Exploring stimulation parameters and individual differences in amygdala-mediated memory modulation

M. K. HOLLEARN[1], L. BLANPAIN[3], J. R. MANNS[5], S. B. HAMANN[5], K. BIJANKI[6], R. E. GROSS[7], D. DRANE[4], J. M. CAMPBELL[2], K. L. WAHLSTROM[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

INMAN LAB
IMMERSIVE NEUROMODULATION AND NEUROIMAGING LAB

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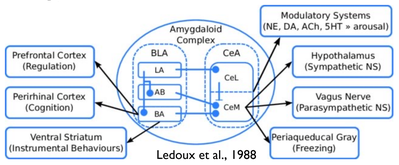
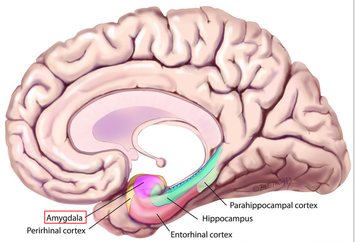
Background

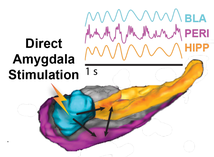
- Deep brain stimulation (DBS) has been successfully at treating drug-resistant neurological conditions like Parkinson's Disease or Major Depressive Disorder.[1]
- Human DBS has in the MTL also shown premise for memory modulation, and most prior studies focused on hippocampus, entorhinal cortex, which have shown mixed results in memory enhancement. [2,3,4,5,6]
- The amygdala has been mainly ignored in human DBS studies despite its established role in emotional memory modulation. [7,8]
- We have previously demonstrated that brief basolateral amygdala (BLA) electrical stimulation enhances memory in rodents[9,10] and humans without eliciting an emotional response. [11]
- ***The present study examined various stimulation parameters and individual differences in patients contributing to the memory modulation effects of prior amygdala stimulation.***



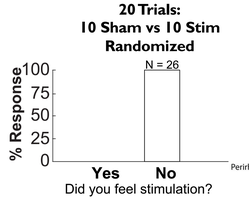
Ledoux et al., 1988

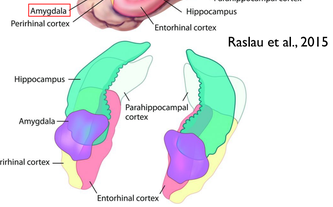


Raslau et al., 2015



Inman, Manns et al., (2018)





Amygdala stimulation will modulate memory retrieval at the one-day delay.

Factors contributing to memory modulation

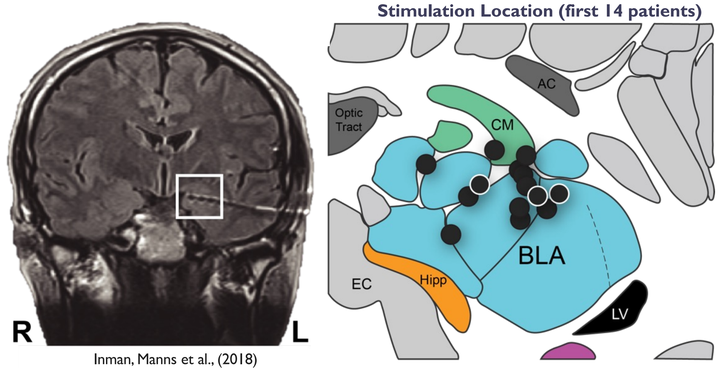
Experimental factors

- **Stimulation duration**
- **Stimulation timing**
- **Stimulation location**
- Memory retrieval length
- Memory paradigm
- Stimulation amplitude
- Stimulation type

Patient factors

- **Demographics**
- **Baseline memory**
- **Neuropsychological tests**
- Sleep deprivation
- Attentional factors

Stimulation Location (first 14 patients)



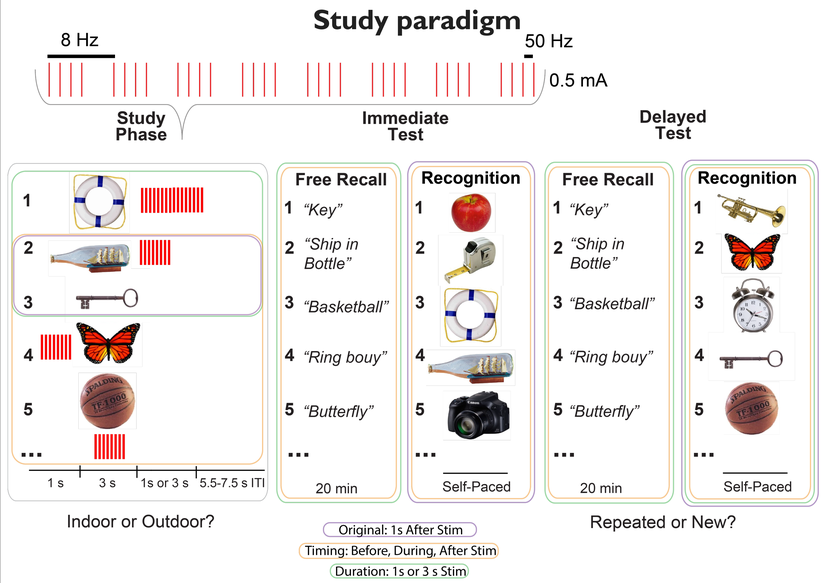
Inman, Manns et al., (2018)

Methods

Participants

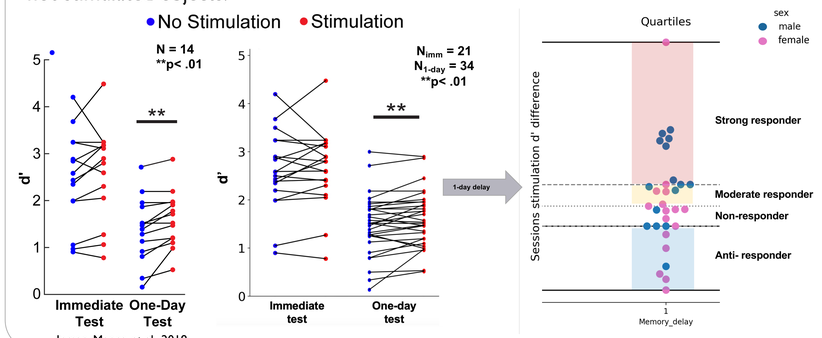
- 31 patients (51% female; $M(SD)_{age}$=34(12), FSIQ = 87(17)) with intractable drug-resistant epilepsy in the Emory University Hospital for intracranial monitoring (iEEG)
- Individual contacts implanted in both hemispheres in the basolateral amygdala
- No epileptiform activity or stimulation awareness was elicited by the stimulation
- Stimulation did not evoke any subjective emotional arousal in patients
- *Stimulation parameters examined:* Duration, Timing relative to stimulus, and Location within the BLA

Experiments	Stimulation condition	Delay	N subjects	N sessions
Original	1 s after	1 day	14	14
Duration	1s and 3s after	1 day	5	6
Timing	1s before, during, and after	1 day	12	14
Total			31	34



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.



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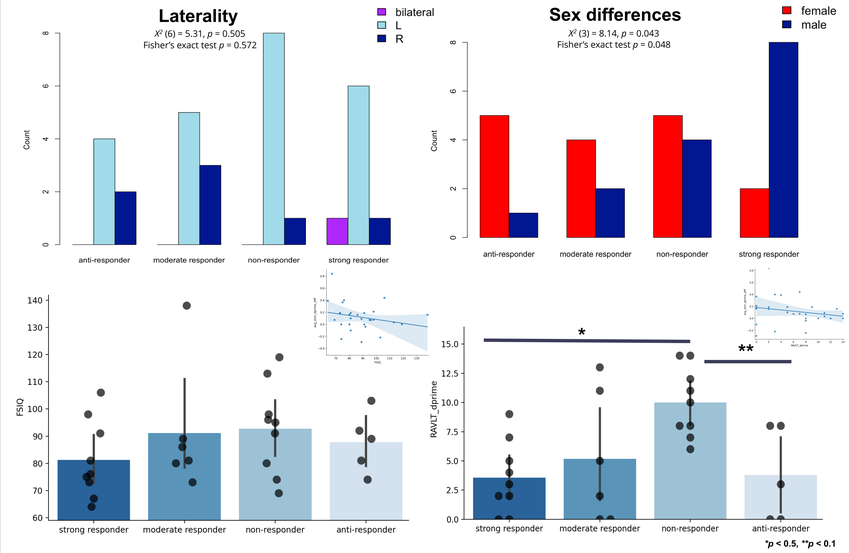
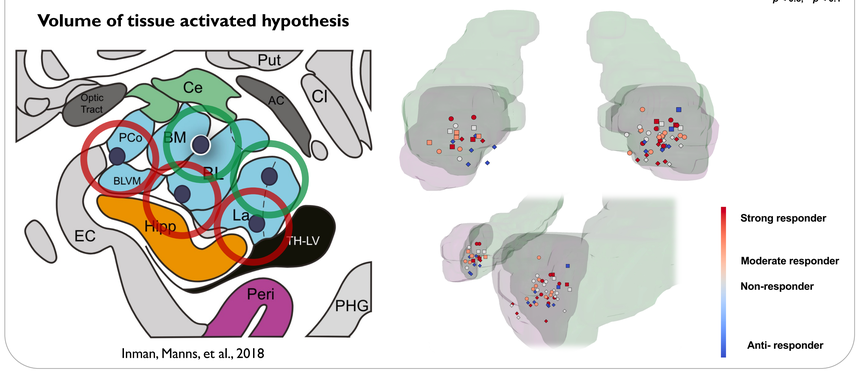
Results continued

- Strength of positive response to prior amygdala stimulation was influenced by individual differences in sex and baseline memory performance on neuropsychological tests of long-term memory like RAVLT (but not intelligence capacity).
- We found no differences between the various stimulation parameters (duration or timing relative to stimulus).
- We found no differences in stimulation-related memory enhancement based on the hemisphere of the stimulated amygdala.



Volume of tissue activated hypothesis



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Conclusion & Current Directions

- Direct amygdala stimulation causes prioritization of *temporally-specific* declarative memories for later recognition without eliciting an emotional response (building onto previous our previous study), and sex differences seems like they may influence the strength of memory prioritization.
- Other stimulation parameters, like timing and duration, we explored do no seem to improve memory more than our original stimulation parameters.
- Baseline memory performance measured by MTL dependent neuropsychological tests (RAVLT d') of long-term memory seem to differentiate between responders and non-responders of memory modulation.
- Location of stimulation and volume of tissue activated might explain the most variability in our results.
- Our next steps are to examine our findings with a multinomial logistic regression to predict responder status based on the ensemble of these patient characteristic and stimulation parameters while accounting for the variance of the factors in the model.

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

Website

@HollearnMartina
@INMAN_Lab

Poster PDF

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