Local field potential of subsequent memory post human amygdala-mediated memory modulation in the medial temporal lobe

INMAN LAB

IMMERSIVE NEUROMODULATION AND NEUROIMAGING LAB

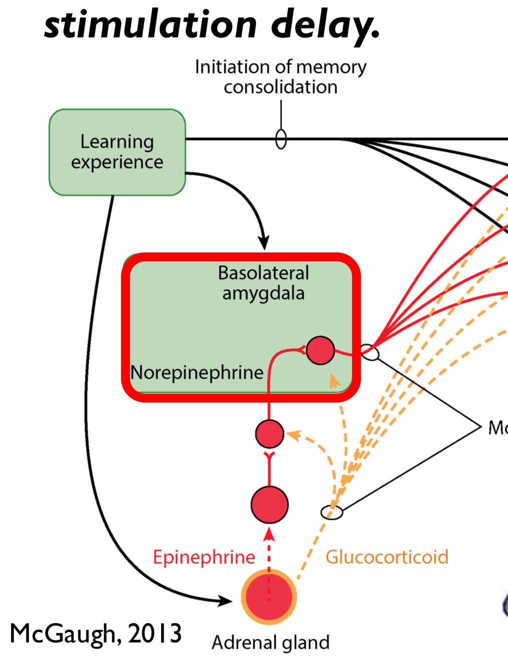
M. K. HOLLEARN[1], J. R. MANNS[5], L. BLANPAIN[3], S. B. HAMANN[5], K. BIJANKI[6], R. E. GROSS[7], D. DRANE[4], J. M. CAMPBELL[2], K. L. WAHLSTROM[1], Light, G. F.[1], Wilson, Z. R.[1], Taševac, A.[1], **J. T. WILLIE*[8], C. S. INMAN*[1]**

[1] Psychology, [2]Interdepartmental Program in Neuroscience, University of Utah, Salt Lake City, UT; [3]Neuroscience, [7]Neurosurgery, [4]Neurology, Emory School of Medicine, Atlanta, GA; [5]Psychology, Emory University, Atlanta, GA; [6]Neurosurgery, Baylor College of Medicine, Huston, TX; [8]Neurosurgery, Washington University School of Medicine and Barnes-Jewish Hospital, Saint Louis, MO

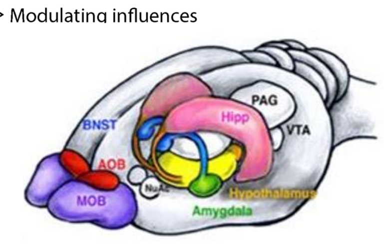
THE UNIVERSITY OF UTAH

Background

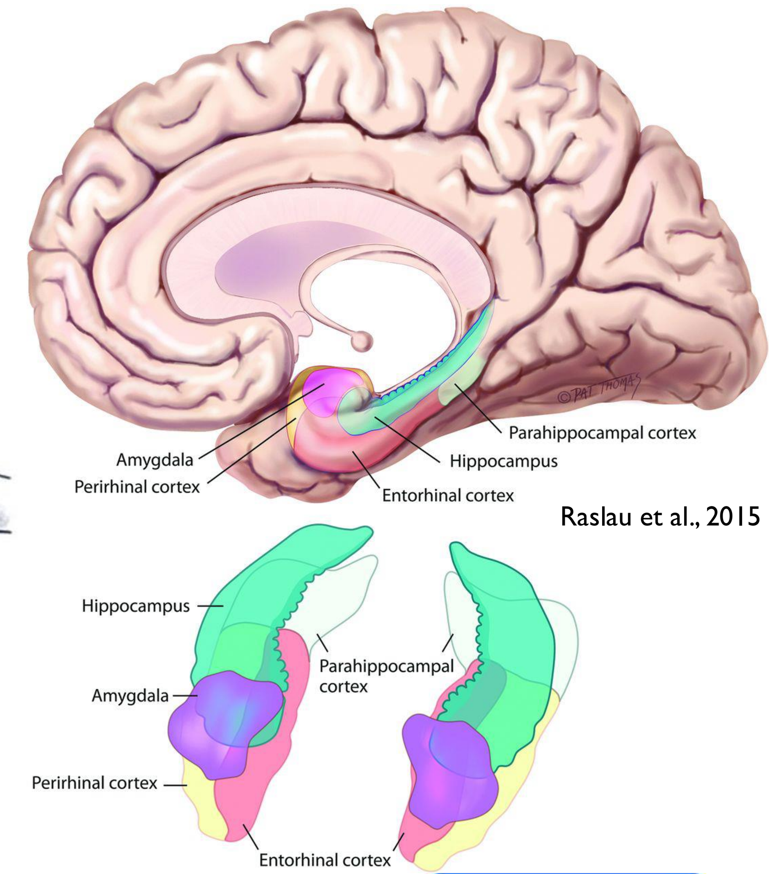
- Human deep brain stimulation (DBS) has been successfully at treating drug-resistant neurological conditions like Parkinson's Disease[1] and various medial temporal lobe (MTL) regions have shown premise for memory modulation but with mixed results.[2,3,4,5,6]
- The basolateral amygdala (BLA), an essential MTL region for emotional memory and consolidation, has been mainly ignored in human DBS despite successful memory enhancement in rodent models[7,8,9,10] and one human BLA stimulation study.[11]
- ***The present study examined various BLA stimulation parameters' effect on the electrophysiology of memory consolidation in MTL regions at a 24-hour post stimulation delay.***



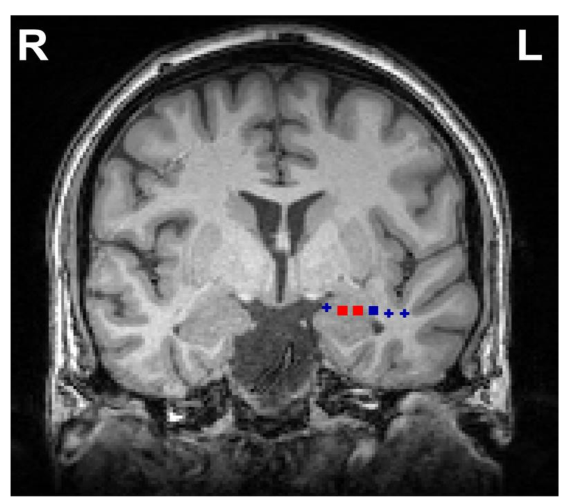
McGaugh, 2013



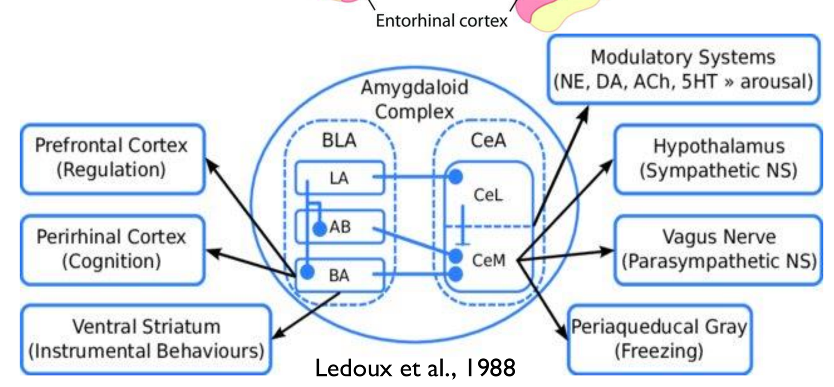
Rodent brain
Gough, 2019



Raslau et al., 2015



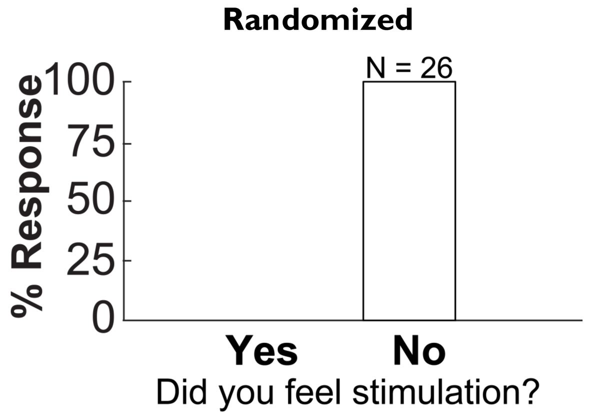
Example BLA stimulation electrode pair (cathode and anode)

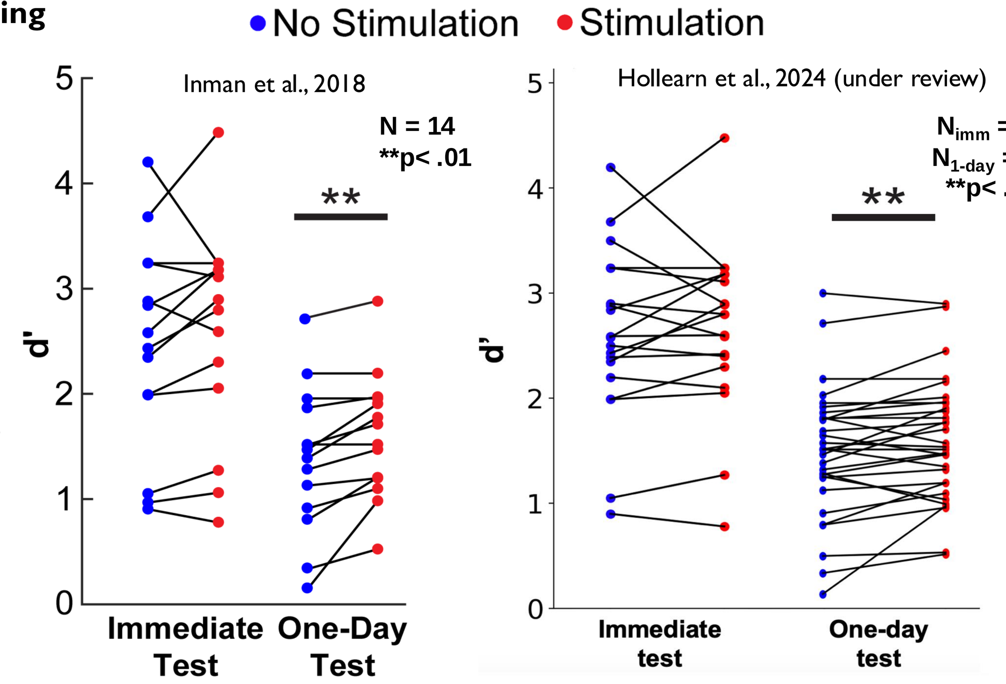


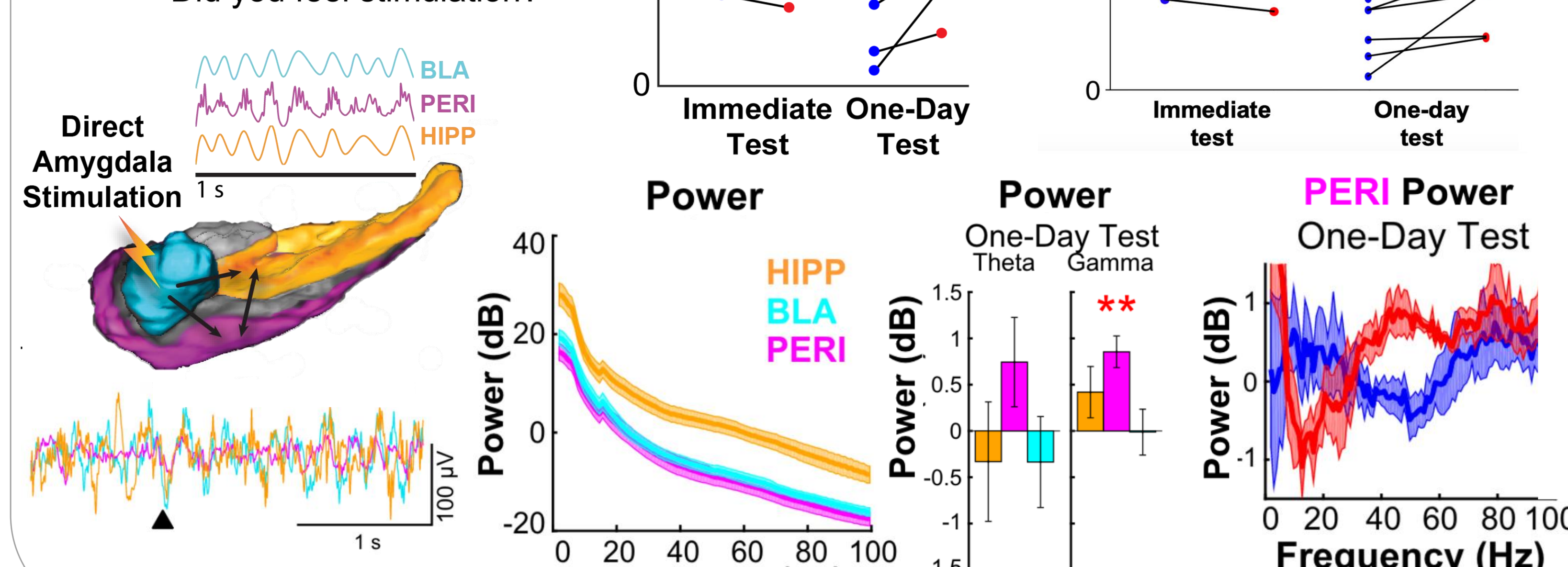
Ledoux et al., 1988

We hypothesize that hippocampus and perirhinal cortices will have higher theta and slow gamma powers for previously stimulated compared to previously not stimulated objects.

Subjective Emotional Awareness Testing
20 Trials:
10 Sham vs 10 Stim
Randomized





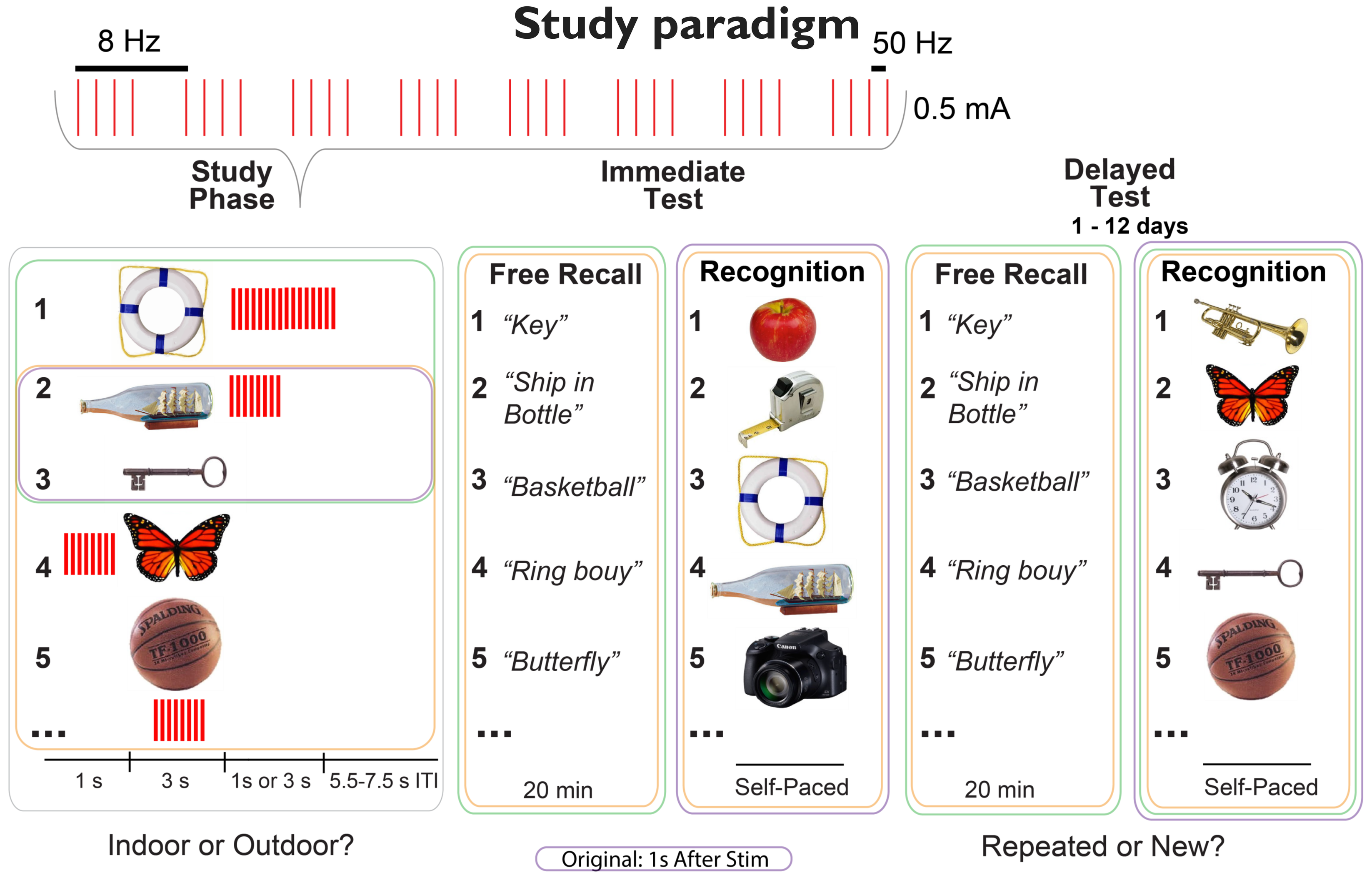


Methods

Participants

31 patients (51% female and 49% male, $M(SD)_{age}$ = 34(12), FSIQ = 87(17) with intractable drug-resistant epilepsy in the Emory University Hospital for intracranial monitoring (iEEG). No epileptiform activity or stimulation awareness was elicited by the stimulation, nor it evoked any subjective emotional arousal in the participants.

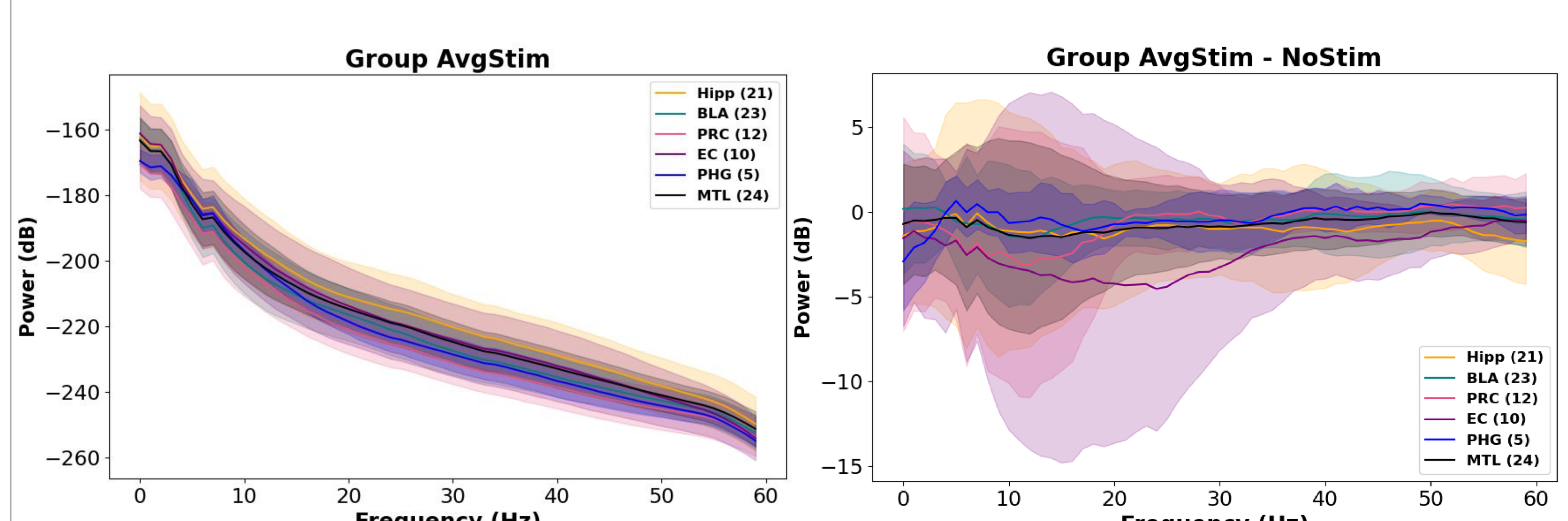
Study paradigm



Results

Building onto our prior work we found an omnibus memory enhancement at the 1-day delay (but not immediate delay) for previously stimulated objects compared to previously not stimulated objects.[12] In this combined dataset we found more variability in memory modulation due to prior BLA stimulation, thus our local field potential (LFP) analyses focus on further understanding the electrophysiology of MTL regions involved in memory consolidation and modulation post BLA stimulation.

Sub-experiments	Stimulation condition	Memory delay	N subjects	N sessions
Original[11]	1 s after and sham	24 hours	14	14
Duration	1 s and 3 s after, and sham	24 hours	5	6
Timing	1s before, during, and after, and sham	24 hours	12	14



Overall power difference in all frequencies for <u>previously BLA stimulated – previously not stimulated objects</u> in MTL regions of interests (ROIs). Number of subjects per ROI is in parentheses after the ROI name, for example, N = 20 for Hippocampus samples (1 per subject). Specifically, we have 20 subjects with one representative Hippocampal channel in the data. The shaded area represents standard deviation, and the lines represent the mean of the sample.

Acknowledgements

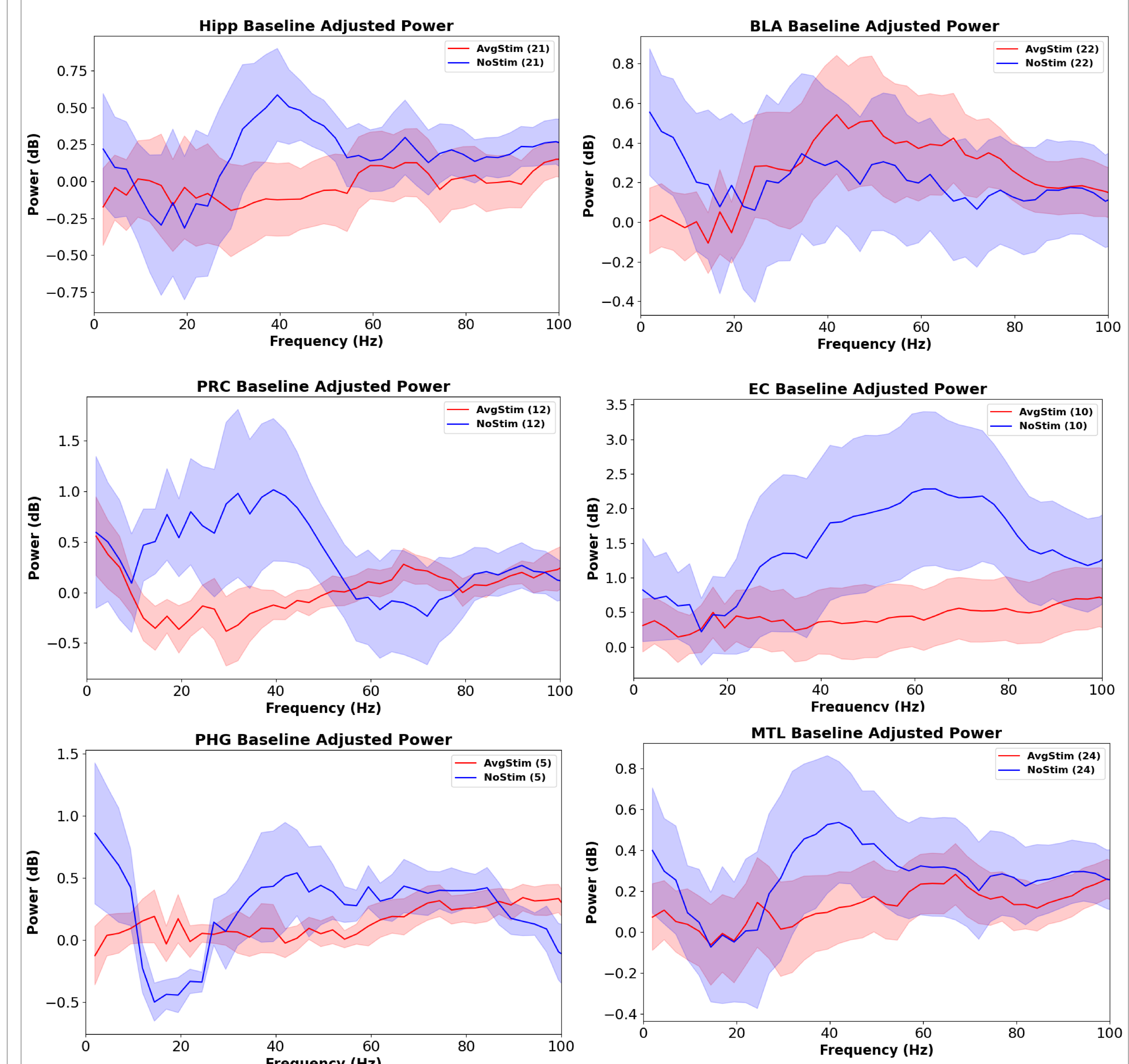
We are grateful for the patient's time and trust in completing this work. Thanks to John Janecek and Phil Demarest for programming assistance. We would also like to thank the EEG technicians and neurology department physicians for their time and assistance in performing these experiments.

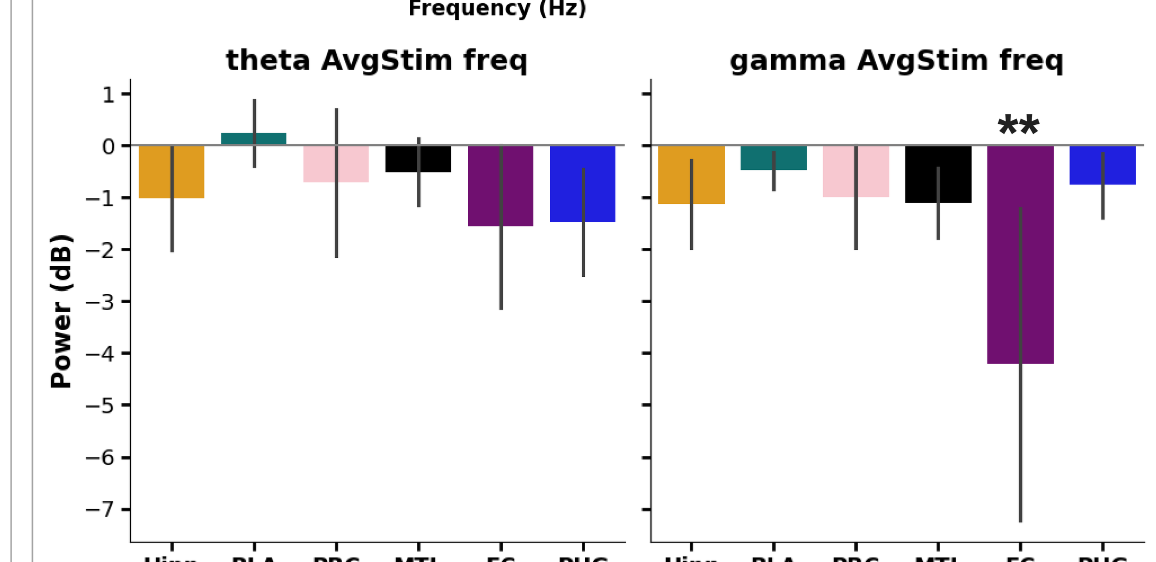
For more information, please email martina.hollearn@psych.utah.edu

@HollearnMartina
@INMAN_Lab

Results continued

Baseline corrected power difference between previously stimulated vs. not stimulated objects in the MTL at retrieval





A linear mixed-effects model evaluating avg stim – stim power differences in theta and gamma frequencies showed a significant difference in power (dB) for entorhinal cortex (p = .001) in the slow gamma band (30-55Hz). This relationship indicated higher slow gamma power in the no prior stimulation remembered objects compared to the previously stimulated objects.

Conclusion & Current Directions

- The LFP results showed no that slow gamma power in the entorhinal cortex was higher for the previously not stimulated objects compared to previously stimulated objects. Also, we found no significant differences in theta (4-8Hz) frequencies between previously BLA stimulated minus not stimulated objects other MTL ROIs observed. These patterns of results contradict our prior findings, which can be due to patient characteristics like baseline memory or additional stimulation parameters introduced in later sub-experiments (e.g., Duration and Timing sub-experiments).
- Next, we will delve into coherence and phase amplitude coupling analyses for the same regions of interest and analysis window (500ms after image onset at retrieval) and will investigate the LFP analysis in the sub-experiments, for example, examining differences in theta and gamma power between 1 sec and 3sec prior BLA stimulation conditions (Duration sub-experiment).
- Finally, future directions include observing power, coherence, and phase amplitude coupling analyses for the above-mentioned MTL regions for the interaction of BLA stimulation and memory accuracy. Specifically, we will examine LFP analyses for contrasts of remembered vs forgotten objects.

References

1. Horn, A., et al (2019). *Brain,* 142(10), 3129-3143.
2. Suthana, N., et al. (2012). *New England J of Medicine*, 366(6), 502-510.
3. Jacobs, J. et al. (2016). *Neuron*, 92(5), 938-990.
4. Titiz, A. et al. (2017). *eLife,* 6, e29515.
5. Hansen, N., et al. (2018). *Hippocampus*, 28(1), 12-17.
6. Khan, I. et al. (2019). *World Neurosurgery*, 126, 638-646.
7. McGaugh, J. L. (2013). *PNAS*, 110,10402–10407.
8. Hamann, S. (2001). *Trends in Cognitive Sciences*, 5(9), 394–400.
9. Bass, D. I. et al., (2012). *Behavioral Neuroscience*, 126(1), 204–208.
10. Bass, D. I., & Manns, J. R. (2015). *Behavioral Neuroscience*, 129(3), 244–256.
11. Inman, C.I., Manns, J. R. et al., (2018). *PNAS*, 115(1), 98-103.
12. Hollearn et al., (2024) under review in Cognitive, Affective, and Beh. Neuroscience