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### HD-tDCS to enhance behavioral treatment for aphasia: A feasibility study

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**Background:** Transcranial direct current stimulation (tDCS) enhances treatment outcomes post-stroke. Effects depend largely on which cortical areas are targeted. Feasibility and tolerability of high-definition (HD) tDCS, a technique that is thought to increase current focality and intensity, for consecutive weekdays as an adjunct to behavioral treatment in a clinical population has not been demonstrated.

**Objective:** To determine HD-tDCS feasibility outcomes, specifically implementation, acceptability, and preliminary efficacy.

**Methods:** Eight patients with chronic post-stroke aphasia participated in a randomized crossover trial with two arms – conventional sponge-based (CS) tDCS and HD-tDCS. Computerized anomia treatment was administered for five consecutive days during each treatment arm.

**Results:** Individualized modeling/targeting procedures and an easy-to-use 8-channel HD-tDCS device were developed for this project. CS-tDCS and HD-tDCS were comparable in terms of implementation, acceptability, and outcomes. Naming accuracy and naming response time improved with treatment for both CS-tDCS and HD-tDCS. Change in accuracy of trained items was numerically higher for HD-tDCS compared to CS-tDCS for most patients post-treatment.

**Conclusions:** Initial feasibility testing shows that HD-tDCS treatment studies can be implemented when designed similarly to documented CS-tDCS studies, and is likely to be acceptable to patients and clinicians. Preliminary efficacy data suggest that HD-tDCS effects, using only 4 electrodes, are at least comparable to CS-tDCS. HD-tDCS holds promise as a clinical technique and warrants further investigation.

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### Exploring structure-function relationships using parallel fMRI and tDCS

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The correlational nature of data from functional magnetic resonance imaging (fMRI) is a primary limitation for investigations aimed at establishing direct structure-function relationships in the human brain. Transcranial direct current stimulation (tDCS) can be used to overcome this limitation. The present work describes an approach for using parallel fMRI and tDCS to more directly investigate structure-function relationships. Experiment 1 used fMRI (n=16) to identify neural correlates of spatial, temporal, and decision-making processes important for causal reasoning – a central cognitive ability. Results from random effects analyses demonstrated three distinct patterns of activation in association with spatial (bilateral fronto-parietal networks), temporal (right hippocampal and cerebellum), and decision-making (inferior frontal

gyrus and insula) components of causal reasoning (Family-Wise Error Cluster Thresholds  $p < .05$ ). A second experiment carried out in a new group of participants (n=16) used tDCS to evaluate the roles of parietal and frontal brain regions identified in Experiment 1. Parietal tDCS stimulation only influenced spatial processing in causal reasoning, while frontal stimulation broadly impacted both spatial and temporal processing (Generalized Linear Model: Session x Location:  $X^2=6.4$ ,  $p=.04$ ). Converging results from fMRI and tDCS indicate that the parietal cortex contributes to causal reasoning because of its specific role in processing spatial relations and the frontal cortices contribute more generally, consistent with their role in decision-making. Multimodal tDCS and fMRI methods provide a strong framework for investigating population-level structure-function relationships, maximizing the strengths of each technique. Ongoing work on simultaneous tDCS/fMRI may provide improved resolution for direct investigation of structure-function relationships in the brain.

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### Cathodal transcranial direct current stimulation (tDCS) suppresses seizures, augments lorazepam potency, and enhances cortical inhibition in the rat pentylenetetrazol epilepsy model

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**Background:** Cathodal tDCS has antiepileptic potential. Yet whether its anti-seizure effect is via GABAergic mechanisms is unknown. We therefore tested in the pentylenetetrazol (PTZ) rat epilepsy model whether cathodal tDCS (1) suppresses seizures, (2) augments benzodiazepine efficacy, and (3) enhances GABAergic cortical inhibition.

**Methods:** Rats (n=20-23/group) received intraperitoneal PTZ (75mg/kg) followed by tDCS (sham or cathodal 1mA; for 20min), and then a second PTZ (25mg/kg) challenge. Two additional groups (n=10-11/group) received a sub-effective LZP dose (0.25mg/kg) after PTZ injection, and then verum or sham tDCS. Clinical and EEG seizures were compared between all groups. In the next experiment, we measured paired-pulse inhibition of the brachioradial is motor evoked potential (MEP) by long-interval paired-pulse transcranial magnetic stimulation (LI-pp TMS). Here, rats (n=7/group), under pentobarbital anesthesia, received PTZ (50mg/kg) or saline with either verum or sham tDCS. Cortical inhibition was measured during a 10-min baseline, 20-min tDCS treatment, and then for 25 more minutes.

**Results:** (1) Cathodal tDCS reduced the number of EEG spike bursts and power in the theta, alpha, beta frequency EEG bands, and improved the clinical seizure outcomes after the second PTZ challenge. (2) Cathodal tDCS in combination with low-dose LZP was more effective in seizure suppression than either tDCS or LZP alone. (3) Cathodal tDCS prophylaxed against the loss of LI-pp TMS motor cortex inhibition that accompanied PTZ injection.

**Conclusion:** These results suggest that cathodal tDCS alone and in combination with LZP can suppress seizures, perhaps by augmenting GABAergic cortical inhibition.