An Exploration of the Therapeutic Potential of Targeted tDCS in Alzheimer's-Associated Agitation & Aggression

Researcher: Sofia Penttilä Supervisor: Dr. Sanjeev Kumar

I. Introduction

Alzheimer's Disease (AD)

- Progressive neurodegenerative disorder causing cognitive, behavioural, and functional decline[1]
- 57 million people live with dementia worldwide[3]
- Involves amyloid-β plaques and tau tangles, leading to synaptic dysfunction, neuronal loss, and brain atrophy[1]
- Disrupts the brain's excitation-inhibition balance, with reduced GABAergic inhibition contributing to cortical hyperexcitability and neuropsychiatric symptoms[6]

Neuropsychiatric Perspective

- Agitation and aggression substantially affect patients, caregivers, and quality of life[4,6]

Transcranial Direct Current Stimulation (tDCS)

- tDCS is a non-invasive neuromodulation technique that can alter cortical excitability and influence GABA/glutamate activity[8,9]
- Cathodal tDCS decreases cortical excitability, making it a potential approach for targeting AD-associated cortical hyperexcitability[8]
- Evidence for tDCS in AD remains mixed

Objective:

This study investigates whether frontal cathodal tDCS improves neuropsychiatric symptoms in patients with Alzheimer's associated agitation and aggression, compared with sham treatment, and whether effects persist at 2-week follow-up

II. Methods

Clinical assessments: NPI-C, CMAI, CGI-S, and CGIC at baseline (T0), post-treatment (T1), and 2-week follow-up (T2)

TMS-EEG: Single- and paired-pulse TMS used to measure LICI and SICI as markers of cortical excitation/inhibition

Demographics: Age, gender, race, and baseline clinical ratings assessed between tDCS and sham groups

Clinical analysis: Linear mixed-effects models tested treatment × time interactions, with participant as a random intercept

- Type III ANOVA assessed treatment, time, and interaction effects

Exploratory LICI analysis: Linear regression tested whether baseline global LICI was associated with changes in NPI-C symptoms at T1 and T2, including LICI × treatment interactions. Change scores were calculated from T0 to T1 or T2, with positive values representing symptom improvement.

Statistical analysis and visualization were conducted in R

III. Results

Clinical Outcomes

- NPI-C Aggression: Significant treatment × time interaction (p = 0.014) (Fig. 1)
- CMAI Physical Non-Aggressive Severity: Significant treatment × time interaction (p = 0.005) (Fig. 2)
- Most other clinical measures showed no significant treatment × time interactions

Exploratory LICI Analysis

- Baseline global LICI showed significant LICI × treatment interactions for: Aberrant motor disturbance (p = 0.003), Dysphoria (p = 0.021), and Irritability (p = 0.045) (Fig. 3)

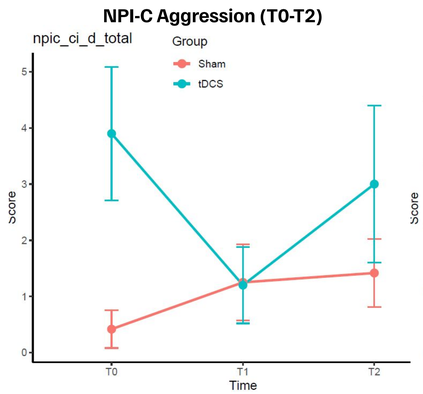


Fig. 1: NPI-C aggression scores across T0, T1, and T2 in the tDCS and sham group. A significant treatment × time interaction was observed (p = 0.014).

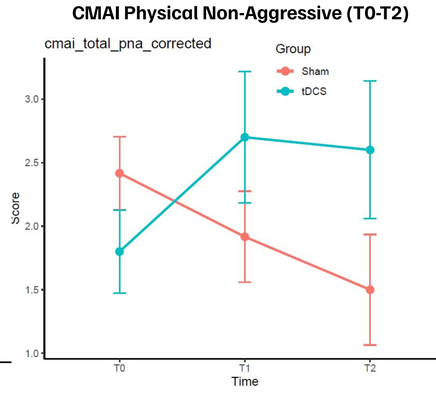
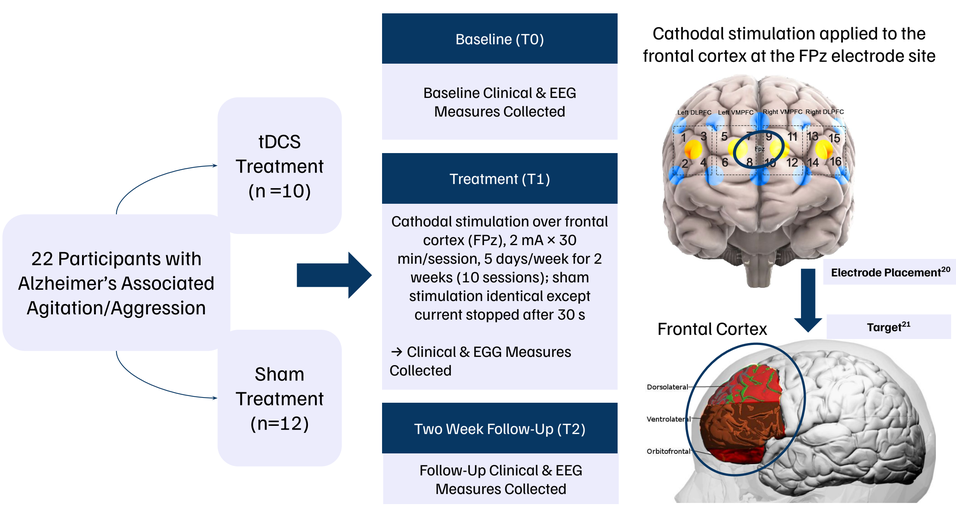


Fig. 2: CMAI physical non-aggressive severity scores across T0, T1, and T2 in the tDCS and sham groups. A significant treatment × time interaction was observed (p = 0.005).

IV. Discussion

- tDCS showed symptom-specific effects, rather than broad clinical improvement.
- Aggression improved immediately post-treatment, but the effect was not sustained
- CMAI physical non-aggressive severity worsened relative to sham
- Baseline LICI may influence treatment response
- Small sample size (N = 22; LICI N = 11)
- Larger studies are needed to confirm effects and identify biomarkers of response



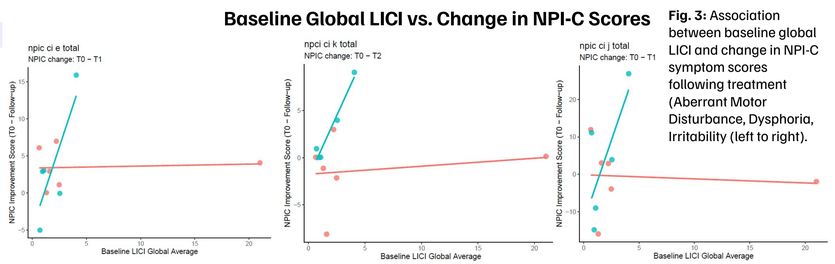


Fig. 3: Association between baseline global LICI and change in NPI-C symptom scores following treatment (Aberrant Motor Disturbance, Dysphoria, Irritability (left to right).

V. Future Directions

- Expand EEG analysis: LICI, SICI, N45, N100, GMFP
- Recruit larger samples to improve reliability
- Use longer follow-up to assess treatment durability
- Identify potential EEG biomarkers of treatment response

References

Research Report

VI. Acknowledgments

- Dr. Sanjeev Kumar
- CAMH Geriatrics Research Team & tTED study
- Laidlaw Foundation
- U of T Laidlaw Scholars Programme