PURE Award Final Report

Evaluation of Neural Connectivity in Stoke Survivors

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Introduction

Strokes are typically caused by an ischemic blockage of the middle cerebral artery, which supplies blood to a number of critical brain areas, including the primary motor cortex, responsible for voluntary movement control, and the primary somatosensory cortex, responsible for perception of body position and movement (Purves, Augustine & Fitzpatrick, 2001). Consequently, stoke patients are often left with sensorimotor deficits rendering simple, everyday tasks difficult, ultimately diminishing the quality of life of stroke survivors.

Traditional tools for assessment of function following a stroke primarily consists of an array of imaging techniques (Lai et al., 2016). One avenue for new, cutting-edge brain damage appraisal methods includes measures of neural connectivity (Campfens, Schouten, van Putten & van der Kooij, 2013) assessing neural system coherence, a measure of connection strength, or the correlation between neuromotor input and output. Corticomuscular coherence (CMC), afferent-cortical coherence (ACC) and afferent-muscular coherence (AMC) are three such measures. CMC refers to the strength of the correlation between cortical activity and lower motor unit activity (Campfens, Schouten, van Putten & van der Kooij, 2013). ACC as tested by Mildren et al. (2017) is a measure of the strength of correlation between sensory afferent stimulation and somatosensory cortex activity. Finally, measurement of AMC evoked by mechanical stimulation as by Peters, et al. (2016) gives us insight into the strength of connection between afferent receptors and lower motor neurons in the spinal reflex pathway (Peters, et al., 2016).

ACC and AMC have never been performed in a stroke population, however, combining these measures with CMC, to our knowledge will provide the most complete assessment of neural connectivity and plasticity performed to date in these patients. ACC has traditionally been measured using electrical pulse train stimulation to evoke cutaneous reflexes, which activates the different mechanoreceptive afferent fibres simultaneously (which does not happen under natural circumstances) and also presumably entrains them to non-physiological frequencies of activation (Peters, et al., 2016). However, the use of mechanical stimulation applied as a vibration at set frequencies provides a potential method for applying stimulation that, at the very least, will bias the afferent input towards different receptor classes (Peters, et al., 2016).

By simultaneously collecting electromyography (EMG) and electroencephalography (EEG) signals during different upper-lib tasks the correlation (both in time and in frequency content) between the two signals can reveal the strength of neural connections along critical pathways involved in human motor control, namely, spinal reflex (AMC), somatosensory (ACM) and corticomuscular (CMC). The use of EEG and EMG in damage appraisal provides advantages including high temporal resolution, mobility, and low cost (Lai et al., 2016). The combination of these novel measures of neural connectivity to supplement current imaging techniques could serve as useful clinical tools to detect stroke induced neurological changes and track recovery.

Methods

Experimental Setup and Procedure

Subjects were instructed to stand while holding a vibrator equipped with a laser pointer between their thumb and index finger with their arm outstretched. Each subject was instructed to maintain postural control of the vibrator by keeping the laser pointer centered on a target placed on the wall in front of them. The perturbations caused by the vibration of the hand-held device required that subjects modulate their grip force throughout trials. Each subject completed 3 trials, each lasting 2 minutes.

EMG Recording

Surface EMG signals were recorded from subjects' right bicep, tricep, anterior deltoid, and lateral deltoid muscles involved in postural control of the arm as well as the flexor digitorum, and thenar eminence to evaluate grip force using bipolar electrodes. The reference electrode was applied to the clavicle. EMG signals were sampled at 5kHz, amplified x2000 and band-pass filtered between 0.03-1kHz.

EEG Recording

EEG electrodes were placed over the approximate hand regions of the contralateral primary motor cortex and primary sensory cortex to measure CMC and ACC respectively. EEG signals were sampled at 5kHz, amplified x 10000 and band pass filtered between 0.3-1kHz.

Data Processing and Statistical Analysis

EMG and EEG signals were processed, and coherence graphs and cumulative density were computed using custom MATLAB software.

Results

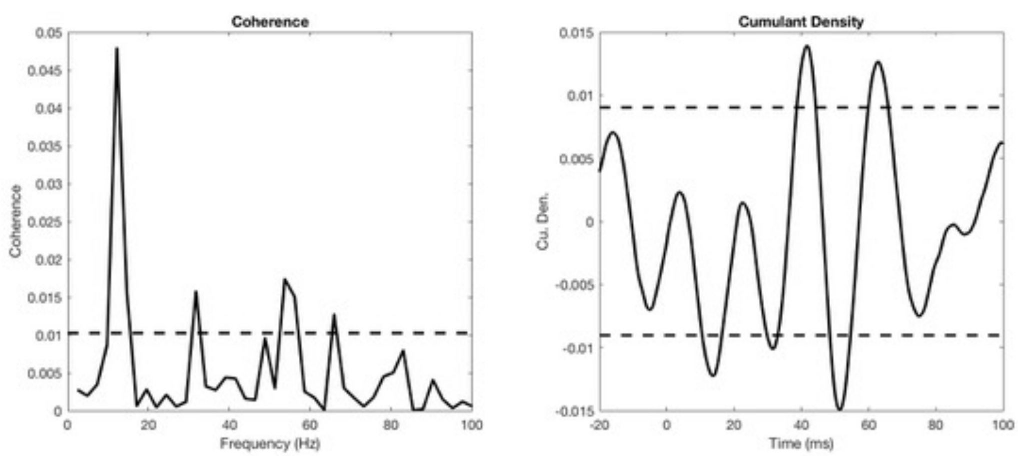

Fig 1. Anterior Deltoid Coherence and Cumulative Density Plots

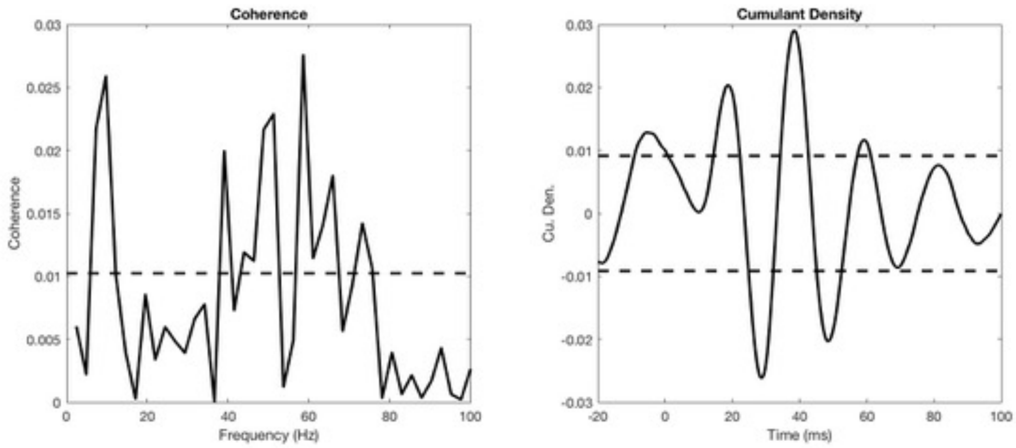

Fig 2. Flexor Digitorum Coherence and Cumulative Density Plots

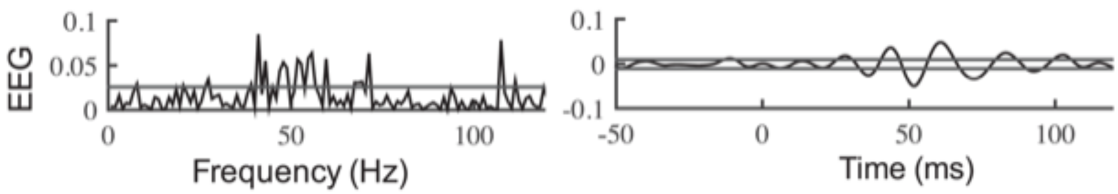

Fig 3. Somatosensory Cortex Coherence and Cumulative Density Plots (Adapted from Mildren et al., 2017)

Discussion

Our results show significant levels of correlation in both frequency and time in the expected bandwidths (Fig 1. and Fig 2.). The strongest coherence between input (vibrator acceleration) and receptor activation was found in the Meissner Corpuscle (FA1) receptor band. These FA1 receptors are sensitive to slippage and code for velocity in an extremely precise manner, being sensitive to microslippage measuring the distance of one fingerprint ridge (Srinivasan, Whitehouse & LaMotte, 1990). This indicates that, in the healthy population we tested, these FA1 receptors have a strong connection onto motor units, which is important for rapid functional force modulation. This detection of slippage and consequent force modulation is impeded in stroke patients, rendering gripping tasks difficult.

These protocols have to potential to be applied to situations requiring a high level of accurate force modulation, such as that required in surgical interventions. The ability to precisely modulate grip on a scalpel is a fundamental ability that well practiced surgeons have mastered. One future avenue for research using these methods is the investigation of quantitative measurement of accuracy in the training of surgeons. By evaluating a trainee's ability to detect minute scalpel slippage and modulate their grip accordingly we could gauge their preparedness to perform surgery.

What I learned

Through this research project I have learned a great deal about the scientific process as a whole. I have gained a deeper understanding of the trial and error nature of this type of work and have learned to adapt, and problem solve for unexpected issues. By only having just read published scientific papers prior to this lab experience, I gained a new appreciation for the challenges that researcher's encounter that do not make it into the final manuscript. Cutaneous reflexes proved to be extremely finicky and required months of problem solving to get right. As a result, I learned the type of patience that is required for neurophysiological research. Additionally, I learned multiple practical skills such as using MATLAB statistical software, 10-20 EEG system positioning, and how to set up EMG systems. While we have not yet reached the ultimate goal of our project we made tremendous progress this summer and I have gained a deeper understanding of many aspects of neurophysiology. This knowledge will serve me well as I continue to work on this research during my honours thesis project in the upcoming year with Dr. Peters.

References

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