Elevated Homocysteine Associated With Levodopa, Peripheral Nerve Dysfunction in Parkinson's Disease

May 18, 2004 — Elevated homocysteine is associated with levodopa and is proportional to peripheral neuronal dysfunction in Parkinson's disease (PD), according to the results of a study published in the May issue of the Archives of Neurology. The editorialist suggests that if the pathogenetic link is proven, available and inexpensive therapy may have a great impact.

"Levodopa metabolism via catechol O-methyltransferase (COMT) increases levels of the neurotoxin homocysteine, which induces an axonal-accentuated degeneration in sensory peripheral nerves in vitro," write Thomas Muller, MD, from Ruhr University Bochum in Germany, and colleagues.

To determine associations between daily levodopa/dopa decarboxylase inhibitor intake, total homocysteine plasma (tHcy) levels, and electrophysiologic sural nerve conduction findings, 31 levodopa-treated patients with PD and 27 control subjects underwent assessment of tHcy levels and bilateral sensory nerve conduction velocity and sensory nerve action potentials.

Although sensory nerve conduction velocities were similar in PD patients and control subjects, sensory nerve action potentials were significantly different in these groups (P < .001). There were also differences in sensory nerve action potentials, but not in sensory nerve conduction velocity, between PD patients with significantly elevated tHcy levels and controls (P < .001), PD patients with normal tHcy levels and those with elevated levels (P = .001), and PD patients with normal tHcy levels and controls (P = .04).

Levels of tHcy were associated with sensory nerve action potentials (R = 0.52; P = .002), sensory nerve conduction velocity (R = 0.47; P = .008), and daily levodopa/dopa decarboxylase inhibitor intake (R = 0.43; P = .02).

"This electrophysiological sign of peripheral neuronal dysfunction may be circumstantial evidence suggesting that, to a certain extent, sensory nerve action potentials are a surrogate marker for the levodopa metabolism-induced elevation of homocysteine levels and the aggravation of the ongoing central neurodegenerative process," the authors write.

In an accompanying editorial, Padraig O'Suilleabhain, MD, from the University of Texas Southwestern Medical Center in Dallas, notes that establishing a cause-and-effect relationship will require additional studies showing that vitamin supplements slow down or even reverse dysfunction of the sural nerve in PD.

Possible therapeutic approaches to reduce tHcy levels include vitamin supplementation, peripherally acting COMT inhibitors, or well-titrated and carefully monitored S-adenosylmethionine (SAM) supplementation with normalizing of reduced SAM levels in PD patients.

"If the pathogenic link is proved, and if potential complications can be shown to be preventable by inexpensive and well-tolerated therapies such as vitamin B supplementation, these early observations would carry great public health significance," Dr. O'Suilleabhain writes. "Repeated epidemiologic and neuroimaging investigations, some funded by companies that market alternative dopaminergic agents, have failed to prove that levodopa accelerated neurodegeneration in PD. On the contrary, it is beyond question that survival and the natural history of PD improved significantly with the introduction of
levodopa. In light of its history we might be particularly cautious before saddling levodopa with further suspicion."


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