Title: **Neural representation of overlapping trajectories and reward acquisitions in the monkey hippocampus**
サル海馬体における重複した移動軌跡および報酬獲得の再現機構

Rafael Bretas Vieira

System Emotional Science, Graduate School of Medicine and Pharmaceutical University, University of Toyama

Objective:

The ability to distinguish overlapping items in time and space is critical to episodic memory. The hippocampal formation (HF) has been implicated in human episodic memory and spatial navigation. Neurophysiological studies have reported that HF place cells code a specific place in the environment that the animals or human subjects navigate. Recent rodent studies have reported that when navigating overlapping trajectories in the different routes place cell activity in the same overlapping trajectories were remapped according to different goal locations in different routes. However, route-dependent neuronal activity in non-human primates remains unknown. Neuronal responses to rewards is another important factor of episodic memory. Recent human fMRI studies reported that overlapping stimuli associated with high reward was less susceptible to interference, which was associated with increased HF activity. However, it is also unknown how HF neurons disambiguate reward delivery in overlapping situations.

This study aims to elucidate the neural mechanisms of disambiguation in episodic memory. In the present study, we recorded monkey HF neurons during performance of three virtual navigation tasks in which a monkey alternately navigated two different routes that included overlapping trajectories (common central path) and acquired rewards in the same locations in overlapping trajectories.

Methods:

Training

Two male adult monkeys were used. The animals were trained to perform three virtual navigation (VN) tasks, where they were required to navigate in a 3D environment by manipulating the joystick. For the tasks, a large 3D open-field space with a 180-m diameter was created. The monkeys could move only inside a limited 24-m diameter space located in the center of the open-field, surrounded by a wall (mobility area). The three VN tasks had different arrangements of the extra-maze distal cues that were located outside the mobility area. The mobility area contained five reward areas (with a diameter of 2.8 m) that were placed in the center and apex of a diamond shape. In the tasks, the animal was required to track the reward areas in a specific order in a figure-8-shaped pathway; the track was navigable by two different routes with a common central stem.

Recording

The subject's head was painlessly fixed in a stereotaxic frame on a restraining chair, and a quartz-insulated platinum tetrode was stereotaxically inserted into the HF. A CCD camera recorded eye movements. Data on the analog signals of neuronal activities, triggers for the juice reward, X-Y coordinates of the monkey in the virtual space, joystick positions, and eye position were digitized and stored on a computer.

Data analysis

For the analysis of place fields where neuronal activity increased, the mobility area in the VN tasks was divided into 30 x 30 pixel grids. Place fields were defined as pixels with over twice the task average firing rate of the neuron surrounded by at least 8 adjacent pixels with over 1.5 times the average firing rate. To analyze effects of different routes on place-related activity in the same trajectory, neural activity in the central common path was analyzed using a two-way ANOVA with zone and route as factors. Reward response was analyzed by comparing firing rates in the 2 s around reward delivery. Furthermore, the mean correlation among population vectors consisting of ensemble pre-reward neuronal activity in the overlapping trajectories was compared to that in the non-overlapping trajectories.

Population HF neuronal activity was examined by Bayesian analyses in order to determine whether ensemble neuronal activity could predict routes, locations, and reward delivery in the overlapping trajectories.

Localization of recording sites

Before recording, 3D MRI scans of the monkey head with a tungsten marker stereotaxically inserted above the recording sites were performed. Three-dimensional stereotaxic coordinates of the recording sites were determined in reference to the marker in the 3D MRI.

Results:

The 106 neurons were recorded from the HF. Of these, 57 neurons displayed place fields in at least one of the tasks (place-related neurons). The 18 neurons displayed significant route-dependent activity in the overlapping path. Bayesian decoding of the route-dependent neurons indicated that ensemble activity of these neurons significantly predicted routes and locations in the central path.

The 75 neurons showed neural correlates to reward delivery (reward-related neurons), whereas 56 of these neurons showed route-dependent reward-related activity in the overlapping trajectories. Bayesian decoding of the reward-related neurons indicated that ensemble activity of reward-related neurons represented routes and reward delivery in the overlapping trajectories. Furthermore, the ensemble activity patterns of the reward-related neurons more distinctly represented overlapping trajectories than non-overlapping trajectories.

Discussion:

The importance of the present results is threefold. First, consistent with rodent studies, the current study provided evidence that the activity of primate HF neurons is also route-dependent. Furthermore, decoding analyses suggest that the ensemble activity of these neurons carries information of route and the monkey's location in the common central path. The present findings extend previous findings in rodents by demonstrating the disambiguation of overlapping trajectories in non-human primates.

Second, 56 reward-related activity neurons showed route-dependent activity, and decoding analyses suggest that the ensemble activity of these neurons also carries information on route and reward delivery (outcome). The present results extend the role of the HF to disambiguation of reward outcome, consistent with the role the HF in episodic memory.

Third, the overlapping trajectories to the same reward areas were more distinctly represented than the non-overlapping trajectories to the non-overlapping reward areas, suggesting that overlapping items are better represented by repeated retrieval with competitive learning, consistent with recent computational studies on neural differentiation rather than those on orthogonalization.