Causally testing the distinctions between anterior-temporal versus posterior-medial hippocampal-cortical network contributions to memory in humans

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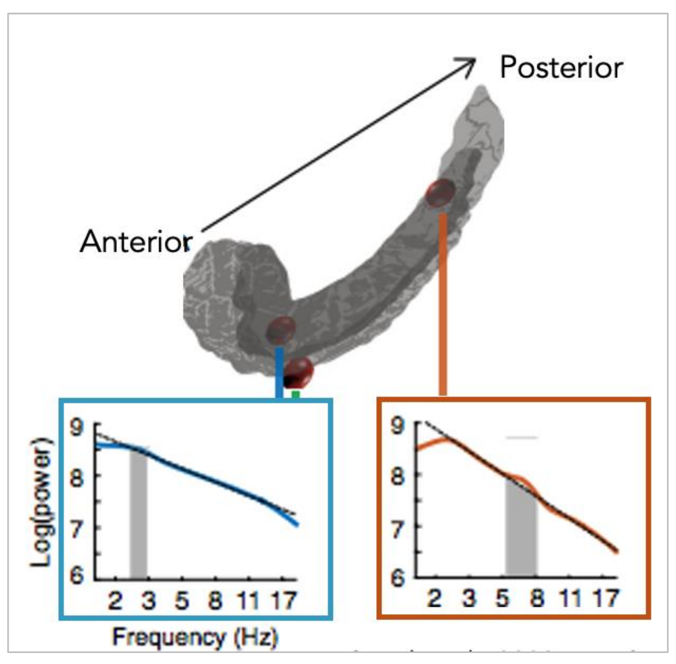
Background

- Synchronous theta-band (4-8-Hz) activity among hippocampal network regions is thought to support episodic memory[1].
- Repetitive transcranial magnetic stimulation (TMS) delivered in a hippocampal network targeted (HNT) manner can modulate network connectivity[2] and memory[3].
- HNT theta-burst stimulation (TBS) caused more robust memory-related connectivity changes among core network regions than other TMS frequencies/patterns[4], possibly due to entrainment with intrinsic hippocampal network rhythms[5].

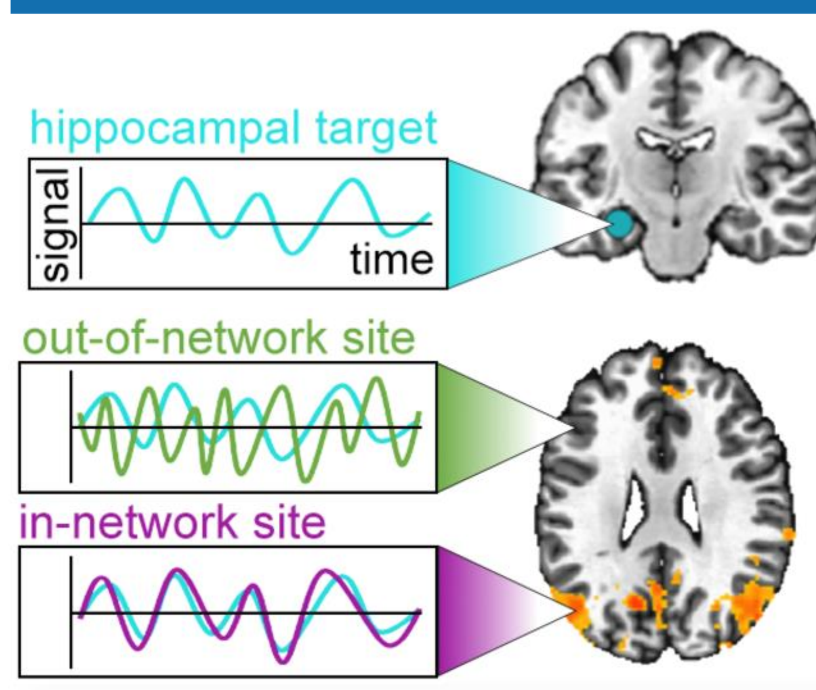


- Growing evidence of theta frequency gradient along hippocampal longitudinal axis[6], akin to rodent type I and type 2 theta rhthyms[7].
- Evidence of functional role of slow versus fast hippocampal theta rhythms in humans is relatively minimal.

Research Goals

- Develop novel fMRI scan sequences to interleave slow (3-Hz) and fast (7-Hz) theta-burst patterned TMS with scan acquisition, building upon previous work (see Hermiller et al., 2020, J Neuro[8])
- Measure immediate impact of slow (3-Hz) versus fast (7-Hz) theta-burst patterned TMS on hippocampal and medial temporal lobe (MTL) fMRI activity during scene memory formation

Individualized Stimulation Targets



Baseline resting-state fMRI used to identify a ***hippocampal target*** for each subject.

Seed-based fMRI connectivity used to define subject-specific left parietal cortical ***stimulation site***.

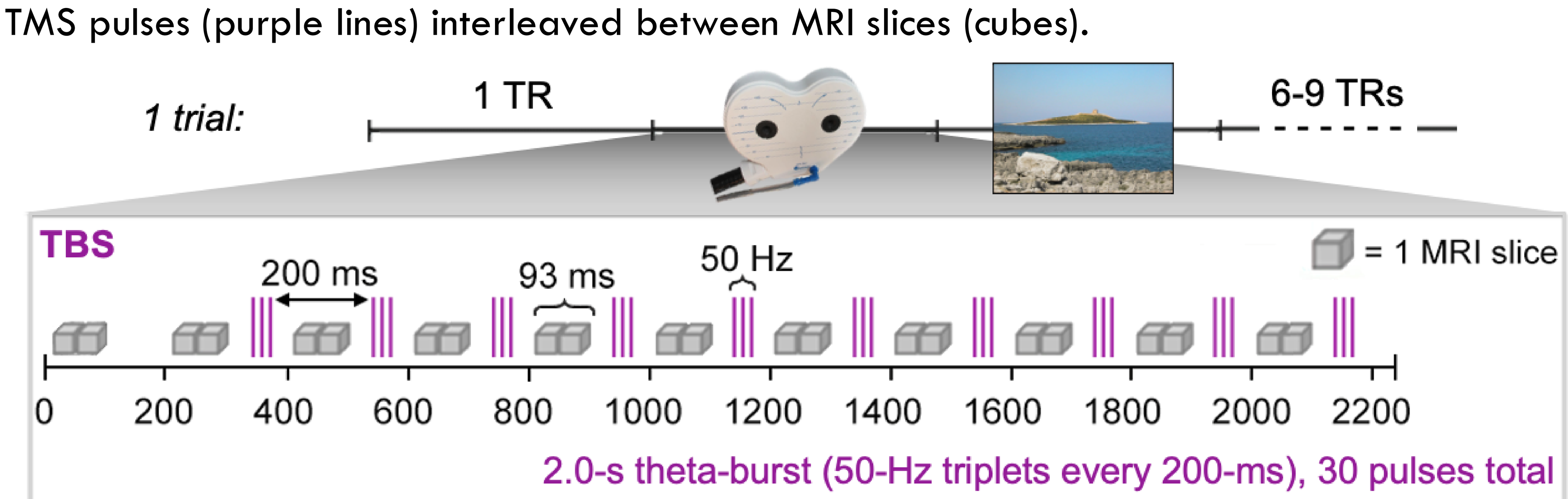
Simultaneous TMS-fMRI

Participants complete a task-based fMRI scan. The task involves forming memories for pictures of complex outdoor scenes.

Stimulation Conditions:

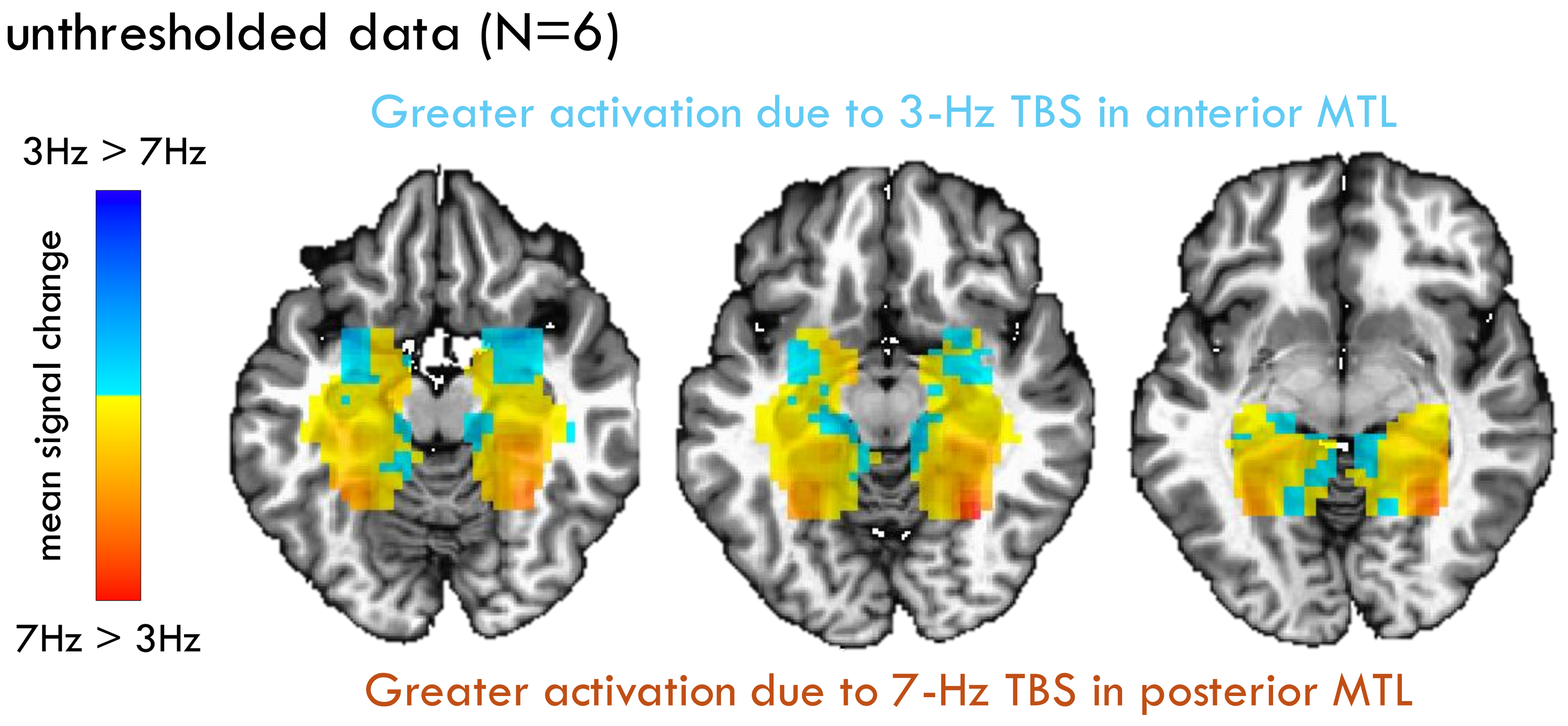
- 39 trials with 3-Hz theta-burst
- 39 trials with 7-Hz theta-burst
- 39 trials no stimulation
- *Trial type interleaved throughout the MRI scan session*

Novel fMRI scan sequences were developed at FSU MRIF to allow for TMS pulses to be interleaved between fMRI slice acquisition. Example of a single trial using 5-Hz theta-burst; TMS pulses (purple lines) interleaved between MRI slices (cubes).

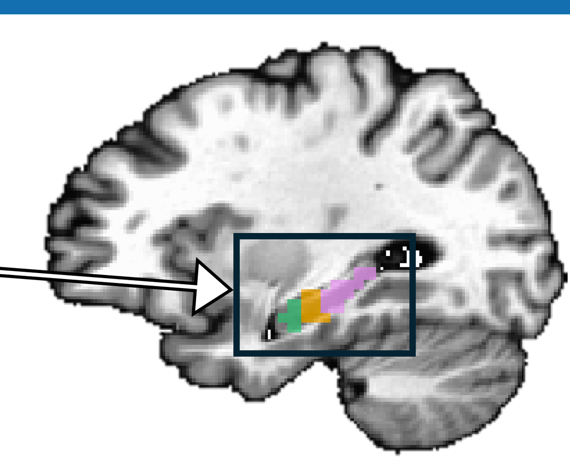


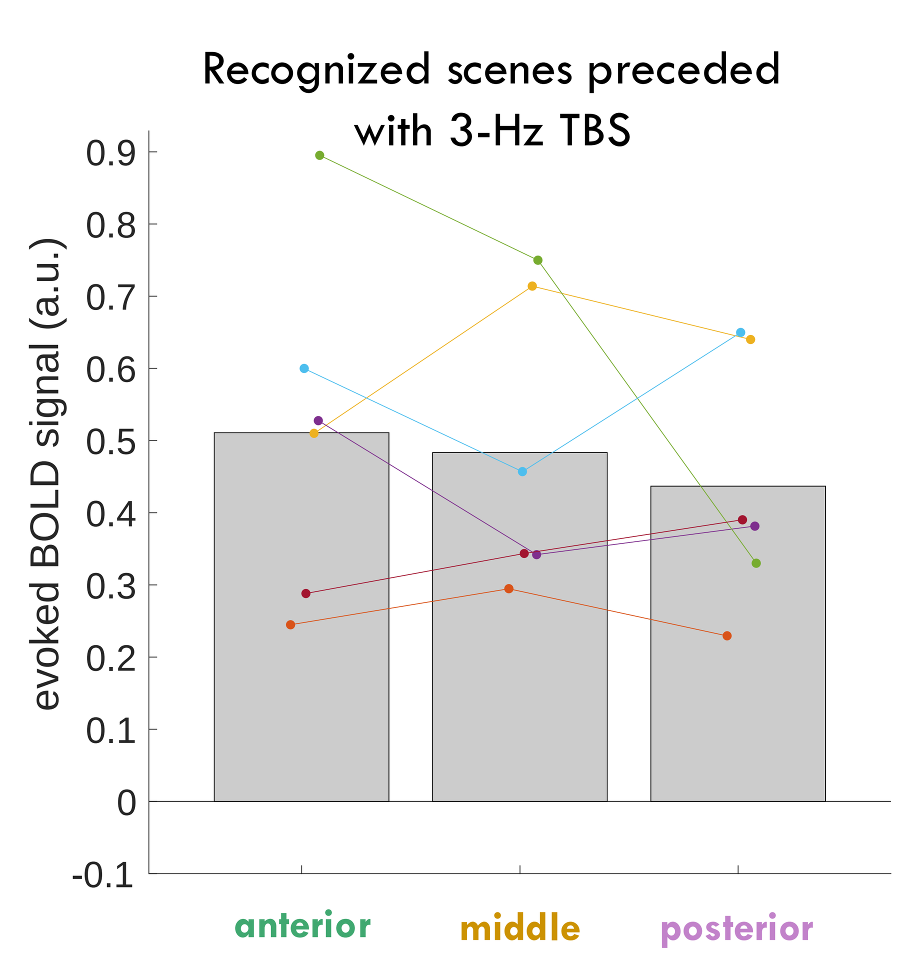
Preliminary Results

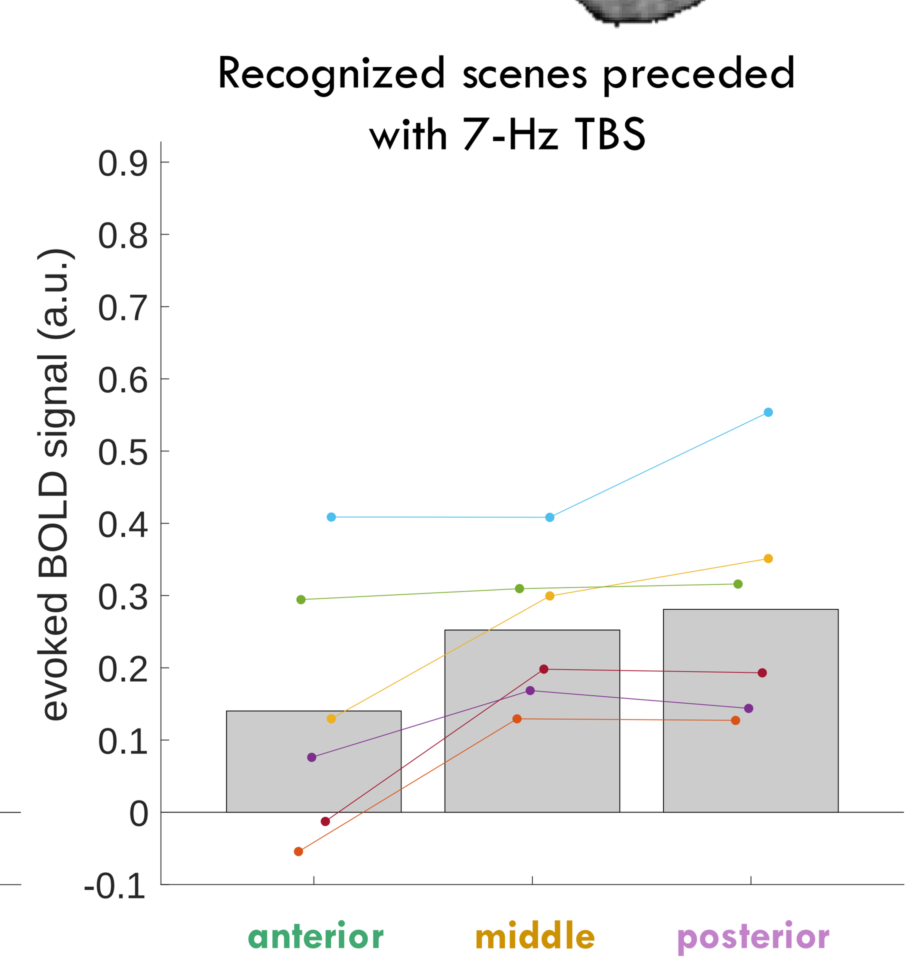
Direct comparison of evoked BOLD signal in the medial temporal lab (MTL) for scenes preceded with 7-Hz vs. 3-Hz theta-burst stimulation; unthresholded data (N=6)



Evoked signal in the anterior, middle, and posterior hippocampus for scenes that were later "Remembered" in a post-scan scene recognition test phase; (N=6).







Conclusions and Future Directions

- The hippocampus and MTL respond differently to HNT TMS delivered at a slow (3-Hz) versus fast (7-Hz) theta-burst pattern
- Future work aims to identify ramification on episodic memory.

Acknowledgements

[1] Buzsaki (2002) *Neuron* [2] Fox et al (2012) *Neuroimage* [3] Wang et al (2014) *Science* [4] Hermiller et al (2018) *Hippocampus* [5] Thut et al (2011) *Front Psychol* [6] Goyal et al (2020) *Nat Comm* [7] Kramis et al (1975) *Exp Neurol* [8] Hermiller et al (2020) *J Neuro*

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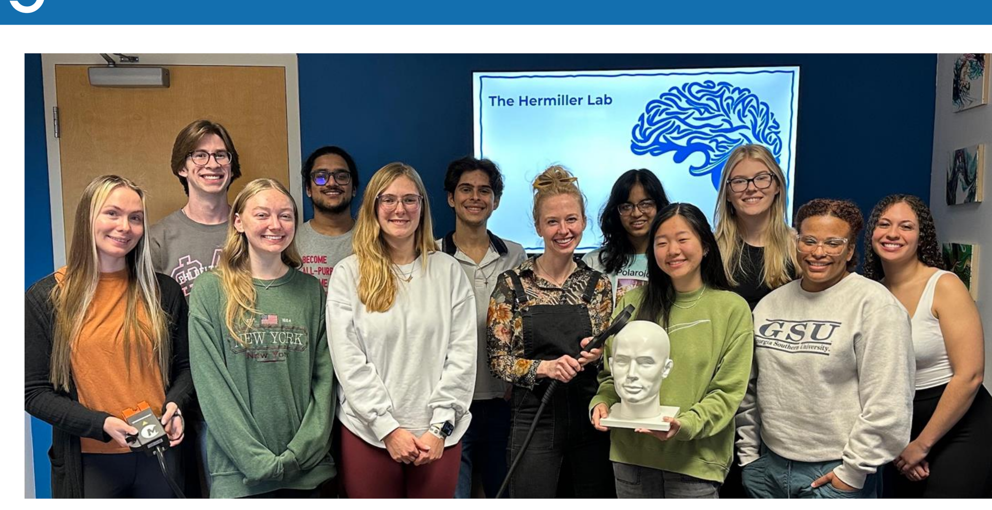

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