Multifocal tDCS in Parkinson's Disease

Connectomic DBS informed multifocal transcranial direct current stimulation (tDCS) in Parkinson's Disease: a crossover double-blinded study

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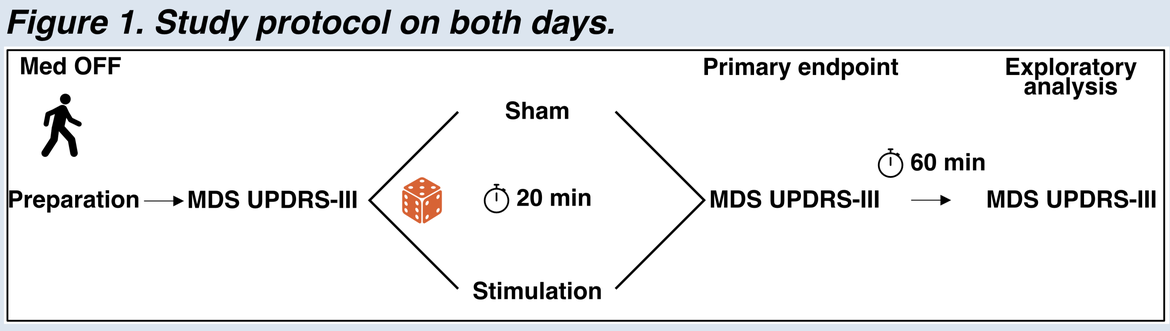
INTRODUCTION

- Deep brain stimulation (DBS) is an effective treatment option in Parkinson's Disease (PD)
- Recent imaging studies have identified specific brain networks associated with clinical improvement during DBS in PD using connectomic analysis approaches
- Transcranial direct current stimulation (tDCS) represents a non-invasive method of neuromodulation
- Using multifocal tDCS, a whole cortical representation of a network may be modulated, potentially leading to higher effects compared to earlier bipolar approaches

STUDY DESIGN & METHODS

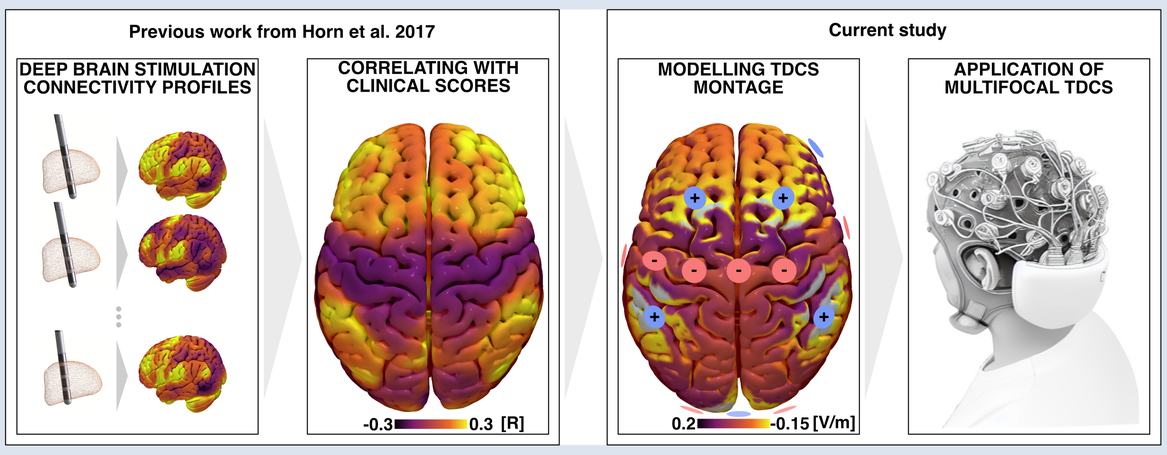
- A double-blinded prospective, cross over trial was designed and preregistered in the German Clinical Trial Register (DRKS00026640). Power analysis revealed that at least N=21 patients have to be included with an underlying power of 70%.

Figure 1. Study protocol on both days.



Patients were included following a minimum 12-hour withdrawal from dopaminergic medication. Stimulation (and sham) were applied for 20 minutes. Directly before and after stimulation, MDS-UPDRS-III scores were recorded on video and rated blinded to stimulation vs. sham condition. As an exploratory endpoint, scores were again recorded 60 minutes after stimulation. Both patients and examiners were blinded to the condition. The same protocol was applied on the second day using the other condition.

Figure 2. Summary of methods.

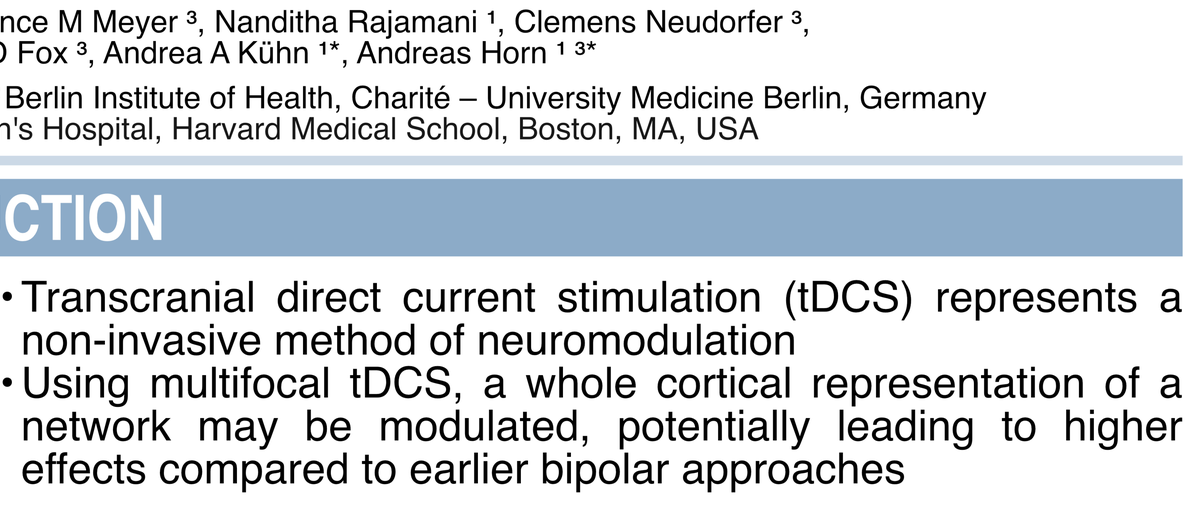


Based on an a priori network published by Horn et al., derived from DBS electrode placement (left two panels), a tDCS montage design was calculated to generate an electrical field maximizing impact on the inverse of the identified network (third panel) (sum of 4 mA). Utilizing this montage, multifocal tDCS was applied according to the design illustrated in Figure 1 (right panel).

RESULTS

- N=23 patients were included in this study
- Mean age 59.9 years, mean H&Y in off-medication 2.4
- No adverse events were observed during this study

Figure 3. Results.



A: ANOVA results. Baseline UPDRS-III were comparable: stimulation days: 37.38 ± 12.5 points; sham days: 36.95 ± 13.9 points. Following stimulation, scores reduced to 33.76 ± 11.19 points (improvement of 3.62 ± 5.29 points ; 9.68 %), while after sham to 36.43 ± 14.15 points (improvement of 0.52 ± 6.11 points; 1.4 %).

ANOVA confirmed significance for main effect contrasting before and after stimulation ($F(1,20) = 4.35$, $p < 0.05$) and for the interaction between stimulation and sham condition ($F(1,20) = 4.21$, $p < 0.05$).

Tukey post-hoc analysis revealed that UPDRS-III scores improved after stimulation ($t=2.9$, $p < 0.03$) but not after sham ($t=0.42$, $p > 0.05$).

B: Pairwise comparison of UPDRS-III baseline and post-intervention.

C: UPDRS-III improvements on sham-days and stimulation-days. After stimulation, improvements were higher ($t=1.76$, $p = 0.043$).

- Exploratory analysis in N=6 patients, who underwent DBS after participating in this study, revealed that DBS outcomes with well-placed electrodes (Fig. 4) correlates with improvements after network-tDCS ($R= 0.81$, $p = 0.025$).

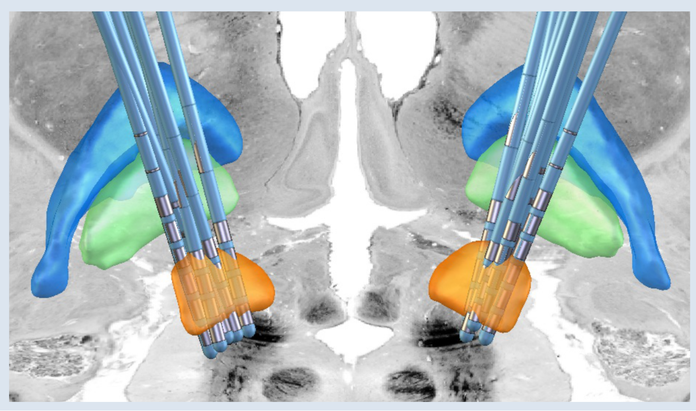


Figure 4. DBS Electrode localization. DBS electrodes from six patients in our sample who sub-sequently underwent DBS were localized using Lead DBS. The backdrop shows a coronal and transversal slice from the BigBrain atlas.

CONCLUSIONS

- Multifocal tDCS under the maximum applicable sum of 4 mA, distributed across the cortex, appears to be a safe method with no reports of adverse events in the current study
- Non-invasive stimulation of a pre-identified PD response network led to a significant improvement in motor symptoms in PD as measured by the UPDRS-III
- This study serves as a proof of principle, demonstrating the possibility of targeting a brain network non-invasively that has been identified through invasive brain stimulation
- The degree of response between multifocal tDCS and DBS targeting the same network may be correlated, potentially motivating for the use of multifocal tDCS as a screening tool before undergoing DBS surgery

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