Modulating Hippocampal Neural States in a Non-human Primate Model of Epilepsy Using Asynchronous Distributed Multi-electrode Stimulation

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Introduction

Neuromodulation is increasingly being investigated for the treatment for medically refractory epilepsy. We have found that asynchronous distributed multi-electrode stimulation (ADMES) of the hippocampus is more effective than macrostimulation (deep brain stimulation) in rodents (1), and is now being evaluated in a non-human primate penicillin (NHP-PCN) seizure model. In this study, we utilize a machine learning approach to characterize the spatial distribution of the effect of ADMES on hippocampal activities in the NHP-PCN model.

Methods

ADMES at 7Hz was applied via two 32-channel electrode arrays in the hippocampus for 10 trials of 2-minute intermittent ADMES and 40 minutes of SHAM stimulation. LFPs were recorded simultaneously using the same electrode array. Power spectral features for each electrode were extracted from 5s windows of LFPs after each ADMES and SHAM stimulation. This data was then used to train a classifier to determine whether the post-ADMES state was discernably different from the sham state.

Results

Cross-validation of the neural state classifier for each electrode-pair indicated that there were specific locations in the array where the ADMES induced observable changes in the hippocampal neural states. Next, we verified that this effect was not due to a difference in the seizure incidence between the two states by classifying between stimulation and sham for the ictal and inter-ictal segments independently. Isolating the effect of stimulation during ictal and inter-ictal segments we achieved AUCs of 0.66±0.08.

Conclusions

These findings suggest that ADMES maximally modulates neural activities at certain locations in the hippocampus in our NHP-PCN model. Analysis of this relationship will allow identifying controllable sub-circuits in the hippocampus. Finally, characterizing the modulated biomarkers of neural state and comparison with seizure biomarkers can be used to optimize this novel stimulation paradigm.

Learning Objectives

Identify the possible advantages of novel stimulation patters for epilepsy treatment.

Understand the role of biomarkers for stimulation optimization

References

1) Desai, SD, Rolston JD, McCracken CE, Potter SM, Gross RE: Asynchronous distributed multielectrode microstimulation reduces seizures in the dorsal tetanus toxin model of temporal lobe epilepsy, Brain Stimulation, 2016:51:899-908. PMID: 26607483