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Relating functional and structural signatures of Parkinson's disease to changes in dopamine signalling: A PET/fMRI study

BrainsCAN . Western University

Penny MacDonald
Western University

Udunna Anazodo
Lawson Health Research Institute

Justin Hicks
Lawson Health Research Institute

Frank Prato
Lawson Health Research Institute

See next page for additional authors

Authors and Researchers
BrainsCAN . Western University, Penny MacDonald, Udunna Anazodo, Justin Hicks, Frank Prato, and Alain Dagher

Western BrainsCAN
Transforming brain research.

Project **Summary**

KNOWLEDGE MOBILIZATION & IMPACT

Relating functional and structural signatures of Parkinson's disease to changes in dopamine signalling: A PET/fMRI study

Background

Parkinson's disease (PD) causes significant cognitive deficits during its progression, with impaired decision-making and attention control being chief among the symptoms.

Cognitive impairments in early PD are known to be linked to complex changes in the dopamine system within the brain. For example, dopamine-producing neurons in one key region of the brain are significantly degenerated, but those in another are spared.

Dopamine-replacement therapy (DRT) has been pursued and it has produced significant improvements in certain cognitive functions - unfortunately it also produced significant impairments in others. A current theory for this effect is that because the degeneration of dopamine-producing neurons is not at the same rate throughout the brain, DRT is successfully addressing a deficit in one region but effectively overdosing other regions that were not yet affected by PD. While this theory does appear to explain the outcomes seen, there is currently no empirical evidence to support it.

The Problem

Currently we have no adequate tools to study these changes in PD. While fMRI can be used to study blood oxygenation as a proxy for neural activity, it does not directly visualize dopamine.

Another form of imaging, positron emission tomography (PET), can allow some targeted exploration of dopamine, but currently it can only identify a single type of dopamine receptor and it is rarely used because the biochemical substance needed to locate the particular type of receptor is challenging to produce.

We need to understand more about the dopamine pathways in the brain and how they relate to cognition in PD, the issues with DRT and the progression of PD to develop cleaner, effective and more selective treatments.

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The Project

Western is in a unique position as it boasts a simultaneous PET-MRI system - few exist in Canada - and the biochemical substance used to locate the specific dopamine receptor (this substance is known as a radioligand). We can understand the changes in this dopamine receptor that arise because of PD and in response to DRT, which will allow us to test the underlying mechanism of dopamine overdose effects.

The foundational milestone for us is to establish this proposed approach with PET-MRI and radioligands in an animal model of PD before we can approach PD patients themselves.

Western Researchers

Penny MacDonald

Lawson Researchers

Udunna Anazodo
Justin Hicks
Frank Prato

McGill Researchers

Alain Dagher