Atripla, Sustiva Component Linked to Neuron Damage

September 28, 2012

A byproduct formed during the breakdown of efavirenz—found in Sustiva and Atripla—appears to damage nerve cells, according to new Johns Hopkins University research published online ahead of print by the Journal of Pharmacology and Experimental Therapeutics and summarized in a news announcement. The scientists hypothesize, but did not conduct the studies necessary to prove, that this may contribute to cognitive impairment in people living with HIV.

Efavirenz is known to be very good at controlling the virus and is one of the few that crosses the blood-brain barrier and can target potential reservoirs of virus in the brain. It may also cause a variety of central nervous system-related side effects, such as nightmares and feeling “buzzed” during the first few weeks of treatment. Now it appears as if 8-hydroxyefavirenz, one of the metabolites created when efavirenz is metabolized by the liver, can damage important “dendritic spines” of neurons—the cells’ critical information processing points.

Is this toxicity clearly associated with, and indeed a cause of, memory declines and other neurocognitive problems in people living with HIV? Additional research, including analyses of data involving people who have been using efavirenz compared with those who have not, will be necessary. The researchers did note, however, that "concentrations of efavirenz and [8-hydroxyefavirenz] in the cerebral spinal fluid of HIV-infected [NorthEastern AIDS Dementia study participants] taking efavirenz were within the range that damaged neurons in culture."

The Johns Hopkins researchers add that a minor modification to efavirenz’s structure may block its effects on nerve cells, without affecting the drug’s effectiveness.

To read the Journal of Pharmacology and Experimental Therapeutics report (paid subscription required), click here.
To read the Johns Hopkins news announcement, click here.

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