

Table 1
Pre/Post treatment fatigue scores

Measure	Before	After	n	p-value
MFIS	48.9 ± 13.1	42.5 ± 11.4	24	0.02
PROMIS Fatigue	27.1 ± 7.4	24.8 ± 6.2	16*	0.21
Daily Fatigue	2.6 ± 1.6	2.1 ± 1.7	25	< 0.01

MFIS and daily fatigue measures showed significant improvement while PROMIS Fatigue did not. It is worth noting that $n = 16$ for the PROMIS Fatigue is due to its late introduction into the study, possibly reducing the power of that specific measure.

4. Discussion and Conclusion

These data indicate RS-tDCS as a possible method for improving fatigue in patients with both relapsing-remitting and progressive MS. While benefit is shown to be significant in two of three fatigue measures, the benefit seems to be small. It is possible that higher amperage, more sessions, or longer sessions could bolster the effect we see. Further studies will look at dose-response and involve a sham arm to help validate findings.

References

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PROCEEDINGS #11. MOOD IMPROVEMENT WITH TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) IS SPECIFIC TO POSITIVE VS. NEGATIVE AFFECT IN MULTIPLE SCLEROSIS

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Introduction

One of the most reliably observed effects of transcranial direct current stimulation (tDCS)¹ is improvement in working memory performance. However, emotional changes have yet to be thoroughly examined. The left dorsolateral prefrontal cortex (DLPFC) is considered to be a neural substrate of specific aspects of mood² and emotion³. For example, studies have shown that it influences emotional stimulus categorization³, emotional evaluation³, and emotional regulation⁴ and thus, is considered to have a major role in top-down emotional control. Here, we explored whether two emotional orthogonal dimensions, positive and negative affect⁵, differentially respond to left anodal tDCS using a DLPFC montage. As part of an open-label feasibility trial⁶, we observed mood changes in a sample of participants with multiple sclerosis (MS). Participants were recruited to develop a remotely-supervised or RS-tDCS protocol where they participated from home using videoconferencing and pairing with cognitively engaging exercises during the stimulation period. A control sample was recruited for comparison where the participants only completed the cognitive training exercise but not the tDCS, otherwise using the same remotely-supervised videoconferencing protocol.

Methods

Eligibility criteria were purposely broad in order to develop the RS-tDCS protocol, and participants were not recruited to treat any specific symptom (including mood).

We enrolled patients with a confirmed diagnosis of MS (all subtypes) between the ages of 18–70 years. Active participants were enrolled in an open label treatment study (RS-tDCS paired with cognitive training), while controls were recruited separately and completed the cognitive training only.

Participants visited the clinic for baseline and follow-up measures. After initial training, they completed 9 remotely-supervised sessions from their homes, consisting either of active (1.5 mA stimulation) paired with the cognitive training (CT) or CT alone. Mood outcome was measured with the self-reported Positive and Negative Affect Schedule⁷, with scores of Positive Affect (PA) and Negative Affect (NA).

Results

A total of $n=24$ participants completed the active condition including the PANAS at both time points and were compared to $n=20$ in the comparison condition. Groups were generally equivalent (Table 1).

Table 1
Demographic and Baseline Clinical Characteristics

Demographic Characteristics			
Characteristic	Active Condition	Control Condition	Significance
Female gender	60.6% (n=20)	38.4% (n=13)	$\chi^2=0.258$
Age (years) mean (SD)	52.5±9.8 (n=25)	51.0 (n=20)	$P=0.671$
Age Range (Years)	30-69	26-67	-
Clinical Characteristics			
EDSS median (range)	4.00 (1.00-8.00)	4.00 (2.00-7.00)	$p=0.585$
Baseline PA mean (SD)	31.9±8.4 (n=25)	30.4±6.6 (n=20)	$p=0.487$
Baseline NA mean (SD)	19.9±8.3 (n=25)	16.7±6.4 (n=20)	$p=0.147$

Paired t-tests indicated that PA trended towards significant improvement in the active condition only (mean change in PA = -3.2 ± 8.3 , $p=0.07$ vs. -1.0 ± 5.8 , $p=0.45$) while both groups showed similarly significantly lowered levels of NA (mean change in NA = 5.1 ± 7.2 , $p=0.002$ vs. 4.2 ± 5.6 , $p=0.003$).

As shown in Fig. 1, the proportion of change from baseline to study end across individuals was disproportionately greater for the active condition for PA, while NA remained the same.

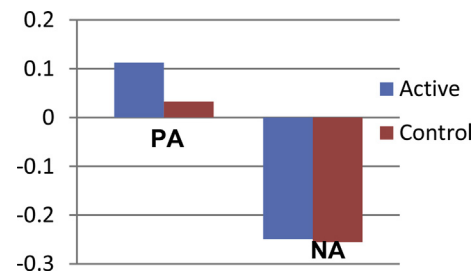


Fig. 1. Proportion of change after 10 sessions in PA and NA by condition.

For both groups, change in NA was significantly predicted by baseline NA, indicating that the higher the NA the more likely for improvement ($r_s = 0.68$ and 0.67 for active and control groups respectively, $p_s < 0.001$). However, change in PA was predicted by baseline NA (and not PA) only in the active condition ($r=0.48$, $p=0.02$).

Discussion:

In this study, exploratory analyses indicated that DLPFC (left anodal) tDCS differentially improves PA compared to NA in MS participants. These findings are consistent with the presumed neurobiological substrates of PA but not NA in the dorsolateral and ventromedial frontal regions. This is supported by PA improvements being independent from baseline PA levels, suggesting a broad and beneficial effect of stimulation to the DLPFC region.

Of note, both conditions had significant reductions in NA across the 10 sessions. Thus, shared features of the cognitive training and contact with the study technician through videoconferencing at each session may have served to generally reduce features of negative affect. This is supported by higher levels of baseline NA predicting a response, indicating a decrease in

features such as irritability and anxiousness as part of general participation in the study.

Future studies will utilize neuroimaging to confirm targeted engagement of the DLPFC in order to enhance changes in mood with tDCS in MS participants. We will also characterize changes in mood in participants with clinically significant mood problems at baseline. We hope that tDCS treatment may be generalizable across conditions.

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PROCEEDINGS #12. REMOTELY-SUPERVISED TRANSCRANIAL DIRECT CURRENT STIMULATION (RS-tDCS) FOR PARKINSON'S DISEASE (PD) CLINICAL TRIALS: GUIDELINES AND FEASIBILITY

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1. Abstract and Introduction

Cognitive and motor deficits are common debilitating symptoms for individuals living with Parkinson's disease (PD). The severity of cognitive and motor impairment in PD is associated with disease burden and quality of life. (1, 2) Transcranial direct current stimulation (tDCS) is a recent therapeutic development with the potential to ameliorate symptoms of PD. Previous studies have associated tDCS with improvement in motor and cognitive function in patients with PD. (3) However, multiple treatment sessions are necessary for a cumulative benefit. The requirement to travel for daily clinic treatment sessions presents an obstacle for many patients, especially those with higher disability and limited access to transportation. In addition to restricting patient access to repeated treatment sessions, such challenges have also limited the design of clinical trials in PD to date. Recently, we have developed a remotely supervised tDCS (RS-tDCS) protocol that delivers computerized cognitive training (CT) paired with tDCS to individuals with MS. (4) Using the same protocol with extensive safety measures, well-defined guidelines, and specially-designed equipment, we explored the feasibility and adaptability of our RS-tDCS approach for participants with PD.

2. Methods

This study was an open-label feasibility study. The eligibility criteria were relatively broad, with the key factors being a definite diagnosis of PD, PD-related changes to cognitive functioning, adequate home facilities, and a score of ≥ -3 standard deviations on the Symbol Digit Modalities Test (SDMT(5)) to measure disease-related cognitive decline and to ensure that participants had the cognitive ability to understand and participate in study procedures.

Each participant completed 10 tDCS sessions (20-minute each, 1.5-2.0-mA, dorso-lateral prefrontal cortex or DLPFC montage, which has been verified for effective targeted engagement of fatigue in patients with PD(6), over a span of two weeks using the remotely-supervised protocol. After the initial session at baseline, participants were sent home with a study laptop and tDCS equipment. The tDCS device (Soterix Mini-CT) is dependent on a code to operate, delivering a single 20 minute "dose" per code. All sessions were supervised in real-time using videoconferencing. The tDCS study technician ensured that the headset was correctly placed before providing the single-use activation code for the session. Additionally, study technicians followed a decision-tree series of checkpoints with "STOP" criteria set forth in the protocol that must be cleared in order to proceed at each step. These checkpoints address compliance (attendance and ability to complete the procedures as instructed) and tolerability (if any predefined events are reported at any time or if pain crosses a threshold, participation will be discontinued). For each study session, participants in both conditions were asked to complete a self-report inventory of adverse events and common side effects before and after their sessions (with items derived from a list of the most common tDCS side-effects in previous trials.(7) During the stimulation sessions, participations completed cognitive activating tasks on the computer. Feasibility of the approach was assessed based on the aforementioned series of checkpoints to address attendance, tolerability, and safety of the sessions.

3. Results

A total of 50 sessions were completed with 100% compliance. In comparison to the MS sample (n=20) in our RS-tDCS pilot study, the PD participants (n=5) are significantly older (mean = 45.15 in MS vs. mean = 69.80 in PD, p=0.004). The PD cohort exhibited a slightly lesser degree of cognitive impairment in their corresponding age groups as measured by the SDMT (mean z-score = -0.94 in MS vs mean z-score = -0.66 in PD, p=0.90). However, this may be influenced by the higher level of education (mean = 17.4 years) achieved by participants in the PD cohort compared to those in the MS cohort (mean = 15.95 years, p = 0.21), and in addition, inter-individual variability will prominently influence a sample's demographic and disease feature composition in a smaller sample size. All participants were able to quickly learn self-administration. In addition, our RS-tDCS protocol provided the opportunity to coordinate sessions with participants' anti-PD medications, ensuring that CT-paired stimulation could occur within the crucial 1-3 hour time window post-medication for maximum benefit (as recommended by study physicians at the New York University Fresco Institute for Parkinson's and Movement Disorders). No serious adverse events were reported. The most commonly reported side effects were skin tingling and burning sensations. The most intense side effect was a burning sensation at an intensity of 4, which qualifies as "mild" on scale from 1 [minimal] to 10 [severe]. The intensity and duration of time that these side effects were noticed by participants tended to decrease throughout the study. Across the 50 sessions, 96% of the daily self-reported pain ratings related to stimulation that were taken before, mid-way, and after tDCS stimulation were reported as 0, which denotes "no pain" on the visual analog scale ranging from 0-10 that participants used to rate pain from the headset. RS-tDCS range of 1.5-2.0mA was tolerable for all participants in the study.

4. Discussion and Conclusion

The RS-tDCS protocol was originally developed and tested in MS participants but designed to be appropriate for more generalizable use. Here, we expand the RS-tDCS protocol for use in PD. The study's high rate of compliance indicates that RS-tDCS is a safe and feasible approach for delivering direct current stimulation for individuals with PD, as with MS, despite the older age of our cohort of participants with PD. Across all 50 sessions, participants with PD found the stimulation to be tolerable. Key concerns for implementing RS-tDCS as an at-home treatment for PD include overall apprehension of technology and the need for technological support among this cohort, given the advanced age range and disabilities. Overall, the data indicate that RS-tDCS is easily implemented to accommodate participants' medication schedules, as well as physical therapy and exercise schedules, to provide maximum benefit and convenience. These findings support the use of the RS-tDCS protocol for clinical study in PD and other movement disorders, as well as the generalizability of the RS-tDCS approach for participant cohort with varying neurological diseases aside from MS.

References

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