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The basal forebrain activity and its contribution to default mode network regulation

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The prominent feature of the basal forebrain is the collection of large cortically projecting neurons that sends cholinergic and non-cholinergic inputs to the entire cortical mantle. Despite its broad involvement in attention, memory and other cognitive capacities, how the BF functionally integrates with the rest of the brain is not well understood. This gap in knowledge arises partially due to the anatomical complexity of the basal forebrain. Numerous studies have conducted single and multi unit recordings in order to understand and characterize the functional architecture of this brain region. For instance based on the findings of individual neuronal types and its correlation with cortical EEG, other investigators described the functional aspects of different intermingled populations including cholinergic, GABAergic and glutamatergic neurons.

This thesis is based on three studies, which aimed to study functional, and behavioral correlates of basal forebrain activity during different states of behavior. In the first two studies we employed the recording of Local field potentials to characterize the localized population level activity of Basal Forebrain and its functional connectivity to its cortical targets such as Visual Cortex (VC) and Anterior Cingulate Cortex (ACC) to understand the systems level functions of the basal forebrain structure in rats. The third study was aimed to understand the exploratory behavior in tree shrew, a small diurnal animal and a close relative of primates in place recognition setting.

We observed pronounced BF gamma (30-80Hz) activity particularly during wake, and to a lesser extent during SWS and REM. During wakefulness, this BF gamma activity exerted a directional influence on VC that was associated with cortical excitation. During SWS but not REM, there was also a robust directional gamma band influence of BF on VC. In this study we reported novel aspects of endogenous BF LFP oscillations and their relationship to cortical LFP signals during sleep and wakefulness.

Having found a profound gamma activity in the BF during wake state while they are in the home cage, we therefore hypothesized that this might be functionally coupled to the Default Mode Network (DMN). We compared BF gamma power in the BF between arena exploration as task condition and home cage as resting state (Default mode) condition. We found functional aspects of the population of BF neurons that are activated during DMN-associated behavioral state, giving rise to pronounced gamma oscillations and they up-regulate cortical gamma oscillations in ACC. The gamma was deactivated during arena exploration task. These findings offer substantial evidence of BF as a regulator of default mode network.

The novel location memory task studied here in tree shrews assessed the ability of animals to form accurate memories of a spatial configuration. After habituation, tree shrews exhibited enhanced exploration when confronted with a novel configuration. During the test session, we also observed an exploration of the location, which had previously been occupied by the displaced object, an effect termed empty quadrant. Our behavioral findings suggest multiple stages of spatial memory formation in tree shrews that are associated with various forms of behavioral responses to novelty. Reduced novelty preference has been linked to major depressive disorder in human patients. We anticipate that the study of the neural circuits of novelty preference and their malfunction during depression may have implications for understanding or treating depression in humans.

This thesis provides novel discovery and insights of the function of Basal Forebrain and its role in regulation of Default Mode Network. The behavioral experiment with tree shrew will serve as a starting point for exploring the electrophysiology of the default mode network in these species since they are one of the closest relatives to primates.

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