Friday, May 11, 2018

ORAL SESSION
Networks and Connectivity
12:30 p.m. – 2:30 p.m.
Chair: Jeff Daskalakis

O17. Connectomics in Subcallosal Cingulate Deep Brain Stimulation: Effective Connectivity as a Biomarker for Target Engagement

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Background: Responders to deep brain stimulation (DBS) in the subcallosal cingulate (SCC) share stimulation on a stereotypic connectome of converging white matter bundles. A tractography-based target selection using a "connectome blueprint" of past DBS responders shows improved results. While this structural pattern is a necessary requirement for antidepressant efficacy, there has been no functional evidence describing the distinction between effective and non-effective contacts.
Methods: Four subjects were implanted with DBS in the SCC using a tractography-based approach. Stimulation from effective and non-effective contacts was performed (2 Hz, 6 V), and the cortical evoked response (ER) was captured with 256-channel EEG.
Results: Magnitude of the ER to unilateral left stimulation is greater following stimulation from effective versus non-effective contacts, with a different signal emerging in dorsolateral prefrontal cortex (DLPFC). Source analysis shows greater ER magnitude from the effective target in left DLPFC between 60ms and 100 ms from the initiation of the propagation pattern. Coincident scalp topography appears as a positive focus over dorsal anterior midline that migrates in the posterior direction and is reliable across individuals.
Conclusions: Absence of objective biomarkers to guide target selection and stimulation parameter setting is a barrier to adequate implementation of SCC DBS. A non-invasive metric of effective connectivity from a white matter target in the subcallosal cingulate has the requisite properties of a biomarker of the effective contacts. This putative biomarker showing involvement of DLPFC in effective stimulation may be informative and relevant to the mechanism of treatment efficacy.
Supported By: Hope for Depression Research Foundation
Keywords: Subcallosal Cingulate, Deep Brain Stimulation, DLPFC, EEG, Treatment Resistant Depression

O18. Changes in Effective Hippocampal Network Coupling Mediate Learning and Memory of Associations Between Temporally Discontiguous Stimuli

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Background: Episodic memory requires linking discontiguous events in time and depends on the hippocampus. This temporal association learning is often modeled using trace fear conditioning. Here we probe the ensemble activity in hippocampal CA1 during trace fear learning to differentiate between candidate activity mechanisms and directly resolve the underlying representation.
Methods: We integrated optogenetics and two-photon calcium imaging with a differential auditory 'trace' fear conditioning (15s 'trace') paradigm in head-fixed, water-deprived mice. We used suppression of licking behavior for water as a measure of conditioned fear. We analyzed CA1 network activity dynamics using linear classifiers (SVM with linear kernel) to decode relevant variables and assess the information encoded by the population with learning.
Results: We find that learning is dependent on dorsal CA1 activity (n=5/group; $p<0.05$, t-test) and mice (n=7) reliably discriminate between fearful and neutral conditioned stimuli (CS). Imaging of CA1 network dynamics (n=1200 neurons/4 mice) show that neither previously proposed mechanisms of temporal sequence nor 'persistent' activity are congruent with the observed population code. Instead, CS identity can be reliably decoded from the covariance of neural activities, which defines the effective network couplings, during both CS and 'trace' intervals.
Conclusions: Our studies suggest that CS identity is encoded by combinatorial patterns of cell activation, which develop with learning but occur at different times across trials. Thus, we propose a new model of trace fear learning where certain CA1 coactivity patterns are transiently potentiated and can be used to query information about the cue identity throughout the trial, without requiring an uninterrupted representation.
Supported By: NIMH K08, T32, and R01; Leon Levy Foundation
Keywords: Hippocampus, Associative Learning, Systems Neuroscience, Two-Photon Imaging, Fear Memory

O19. Electroconvulsive Therapy Modulates Gray Matter Increase in a Hub of an Affect Processing Network

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