Electrophysiological correlates of combined working memory training and transcranial direct current stimulation (tDCS) in Neurofibromatosis Type 1: A pilot study

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1. Background

Neurofibromatosis Type 1 (NF1) is a neurodevelopmental disorder:

- Clinical symptoms include dermal neurofibromas and pigmentary lesions
- **Cognitive impairments include working memory (WM)** and attention deficits

Neuroimaging studies have revealed aberrant neural activity during rest and WM performance relative to typically developing children[1,2].

At present there is no standardised treatment for the cognitive impairment associated with NF1.

One existing non-pharmacological intervention study:

- Pilot study investigating WM training (WMT) in NF1[3]
- Improvements in working memory, attention, executive functioning, and short-term memory on untrained tasks[3], alongside regionally specific changes in resting state fMRI[4]

Aim

To investigate the effects of combined WMT and tDCS on EEG activity in adolescents with NF1.

2. Methods

Participants & design

- Single site randomised control trial
- N = 16:
  - Active-tDCS (n=8; 13.16±1.61 years; female: n=3)
  - Sham-tDCS (n=8; 12.89±1.89 years; female: n=3)

Intervention

- 3 x 20 min sessions of combined working memory training (WMT) + tDCS
- WMT task: adaptive spatial n-back task

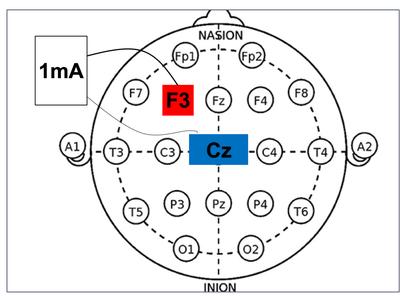

Fig 1. tDCS montage (anode (+): red, 5x5cm; cathode (-): blue, 5x7cm)

Procedure

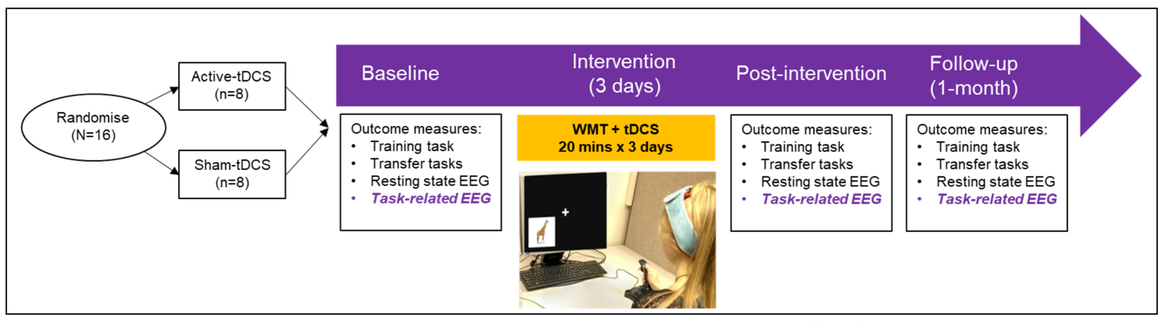

Fig 2. Intervention procedure

Electroencephalography (EEG) recorded during rest and during a visual n-back task

Task-related analysis

P300:

- Correct target trials only
- Time-window: early (300-500ms); late (500-700ms)
- Region of interest: Pz

Theta power:

- Time-window: 900-1900ms post-stimulus onset (maintenance period)
- Frequency band: 4-7Hz
- Region's of interest: left-frontal, mid-frontal, and right-frontal

Theta phase coherence:

- Time-window: 900-1500ms post-stimulus onset (maintenance period)
- Laplacian filtering
- Inter-site phase clustering over trials
- Region's of interest: left and right-frontoparietal

3. Results

P300:

- P300 component sensitive to training: significant reduction in early (300-500ms) and late (500-700ms) P300 amplitude across groups from baseline to post-intervention. This reduction persisted at follow-up in both time-windows.
- Late portion of the P300 component sensitive to stimulation: significant decrease in P300 amplitude from baseline to post-intervention for the active stimulation group only.

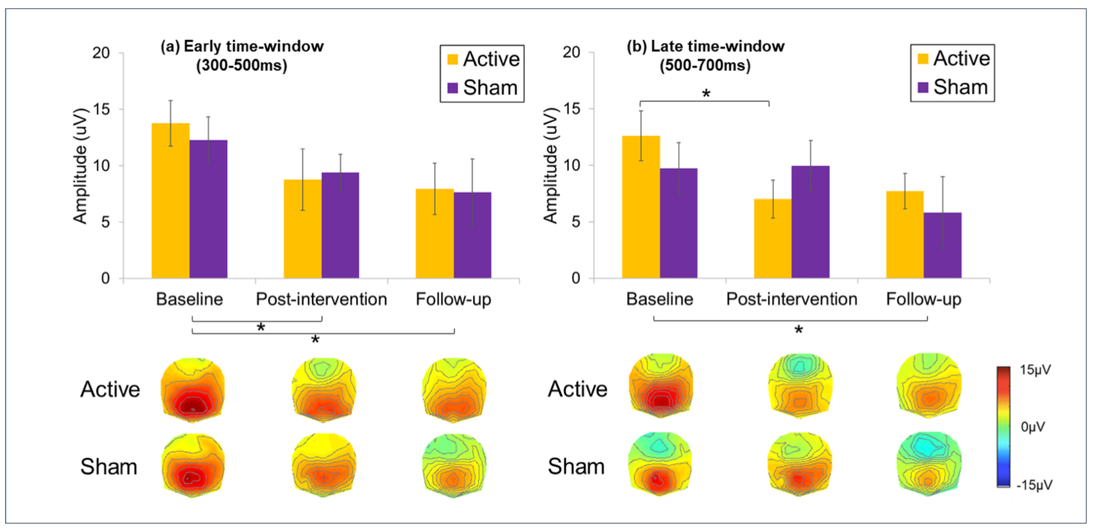

Fig 3. (a) early and **(b)** late P300 amplitude at Pz (top) and as topography plots (bottom).

Theta power:

- No training or stimulation effects on frontal theta power

Theta phase coherence:

- No training or stimulation effects on frontoparietal theta coherence

4. Discussion

- Early (300-500ms) and late (500-700ms) P300 amplitude was robustly sensitive to WMT effects with amplitude reductions across the board. Promisingly, WMT effects persisted at follow-up.
- Late portion of the P300 component (500-700ms) was sensitive to stimulation, with amplitude reductions driven by the group that received active stimulation.
- P300 is a complex component with multiple cognitive contributors (e.g., allocation of attention, task-relevant target detection, updating of working memory etc.), and so it is difficult to provide a mechanistic explanation for the observed effects without further research to tease these contributors apart.
- No significant training or stimulation effects on task-related theta power or frontoparietal theta coherence. In line with a recent investigation in adolescents with ADHD that observed no significant effect of WMT + tDCS on spectral power[5].
- This pilot study provides a useful foundation for future investigation using larger, sufficiently powered, samples to draw stronger conclusions with regards to the effect of combined working memory training and tDCS on EEG activity in NF1.

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