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Long-lasting therapeutic effects of desynchronizing brain stimulation

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Abstract

Within the last standard high-frequency (HF) deep brain stimulation became the standard therapy for medically refractory movement disorders. HF deep brain stimulation has been developed empirically, mainly based on observations during neurosurgical procedures. In contrast, to overcome limitations of standard HF deep brain stimulation, we use a mathematical modelling approach. To this end, we make mathematical models of affected neuronal target populations and use methods from statistical physics and nonlinear mathematics to develop mild and efficient control techniques. In particular, we specifically utilize dynamical self-organization principles and plasticity rules. In this way, we have developed multi-site coordinated reset (MCR) stimulation, an effectively desynchronizing brain stimulation technique. The goal is not only to counteract pathological synchronization on a fast time scale, but also to unlearn pathological synchrony by therapeutically reshaping neural networks. We examined the effects of MCR stimulation in seven patients with severe PD or essential tremor during the first week after electrode implantation with our novel portable brain stimulator. According to our theoretical predictions, in all seven patients epochs of MCR stimulation caused pronounced therapeutic effects, which outlasted MCR stimulation during the whole post-MCR observation period prior to dismissal (i.e. during at least four days), even in patients with severe fluctuations. Current delivery of MCR stimulation was considerably smaller compared to HF stimulation.