Objective/Hypothesis: Here, we characterized brain-wide changes in functional network segregation (i.e., the balance of within vs. between-network connectivity strength) induced by high-definition (HD) tDCS in older adults with mild cognitive impairment (MCI) during virtual spatial navigation.
Methods: Participants were a mixed neurologic sample comprising 20 MCI patients and 22 cognitively intact older adults (healthy controls – HC), part of a double-blind, cross-over, randomized controlled trial (NCT01958437). All participants underwent functional magnetic resonance imaging (fMRI) following two counterbalanced HD-tDCS sessions (one active, one sham) that targeted the right parietal cortex (center anode at P2) and delivered 2mA for 20 minutes.
Results: Compared to HC, MCI patients showed lower brain-wide network segregation following sham HD-tDCS. However, following active HD-tDCS, MCI patients' network segregation increased to levels similar to those in HC, suggesting functional normalization. Follow-up analyses indicated that the increase in network segregation for MCI patients was driven by HD-tDCS effects on the "high-level"/association brain networks, in particular the dorsal-attention and default-mode networks.
Conclusion(s): HD-tDCS over the right parietal cortex may normalize the segregation/integration balance of association networks during spatial navigation in MCI patients. This highlights the potential utility of employing HD-tDCS as a targeted system-level intervention for restoring brain activity in Alzheimer's disease and related dementias.
Keywords: neuromodulation, transcranial electrical stimulation, network neuroscience, restoration

P2.083

A 6-MONTH NATURALISTIC STUDY OF DEPRESSION AND INSOMNIA USING TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN 100 PATIENTS WITH TREATMENT-RESISTANT DEPRESSION DEMONSTRATING RESPONSE AND DURABILITY

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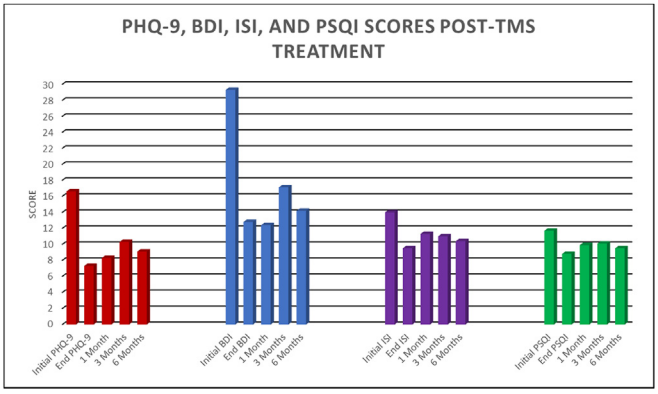
Abstract
Background: 100 patients were selected, with 72 completing treatment (using only their data). The average age of the patients was 50.8 years, and 49 were females.
Design/Methods: Using the *Brainsway* H1 dTMS system to the left dorsolateral prefrontal cortex (LDPFC) at 120% motor threshold and 18 Hz, the patients received on average 31.2 dTMS treatments. Following the Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI), before, after treatment, at three months, and six months post-treatment, results were analyzed using paired sample t-tests. Scales were completed/returned by 100% at the end of treatment, 69% at one month, 44% at three months, and 38% at six months.
Results:

	Initial	End	1 Month	3 Months	6 Months
PHQ-9	16.6	7.3	8.3	10.5	9.1
BDI	29.3	12.8	12.4	17.1	14.2
ISI	14	9.5	11.3	11.0	10.4
PSQI	11.7	8.8	9.9	10.1	9.3

The study demonstrated improvement on all four scales. Changes in depression inventory scores were statistically significant at $P < .001$ for both: **after** treatment and **six months post-treatment**. Both insomnia scales demonstrated statistically significant changes ($P < .01$) **after** treatment. The difference in ISI scores from **six months after treatment** was statistically significant ($P < .05$), as was the change in PSQI scores ($P<.01$). Treatment showed overall durability. Even from the **end** of initial TMS treatment to **six months after treatment**, there were no statistically significant changes in the BDI, ISI, or PSQI scores, but a difference was noted in the PHQ-9 ($P<.05$). Also, 31 patients eventually required some form of preservation/maintenance treatment.
Conclusions: Statistically significant improvement in both insomnia and depression scales were found and maintained at least 6-months with dTMS treatment.



Conflict of Interest: The authors have no conflicts of interest to report. No funding was provided for this research.
Keywords: Transcranial Magnetic Stimulation, Depression, Insomnia, Durability

P2.084

COGNITIVELY IMPAIRED OLDER ADULTS EXHIBIT DIMINISHED RISE IN I/O CURVE WITH TMS

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Abstract
When single-pulse transcranial magnetic stimulation (TMS) is applied to the motor cortex, the electromyogenic response that results from the summation of synchronous descending volleys can be readily measured (Motor Evoked Potentials; MEPs). When TMS intensity increases there is an increase in the MEP amplitude. This reflects that stronger TMS stimuli depolarize a larger pool of neurons, which summate to generate a larger motor response. However, even at the strongest TMS intensities, MEP amplitude is smaller than what could otherwise be observed with direct stimulation of the proximal peripheral nerve. This relative reduction in TMS-MEP suggests that some 'signal' is inevitably lost due to phase cancellations in the motor cortex as a function of cortical de-synchrony.
This study enrolled 40 older adults (mean age 69±2), 20 with intact cognition and 20 with evident cognitive decline (MCI). We generated I/O curves by sampling MEPs across 16 intensity levels in two conditions: at rest and in presence of background voluntary contraction. We analyzed the effect of cognitive status on different components of this I/O relationship.
When evaluating model parameters for the sigmoidal curve generated across the entire I/O curve, there is significantly flatter rise in MEP amongst MCI cohort ($p < 0.01$). Further, in the intensity band where steepest rise is expected (110-140% MT), an ANOVA revealed significantly reduced area under the curve ($p<0.05$) amongst MCI cohort. Similarly, a hierarchical linear model within this same band of intensities also indicates a significantly blunted effect of increased TMS intensity on rise in MEP in MCI cohort ($p < 0.05$). This effect was most pronounced in the active condition.
This novel finding of a diminished rise in MEP amplitude across the I/O curve in MCI could be interpreted as increased cortical de-synchrony. Further investigation into this preliminary finding is required.
Keywords: Aging, Cognitive Decline, TMS, Input/Output Curve