The Causal Role of Theta and Alpha Oscillations in Output-Gating

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Study Rationale

- Cognitive control is the ability to dynamically allocate limited resources to process input from the environment and manipulate internal representations as a function of behavioral demands (output-gating)
- Two intertwined cognitive processes comprise output-gating: the selection of relevant information and the suppression of irrelevant information
- Neural oscillations are implicated in output-gating: theta oscillations (4-7 Hz) in selection and alpha oscillations (8-12 Hz) in suppression [1,2,3,4]
- The functional interaction between these oscillations may be critical to an understanding of how the brain instantiates output-gating

What We Did

- We recorded high-density EEG to localize task driven theta and alpha oscillations during a working memory (WM) task that manipulated output-gating using retro-cues
- We targeted task driven brain dynamics with online rhythmic TMS at individualized theta and alpha frequency at a frontal and parietal site
- We measured the immediate effect of rhythmic TMS on power and phase entrainment

What We Found

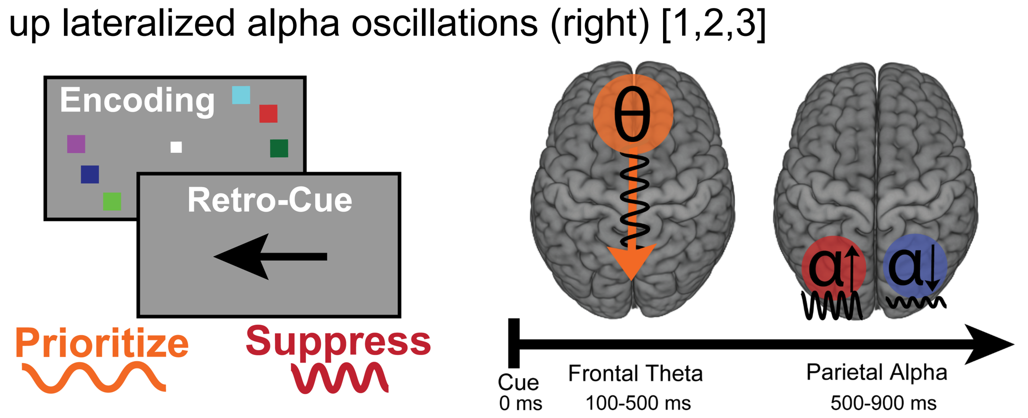
- Cues in the delay period of a WM task drive frontal theta oscillations, and retro-cues drive parietal alpha oscillations contralateral to irrelevant information
- Left parietal alpha oscillations explained individual differences in retro-cue benefit
- Theta TMS increased theta and decreased alpha power in both frontal and parietal
- Alpha TMS increased alpha power in parietal and decreased theta power in both
- Phase entrainment was strongest when TMS was matched to endogenous dynamics
- Participants performed better when TMS was matched endogenous dynamics

Pre-registration

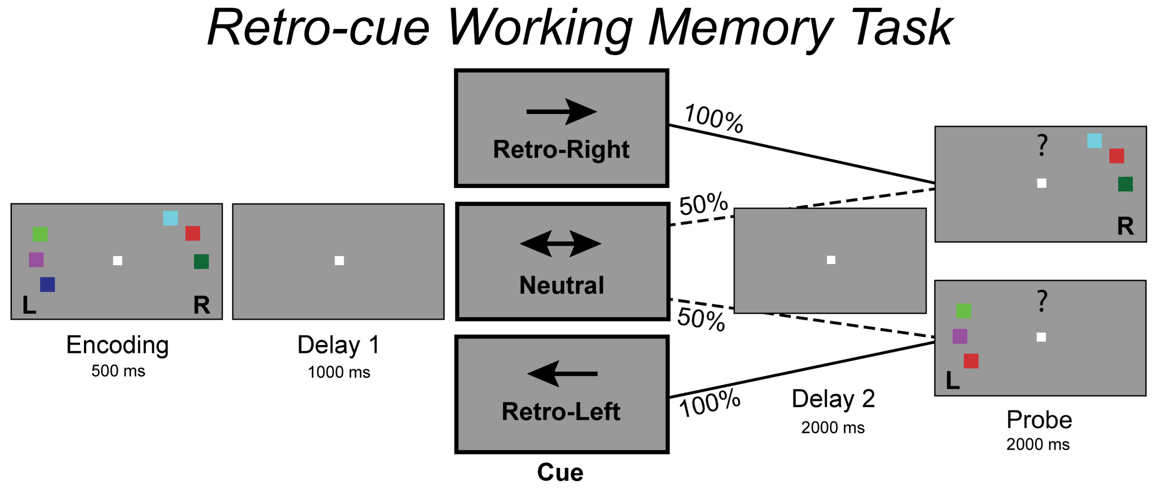
- Study preregistered through the Open Science Framework [5]
- Accessible through the following link or QR code: *https://osf.io/vxdkb*

Experimental Design

- A retro-cue during the delay period of a working memory task drives *prioritization* of some representations held in working memory and *suppression* of others (left)
- Lateralized stimulus arrays at encoding enable EEG analysis of left versus right hemispheres
- Frontal theta oscillations activate early in the delay followed up lateralized alpha oscillations (right) [1,2,3]



Retro-cue Working Memory Task

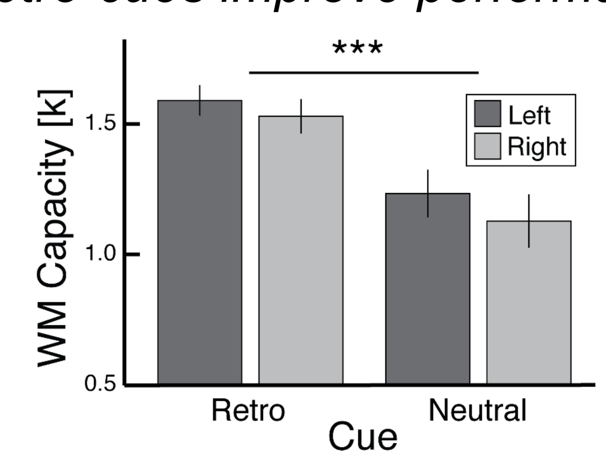


Experimental Design

- **Session 1** Behavioral Screening (N=77): Participants performed the retro-cue task with a variable WM load (2-4 items bilaterally) to titrate the difficulty of task. Three-factors: load (2,3,4), cue (retro & neutral) and side (left & right) with 40 trials per condition. Participants with accuracy >60% and <90%, and a retro-cue benefit of accuracy >5% proceeded to subsequent sessions.
- **Session 2** Target Identification (N=58): Fixed WM load from screening. Two factors: cue (retro & neutral) and side (left & right) with 60 trials per condition. High-density EEG (128 channels EGI) used to determine individualized alpha (left-retro minus right-retro) and theta frequency (retro minus neutral) for rhythmic TMS.
- **Sessions 3&4** Target Engagement & Validation (N=48, analysis N = 42): Fixed WM load, only retro-cues, two-factors: stimulation (individualized theta TMS, arrhythmic TMS duration matched to theta, individualized alpha TMS, arrhythmic-alpha TMS) and side (left & right). 40 trials per condition. High-density EEG with online TMS (5 pulse trains) 100 ms after retro-cue. TMS targeted to parietal (L-IPS) or frontal (L-MFG), order randomized and counterbalanced.

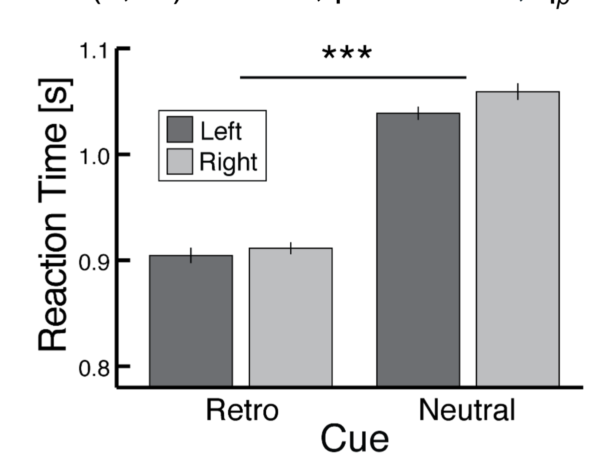
Behavioral Screening

Retro-cues improve performance



Two-way repeated-measures ANOVA

Cue: $F(1,76) = 28.03$, $p = 1.12e\text{-}6$, $\eta_p^2 = .269$



Two-way repeated-measures ANOVA

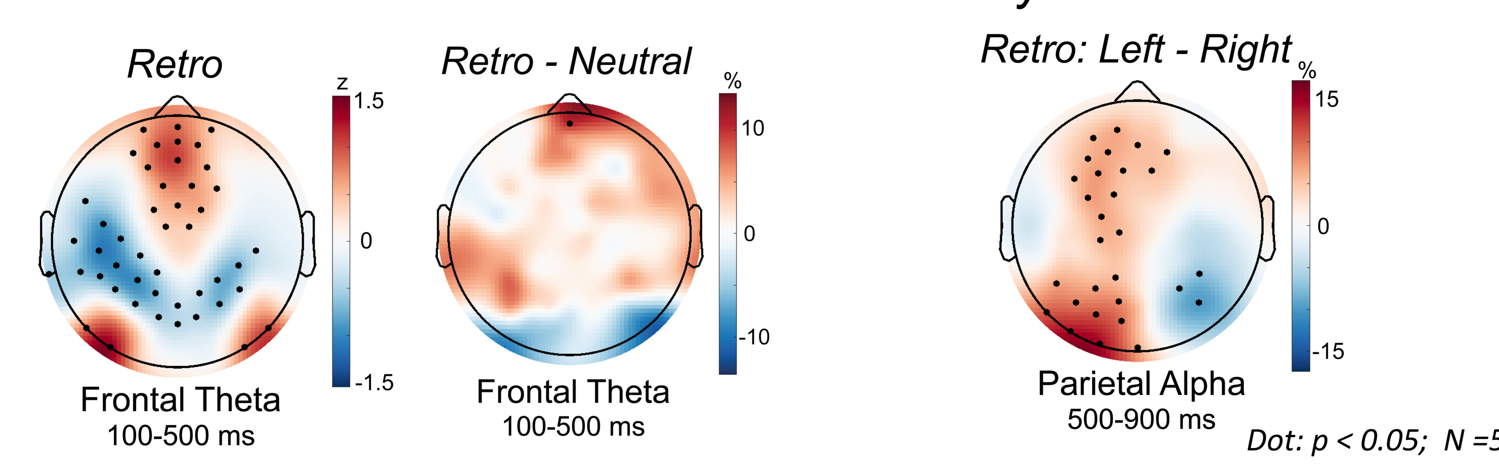
Cue: $F(1,76) = 583.8$, $p = 2e\text{-}16$, $\eta_p^2 = .885$

**** p < 0.005; error bars within-participant SEM; N = 77*

Target Identification

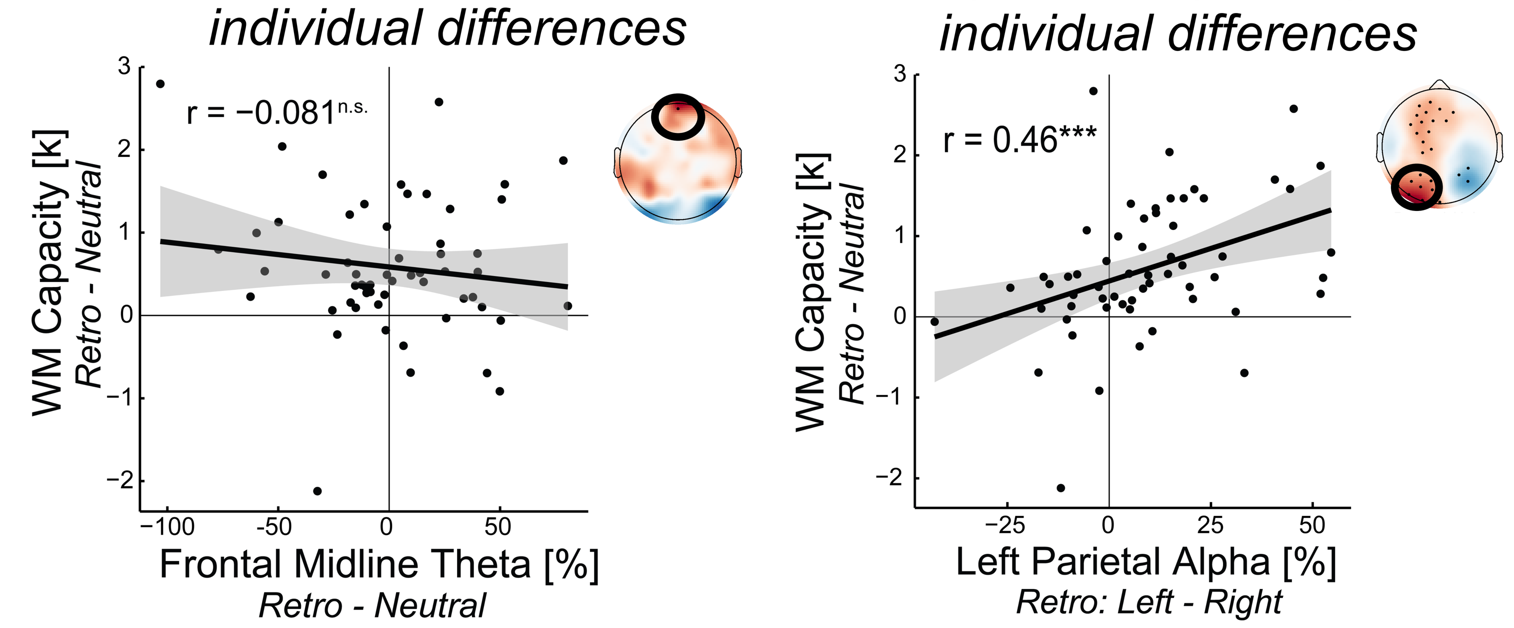
Retro-cues drive frontal theta, but not more than neutral cues

Parietal alpha lateralization driven by retro-cue direction



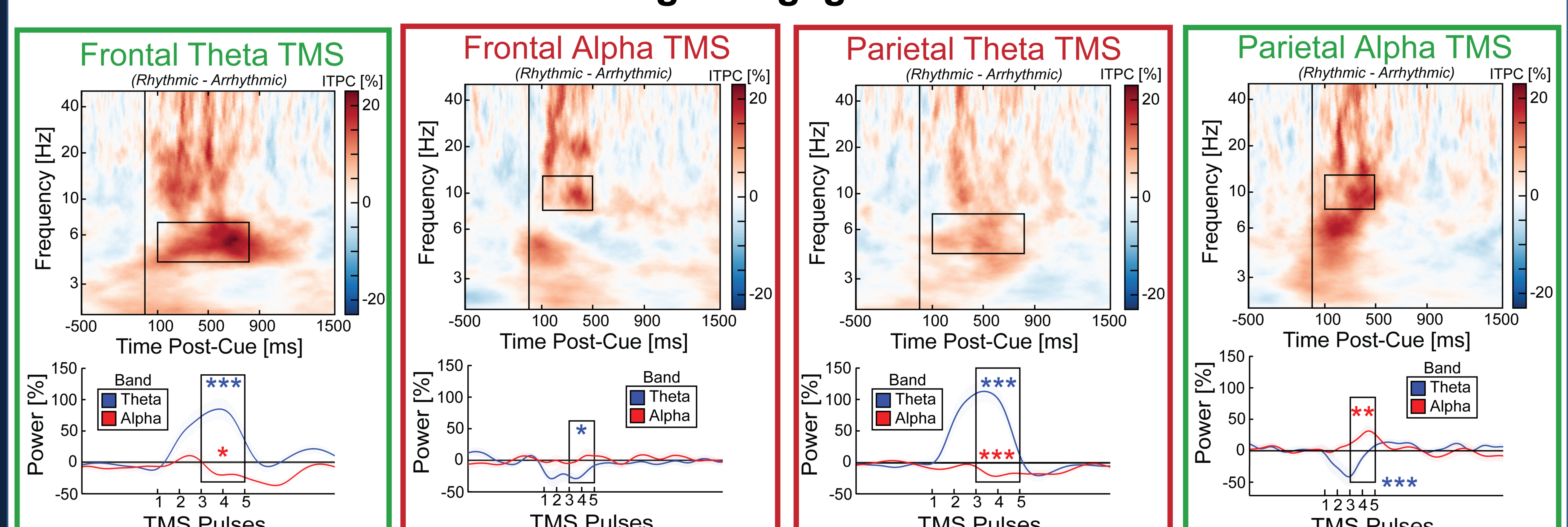
Frontal theta does not explains individual differences

Left parietal alpha explains individual differences



**** p < 0.005, spearman correlation; shaded area 95% CI; N = 58*

Target Engagement



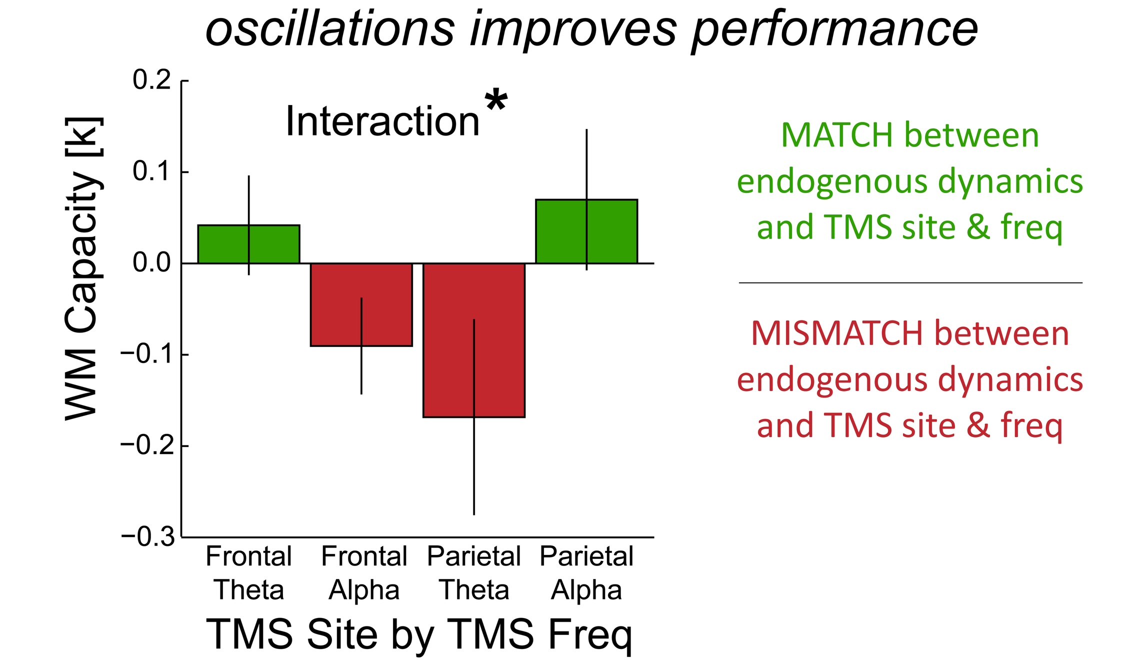
Inter trial phase coherence (ITPC) strongest when TMS frequency is matched to endogenous dynamics

Theta TMS drives theta power in both sites, alpha TMS drives alpha power only in parietal

* p < 0.05, ** p < 0.01, *** *p < 0.005; Power: aligned to individualized frequency of TMS, error bars are within-participant SEM; N = 42*

Target Validation

Stimulation matched to endogenous neural oscillations improves performance



Two-way repeated-measures ANOVA

Interaction: $F(1,41) = 4.93$, $p = 0.032$, $\eta_p^2 = 0.107$

** p < 0.05; N = 42*

Discussion

- Retro-cues can be used to study output gating and to drive similar neural dynamics to input-gating
- Rhythmic TMS drives frequency-specific entrainment (phase alignment) and power relative to arrhythmic control stimulation
- Power response to TMS suggest an antagonistic relationship between theta and alpha oscillations
- Frontal cortex did not increase alpha power from alpha TMS, suggesting an indirect mechanism via theta suppression
- Entrainment from rhythmic TMS was strongest when TMS was matched to the endogenous activity
- Entrainment from rhythmic TMS aligned more closely with our behavioral findings than did power
- Future work will test the causal role of functional connectivity using multiple TMS coils and weighted phase lag index analysis

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FF is the lead inventor of IP filed by UNC. FF is the founder, CSO, and majority owner of Pulvinar Neuro LLC. Pulvinar Neuro had nothing to do with this study.

References

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