BRAIN PLASTICITY CHANGES IN MOTOR REGION AND DYNAMIC CHANGES IN WHITE MATTER AFTER STROKE INDUCED BY A NEURAL ACTIVITY-TRIGGERED REHABILITATION DEVICE

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Introduction There is growing evidence that closed-loop functional neural stimulation is a viable means of driving plasticity in the intact and damaged nervous system. Recent studies have shown that noninvasive Brain Computer Interface (BCI) devices coupled with functional electrical muscle stimulation (FES) have the potential for improving motor function after stroke [1]. Other work has shown that improvement of sensorimotor, cognitive, and affective function is possible in patients (e.g., Vestibular Disorders, Multiple Sclerosis, Stroke) through tongue stimulation (TS) in coordination with salient environmental cues [2-3]. In this study, we investigate whether a closed-loop neurological feedback device which combines BCI-EEG, FES and TS, can increase the extent of stroke recovery as indexed by behavioral measures and induce brain plasticity as measured by fMRI and diffusion tensor imaging (DTI).

Intervention The proposed closed-loop device consists of three components: (1) a BCI-EEG system for detecting real-time volitional command signals from motor cortex and providing visual feedback that allows subjects to monitor and modulate their brain activity. (2) a TS module to provide sensory feedback and increase the general excitability of the afflicted sensory-motor system through latent intact neural pathways. The TS consists of a thin-film array of 144 electrodes and sits on the surface of the tongue. (3) a FES component for activating muscle contraction in the affected limb. The BCI-FES-TS intervention consisted of trials of either attempted finger/hand movement contrasted with relax conditions or imagined movements and relax conditions. The subtraction of EEG signals between contralesional and ipsilesional sides of the brain were used to trigger FES for movement practice. All patients underwent minimum 9 and maximum 15 intervention sessions, 2 hours per session per day, and typically 3 days per week. Two chronic stroke patients (mean age = 57 years, 1 male, both greater than 1 year from stroke onset) and one sub-acute stroke patient (age = 68 years, male, 3 months from stroke onset) with upper extremity motor deficits were tested. The two chronic patients had left hemisphere strokes, with severe right arm hemiparesis and mild language impairment. The sub-acute stroke patient had mild right arm hemiparesis and intact language function.

Imaging data and analysis fMRI and DTI scan images were collected before (t1), in the middle of (t2), and immediately after intervention (t3) as well as one month later (t4) from the patients while attempting or imagining motor tasks in the scanner (3T GE scanner). A series of 70 scans were acquired with TR = 2.6 sec, 42 sagittal slices, and 3.5 x 3.5 mm³ voxel resolution. Diffusion weighting was isotropically distributed along 66 directions (66 directions + 1 baseline). fMRI data was preprocessed in AFNI and DTI data was preprocessed in FSL. A single-subject white matter atlas-JHU-DTI-MNI atlas with a matrix size of 91 x 109 x 91 (2mm isotropic resolution) was registered to each subject's native space.

Results (1) All patients showed improvement in accuracy on the BCI tasks over time across sessions. (2) fMRI data (**Figure 1**) showed significant greater activity in ipsilesional side (left for all subjects) of the brain during finger tapping after 6-15 intervention sessions (clusterwise significance p < .001). (3) DTI data (i.e., fractional anisotropy-FA) showed overall significant changes in the motor (i.e., corticospinal) tracts in comparison to language (i.e., superior longitudinal fasciculus) (paired *t*-test: *p*-value = 0.027) and memory (i.e., uncinate fasciculus) tracts (paired *t*-test: *p*-value = 0.058).

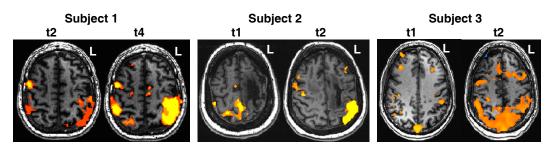


Figure 1 fMRI images show brain activation due to attempted finger tapping compared across time. (Radiological convention: right side of brain images shows patients' left hemisphere)

Conclusions Preliminary results suggest that this device could be used during post-stroke rehabilitation procedures and may reduce the duration of rehabilitation and increase the level of recovery. All subjects showed brain plasticity changes in terms of brain activity and white matter tract changes that are relevant for motor recovery due to the intervention.

References

- 1. Daly JJ, Cheng R, Rogers J, Litinas K, Hrovat K, Dohring M. J Neurol Phys Ther, 33(4): 203-11, 2009.
- 2. Danilov YP, Tyler ME. J Integr Neurosci, 4(4): 537-50, 2005.
- 3. Wildenberg JC, Tyler ME, Danilov YP, Kaczmarek KA, Meyerand ME. Brain Imaging Behav, 4(3-4): 199-211, 2010.