Project Details	
Project Code	MRC22NMHBr Fischer
Title	Developing individualized somatosensory stimulation tools to understand and manipulate dysfunctional network activity in dystonia
Research Theme	Neuroscience & Mental Health
Summary	Dystonia is a movement disorder that causes involuntary muscle contractions and is challenging to treat. By combining EEG recordings with non-invasive somatosensory stimulation, this project will test the hypothesis that pathological synchronization of sensorimotor network activity causes motor symptoms. Data analyses and computational modelling techniques will be used to optimize stimulation protocols that aim to ameliorate dystonia symptoms.
Description	Dystonia is a disabling and highly heterogenous movement disorder, which can cause involuntary twisting of the neck, cramping of the hand, tremor, or tonic muscle contractions in multiple parts of the body. In the UK an estimated 70 000 people are affected by dystonia. The causes of dystonia are still poorly understood and the efficacy of current treatments, including medication, repeated injections of botulinum toxin and deep brain stimulation is highly variable. Dystonia is classed as a network disorder involving reduced cortical inhibition and maladaptive plasticity. Neurophysiological studies have reported excessive synchronization of neural activity across motor units and motor cortex, expressed as low-frequency oscillations (LFOs, 4-12 Hz). Conversely, beta synchronization (13-30 Hz), which plays a role in movement inhibition, is reduced. Currently it is still unclear to which extent excessive LFOs or diminished beta synchronization play a causal role in the emergence of symptoms. This PhD project will specifically test the hypotheses that 1) suppressing LFOs will reduce dystonia symptoms and 2) boosting beta oscillations will improve inhibitory control and thus also attenuate symptoms. The student will learn to combine high-density electroencephalography (EEG), which measures cortical synchronization, and non-invasive peripheral somatosensory stimulation tailored to the individual patient's pathophysiology. Somatosensory stimulation in the form of vibrotactile stimulation has recently shown promise for alleviating Parkinsonian symptoms. It has previously also been trialled to improve dystonia, but without considering the oscillatory nature of sensorimotor neural activity. Our project is novel in that vibrotactile stimulation will be used in a temporally specific fashion to manipulate synchronization patterns associated with dystonia. The project contains four parts: 1) First, we will characterize individual pathological synchronization linked to dystonia symptoms in each participant using EEG and electromyography (EMG) recordings of the affected muscles. We will specifically recruit patients with neck or focal hand dystonia, as well as genetic and idiopathic forms to compare the pathophysiology and response to the stimulation protocol between groups. 2) We will test if somatosensory stimulation can help attenuate cortical LFOs and improve symptoms. Our closed-loop approach will involve real-time tracking of cortical oscillations associated with the symptoms. Vibrotactile stimulation will be delivered also in an oscillatory pattern, but phase-shifted relative to the central oscillation such that destructive phase interference is achieved (akin to noise-cancelling headphones). A

	similar phase interference approach has previously been successfully used to reduce tremor. 3) EEG will be measured in a simple movement inhibition task to identify the person-specific beta peak frequency. Vibrotactile stimulation will then be applied at this frequency to assess if cortical beta synchronization can be boosted and LFOs will be reduced. Both stimulation protocols will be evaluated based on EEG and EMG activity in symptom-provoking situations, capturing changes in synchronization and the severity of muscle co-contractions. Any changes outlasting the stimulation episodes will also be monitored to test whether the protocol induced plastic changes in connectivity. 4) Computational modelling (Kuramoto models and theta-neuron neural mass models, supervised by JZ&CH) will be used based on the experimental data to understand how sensorimotor network activity responds to external perturbations and to optimize stimulation patterns. In summary, targeted manipulation of synchronization with non-invasive peripheral stimulation will help us gain insights into the functional role of synchronization for sensorimotor control and might help us develop treatments to promote rewiring of networks and restore their function.
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