Enhanced neural reinstatement and memory for naturalistic episodes following hippocampal-targeted noninvasive stimulation



Melissa Hebscher¹, Joel L. Voss¹

1) Northwestern University Feinberg School of Medicine

Background

- Episodic memory depends on widespread network of regions including hippocampus and posterior parietal lobe
- Transcranial magnetic stimulation (TMS) of lateral parietal regions with high functional connectivity to hippocampus can alter episodic memory and its neural correlates¹
- Stimulation-induced improvements in paired-associates, word-list, spatial precision tests of episodic memory^{2,3,4}
- Associated improvements in resting state functional connectivity
- Currently unclear whether effects of hippocampal-targeted stimulation generalize to more naturalistic forms of episodic memory, which involve distinct neural mechanisms⁵
- Parietal stimulation has been shown to alter autobiographical memory^{6,7}, but findings are inconsistent perhaps due to lack of control
- Effects of stimulation on memory-related neural activity unclear
- Neural reinstatement thought to underlie episodic memory

Present Study

Current study investigated effects of hippocampal-targeted parietal stimulation on memory for naturalistic video-clip episodes.

- Does hippocampal-targeted stimulation affect memory for naturalistic, complex events?
- What are the effects of hippocampal network-targeted stimulation on large-scale, multivariate memory-related neural activity?

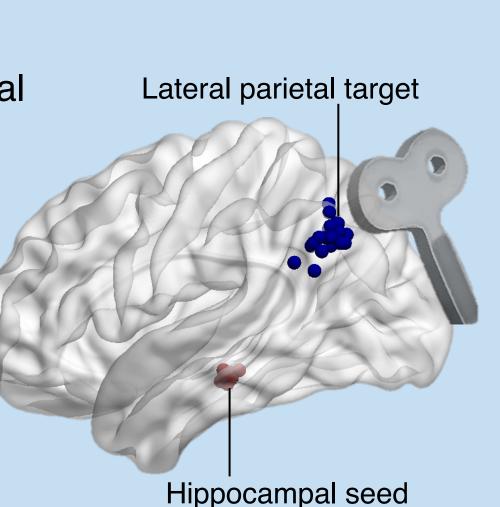
Methods

Study design

• 40s of TMS immediately followed by 45 min episodic memory task with fMRI (n=20)

TMS methods

- Active stimulation: subject-specific lateral parietal target with high functional connectivity to hippocampus
- <u>Control stimulation</u>: vertex stimulation (low connectivity to hippocampus)
- Continuous theta burst stimulation (cTBS) – bursts of 3 50 Hz pulses delivered at 5 Hz

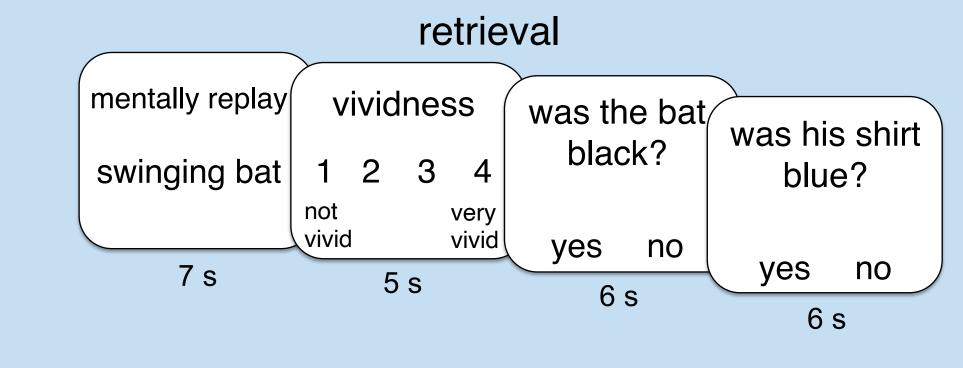


Episodic memory task

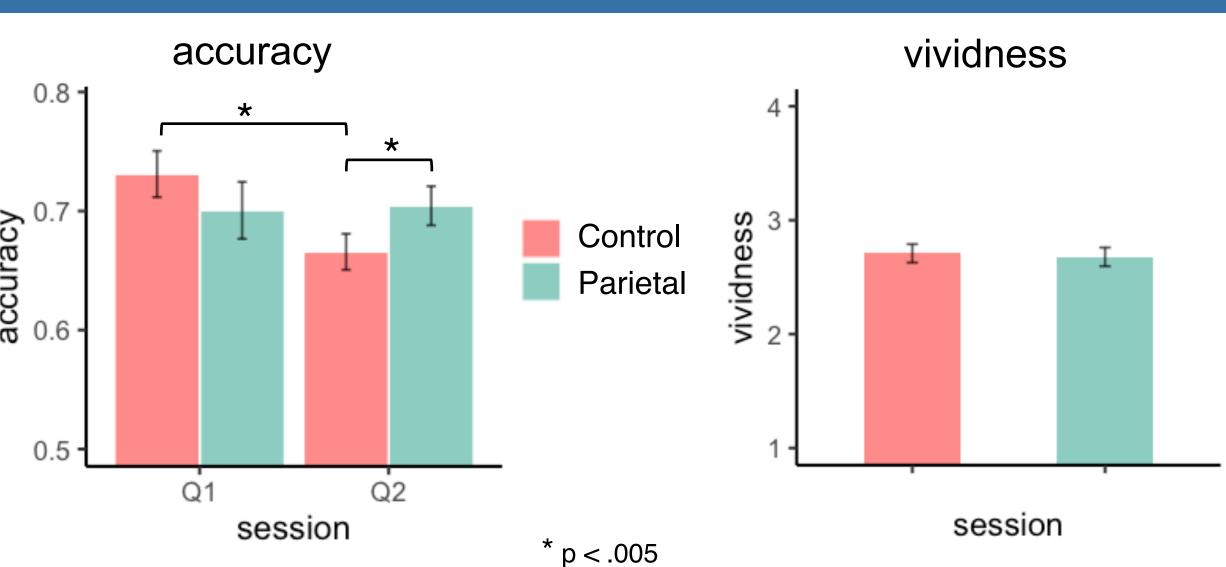
- Encoding: 50 short videos depicting everyday events per session
- Retrieval: subjective and objective memory measures

encoding





Behavioral Results



- Parietal stimulation improves objective memory accuracy on the second question (p < .005) but not the first (p > .05)
- Accuracy on the second question is worse than on the first for control stim, but not for parietal stim
- May reflect interference, rescued by parietal stimulation
- No effect of stimulation on subjective vividness (p > .05)

Neural Reinstatement

Precuneus

Angular gyrus

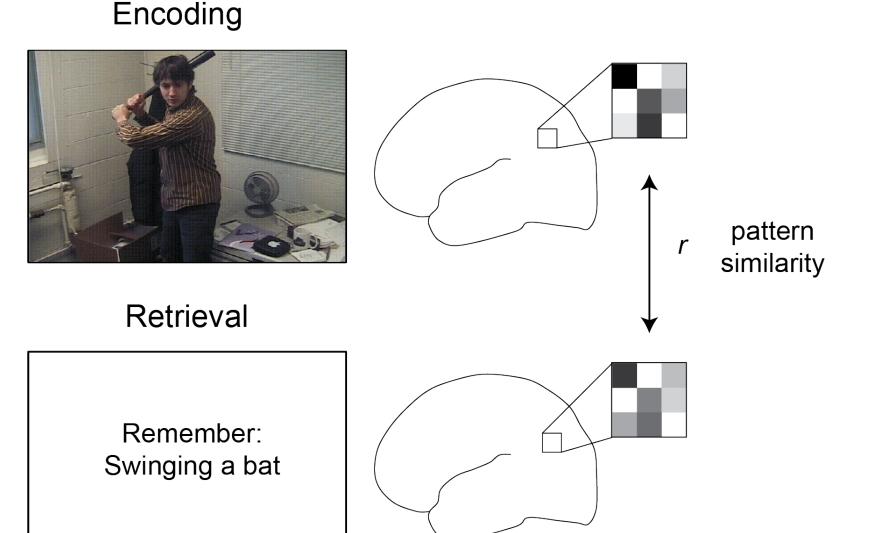
Fusiform gyrus

* p < .05, corrected for multiple comparisons

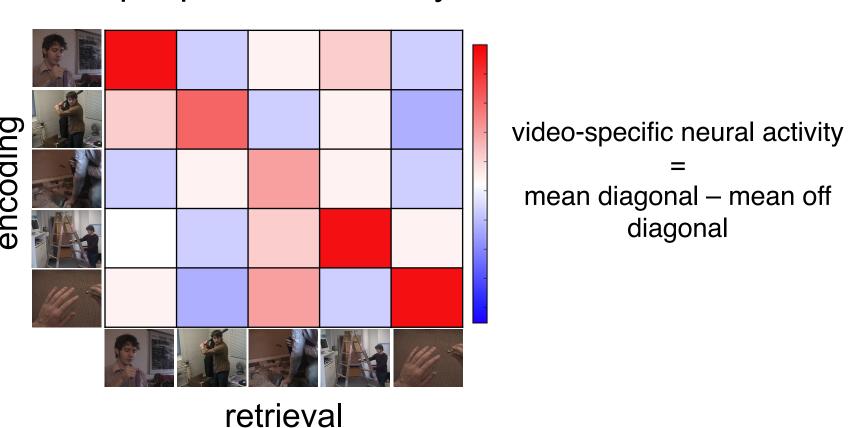
Mid. Occipital gyrus

Mid. Temporal gyrus

Pattern similarity analysis



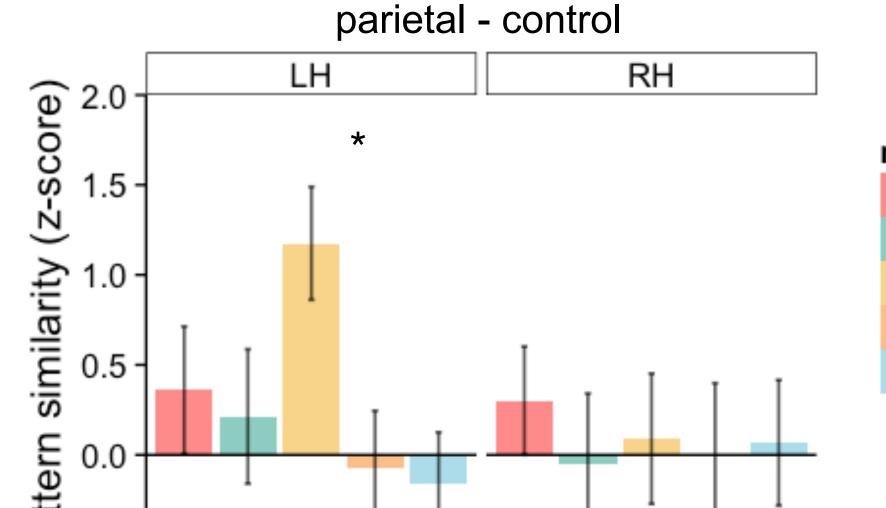
Example pattern similarity matrix



Regions of interest (ROIs)

5 bilateral regions of interest: precuneus, angular gyrus, middle occipital gyrus, middle temporal gyrus, fusiform gyrus

Pattern similarity results

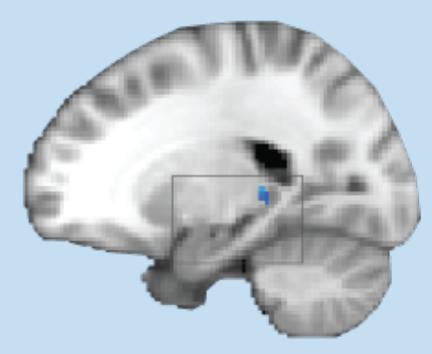


ROI

- Posterior parietal and occipital regions show reinstatement of video-specific multivariate patterns of neural activity
 Parietal stimulation enhances
- Parietal stimulation enhances reinstatement in left middle occipital gyrus

Univariate Results

parietal > control stimulation

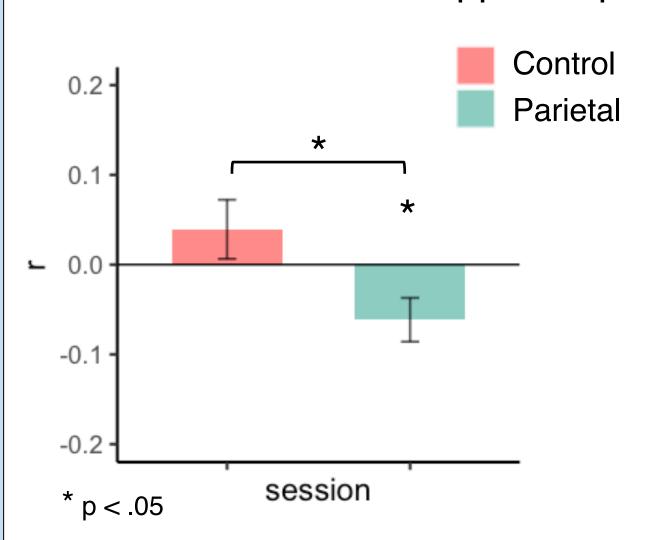


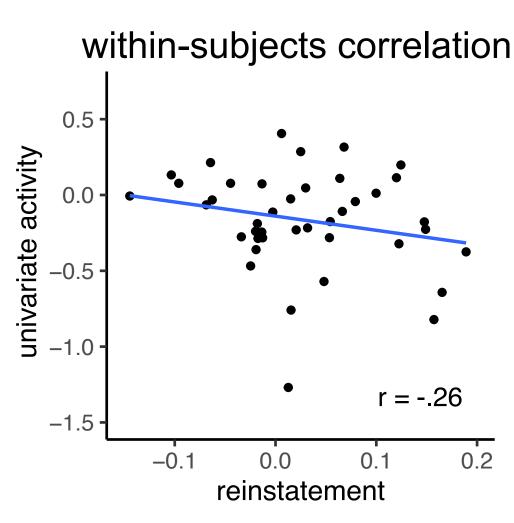




 Parietal stimulation leads to decreased left posterior hippocampal activity during memory encoding (cluster corrected threshold p < .005)

Correlation between hippocampal activity and reinstatement





 Stimulation leads to a negative within-subject correlation between univariate left posterior hippocampal activity at encoding and reinstatement in left medial occipital gyrus

Conclusions

- Lateral parietal stimulation alters objective but not subjective memory for naturalistic episodes
- Accuracy improved on the second question only, suggesting reduced interference
- Memory for lifelike events supported by reinstatement of eventspecific patterns of neural activity in posterior midline regions
- Lateral parietal stimulation alters reinstatement of event-specific multivariate activity
- Stimulation decreases posterior hippocampal univariate activity during memory encoding
- Stimulation alters within-subject association between univariate hippocampal activity and medial occipital reinstatement
- Hippocampal-targeted stimulation alters large-scale, eventspecific multivariate patterns of neural activity and objective memory for naturalistic episodes

References

- 1. Wang, J.X., Rogers, L.M., Gross, E.Z., Ryals, A.J., Dokucu, M.E., Brandstatt, K.L., Hermiller, M.S., Voss, J.L. (2014), *Science*
- 2. Nilakantan, A.S., Bridge, D.J., Gagnon, E.P., VanHaerents, S.A., Voss, J.L. (2017), *Curr Biol*
- 3. Hermiller, M.S., VanHaerents, S., Raij, T., Voss, J.L. (2019), Hippocampus
- 4. Tambini, A., Nee, D.E., D'Esposito, M. (2018), J Cogn Neurosci
- Chen, H.-Y., Gilmore, A.W., Nelson, S.M., McDermott, K.B. (2017), *J Neurosci* Hebscher, M., Meltzer, J., Gilboa, A. (2019), *Elife*
- 7. Thakral, P.P., Madore, K.P., & Schacter, D.L. (2017), J Neurosci