RECOVERY OF REWARD FUNCTION IN PROBLEMATIC SUBSTANCE USERS USING A COMBINATION OF ROBOTICS, ELECTROPHYSIOLOGY, AND TMS

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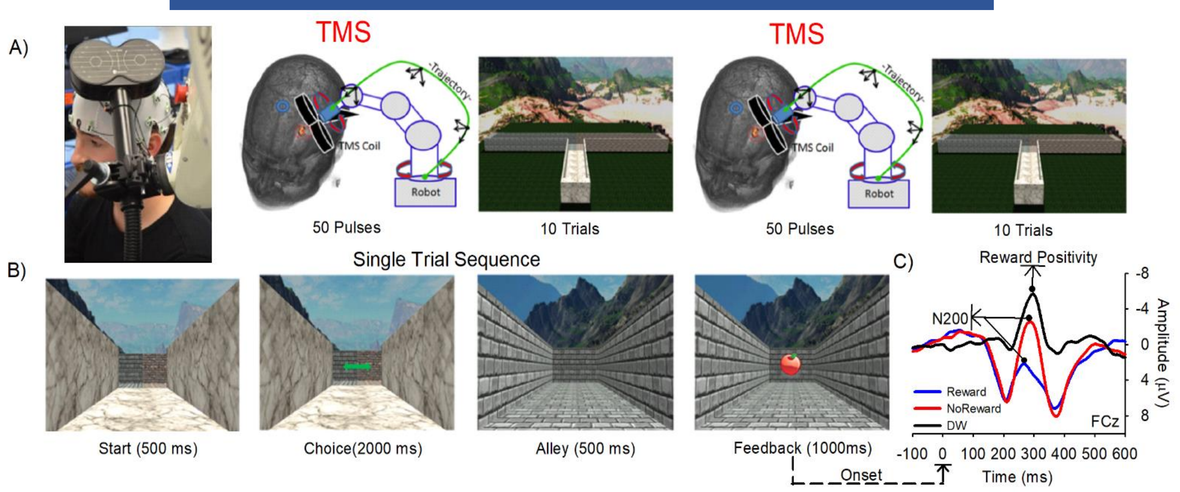
BACKGROUND AND AIMS

- Reward processing function is impaired across various substance use disorders (SUDs)
- The anterior midcingulate cortex (aMCC) and basal ganglia play pivotal roles in reward processing and the cognitive control of action
- Dopaminergic reward prediction error signals (RPEs) are used by these areas to learn the value of rewards and motivate goal-directed behavior
- 10-Hz rTMS applied to the left dlPFC has been shown to enhance dopamine release, neuronal activity, and cerebral blood flow in the aMCC and basal ganglia
- Reward function can be measured by the amplitude of the reward positivity and reward learning behavior
- **Aim:** *To test whether 10-Hz TMS can enhance the reward positivity and reward learning in SUD*

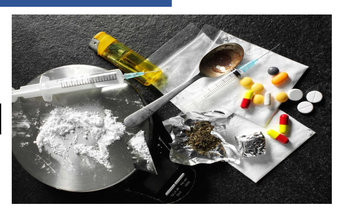
METHODS



- **TMS paradigm:** A) Robot-guided 10Hz (excitatory) TMS over dlPFC (F3) or SHAM. Participants completed 400 trials of T-Maze task: 4 blocks, 100 trials each. ERPs were recorded from Fz. B) Single trial sequence. C) Simulation of "normal" ERPs elicited by reward feedback (blue), no reward feedback (red) and associated difference wave (black). The reward positivity is assessed as the amplitude of the difference wave. Negative is plotted up by convention.
- **Probabilistic selection task (PST)**: Reward learning task. Participants learn to select the more frequently rewarded stimulus in a set of pairs (AB, CD, EF). Rewards are probabilistically allocated (80/20%; 70/30%; 60/40%). Participants must learn that particular stimuli are associated with relatively more reward (A, C and E), or with relatively more punishment (B, D and F).

PARTICIPANTS

- 22 problematic substance users:
  - 11 active TMS; 11 SHAM; age -matched
  - Used a wide range of illicit substances



RESULTS

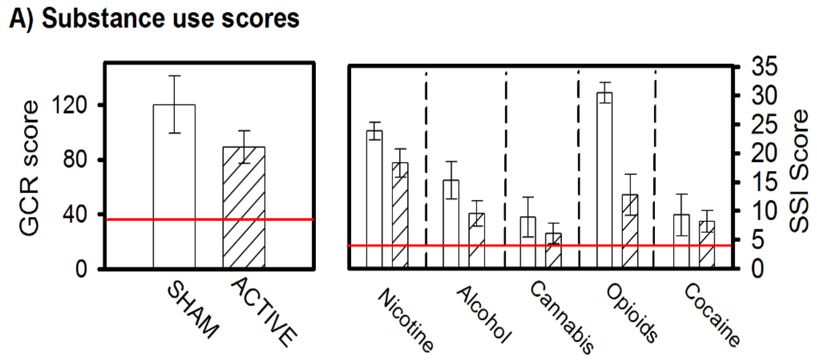


Figure 1. GCR score [Left Panel] and Specific Substance Involvement (SSI) Score of the ASSIST.

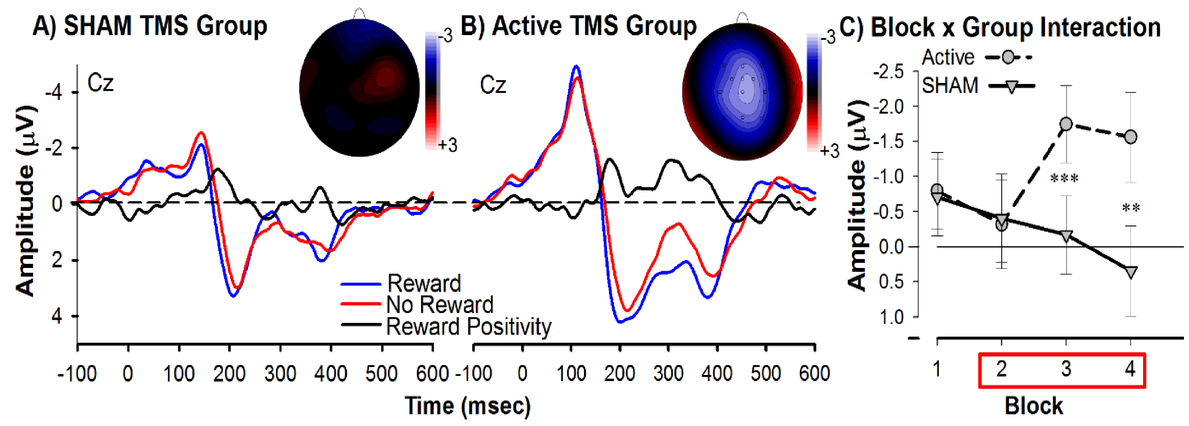


Figure 2. Significant Block x TMS group interaction, $F_{3, 54}$ = 2.98, $p < .05$, $\eta^2 = 0.14$. The amplitude of the reward positivity decreased across blocks for the SHAM group, but increased across blocks 3 and 4 for the Active group

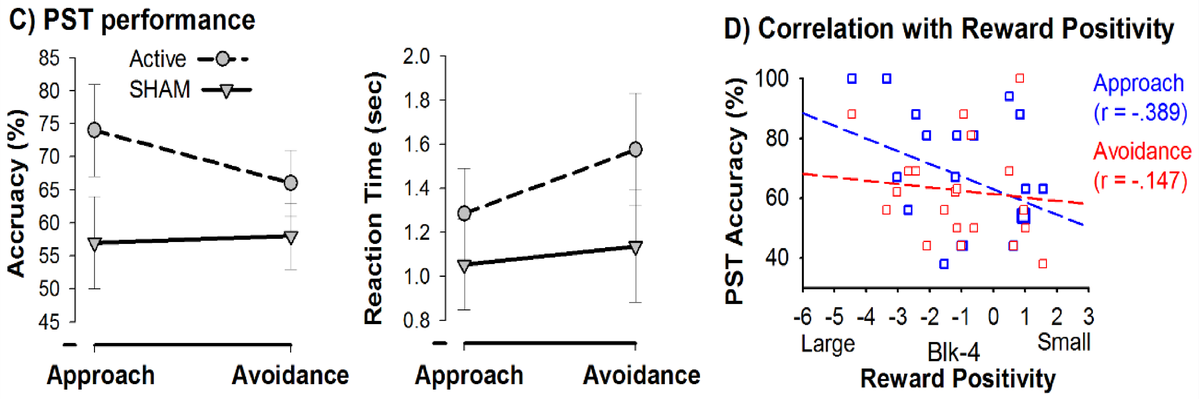


Figure 3. Reward positivity amplitude recorded at Block 4 was correlated with PST approach accuracy (r = -.389, $p < .05$, *one-tailed*)

CONCLUSIONS

- Excitatory TMS appears to alleviate reward processing impairment in the aMCC of SUD
- Also enhances approach learning in the basal ganglia
- Both via enhancement of dopaminergic RPE signaling
- Repeated TMS sessions may improve the effect of TMS
  - Using targets other than F3 (e.g., diffusion weighted imaging, cortical thickness) may improve specificity of targeting procedure and increase the effect of TMS
- These results have implications for relapse monitoring and treatment of OUD

FURTHER INFO AND CONTACT

- ***See**:* Biernacki, et al., (2020). *International Journal of Psychophysiology.* doi: 10.1016/j.ijpsycho.2020.08.008
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