

Pacific Parkinson's RESEARCH INSTITUTE

2022 IMPACT REPORT

Functional Segregation in Parkinson's Research

Partnering in the Search for a Cure

The Pacific Parkinson's Research Institute (PPRI) partners with the UBC Faculty of Medicine to fund the strategic research priorities of the Pacific Parkinson's Research Centre (PPRC), a Centre of Excellence for the diagnosis and management of Parkinson's disease and related disorders. This partnership enables our world-leading experts to apply the novel technology of hybrid positron emission tomography and magnetic resonance imaging (PET-MRI) to study altered striatal plasticity in established Parkinson's disease. This investigation has significant potential to increase our understanding of the pathological features and compensatory processes associated with Parkinson's and to assess the impact of therapeutic interventions such as exercise, other lifestyle modifications as well as emerging pharmacological and biological treatments.

The University of British Columbia Faculty of Medicine and the Pacific Parkinson's Research Centre (PPRC) thank the Pacific Parkinson's Research Institute (PPRI) for advancing our understanding of a key characteristic of Parkinson's disease: the structural and functional changes it brings about in the striatum, the part of the basal ganglia that receives dopamine projections that degenerate in Parkinson's, and whose circuits are critical for motivation and motor planning. The PPRI's visionary support of the leadership of principal investigator Dr. Jon Stoessl, Professor & Head of Neurology, and former Director of the Djavad Mowafaghian Centre for Brain Health at UBC & Vancouver Coastal Health, is essential to advancing our understanding of PD. This research has great potential to allow innovation in shaping its progression.

For more information, please contact:

Pacific Parkinson's

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The UBC Faculty of Medicine, Dr. Stoessl and his team are pleased to prepare the following progress update.

Thank You



THE UNIVERSITY OF BRITISH COLUMBIA

Summary of Project Achievements to Date



This project is being led by Alexandra Pavel, MSc student in Neuroscience, under the supervision of principal investigator Dr. Jon Stoessl. Ethics approval was received for the project on February 3rd, 2020, with data collection commencing on January 25th, 2021, due to COVID-19 in-person research restrictions.

To date, nine Parkinson's disease (PD) and ten healthy control (HC) participants have been enrolled. The team have conducted a total of 70 hybrid PET/MRI scans completed so far. We aim to recruit 20 participants (10 PD and 10 HC) and conduct 80 PET/MRI scans overall during the project.

Dr. Jon Stoessl

Parkinson's disease is known to result in loss of dopamine projections to the striatum (a structure in the forebrain) that, in addition to facilitating movement, coordinates many aspects of cognition such as reward perception and decision making. In PD, dopaminergic projections innervating the striatum degenerate in a selective manner. While a back-to-front pattern of progression is supported by previous imaging studies, the possibility of an additional top-to-bottom gradient is less established. Control of motor functions of different body parts (i.e. face vs. hand vs. leg) is thought to be anatomically separated within the striatum, but it is not known if this separation is respected in Parkinson's.

Additionally, while it is widely accepted that the complex loops from cortex to striatum to basal ganglia outflow, thalamus and back to cortex are segregated with respect to function (motor vs. cognitive vs. reward), it is also not known whether this segregation of function is maintained in Parkinson's. As dopamine enhances the signal to background activity in the brain, leading to the capacity to fine tune discrete responses, knowledge about this separation of function is critical to understanding the deficits associated with Parkinson's. It is also not known whether a loop that is working better might take over the function of a loop that is not working well in Parkinson's. This could be a form of compensation for the loss of dopamine, but may also lead to loss of the ability to combine different types of brain functions. Furthermore, based on prior research supported by PPRI, we believe that changes in brain plasticity in Parkinson's may be amenable to exercise.



Using hybrid PET-MR imaging data, the project is assessing functional reorganization of connections in PD and healthy controls, to study simultaneously the pattern and degree of dopamine release as well as activation of connected networks in the brain.

The scans obtained are currently undergoing analysis by the research team. The exciting preliminary results point towards a confirmation of Dr. Stoessl's hypothesis that the spatial distribution of striatal dopamine release - the process whereby dopamine neurons regulate activity in the striatum, differs between PD and HC subjects and that people with PD do not demonstrate the discrete localization of dopamine release that is seen in healthy control subjects.

Alexandra Pavel (MSc)

The Team

Dr. Stoessl initiated a recruitment exercise to drive the project forward, resulting in the following team:

Jess McKenzie (Coordinator)

Jess McKenzie has worked at the PPRC as a nurse research coordinator in the PET imaging program, and she feels fortunate to have worked with an excellent team of people under the direction and leadership of Dr. A. Jon Stoessl and Dr. Vesna Sossi on a variety of academic projects investigating the characterization, progression, and complications of Parkinson's disease.

Sahib Dhaliwal (Research Assistant)

Sahib Dhaliwal joins us a Research Assistant who provides integral support for the day to day aspects of the project. She is responsible for screening, recruitment, communications, and secondary financial details associated with the conduct of the project.

Shairy Sifat (Coordinator)

Shairy Sifat joins us as a Nurse Research Coordinator who provides expertise in the clinical aspects of care for research participants undergoing the assessments and procedures associated with participating in this project.

Elham Shahinfard, PhD (PET Lab Manager)

Elham has been working as a manager involved in the development of the Charles Fipke Integrated Neuroimaging suite, daily operations of the PET imaging centre and liaising with other researchers and collaborators about their research studies.

Student Supervision

During the course of the project, Dr. Stoessl has supervised Polina Timofeeva and Christopher Mok (work-learn co-op), Alexandra Pavel (MSc) and Dongning Su (PhD student visiting from Beijing).

Collaborations

During this reporting period, Dr. Stoessl has strengthened his national and international collaborations with researchers who are renowned in their fields as he has advanced his research into the structural and functional changes in striatal projection neurons associated with PD:

Professor Vesna Sossi (UBC)

Vesna Sossi is currently a Professor in the Physics and Astronomy Department and Adjunct Professor in Medicine at UBC. She has been leading the UBC Positron Emission Tomography (PET) brain imaging program since 2009. She has collaborated with Dr. Stoessl on the following studies: Functional segregation, bioenergetics in PD and Tau imaging in PD.

Dr. Tao Wu, Dr. Tao Feng (Capital Medical University, Beijing)

Dr. Wu is a Professor in the Department of Neurobiology at the Capital Medical University China and Dr. Feng is the associate chief physician of the Neurology Department of Beijing Tiantan Hospital, which is affiliated to the Capital Medical University. They have collaborated with Dr. Stoessl on supervision of Dongning Su, imaging projects on gait, and levodopa-induced dyskinesias.

Cheryl Wellington, Will Panenka, Mypinder Sekhon

Dr. Wellington is a Professor with the Department of Pathology and Laboratory Medicine, UBC, Dr. Panenka is a dually certified psychiatrist, and neurologist and assistant professor in the department of psychiatry at UBC and Dr. Sekhon is an intensive care physician and clinician-scientist at Vancouver General Hospital. They are collaborating with Dr. Stoessl on CNS Effects of COVID-19.

Canadian Open Parkinson Network

Dr. Stoessl is a founding member and sits on the Executive Committee for this initiative which is funded by Brain Canada and Parkinson's Canada.

Presentations and Publications:

Presentations

The ongoing COVID-19 pandemic has restricted Dr. Stoessl's opportunities for in-person presentations. However, he has been pleased to give the following during the reporting period:

Why have we failed to develop effective neuroprotective strategies in PD? Movement Disorders Society of India (virtual). Invited plenary speaker. *February 20, 2021*

Imaging in PD: Great Opportunities. PMD Alliance (virtual). *March 15, 2021.*

What's new in imaging? World Parkinson Virtual Congress. *May 19, 2021.*

Imaging Biomarkers in Neurodegeneration. Indian Academy of Neurology (Baldev Singh plenary oration). *November 12, 2021 (virtual)*

Can MRI & PET Imaging Determine Disease Subtype, Monitor Disease Progression & Individualize Treatment in PD: NO. Invited Plenary Debate, International Association of Parkinsonism & Related Disorders. Prague, CZ; *May 4, 2022.*

In the Mind's Eye: Molecular Imaging Insights into Parkinson's Disease. Invited Keynote Lecture, CNS Research Day, Western University; *May 17, 2022.*

Meet the Expert. Movement Disorders International Congress, September 21, 2021 (Virtual) Tips on Peer Review. American Academy of Neurology Movement Disorders Section Meeting, September 9, 2021 (Virtual)

Publishing in the Journals. Movement Disorders Society Cybertalk, June 21, 2021 (Virtual) Molecular Imaging Studies in Parkinson's. Parkinson Society BC World Parkinson's Day, April 13, 2022.

Publications

Serotonergic System Impacts Levodopa Response in Early Parkinson's and Future Risk of Dyskinesia. Fu JF, Matarazzo M, McKenzie J, Neilson N, Vafai N, Dinelle K, Felicio AC, McKeown MJ, Stoessl AJ, Sossi V (2021) *Mov Disord* 36: 389-397. DOI: 10.1002/mds.28340.

Looking Forward (editorial). Stoessl AJ (2021). 2021: Looking forward (editorial). *Mov Disord* 36: 11-12. doi: 10.1002/mds.28455; PMID: 33492792.

Clinical Role of Neuroimaging and Liquid Biomarkers in Patients with Cognitive Impairment. Brisson M, Brodeur C, Letourneau-Guillon L, Masellis M, Stoessl AJ, Tamm A, Zukotyunski K, Ismail Z, Gauthier S, Rosa-Neto P, Soucy JP (2021). *CCCDTD5: Alzheimers Dement* 6:e12098. doi: 10.1002/trc2.12098; PMID: 33532543.

Weeding Through the Haze: A Survey on Cannabis Use Among People Living with Parkinson's Disease in the US. Feeney MP, Bega D, Kluger BM, Stoessl AJ, Evers CM, de Leon R, Beck JC (2021). *NPJ Parkinson's Disease* 7: 21. Doi: 10.1038/s41531-021-00165-y; PMID: 33658517

Dopamine Receptors in Parkinson's Disease: A Meta-Analysis of Imaging Studies. Kaasinen V, Vahlberg T, Stoessl AJ, Strafella AP, Antonini A (2021). *Mov Disord* 36: 1781-1791. doi: 10.1002/mds.28632; PMID: 33955044.

Emerging Neuroimaging Biomarkers Across Disease-Stage in Parkinson's Disease: A Review. Mitchell T, Lehericy S, Chiu SY, Strafella AP, Stoessl AJ, Vaillancourt DE (2021). *JAMA Neurol* 78: 1262-1272. doi: 10.1001/jamaneurol.2021.1312.

Cortical Morphology Predicts Placebo Response in Multiple Sclerosis. Cherkasova M, Fu JF, Jarrett M, Johnson P, Abel S, Tam R, Rauscher A, Sossi V, Kolind S, Li DKB, Sadovnick D, Machan L, Girard JM, Emond F, Vosoughi R, Traboulsee A, Stoessl AJ (2022). *Sci Reports* 12: 732. doi: 10.1038/s41598-021-04462-7.

Submitted and In Preparation Journals

Does Protein Aggregation in Parkinson's Disease Start in Axonal Terminals? Matarazzo M, Perez-Soriano A, Vafai N, Shahinfard E, Cheng KJ-C, McKenzie J, Neilson N, Miao Q, Shinotoh H, Sossi V, Stoessl AJ. A 11C-PBB3 study (*under revision*)

Altered Visual Network Dynamics Associated with Freezing of Gait in Parkinson's Disease. Su D, Ji L, Cui Y, Gan L, Ma H, Liu Z, Duan Y, Stoessl AJ, Zhou J, Wu T, Liu Y, Feng T. Submitted to Journal of Neurology, Neurosurgery & Psychiatry May 2022.

Thank You

The UBC Faculty of Medicine and the PPRC are deeply grateful to the PPRI for supporting our investigations into the role of hybrid positron emission tomography and magnetic resonance imaging (PET-MRI) to study the altered striatal plasticity in established prodromal Parkinson's disease, contributing to the development of an integrated approach to new opportunities for wellbeing for patients and care partners. Thank you for enabling our experts in neurology, microbiology, immunology, nutrition, exercise, metabolomics, psychiatry and other fields to proceed with this extensive research program to inform the development of much-needed therapies and interventions for Parkinson's disease.