A Computational Model for the Effects of Norepinephrine on a Pyramidal Cell

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Objective. To reproduce the effects of norepinephrine (NE) on the firing characteristics of a cortical pyramidal cell. The long-range goal is to explore the effects of NE on realistic models of cortical networks as a means for understanding the mechanisms surrounding NE-facilitated stroke recovery.

Background. The mechanisms of how NE-facilitated stroke recovery is achieved is unclear; "unmasking" of existing pathways, acceleration of recovery from diaschisis, and enhancement of LTP have all been proposed. Some knowledge of the effects of different drugs (such as NE) at the ion channel level is known. What is unclear, however, is how these local effects translate into the macroscopic phenomena seen clinically. A first step would be to develop a model of a single pyramidal cell that can reproduce the firing pattern changes seen experimentally when NE is applied.

Methods. We used a reduced compartment model of one cell developed by Bush and Sejnowski (*J Neuroscience Methods,* 1993). The model has eight compartments (soma and seven dendrites), and incorporates Hodgkin-Huxley-type conductances, including fast potassium and sodium currents (for generation of action potentials), a high-threshold Ca++ conductance, a Ca-dependent K+ conductance, and a first-order calcium pump. A simulated 300 msec 1 nA constant current pulse was injected into the soma to assay bursting properties and adaptation. The effects of NE were modeled by reducing the conductance of the Ca-dependent K+ channel. All simulations were carried out on a SPARC10 Sun workstation using the program NEURON 3.0 (Hines and Moore, 1994).

Results. Injection of the current pulse resulted in a burst of about six action potentials, with a reduction in the firing frequency as time progressed (adaptation). Addition of NE was simulated by the reduction in the adaptation current. This resulted in an increase of firing to about 8 to 10 spikes in the interval. These results are consistent with those observed by McCormick et al. (*Progress in Brain Research* 1991;88:295).

Conclusion. The simulations were able to reproduce some of the effects of NE on the firing characteristics of a single cell. This is a first step in producing realistic network models for the effects of NE and other neuromodulators on cortical networks.

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