Structured thalamocortical dynamics in monkeys during loss and recovery of consciousness

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Introduction

- Anesthesia is a reversible state of unconsciousness characterized by analgesia, amnesia, unresponsiveness, and immobility.
- Despite anesthetic agents and their effects being fairly well understood at a molecular level, a systems-level description is largely lacking. The present work examines propofol, which is widely used in human clinical settings and has relatively simple molecular targets.
- Propofol is a GABAa agonist, and it primarily acts to lengthen the time decay constants on IPSPs (Kitamura et al., 2002).
- We utilized a non-human primate model of general anesthesia to investigate how various cortical and subcortical networks mediate the transition into and out of propofol-induced unconsciousness.

Methods

- Simultaneously recorded spiking and LFP activity from chronically implanted Utah arrays in ventrolateral PFC (vlPFC), frontal eye fields (FEF), posterior parietal cortex (PPC), and superior temporal gyrus (STG).
- Bilateral laminar thalamic electrodes for recording LFP activity were implanted chronically, targeting the mediodorsal (MD) and intralaminar thalamic nuclei.
- Recording sessions consisted of propofol being delivered intravenously for one hour.

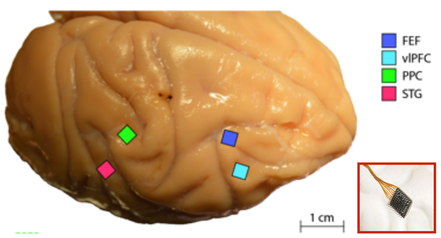


Fig 1. Cortical placement of Utah arrays, targeting the fronto-parietal network, which has previously been implicated in various executive function tasks.

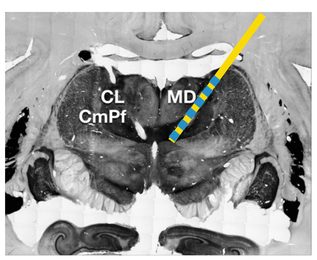
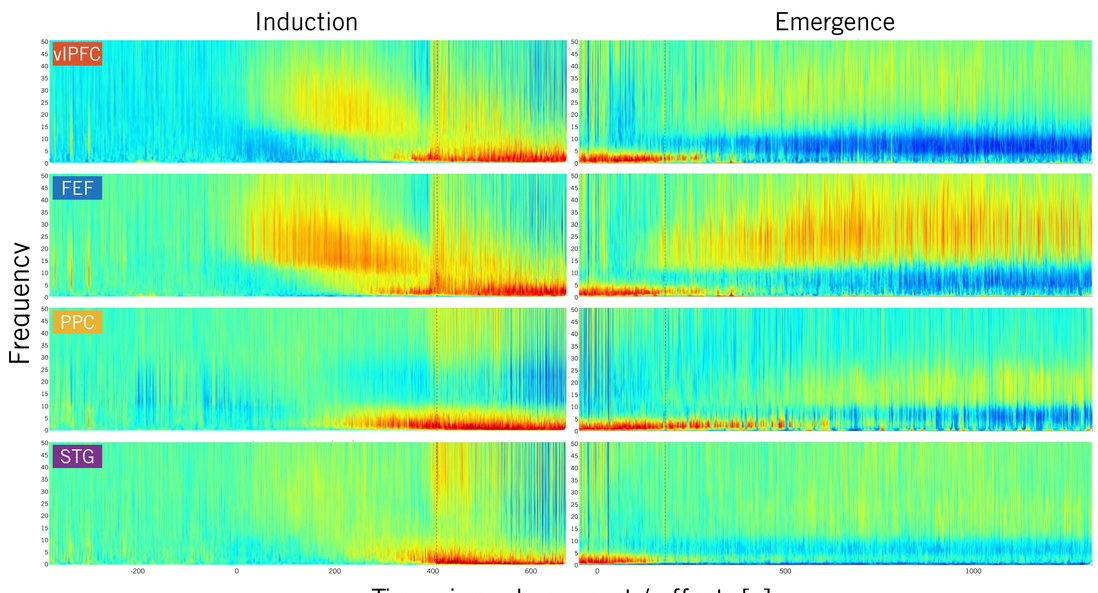


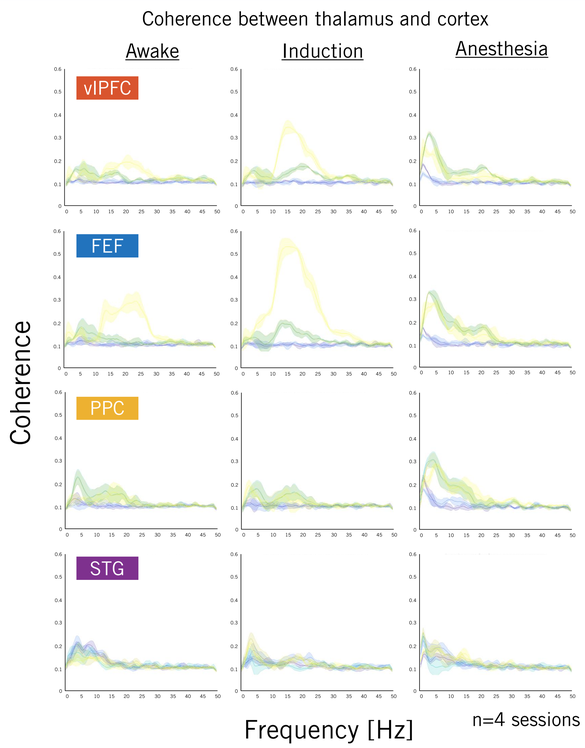
Fig 2. Coronal cross-section showing targeted thalamic nuclei, including the mediodorsal (MD) thalamus, which is highly connected with PFC, and the intralaminar nuclei (centrolateral, CL; centromedian, Cm; parafascicular, Pf), which diffusely innervate superficial cortex.

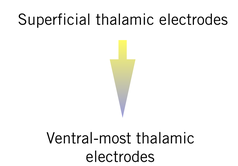
Loss of and recovery of consciousness carry different spectral signatures



- Frontal regions are the first to be affected, reliably exhibiting a strong beta oscillation between approximately 10 - 40 Hz immediately prior to loss of consciousness (LOC). This activity, often termed paradoxical excitation, has been thought to be a coherent oscillation between frontal cortex and thalamus.
- Induction shows widespread cortical delta oscillations (1.5 - 4 Hz) which transition into a slow (<1 Hz) rhythm. This slow oscillation is a well-known signature of GABA-ergic anesthetics, and is primarily generated cortically.
- FEF and PPC seem to be the most sensitive to the anesthetic, taking longer than other regions to return back to baseline.

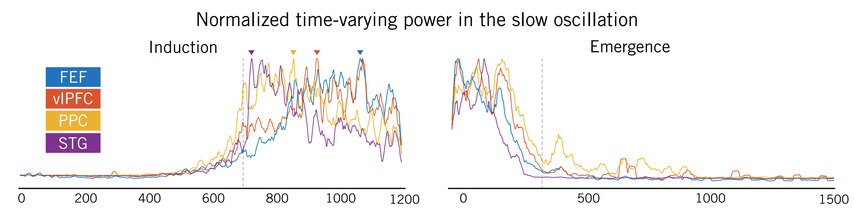
Beta coherence between MD thalamus and PFC is lost during anesthesia



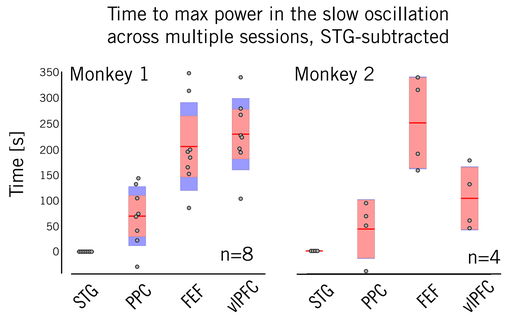


- Resting wakefulness is characterized by a coherent beta rhythm between MD thalamus and frontal cortex.
- This coherence is amplified during paradoxical excitation prior to LOC and lost during stable anesthesia, suggesting a functional disconnection between thalamus and cortex during unconsciousness.
- The cortical slow oscillation is largely discoherent from thalamus, supporting the idea that it is cortically-generated and cortically-maintained.

Slow oscillations come online in a stereotyped posterior-anterior ordering during induction



- The anesthetic slow oscillation reaches maximum power in posterior regions before anterior regions, during LOC. STG is typically the first to reach max power, and the first to lose the slow oscillation.
- Slow oscillation power returns to baseline in PPC last.



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