TRANSCRANIAL STIMULATION AND COGNITIVE RESERVE:
MEANS OF COGNITIVE ENHANCEMENT IN MCI AND HEALTHY AGING

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The ability to hold and manipulate information in working memory (WM) declines with aging and across neurodegenerative diseases. Impaired synchronization of the frontoparietal network (FPCN) is recognized as a potential neurological root. We aimed to evaluate the efficacy of various multifocal transcranial alternating current stimulation (tACS) protocols in improving WM performance by synchronizing theta oscillations in the FPCN. Additionally, we assessed whether tACS improves performance depending on baseline cognition and induced functional connectivity changes in the FPCN.

METHODS

Protocol (Figure 1): Session 1: Assessment of individual targets in the right medial frontal gyrus (rMFG) and inferior parietal lobule (rIPL) areas. Sessions 2-5: Randomized within-subject tACS at θ frequency of 4.51 Hz concurrently with the visual N-back task.

Subjects:

	HC = 31	MCI = 24	*p*
Age	68.19 ± 5.25	68.33 ± 5.38	n.s.
YoE	16.44 ± 3.99	13.81 ± 2.97	.005
Sex F/M	9/8	8/7	n.s.

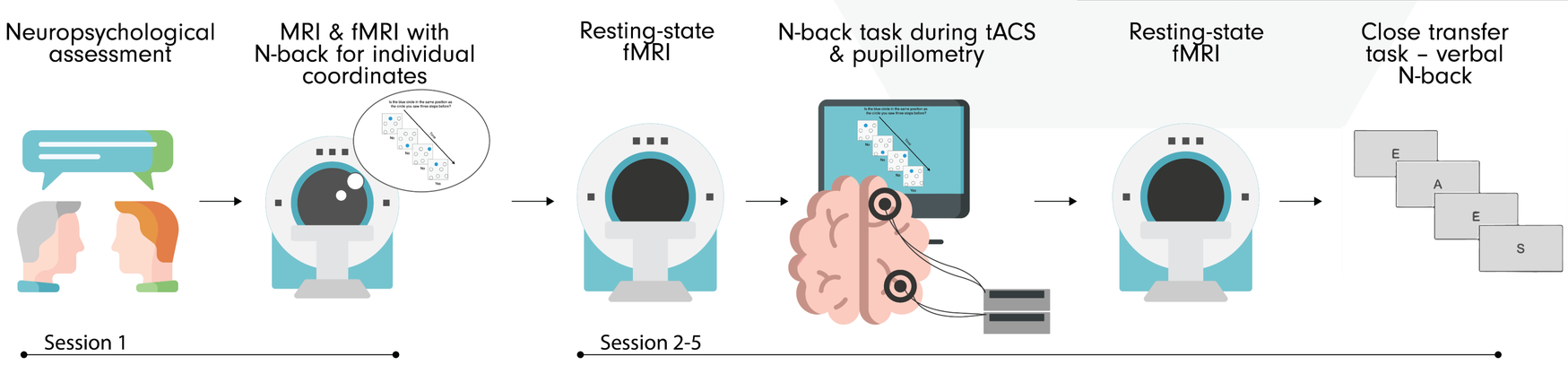

Figure 1 | Experimental protocol

RESULTS

Frontoparietal stimulation, compared to sham, significantly enhanced accuracy on the 2-back task in the HC group (Figure 2; β = -2.70, p = .037), with a mean improvement of 2%. Both groups also improved with task training (β = 4.59, t(1547) = 5.03, p < .001).

On the 3-back task, only HC participants showed improvement (Figure 2; β = -2.64, p = .058) with **frontal stimulation**, achieving a mean difference of 3%, while the performance of MCI did not change.

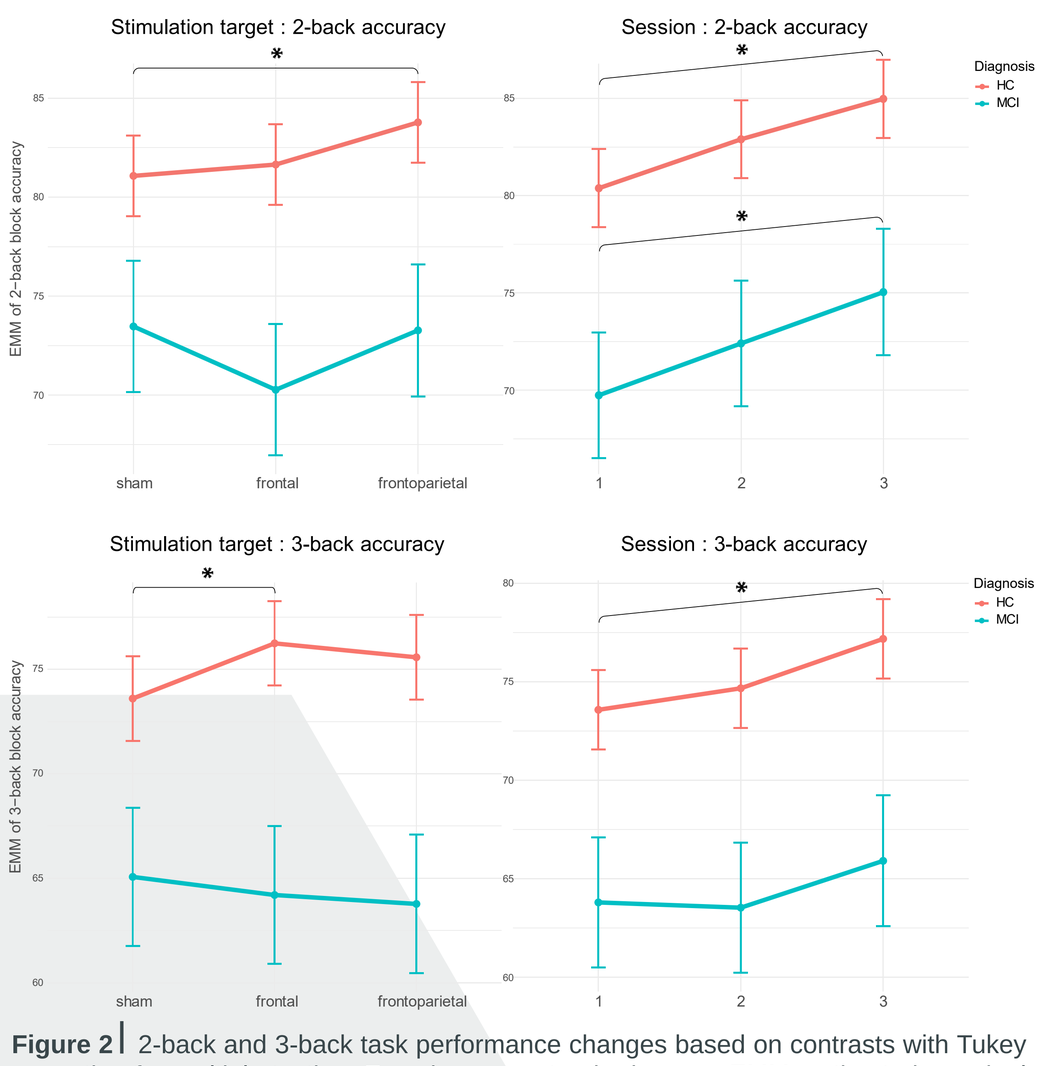

Figure 2 | 2-back and 3-back task performance changes based on contrasts with Tukey correction for multiple testing. Error bars are standard errors. EMM: estimated marginal means.

Association with FPCN connectivity

Improvement in the 2-back task was correlated with post-stimulation changes in FPCN functional connectivity (Figure 3), specifically in the clustering coefficient (β = 13.74, p = .032) and node strength (β = .16, p = .032). Baseline pre-stimulation task functional connectivity was not associated with performance.

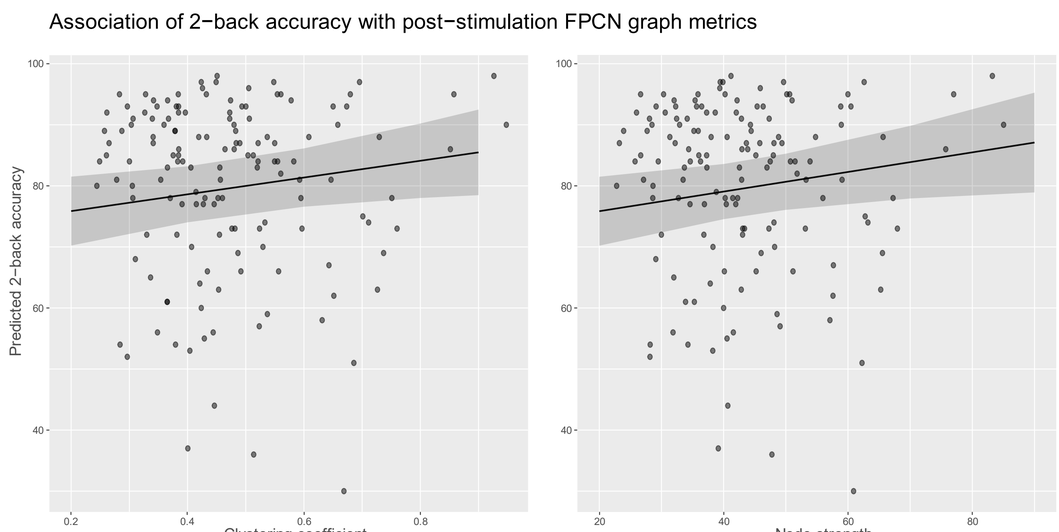

Figure 3 | Scatterplots of associations between 2-back task performance and post-stimulation FPCN clustering and node strength. Ribbons are standard errors.

DISCUSSION

Our findings indicate that in-phase frontoparietal tACS enhanced performance on the 2-back task, while frontal tACS improved performance on the more demanding 3-back task. This enhancement was evident only in HC, whereas individuals with MCI showed improvement primarily on the less demanding 2-back due to the training aspect of the intervention. Additionally, we observed that participants who successfully increased the clustering and node strength within the FPCN from their pre-stimulation baseline demonstrated greater performance gains. This increase in node strength and clustering likely reflects a compensatory mechanism utilized by HC. Our results emphasize that the efficacy of tACS interventions is closely tied to an individual's baseline cognitive capacity, aligning with established theories of cognitive aging and compensation, such as the Scaffolding Theory of Aging and Cognition (STAC).

Acknowledgment

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