



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Parkinson's disease and the gastrointestinal microbiome	
Name	Dr Michal Lubomski	
Award Received	2020 RACP Fellows Research Entry Scholarship	
Report Date	January 2021	
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	Finish Date:	31/12/2020

PROJECT SUMMARY

I have been evaluating gastrointestinal dysfunction and the gut microbiome in a cohort of 103 Parkinson's disease patients and 81 healthy control spouses / relatives. My investigations have shown a number of interesting, insightful and clinically relevant findings linking gastrointestinal dysfunction with gut microbiome changes in Parkinson's disease. In my preliminary studies, I was able to determine that Parkinson's disease patients more commonly experienced symptoms of gastrointestinal dysfunction and that these were more severe in nature. Specifically, Parkinson's disease patients were three-times more likely to experience constipation than the healthy controls, (78.6% vs 28.4%), and their constipation was four times worse. This was also associated with chronic pain and more frequent upper gastrointestinal tract symptoms, in the form of indigestion, nausea, excessive fullness and bloating. Interestingly, I found that Parkinson's disease patients undertaking more physical activity were (among other things) less likely to be constipated, supporting the idea that adjusting lifestyle factors could have a beneficial impact on disease.

My ongoing research is exploring relationships between the gut microbiome and Parkinson's disease. My initial analysis of the gut bacteria at a single time point has identified numerous differences in the Parkinson's disease patients, which are supportive of the theory of 'gut leakiness' and inflammation involvement in Parkinson's disease. A variety of other changes relating to various disease characteristics have also been identified and testing of predictive models has identified a potential gut microbiome biomarker in Parkinson's disease, which may further improve with incorporation of patient nutritional data. I have also investigated the acute and long-term impacts of standard and device-assisted therapies on the gut microbiome, showing unique microbiome change in response to initiating device-assisted therapies. Furthermore, preliminary results indicate that several bacterial differences remain consistent when evaluating the gut microbiome over time, further supporting the possibility of utilising the gut microbiome as a biomarker in Parkinson's disease.

PROJECT AIMS / OBJECTIVES

Aims:

1. To evaluate differences in the gut microbiome composition between Parkinson's disease patients and healthy controls.

2. To assess acute and longitudinal changes in the gut microbiome composition in response to standard and advanced Parkinson's disease therapies (Duodopa and Deep Brain Stimulation).

Objectives:

To determine temporal changes in gut microbiome profiles in relation to lifestyle and therapy and relate these changes to clinical motor and non-motor Parkinson's disease features.

The study's aims and objectives were achieved by completing three timepoint analyses in a cohort of 103 Parkinson's disease and 81 healthy control patients. These three distinct analyses formed the basis of each manuscript that are in preparation and will be submitted over the next 6 months.

An initial cross-sectional study identified a variety of clinical motor and non-motor characteristics that were associated with various microbiome profiles in Parkinson's disease, as well as showing differing bacterial compositions between Parkinson's disease patients and healthy controls.

Evaluation of acute influences from initiation of device-assisted Parkinson's disease therapies (Duodopa and Deep Brain Stimulation) again identified specific microbiome changes. It was proposed that these reflected impacts from the physical properties of these therapies, as well as influences from environmental factors associated with their initiation. This objective has been a novel research interest in the rapidly expanding global scientific field.

Lastly, preliminary longitudinal analyses over 12 months, utilising three- time intervals, has suggested persistent alterations in microbiome profiles for Parkinson's disease patients compared to healthy controls, supporting a potential role of a gut microbiome biomarker that could be used to aid in the management of Parkinson's disease, particularly in reference to disease progression.

SIGNIFICANCE AND OUTCOMES

Globally there is increasing research interest into the composition of the gut microbiome, how it impacts various diseases and whether it can be modified to alter disease and patient outcomes. My research has provided unique insights to this field by advancing the understanding of gut microbiome changes in response to the initiation of certain device-assisted therapies, as well as longitudinally characterising the gut microbiome profiles between Parkinson's disease patients and healthy controls. This work has identified changes in the abundance of certain bacterial taxa that appears to be temporally stable under various disease and treatment circumstances, which could be utilised as a potential disease biomarker to aid disease diagnosis and more importantly to assist clinicians in determining patterns of disease progression.

Potential avenues of ongoing research in this field, (although these interests are not currently planned, they could potentially be considered) include transplanting the gut microbiome of a healthy individual into a Parkinson's disease patient, supplementing the microbiome by introducing "beneficial" bacteria (probiotic supplementation) or supporting the "good" bacteria that are present in the gut (prebiotic supplementation), as well as developing specific drugs to block the gut microbiome from disrupting how certain Parkinson's disease drugs work.

It is hoped that with further well-designed study's, the analysis of a person's gut microbiome may one day be used to identify individuals at- risk of Parkinson's disease and those with early Parkinson's disease, in addition to offering patients more effective and tailored.

PUBLICATIONS / PRESENTATIONS

Publications:

1. Lubomski M, Davis RL, Sue CM. Gastrointestinal dysfunction in Parkinson's disease. J Neurol. 2020 May;267(5):1377-1388. doi: 10.1007 /s00415-020-09723-5. Epub 2020 Jan 27.

2. Lubomski M, Tan AH, Lim SY, Holmes AJ, Davis RL, Sue CM. Parkinson's disease and the

gastrointestinal microbiome. *J Neurol.* 2020 Sep;267(9):2507-2523. doi: 10.1007/s00415-019-09320-1. Epub 2019 Apr 30. PMID: 31041582.

3. Lubomski M, Davis RL, Sue CM. The gut microbiota: A novel therapeutic target in Parkinson's disease? *Parkinsonism Relat Disord.* 2019 Sep;66:265-266. doi:

10.1016/j.parkreldis.2019.08.010. Epub 2019 Aug 12. PMID: 31445904.

4. Lubomski M, Davis RL, Sue CM. Depression in Parkinson's disease: Perspectives from an Australian cohort. *J Affect Disord.* 2020 Dec 1;277:1038-1044. doi: 10.1016/j.jad.2020.09.032. Epub 2020 Sep 11. PMID: 33065812.

5. Lubomski M, Davis RL, Sue CM. Health-Related Quality of Life for Parkinson's Disease Patients and Their Caregivers. *Movement Disorder Journal.* Accepted for publication

6. Palavra, N., Lubomski, M., Flood, V., Davis, R.L., Sue, C.M. Increased added sugar consumption is common in Parkinson's Disease. *Frontiers in Nutrition.* Under review.

7. Lubomski M, Davis RL, Sue CM. Cognitive influences in Parkinson's disease patients and their caregivers: Perspectives from an Australian cohort. *Journal of Geriatric Psychiatry and Neurology.* Under review.

Abstracts:

Movement Disorder Society - Virtual Congress September 2020.

1. Gut Microbiota in Parkinson's disease: influences of device-assisted therapies.

Awaiting three planned publications, now in 2021, due to delays throughout 2020 from COVID-19:

1) Influences of device-assisted therapies to the gastrointestinal microbiome in Parkinson's disease.

2) Cross-sectional study of the gut microbiome in an Australian cohort of Parkinson's disease patients.

3) Longitudinal study of the gut microbiota in Parkinson's' disease

ACKNOWLEDGEMENTS

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5. Lubomski M, Davis RL, Sue CM. Cognitive influences in Parkinson's disease patients and their caregivers: Perspectives from an Australian cohort. *Journal of Geriatric Psychiatry and Neurology.* Under review.

Anticipated: *Parkinson's New South Wales - Magazine.* Stand by me. 2021 edition.