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Comparison of cortical network effects of high-definition and conventional tDCS during visuomotor processing

tDCS is a non-invasive brain stimulation approach in which low level currents are applied across the scalp to influence underlying brain function [1–3]. The Serial Reaction Time Task (SRTT) is commonly used to investigate neural mechanisms underlying motor-learning [4]. In the SRTT, subjects make a series of button presses based upon visual location cues. When the sequence is random, mean RT remains relatively stable over time. However, when the sequence is repetitive and fixed, individuals show a progressive motor learning reflected in a reduction in reaction time (RT) across trials even if they are not told of the sequence in advance. The rate of motor learning may be modulated by tDCS applied to the visuomotor learning circuit consisting of dorsal-stream visual cortex and motor/premotor regions of frontal cortex [5,6].

We recently [7] demonstrated that RT distributions during the fixed version of the SRTT are bimodal, with intermixed fast, "proactive" and slow, "reactive" trials, and that tDCS functions primarily by altering the ratio between trials reflecting enhanced motor learning. Further, we have demonstrated that the different trial types are associated with differential connectivity patterns within the visuomotor network. Finally, we demonstrated that the shift in connectivity pattern explained the shift in RT distribution. Specifically, cathodal stimulation of dorsal-stream visual cortex, with cathode at POz and anode at Cz according to the 10–20 EEG system, brought about a change in connectivity between motor and visual cortices accompanied by improved task performance.

Traditional tDCS uses relatively large (3 × 3 cm) pads placed over specific scalp regions, which leads to relatively coarse targeting of the electrical field within underlying brain regions. More recently, high-definition (HD-tDCS) approaches have been developed to better focus the energy to key underlying brain regions [8]. Here we investigate the relative effectiveness of HD-vs. conventional tDCS [9] in improving motor learning when applied to the visual node of the visuomotor network, along with the relative effects on underlying brain connectivity patterns. We predicted increased efficacy of HD-vs. conventional tDCS, reflecting its greater focality within target regions.

This study involved 10 healthy participants (3 females, 7 males), mean age 41.7 ± 9.6. All subjects provided written informed consent, and the procedures were approved by the Nathan Kline Institute Review Board. All participants reported normal vision. All were right-handed.

Cathodal (2 mA) or sham tDCS over visual cortex was administered using the Soterix Medical HD-tDCS 4 × 1 stimulator while subjects performed repeat trial blocks ("runs") of the SRTT using a previously described paradigm. Simultaneous EEG was recorded using an AC-coupled BrainVision recording system. Participants received four tDCS conditions on separate days in random order: HD-active, HD-sham, conventional-active, and conventional-sham (see Figs. A, B). Separate analyses were performed for random and fixed conditions using 2 × 2 mixed-model regression with factors of run-number, active/sham and HD/conventional stimulation as described previously [7].

Mean RT Results: No significant tDCS effects were observed during the "random" sequences as reflected in a non-significant effect of run ($F_{1,140} = 0.76$, $p = .39$). During "fixed" sequences, significant main effects of run-number ($F_{1,781} = 18.3$, $p < .0001$), active/sham stimulation ($F_{1,781} = 18.3$, $p < .0001$), and tDCS type (HD/conventional, $F_{1,781} = 18.8$, $p < .0001$), the 2-way interactions between active/sham X run# ($F_{1,781} = 4.13$, $p = .043$), tDCS type X run# ($F_{1,781} = 12.1$, $p = .001$) and active/sham X type ($F_{1,781} = 5.74$, $p = .018$) as well as the 3-way interaction between factors ($F_{1,781} = 5.85$, $p = .016$) were observed. Across all runs, active stimulation was significantly superior to sham ($F_{1,781} = 27.9$, $p < .0001$) and HD was significantly superior to conventional ($F_{1,781} = 7.29$, $p = .007$) (Fig. 1C, D).

Single-trial RT Results: Across all random conditions, data fit best to a 1-Gaussian distribution ($R^2 = 0.999$) with mean RT across conditions of 2.676 ±.001 log-ms (474.2 ms) (Fig. 1E). By contrast, in the fixed condition, a 2-Gaussian solution was statistically superior ($F_{3,23} = 220.9$, $p < .0001$, $R^2 = 0.989$), with mean RT of the fast and slow trials of 2.305 ±.009 and 2.635 ±.006 log-ms (201.8 and 431.5 ms), respectively.

When analyses were conducted across conditions, the ratio of fast to slow trials was significantly higher (F1,50 = 40.3, $p < .0001$) in the HD (62.5 ±.01) than conventional (49.6 ±.02) condition, consistent with mean RT results. Furthermore, when a cutoff value of 2.47 log-ms (295 ms) was used to differentiate fast vs. slow responses, the 3-way run X active/passive X type (HD/conventional) interaction ($F_{1,797} = 13.2$, $p < .0001$) was also significant (Fig. F).

Electrophysiological Results: As reported previously [7], under sham condition significant coherence is observed across Motor, SMA, Visual cortical regions revealing a functional network engaged in SRTT task performance (Figure, Panel G *left*). Conventional visual-cathodal tDCS significantly modulated coherence across the visual-motor nodes of this network compared to sham (Figure, Panel G *middle*). HD-tDCS however not only modulated the coherence across the visual-motor nodes but also across visual-SMA and motor-SMA regions compared to sham. Moreover, when comparing HD-tDCS vs. conventional, HD-tDCS brought about a significantly higher coherence between the motor-SMA

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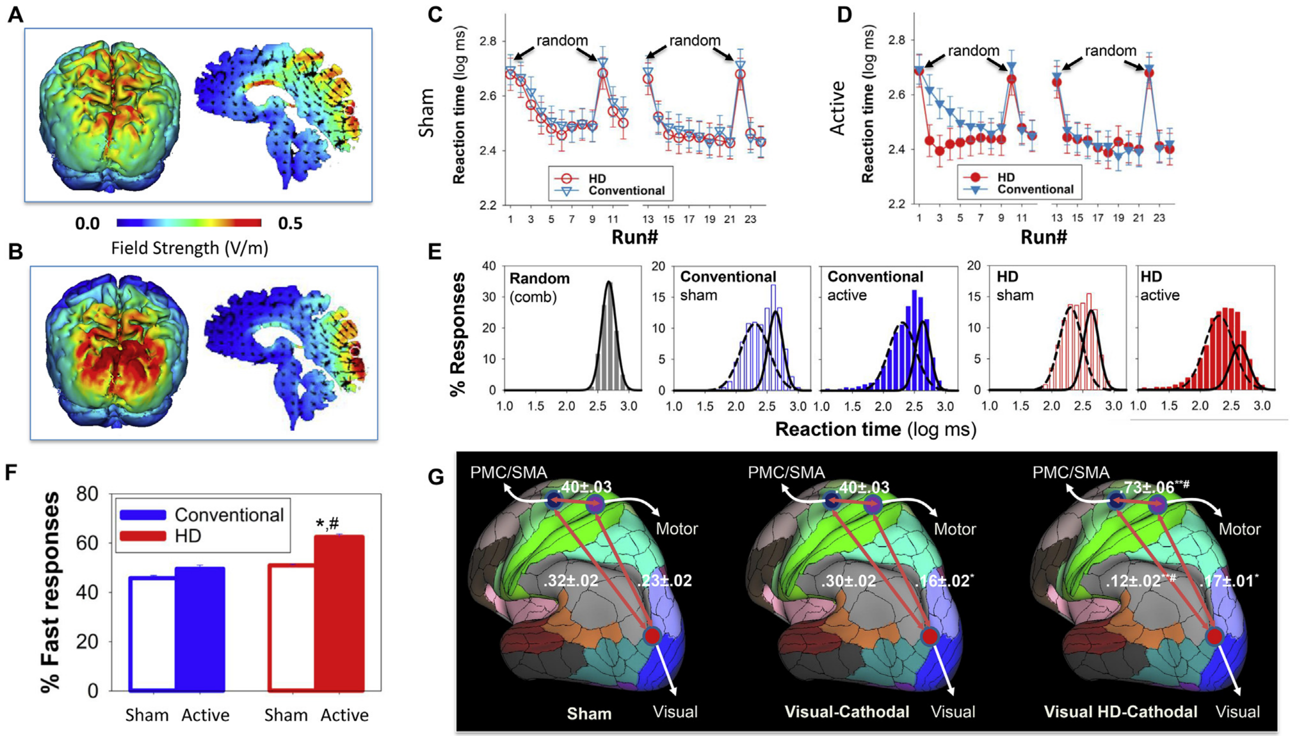

Fig. 1. A. Occipital and sagittal views of electric field (EF) intensity map under conventional tDCS condition computed [10,11] using Soterix HD-Targets software. The conventional tDCS conditions used a pair of surface 3 × 3 cm rubber electrodes each fitted in a snug sponge sleeve, the anode (2mA) was placed over the vertex (Cz) and the cathode (-2mA) over the scalp area (POz) according to the 10–20 EEG system.
B. Occipital and sagittal views of EF intensity under HD-tDCS condition, indicating greater intensity and more focal EF distribution compared to conventional tDCS. The HD-tDCS conditions used one cathode electrode centred over POz (-2mA) and four anode (0.5mA each) electrodes arranged symmetrically around the cathode (CP1, CP2, PO3, PO4). The HD electrodes were placed in specially designed holders filled with conductive gel.
C. Log-RT by run during sham stimulation showing two SRTT blocks each consisting of 12 runs. Random runs [1,10] are indicated; all other runs used fixed sequences.
D. RT by run during active stimulation.
E. Single-trial response distribution during indicated conditions. Given absence of tDCS and learning effects, the distribution was collapsed across conditions for the random sequences. Dashed curves indicate fast trial distributions; Solid curves represent slow trial distributions.
F. Using a cut-off value of 2.47 log-ms (295 ms) to differentiate fast vs. slow responses, analysis by run showed highly significant increases across runs ($F_{19,797} = 146.6$, $p < .0001$), as well as significant main effects of active vs. passive stimulation * ($F_{1,797} = 206.8$, $p < .0001$) and HD vs. conventional # ($F_{1,797} = 287.4$, $p < .001$).
G. Left: Coherence measures during task for each source pair (mean ± sem) under sham stimulation condition within the beta-frequency range (10–24Hz) in the 100-ms pre-response window showing significant coherence ***p < .001 between each pair versus baseline. The baseline coherence measures for these pairs were: SMA-Motor: 0.03 ± 0.02; SMA-Visual: 0.04 ± 0.01; Motor-Visual: 0.03 ± 0.02.
Middle: Coherence measures during task under conventional tDCS. Significant *p < .05 coherence difference for visual-cathodal conventional tDCS versus sham condition.
Right: Coherence measures during task under HD-tDCS. Significant *p < .05, **p < .01 coherence difference for visual-cathodal HD-tDCS versus sham and significant #p < .01 coherence difference for visual-cathodal HD-tDCS versus visual-cathodal conventional tDCS.

and lower coherence between visual-SMA regions (Figure, Panel G *right*).

In summary, tDCS alters mean RT during motor learning primarily by facilitating a shift from slow, “reactive” to fast, “proactive” responses, in which the subject can predict in advance where the stimulus will appear. Here, we show performance improvement with HD-tDCS also follows the same pattern albeit more so compared to conventional configuration. We also show HD-tDCS modulated the coherence across all the cortical nodes engaged in SRTT with greater effectiveness compared to conventional tDCS. This is note-worthy considering the current flow distribution of HD-tDCS shows minimal direct current spread to non-visual nodes of the visuomotor circuit. This suggests the observed significant change in coherence between the motor and SMA regions result from more efficient use of visual information, rather than local modulation of the interaction between these regions.

tDCS has been shown to have robust effects on brain plasticity across a range of paradigms. Nevertheless, effects of conventional tDCS may be limited by non-focality of conventional stimulation approaches. HD-tDCS produces greater focality by surrounding a central “active” electrode with multiple “returns”, limiting current spread. Here, we show both superior behavioral and superior neurophysiological effects of HD-vs. conventional tDCS, supporting its more widespread use across learning paradigms.

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Declaration of competing interest

The City University of New York holds patents on brain stimulation with Marom Bikson as inventor. MB has equity in Soterix Medical Inc. MB consults, received grants, assigned inventions, and/or serves on the SAB of Boston Scientific, GlaxoSmithKline, Mecta, Halo Neuroscience, X. The rest of the authors wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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