INTERIM REPORT

Transcranial direct current stimulation (tDCS) combined with cognitive training to enhance memory in patients with amnestic mild cognitive impairment (aMCI)

Dementia Collaborative Research Centre
Assessment and Better Care

December 2014
Corresponding Author

Adith Mohan a.mohan@unsw.edu.au

Acknowledgements

This project has been funded by an NHMRC Program Grant (ID568969) and by the Dementia Collaborative Research Centre – Assessment and Better Care, University of New South Wales as part of an Australian Government Initiative.

Disclaimer

The views expressed in this work are the views of its author/s and not necessarily those of the Australian Government.
Transcranial direct current stimulation (tDCS) combined with cognitive training to enhance memory in patients with amnestic mild cognitive impairment (aMCI)

**BACKGROUND**
Currently, there is no effective intervention available for people at risk for dementia, with pharmacological approaches having so far proven ineffective. However, behavioural interventions, such as cognitive training have shown promise for improving cognition, particularly memory. Improving memory is especially important for people who are at risk and have objectively measured memory impairment, i.e., diagnosed with amnestic mild cognitive impairment (aMCI). aMCI is considered the symptomatic predementia phase of Alzheimer’s disease (AD), the most common form of dementia.

Currently, there is no effective intervention available for people at risk for dementia. Many different approaches have been trialled, both pharmacological and non-pharmacological. This research has shown that pharmacological approaches (e.g., cholinesterase inhibitors) have minimal effects. Attention has therefore turned to non-pharmacological interventions, with recent systematic reviews highlighting early promising results for psychological interventions (e.g., cognitive training (CT)), particularly for improving memory. However, RCTs into CT interventions have so far shown limited efficacy, primarily due to small sized treatment effects and insufficiently powered studies.

This double-blind randomized controlled study aims to investigate an exciting novel approach we have developed for improving memory in people diagnosed with aMCI; cognitive training (CT) combined with mild non-invasive brain stimulation (transcranial direct current stimulation (tDCS)). tDCS is a safe and non-invasive technique which can be used to improve attention and cognitive performance. Based on our prior work in healthy participants, we expect that this combined approach (i.e., tDCS + CT) will be more effective in improving memory and cognition than CT alone.

**OBJECTIVES & HYPOTHESES**
There is preliminary evidence that CT can improve memory in people diagnosed with MCI. The primary objectives of this study are thus: 1) To investigate whether active tDCS combined with CT (Active tDCS + CT) improves memory more than CT alone (Sham tDCS + CT), and 2) To determine whether the memory improvement from Active tDCS + CT is maintained over time.

Our hypotheses are as follows:
1) Active tDCS + CT will show significantly greater improvement from baseline (T1) to post-intervention (T2) on a non-trained verbal memory task compared to Sham tDCS + CT.
2) The difference in performance between Active tDCS + CT and Sham tDCS + CT on the non-trained verbal memory task at post intervention will remain significant at 3 month follow-up.

**STUDY DESIGN**
The study will use a double-blind, sham-controlled, parallel group, experimental design. Participants will be randomised using a computer generated random number list and matched based on estimated premorbid IQ (e.g., low average, average, high average, etc.) to one of two conditions (1:1 ratio): 1) Active LDLPFC tDCS during CT (Active tDCS + CT) or 2) sham tDCS during CT (Sham tDCS + CT). Both conditions will require attendance for 15 sessions, conducted over approximately 5 weeks (3 sessions per week) at the Neurostimulation Research Centre, Black Dog Institute, Sydney. Primary and secondary outcome measures will be completed at T1 (i.e., pre training day 1), T2 (i.e., post-intervention, 1-3 days post day 15), and at T3 (i.e., 3 months follow-up).
METHODS

Transcranial direct current stimulation (tDCS)
Active tDCS will be given continuously for 30 minutes at 2 mA, 3 times a week during CT. The anode will be placed over the left F3 electrode site (overlying the LDLPFC and identified on the scalp using an EEG cap based on the 10/20 system) and the cathode over F8. Conductive rubber electrodes covered by sponges soaked in saline will be used, held in place by a head band. For sham stimulation, the current will be gradually increased to 1 mA and then left on for another 30 seconds before being ramped down to zero over another 30 seconds.

Cognitive Training (CT)
CT will be administered using the COGPACK (Marker, 2001) computer-administered CT software. This software was chosen because researchers in our team have found it to be well-tolerated in people with MCI and because it has previously been shown to be effective for improving memory in older adults. Several CT tasks were specifically chosen to train cognitive abilities important for learning and memory (i.e., working memory, processing speed, attention), in addition to memory CT tasks.

Outcome Measures
Primary outcome measure
The primary cognitive outcome measure will be the Total Learning score from the CVLT-II, a non-trained test of verbal learning and memory (2 parallel forms).

Secondary outcome measures
Additional outcome measures will examine for potential transfer effects to other non-trained cognitive tests assessing visual memory, processing speed, working memory/sustained attention, subjective cognitive complaints, and functional and quality of life outcomes.

PRELIMINARY RESULTS
Data collection commenced in January 2013. As of June 2014, 20 participants have completed the T2 assessment. Preliminary results suggest an advantage for Active tDCS + CT condition on the primary outcome measure (CVLT-II), as well as on a secondary outcome measure assessing speed of information processing.

SIGNIFICANCE
Preliminary results suggest that tDCS combined with CT causes greater memory improvement than CT alone in patients with aMCI. Moreover, we expect that memory improvements with Active tDCS + CT will be maintained over time. Should this intervention be found effective, potential large-scale translation to the community is feasible as CT can be manualised and completed at home on computer/tablet. tDCS technology is also simple to use, inexpensive, and portable. Furthermore, the next generation of tDCS technology in development will enable home use.

FUTURE DIRECTIONS
This clinical trial is powered so that a total sample size of N = 100 is required, allowing for ~10% attrition. A NHMRC project grant for the study was submitted in 2014 for potential commencement in 2015. Recruitment will continue for the study throughout 2014.