



Hippocampal network targeted theta-burst stimulation immediately enhances medial temporal lobe memory processing

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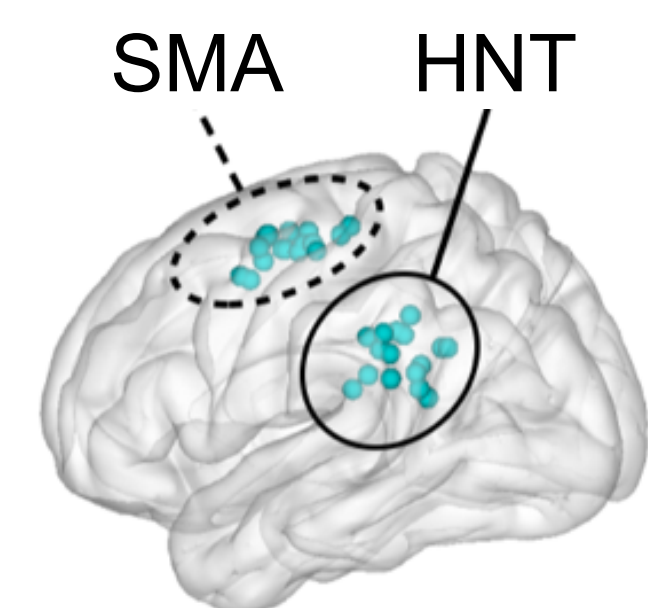
LABORATORY FOR HUMAN NEUROSCIENCE

Introduction

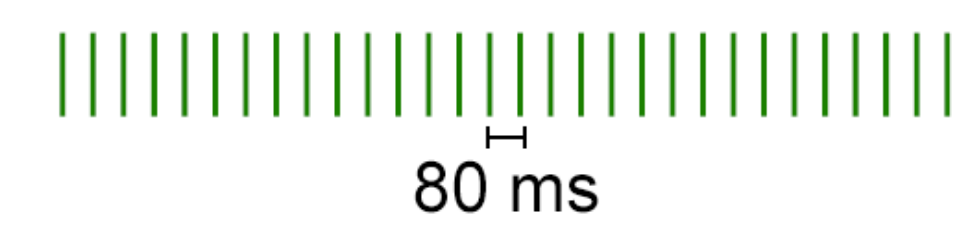
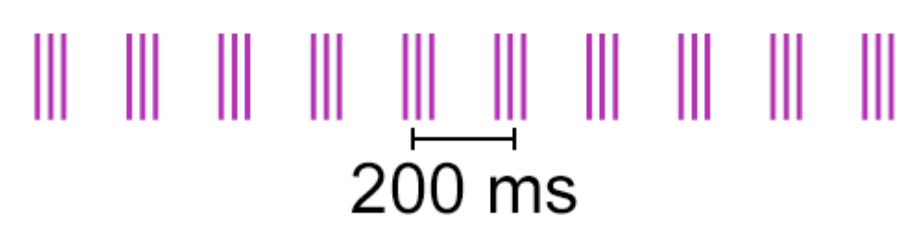
- Synchronous theta-band (4-8-Hz) activity among hippocampal network regions is thought to support episodic memory¹.
- Repetitive transcranial magnetic stimulation (TMS) delivered in a hippocampal network targeted (HNT) manner can modulate network connectivity² and memory³.
- HNT theta-burst stimulation (TBS) caused more robust memory-related connectivity changes among core network regions than other TMS frequencies/patterns⁴, possibly due to entrainment with intrinsic hippocampal network rhythms⁵.
- The immediate impact HNT TBS on medial temporal lobe (MTL) memory processing is unknown.**

Research Goals

- Measure immediate impact of stimulation on MTL fMRI activity during scene memory formation (versus numerical judgments).
- Test the selectivity of effects for HNT (versus out-of-network SMA).

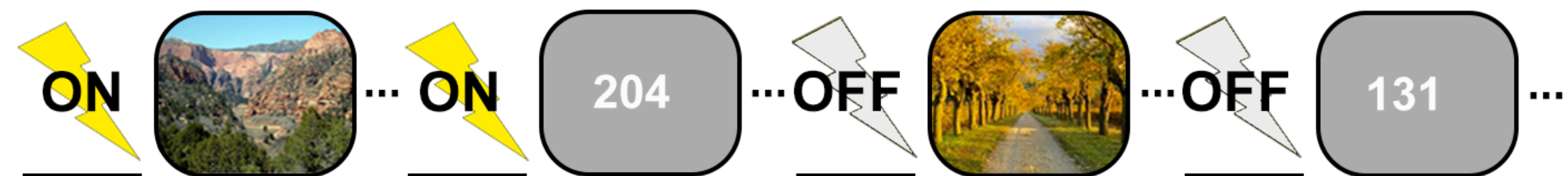


- Test the frequency-specificity of effects for TBS (versus beta, 12.5-Hz).

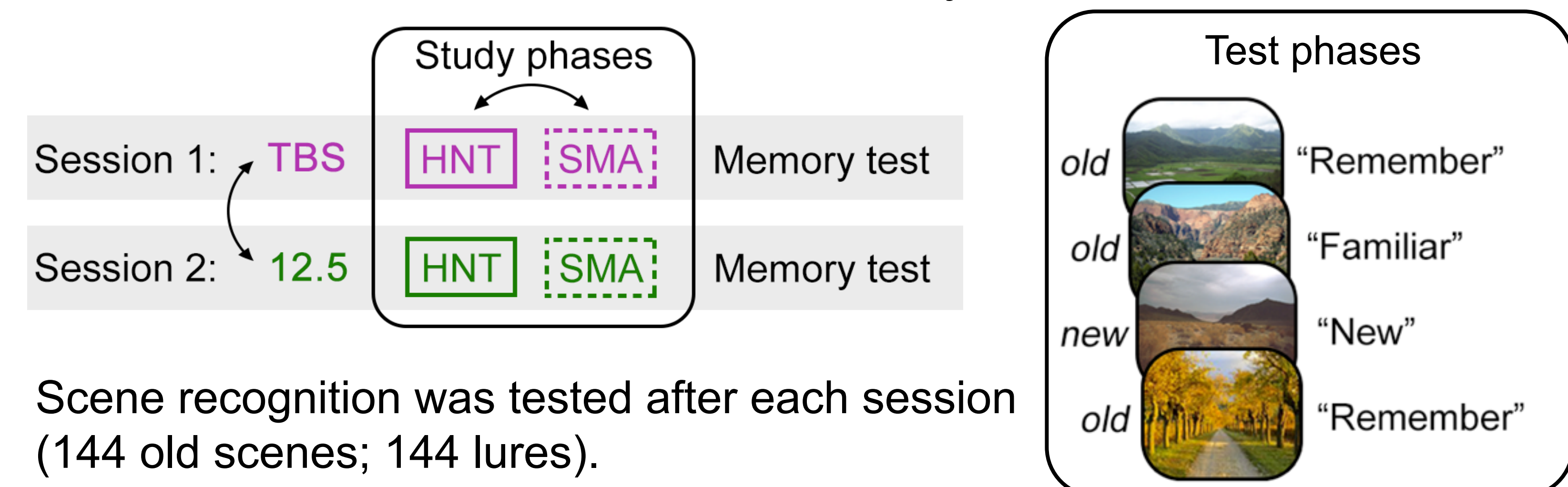


Experiment Design

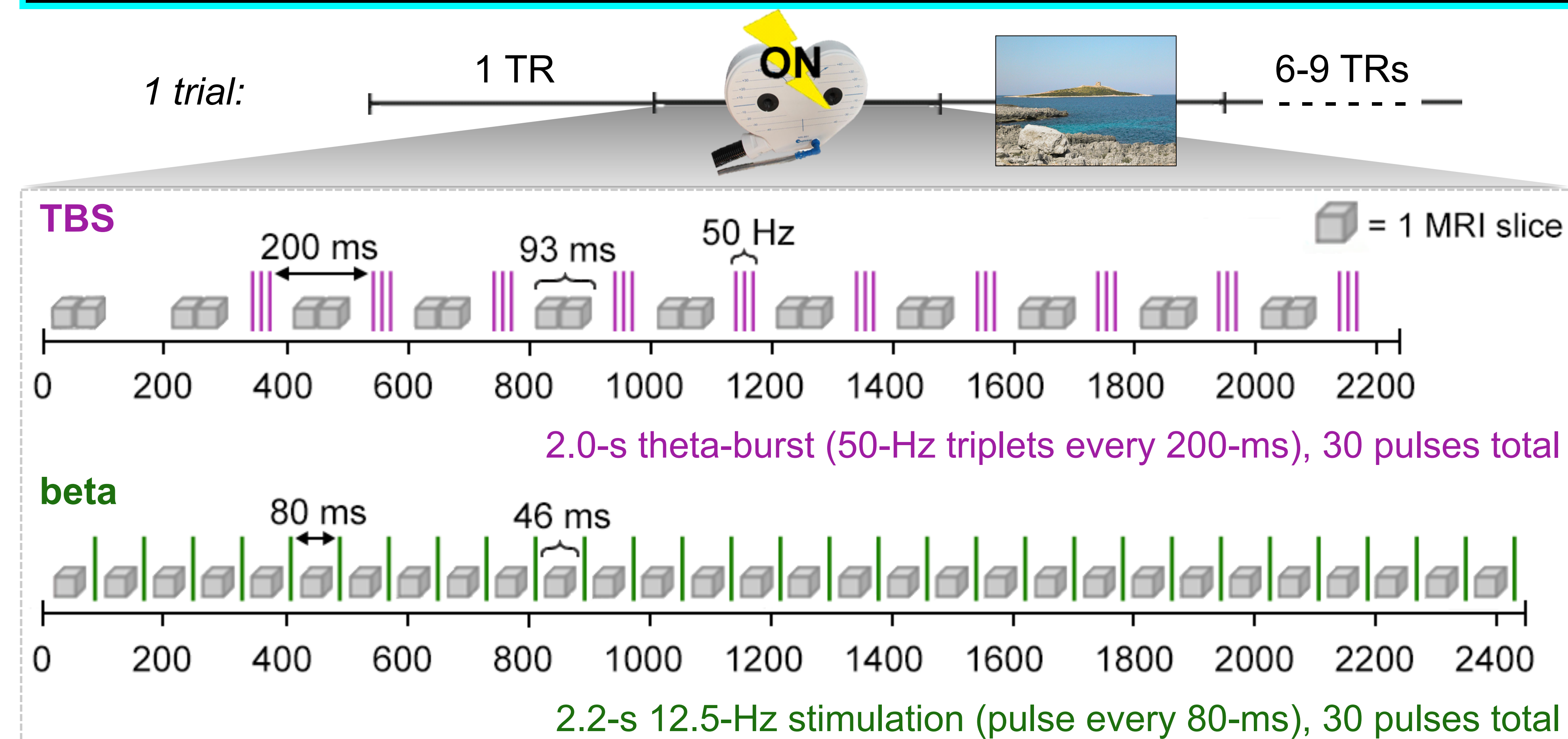
Participants (N=16) completed a simultaneous TMS/fMRI memory task on two days, with a different stimulation pattern (TBS or beta) delivered each session



TMS was delivered to the HNT and SMA locations during both sessions.
 TMS was OFF for one third of the trials (randomly interleaved).
 Conditions were counterbalanced across subjects.

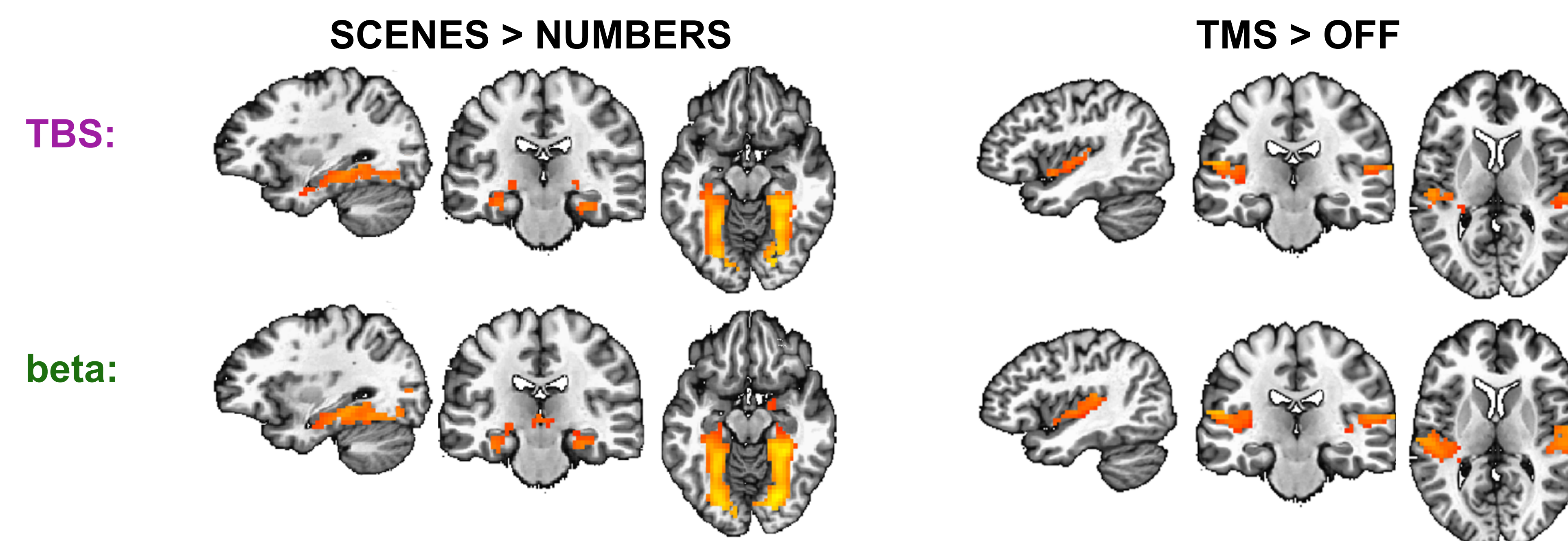


Interleaved TMS/fMRI



Validation of Approach

Expected activation patterns observed in both scan sequences validate the methodology and experimental design.



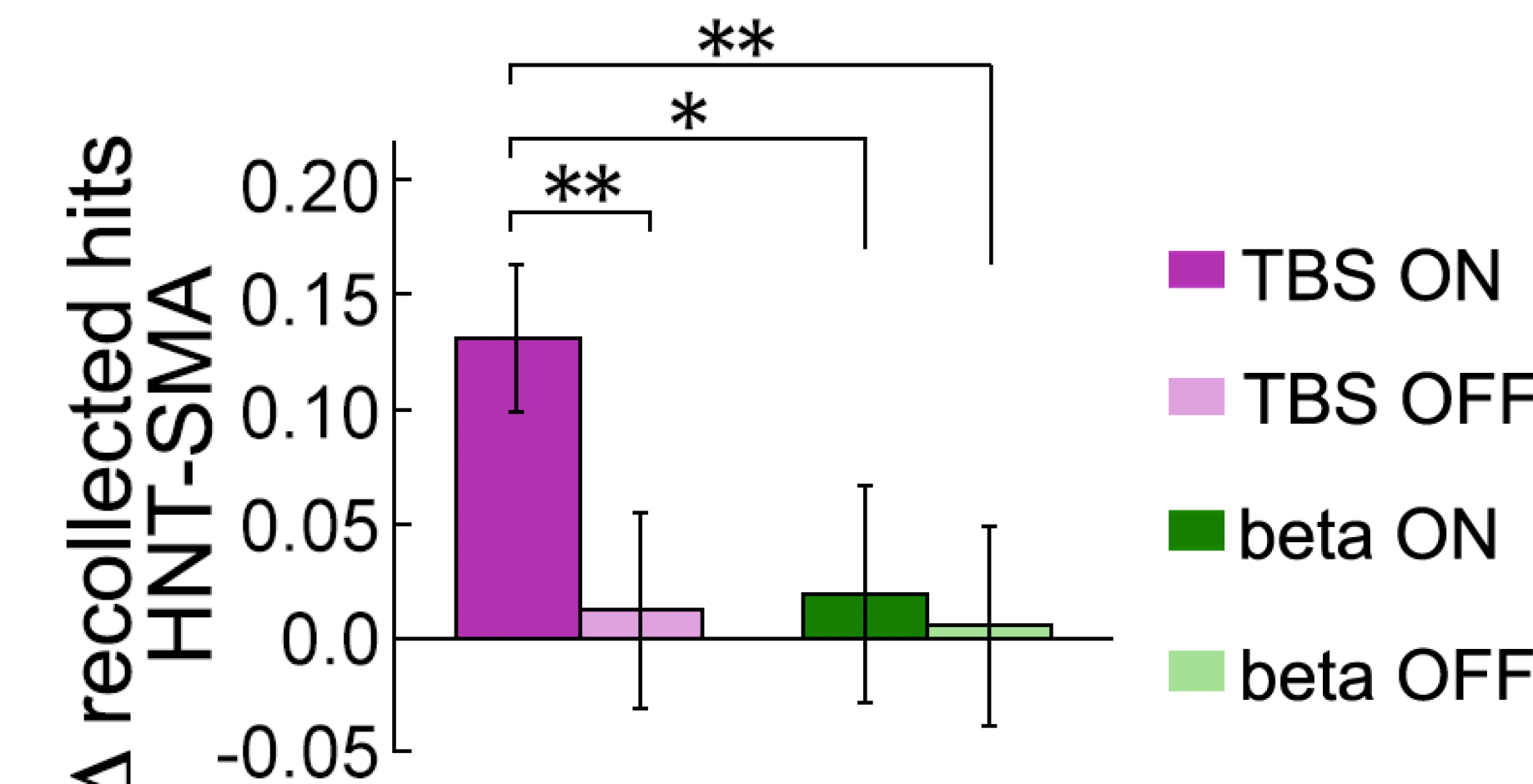
Memory Enhancement

Overall hit rate ("Remember" and "Familiar" responses combined) did not vary.

The proportion of **recollected hits** varied significantly by stimulation presence (on versus off), pattern (TBS versus beta), and location (HNT versus SMA) (3-way interaction $F_{1,11}=6.63, P=0.02 \eta^2_p=0.44$; rMANOVA).

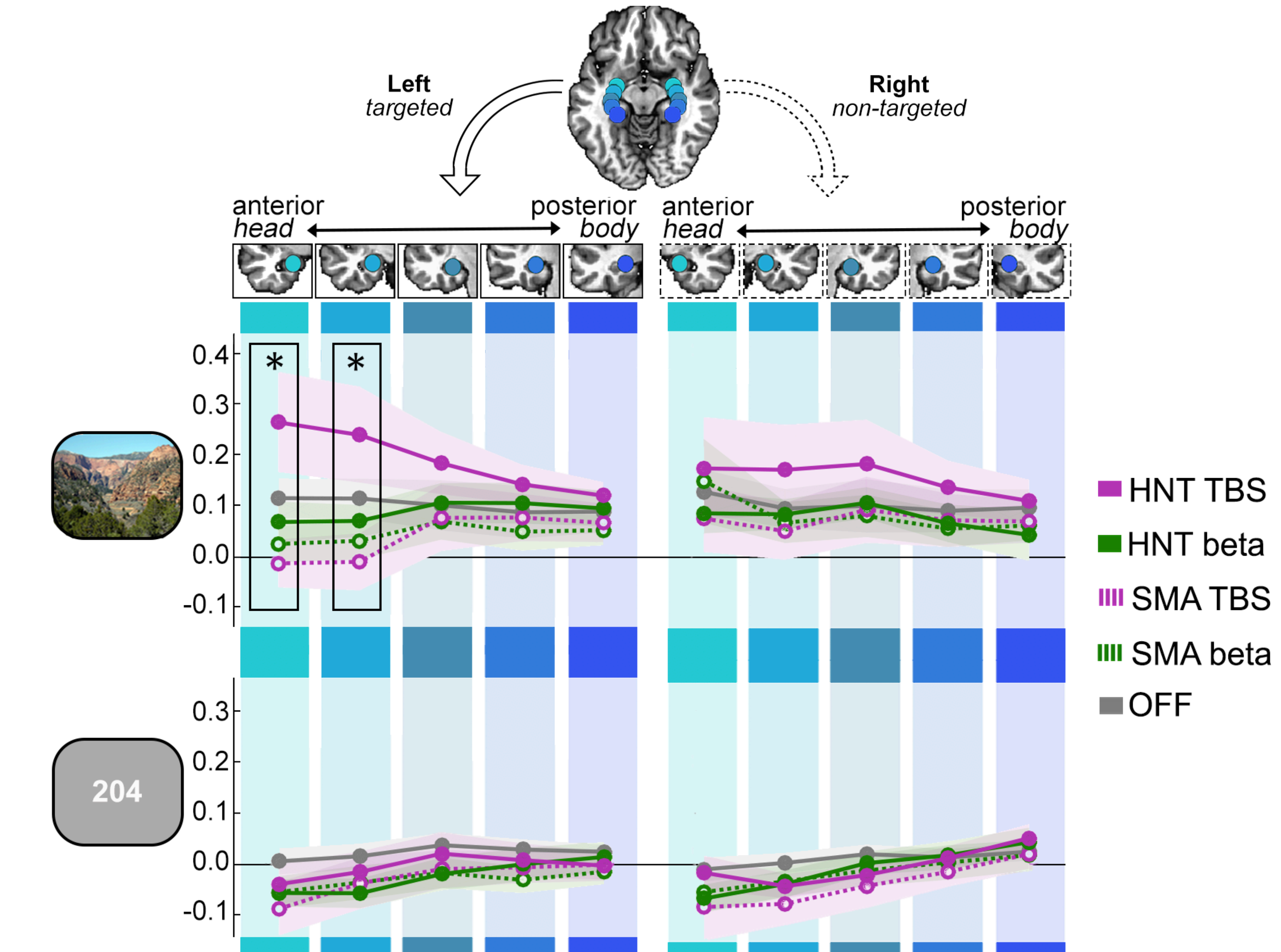
The difference in the proportion of recollected hits was assessed within session (i.e., HNT minus SMA, for each pattern) was assessed.

Recollection was enhanced for scenes presented in the HNT TBS condition relative to all control conditions (* $P<0.05$, ** $P<0.01$).



Hippocampal/MTL Activity Increases

Stimuli-evoked activity due to later-recollected scenes (top) and to numbers (bottom) was extracted from five spherical ROIs along the longitudinal axis in both the left and right hippocampus for each stimulation condition.



Activity for recollected scenes was significantly greater for HNT TBS in the two left anterior ROIs ($P<0.05$, 1-way rMANOVA)

Discussion

- HNT TBS led to greater memory-related scene-evoked fMRI activity in the anterior MTL and enhanced memory formation.
- These findings suggest that HNT TBS can directly influence hippocampal/MTL memory processing.
- This contributes causal evidence supporting the role of theta rhythms in episodic memory.
- Future directions include investigating the effects of stimulation on encoding versus retrieval process and testing for differential effects of low versus high theta and gamma burst frequency ranges on memory and MTL activity.

Acknowledgments

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*

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