Category: Nursing issues

Study type: Quantitative study - other

Author's declarative title: Combined transcranial direct current stimulation and cognitive remediation therapy modestly slows cognitive decline in older adults with remitted depression but not mild cognitive impairment alone

Commentary on: Rajji TK, Bowie CR, Herrmann N, et al. Slowing Cognitive Decline in Major Depressive Disorder and Mild Cognitive Impairment: A Randomized Clinical Trial. *JAMA Psychiatry.* 2025;82(1):12–21. doi:10.1001/jamapsychiatry.2024.3241

Commentary

Implications for practice and research

- The combination of transcranial direct current stimulation (tDCS) and cognitive remediation (CR) therapy slows cognitive decline in older adults with remitted depression and mild cognitive impairment (MCI), though the effect sizes are small and may not yet justify routine clinical use.
- It remains unclear whether the observed benefits stem primarily from CR, tDCS, or their combination. Future trials should examine the interventions independently, assess cost-effectiveness, and evaluate real-world applicability.

Context

Late-life depression and MCI are both associated with increased dementia risk and are widely recognised as prodromal conditions.[1,2] Depression commonly presents with cognitive symptoms that are often resistant to standard treatment and can persist into remission.[3,4] Moreover, depression and MCI frequently co-occur, with a pooled prevalence of depression in individuals with MCI estimated at 32%.[5]

Targeting cognitive function in these high-risk groups is important, as cognitive reserve may be a modifiable factor that contributes to delaying or even preventing progression to dementia. CR, a behavioural intervention involving structured cognitive training, and tDCS, a non-invasive brain stimulation technique that may enhance cortical plasticity, have both been proposed as promising therapeutic strategies to boost cognitive function in older adults.

The PACt-MD trial is the first large-scale, long-term, randomised controlled trial (RCT) to investigate the combined effects of CR and tDCS in older adults with remitted major depressive disorder (rMDD), with and without MCI, prior to conversion to dementia.[6]

Methods

This double-blind RCT recruited 375 older adults (>65 years) with rMDD (with or without MCI), or MCI alone, from five academic hospitals in Canada. Participants received either active CR + active tDCS, or sham equivalents of both interventions, over an eight-week acute phase, followed by biannual booster sessions and home-based daily cognitive exercises. Follow-up lasted for up to seven years (median four years).

The primary outcome was change in a composite cognitive score derived from performance across six cognitive domains. Secondary outcomes included domain-specific changes, short-term (two-month) cognitive improvements, progression to dementia. Subgroup analyses explored the impact of diagnosis and APOE ε4 genotype on any changes.

Findings

Compared to the sham group, participants receiving CR + tDCS showed a slower rate of global cognitive decline, with an adjusted Z-score difference of 0.21 (corresponding to a small effect) at 60 months. However, no significant cognitive benefit was observed at two months, and the intervention did not significantly reduce conversion to dementia or MCI. Interestingly, APOE ε4 carriers, who are at higher genetic risk of Alzheimer's disease, showed no significant benefit of the combined intervention. The most pronounced cognitive improvements were observed for executive function and verbal memory—domains commonly affected in depression.

Commentary

Rajji and colleagues' PACt-MD trial is a timely and high-quality investigation into the potential for non-pharmacological interventions to mitigate cognitive decline in older adults with rMDD and/or MCI. The study has several strengths, including its sample size, long follow-up period, robust and effective blinding procedures, and in-depth analysis of treatment effects across diagnostic and genetic subgroups.

Nonetheless, several limitations merit comment. First, the trial design using a combined intervention strategy makes it impossible to determine the individual contributions of CR and tDCS; we cannot tell whether one or both interventions, or their interaction, are driving the observed effects. Second, although statistically significant, the observed effect sizes were small - equivalent to less than one point on commonly used clinical tools such as the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA) over five years. Third, the lack of significant benefit in slowing conversion to dementia, or in APOE ε4 carriers, suggests that this intervention may be less effective in individuals with underlying Alzheimer's pathology.

Despite these limitations, this trial represents an important advance on previous work, as there are currently no established treatments for cognitive impairment associated with depression. The PACt-MD trial provides robust evidence supporting the potential of tDCS + CR as a feasible, non-invasive approach that warrants further exploration in targeted populations.

References

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Commentator details

Name: Professor Jonathan Roiser
Affiliation: University College London, Institute of Cognitive Neuroscience
Correspondence address: UCL Institute of Cognitive Neuroscience, Alexandra House, 17-19 Queen Square, London WC1N 3AZ
Email: j.roiser@ucl.ac.uk

Name: Dr Harry Costello
Affiliation: University College London, Division of Psychiatry
Correspondence address: UCL Division of Psychiatry, 6th Floor, Wings A and B, Maple House, 149 Tottenham Ct Rd, London W1T 7NF
Email: harry.costello@ucl.ac.uk

Competing interests

No competing interests to declare.