Suppression of pathological tremor using electrical stimulation of afferent pathways

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PATHOLOGICAL tremor is a rhythmic oscillation of body parts, symptomatic to several neurological disorders. Current treatments include medication and deep brain stimulation, but both suffer from side-effects and variable efficiency. The use of electrical stimulation for tremor suppression has been suggested [Javidan et al. 1992], but the proposed methods require substantial stimulation amplitudes that may involve discomfort and fatigue for the patient. In this study we propose a novel stimulation strategy relying on low-level stimulation of afferent pathways, instead of motor pathways, for antagonist muscle pairs. This strategy relies on the stimulation of type Ia fibers (with lower rheobase current than motor axons) to increase motor neuron (MN) excitability in the homonymous MN population (agonist), while simultaneously decreasing heteronomous MN excitability (antagonist). If delivered out of phase with the neural tremorogenic input, we hypothesize that this neuromodulation can suppress tremor while overcoming the drawbacks of previous methods. Here, we investigate this approach based on a computational model of the peripheral nervous system. Furthermore, we present preliminary experimental data from 5 tremor patients.

The computational model integrated previously published models of various parts of the peripheral nervous system and contained two antagonist musculotendon segments (series elastic and parallel elastic and viscous elements) acting on a limb. Each muscle was innervated by 180 MNs modeled as two-compartment Hodgkin-Huxley models. Furthermore, each muscle contained 54 muscle spindles projecting directly to a subset of the homonymous MNs and to the heteronomous MNs via interneurons. The nerve rheobase current was inversely related to the axonal conduction velocity (Ia: 106±8 m/s; α: 84±8 m/s). The modeled spinal connectivity was validated by simulating classic protocols for H-reflex recruitment curves and reciprocal inhibition strength. A 5-Hz sine wave current was injected in the MN populations to simulate descending oscillations (opposite phase for each muscle), while a constant current was injected into the MNs to induce light baseline contraction levels (~10% of maximum contraction). In addition, the simulated electrical stimulation was delivered to the axons. Stimulation intensity was varied between levels required for 20% and 50% of total axonal recruitment, while stimulation frequency was varied between 30 and 200 Hz. Furthermore, stimulation timing, contraction level and tremor amplitude were varied. The simulations consisted in intervals of 2 s, alternating with and without stimulation.

In the experiments, the level of electrical current was set to the lowest level where muscle contraction was palpatable. To assess suppression efficiency, the integral power spectra of the musculotendon length power spectrum in a 3-12 Hz range of the periods with and without stimulation were compared.

In the simulations, the highest level of tremor suppression achieved was 41±12% at a stimulation frequency of 60 Hz. The optimal stimulation amplitude generated the activation of 22±8% of the Ia axons, without activation of any of the α fibers. This condition was equivalent to 33% of the maximum H-reflex amplitude. Suppression efficiency was most sensitive to the delay between the imposed MN oscillations and the center of the stimulation bursts. While optimal suppression was achieved by shifting pulse-centers by -15 ms with respect to the oscillations, deviations of more than 25 ms from this value enhanced tremor. Suppression efficiency was correlated to tremor amplitude and, to a lesser extent, voluntary contraction level. In the experiments, a similar level of tremor suppression as predicted by the simulations was obtained (mean: 49%). The effect was however very variable within and between the patients, possibly due to the fact that the stimulation timing was not adjusted with fine precision, which the simulations predicted to be a critical factor for tremor suppression efficacy.

The results indicate the potential of tremor suppression based on low level electrical stimulation of Ia afferent fibers without activation of α axons. While tremor amplitude at optimal settings was significantly reduced, the sensitivity of the approach to the timing of the stimulation implies the need for robust and accurate methods for tremor analysis to drive the stimulation.

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