

# New Treatment Insights Into The Dopamine Dilemma

by Jonathan Davies

Current treatments for Parkinson's disease may be putting sufferers at higher risk of peripheral nerve damage, according to a new study published in the July 2010 edition of *Annals of Neurology* by Drs. Cory Toth, Oksana Suchowersky, and Douglas Zochodne, researcher clinicians in the Department of Clinical Neurosciences (DCNS) and members of the Hotchkiss Brain Institute (HBI) in Calgary.



According to the Parkinson Society of Canada, an estimated 80,000 Canadians suffer from Parkinson's disease (PD), in which a lack of production of the neurotransmitter dopamine prevents the region of the brain responsible for movement, the motor cortex, from accurately relaying motor commands to muscles. This progressive, degenerative disease can lead to patients developing tremors and impaired movement and speech. Levodopa (L-dopa), a compound that neurons use to make more dopamine, is routinely used as a treatment for PD, to restore proper functioning of the motor cortex in the brain.

Neurological complications regularly occur alongside Parkinson's disease. One possible contributing factor to these problems is peripheral neuropathy – or damage to nerves in the peripheral nervous system that feed information into and out of the brain and spinal cord. Peripheral neuropathy poses a significant problem in Parkinson's disease because any additional numbness and impaired balance in a patient who is already experiencing difficulty with movement can lead to a higher risk of falling and further loss of mobility. Yet no studies had been conducted to understand why those additional neurological issues were seen along with Parkinson's disease.

“As far back as my residency, we were seeing about a 10% incidence of peripheral neuropathy along with Parkinson's disease,” says Dr. Cory Toth, a neurologist with Alberta Health Services and a researcher at the Faculty of Medicine, UCalgary. “But when I asked the specialists about it, they didn't think it was attributable to the treatments we were using.”

Toth wanted more definitive answers, so in collaboration with Drs. Suchowersky and Zochodne, he conducted a longitudinal study of 58 Parkinson's disease patients to test for links between Parkinson's disease and peripheral neuropathy. The results were surprising. In their study, Dr. Toth and his team found over half of the Parkinson's disease patients tested had peripheral neuropathy. And the severity of the peripheral neuropathy suffered went up with increased exposure to L-dopa as a treatment.

Comprehensive blood testing showed that the Parkinson's disease patients who also had peripheral neuropathy had increased serum levels of methylmalonic acid (MMA). MMA is a potentially toxic substance believed to damage neurons, which Toth believes may account for the high prevalence of peripheral neuropathy seen.

“With L-dopa, you get the good effects of reducing Parkinsonian symptoms, but you could also get the bad effects of peripheral neuropathy,” he says.

Dr. Toth and his team also found similar effects in the laboratory. They've shown that when neuronal cultures are exposed to elevated MMA, they exhibit multiple toxic effects including stunted axonal outgrowth. Together, these findings suggest that L-dopa use may create other unintended problems, and – hopes Toth – will make clinicians reconsider how they treat the disease.

Diagnosed with Parkinson's in 2003, Sharon Strachan knows first hand what it's like to suffer from the disease. Starting with an almost imperceptible tremor in her left hand, symptoms progressed quickly. Soon her neurologist noticed a diminished arm swing on the left side, a facial mask, and a gait that slowed with each day.

"At the time my friends would joke around with me saying, 'hurry up, Speed! After a while though it was difficult to keep laughing," says Sharon. "With the progression of PD, walking felt like moving through wet sand."

With a demonstrated link between L-dopa and peripheral neuropathy, Drs. Toth, Suchowersky, and Zochodne can now focus on developing therapies that will stop that damage from happening in the future.

One treatment change that Toth thinks might work is supplementing L-dopa therapy with cobalamin. Treatment with cobalamin (a form of Vitamin B12) promises to prevent the process by which L-dopa contributes to the formation of MMA, and thus could help protect against peripheral neuropathy during long term L-dopa therapy.

Toth plans to continue investigating the links between L-dopa and peripheral neuropathy, but will now focus on understanding possible protective mechanisms that could help provide improved treatment options for Parkinson's disease.

"Parkinson's disease in all its symptoms is difficult enough, let alone with added problems incurred by the medications we need, like l-dopa," says Sharon. "This new research is exciting because it gives hope to all of us who struggle daily with the limitations of PD - hope for better management of the disease now, and hope for a cure in the future."