

Poster presentation

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5HT neuromodulation of hippocampal pyramidal cells: effects of increased I_h on cell excitability

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Background

During waking, serotonin (5HT) levels in the hippocampus are high but during REM sleep hippocampal 5HT levels drop so low that it is virtually absent. We investigate how differing levels of 5HT affect the properties of hippocampal pyramidal cells through analysis of biophysical models of CA1 pyramidal neurons. Studies in the hippocampal slice show that 5HT increases I_h , the hyperpolarization-activated current, by affecting its maximal conductance and its half-activation voltage [1]. In hippocampal pyramidal cells, I_h has been shown to have a normalizing influence on the temporal summation of dendritic synaptic inputs [2] that has been analyzed in modeling studies where I_h was the only active conductance in the model cell membrane [3-5]. Recently, dopaminergic neuromodulation of I_h has been shown to influence excitability of pyramidal cells in the entorhinal cortex [6]. While the action of dopamine on the kinetics of I_h was not determined in these cells, dopamine had the general effect of increasing I_h which resulted in a decrease of excitability. We consider how the specific 5HT modulation of I_h affects cell excitability in model hippocampal pyramidal neurons. Our analysis pays particular attention to rectifying the well-known depolarizing effects of I_h on resting potential with its inhibitory effect on excitability.

Methods

To concentrate on the interaction of I_h with spike generating currents, we constructed a single compartment model neuron that contains biophysically accurate Na^+ , K^+ -

delayed rectifier and h currents with parameters set to replicate CA1 pyramidal cell subthreshold and firing behaviors [4]. We also constructed a simplified single compartment model that includes I_h and the Morris-Lecar model equations for spike generating currents in order to analyze I_h effects on cell firing using phase plane techniques. In these models, we simulate the changes to I_h that the slice studies indicate occur when 5HT is present.

Results

Preliminary simulations using both the biophysical and simplified models show that neuronal excitability decreases with increased I_h . However, there is a voltage-dependence of the effects of increased I_h : if cell voltage is held around -70 mV and a current pulse is given, excitability decreases but if cell voltage is held around -50 mV when the pulse is given, excitability increases. We also investigate how the changes to I_h due to variations in serotonin level affect the cell response to a stimulus.

Conclusion

While the rectifying effects of I_h on resting potential are well understood, we concentrate on understanding the interaction of I_h with spiking currents and its nonintuitive effects on cell excitability. 5HT modulation of I_h suggests that excitability and, hence, synaptic processing in hippocampal pyramidal cells may change in different behavioral states such as waking and REM sleep. Understanding this change in neuronal processing during waking hippocampal activity which is involved in memory formation

and during reactivation firing in REM sleep may lead to insight into the role of REM sleep in learning and memory.

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