Popular Antidepressants Boost Brain Growth

The beneficial effects of a widely used class of antidepressants might be the result of increased nerve-fiber growth in key parts of the brain, according to a Johns Hopkins study being published in the January 2006 issue of the Journal of Neurochemistry.

The study on rats, led by Vassilis E. Koliatsos, M.D., a neuropathologist at the Johns Hopkins University School of Medicine, found that selective serotonin reuptake inhibitors (SSRIs) increase the density of nerve-impulse-carrying axons in the frontal and parietal lobes of the neocortex and part of the limbic brain which control the sense of smell, emotions, motivation, and organs that work reflexively such as the heart, intestines and stomach. “It appears that SSRI antidepressants rewire areas of the brain that are important for thinking and feeling, as well as operating the autonomic nervous system,” said Koliatsos.

Axons are long, filament-shaped extensions of neurons that, together with myelin, are the main constituents of nerves. Axons conduct chemically driven nerve impulses away from the cell body toward a narrow gap known as a synapse. Among the chemicals involved are such monoamines as norepinephrine and serotonin, which, at the synapse, are transferred to another neuron.

Antidepressants, such as Prozac, Zoloft and Paxil, have long been thought to exert their clinical effects by increasing synaptic concentrations of serotonin and norepinephrine, enhancing or stimulating their transference.

“But our findings -- that serotonin reuptake modulators increase the density of nerve synapses, especially in the front part of the brain - may offer a better explanation of why antidepressants are effective and why they take time to work,” according to Koliatsos.

For example, antidepressants increase synaptic monoamines within hours, and the regulatory effects on receptors are complete within a few days, yet clinically meaningful results from antidepressants usually require a two- to four-week delay.

“This disparity between simple pharmacological effects and clinical experience might be due to the time it takes for serotonin axons to grow,” Koliatsos said.

“For the patient, this hypothesis provides more tangible evidence of a real effect in the brain,” he added.

In the Hopkins study, Koliatsos and his team gave either the selective serotonin reuptake inhibitor fluoxetine (Prozac), the selective serotonin reuptake enhancer tianeptine (a drug approved only for human use in France) or the selective norepineprine reuptake inhibitor desipramine, a so-called tricyclic antidepressant, to groups of rats for four weeks and studied anatomical patterns of serotonin stimulation on various parts of the brain. The results showed that fluoxetine and tianeptine, but not desipramine, increased the density of serotonin axons in the frontal and parietal neocortex and certain limbic cortical and subcortical areas.

One possible explanation for this action is the brain-derived growth factor (BDNF). BDNF is regulated by levels of
serotonin and is known to be a prime candidate for causing serotonin axon growth, Koliatsos said.

In general, the relationships between brain serotonin concentrations and BDNF expression are very complex, but previous studies have suggested that both higher (such as caused by serotonin reuptake inhibitors) and lower (such as effected by tianeptine) concentrations of free serotonin might induce BDNF expression in such brain regions as the frontal and parietal cortex.

The researchers caution that since a previous study failed to show a correlation between tianeptine treatment and BDNF levels, further investigation of the complex regulations of BDNF by antidepressants is needed.