Guest lecture: Jeneva Cronin

[00:00:00.24] Hi, I'm Jeneva Cronin. I'm getting my PhD in bioengineering and all of my research focuses on neural engineering. And in today's video I'll talk about stimulation for somatosensory restoration.

[00:00:14.25] So you've already talked about brain-computer interfaces but just as a quick review-- in the bottom left you can see different layers of the brain. A brain-computer interface is the device that records those brain signals, sends them to a computer to decode the signals, and create some type of control signal which it can send to an end effector, which could be something like a prosthetic.

[00:00:35.28] Typically, a user in a brain-computer interface would receive some type of external feedback in the form of visual or audio cues, however, there's also a need for somatosensory feedback. Somatosensory sensations include tactile sensations-- the sensations you get when you touch something-- and proprioception sensations, which are the sensations that you experience when you know where your body or your limbs are in space, even if you're not touching anything.

[00:01:06.42] In the US, there are 2 million people living with the loss of a limb and there are 5 and 1/2 million Americans that are paralyzed to some degree. In a 2014 study, quadriplegics ranked their priorities in gaining arm and hand function back. Paraplegics ranked regaining sexual function the highest and both groups ranked regaining bladder and bowel control very highly. What's similar amongst all of these priorities is that we'll need to restore somatic sensation-- or that tactile sensation-- so that people can feel what they're touching or get internal signals, like needing to use the restroom.

[00:01:47.42] So how can we restore somatosensory feedback in a brain-computer interface? This is where we get into the idea of a bi-directional brain-computer interface which not only decodes the signal, but it also gets some kind of state awareness of that end effector-- like a prosthetic, for example.

[00:02:03.59] So the computer can encode sensory feedback in the form of stimulation for the brain or any part of the nervous system. And in that way, you've created a Bi-directional Brain-Computer Interface-- or a BBCI-- which both decodes motor signals, in order to control some end effector-- like the prosthetic-- and then re-encodes somatosensory feedback so that the user has an idea of what that end effector is doing. And they could still receive the external feedback in the form of visual or audio cues. Many users will also have external feedback in the form of visual cues if they have a typically functioning visual system.

[00:02:46.29] So as a quick review of the somatosensory pathway. You've already discussed this in other videos, but there are-- on the left hand side, you can see that there are four different types of mechanoreceptors. They have different receptive fields and different response types so they respond differently temporally, meaning their timing of their response is different. Those signals travel from the mechanoreceptors-- and there are a lot of those in your fingertips-- to your spinal cord, up through spinal cord, they cross from one side of the cord to the other side in your brainstem-- specifically in the medulla-- and then they continue traveling up the brainstem, through the thalamus, into your cortical sensory areas.

[00:03:26.94] In the primary sensory cortex, that somatosensory information that's traveled up from those mechanoreceptors, your fingertips, or any other part of your body is represented spatially. So your hands are represented in one area, your face is represented another area, your arms, your legs, they're all represented spatially based on the body part that they came from.

[00:03:49.27] We can also describe the spatial resolution of tactile sensations using something called a two-point discrimination threshold. So you can see at the top of this chart, fingers have very low two-point discrimination thresholds. Meaning in the x-axis you see the mean threshold, or millimeters, and that's how far apart two points have to be for a user or subject to experience those two points touching-- their body touching their fingertips, for example-- as separate points and not as one point.

[00:04:22.47] So the fifth finger, for example, has a two-point discrimination-- reading from this graph-- of about maybe 5 millimeters. That means that the two points can be separated by 5 millimeters and they can tell them apart. If they come closer together-- say that those points are separated by only a millimeter or less-- they would probably experience it as a single point touching their hand and not two points.

[00:04:47.61] You can see that the back has a very high two-point discrimination threshold, meaning that it's mean threshold of separation between those two points has to be much higher-- in the range of 35 to over 40 millimeters separation-- for the subject to experience them as two different points. This is important to keep in mind because if we want to restore a somatosensation-- specifically in a hand prosthetic-- we're going to need to have a high spatial resolution. Meaning that the user could experience touch on one fingertip as distinct from touch on another fingertip, or distinct from touch on the palm of their hand, or perhaps even on the back of their hand.

[00:05:29.29] So let's go through some examples of sensory feedback in brain-computer interfaces that have been demonstrated in humans or in monkeys-- also known as non-human primates. We'll talk about two general feedback approaches-- one is peripheral approaches and the other is cortical approaches.

[00:05:47.24] So, peripherally, we can consider restoring sensory feedback in two ways-- targeted muscle reinnervation and peripheral nerve stimulation. These are two methods that have been demonstrated in prior research and literature and they both interface with the peripheral nervous system. Cortical approaches will interface with the cortical nervous system. And we've demonstrated intracortical microstimulation and direct cortical stimulation so we'll go through those in more detail in a moment but first, let's start with peripheral approaches.

[00:06:22.52] To begin, we'll look at targeted muscle reinnervation. In Targeted Muscle Reinnervation-- or TMR-- a doctor or a surgeon removes the residual nerves that are left in an amputation. So even after an amputation, there are residual nerves running down to that end of that amputation. Those nerves can be redirected to grow into the chest area near the pec muscle.

[00:06:49.58] So those residual nerve endings are moved from the amputated arm into the pec muscle and then they eventually will reinnervate. And when a patient imagines moving or tries to move that arm that's been amputated, instead, they will have a response in those pec muscles. So if, for example, I'm imagining moving some part of my arm that's been amputated, I could instead have a muscle response in my pec muscle. Then, sensors that are placed on the pec muscle can pick up those electrical signals and use them to send some type of control signal to, say, a prosthetic.

[00:07:28.31] So in addition to being able to restore some degree of motor function with targeted muscle reinnervation, there have also been demonstrations of restoring some degrees of sensory feedback. So with the same idea of TMR, with the residual nerves reinnervate into a different muscle-- in this case, the pec muscle-- touching that area-- so touching the chest. And if an experimenter touches the subject's chest, that subject can experience a somatosensory sensation, like a tactile touch sensation, on their hand.

[00:08:02.44] And you can see on the graph on the right, those different colors represent either sensations that were localized either to the palmar side of the hand-- meaning the side with your palm; those are in red-- or to the dorsal side of the hand, which is the back side of your hand. The dark red and dark green colors are a strong sensation, whereas the lighter red and lighter green colors are more diffuse, or less intense sensation. And the dots on the chest show where the experimenter touched the subject's chest in order to get those sensations that localized to the hand. So again, even though the experimenter wasn't actually touching the subject's hand-- in fact, their hand has been amputated-- the experimenter is only touching the chest, the subject still localizes or perceives the sensation as if it's coming from their hand.

[00:08:58.13] Now look at peripheral nerve interfaces. In a peripheral nerve interface-- as demonstrated here-- you can have an electrode that wraps around the peripheral nerve. There are different shapes to these electrodes. You can see in the left side of the image, a kind of circular electrode cuff, on the middle part of the image, there's a flat electrode cuff. So these cuffs have different shapes but they all wrap around the nerves-- still that residual nerve that's heading towards a limb that has now been amputated-- and stimulating through those electrodes can elicit sensations.

[00:09:30.71] So you can see on the bottom left picture with the hand and the different colors, those are examples of stimulating different nerve endings out of the radial, ulnar, median nerves, creating sensations that are localized. And then, again, they're tactile sensations that are localized to that hand in those different areas.

[00:09:50.55] Using peripheral nerve interfaces, researchers have demonstrated that subject can improve their performance on different tasks. So here in the top pictures, you see a subject whose right hand is prosthetic, their left hand is still their intact arm, and his job, or his task, is to pick up each cherry and pluck the stem from the cherry. When there's no feedback-- that's in red, feedback off, meaning that the stimulation is not turned on-- he still has motor control of the prosthetic but there's no sensory feedback. You can see that he's squishing the cherry. On the top right hand side with the feedback on, which is in blue, you can see that he plucked the stem from the cherry without breaking it or squishing it.

[00:10:33.87] If you look at the bottom graph, which demonstrates his success rate or the percent of times that he successfully plucks the stem from the cherry without squishing the cherry, you can see in the dark red versus dark blue bars, dark red and dark blue are both blinded, meaning he's wearing a blindfold so he has no visual feedback. He's much more successful when the stimulation is turned on as represented by the dark blue bar.

[00:11:03.54] Even when he has visual feedback, which are in the sighted trials-- so the light red and the light blue bars-- you can still see that his sighted trial with the feedback on is a better performance than in the sighted trial with the feedback off. So that's saying that even with visual feedback, we still benefit from having our somatosensory feedback.

[00:11:23.88] Here's another example of a peripheral nerve interface. Again, you can see that it's improving performance. On the left hand side of this video-- so same subject both times-- on the left hand side of the video, the subject's stimulation is turned off, so he does have motor control of the prosthetic but he doesn't have the sensory feedback via the stimulation.

[00:11:42.90] On the right hand side, the stimulation is turned on. And at this point, he's moved a couple of blocks off the table onto the lower table, whereas when the stimulation's off, he's having trouble moving any of them. So, again, this just demonstrates that sensory feedback can improve subjects' performance on motor tasks.

[00:12:06.81] So we talked a little bit about peripheral approaches, including targeted muscle reinnervation and peripheral nerve stimulation. We can now look at cortical approaches, which will include intracortical microstimulation and direct cortical stimulation. Intracortical microstimulation penetrates the cortex, so you use small electrodes that penetrate the surface of the cortex. Direct cortical stimulation-- which we'll specifically talk about micro and macro-ECoG-- sit on the surface of the cortex. So they don't actually penetrate the cortex but they both are underneath the skin, the scalp, and skull.

[00:12:45.50] In sensory feedback through an ICMS device or intracortical microstimulation-- in the top left, again you can see that those intracortical microstimulation means the electrodes penetrate into the cortex. In the bottom left, we see another demonstration that sensory feedback can improve performance. So in this specific research, a non-human primate or monkey was supposed to search for a virtual object or a virtual target; it didn't know where that target was.

[00:13:14.79] In the control condition, the monkey got no feedback at all. In the sound condition, the monkey got auditory feedback. In the stimulation condition, the monkey got intracortical microstimulation feedback. And in the stim plus sound condition, the monkey got both stimulation and that auditory feedback.

[00:13:34.08] And you can see that in every case, the feedback-- the sound, the stim, or the stim plus sound-- they all do better than the control condition alone, meaning they all do better than having no feedback at all. And it's important that that stimulation alone-- whether it's with the sound or without the sound-- so the stimulation alone still does better than the control trial. And that suggests that continuing to research methods of sensory stimulation for feedback in these devices and in bi-directional brain-computer interfaces could work and could improve subjects' performance.

[00:14:07.66] On the bottom right hand side, this is a different research experiment where, again, a monkey with intracortical microelectrodes implanted is supposed to search for different targets. So you can see those three different targets-- they're represented as gray and black circles. One is the target and it's based on a different type of stimulation pattern so it should feel different to the monkey that's getting the intracortical microstimulation. One is the target, the other two are not correct and the monkey is able to search that space using the intracortical microstimulation and land on the correct target.

[00:14:41.75] And these researchers, in this case, demonstrated this both with the monkey using hand control-- as in he's moving that yellow joystick with his hand and receiving the ICMS as his sensory feedback-- and in another condition, the monkey is controlling the movement of the virtual hand on the screen using intracortical electrodes over the motor cortex. So those electrodes are decoding his movements, making the virtual hand move on the screen, and he's getting intracortical microstimulation as a feedback.

[00:15:14.32] In humans, one group has also demonstrated sensory feedback through intracortical microstimulation. There have been many examples of motor control with intracortical microstimulation but this is the first one using stimulation of the sensory cortex to provide sensory feedback. On the left hand side, you see the picture of a subject's hand where the different colors represent where stimulation through different electrodes on the middle column elicited sensations. So you can see that the electrodes in the middle column that are colored in purple elicited sensations on the index finger, whereas some of the orange electrodes that are in that middle column elicited sensations kind of at the bottom part of the pinky finger, or the little finger.

[00:16:01.11] The right hand side of this chart just demonstrates where those electrodes were placed in the subject's brain. And again, these are intracortical microelectrodes so they do penetrate the cortex.

[00:16:16.51] Index, ring, pinky, index, middle, middle, middle, ring, ring.

[00:16:44.91] On the next slide, I'll show you a video of this same subject completing a task in which the experimenter touches the fingers of a prosthetic and those fingers have sensors at the ends of them. So the sensors can pick up when the experimenter touches which finger, and then based on which sensor is activated, the computer decides which electrodes in the subject's brain to stimulate. You'll be able to see that when the experimenter touches, say, the middle finger. The subject can identify that the middle finger has been touched even though he's wearing a blindfold. So let's take a look at that.

[00:17:18.33] Index.

[00:17:20.81] As I mentioned, there have also been a number of demonstrations of using intracortical electrodes to decode movement. So in both of these videos, each woman has intracortical microelectrodes implanted in their motor cortex. Unlike the previous video that was using stimulation to stimulate the sensory cortex and elicit those sensory sensations-- like touch on a fingertip-- in this case, the subjects are imagining moving the prosthetic in a certain direction. The woman on the bottom left is trying to drink from a cup, the woman on the top right is trying to take a bite of a piece of chocolate, and those electrodes are decoding their motor intentions and using it to move those robotic arms.

[00:18:06.27] So we've just gone over intracortical microstimulation and intracortical electrodes for motor decoding in humans and non-human primates. Another method of a cortical approach to providing sensory feedback is electrocorticography. So electrocorticography electrodes sit on the surface of the cortex. They can be subdural or epidural depending on which layer of the dura they lay on. Primarily, my research deals with subdural electrodes. So they sit underneath the dura, right on the surface of the brain, and you can record through them or you can stimulate through them.

[00:18:39.84] When we stimulate through electrocorticography electrodes, we call it direct cortical stimulation because we're stimulating the surface of the cortex. On the bottom chart, you can see examples of ECoG electrodes implanted on the surface of the brain and then images that show where they are relative to the rest of the brain and the skull.

[00:19:01.08] There are different sizes of electrocorticography electrodes or electrocorticography grids. Oftentimes they're called micro-ECoG or macro-ECoG, depending on their size. Some specific sizing details are given on the left hand side of this slide, but what we want to focus on is just the difference in size. So on the right hand side images, you can see that the macro-ECoG electrodes are spaced further apart and they just cover a larger surface of the brain, whereas the micro-ECoG grid, those electrodes are spaced closer together and they cover a much smaller portion of the brain.

[00:19:37.71] In my research, which we'll talk about in a few minutes, we use macro-ECoG electrodes. In a different research study, which was published very recently, they used micro-ECoG stimulation.

[00:19:52.28] When we stimulate it through ECoG, we can do it in different ways. We can do a bipolar stimulation which uses two electrodes, and we stimulate both of them so you keep that current relatively focal in that area. You can also do what's called monopolar stimulation which stimulates just through one of those electrodes.

[00:20:10.69] And you can see an example of the bipolar simulation in the top figure with those two white electrodes just demonstrating that you could stimulate through both of those two electrodes. We often use what's called biphasic stimulation pulses, meaning they go in both a positive and a negative direction. So there's a positive current and a negative current, relative to a baseline level.

[00:20:32.41] The most important thing to note here is that there are a number of different parameters when it comes to this type of stimulation. We have the current amplitude, there's the pulse frequency-- or how quickly those pulses follow one another-- there's the pulse duration-- or the duration in time that each phase the pulse lasts for-- there's the train duration-- the length of time that the entire train takes-- and there's an inter-train interval. This picture is just a demonstration. Oftentimes in the research that I do, we use anywhere from 20, to 40, to 80 pulses per train duration; not just three as is shown here. But this is just for illustrative purposes.

[00:21:13.99] Let's take a look at what's been done in macro and micro-ECoG in humans. In macro-ECoG, a study published in 2013 demonstrated that subjects could differentiate the stimulation of the percepts-- meaning the sensations they experienced after stimulation-- using either the current amplitude or the frequency-- that pulse frequency. In the top graph, you can see-- in the top, excuse me, chart you can see the differences in frequency.

[00:21:43.39] So, for example, in the top yellow-colored line where the subject got the question or the task correct, the subject was able to tell that one direct cortical stimulation train using a frequency of 75 hertz was the same as another direct cortical stimulation train using a frequency of 75 hertz. Later in another trial-- another correct trial-- the subject could tell that the frequency of 75 hertz was less than the stimulation with a frequency of 100 hertz.

[00:22:14.49] There are similar differences when you change the current amplitude but most importantly here, subjects experienced these differences in frequencies or amplitude as a change in the intensity of the stimulation or a change in the intensity of the sensation, or the percept, that they experienced. The reason we're interested in studies like this and in how subjects can discriminate between different direct cortical stimulation waveforms is you can probably imagine that when we use our hands with intact tactile sensation to, say, pick up a cup or to brush our teeth, we get a lot of tactile feedback from our fingertips and from all parts of our hands.

[00:22:54.30] Picking up a water bottle feels different than touching a soft blanket and that feels differently than touching, say, sandpaper. So we have a lot of tactile experiences that are normal to our everyday lives and, ideally, we'd be able to encode different types of tactile sensations in a somatosensory feedback device for a bi-directional brain-computer interface. So we want to know how we can change the different stimulation waveform parameters, including current amplitude and pulse frequency as illustrated here, and how much we can change those different parameters so that subjects can experience unique sensations.

[00:23:35.01] In a recent study with micro-ECoG stimulation, a subject experienced sensations in different areas of his hand. This happens in macro-ECoG as well, but here we've illustrated the micro-ECoG study. You can see that on the left hand side, the electrodes are color coded-- so they're outlined in different colors.

[00:23:51.39] The electrodes outlined in red, labeled as P1, correspond to the P1 sensations and the blue is where the subject experienced a sensation. So those P1, outlined in red, sensations were experienced on all five fingers, whereas you can see the single-electrode, outlined in yellow and labeled as P4. And then on the right hand side of the slide, the subject experienced that sensation only on his little finger.

[00:24:21.54] So this demonstrates that by stimulating different micro-ECoG electrodes or macro-ECoG electrodes-- it works in both-- subjects can experience or localize the percept to different areas of their hand. They're feeling a sensation on their hand in the case of these last two studies I showed you because the experimenters are specifically targeting the hand sensory area and they're purposefully stimulating that hand sensory area to elicit sensations over their hand.

[00:24:53.69] So let's take a look at some research that I've done more recently. Even knowing that subjects can discriminate between different pulse frequencies and different current amplitudes, and knowing that it can localize these percepts or sensations to different areas on their hand-- depending on what electrodes you stimulate-- there is still a question of whether or not subjects could use Direct Cortical Stimulation-- or DCS-- as feedback in a task.

[00:25:20.31] So in this experiment, what we did was ask subjects to wear a glove-- and you can see that picture in the bottom right hand corner-- and this data glove could pick up different positions of their hand by measuring their joint angles. We asked subjects to move their hand in a grasping motion-- as if they are graphing a water bottle and then releasing it-- to find and follow a target hand position.

[00:25:41.66] There were three different states. The first state was their hand was too open, the second state was their hand was within the target position, and a third state was their hand was too closed. Our computer then encoded that sensory feedback in the form of different types of stimulation delivered to their hand sensory cortex.

[00:26:01.49] In the first state, which corresponded to the subject's hand being too open, the subject received no stimulation. That's shown in the light gray on the top of the graph on the left. When the subject's hand was within the target position-- shown in red here-- the subject received a low current amplitude stimulation. And if the subject's hand was too closed, they received a high current amplitude stimulation. And remember that low current amplitude stimulation is experienced as a less intense sensation than the high current amplitude stimulation.

[00:26:41.51] So in this case, most of the stimulation parameters were held constant except for the stimulation current amplitude, which was varied based on the position of the subject's hand. We can see here on the top graph, the blue line is a trace of the subject's hand opening and closing. The dashed lines, in a sort of sinusoidal shape, are the targets the subject is supposed to stay in and below that, the black vertical lines show the different levels of stimulation the subject's receiving.

[00:27:18.05] So when the subject's hand is too open or it's above that target area, there's no stimulation. There's a low intensity stimulation, or a low current amplitude stimulation, when the subject's hand is within the target and a higher current amplitude stimulation when the subject's hand is too closed or below that target, as illustrated in this graph. You can see by that blue trace, the subject's hand primarily stays within the target. This was their trial 9 and you can see their accuracy and how well their hand movements met kind of an ideal position or ideal hand movements which would have been demonstrated by this following just through the center of the target.

[00:27:59.42] Blue, in the accuracy in the r-squared performance, represent the subject's performance. Those orange bars represent a random chance. So if the subject was just performing this randomly, what would their chance level be of success of performance-- accuracy or r-squared? You see in both cases, the subject does better than just base chance.

[00:28:23.00] We can take a look at all the subjects trials together. In trials two through four, you can see that the subject received visual stimulation. We even see that in general, after trial 2, all of the trials the subject performs better than chance, except for the catch trial. So trial 10 was a catch trial, and in that trial subjects received the same current amplitude waveform during the entire trial, and that was independent of the state. So no matter where their hand was-- whether it was within the target, outside of the target, too opened or too closed-- the subject got the exact same stimulation feedback. You can see the performance drops.

[00:29:05.99] So researchers experimenters often include trials like this-- they're sometimes called catch trials, other times they're types of controls-- to demonstrate and try to weed out exactly how subjects are performing a task. The fact that the subject wasn't able to perform above chance during this catch trial suggests that the subject was using the direct cortical stimulation as feedback to complete the task. And that suggests that subjects may be able to, in the future, use direct cortical stimulation as feedback in motor tasks which is what we would want in a bi-directional brain-computer interface.

[00:29:46.25] Our lab has also completed research on the rubber hand illusion using direct cortical stimulation. So for a moment, let's just talk about the rubber hand illusion. Part of the rubber hand illusion is illustrated in that top figure.

[00:29:58.82] You can imagine yourself sitting on a table, your real right hand is placed behind a screen so that you can't see it, and a sheet or a towel is placed over your shoulder and over that screen so that you can really just cannot see your true right hand. A rubber hand that looks similar to your right hand is then placed in front of you but it's in front of the screen so you can see the rubber hand and you cannot see your real hand. If an experimenter then touches your real hand and the rubber hand at the same time, you'll get the visual cues from the rubber hand, you'll get the tactile cues from your real hand, and oftentimes many subjects, or users is in this experiment, start to feel a sense of ownership over the rubber hand. So even though the rubber hand is not their true real hand and their real hand is just behind the screen, they feel a sense of ownership over the rubber hand.

[00:30:58.55] We wanted to try this same illusion but rather than touching the real hand, we wanted to stimulate the subject's brain using direct cortical stimulation through those electrocorticography electrodes. So in this case, we used a digital touch probe-- that's shown in black-- to touch the rubber hand. And whenever it touched the rubber hand, it also triggered cortical stimulation through those ECoG electrodes.

[00:31:28.13] You can see by the bottom graph-- in the line that's colored in turquoise, which was the illusion condition-- the subject experienced the illusion and rated their ownership level at somewhere between plus one or plus three. And their ownership rating is them rating how much they agree with the statement, "It feels as if the rubber hand were my own hand."

[00:31:51.25] So in the illusion condition, the subject rates that ownership experience above zero, whereas in all of the controlled conditions-- which are all of the other conditions colored in black and white here-- the subject rates their ownership condition lower, below zero. This again suggests that direct cortical stimulation can elicit a sense of ownership over an artificial limb. We used a rubber hand here, but one can imagine that in the future, in a bi-directional brain-computer interface, if it used direct cortical stimulation through ECoG electrodes, subjects may experience that same sense of ownership over a prosthetic.

[00:32:32.48] So we've discussed research using peripheral approaches and cortical approaches to provide sensory feedback. And while some research has demonstrated great success in eliciting sensory percepts, there are still a lot of questions about how useful somatosensory stimulation will be, whether it's intracortical microelectrodes or direct cortical studious stimulation. How useful can that feedback be as a signal? So, specifically, how natural does the direct cortical stimulation percept feel? And where is the percept localized?

[00:33:02.69] We looked at this a little bit. You saw that in some experiments in the one subject that has micro-ECoG and in a number of subjects that have had macro-ECoG stimulation, subjects experienced a sensation, they can localize it to some part of their hand. Sometimes it's a single finger, sometimes it's multiple fingertips, or larger areas of their hand.

[00:33:22.14] We also know that in general in the research that's been done so far, using direct cortical stimulation of the cortex, subjects can experience sensations that are generally abstract. So they don't really feel normal; they don't feel like they were touching a water bottle, or touching a soft blanket, or touching something that's vibrating, or experiencing a lot of pressure. They feel more abstract. Subjects use words like "tingling," "buzzing," or some subjects have said it feels like wind rushing over my skin, or like pins and needles. So subjects use different words to describe it but in general, it doesn't feel like a typical sensation.

[00:34:02.80] Using intracortical microstimulation, one subject may have experienced more natural sensations. But we need a lot more research to understand how subjects will really experience and describe those sensations and where the sensations will be localized to. There's also the question of, "Can subjects use direct cortical stimulation as feedback in a task or a motor task?" And not only direct cortical stimulation, but can they use intracortical microstimulation or other types of stimulation?

[00:34:28.66] In the aperture tasks that I showed you, one subject was able to complete the task and use that sensory feedback of that direct cortical stimulation as feedback in a task, but only one subject was able to complete that task as well as the subject I showed you. So there's still a open question as to how can we help more subjects to complete tasks like this? How can we make direct cortical stimulation or intracortical microstimulation more useful in feedback tasks?

[00:34:58.77] There's a little question of what different parameters of stimulation-- whether it's for direct cortical stimulation or intracortical microstimulation-- can subjects experience? And how will they experience the stimulation with different parameters? What percepts will be elicited? If we change parameters, will it elicit different percepts? These are all open questions that remain to be researched in more depth and more details so that we can understand how to build future devices such as bi-directional brain-computer interfaces.

[00:35:29.74] There's also a question as to what happens if users aren't paying close attention? Often when we're doing these experiments, we are asking subjects to really focus in on the task at hand. But as we know, when we go about our typical everyday lives, we often are opening a door while talking to somebody else, or searching around in our backpack or a purse trying to find, say, a pen, and you're chatting with someone else, or watching your teacher. So you're doing a lot of other things while you get that tactile information about your environment. So the question is how will these somatosensory stimulation feedback methods work if the subject isn't paying very close attention?

[00:36:11.92] We talked about this briefly, but there is still a question of the range of stimulation trains and parameters that subjects can discriminate between. Again, that's important because we want subjects to be able to experience unique percepts so they could, say, experience light pressure, medium pressure, higher pressure. They could experience softness or roughness like sandpaper. We want subjects to be able to experience those unique percepts. So again, we're asking the question "how many percepts can we encode with these types of stimulation?"--whether it's direct cortical stimulation or intracortical microstimulation.

[00:36:51.97] And finally, can we improve any of these? Are there changes that we can make to the electrodes, to how we deliver the stimulation, the timing of delivery, or the parameters that we use for the stimulation waveforms that will improve any of these other questions that we've discussed? Can we improve the spatial location? Make a more high resolution spatial location?--meaning that subjects could experience small points on their fingers or their hand.

[00:37:21.52] Can we make it easier to use in a motor task? Could we make it easier to perceive? Or make subjects more likely to perceive the direct cortical stimulation? And can we help subjects to discriminate between different types of stimulation or different stimulation parameters so that they can experience more unique percepts?

[00:37:42.22] These are all open research questions that some of my research focuses on and many other research labs are looking into. So that's a bit about somatosensory stimulation for feedback, and thanks for listening.