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Closed-Loop Deep Brain Stimulation for Mental Disorders: Progress Towards a Circuit-Directed Treatment

Abstract: Mental disorders are arguably the largest public health problem of our age. They are the largest cause of disability worldwide, and yet current treatments work poorly for most patients. Neuroscience increasingly suggests that mental disorders arise from dysfunction in specific brain circuits, but medication and talk therapy do not target those circuits. More recently, multiple groups have used implantable systems (deep brain stimulators, DBS) to electrically stimulate those circuits. DBS had strong initial promise, but large-scale clinical trials had poor outcomes. A key cause of that failure is that all prior investigations have been open-loop, delivering energy without measuring how or whether the brain changes in response. By shifting to closed-loop approaches, we could better identify which patients should receive DBS and what stimulation patterns might produce clinical response. The core barriers to that shift are a need to identify biomarkers (control signals) and a need for stimulation protocols that change those markers. I will present data from electroencephalographic (EEG) studies of patients who had previously received implants for depression and obsessive-compulsive disorder (OCD). I have identified EEG signals that are important for flexible thinking, a key aspect of recovery from both illnesses. Those signals change in response to DBS and may drive clinical response. In the second part of the talk, I will show examples of how we have used those insights to design new stimulation protocols, in humans and animal models, that show promise as rationally-designed, circuit-oriented therapies.