Brain Stimulation: Therapeutic Approach

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For approximately 30% of patients with epilepsy there are no therapies available to control their seizures. Therefore, there is a need for new antiseizure therapies that are effective and safe. Deep brain stimulation delivered at a high frequency with short duration pulses has been approved by the FDA and while effective in some patients, there are still many patients who do not respond. To expand the number of stimulation therapies available to treat these patients our research has focused on assessing the efficacy and safety of low frequency, 1Hz stimulation (LFS). The goal is to generate preclinical data to obtain FDA approval to incorporate this stimulation paradigm in an implantable stimulator. Our initial studies tested preemptive 1Hz sine wave stimulation using the amygdala kindling seizure model. When LFS was delivered for 30 sec before the delivery of the kindling stimulus it significantly: 1) raised afterdischarge (AD) threshold, shortened AD duration, delayed kindling acquisition, and decreased the incidence of Stage 5 behavioral seizures in fully amygdala-kindled rats. Similar results were obtained when the animals were kindled in the hippocampus. To build upon these findings, the efficacy of voltage controlled LFS (VCLFS) was then tested in the tetanus toxin (TX) model of spontaneous seizures. The stimulus voltage was adjusted to 1 V peak-to-peak or safety. The efficacy and safety of scheduled VCLFS delivered continuously to the hippocampus for one minute out of every hour was evaluated. VCLFS significantly decreased the incidence of TX-induced epileptiform events with no evidence of histologic damage.