

Researchers identify why dopamine replacement therapy has a paradoxical effect on cognition

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Dopamine replacement therapy, which is used to manage motor symptoms associated with Parkinson's disease, can, at times, adversely affect cognition.

Dr. Oury Monchi, Ph. D. in neuronal modeling and Head of the Neurophysiological and Neuroimaging Research theme at the Centre de recherche de l'Institut universitaire de gériatrie de Montréal (IUGM), which is affiliated with the Université de Montréal, and Dr. Penny A. MacDonald, Neurologist and postdoctoral fellow in Dr. Monchi's laboratory, have identified the reasons why within the framework of a clinical study recently published in *Brain: A Journal of Neurology*. This marks the second time in three months that *Brain* has published the results of IUGM researchers.

"The aim of our study was to understand the effects of dopamine replacement therapy on various aspects of cognition in patients with Parkinson's disease. When it comes to this particular disease, the part of the brain most affected by dopamine depletion is the striatum which is divided into several structures. In Parkinson's disease, the dorsal striatum is more severely affected than the ventral striatum, which remains relatively unaffected, at least during the first phases of the disease. We observed that while dopamine replacement therapy enhances the functions of the dorsal striatum, it is at the expense of the ventral striatum which suffers a dopamine overdose, impairing its function",

states Dr. Monchi.

Until now, the effect of dopamine replacement therapy on cognition in individuals with Parkinson's disease was controversial. The purpose of this study however, was to further investigate. This led to a series of laboratory tests and neuroimaging studies that allowed researchers to clearly define the distinct [cognitive](#) functions performed by the dorsal and ventral striatum, thereby shedding some light on the issue.

"The best treatment option for managing the motor symptoms of Parkinson's disease remains dopamine replacement therapy. In some patients however, it can have a negative effect on specific aspects of cognition. Our discovery will therefore enable us to explore different medication and non-medication based avenues that could help improve the overall health of those affected. Our findings may contribute to helping develop personalized medicine - an avenue that is currently commanding a great deal of attention", exclaims Dr. MacDonald.

Twenty two Parkinson's disease patients without dementia and twenty two healthy individuals were included in the first part of the study (behavioural), while thirteen healthy young adults participated in the second part of the study (neuroimaging). Each participant was asked to repeatedly choose numbers (288 times) such as selecting the higher of two numbers, for example. On some occasions, patients were given no reinforcement, while on other occasions, they were influenced by various cues that made it easier to answer (a function usually associated with the dorsal striatum), or more difficult to answer due to interference (associated with the ventral striatum). Parkinson's patients were tested on or off medication. Selection was validated with functional magnetic resonance imaging which was used to observe cerebral activity during the exercises. Results demonstrated that while dopamine replacement enhances results for conditions associated with interference (dorsal striatum), it reduces results for conditions associated with facilitation

(ventral striatum).

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease. Onset usually begins between the ages of 45 and 70 years. For reasons that remain unknown, the cells that produce dopamine, a chemical that relays signals to the striatum, die. Since dopamine controls movement, the motor symptoms of Parkinson's disease gradually begin to appear. Motor symptoms manifest as tremor, rigidity and akinesia (inability to perform certain simple voluntary movements). Symptoms can also affect cognition and mood and may even lead to depression. According to Health Canada, it is estimated that 1 in 100 Canadians over age 60 are diagnosed with this condition. The direct and indirect costs associated with Parkinson's disease exceed \$450 million a year.

Provided by University of Montreal

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