

# Memory Loss After Brain Injury Is Improved by Theta Burst Stimulation of the Fornix

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#### Introduction

Memory loss after brain injury can be a source of considerable morbidity, but there are presently few therapeutic options available for this condition. We have previously demonstrated that burst stimulation of the fornix is able to significantly improve memory in a rodent model of traumatic brain injury. The purpose of this study is to determine the effect of theta burst stimulation of the fornix on memory in humans.

# Methods

Five patients undergoing stereo-EEG evaluation for medically intractable epilepsy were enrolled. All patients were implanted with an electrode into the proximal fornix and dorsal hippocampal commissure on the dominant (n=3) or non-dominant (n=2)side (Figure 1), and stimulation of this electrode reliably produced a diffuse evoked potential in the head and body of the ipsilateral hippocampus. Each patient underwent testing of verbal memory (RAVLT), visual memory (MCG Complex Figures Questionnaire), and visual confrontational naming (BNT Short Form) once per day over two or four consecutive days. For 50% of the trials, the fornix electrode was continuously stimulated using a burst pattern (200 Hz in 100 msec trains, five trains per second, 100 microseconds, 7 mA, Figure 2), and this was compared with sham stimulation. Participants and examiners were blinded to whether stimulation was active or not, and the order of stimulation was randomized. The results were compared using a paired sample Student's t-test with correction for multiple comparisons.

# Figure 1. Targeting of fornix and hippocampus.



(A, B) Preoperative MRI was used to identify a trajectory passing through the fornix and terminating in the dorsal
hippocampal commissure. (C-E)
Fusion between preoperative MRI and postoperative CT was used to demonstrate electrodes
located in the fornix on coronal
(C) and axial (D) views, as well as electrodes in the hippocampal head (E) and body (F). White arrows indicate the relevant electrode contact. Figure 2. Theta burst stimulation parameters.

The External Neurostimulator Unit was programmed to deliver 0.1 msec pulses at 200 Hz in 100 msec trains, 5 trains per second.

1 second

This was accomplished by activating the cycling setting of the neurostimulator 0.1 second on and 0.1 second off.

#### Results

Burst stimulation of the fornix was not perceived by any of the participants but was associated with a significant reversible improvement in immediate (p<0.01) and delayed (p < 0.05) performance on the MCG Complex Figure Test (Figure 3). There were no significant differences in RAVLT or BNT. There was no correlation between performance and stimulation of the fornix on the dominant or nondominant side. There were no complications.



### Conclusions

Burst stimulation of the fornix is associated with significantly improved performance on memory for complex figures.

# **Learning Objectives**

 Outline the effects of burst stimulation on memory and word finding.
 Describe the utility of stimualation of white matter tracts for diffuse activation of a neural structures.
 Discuss the potential for neuromodulation to treat cognitive disorders.

# References

Sweet J, Eakin K, Munyon C, Miller J. Improved Learning and Memory With Theta-Burst Stimulation of the Fornix in Rat Model of Traumatic Brain Injury. Hippocampus 2014 (accepted).