Do Working Memory Differences Exist Dependent Upon Dorsolateral Prefrontal Cortex or Medial Orbitofrontal Cortex Repetitive Transcranial Magnetic Stimulation Treatment for Smoking Cessation?

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Background

- In the United States, cigarette smoking yearly claims about one in every five deaths, with mortality rates continuously rising.[1]
- High-frequency repetitive transcranial magnetic stimulation (HF-rTMS) over the dorsal lateral prefrontal cortex (DLPFC) as well as low-frequency (LF-rTMS) over the medial orbitofrontal cortex (mOFC) has historically demonstrated high efficacy in curbing nicotine cravings and worked as progressive neurostimulation therapy for smoking cessation.[2,3,4,5]
- While rTMS reports positive findings for smokers and those suffering from tobacco use disorder (TUD), its consequential effects upon working memory are not well known.
- This study investigated rTMS for smoking cessation in DLPFC and mOFC placements to expose participants' potential cognitive memory impairments, as tested using the N-back working memory task.

Aims

To access whether working memory differences exist when undergoing rTMS treatment for smoking cessation comparing DLPFC and mOFC brain stimulation.

Methods

MUSC conducted a double-blind, sham-controlled, randomized clinical trial ("RTMS manipulates imbalanced drive-reward and executive control circuitry for smoking cessation") with recruitment beginning in 2021-present.

Sample

- n=18 (9 female), aged 49.8 [9.7] (mean [SD]) from the Charleston, South Carolina vicinity
- Voluntarily enrolled in daily rTMS treatment for smoking cessation totaling 15 sessions over 3 weeks

Inclusion	Exclusion
18-65 years old, smoke ≥10 cigarettes/day, meet DSM-5 TUD criteria, motivated to quit smoking	Current moderate-severe substance use (alcohol, cannabis, psychoactives), lifetime history of Axis I disorders, use of tobacco other than cigarettes

Procedure

- Sham or active MRI-guided rTMS to the DLPFC (10 Hz, 3000 pulses each session) for facilitation protocol or to the mOFC (1 Hz, 900 pulses each session) for inhibition protocol.
- N-back studies occurred once a week, prior to rTMS treatment #1, #6, #11, #15, and 1 month after the 15th rTMS.

Results

Number of Participants Who Started Selective rTMS Treatments
(Sham & Active)

Number of Those Participants Included in Study Analysis
(Sham & Active)

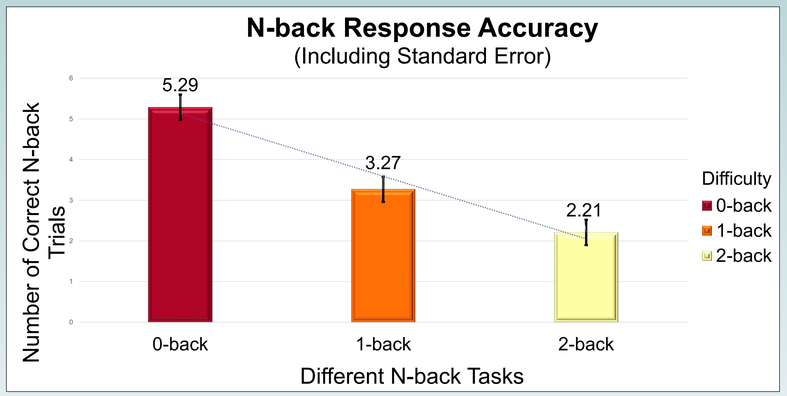

Figure 1: Mixed model results showed significantly different correct trials between 0-back (5.29±0.31), 1-back (3.27±0.31), and 2-back (2.21±0.31), ($p < 0.01$). With increasing task difficulty (increasing *n*s), accuracy decreased.

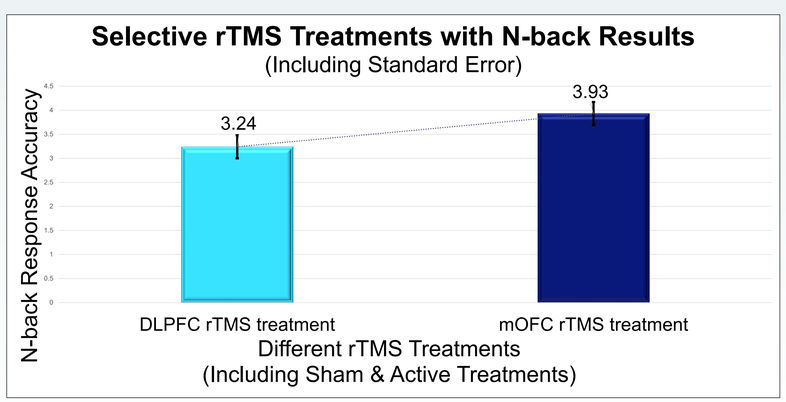

Figure 2: A trend difference existed between DLPFC treatment (3.24±0.24) and mOFC treatment (3.93±0.25), ($p = 0.054$). Treatment to mOFC generated higher N-back result accuracy.

Results

- No significant change in N-back response accuracy was found between treatment weeks.
- N-back response time did not show a significant difference between DLPFC and mOFC rTMS treatment.

Conclusions

- **Initial findings softly suggest dorsal lateral prefrontal cortex (DLPFC) rTMS and medial orbitofrontal cortex (mOFC) rTMS affect working memory differently, as measured with N-back. Noticeably, both DLPFC and mOFC included sham and active treatments.**
  - Slight trend difference in **favoring** mOFC rTMS treatment over DLPFC rTMS treatment in stimulating working-memory accuracy.
    - Though the DLPFC does control over working memory,[6,7] the mOFC mediates task retrieval, outcome-specific information, and goal-oriented action.[8,9]
    - **Hypothesis:** Participants viewed succeeding at N-back testing as their main goal, with potential added pressure to succeed because the researcher was present in the room during N-back testing. Their subset goal was to remember the correct N-back letter. Thus, participants' mOFC was working overtime and was also stimulated by the rTMS, possibly causing the slight shift in N-back accuracy when compared to DLPFC placement.
- 12 study participants took 5 N-back tests, but their accuracy scores did not significantly change with increased practice.
  - Possible ceiling effect in response accuracy leading to higher variability in response times, as found in prior working-memory studies.[10]
- Study limitations included small sample size.
  - Note p-value of 0.054 in Figure 2. More participants are needed to reveal potentially true statistical significance.
  - However, very low standard error shows sample mean accurately reflecting population mean.
- Future studies necessary to aid in choosing mOFC rTMS over DLPFC rTMS when considering working memory precision and preservation.

References

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Acknowledgements

This work was supported in part by NIH grant R25 DA020537, as well as NIDA grants 1UG3DA048507-01A1 and 5UG3DA048507-02.