Functional MRI in stroke following tDCS and brain-computer interface-assisted motor imagery rehabilitation

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Introduction

Recent advances in stroke rehabilitation include motor imagery (MI) [1, 2], and transcranial direct current stimulation (tDCS). In chronic stroke patients, recovery in the affected arm can be improved with cathodal tDCS to the unaffected M1 cortex [3], or anodal tDCS to the affected M1 cortex [3, 4]. Functional imaging studies post-tDCS have shown increased activations in the SM1 and SMA [5] and increased regional cerebral blood flow in M1, SM1 and posterior brain regions [6]. These underscore the effectiveness of tDCS in modulating regional neuronal activity. Pilot data in seven subjects with traumatic brain injury (TBI) demonstrated a significant improvement (Fugl-Meyer and Jebsen-Taylor Hand Function scores) with combined tDCS and robotic arm therapy [7]. Here we investigate the imaging outcomes of a novel approach combining tDCS with robot-assisted MI and brain-computer interface (MI-BCI) therapy to facilitate motor recovery in chronic stroke patients with moderate to severe impairment of upper extremity function.

Methods and Materials

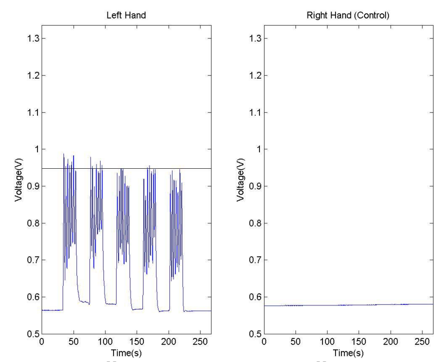
We conducted a randomized, double-blind study of combined tDCS and MI-BCI vs sham-tDCS and MI-BCI in a population of chronic stroke subjects. We present preliminary fMRI findings in one patient with left upper limb hemiparesis who underwent the former. The subject was scanned three times, at Weeks 0, 2 & 6. Combined tDCS and MI-BCI therapy was carried out in ten sessions over two weeks, starting at Week 2 after the 2nd MRI scan. Each therapy session consisted of 20 minutes of brain stimulation with electrodes placed on the bilateral cortical M1, followed by 40 minutes of MI-BCI where the subject performed a reaching task while being presented with the clock game interface of the MIT-Manus robotic system.

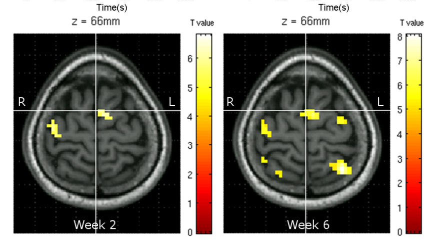
MRI data were acquired using a Siemens 3T Trio scanner (Erlangen, Germany). Prior to each scan, the subject's bilateral maximum grip strength or maximum voluntary contraction (MVC) was measured using an in-house developed pneumatic rubber bulb hand manipulandum (Honeywell, MN, USA). The subject then lay supine in the scanner, with a rubber bulb in each hand and resting in custom hand supports that allowed a trained operator to manually compress the subject's fingers, and thus bulb indirectly, without any direct operator-subject contact. The motor paradigm consisted of 5 active blocks, each comprising repeated grip-release motions, and interleaved with rest. The task was a dynamic hand grip cued by a visual stimulus of a moving red circle. Four functional scans were performed in a randomized order: Active left (AL), Active right (AR), Passive left (PL) and Passive right (PR), where left and right refer to the subject's hand, active movements were self-initiated and passive movements were performed by a trained operator with the subject relaxed. The target grip strength for the active and passive paradigms was 30% MVC of the respective and non-affected hand respectively. fMRI data were acquired with a single-shot gradient echo EPI sequence with TR=3000ms, TE=30ms, Matrix=64x64, voxel size=3.4mm isotropic, no. of slices=42, slice gap=0.34mm and number of measurements, N=89. T1-weighted data were acquired with a 3D-SPGR sequence with inversion recovery and TR=1900ms, TE=2.5ms, Matrix=256x256, voxel size=1mm isotropic, GRAPPA=2. The functional and structural data were analysed with Matlab r2011b (Mathworks, Natick, USA), SPM8 (UCL, London, UK) and Freesurfer (MGH, Boston, USA). Significant active voxels and laterality indices [8] were calculated for each fMRI dataset, and their centres of activation mapped to Talairach coordinates for anatomical referencing [9].

Results and Discussion

Pressure readings indicated good compliance with all motor paradigms. Even when the subject was unable to rapidly fully relax the grip in the stroke-affected hand during the most taxing AL paradigm (See Figure 1), the requirements for grip timing, peak grip force and lack of mirror movements were still observed. Subject motion was acceptable and typically <1mm translation and <0.02° rotation across all scans. A simple block paradigm with unilateral hand grip and calibrated visual stimulus was deliberately chosen to insure good compliance to the paradigm, and this was observed in all cases.

Our key findings following treatment are (i) a reduction in activation in bilateral SM1, PMC and SMA during the AR paradigm, and (ii) an increase in activation in the SMA, contralateral SM1, and ipsilateral PMC and PPC during the AL paradigm (See Figure 2). Table 1 summarizes the voxel counts and laterality indices at specified brain regions for the AL and AR paradigms, excluding areas primarily involved in visual processing. The test-retest data (Weeks 0 & 2) were in good agreement. The increase in activation in the contralateral SM1 during stroke-affected hand movement was consistent with our separate transcranial magnetic stimulation (TMS) findings that detected a reduction in resting motor threshold in the contralateral M1. We hypothesize that the overall reduction in activation during the AR paradigm could be due to our application of inhibitory cathodal stimulation to the unaffected hemisphere, as well as an increase and normalisation in interhemispheric inhibition of the unaffected motor cortex. These early findings present evidence of training-induced cortical plasticity, sustained at two weeks post-treatment that underscore the therapeutic potential of a combined tDCS and MI-BCI approach. Complementary structural and functional connectivity data collected, including data from passive paradigms, will further inform on the mechanisms involved.





Voxel Count	Active Right (AR)									Active Left (AL)								
	Wk0 (Pre1)			Wk2 (Pre2)			Wk6 (Post)			Wk0 (Pre1)			Wk2 (Pre2)			Wk6 (Post)		
	C	I	L	C	I	L	C	I	L	C	I	L	C	I	L	C	I	L
SM1	126	25	0.67	167	82	0.34	50	19	0.45	14	0	1.00	26	0	1.00	55	0	1.00
PMC	9	57	-0.73	5	78	-0.88	0	50	-1.00	17	0	1.00	7	0	1.00	16	26	-0.24
SMA	17	27	-0.23	30	26	0.07				9	0	1.00	0	20	-1.00	15	14	0.03
PPC	8	127	-0.88	0	72	-1.00	0	87	-1.00	16	0	1.00				0	22	-1.00

Figure 1. (Top) Measurements from pressure transducers show good compliance to the block motor paradigm (AL), with grip strength close to the target 30% MVC (black horizontal line) and minimal contralateral movement. **Figure 2.** (Middle left & right) Activation maps (AL) from Weeks 2 & 6 respectively. **Table 1.** (Bottom) Active voxel counts (P<0.05 FWE corrected) associated with centres of activation in the sensorimotor cortex (SM1), premotor cortex (PMC), supplementary motor area (SMA) and posterior parietal cortex (PPC). AR & AL data from three timepoints shown. C/I = hemisphere contra/ipsilateral to active hand, L = laterality index.

References

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