Mechanism of nicotine's learning effects explored

April 4 2007

While nicotine is highly addictive, researchers have also shown the drug to enhance learning and memory—a property that has launched efforts to develop nicotine-like drugs to treat cognitive deficits in Alzheimer's and Parkinson's diseases, schizophrenia, and attention-deficit/hyperactivity disorder.

A key problem in designing such drugs has been that little was known about the detailed mechanism by which nicotine exerts its learning-enhancing effects.

Now, researchers have discovered important details of how nicotine adjusts the signaling properties of neuronal wiring to enhance memory. Such signaling properties include the strength of the connections by which one neuron triggers another. Huibert Mansvelder and colleagues reported their findings in the April 5, 2007, issue of the journal *Neuron*, published by Cell Press.

The researchers made their discoveries by analyzing the electrophysiological properties of neurons in slices of mouse brain, as they treated the slices with nicotine or with drugs that prevent nicotine's action. Specifically, the researchers studied the neurons of the prefrontal cortex, which contain centers for learning and memory.

Researchers had known that nicotine enhances learning by activating receptors for the neurotransmitter acetylcholine. Such neurotransmitters are the chemical signals that one neuron launches at another to trigger a

nerve impulse in the receiving neuron.

In their studies, Mansvelder and colleagues found that by activating acetylcholine receptors, nicotine affects a process called “spike-timing-dependent potentiation” that governs changes in strength of signaling connections among neurons. What’s more, the researchers traced this effect to nicotine’s action on specific kinds of neurons, called GABAergic neurons, in the learning centers. In turn, the effects on GABAergic neurons affected signaling between neurons mediated by the key substance calcium.

The researchers also discovered key details of the mechanisms by which nicotine excites different kinds of “interneurons” in the prefrontal cortex. Interneurons are the way-stations for neuronal impulses, passing neuronal signals from one neuron to another.

Source: Cell Press