Patient-specific approach may improve deep brain stimulation used to treat Parkinson's

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Researchers have developed a method to measure how the brain responds to electrical stimulation and use the response to maximize efficacy of deep brain stimulation (DBS) - a therapy that has been successfully used to treat advanced stages of Parkinson's disease. The study, published in *PLOS Computational Biology*, provides a patient specific approach to tuning parameters that may dramatically improve efficacy of deep brain stimulation.

Deep brain stimulation uses an electrode placed deep in the brain to deliver electric stimulation for the treatment of diseases such as Parkinson's disease. For Parkinson's disease it is hypothesized, but still controversial, that electrical stimulation suppresses pathological neural oscillations, called beta rhythms.

Deep brain stimulation amplitude and frequency must be set by a clinician, who usually watches the patient's symptoms and side effects to select parameters. Setting stimulation parameters is a time intensive and laborious process, and does not guarantee that the settings are optimal for the patients, which can result in stimulation that requires more energy or greater side effects than necessary.

The current deep brain stimulation devices deliver stimulation like a metronome, completely blind to the patient's neural activity. New devices are being developed by Medtronic and other medical device companies that can allow both stimulation and monitoring of the neural activity which can facilitate tuning of the parameters and even delivery of stimulation triggered by neural activity.

Holt et al, at the University of Minnesota, with collaborators at UC Santa Barbara, demonstrate their approach in a computational model of the brain. They hypothesize that triggering stimulation at a particular phase of a neural oscillation may be more effective at suppressing the pathological activity than periodic stimulation. Furthermore, applying bursts of stimulation at select phases of the oscillation may be even more effective than a single pulse.

By applying stimulation and measuring how each pulse shifts the oscillation, they can generate a measure of the brain's response, called a "Phase Response Curve". This curve allows them to predict how the oscillation will respond to any stimulus pattern (within reason). The authors, utilizing control theory approaches, were then able to use the phase response curve to then design stimulus patterns optimized to suppress the oscillation.

In this study they measured phase response curves from a computer simulation of brain activity, predicted what stimulus patterns would suppress the neural oscillations, and then demonstrated that the stimulation patterns predicted to suppress the oscillations were in fact effective.

This method therefore provides a patient specific approach to tuning parameters that may dramatically improve efficacy of deep brain stimulation. In the future, they plan to test this in animal models of Parkinson's disease and translate it to humans.

More information: *PLOS Computational Biology*, dx.plos.org/10.1371/journal.pcbi%201005011

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