Joint and independent contributions of the frontal cortex and central thalamus to executive function

201.11

Jonathan L. Baker, Sudhin A. Shah, Jae-wook Ryou, Nicholas D. Schiff, Keith P. Purpura

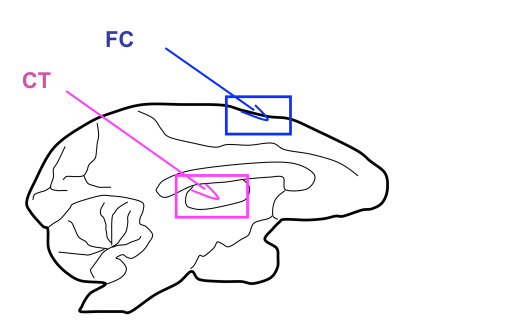
Department of Neurology and Neuroscience, Weill Cornell Medical College, New York, NY, 10065

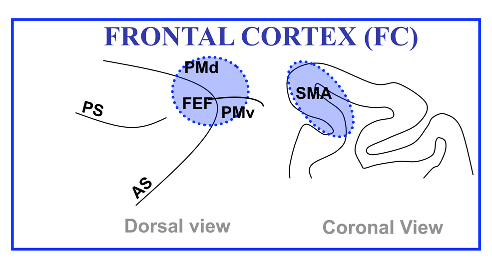
INTRODUCTION

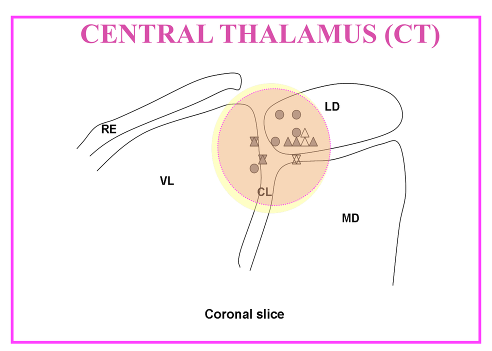
The involvement of the frontal cortex (FC) and central thalamus (CT) in executive components of behavior is suggested by anatomical connectivity, clinical studies and physiological evidence. Although certain components of executive function have been studied in both areas independently, there is a dearth of evidence comparing their independent and joint engagement during tasks that require the temporal organization of goal-directed behavior. In this study, we investigated two processes central to most executive functions – sustained attention and working memory, while conducting simultaneous microelectrode recordings within the frontal cortex and central thalamus of an awake behaving non-human primate. In a second animal, we included a grid of EEG electrodes to investigate brain-wide interactions during the tasks.

GENERAL METHODS

NEUROPHYSIOLOGY





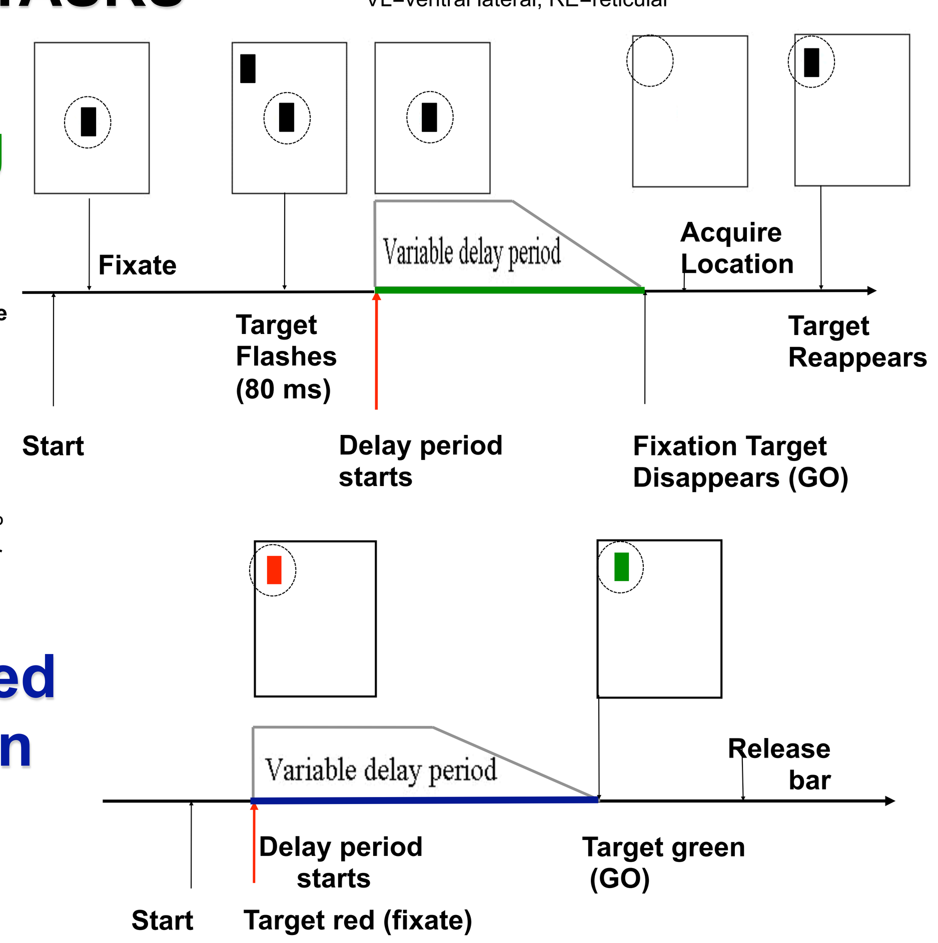


Paired single-unit recordings were conducted in the frontal cortex and central thalamus as illustrated above. Recordings were made with epoxy-insulated tungsten FHC microelectrodes (1-4 MΩ). Broadband neural signals were streamed to disk at 20 KHz and synchronized with eye movements and behavioral markers. Local field potentials (LFP) were filtered digitally (1-200Hz) and spike-sorting was conducted off-line using standard sorting techniques. Histology confirmed the recording locations.

AS=arcuate sulcus; PS=principal sulcus; FEF=frontal eye fields; PMd=premotor dorsal; PMv= premotor ventral; SMA=supplementary motor area; CL=central lateral nucleus; MD=medial dorsal; LD=lateral dorsal; VL=ventral lateral; RE=reticular

DELAY TASKS

Working Memory



= direction of gaze

Gaze direction monitored by infrared eye tracker, sampling rate = 120 Hz. Fixation restricted to a 1° x 1° window at the center of gaze.

Sustained Attention

The variable delay period was a normally distributed time interval with a mean duration of 1350 ms and standard deviation of 350 ms. Performance was variable over experimental sessions that included ~1000 trials and that often switched between blocks of the sustained attention and working memory tasks. Peak performance was typically 75-80% correct on both tasks.

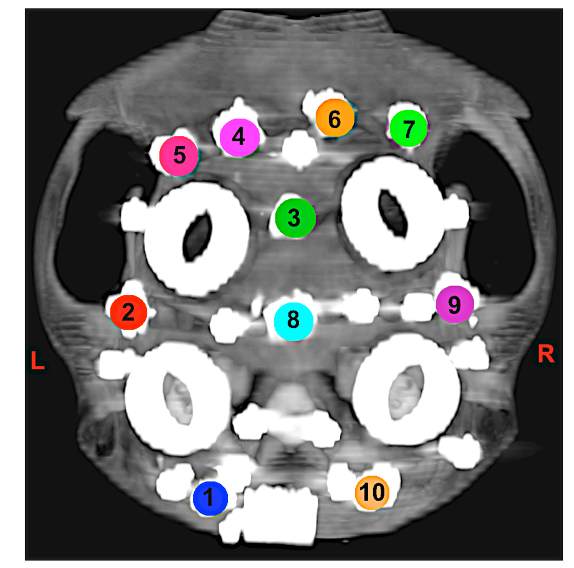
CURRENT APPROACH: LARGE-SCALE CORTICAL AND CENTRAL THALAMIC RECORDINGS

MOTIVATION

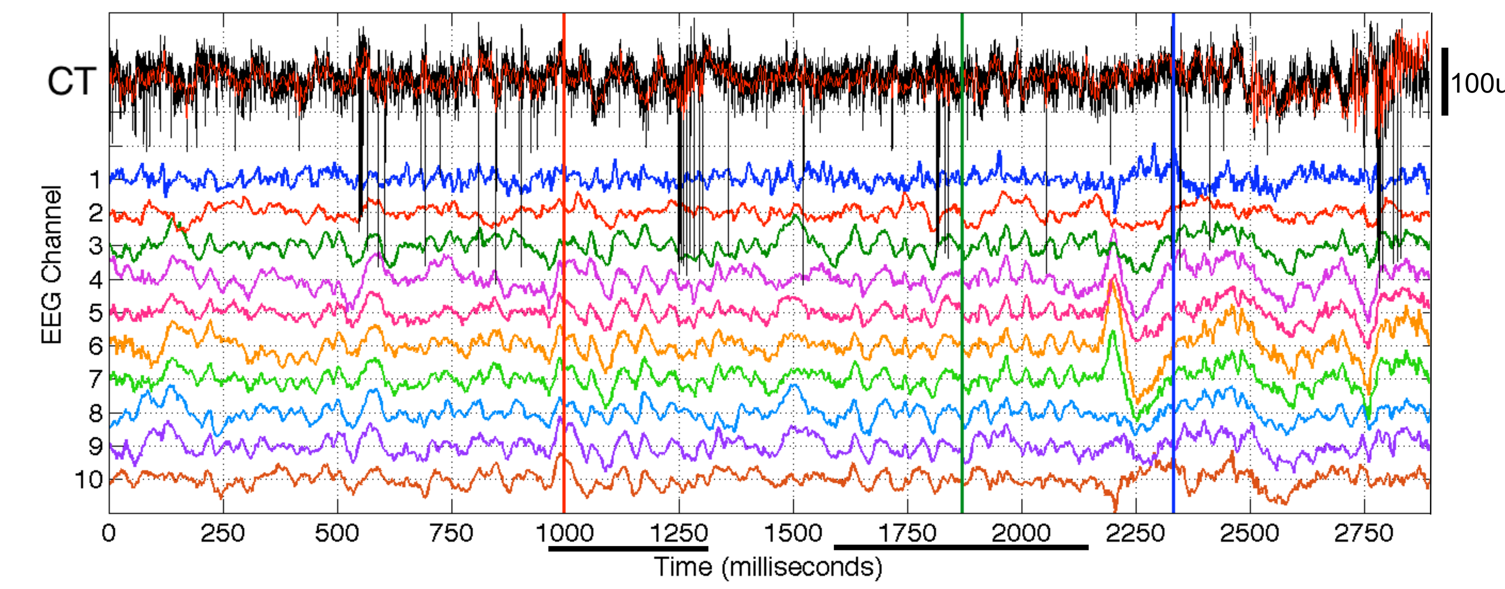
Central thalamic deep brain stimulation (CT/DBS) has been proposed as a strategy to remediate impaired consciousness resulting from severe brain injuries (Schiff and Purpura, 2002) and is the subject of ongoing human clinical trials. A recently published single-subject human study has demonstrated that CT/DBS facilitated behavioral recovery after longstanding severe traumatic brain injury (Schiff et al., 2007). However, the precise physiological mechanisms underlying this promising intervention are not well understood and have only recently been investigated. Understanding the neurophysiological basis of measured behavioral effects, from both human and non-human primates, and how to optimize the efficacy of CT/DBS motivate current studies within our group.

METHODS

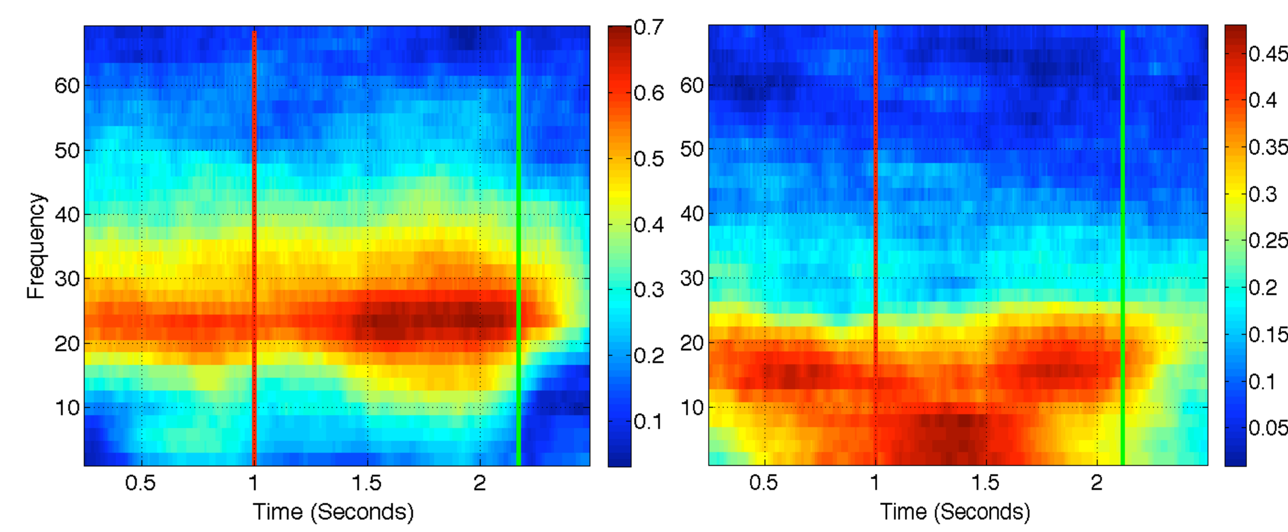
We implanted a nonhuman primate with a fixed set of 10 EEG electrodes and 4 Gray Matter Research (GMR) recording chambers in order to investigate the interactions among large cellular populations within the central thalamus, the prefrontal cortex and more broadly across the cerebral hemispheres while the animal performed a set of behavioral tasks. This approach mirrors aspects of the clinical setting and results may guide ongoing clinical interventions. Broadband neural activity and behavioral signals were acquired with a TDT RZ2 system and the data and results were analyzed using Chronux (chronux.org) and in-house software routines.



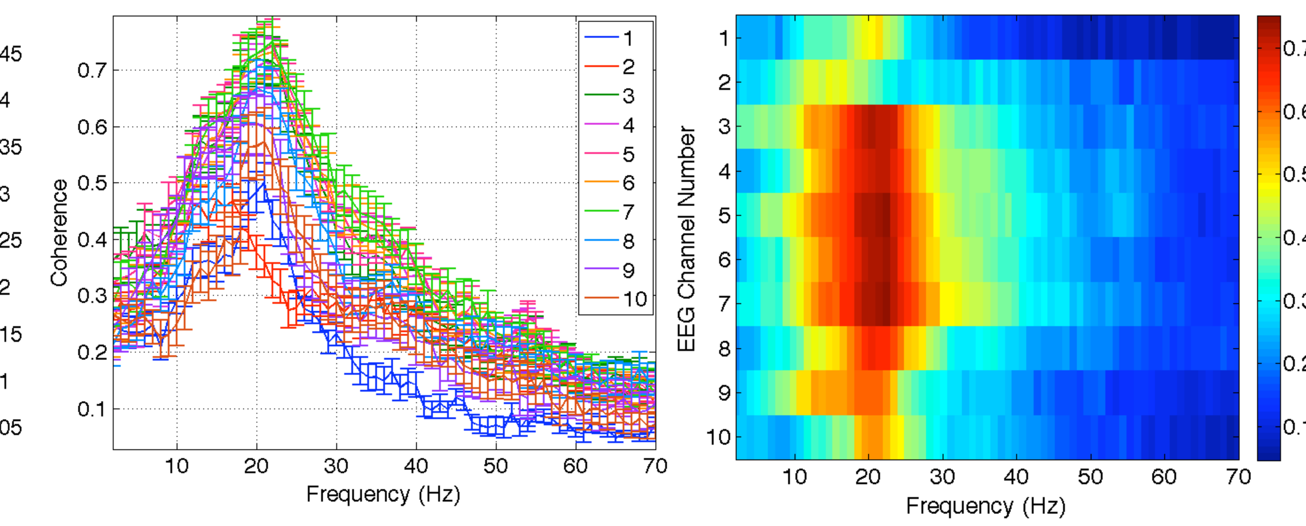
Above: CT image of the second animal implanted with four GMR recording chambers, two over the arcuate sulci and two centered and angled for bilateral access to the central thalami. A set of 10 EEG electrodes (BioPac Systems Inc.) were fixed to Ti bone screws (Salvin Dental) embedded within the acrylic implant. The system was designed to provide a simultaneous macroscopic (EEG), mesoscopic (LFP), and microscopic (SUA, MUA) portrait of the ongoing evolution of neural activity within the thalamocortical circuits of interest throughout the behavioral performance of the animal.



Above: Broadband neural activity recorded in the central thalamus (CT) and simultaneous recordings from the 10 EEG channels while the animal performed a sustained attention trial. The color code of the EEG channels is conserved in the CT image (*left*) and the average coherence plots displayed below. The vertical **red** and **green** bars indicate the delay period and the vertical **blue** bar indicates the bar release. Prominent beta (20-30Hz) coherence among the EEG channels is marked by the **horizontal bars**. Large amplitude excursions observed within EEG channels 4, 5, 6 and 7 correspond to saccade evoked potentials.

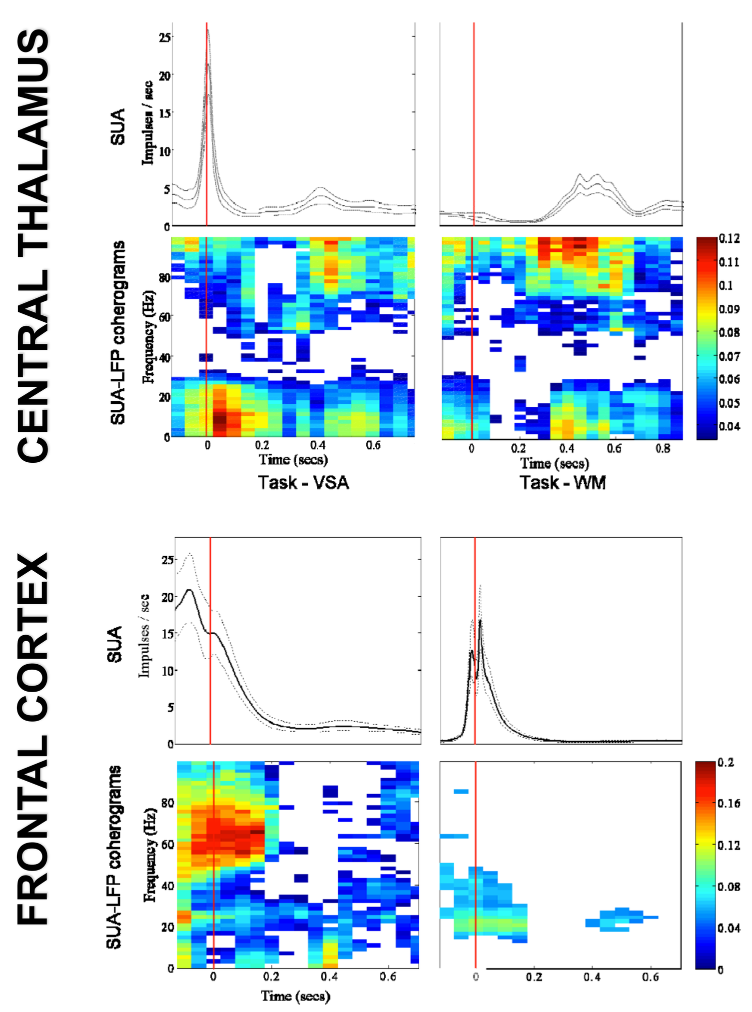


Left: Average coherence (120 sustained attention trials) between the local field potential recorded in left central thalamus and the right frontal EEG channel 7. **Right:** Average coherence (195 sustained attention trials) between the local field potential recorded in right central thalamus and the left temporal EEG channel 2. The colorbar represents the coherence, from 0 to 1. The vertical red and green bars indicate the start and average end points of the delay periods. Note the prominent beta (20-30Hz) coherence during the delay period and the significant shift in coherency, from beta-alpha-beta for a different electrode.

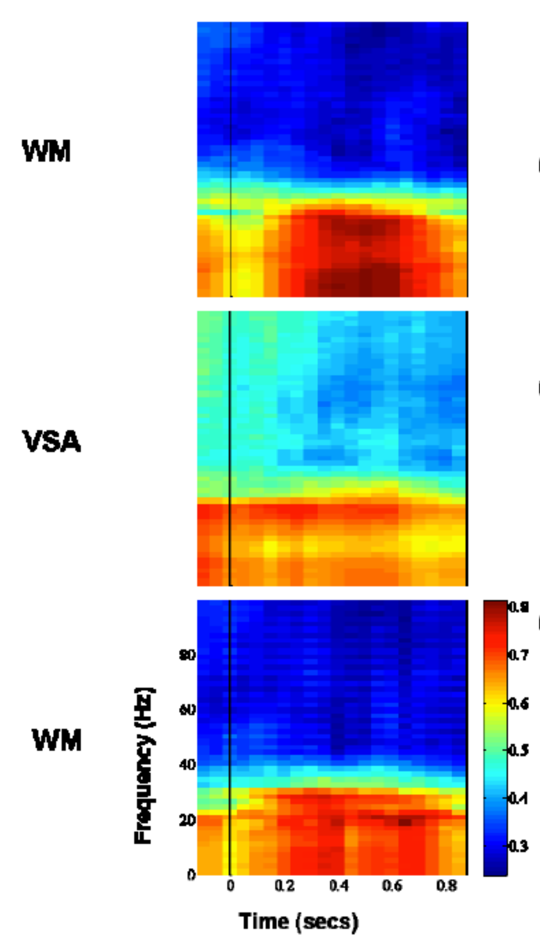


Left: Mean +/- SE coherence between the local field potential within the central thalamus and the 10 EEG channels. The data above includes 1670 sustained attention trials and including all 15 thalamic recording sessions and locations. The 2-D histogram **(Right)** illustrates the greater power and broader range of significant frequencies within the 5 frontal EEG channels (**3-7**) consistent with the known reciprocal connectivity between the frontal cortex and central thalamus and their graded functional interaction during a task known to engage these structures. The colorbar represents the coherence, from 0 to 1.

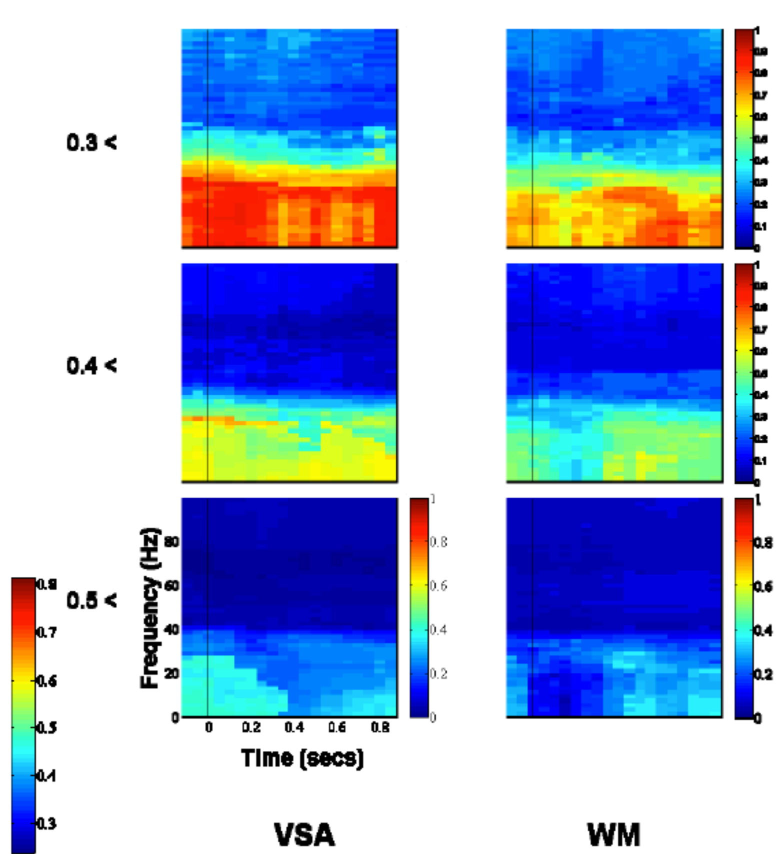
RESULTS: SINGLE UNIT AND LFP ACTIVITY



Upper Panel: Task dependent coherence in a central thalamic spike-LFP coherogram in both the visual sustained attention (VSA) and working memory (WM) tasks. Top panels: Firing rate modulations. Bottom panels: Corresponding spike-LFP coherograms. The red vertical lines represent the start of delay period. **Lower Panel:** Task dependent coherency in a frontal cortex spike-LFP coherogram: Colorbar sets the coherency.



Task dependent coherency between the frontal LFP and central thalamic LFP. The black vertical line represents the start of delay period. During the recording session, the animal switched between working memory and sustained attention tasks.



Summary distribution of thresholded coherency between local field potentials recorded in the frontal cortex and central thalamus. VSA task(n=53) and the WM task (n=49). The black line indicates the start of delay period. The colorbar denotes the fraction of recording sites.

SUMMARY & CONCLUSIONS

- **Neurons recorded within the frontal cortex and central thalamus exhibit a variety of response profiles during both tasks, *see poster 201.12*.**
- **Significant coherence in the upper gamma (60-100Hz) and beta (15-30Hz) bands were observed between single units and local field potentials recorded within multiple frontal and central thalamic locations. Significant frontal LFP and central thalamic LFP coherence from DC-25Hz was observed for a large percentage of recordings and exhibited task dependence.**
- **We observe consistent and significant thalamocortical interactions, based on LFP/EEG coherency, most prominently within the beta band (20-30Hz), but not exclusively, as other frequency bands, including alpha and gamma, also exhibited significant coherency associated with the behavioral task.**
- **Thalamocortical coherency was most pronounced within the frontal cortex, consistent with the known anatomy and physiological role of the central thalamus, as a rostral extension of the midbrain reticular formation and in the modulation of global forebrain arousal and facilitation of executive function.**

References:

Schiff, N.D. and Purpura, K.P. (2002) Towards a neurophysiological basis for cognitive neuromodulation through deep brain stimulation. Thalamus Related Systems 2, 55–69.

Schiff, N.D. et al. (2007) Behavioral improvements with thalamic stimulation after severe traumatic brain injury. Nature 448, 600–603.

Shaw S.A. (2010) Joint and independent contributions of the frontal cortex and central thalamus to executive function. PhD dissertation.

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