanobot, a device from the Technion that would be put in to the bloodstream and ultimately manipulated in to the nervous system. This is a new technology for reversible modulation or stimulation of cortical function using ultrasound that a colleague is developing at Harvard MGH. Actually, a number of groups are working on this that would be a noninvasive spatially localized stimulation method since they're set up in rats.
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>> They're currently in animal studies trying to do this using something that's quite similar to a conventional ultrasound transducer. This is a result that I particularly wanted to stress from the Kamatani group in Japan at ATR. This is what you've mentioned in the introduction, this is mind reading. What you see here is a set of visual stimuli that were presented to a person while they were inside an MRI scanner. So this is what they saw on a screen, they saw one of these images at a time, or they saw another one. What these investigators then did is they took the data that they were able to measure from the person's brain using fMRI. And they asked using only what we've measured from the person's brain to what extent can we reconstruct what the person is seeing. In other words, to what extent can we read their vision, read their mind? To what extent can we guess or reproduce, or reconstruct, or decode the image that they're seeing in front of them without any other knowledge of what that image would be. And each one of these is a single example of one of those reconstructions. So for example, in this case, the person saw the N and this was a single reconstruction that they were able to make from the brain of what that person was experiencing. They were able to literally read out this N from the person's

brain. This down here is the average of multiple repetitions, and you can see the signal gets somewhat clearer. But I would argue that images like these represent the dawn of an era when we can actually read the brain and the mind that goes with it. So now I'm gonna talk about some of our technology for brain reading and for controlling the functions of the brain. So, brain imaging like the data that you just saw has up until recently suffered from a real problem. And that's that it took hours, days, weeks, even months of pain-staking effort of a team of post docs to go off and crunch the numbers to produce images like the one that I just saw. Ultimately, produce pictures like these that you hope to send off to the journals and put on your wall. This has been pretty prevalent in the press. I think that most everyone here has probably seen this. I can't hardly go to an economics lecture anymore without hearing about the brain and the limbic system. But the fundamental limitation has been the amount of time that it's taken to produce these images. So what we've done, and this is the core of our own work, is that we've compressed these down from days into milliseconds so that you can read out the pattern of activation in the brain in real time. While someone is in the scanner, they can see what's happening in their own brain as its happening and that allows you to do fundamentally new things. We believe that this has a potential to offer an alternative to the prior ways of changing brain functions which were the couch, pills or the knife. And we're trying to develop technologies for turning these patterns of brain activation and whole brain models of brain activation into methods for treating patients. So for example, we select brain regions that we want to control in a chronic pain patient here. We then show the patient these channels of brain activation that correspond to their own experience of chronic pain. And we ask whether they can learn to take control of the very processes, the very pathways in their brain that are producing their pain experience. We showed them their brain, we showed them an image like this that corresponds to our reconstruction of their pain. And we try to ask whether they can learn, instead of being the victim of pain, to be the person who controls it, who controls their own nervous system. And thereby whether they can make their pain go away and hopefully, through neuro plasticity, fundamentally change the processes that produced the pain in the first place in an enduring fashion. That's our primary goal. So what does this mean in the broader human context? Well, for millennia, people of course have wanted to understand the mind brain interface, they wanted to understand exactly what you just saw. How is it that when I open my eyes and I see the world around me that can come from a piece of meat the size of grapefruit? How can that be? Descartes used introspection, imagine his glee if he could have looked inside his own brain during his experience. Well, that's what we're doing today. While you're inside the scanner you can have your own subjective experience. And in the same moment you can look at complex images like the ones I was just showing you of what's going on in your own brain second by second. You can try to learn how to understand it, do experiments on yourself. And ultimately you can try to learn how to control it, how to do things that you fundamentally can't do today. If I asked you to control activation in a particular area of your brain, you have no idea how to start because you don't even know what you're doing there. Much of what we learn we learn through mimicry. When you want to learn the backswing of a tennis stroke, you learn it from mimicking your buddy, you brother, your coach. That's how we learn so much. Imagine the possibility of being able to first of all see your own patterns of brain activation in the hundreds of brain areas that you have and see the pattern of a training example. See an expert's pattern of brain activation, and then learn through successive approximation through mimicry, to produce the pattern of brain activation that you seek. That's what we see as the promise of being able, part of the promise of being able to look inside the brain in real time. You can target your manipulation based on what you see there. So I think I've got here an example of what the anatomical fly in looks like. This is the modern day update of the Fantastic Voyage. This is my colleague Peter's brain, this is what we do with MRI, we can literally fly in to the structure and see the anatomy, but more interestingly, we can see the physiology. That's the spot in Peter's brain that lights up when Peter moves his hand, and we can do that in real time. So Peter can see this taking place and Peter can ask questions like what happens if I try to control this activation. What if Peter wanted to try to increase that activation or move it to a different area, or treat disease, for example, if Peter had a stroke right here, god forbid. This technology potentially allows the possibility to try to change the pattern of activation that we see. So imagine if you're a clinician or if you work with a clinician what this means. This is a colleague who is a clinical therapist working with someone while they're inside the scanner. This is the first real-time brain imaging augmented psychotherapy. So that while inside the scanner I'll be at a difficult scenario for psychotherapy. Both the patient and the treating physician can see what's happening inside the brain in real time. So the project of therapy, which is of course to understand and change ultimately what's happening in cognition and experience, and presumably ultimately in the brain, can be seen as it unfolds. This is what some of the software that we use to do this looks like on some of our monitors. You can pick brain regions, select targets, display the data in a whole variety of ways, essentially reproduce the offline fMRI analysis again in real time. We've also then taken a data and constructed elaborate representations that are more meaningful to patients. So, patients don't often like to look at squiggly graphs 'cause they're not scientists. They like to look at things often that are more representative to them. So, for example, in pain patients we take a signal from areas of the brain, in this case three areas, that are part of the pain matrix that produces pain and it allows for pain control and we show them as virtual reality fires on a beach and the subjects are then able to relate to that and try to learn how to use cognitive strategies to control the level of fire that they see and thereby control their own brain activation and ultimately their own pain. So, can this actually be used in clinically important areas? That's what we're in clinical trials doing today. Unfortunately, I don't have the results of those trials for you today. They're ongoing but let me show you an example of how we do it and these are published results for those that are interested.

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>> We've picked an area here called the rostral anterior cingulate cortex, a brain area that's for some length of time been known to be involved in chronic pain. We target this brain region. We can also target complex patterns of brain activation. We show the subjects either of this squiggly line of the activation level in that brain region or something that looks more like this fire that gets bigger when the activation goes up or smaller when the activation goes down. We train them over a repeated period of cycles to try to learn how to take control for themselves to flex their brain, be able to make this brain region volitionally go up and go down. Then we ask the following question, if a subject turns the brain region that produces pain down, does the pain itself go down? If they turn the brain region that produces pain up, does the pain itself go up? And in order to do that in healthy subjects we actually apply a painful stimulus. We use a heat stimulus on the hand of the subject, I've been a subject, it hurts and we ask does it hurt differently when you take control of the system. So, we're not doing a normal fMRI experiment here where you apply a stimulus and you see what lights up in the brain. Instead, we are asking if you take control of your own brain, what does that do to your experience. So, the

first step in that is to ask for the first time, it was never a technology previously available that would allow you to ask such a thing, can people even do it? Can people take control over a spatially localized area of the brain? And the answer is yes. The area that we targeted is here in red and this is showing the difference in their ability to control every area of the brain before training versus after and what you see is that the largest increase in the entire forebrain takes place in the area that we had targeted. You also see as you would expect that other related regions of the pain matrix are also activated by this task because the brain is a complex cognitive structure and they're using this whole system, not just the region that we're targeting. Nonetheless, it was a very selective effect. This was the region that showed the greatest increased. We did this once comparing the start and the end of training, this is in a follow on reproduction after training where you can see we again got a very, very similar patterns. We're pretty convinced that this is reproducible. So, over the course of training, what does this look like? Let me show you a little bit of hard data. This is at the outset of training. People are pretty bad at it. Now given the cognitive strategies that we started them off with, it's already possible to produce some amount of modulation of this brain area by using the cognitive strategies. This is what you can do simply by instructing the patient. But over the course of training, you can see that there's a monotonic and statistically significant increase in their ability to control the brain signal. And that this is reproducible in a test run that we give them after training. So that says people can learn how to produce activation in particular targeted regions of their own brain. Never do that before because we didn't have a way to measure it. Now, the real question is when they do this, what happens to their pain experience? This is no longer a measure of brain activation. This is a measure of their pain experience and the extent to which they have control over it, specifically. The difference in their pain that they rate psychophysically between the increased period and the decreased period and what this says is that at the outset the pain hurts just about the same in these two periods as you would expect 'cause it's the exact same stimulus every time. So when you presented during the increased period, presented during the decreased period, they give it the same rating. There's no difference. But over the course of training as they learn how to control this brain region, when the brain region goes up, the pain goes up. When the brain region goes down the pain goes down and there is a corresponding change in their pain experience that very closely mirrors what we see and they see in their brain activation. So, we hope that this is a first glimmer of the fact that through changing your own brain's activation, you can change your experience. You can change something as fundamental as pain. We did a whole variety of control groups that I won't take you through into much detail but just to point out that we wanted to make sure that this was a specific effect of the real-time fMRI brain signal. So this is the experimental group that I already told you about that showed a significant improvement in their pain ratings. This is the first control group who received training in attention only. This is the second control group who received essentially identical training to the first one but in the absence of real-time fMRI signal. This is the third control group who received real-time fMRI and a scanner and identical instructions and they were blind to this but we showed them activation from essentially the wrong brain region, a brain region not specifically involved in pain to make sure that any of the variety of placebo effects are non-specific. Physiological effects are not leading to this. This is a yoked control group. We got a little crafty here. We took the brain activation from one subject in the experimental group and showed it to another subject who are in the control group but they thought it was coming from their own brain. In other words, any expectation that they would have had that the pain would change because of what they saw on the screen was identical, literally identical to what a previous experimental subject had seen and yet in all four of these control groups, there was no statistically significant change from zero. They bounced around a little bit and all four are significantly different from the experimental group. We also measured--'cause I don't have the slide--but we measured their affect in response to the pain. How unpleasant the pain was as in addition to how intense and we saw a very similar pattern. The experimental group showed a significant change. None of the other four control groups did. So as a wrap up, I wanna leave you with this thought for the future. What's it gonna mean for humanity as we start to be able to go inside our own nervous system, go inside the organ that produces all of our experience and change what we find there through all of the technologies that I've talked about but with respect to our own, asking the question to what extent can someone go to a brain state that they've never been to before? To what extent can a person go to a place in their own mind in their own nervous system where they've never been? And when they get there, what is that experience like? How can that change them as a person and what are they capable of achieving? Thanks very much.

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[Applause]

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>> And I would love to entertain questions.

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[Inaudible Question]

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>> We have not. A question that I'm often asked whether we have done this in professional meditators or yogis, we have not yet done that although it's a fascinating question partly because I'm not sure that they in comparison to other types of specialists are or are not going to be in a privileged position to be able to control this particular signal. The brain of course has hundreds, even thousands of different brain regions with particular functions. If you take a pianist, they're gonna be very good at controlling their motor cortex areas to do with rhythm and so forth. If you take a mathematician, they're of course gonna be good at controlling those parts of their brain. It's possible that a meditator or a yogi is gonna have unique abilities to control more complex patterns of their brain or more fundamental ones. But I think it's also possible that other kinds of specialist in other areas are each going to be able to control the area that they are a specialist in. To directly answer your question, however, we've not yet explored that in detail.

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[Inaudible Question]

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>> So we have looked at training the somatosensory cortex. In fact, we were just doing a bit of that last week that the first paper that week for publishing this was in the somatomotor system broadly. It does turn out that people can control that region. We've not yet been able to systematically dissect which brain regions would have what impact on pain. We're of course looking at that and we're also looking at patterns of activation. From the data that we've seen to date, my belief is that this interconnected network of brain regions in some sense functions together. And so our hope is that as we choose one node in this network and a person learns to control it, they're in fact doing that by controlling the entire network.

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>> Now that's speculation today but that's why we have hope that we may be able to impact the entire pain network even though we're not necessarily training every single spot within it.
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[Inaudible Remarks]
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>> Okay, so if I understand the question, it was about some of the technical aspects of fMRI and how we're able to perform this training given the many types of noise that there are in the fMRI signal. For example, drift, physiological noise, subject motion and so forth, and these are all limitations that we have to face. Ultimately, of course, we hope as technology develops, this will be overcome. The way that we overcome them today is by correcting them as well as we can. So the issue of head motion we correct both by trying to get very precise re-registration of the subjects from scan to scan so that we can pick the exact same spot each time even though the subject may have moved. We also use real-time motion correction so that if the subject moves during a scan, we can essentially maintain targeting of a very small structure. We both give the subjects instruction on how to try to minimize physiological noise like for example through respiration and changes in heart rate and we're increasingly working towards being able to directly correct for that and fundamentally, I think, the answer is that the fMRI signal that we're measuring has many limitations in its spatial and temporal scale, but it nonetheless seems to work and so as pragmatists, we're simultaneously working on trying to get the signal to be improved as many groups are but we're finding that even with the limitations of the current signal, people can use it successfully as a training signal and I think the grounds for optimism comes from matching the cognitive process that you want to train with the characteristics of the signal. If you wanted to use the fMRI signal which is relatively slowly modulating with very rapid motor control kinds of test, you would probably not succeed. So we are interested in finding tasks that will exploit the nature of the signal, that change over seconds or tens of seconds and thereby that we believe a subject will be able to learn using the signal even in the presence of its noise.
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[Inaudible Question]
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>> Yeah, so the challenge here is neurons code, as I was saying, on the timescale of milliseconds, at least certain parts of the code where we have a signal that is reading in the timescale of seconds. Essentially, it's integrating over a whole second or a few seconds and that's the signal that we read out and the reason that I think that this has potential to be successful is that we're ultimately training somebody on a correlate of their own cognitive experience. And if we choose a correlate of a cognitive experience that itself changes on a slow time scale, we don't necessarily need to look at the details of precise temporal coding because, for example, if you can only change your cognitive process every few seconds and some of the cognitive processes we look at, you may not even be able to change that quickly. The thing that the subject is learning to control is not changing on the timescale of milliseconds even though the neurons may be firing on that timescale. So again, we think that there is promise here because we've chosen processes that can be read out on the slower timescale of fMRI and in that sense, we use the fMRI signal to average for us the neuronal signal over thousands of milliseconds, maybe over a few seconds, and we allow the technique to do the very averaging that we would probably have to do as the first step where we able to measure the individual action potentials of neurons anyway since we are trying to train a subject to control something that changes on the order of seconds.

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[Inaudible Question]
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>> I'm not sure I completely got the question. Can you try to come at that in a different direction? I want to make sure I can answer it clearly.
>> Okay. I believe with the mapping [inaudible] to activity of the brain area is not one by one projection. So different experiment or condition may correspond to one brain stage, so how do you divide this stage?
>> So this is a very subtle and complex question. The brain is, of course, very complex and the activation in a particular area does not, as you say, have a one-to-one correspondence with a particular task. Brain region like the one that we're interested in that I mentioned the data for like the rostral anterior cingulated is actually involved in many, many different tasks and so you could ask well, how is it that by training this brain state you would produce the result on the desired task instead of on some other tasks and I think that the way that you can hope to do that is by putting together what we think are the two fundamental elements needed to make this succeed. One is the one that I've already talked about a lot which is the brain signal from the structure or structures that you're interested in but the other is appropriate cognitive training instructions that are gonna allow the subject to use viable strategies that you hypothesize are going to have the specific function and result that you're interested in. So, taking the example of rostral anterior cingulated, there are other kinds of strategies that the subject could employ that would very likely activate the structure that would have nothing to do with pain because the mapping is not one to one. So we believe that it's the interplay between the signal that the subject gets when they perform particular strategies that are related to the brain state and behavioral state that you're interested in, that that combination is what allows you to produce the successful outcome that you're looking for.
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[Inaudible Question]
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>> We have not looked at [inaudible]. There are literally dozens and probably hundreds of different kinds of clinical applications and development applications of which that I guess would be one that we have just simply not have time to look at and so we're again at the very early stage. So the short answer is no and the broader answer is what we see is a long progression of trying to use this technique and later techniques that will develop to understand and be able to look inside the organ of the brain as each of these different kinds of therapeutic and development based modalities gets used so that hopefully, we can learn how to improve them and understand their mechanisms while they're being used.
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[Inaudible Question]
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>> So the question is--I'm not sure if everyone could hear it, was if you train somebody in the context of pain to suppress activation in one area, is it just gonna pop up somewhere else? And of course we don't know the answer to that question today. But our hope is that in fact experience-dependent plasticity can suppress activation and I don't think there's compelling evidence that it necessarily does pop up somewhere else. If you look at areas that show decreased mapped real as data as it were when you don't engage in a task for example. They don't necessarily, I don't think pop up somewhere else. The fact that you don't have very much area dedicated to the center of your back, as I was mentioning in the somatomotor map, I don't think implies that that space is

showing up somewhere else. I think the implication is that when you don't engage a particular brain area, the processing hardware simply diminishes. And so I don't think that there would be too much concern that if you can decrease the activation, for example, in the areas of the pain matrix that it's going to reemerge somewhere else. I suppose it would be possible. But I guess I would say I'm optimistic that you would simply be able to take the person who went along the path of becoming a chronic pain patient and turn them into someone who's not. Because an interesting fact is that many patients who have seemingly identical or very similar injuries, you may have two patients, one of them in six months is well. The other one, six months later is still in chronic pain and may be in chronic pain for the rest of their life. I think there's a very real hypothesis that what's happened here is that plasticity in the chronic pain individual has worn through as it were connections in the nervous system which are maintained that continue to produce the chronic pain, which is no longer serving them. Chronic pain is almost by definition no longer serving a positive function. It's just destroying the person's life and if you could decrease the activation in that system and/or channel it in towards, into more positive patterns of activation, we hope that you could turn that chronic pain patient into a person more like the person who no longer experiences their chronic pain. And it's possible again that the difference between the two in the first place may have been that for whatever reason, the person who didn't end up with chronic pain started with the nervous system or built a nervous system through their own experience. That allowed them to figure out what strategies would allow them to overcome the pain. So that it didn't get stronger and stronger, it got weaker and weaker. And our hope is that we might be able to use direct knowledge of what's happening in the brain to teach somebody else that trick.
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[Silence]
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>> Okay, I lost my voice so much. What if you overwrite part of the brain? Like you're saying that you want to redirect the pain sensors or wherever they may be feeling it. But what if they redirect it to some other area of their brain and then they overwrite what was there. Is that possible or would that, or wherever they have redirected that to would that just adopt and host both functions, or what would happen with that?
>> So I think that question is similar. Again, to date we are not trying to train people, certainly not the pain patients, to move activation from one place to another. We're trying to get them to either produce or inhibit particular patterns of brain activation. So we don't think, we don't have yet, I think, data to suggest a reason to believe that we're moving the activation someplace else and thereby overwriting potentially some other function. Now, there are cases where you might want to do that. So I brought up the example of stroke. It may be that in stroke where you've lost a substantial portion of neural tissue, you actually would want to take the functions that were represented in the tissue that was lost and put them into other neural real estate because the nervous system does have the capacity for redundancy. And it's entirely possible that that place where you've put them, that other brain tissue might be able to accomplish both functions. Or at least partially allow you to accomplish the task that you might no longer be able to accomplish if you were a stroke victim. So for example, if you had a stroke and were no longer able to use precise motor control on one side, perhaps you can get the surrounding tissue around the area of the stroke to allow you to regain that function, perhaps even the tissue on the other side of the brain. Similarly for language, it may be that other tissue can take over the function that has been lost. So I think there's a positive side of the issue that you raised and it may be that by

imaging the brain in real time in individual subjects, it's possible to facilitate this process that data suggests is already going on during the process of recovery from stroke normally.
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[Inaudible Question]
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>> So the philosophy of mind is of course a very complex subject. I'm not a philosopher, I'm a pragmatist. And so my view is that I get in the scanner and I do think it's of course fascinating to be able to see the physical substrates taking place in real time and potentially change them. And if I can do that then I would say, well never mind about the philosophy. And I don't mean to put that very fundamental philosophical question to the side, but just to say that's not our area of specialization. I think that I'd be eager to have already been talking to a lot of philosophers who find what we're doing fascinating, but that's not our primary goal. Our primary goal is very pragmatic. And it may be that having a clear understanding of mind is important to the pragmatism. But so far, we're mostly interested in trying to see the activation and allow us to have an impact on experiential and behavioral consequences. And I think we've been able to avoid some of the hairiest depths of philosophical conundrum thus far and we'll keep trying.
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[Inaudible Question]
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>> Yeah, that's again a very complex subject. There are obviously important differences between individuals. It's not clear that you would necessarily want one person's brain to function in the same way as another. There are many complex questions, for example, what if you took two people who are of different gender. What if you took the normal differences in mapping between a left-handed person and a right-handed person, the many types of variability between different brains that are what makes us all ourselves. What does it mean even to take the pattern of activation from one person's brain and try to get someone else to mimic it?
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>> There are many complicated issues here. However, I would fall back to the view that in many ways the brains of different people are similar. No people--no two people have the same backswing on a tennis court but you can learn from others. And I believe that similarly, we'll be able to use the similarities in different people's brains, and we already are, to meaningfully train one individual to benefit from what we know about the brain either of a particular prior individual or from a large population of people from which we've aggregated to gather data, for example, about which brain regions you want to have active and which ones you might not want to have active.
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[Inaudible Question]
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>> Sure. So I'm volunteer number 1. I think the most exciting seat in the house is, of course, within the scanner. Being in the cockpit and trying to fly your own virtual reality simulator while you watch it functioning is, of course, the most fun seat of all. We recruit from a variety of sources. We recruit from the local community. We get healthy controls, Stanford undergrads, some of them people that work in the community. We recruit disease populations either through working with clinical collaborators or increasingly, again, just through advertisements in the local media. And they are typically people--in fact, we look for those who are highly motivate, who are cognitively high functioning. This is a technique that's more like going to the gym than taking a diet pill.

So we need people who are gonna be active and engaged and want to succeed and, typically, not surprisingly, people who are interested in understanding their own mind and learning how to control it.
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[Inaudible Question]
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>> So what is the limit of the spatial resolution of imaging? Boy, there'd be many ways to approach that question. I think you could approach it from the perspective of current technology--
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[Inaudible Question]
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>> You know, I think it's very difficult to say. So there's a number of groups that are working and, you know, I think there's every reason to be optimistic that over the coming decades there are gonna be better and better techniques for better and better spatial resolution and I would feel a pretty high degree of confidence that as we understand the brain better and we are able to image it at more precise resolution, there are gonna be things that we can do that you can't do today. For example, I think it's pretty remarkable to see the letter N that I showed you that they were able to read out, but of course, that's nothing like the spatial resolution that I see when I look before me. And as our ability to read out the nervous system becomes more and more precise, we may be able to do things like read out individual memories at this kind of fidelity that may one day be possible. And presumably, there will be a commensurate increase in the ability to train subjects to both understand their own nervous system and to control it. The rate limiting step that's inherent in a technique that we're using is that it is fundamentally based on changes in blood flow and so that has a--its physiological limit both spatially and temporally, which is in a sense more fundamental than the technological limit. But again, I think that those are probably limitations of today, not limitations that are gonna be around for the long term.
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[Inaudible Question]
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>> So we believe there--
[Inaudible Question]
>> Both. So, in some of our successful patients, they report both things, like the two examples. There was one woman who said I used to wake up in the middle of the night and I would have shooting back pain and I would have to go and take my pain meds. What I now do is I lie in bed, I use the cognitive strategy that you taught me that I learned myself, and I know how I can bring my pain back down without going and using my meds. That's one example. The other example is that we hope that the brain being a plastic organ can change and that through repeated exercise you can bring your pain down even when you're not actively engaged in trying to control it. Just like when you walk out of the gym, you may still be stronger. We hope that the changes in your brain may lead to enduring decreases in chronic pain even when you're not actively engaged in cognitive tasks. And we've seen that in example subjects as well. And, of course, we're in the midst of clinical trials to see the extent to which those example subjects are replicated across groups.
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[Inaudible Question]
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>> So there is a question of wanting to change pain and then there's a question of whether you want to wanna change pain.

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[Inaudible Question]
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>> We've not tried to do that. I think it's a very interesting question. I think in many patients, for example, chronic pain patients they have important secondary gain from being chronic pain patients. Like, for example, their livelihood in some cases, their emotional support network, their sense of self. So many people have important profound reasons that they may not want to get over their pain or some parts of them may not want to get over their pain. And it is possible that we could try to use neuro imaging as a tool to understand how that aspect differs in different people. To date, we've not tried to do that. We've tried to select patients who are highly motivated to get over their chronic pain. But I think it's an interesting question that would be something that you could potentially try to explore in the future, although, quite complex cognitively I would point out.
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[Inaudible Question]
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>> I think that that's a fascinating question and in a sense, the question is whether we can become aware of parts of ourselves that we are not aware of today, and that's exactly what the technology is giving us. By definition, things that are in our unconscious, we are not conscious of and this technology allows us to potentially look inside and probe those processes and bring them into consciousness and that's how they have the potential for us to be able to both understand ourselves and change ourselves. So, yes, I think that the, in a sense, almost by definition, this is a technology that allows us to look at the parts of ourselves that we do not currently have access to and have the potential to thereby be able to come to understand ourselves in fundamentally new ways and potentially change who we are in fundamentally new ways as well.
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[Inaudible Question]
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>> It's quite difficult to put into words our cognitive strategies for controlling brain activation and I think that is similar to trying to put into words most cognitive processes. I really like raspberries. Why is that? Well, you know, they are kind of sweet and they're kind of, I don't know, juicy and a little tangy. But can I really bring that experience of a raspberry down into a way that I could convey it to you that you meaningfully understand why it is, what--that I like raspberries, what my cognitive process is. It's extremely difficult and extremely important because if we could teach people how to replicate a cognitive process without needing the fMRI scanner, we could and perhaps one day we'll be able to impact large numbers of people with a lot less technology. But I think what I would say to answer your question directly is it's very difficult for me to meaningfully put in to words the kinds of cognitive strategies that I use to try to control my pain. I would say things like I tried to focus on it in such a way that I experienced it as being tactile in nature and not harmful. But that's really only sort of the beginning because that's what I was doing when I started as well. So I think to date, again, you need this potent combination of strategies that you can verbalize or instantiate into tasks to give subjects a start paired with the brain signal that allows them to shape what they do and to discover for themselves in their own nervous system what strategies will allow them to control their processes of mind.
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[Inaudible Remark]
^M01:32:05

[Applause]
>> Thanks very much.