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Non-invasive electric stimulation using deep targeting techniques modulates hippocampal theta in the urethane-anesthetized rat

Electrical brain stimulation has a large potential to study normal and treat abnormal brain function due to the brain's electrical nature. Less invasive techniques are of great interest because they can be inexpensive, easy to use, and carry minimal risk. However, efficacy and mechanisms aren't well understood. We use Temporal Interference (TI) stimulation because of its ability to target deeper structures with minimal influence on surface regions. Using a virtually reconstructed rat head model, we found the best locations for skull-mounted electrodes for targeting the hippocampus. The hippocampus is an ideal target for our study because 1) it tests our ability to target deep 2) it generates, theta, the largest amplitude rhythm the brain 3) theta is an important brain rhythm, associated with learning and memory, and possible antiepileptic effects. In urethane-anesthetized rat, which generates theta spontaneously, we use short (1.5 sec) bouts of TI stimulation or sine wave stimulation of randomly ordered intensities. The stimulation frequency is the average recorded frequency of the peak amplitude before stimulation onset. When no theta is present, a random frequency was generated between 4 and 5 Hz. Our results for the sine wave group showed a theta amplitude increase during stimulation with its initial increase dependent on theta's phase at the stimulation onset. For the TI group, we found a phase-independent theta amplitude increase, which lasted seconds after stimulation. Also, we found an increased likelihood of theta's initiation during the TI stimulation period. All effects were dose-dependent -- with larger effects at the higher stimulation intensities. Thus, we elucidate TI to be significantly better at targeting deep brain than sine wave stimulation. This is significant because our increased ability to modulate brain activity means we can better test normal function of brain rhythms and their role in mitigating or propagating pathological brain states.