Researchers probe link between theta rhythm, ability of animals to track location

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In a paper to be published today in the journal *Science*, a team of Boston University researchers under the direction of Michael Hasselmo, professor of psychology and director of Boston University's Computational Neurophysiology Laboratory, and Mark Brandon, a recent graduate of the Graduate Program for Neuroscience at Boston University, present findings that support the hypothesis that spatial coding by grid cells requires theta rhythm oscillations, and dissociates the mechanisms underlying the generation of entorhinal grid cell periodicity and head-direction selectivity.

Theta Rhythm - The hippocampal theta rhythm is an oscillation that can be observed in EEG recordings from the hippocampus and other brain structures in numerous species of mammals including rodents, rabbits, dogs, cats, bats, and marsupials. In rats, the most frequently studied species, theta rhythmicity is easily observed in the hippocampus, but can also be detected in numerous other cortical and subcortical brain structures. Hippocampal theta, with a frequency range of 6-10 Hz, appears when a rat is engaged in active motor behavior such as walking or exploratory sniffing, and also during REM sleep. Models have proposed a role for theta rhythm in spatial navigation and episodic memory function.

Grid cells and Self-Localization - Early studies on navigation revealed that most animals have an exceptional ability to keep track of their location, even in complete darkness. Research now suggests that this ability may involve computations in the entorhinal cortex. Single cell recordings from the entorhinal cortex during navigation have revealed a specific type of neuron that is able to track a rat's position. These cells have been termed 'grid cells' based on the fact that they fire when the rat is at regularly spaced locations in the environment, forming a hexagonal 'grid' in the environment. These cells might allow animals to keep track of their current location.

Computational neuroscientists, including Michael Hasselmo, have demonstrated how these grid cells could generate this regular spatial pattern based on theta oscillations in models. The models proposed that theta oscillations in the entorhinal cortex provide a baseline clocking mechanism. The model requires input from other cells that respond based on the current head direction of the animal or its current running speed. In the model, running speed and head direction inputs modulate the frequency of other oscillators, such that when these oscillations interact to influence the firing of a grid cell, they cause the grid cell to fire systematically dependent on the location of the animal.

Brandon et al., support this theoretical model by demonstrating that grid cells in the entorhinal cortex need the theta rhythm as a clock to help keep track of the animal's location. In the article, "Reduction of Theta Rhythm Dissociates Grid Cell Spatial Periodicity from Directional Tuning," Brandon et al., report that grid cells recorded in the medial entorhinal cortex of freely moving rats exhibit firing at regular spatial locations and temporal modulation with theta rhythm oscillations (4 to 11 hertz). The researchers analyzed grid cell spatial coding during reduction of network theta rhythm oscillations caused by inactivation of the medial septum (MS) with the drug muscimol. During MS inactivation, grid cells lost their spatial periodicity, whereas head-direction cells maintained their direction signal. Conjunctive grid - by - head-direction cells lost grid cell spatial periodicity but retained head-direction specificity. All cells showed reduced rhythmicity in autocorrelations and cross-correlations.

This finding provides experimental support for the role of oscillations in coding spatial location by neural circuits. Consistent with this data, other laboratories have shown that the same manipulation of MS that reduces theta rhythm can severely disrupt the behavioral ability of a rat to remember the location of prior events. The alteration of oscillatory dynamics in the entorhinal cortex could underlie impairments in the ability to remember the spatial location of events in an episode. For example, drugs that cause amnesia may do so through an influence on theta rhythm oscillations, and a change in oscillations could contribute to the influence of Alzheimer's disease on the formation of new memories.

More information: "Reduction of Theta Rhythm Dissociates Grid Cell Spatial Periodicity from Directional Tuning," *Science*, in press

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