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

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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.
- Human DBS has shown promise for memory modulation, and most prior studies focused on hippocampus, entorhinal cortex, which have shown mixed results in memory enhancement.
- The amygdala has been mainly ignored in human DBS studies despite its established role in emotional memory modulation.
- We have previously demonstrated that brief basolateral amygdala (BLA) electrical stimulation enhances memory in rodents.
- The present study examined various stimulation parameters and individual differences in patients contributing to the memory modulation effects of prior amygdala stimulation.

**Experimental factors**

- Differences in patients contributing to the memory modulation effects of prior amygdala stimulation.
- Stimulation enhances memory in rodents and humans without eliciting an emotional response.
- The present study examined various stimulation parameters and individual differences in patients contributing to the memory modulation effects of prior amygdala stimulation.

**Methods**

**Participants**

- 31 patients (15 female, M<SD>age=34.7, SD=8.7) 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

**Experimental conditions**

- Original: 1 s after
- Duration: 1 s and 3 s after
- Timing: 1 s before, during, and after

**Results**

- 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 and delayed recall.
- 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.

**Results continued**

- Direct amygdala stimulation causes prioritization of temporally-specific declarative memories for late recognition without eliciting an emotional response (building onto previous studies), and sex differences seem like they may influence the strength of memory prioritization.
- Other stimulation parameters, like timing and duration, we explored do not seem to improve memory more than our original stimulation parameters.
- Baseline memory performance measured by MTL dependent neuropsychological tests (RAVLT) 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.

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

**Factors contributing to memory modulation**

- **Experimental factors**
  - Stimulation duration
  - Stimulation time
  - Stimulation location
  - Memory retrieval length
  - Memory paradigm
  - Stimulation amplitude
  - Stimulation type

- **Patient factors**
  - Demographics
  - Baseline memory
  - Neuropsychological tests
  - Sleep deprivation
  - Antenna factors

**Study paradigm**

- 8 Hz
- 50 Hz
- 0.5 mA
- Immediate Test
- Delayed Test
- Free Recall
- Recognition

**Study Phase**

- Indoor or Outdoor?
- Original: 1 s after
- Timing: before, during, after
- Duration: 1 s, 3 s
- Delayed: 20 min

**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 unstimulated objects.

**Conclusion & Current Directions**

- Direct amygdala stimulation causes prioritization of temporally-specific declarative memories for late recognition without eliciting an emotional response (building onto previous studies), and sex differences seem like they may influence the strength of memory prioritization.
- Other stimulation parameters, like timing and duration, we explored do not seem to improve memory more than our original stimulation parameters.
- Baseline memory performance measured by MTL dependent neuropsychological tests (RAVLT) 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.
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**References**