CNS 2017 ANNUAL MEETING
BOSTON, MASSACHUSETTS
OCTOBER 7–11, 2017

Improvement in Delayed Recognition Using a Novel Neural Prosthesis for the Human Hippocampus

Robert Thomas Wicks MD; Mark Witcher; Dong Song PhD; BR Robinson; Dustin Fetterhoff; Alexander Dakos; Brent Roeder; Daniel Edward Couture MD; Adrian Walter Laxton MD; Heidi Monger-Clary; Gautam Popli MBBS; M Sollman; Vasilis Marmarelis; Theodore W. Berger PhD; Samuel A Deadwyler PhD; Robert E. Hampson PhD

Introduction

Linear, fixed stimulation applied directly to the hippocampus has been demonstrated in several reports to produce an impairment of human memory. Pattered stimulation, modeled from native spatio-temporal connectivity of CA3 and CA1 neurons, may facilitate memory. We predict that hippocampal stimulation with the use of a multi-input/multi-output (MIMO) stimulation paradigm will significantly improve short-term memory recall.

Methods

Three patients with medically-refractory epilepsy underwent implantation of intracranial depth electrodes for planned seizure monitoring and localization. At least one macro-micro (EEG and single-unit) depth electrode was placed within the head of the hippocampus and localized to the CA1 and CA3 cell layers. Patients performed a delayed-match-to-sample (DMS) memory task, in which they encoded specific screen images during presentation in the task sample phase, and then recalled that image after a delay of 1-70sec, in the Match phase of the task, which included simultaneous display of 2-6 non-match images. CA3 and CA1 neural firing patterns were recorded and processed to predict from temporally coupled CA3 neuron activity, the CA1 cell discharges that corresponded to correct match responses. After 2-4 days, Patients were given a second DMS task during which the MIMO model predicted electrical stimulation was delivered to CA1 neurons during the sample phase. For each sample presentation, patients were given MIMO stimulation, random stimulation, or no stimulation. A delayed recognition task was then performed. A sample image and two non-match images were displayed and patients were asked to rank the familiarity on a scale of 1-5. Total delay of 30-50min occurred from initial presentation in the DMS trial to assessment of the delayed recognition.

Results

MIMO stimulation of CA1 neurons during Sample presentation significantly improved delayed recognition when compared to no stimulation or random stimulation($p<0.001$).

Conclusions

Results support the basis for development of a possible neural prosthesis.

Learning Objectives

1)A linear, fixed pattern of stimulation applied directly to the human hippocampus has been previously shown in published reports to inhibit human memory.

2)Single neurons were recorded in vivo from the human hippocampus, and pairs of neurons were localized within the CA3-to-CA1 neural circuit via analysis of functional connectivity between pairs.

3)Short-term memory was successfully facilitated in human epilepsy patients via application of a multi-input/multi-output (MIMO) nonlinear simulation model to individual CA1 neuron firing in the hippocampus of each subject.

References

1) Jacobs J, Miller J, Lee SA, et al. Direct Electrical Stimulation of the Human Entorhinal Region and Hippocampus Impairs Memory. Neuron 2016;92(5):983-90. doi: 10.1016/j.neuron.2016.10.062

2) Lacruz ME, Valentin A, Seoane JJ, et al. Single pulse electrical stimulation of the hippocampus is sufficient to impair human episodic memory. Neuroscience 2010;170(2):623-32. doi: 10.1016/j.neuroscience.2010.06.042

3) Berger TW, Song D, Chan RH, et al. A hippocampal cognitive prosthesis: multi-input, multi-output nonlinear modeling and VLSI implementation. IEEE Trans Neural Syst Rehabil Eng 2012;20(2):198-211. doi: 10.1109/TNSRE.2012.2189133

[Default Poster]