Abstract:

In vivo rasts show two very different EEG patterns in the hippocampus: theta waves or sharp waves (SPWs). The hippocampal theta waves appear when the animal is exploring. During immobility (e.g., eating or grooming), the prominent theta waves disappear and the SPWs occur. In a CA3 hippocampal network model, we analyze how the presence or the absence of external interactions with the hippocampus, and their known modulatory and phasic effects of these inputs can influence the dynamics of this CA3 network for the occurrence of either theta waves or SPWs.

Summary:

The hippocampal formation displays two distinct EEG phenomena, which are related to different behavioral states: theta rhythm and sharp waves (SPWs). These two patterns rely intimately to interactions among different regions of the hippocampal formation and the projections between the septal area and the hippocampus. The theta wave can be generated by different mechanisms, but SPWs seem to result from the recurrent network of CA3.

The major cortical input to the CA3 hippocampal region is provided by the entorhinal cortex (EC) via the perforant path. This projection is essentially glutamatergic.

The medial septum and the diagonal band of Broca (MS-DB) projects throughout the hippocampus, but primarily in region CA3 and the dentate gyrus. This input includes both cholinergic and GABAergic fibers. In fact, most of the cholinergic input to the hippocampus comes from the the MS-DB. This projection is very specific, and while cholinergic terminations are to all type of hippocampal cells, GABAergic terminations innervate only GABAergic interneurons [4]. The cholinergic input induces a tonic level of depolarization in pyramidal cells and interneurons due to the effect on muscarinic and nicotinic receptors. At the network level, acetylcholine (ACh) reduces the strength of the excitatory synaptic connections and of the inhibitory synaptic connections. In contrast, the GABAergic septal input causes a phasic disinhibition of the hippocampal pyramidal cells. This phasic input seems to provide the theta rhythm in the hippocampus via a inhibition-disinhibition mechanism of the pyramidal cells [5]. These two inputs to regions CA3 create current generators for the hippocmapal theta, that together with the properties of the CA3 network itself need to be integrated to generate the prominent theta rhythm seen when the animal is carrying on some exploratory activity.

SPWs appear in the absence of theta rhythm, i.e., during slow wave sleep and related awake immobility behaviors such as sitting still, eating, or drinking [1]. The emergence of the SPWs is correlated with the suppression of cortical inputs to the hippocampus. By definition, SPWs are irregular, slow (40-100 msec), large amplitude (1-3 mV) field potentials seen in the stratum radiatum of CA1. Their incidence ranges from 0.02 to 3/s. They result from a population discharge of CA3, which, in fact, provides the major input to CA1. Even though technically SPWs are in CA1, we will also refer to the population discharge in CA3 as SPW. They have been hypothesized to be the output wave form used to transfer memories from the hippocampus to the neocortex during the consolidation process [2].

Using a CA3 hippocampal network model constructed from Pinsky-Rinzel pyramidal cells and Wang-Buzsaki interneurons, we have analyzed how the modulatory input from medial septum could regulate the appearance of theta and SPW during different behavioral states. In particular, we evaluate potential mechanisms for the onset of SPW, addressing both the broad distribution of activity and the variability of SPW appearance. We compare theoretical mechanisms for SPW onset, including the synchronous firing of spontaneously active pyramidal cells, and the changes in spontaneous firing of inhibitory interneurons which allow onset of excitatory feedback. Both mechanisms could contribute to the onset of SPW, but the change in interneuron activity appears important for replicating firing activity of interneurons [3] and for obtaining greater variability in SPW onset times.

References:

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