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Poster presentation

K_A channels suppress cellular responses to fast ripple activity – implications for epilepsy

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Background

During cognitive tasks, synchrony of neural activity varies and is correlated with performance. There may however be an upper limit to the level of normal synchronicity and epileptogenic activity is characterized by excess spiking at high synchronicity. Very high field oscillations (fast ripples), in the range of 250–600 Hz, have been recorded from patients with mesial temporal lobe epilepsy [1]. Furthermore, in epilepsy an A-type potassium channel (K_A) has been implicated. More specifically, a mutation in a K_A gene was found in a temporal lobe epilepsy patient [2] and a highly selective blocker of K_A induced seizures [3]. In previous work we have showed that K_A can suppress synchronized synaptic input to a neuron while minimally suppressing semi-synchronous input. As high frequency implies high synchronicity we set out to investigate if K_A could suppress the cellular response from fast ripple activity.

Methods

We used a cell model of a hippocampal CA1 pyramidal neuron based on [4]. It is a detailed compartment model with Na, K_{dr} and K_A-type currents of Hodgkin-Huxley type. The high frequency of fast ripples has been hypothesis to occur from combining two ripples with lower frequency [5]. According to [6], only 11% of the neurons participating in a ripple are activated at each ripple. Due to these two factors we used 60 Hz as the frequency of individual neurons. In a fast ripple, the 50 synaptic inputs were activated simultaneously and in control/desynchronized the input were evenly distributed in time.

Results

K_A channels suppress cellular responses to fast ripple activity. The left figures of Figure 1 represent the simulation K_A present and the right with K_A absent. Top figures represent fast ripple activity and bottom figures the case when the input is control/desynchronized. Note that when K_A is present there is no spike activity from fast ripple input even though it is present in control/desynchronized.

Discussion

Our model shows that K_A can prevent the cell form getting activated by fast ripple activity. Understanding how K_A can reduce synchronized and fast ripple activity can provide insight in how epileptic drug work or suggests new drugs targeting K_A.

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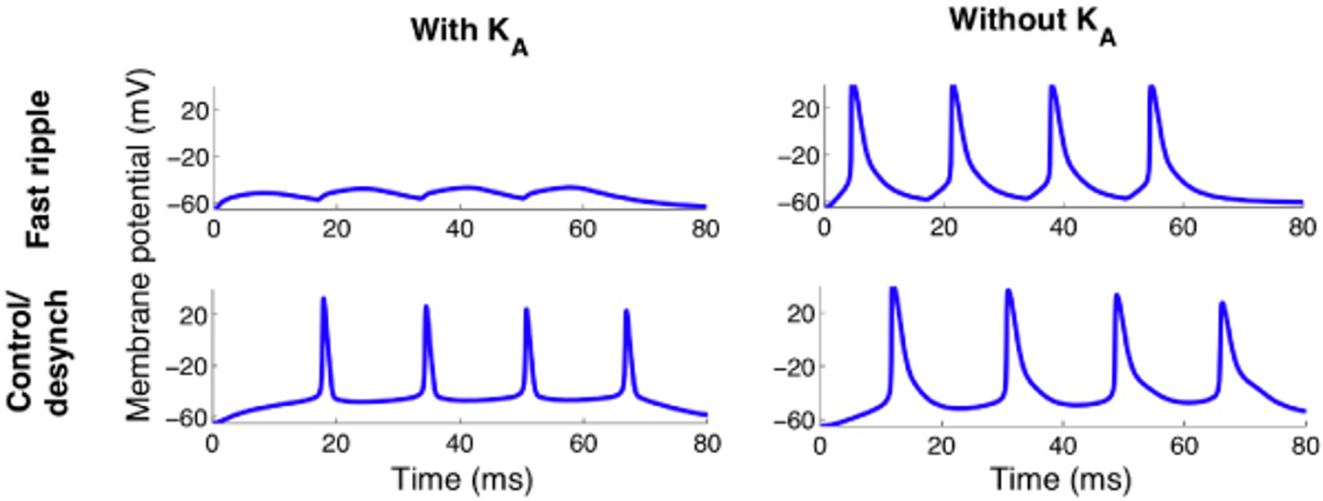

Figure 1

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