Targeted Brain Stimulation Alters Resting State EEG and Reduces Post-Stroke Impairment

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Abstract— **Transcranial direct current stimulation (tDCS) is a potentially effective intervention for stroke rehabilitation. However, conventional tDCS is limited by spatial resolution to specifically target a brain region. Therefore, this study utilized TMS, and computational modeling-guided high-definition tDCS (HD-tDCS). Stroke participants had three visits 1) anodal HD-tDCS stimulation of the primary motor cortex to improve function of the corticospinal tract in the lesioned hemisphere, 2) cathodal stimulation of the dorsal premotor cortex to inhibit use of the cortico-reticulospinal tract in the contralesional hemisphere, and 3) sham. The effect was assessed by qualitative EEG metrics Delta-Alpha Ratio (DAR) and Delta-Theta-Alpha-Beta Ratio (DTABR) as objective outcome measures. Both anodal and cathodal stimulations significantly decreased the DAR and improved Fugl-Meyer Upper Extremity scores. No significant changes in DTABR. Targeted HD-tDCS may improve brain function and reduce post-stroke impairments which could be integrated with robotic based therapy as future work. DAR could be an objective method to assess alteration of brain activity in stroke rehabilitation.**

I. Introduction

Stroke is the second leading cause of death and disability worldwide. Long-term effects of stroke can include cognitive impairment and motor deficits, leading to significant psychosocial consequences and difficulty with activities of daily living[1]. Stroke recovery is highly variable since the long-term effect is determined by the site and size of the initial lesion. Individuals post stroke can experience continued upper extremity motor impairment including hemiparesis, spasticity, and abnormal muscle synergies[2]. Previous studies found that post-stroke motor impairments are associated with damage to the lesioned corticospinal tract and a maladaptive hyperexcitability of the contralesional cortico-reticulospinal tract (CRST). The medial CRST primarily originates from the dorsal premotor cortex (PMd) and travels through the pontine reticular formation to the spinal cord.

Transcranial direct current stimulation (tDCS) is an emerging intervention that has potential to improve motor function by modulating cortical excitability using weak electrical current. Different from other technologies such as robots, functional electrical stimulation, and local vibrations that manipulate the periphery, tDCS modulates brain circuitry directly and facilitates neuroplasticity. Current research suggests that anodal stimulation to the lesioned hemisphere and cathodal stimulation to the non-lesioned hemisphere can improve upper extremity motor function in stroke patients[3, 4]. However, the effect is limited as conventional tDCS uses large sponge electrodes making it difficult to target a specific area of the brain. Therefore, this study uses a targeted high-definition tDCS (HD-tDCS) technique. Qualitative EEG (qEEG) metrics taken at resting state have been studied as a potential indicator of functional impairment following stroke[5]. When measured in subjects 24 hours after stroke, brain activity in delta and/or theta band(s) increases, and alpha and/or beta activity decreases, leading to increased delta/alpha ratio (DAR) and delta-theta/alpha-beta ratio (DTABR)[5]. These changes have also been shown in chronic stroke [6]. The aim of this study is to use qEEG as a objective metric to investigate the impact of facilitating the ipsilesional corticospinal tract via anodal HD-tDCS stimulation, and inhibiting the contralesional cortico-reticulospinal tract (CRST) via cathodal HD-tDCS stimulation.

II. Methods

Twelve individuals at least 3 months post stroke (Mean age = 60.42; SD = 13.09, 3 female) were given a baseline assessment of their Fugl-Meyer Motor Score of the upper extremity and a 3-minute resting-state continuous EEG. The EEG was recorded using the 16 channel OpenBCI Cyton Daisy Biosensing Boards sampled at 125 Hz, After the baseline, the participants completed three visits in a computed randomized order: 1) anodal high-definition transcranial direct stimulation (HD-tDCS) over the ipsilesional M1, 2) cathodal HD-tDCS over contralesional PMd, 3) sham stimulation, with a two-week washout period. To ensure there is no carry-over effect, we compared the outcomes of pre-stimulation measurements with the baseline for each visit.

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The HD-tDCS method used five 1-centimeter electrodes with the main stimulation electrode in the center, and four surrounding co-centric electrodes with opposite polarity 40-45 mm from the center. The stimulation dosage was set as 2 mA, for 20 min. For sham stimulation, the HD-tDCS unit was set to the sham feature, which produces a sham waveform based on the indicated "real" waveform by only ramping the current to 2mA at the start and end of the stimulation to provide the same feeling as active stimulation The stimulation location was identified using subject-specific 1.5T MR images and verified by the TMS-induced MEP. The paired-pulse TMS was applied at the respective hotspots for the elbow flexor muscle at the paretic arm, over ipsilesional M1 and contralesional PMd with reference to the paretic arm. The MEP status was determined using criteria previously reported[7]. Electrical fields in the brain were estimated using the Realistic Volumetric Approach to Simulate Transcranial Electric Stimulation (ROAST) toolbox[8] to confirm that the targeted brain area was stimulated.

The EEG data was preprocessed using EEGLAB v 2020.0 toolbox in MATLAB[9]. The data was visually inspected for artifact removal. The power spectrum was calculated average using the Fast Fourier Transform. From this, mean power was computed across the following frequency bands: delta (1-4 Hz), theta (4.1-8 Hz), alpha (8.1 – 12.5 Hz), and beta (12.6-30 Hz)[5] with only electrodes in the sensorimotor area (C3/C4, F3/F4, and P3/P4). DAR and DTABR qEEG metrics were calculated with the following formulas:

$$DAR = \frac{\delta}{\alpha} \quad (1)$$

$$DTABR = \frac{\delta+\theta}{\alpha+\beta} \quad (2)$$

Statistical analysis was completed using commercial software Statistical Analysis Systems (9.4, SAS, Carey, NC, USA) with alpha = 0.05. DAR, DTABR and FMUE scores were analyzed using generalized estimating equations (GEE) in PROC GENMOD. All procedures performed involving human participants were in accordance with the ethical standards of the internal review board (IRB) of the University of Oklahoma Health Sciences Center (IRB # 14011)

III. Results

GEE analysis revealed anode stimulation significantly reduced DAR compared to sham stimulation (p=0.0260) and the cathode stimulation also altered DAR significantly in comparison to sham stimulation (p=0.0108). For DTABR, while the mean change for cathode (-0.98) and anode (-1.06) are greater than the sham (-0.04) there were no statistically significant changes found between cathode and anode compared to sham over time (p=0.2590 and p=0.1044 respectively) (Fig. 1). FMUE mean scores after anode and cathode stimulation increased significantly over time compared to the sham (anode: p=0.0076 and cathode: p= 0.0015) (Fig. 2).

IV. Conclusion

HD-tDCS may improve the function of the lesioned corticospinal tract and reduce the excitability of the contralesional cortico-reticulospinal tract, showing the benefit of subject specific precise neuro-navigation to guide the stimulation. Both anodal and cathodal HD-tDCS may improve brain function and reduce post-stroke impairments as FMUE increased post stimulation, which can be combined with robotic-based therapy as future work. As well as additional visits to explore the lasting effect of this protocol. Further, DAR could be a potential method to assess alteration of brain activity in stroke rehabilitation, and future analysis during functional tasks could be explored. This is important as qEEG could be used as a more objective method, compared to clinical assessments, to track stroke rehabilitation.

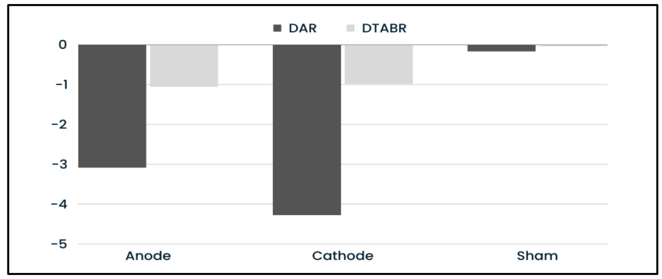

Fig. 1. Mean Change in DAR and DTABR (Post minus Pre) for Anodal, Cathodal, and Sham Stimulation

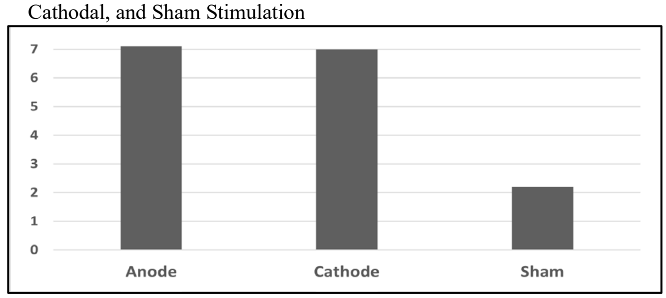

Fig. 2. Mean Change in FMUE (Post minus Pre) for Anodal, Cathodal, and Sham Stimulation

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