

Pacific Parkinson's

RESEARCH INSTITUTE

2019 IMPACT REPORT

Exercise and Parkinson's Disease

Partners 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 Canadian Centre for Excellence for the diagnosis and management of Parkinson's disease and related disorders. The strong partnership between the PPRI and PPRC mirrors the special bond between patients and clinician-scientists at PPRC—decisions on the best ways to improve the lives of people with Parkinson's disease in British Columbia are made locally and collaboratively.

For more information, please visit www.pacificparkinsons.org

Project Summary

With leadership from Dr. Jon Stoessl, Professor and Head of Neurology and Director of the Djavad Mowafaghian Centre for Brain Health, the PPRC's exercise team is publishing the findings of the PPRI-funded exercise study and continuing three-year follow-up with study participants. The PPRC also advanced an ambitious proposal for a Parkinson Foundation Research Centres of Excellence at UBC that integrates exercise with several cutting-edge approaches to advancing our understanding of how Parkinson's disease develops.

For more information, please contact:

Pacific Parkinson's Research Institute

210 - 1095 West Pender Street
Vancouver, BC V6E2M6
Telephone: 604 681-5031
Email: ppri@telus.net

Thank You

The UBC Faculty of Medicine is grateful to PPRI and Mr. Kurt Gagel for enabling the PPRC to investigate the mechanisms underlying the benefits of exercise for people with Parkinson's disease. Thanks to your support, we came very close to securing a new grant that would form an interdisciplinary research team around the potential of exercise in improving the lives of people with Parkinson's.



Key Findings

In December 2018, a manuscript entitled “Habitual exercisers versus sedentary subjects with Parkinson’s disease: multimodal PET and fMRI study” was published in the journal *Movement Disorders*. This article describes the initial pilot study funded by PPRI, which examined differences in dopamine release, reward signaling, and clinical features between habitual exercisers and sedentary subjects with Parkinson’s disease.

Imaging analysis before and after stationary cycling demonstrated greater dopamine release in habitual exercisers compared to sedentary subjects. Habitual exercisers revealed greater brain activation during the functional reward task and lower apathy compared to sedentary subjects. The study concludes that habitual exercise is associated with preservation of motor and non-motor function, possibly mediated by increased dopamine release. This study is the foundation for future randomized controlled trials.

Also this year, a manuscript was submitted to *Movement Disorders*. In this double-blind study funded by PPRI, the effects of aerobic exercise on dopamine release evoked by cortical stimulation and activity of the brain’s reward pathways were examined in Parkinson’s disease using PET and fMRI. Aerobic exercise was found to alter the responsivity of the reward pathways in the brain, presumably related to changes in dopamine pathways, and also to result in increased dopamine release in the dorsal striatum evoked by cortical stimulation. This suggests the therapeutic benefits of exercise are in part related to brain plasticity and enhanced dopamine release.

In addition to these publications, a brief manuscript on inflammation is planned, and presentations were made to Parkinson Canada and an International INSIGHT into Parkinson’s online meeting.

Follow-up Study

The research team continues to conduct follow-up testing with the initial 25 subjects three years later to assess how exercise may continue to benefit brain behaviour and wellness over time. We expect to complete a total of 22 follow-up tests by spring of 2021 (three subjects were lost due to illness or claustrophobia). Four subjects have already returned for testing, and another eight subjects are expected to return by year-end.

New Opportunities

Using PPRI funding as leverage, the PPRC applied for a Parkinson Foundation Research Centres of Excellence. We were among 66 leading centres around the world to submit a letter of intent, among the 13 invited to submit a full proposal, and among the six centres selected for a final interview. Although the interview went well and the reviews were for the most part very positive, unfortunately, our application was not funded. The five key projects included in our application are relevant to the PPRI funding received to-date and for this reason are briefly summarized below:

1. **Bioenergetics:** With partial funding from PPRI, Dr. Vesna Sossi will lead the examination of brain energetics in healthy aging and Parkinson's and the effects of exercise on altered bioenergetics in Parkinson's.
2. **Neuroinflammation:** Novel biomarkers will be used to study neuroinflammation in Parkinson's, with findings linked to the PPRI-funded microbiome study. Once the preliminary studies are complete, the PPRC will examine the effects of exercise on inflammation in Parkinson's and what happens during early phases of disease.
3. **Somatotopy:** This is the point-for-point correspondence of an area of the body to specific regions in the central nervous system. Neurons are selectively lost in Parkinson's, and the pattern of loss is thought to be associated with the area of the body that is affected first (arm, leg). Also, motor functions should be affected more than cognitive and reward functions, but the normal segregation of function may be disrupted in Parkinson's, reflecting the loss of dopamine. This study will assess the effects of Parkinson's on dopamine release and functional activation of the striatum, and whether exercise has an impact on the degree of segregation.
4. **Exercise:** The hub of the proposal, exercise is linked to all the other projects. The PPRC will examine the effects of exercise on bioenergetic defects and neuroinflammation in one cohort, and the effects of exercise on functional activation, functional connectivity, dopamine release, and functional segregation in Parkinson's in a separate cohort.
5. **Mood, apathy, and engagement:** Exercise is a form of engagement, therefore the PPRC plans to pilot a self-management program and link the findings to imaging from the main exercise study. Mood, apathy, patient-reported outcomes, quality of life, and care partner evaluations will be assessed. This project is linked to the PPRC's broader program on brain wellness led by Dr. Silke Cresswell.

In the future, PPRC plans to extend these projects to examine prodromal Parkinson's to identify whether abnormalities are present before the motor symptoms of disease manifest. Our long-term plans also include assessing the therapeutic potential of exercise in subjects at high risk of developing Parkinson's disease.