Freezing Parkinson's in its tracks

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Parkinson's disease, a disorder which affects movement and cognition, affects over a million Americans, including actor Michael J. Fox, who first brought it to the attention of many TV-watching Americans. It's characterized by a gradual loss of neurons that produce dopamine. Mutations in the gene known as DJ-1 lead to accelerated loss of dopaminergic neurons and result in the onset of Parkinson's symptoms at a young age.

The ability to modify the activity of DJ-1 could change the progress of the disease, says Dr. Nirit Lev, a researcher at Tel Aviv University's Sackler Faculty of Medicine and a movement disorders specialist at Rabin Medical Center. Working in collaboration with Profs. Dani Offen and Eldad Melamed, Dr. Lev has now developed a peptide which mimics DJ-1's normal function, thereby protecting dopamine- producing neurons. What's more, the peptide can be easily delivered by daily injections or absorbed into the skin through an adhesive patch.

Based on a short protein derived from DJ-1 itself, the peptide has been shown to freeze neurodegeneration in its tracks, reducing problems with mobility and leading to greater protection of neurons and higher dopamine levels in the brain. Dr. Lev says that this method, which has been published in a number of journals including the *Journal of Neural Transmission*, could be developed as a preventative therapy.

Guarding dopamine levels

As we age, we naturally lose dopamine-producing neurons. Parkinson's

patients experience a rapid loss of these neurons from the onset of the disease, leading to much more drastic deficiencies in dopamine than the average person. Preserving dopamine-producing neurons can mean the difference between living life as a Parkinson's patient or aging normally, says Dr. Lev.

The researchers set out to develop a therapy based on the protective effects of DJ-1, using a short peptide based on the healthy version of DJ-1 itself as a vehicle. "We attached the DJ-1-related peptide to another peptide that would allow it to enter the cells, and be carried to the brain," explains Dr. Lev.

In pre-clinical trials, the treatment was tested on mice utilizing well-established toxic and genetic models for Parkinson's disease. From both a behavioral and biochemical standpoint, the mice that received the peptide treatment showed remarkable improvement. Symptoms such as mobility dysfunctions were reduced significantly, and researchers noted the preservation of dopamine-producing neurons and higher dopamine levels in the brain.

Preliminary tests indicate that the peptide is a viable treatment option. Though many peptides have a short life span and degrade quickly, this peptide does not. Additionally, it provides a safe treatment option because peptides are organic to the body itself.

Filling an urgent need

According to Dr. Lev, this peptide could fill a gap in the treatment of Parkinson's disease. "Current treatments are lacking because they can only address symptoms — there is nothing that can change or halt the disease," she says. "Until now, we have lacked tools for neuroprotection."

The researchers also note the potential for the peptides to be used preventatively. In some cases, Parkinson's can be diagnosed before motor symptoms begin with the help of brain scans, explains Dr. Lev, and patients who have a genetic link to the disease might opt for early testing. A preventative therapy could help many potential Parkinson's patients live a normal life.

Provided by Tel Aviv University

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