Neuroscience 2003 Abstract

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Abstract Title:	Computational analysis of the effects of chronic stress on hippocampal excitability: from neurons to network.
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Chronic stress induces dendritic atrophy in hippocampal CA3 pyramidal neurons and is believed to be one of the key factors contributing to the consequent deficits in hippocampal function. In the present study, we perform computational simulations using NEURON to analyze the effects of stress-induced dendritic remodeling on hippocampal excitability at both single-cell and network levels. To this end, we first developed a statistical algorithm that systematically pruned dendritic arbors of three-dimensional CA3b pyramidal cell reconstructions (from the Duke-Southampton archive) to replicate experimental data on stress-induced debranching and atrophy (Vyas et al., J.Neurosci., 22(15), 2002). Next, we impose passive and active membrane properties on these reconstructions as in (Migliore et al., J.Neurophy., 73(3), 1995). Our simulations indicate that dendritic atrophy leads to: (i) enhanced cell excitability as manifested by increased firing frequencies; (ii) transition from a bursting to regular-spiking pattern; and (iii) differential increase in back-propagating action potential amplitudes along basal and apical dendrites. To study the effects of these single-neuron changes on emergent properties at the population level, we constructed networks with reduced models of pyramidal cells (Pinsky-Rinzel (P-R) model) and interneurons (Wang-Buzsaki Model). The CA3 area, with extensive recurrent connectivity and intrinsically bursting cells, is considered a region with high seizure susceptibility. To analyze the effects of stress on the form and duration of an ictal event, we built on the network model in (Traub et al., Epilepsia, 37(9), 1996) and introduced (i) atrophy (by reducing the size of the dendritic compartment in the P-R cell); and (ii) variations in synaptic currents (Kole et al., Eur.J.Neurosci., 16, 2002). Preliminary results from these simulations suggest that seizure susceptibility of the CA3 region increases with stress.

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