Cognitive assessment for the prediction of transcranial electrical stimulation effects on memory improvement

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Introduction

Neuropsychiatric disorders, including Alzheimer's Disease (AD), impose substantial personal and financial burdens, and despite being one of the leading causes of death globally, treatment strategies are generally ineffective. The MEMORI Study (NCT05077826), a randomized double-blind clinical trial of older adults with and without Mild Cognitive Impairment (MCI), investigated the efficacy of transcranial direct-current stimulation (tDCS) to improve learning and potentially mitigate the effects of dementia. This study investigated whether variation in treatment efficacy can be predicted by cognitive assessments given prior to treatment.

Methods

- Cognitive assessments were used to evaluate cognitive function and impairment among participants who received either a sham (0.1 mA) or verum (2.0 mA) dose of tDCS.

- Correlation coefficients were computed to investigate the relationship between these cognitive measures and the scores from the PRETXT discovery learning task after training [3].

- The scores from the PRETXT task were calculated using the last test minus the baseline, converted to Z-scores.
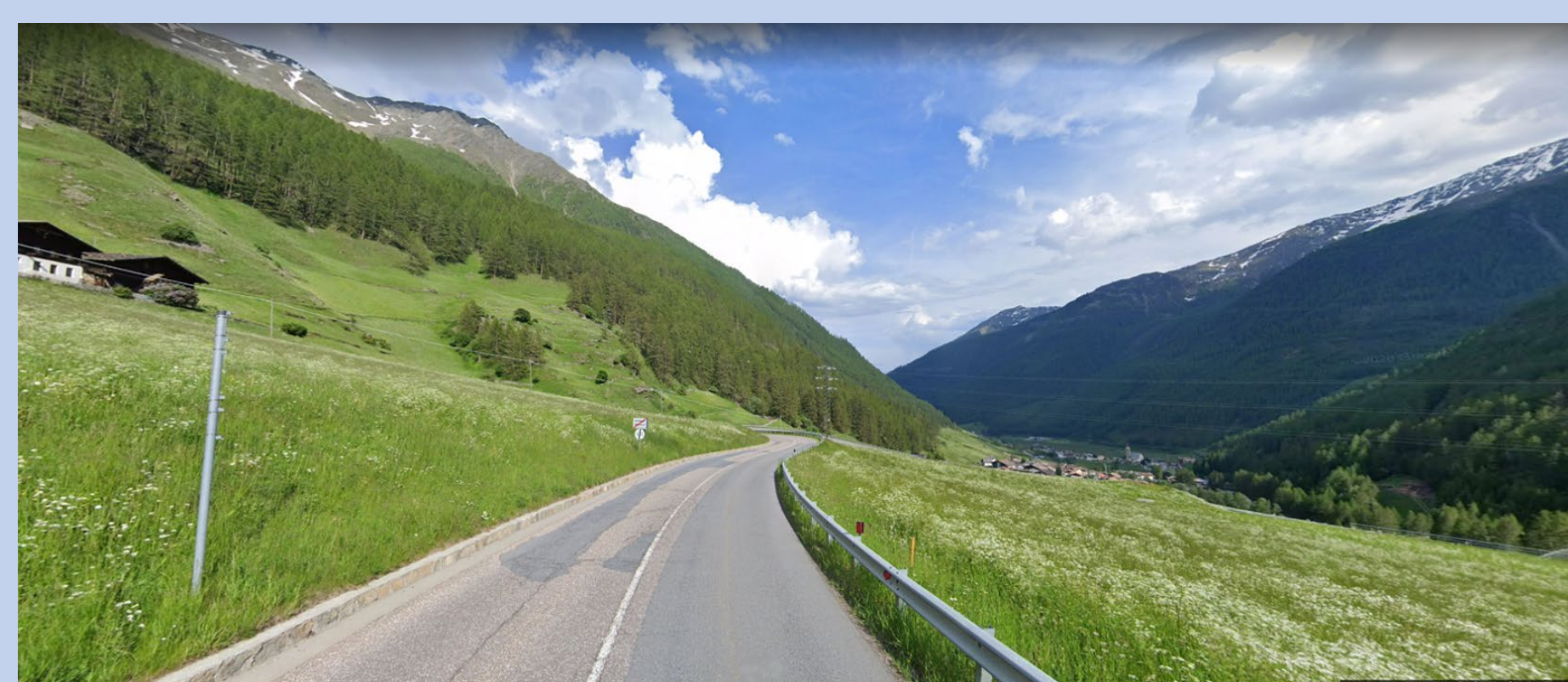
PRETXT Learning Task: Participants are shown a series of pictures from European streets and asked to decide if the picture represents 'Category 1' or 'Category 2'. This task was used in MEMORI to determine participants' improvements in learning and memory [3].
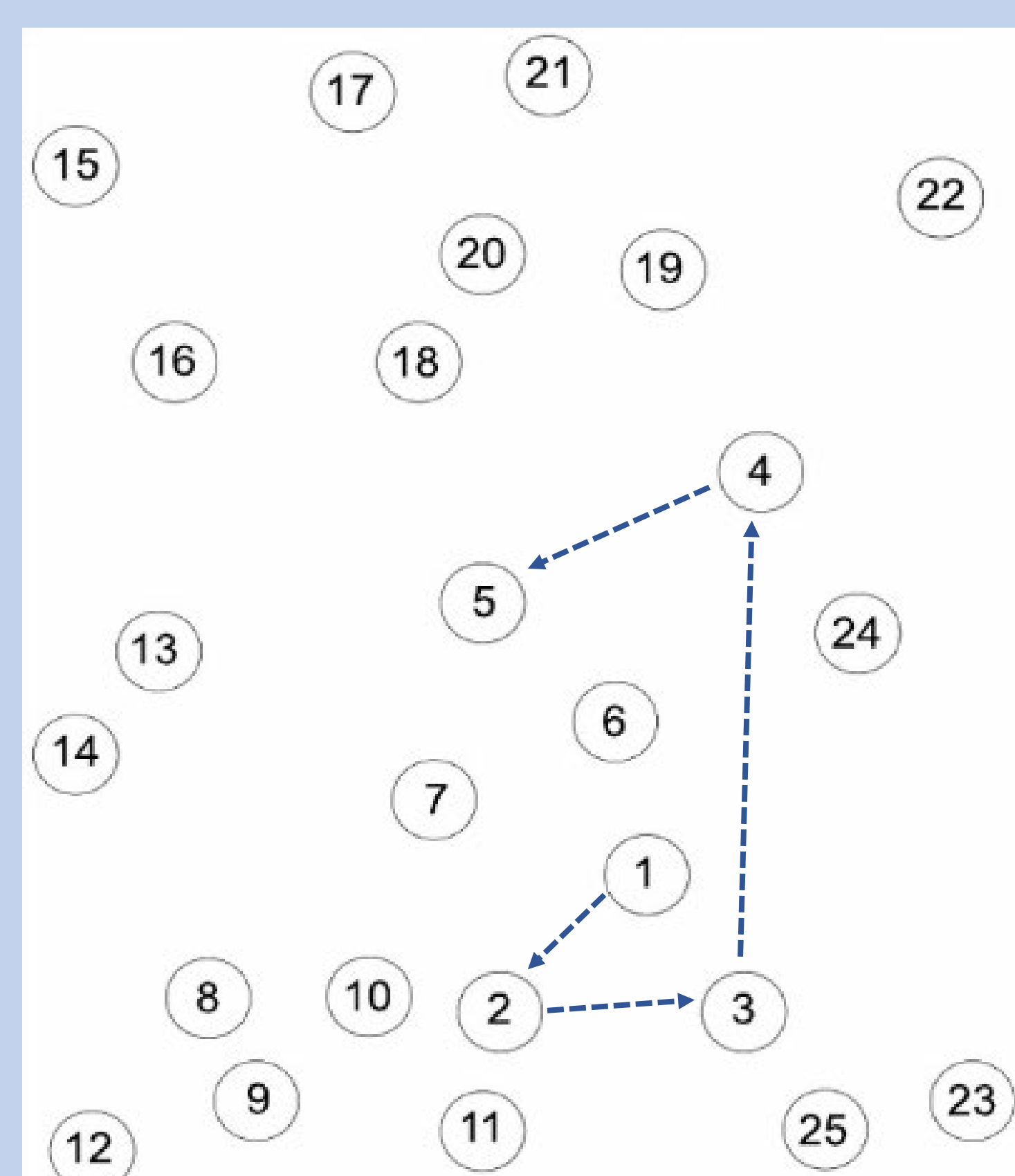
Trail Making Test A (TMT A): Participants are tasked with drawing lines in numerical order. Their time is scored, with no penalties for mistakes made. This test is used to evaluate working memory [1].
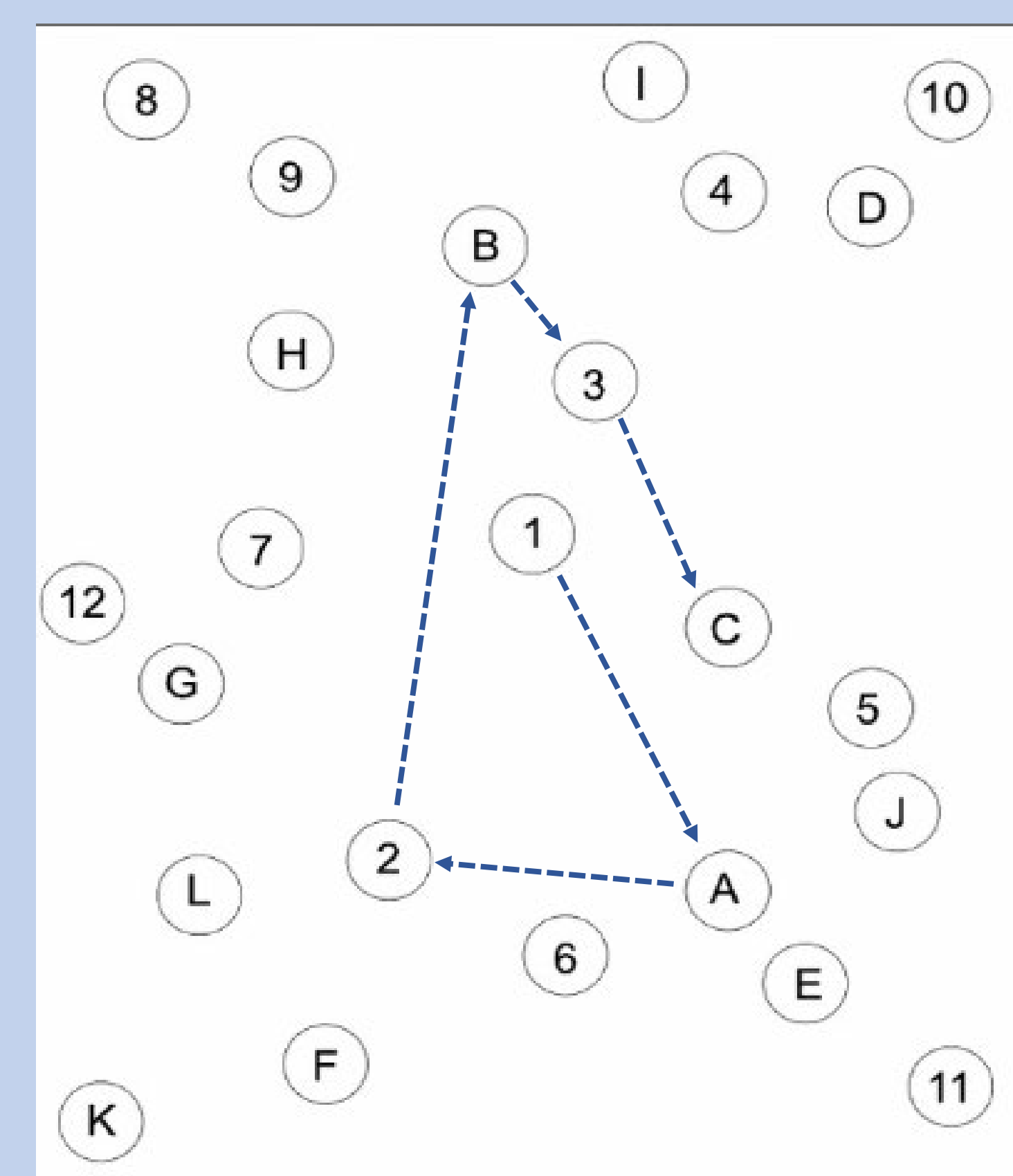
Trail Making Test B (TMT B): Participants are tasked with drawing lines in numerical and alphabetical order, alternating with numerical and alphabetical. Their time is scored with no penalties for mistakes made. This test is used to evaluate mental flexibility and processes [1].

Future Directions

The Trail Making Tests are a commonly used screening tool for dementia. The TMT scores were found to have a significant positive correlation with cognitive ability and learning task performance in participants receiving verum tDCS, but not sham. TMT A had a larger significance compared to TMT B. This could be due to the increase in complexity and since the age-related differences in processes are smaller and more variable in TMT B compared to TMT A [4]. TMT A also measures working memory, which is more readily utilized and quantified by the learning task [1].

Limitations include; the TMT data being difficult to stratify since age, education, and intelligence affect TMT performance, the normative cutoffs for TMT's being difficult to analyze [4], and the relatively small sample size.

In the meantime, these results suggest a simple and cost-effective strategy for predicting the beneficial effects of this neuromodulation technique on individual patients.

Highlights

- Participants of all cognitive abilities were randomly assigned to either condition.
- A significant positive correlation was found between TMT performance and tDCS enhancement in learning for the active tDCS group.
- No correlation of TMT performance with learning in sham tDCS.
- TMT A has a more significant correlation than TMT B, since the learning task measures improvements in memory and learning. Working memory (TMT A) may have a larger impact on the scores as opposed to executive functioning (TMT B) [4].

Correlation of TMT A and 4th Test Minus the Baseline
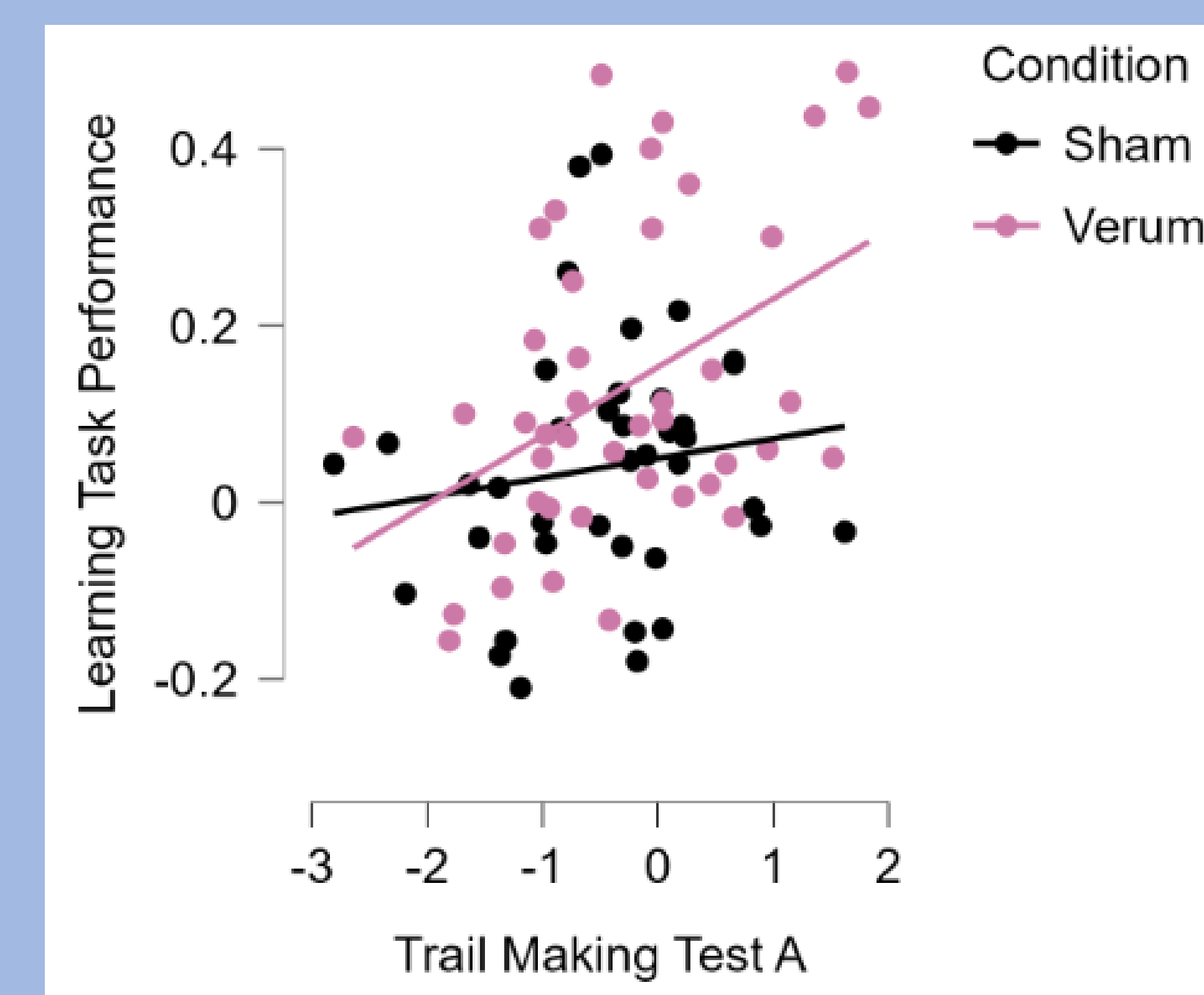
Correlation of TMT B and 4th Test Minus the Baseline
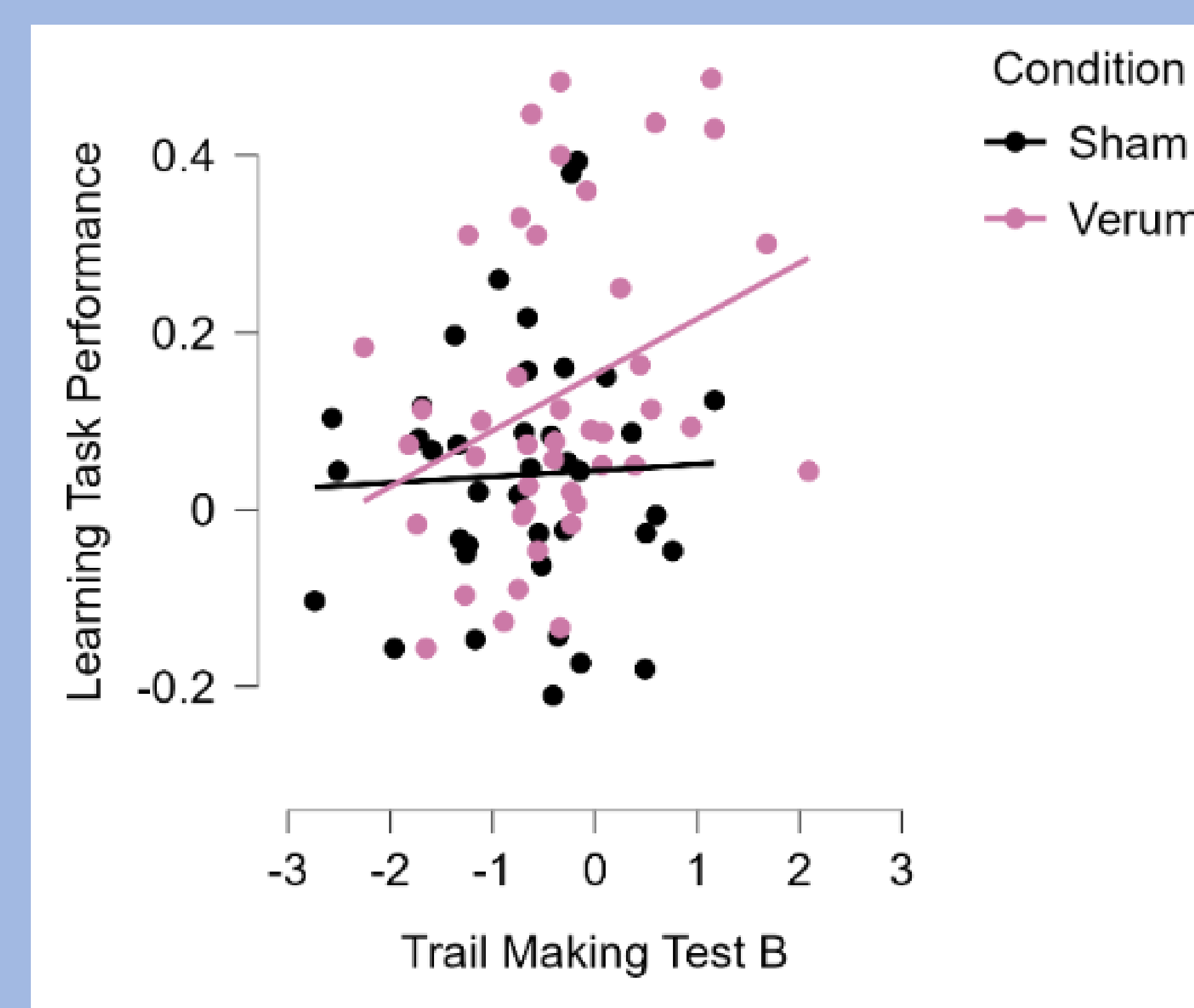
Results

In the verum tDCS group, a significant positive correlation was found between Trail Making Tests A and B and the amount of learning in the PRETXT task ($r=0.4415$, $p=0.0030$ and $r=0.3270$, $p=0.0324$, respectively). In contrast, the sham tDCS group showed nonsignificant correlations ($r=0.1453$, $p=0.3468$ for Test A and $r=0.0446$, $p=0.7740$ for Test B).

References: [1] Esther Heerema, MSW. The Trail Making Test and Its Use as a Screening Tool for Dementia. *Verywell Health*, Verywell Health, 27 May 2023. [2] Gibson, Benjamin C. Effects of Transcranial Direct Current Stimulation on Category Learning in Older Adults. *University of New Mexico*, Digital Repository UNM, 2023. [3] Gibson, B. C., Mullins, T. S., Heinrich, M. D., Witkiewitz, K., Yu, A. B., Hansberger, J. T., & Clark, V. P. (2020). Transcranial direct current stimulation facilitates category learning. Brain Stimulation, 13(2), 393–400. [4] Salthouse, Timothy A. What Cognitive Abilities Are Involved in Trail-Making Performance? *PubMed Central NIH*, U.S. National Library of Medicine, July 2011.