Patterned pulses boost the effects of deep brain stimulation, research shows

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Electrical stimulation has been used as a sort of defibrillator of consciousness, rousing a victim of traumatic brain injury to at least partial awareness, after years in a coma. The procedure, termed deep brain stimulation, has also been used to treat Parkinson's disease and has shown some promise for use in epilepsy, cluster headaches and treatment-resistant depression. But new research shows that the even, equally spaced electrical pulses typically used in the procedure now are not necessarily the most effective. Complicating the temporal pattern, Rockefeller University researchers say, may improve outcomes by more closely mimicking the dynamic signals that comprise the natural traffic of neurons.

The researchers, led by graduate student Amy Wells Quinkert and Donald W. Pfaff, head of the Laboratory of Neurobiology and Behavior, stimulated the brains of mice with two unconventional pulse patterns and found that one had a substantially greater effect in measures of the mice's arousal than the conventional monotonic pattern that is the clinical standard of the day.

"The idea was that if we're mimicking what the brain does naturally, rather than using a fixed frequency, then we may be increasing the efficacy of the treatment and decreasing the possibility of adverse effects," Quinkert says. "And we got a pretty striking result."

With colleague Nicholas Schiff, head of the Laboratory of Neurophysiology at Weill Cornell Medical College, the scientists used a simple, nonlinear equation — thought to describe the activity in some biological phenomena — to generate temporal series of pulses that were applied to the hippocampus, a brain region connected with a wide variety of emotional, visceral and memory functions. Using implanted electrodes, they also stimulated the thalamus, a deeper brain structure that receives input from the brain's arousal systems and projects to the cerebral cortex.

The stimulus, which was applied for 10 minutes, varied in the length of the sequence of pulses that was repeated — 10 pulse repeat in one experiment and 50 pulse repeat in another. The researchers observed the arousal of the mice before, during and after 10-minute stimulation periods and compared it to that of mice that received the conventional fixed frequency pattern. They found that in several measures that reflect behavioral arousal, including fidgeting movements, total distance traversed and whole body movements, the 10-repeat nonlinear pattern, applied to the hippocampus, increased activity more than either the 50-repeat or the fixed frequency. However, the 10-repeat pattern had less effect than the alternatives when applied to the thalamus, an indication of the neuroanatomical particularity of the factors involved, the researchers report in experiments published online in *Behavioural Brain Research*.

"Not only does temporal pattern make a difference, but also the response to the temporal pattern is different in each stimulation target," the researchers say. "This difference between brain regions likely depends on the physiology of the target of stimulation and its function within the particular neuronal circuit of interest."

The results lend credence to the long-held hypothesis that a portion of the information trafficked in the brain is encoded in the temporal patterning of firing neurons that has been observed, and not simply the absolute number of neuronal pulses. Quinkert plans to explore whether there is something specific to the equation they used to determine the pulses that is responsible for the observed effect, or whether the effect could be achieved by random series or by other variations in the pulse series.

“Amy’s experiments represent the first time that a mathematical equation was used to determine a pattern of deep brain stimulation,” Pfaff says. “We hope that our findings in mouse brain can be applied to Professor Schiff’s studies in monkey brain, in the future.”

More information: *Behavioural Brain Research* 214: 377-385 (December 25, 2010);Temporal patterning of pulses during deep brain stimulation affects central nervous system arousal, Amy Wells, et al. dx.doi.org/10.1016/j.bbr.2010.06.009

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