Can depression and anxiety be treated by stimulating brain signals?

October 17 2019

Maryam Shanechi, the Andrew and Erna Viterbi Early Career Chair and assistant professor of electrical and computer engineering. Credit: USC Viterbi

Maryam Shanechi, the Andrew and Erna Viterbi Early Career Chair and assistant professor of electrical and computer engineering, is trying to do something that has never been done before: treat neuropsychiatric disorders using brain-machine interfaces (BMIs). This work, in part, just landed her on *Science News* magazine's Top Ten Scientists to Watch. In her perspective article published last week in *Nature Neuroscience*,

Shanechi lays out how she intends to solve this challenge.

BMIs provide a direct pathway to the brain to translate brain signals into actions. They have already been used in clinical trials to restore lost motor function in people with paralysis. But, in case you didn't know, our brains don't only control our movement. They regulate our thoughts and emotions as well. Below, Shanechi answers some questions about her work and what the future might hold for our understanding and treatment of mental disorders.

You're not the first person to work with BMIs. What makes your research so different?

We are developing the first generation of BMIs that can restore emotional function in people with neuropsychiatric disorders like depression, anxiety and more. These new BMIs aim to solve the challenging problem of regulating the abnormal neural activity patterns that underlie emotional dysfunction in these disorders. In other words, we aim to restore healthy emotional function to our patients in cases where medication or therapy will not work.

Why is recording and understanding something like mood or emotion so difficult?

I don't think I'd be the first one to tell you that emotions are complex. Simply observing someone's behavior is not always a great indicator of what they're feeling inside. So we have to first find a reliable way of assessing how someone's mood changes in time, which is very difficult. For example, if we use a questionnaire, we can only give it to the patient a few times a day at most. Understanding how someone's mood state is represented in brain activity is even harder because mood states involve multiple distributed brain regions and it's not always clear how these

regions coordinate their activity to represent mood. So, there's a lot of computational and machine learning challenges that we need to solve to understand how mood is represented in the activity of these brain regions.

Finally, even IF we understand how mood or emotions are represented in the brain, and even IF we can perfectly decode them from brain signals, we're still not done. We still need to solve another challenging problem: how can we change these distributed brain signals using electrical stimulation to regulate them and the abnormal mood symptoms they represent? This is a largely unresolved standing challenge that we are focused on solving in my lab.

What potential does this hold for the future not just of mental health, but of understanding our brains as a whole?

Neuropsychiatric disorders are a major cause of disability worldwide with depressive disorders being the most disabling among them. About 30% of major depression patients are treatment-resistant—that's about 5 million people in the US alone. Having an alternative therapy in the form of a BMI that selectively targets brain signals that are the cause of emotional dysfunction can revolutionize treatment for neuropsychiatric disorders.

But BMIs are not just a tool to cure mental disorders, they're a tool for discovery about mental health in general. BMIs can help us better understand the neural mechanisms of emotion regulation (how we start, stop, or change the trajectory of our emotions). One way to do this is to have participants engage in emotion regulation while we monitor their brain signals to study these fundamental questions.

Having a BMI that interacts with the brain might sound a little scary to some people. What are you doing to address to moral questions that might arise from this kind of work?

First, we are designing these BMIs as alternative therapy only for patients with very severe cases of depression and anxiety who do not respond to any other therapy. Second, of course, the ethical considerations for human BMIs are extraordinary and should be closely guided by neuro-ethicists. But engineers have a role to play as well. Engineers of every discipline are developing all kinds of tools that are fundamentally changing society and the world as a whole. It's important for all of us to approach our work, which we do for the good of everyone, from an ethical perspective.

BMI studies in humans are no different and should be performed with strict selection criteria. There are already strict ethical standards in place for epilepsy patients, and this could be a good starting point for how to address future studies on the human brain. As recently stated by Yuste and colleagues, BMIs "must respect and preserve people's privacy, identity, agency, and equality." I reference their work in my paper.

What's the next step in your research?

We need to build models that allow us to predict how brain signals respond in real-time to ongoing changes of electrical stimulation. Then we can predict how a change in stimulation changes brain signals and thus how it can help regulate abnormal mood states. With this last step in place, we can finally build the controllers that change electrical stimulation in real-time to drive abnormal brain activity toward a healthy therapeutic regime. We are currently working on these directions.

More information: Maryam M. Shanechi. Brain–machine interfaces from motor to mood, *Nature Neuroscience* (2019). DOI: 10.1038/s41593-019-0488-y