INTRODUCTION
Non-invasive brain stimulation has the potential to maximize neurorecovery in children with hemiparesis. An innovative form, transcranial direct current stimulation (tDCS), has many clinical and translational advantages - it has not produced seizures, is affordable, and is portable, allowing for potential simultaneous use in clinical rehabilitation settings for motor improvements. To begin use of this device, optimal electrode location must be verified. Current tDCS treatments rely on traditional EEG landmarks but, in children with unilateral lesions, the location of the motor hotspot may vary. Research Question: where is the optimal site of tDCS stimulation? Specific Aim: Determine the optimal location for tDCS motor cortex stimulation. Conventional EEG landmarks differ from the motor hotspot in both the ipsilesional and contralateral hemisphere in children with congenital hemiparesis.

METHODS

Dosage Determination. An individual head model from a 10-year-old female diagnosed with congenital left-hemiparesis was created from 1 mm-resolution T1-weighted and T2-weighted magnetic resonance imaging (MRI) scans. The model was individualized for tDCS current flow for C3 cathodal-C4 anodal and contralateral M1 cathodal—Supraorbital reference electrode configurations for tDCS. Using the peak cortical electric field (EF) for each montage and comparing to previous data in adults and children ages 8 and 12 years, the determination was made to proceed with a dose of 0.7mA with an electrode size of 3 x 5 cm sponge-based electrodes for one 10-minute session.1,2

For this one-time application of tDCS we computed the mean difference in scores between sessions along with a pooled standard deviation (SD). We evaluated whether the mean difference was greater than two times the pooled SD to decide whether to stop the study, and review the protocol and results for modifications with our medical monitor. Means and SD were analyzed for hotspot to C3/C4 distance in ipsilesional and contralateral hemispheres.

METHODS (continued)

TMS Landmarks. Single pulse, transcranial magnetic stimulation (TMS) delivered by a Magstim 200 coil (Magstim, UK). An individual head model for bilateral M1 hotspots for the first dorsal interosseous (FDI) muscles defined as the minimum intensity required to elicit EMG motor evoked potentials ≥50 µV peak-to-peak in at least 3 of 5 trials with the first dorsal interosseous (FDI) muscle at rest. Motor thresholds and standard EEG C3/C4 locations were obtained. The lesioned cerebral hemisphere was identified by MRI images and confirmed by the study team Neurologist. The distance between the conventional C3/C4 EEG and TMS hotspot landmarks were then noted bilaterally.

Intervention. Bi-hemispheric tDCS was delivered by a Soterix LTE tDCS Stimulator (NY, NY) via rubber electrodes attached to single-use sponges dampened with normal saline and placed over the M1 hotspot. The tDCS mode was positioned over the ipsilesional M1, the cathode over the contralateral M1. Subjects were randomized to tDCS or sham stimulation. tDCS was applied for 10 minutes at 0.7mA. The sham group received a 30-second ramp up and ramp down active stimulation phase with no stimulation during the interim phase. During the session, continuous monitoring included 1)EMG of ipsi and contralateral biceps brachii and FDI musculature and 2) subject symptom assessment to identify adverse events.

For the interim analysis using n=10 subjects who have completed the study showed no serious adverse events including seizure. The most commonly reported side-effect was transient scalp tingling during the tDCS stimulation (n=4). Our analysis includes 1) Physician evaluation using a modified Pediatric Stroke Outcome measure, 2) Continuous upper extremity EMG monitoring, and 3) Cognitive and Behavioral testing. The interim analysis for the items related to safety to date found no mean difference greater than the associated pooled SD, allowing for continuation of the study.

Electrode Placement. The interim analysis revealed variation between the location of the conventional EEG C3/C4 landmarks and the TMS-guided motor hotspot for the FDI in both ipsi and contralateral hemispheres. (Figure 4) Seventy percent of children had variation in the ipsilesional hemisphere, and eighty percent in the contralateral hemisphere.

Safety and Efficacy. The interim analysis using n=10 subjects who have completed the study showed no serious adverse events including seizure. The most commonly reported side-effect was transient scalp tingling during the tDCS stimulation (n=4). Our analysis includes 1) Physician evaluation using a modified Pediatric Stroke Outcome measure, 2) Continuous upper extremity EMG monitoring, and 3) Cognitive and Behavioral testing. The interim analysis for the items related to safety to date found no mean difference greater than the associated pooled SD, allowing for continuation of the study.

RESULTS

For Locating the Optimal Stimulation Site

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respectively. (Collaboration with the Department of Biomedical Engineering The City College of

Figure 1. Study Design. A)Dosage Determination. B) Electrode Placement.

Figure 2. Predicted electric field magnitude. A) As compared to other models. B) Predicted electric field on cortical surface. (Collaboration with the Department of Biomedical Engineering The City College of New York of CUNY)

Figure 3. Segmented tissue masks (skin, skull, cerebrospinal fluid, gray matter, and white matter respectively. (Collaboration with the Department of Biomedical Engineering The City College of New York of CUNY)

Figure 4. Overlapping EEG grid with individual hotspot coordinates. Superposition of all points to display bilateral hemispheres designated on left (blue arrow C3) and contralateral hemisphere on right (blue arrow C4). The position of the hot spots shown are in relation to the C3 or C4 position. Red dots correspond with contralateral motor hotspots. Yellow dots correspond with ipsilateral motor hotspots.

Table 1. Average pooled distance from Motor Hotspot to International 10-20 EEG C3 C4 Coordinates.

CONCLUSIONS/SIGNIFICANCE
Group analysis confirms the safety of the one-time tDCS application in pediatric hemiparesis. The use of tDCS alone or combined with behavioral intervention has been studied in adults with stroke with beneficial outcomes, yet little research has been performed on the safety of tDCS in children. Such research proposes a synergistic approach to improving hand function and enhancing quality of life. Critical consideration of tDCS-generated effects must be assessed: current intensity at the stimulation magnitude, electrode location, and duration of stimulation.4 Variation in the location of responsive motor cortex can directly affect the optimal electrode placement and the intended target area of application of tDCS in subjects with functional or anatomic reorganization. Our research indicates that EEG landmarks do not consistently indicate the optimal site of tDCS motor cortex stimulation in children with unilateral lesions. The size of the tDCS electrode may vary and the area of influence is in large part based upon placement of the electrode. This variation can directly affect the optimal electrode placement and the intended target area of application of tDCS. Using TMS to guide tDCS electrode placement may therefore be optimal. Future studies are indicated to compare EEG and TMS landmark measurement techniques in a cohort of typically developing children and children with hemiparesis. Such research could benefit from incorporation of Stereotactic Neuronavigation.

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REFERENCES


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