**Clinical feasibility and mechanistic underpinning of proprioceptive modulation as a novel and non-invasive treatment of common movement disorder: tremor.**

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Tremor affects more than 7 million people in the United States and results in substantial social and physical disability. Essential tremor is the most common form of tremor, about 6% of people above age of 65 and 21% above the age of 80 suffer from common forms of tremor such as essential tremor. Dystonic tremor is the second most common form of isolated tremor affecting more than 3 million people worldwide. Clinical manifestations of both forms of tremor disorders are chronic, there is no cure, and there are few symptomatic treatments that are effective. The **theme** of our research is to determine if non-invasive modulation of peripheral proprioceptive feedback can be an effective treatment of essential tremor and dystonic tremor. We also delineated the mechanistic underpinning of such novel therapeutic approach to treat tremor. The research included three experiments. ***Experiment 1*** asked whether non-invasive modulation of proprioceptive feedback changed characteristics of tremor. We utilized custom-built vibration delivery system that utilized wearable coin vibrators. The motor delivered vibration to the sternocleidomastoid muscles. We were able to precisely modulate the amplitude and frequency of vibration. We discovered that muscle vibration significantly diminishes the tremor amplitude, the effects are instantaneous and reproducible. ***Experiment 2*** asked whether proprioception modulates the activity of movement sensitive neurons in the human basal ganglia – the critical neural structures responsible for precise and coordinated human movements. We measured the effects of neck muscle vibration on the activity pattern of basal ganglia single neurons intraoperatively during deep brain stimulation surgery. We discovered muscle vibration has instantaneous effect on the output of movement sensitive single neurons. We also found that neck vibration also reduces synchronous neural discharge that may lead to oscillations in the neural network causing tremor. ***Experiment 3*** asked whether vibration also affects other areas of the human nervous system connected with the basal ganglia and responsible for voluntary movements. Using functional MRI (fMRI) we discovered that proprioceptive modulation using vibration correlated with the activity pattern in the somatosensory cortex, thalamus, cerebellum, and basal ganglia. The **key impact** of this research is that it is the first study objectively establishing the efficacy of a novel treatment of tremor using non-invasive proprioceptive modulation with tactile vibration. In addition to establishing the clinical feasibility and therapeutic efficacy, our study also delineated the mechanism how proprioceptive modulation may treat common and refractory movement disorder – tremor.