independent diffusion encoding directions (b=1000 s/mm^2) and 5 unweighted images, with in-plane resolution of 2mmx2mmx2mm over the whole brain and TR/TE=7200/82ms. T1-weighted imaging was performed using a inversion-prepared fast spoiled gradient echo sequence, 1x1x1.2mm resolution over the whole brain.

3. Results

Fig. 1 provides an overview of how connectivity might be rendered in a way useful for surgical planning for DBS. The individual tracks provide a useful visualization of the tracks (Fig. 1a) but require specialized software not typically supported in planning workstations. Connectivity analysis reduces the tracks to a concise matrix representation that can be shown in a chord diagram (Fig. 1b) providing a quick display of connections that may be affected by DBS treatment. The connectivity can be computed for each location in the image so various scalar representations are possible for display. In one, 3 regions (Pre-, Post-central, and Superior Frontal Gyri) are selected and rendered in the red, green and blue channels (Fig. 1c). In another the connectivity is clustered and the clusters are shown (Fig. 1d). In both the scalar maps are easily ported to existing workstations and might be a way to deliver structural connectivity data to surgeons.

4. Discussion and Conclusion

Structural connectivity analysis provides a potentially powerful tool to aide in surgical planning. A recent case study shows how side effects might be predicted by connectivity analysis [1]. This information can be displayed in planning workstations using methods like those proposed here. More work is needed to determine the connectivity patterns to target for successful DBS. When long-term clinical outcome measures are available for these subjects we will determine the connectomic correlates.

References

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Acknowledgements

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PROCEEDINGS #10. REMOTELY-SUPERVISED TRANSCRANIAL DIRECT CURRENT STIMULATION (RS-TDCS) IMPROVES FATIGUE IN MULTIPLE SCLEROSIS

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1. Abstract and Introduction

Fatigue is a common and debilitating symptom of multiple sclerosis (MS) with estimates of up to 75% of patients reporting fatigue as their most disabling symptom [1]. Despite its prevalence, fatigue remains a frustrating symptom lacking reliable treatment options.

tDCS has been previously shown to improve fatigue in MS patients, but requires daily sessions to be effective [2]. The necessity of daily sessions limits many studies to small sample sizes and few sessions studied, especially for patient populations with disability who may have additional physical barriers to attending daily sessions on top of personal and professional obligations. In response to this issue, we have developed a remotely-supervised tDCS (RS-tDCS) protocol that allows participants to complete tDCS sessions from home. The accessibility of our remote protocol increases both enrollment and compliance; moreover, it allows for an extended number of sessions to be studied [3].

Participants were enrolled in a RS-tDCS feasibility study in which they completed baseline, daily, and study-end measures of fatigue.

2. Methods

This study was an open label, exploratory pilot study. Eligibility criteria were relatively broad, enrolling patients with a confirmed diagnosis of MS (all subtypes) between the ages of 18-70 years and a range of neurologic disability as measured by the Expanded Disability Status Scale (EDSS). Those with greater disability (EDSS $\geq$ 6.5) participated with the assistance of a caregiver proxy.

Participants visited the clinic for baseline and follow-up measures. Here they completed self-report measures of fatigue, the Modified Fatigue Impact Scale (MFIS), and the PROMIS Fatigue measure (with lower scores associated with benefit). The baseline visit also consisted of tDCS training and the first of 10 sessions.

Participants completed 9 daily tDCS sessions from home (20 minutes; DLPFC montage; left anodal) paired with brain training games. Before and after each session, participants rated their fatigue on a visual analogue scale. After all sessions were complete participants returned for a follow-up visit where baseline measures were repeated.

Paired t-tests were used to analyze change in scores from baseline to follow-up.

3. Results

A total of 25 participants were enrolled with all MS subtypes (n = 6 relapse-remitting; n = 19 progressive) and a range of disability (EDSS scores ranged from 1.0 to 8.0).

Most participants saw positive change in fatigue measures indicating an overall beneficial effect. Individuals' data points are shown in Fig. 1.

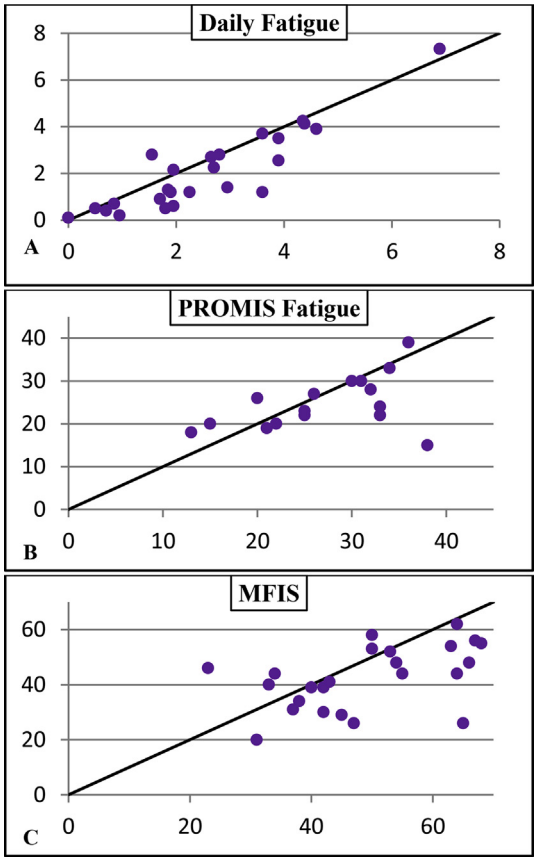

Fig. 1. Graphs show individual data points for each participant. x-axes are baseline scores and y-axes are follow-up scores. Points falling under the plotted line indicate improved score for that individual.

Paired t-tests were performed to test for significance of the effect, summarized in Table 1.

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.

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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 mood [2] and emotion[3]. For example, studies have shown that it influences emotional stimulus categorization[3], emotional evaluation[3], and emotional regulation[4] 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 affect[5], differentially respond to left anodal tDCS using a DLFPC montage. As part of an open-label feasibility trial[6], 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 Schedule [7], 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)	χ^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.

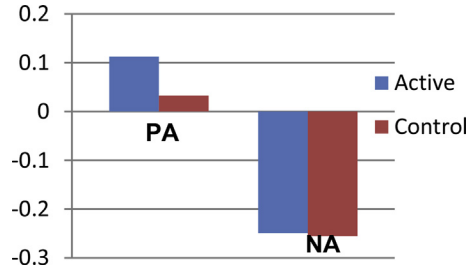

Fig. 1. Proportion of change after 10 sessions in PA and NA by condition.

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