

Title: Using Combined EEG and Non-invasive Brain Stimulation to Examine and Improve Reward Functioning in Opioid Use Disorder

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Statistical analysis. First, we predict that people with OUD will exhibit a truncated reward positivity elicited by monetary rewards, compared to healthy controls. This finding would indicate that OUD individuals are impaired at using normal rewards to develop internal representations of action value, and thus are impaired at using these action values for cognitive control. Second, we predict that repetitive TMS will lead to increases in dopamine release and neuronal activity in the ACC, thereby leading to a positive shift in the ACC valuation of monetary rewards in OUD as revealed by an increase in reward positivity amplitude in the active TMS group relative to the sham group. To test these predictions, we will conduct a 2 x 2 repeated measures analysis of variance with TMS (active vs sham) and Group (OUD vs. controls) as factors.

We anticipate the following results:

- *Aim 1:* A Group (OUD, control) by TMS (active, sham) interaction, where OUD participants in the sham condition will demonstrate an attenuated reward positivity signal relative to the control participants in the sham condition.
- *Aim 2:* A within-group main effect of TMS (active, sham) where participants receiving active TMS will demonstrate a larger reward positivity compared to participants in the sham condition. We also anticipate a 2-way TMS (active, sham) by Group (OUD, control) interaction, where control participants receiving the active TMS will demonstrate a larger reward positivity signal relative to the SHAM control group. We also anticipate OUD participants receiving active TMS will demonstrate a larger reward positivity relative to OUD SHAM.

Linear regression models will be used to compare groups while adjusting for potential confounds within each age group and for the whole sample while controlling for age and education. Post hoc analysis (e.g., Tukey HSD) will be performed when linear regression shows any significant main effects or interactions. In all comparisons, sex will be considered as a biological variable to assess trends to be explored further in the R01 longitudinal study.