THETA ACTIVITY IN THE MONKEY HIPPOCAMPUS DURING VIRTUAL NAVIGATION

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**Highlights**
- We trained a rhesus macaque to navigate an immersive 3D virtual environment to perform a basic foraging task.
- Recordings in the hippocampus revealed prominent theta-band (4-10 Hz) oscillatory activity that was closely associated with movement.
- These oscillations were specifically correlated with eye movements, such that the highest amplitude oscillations were seen during regular saccadic activity, as such when the monkey was scanning the environment for targets. Furthermore, there was a direct correlation between saccadic frequency and theta frequency.
- We also observed significant cross-frequency coupling between theta-band (3-12 Hz) phase and amplitude within multiple frequency bands in the beta to high gamma (20-150 Hz) range.

**Introduction**
- Theta and lower frequency oscillations are widely observed in the CA1 subfield of the dorsal hippocampus in rodents during spatial navigation.
- Theta oscillations are also observed in the human hippocampus during navigation in a virtual environment, whereas they are modulated by movement (Ekstrom et al., 2005) as well as viewing behavior (Watsalo et al., 2011).
- Our lab has previously shown evidence of 8-10 Hz oscillatory activity in the monkey hippocampus during free-viewing (Jutras et al., 2013), suggesting a role for low frequency oscillations in the processing of visual information relevant to the environment.

**Virtual Foraging Task**
- The monkey is trained to use a joystick mounted inside the primarix chair to navigate through a virtual environment, obtaining reward for navigating to specific targets in the environment, i.e., bananas. The virtual environment is rendered using Panda3d (Gibson et al., 2012) as well as additional programming in Panda3D. The joystick's interaction with the virtual environment is recorded by Cygolite.
- Each trial begins with the placement of ten bananas at random locations in a virtual arena. The monkey navigates to each banana, upon reaching the target, he receives a reward (food kibbles) and the banana disappears. After obtaining all ten rewards, a new trial begins with the appearance of new items in ten randomly new locations.

**Hippocampal Recordings**
- Local field potentials (LFPs) were recorded from single electrodes (PAC Inc., Bowdoin, ME) in the hippocampus of a rhesus macaque. Eye movements were monitored non-invasively using a Passive EYE-tracking system (EGBA, Washington, MA).
- Left: positive, green line of recordings yielding high amplitude low-frequency (theta) oscillations during virtual foraging tasks.
- Right: example hippocampal LFP traces from a single electrode channel taken during foraging task.
- Below, right: histograms depicting total duration and interburst interval for the same example LFPs.

**Example LFPs with prominent theta (-4 Hz)**
- Right: example hippocampal LFP traces from a single electrode channel taken during foraging task.
- Below, left: autocorrelation taken from example LFP during slow oscillations ("slow") (Cajal et al., 2001) of theta (3.5-5.5 Hz).
- Below, right: histograms depicting total duration and interburst interval for the same example LFPs.

**Behavioral categorization: Exploring vs. Acquiring**
- The monkey alternates between two general movement types: "exploring" (i.e., scanning the environment to select a target) and "acquiring" (i.e., initiating and maintaining a forward trajectory of the avatar in order to collide with a target). During both behaviors, the monkey exhibits a theta-like eye movements to scan the environment, obtain information about target locations and other visual cues (i.e., scene boundaries and landmarks).
- Right: histograms depicting the distribution of instantaneous saccadic rates for the two behavioral categories in an example session.

**Instantaneous theta frequency increases with saccadic rate**
- Above: LFP power for an example hippocampal LFP calculated across all timepoints (green) and normalized for exploratory movements (blue).
- Right: instantaneous saccadic rates and time-locked waveform values were calculated for each timepoint in the recording session for the example LFP. The waveform was time-locked across all timepoints in each bin (i.e., are defined on the appearance of one stimulus). The line in each panel represents the frequency of the instantaneous LFP power in each bin (i.e., the instantaneous theta frequency).
- Bottom: average LFP power across all timepoints in the recording session.
- Middle: saccade-triggered averaged LFPs during exploratory movements only.

**Hippocampal LFPs exhibit cross-frequency phase-amplitude coupling during virtual navigation**
- Example hippocampal LFPs exhibit cross-frequency phase-amplitude coupling during virtual navigation.
- Above: Correlation Index (derived using methods described in Canady et al., 2009) for an example hippocampal LFP for four timepoints in the recording session.
- Right: cross-frequency coupling derived using generalized linear model (GLM-IFC), based on methodology in Kramer and Eden, 2013.
- Conclusions for GLM-ICF are depicted with dashed red lines.
- Top: GLM-ICF between 3-12 Hz phase and 90-140 Hz amplitude.
- Middle: GLM-ICF between 3-12 Hz phase and 50-70 Hz amplitude.
- Bottom: GLM-ICF between 3-12 Hz phase and 20-40 Hz amplitude.

**Conclusions**
- Strong theta-band (4-10 Hz) activity in the monkey hippocampus is observed during a task of virtual navigation.
- These data provide evidence for a high degree of association between theta-band oscillations in the monkey hippocampus and saccadic movements during multiple behavioral phases of a virtual navigation task, suggesting a close relationship between hippocampal network activity and the role of sensory input.
- The presence of cross-frequency oscillatory interactions provides evidence for a hierarchical organization of hippocampal activity in the primates hippocampus, similar to that seen in the rodent (Cajal et al., 2013), and suggests that neuronal coding may be highly modulated by these oscillations associated with saccadic oscillations.
- The neural network architecture leads to a high degree of manipulation, allowing for more directed navigation and memory processing.
- Additional recordings are needed to assess the spatial distribution of this activity in the primatized hippocampus.

**References**

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