INFORMATION and CONSENT to PARTICIPATE in RESEARCH

Investigating the relationship between performance fatigability and Parkinson's Disease-related fatigue

This study is funded by Parkinson Canada

Introduction

Fatigue is reported to be one of the most debilitating symptoms of Parkinson's disease. However, recent work has shown that aerobic exercise training improved neuromuscular performance fatigability but not perceived fatigue. Participants reported less desire to exercise when they had high perceived fatigue – even though these ratings showed no link to actual lab-based performance fatigability measures.

Purpose of the study

Owing to the multiple origins of fatigue, it has been difficult to determine the best ways to approach measuring fatigue in general and clinical populations. There is confusion regarding whether or not self-reported measures of fatigue reflect laboratory based objective measures. Some studies assess only the psychological factors that contribute to feelings of fatigue and tiredness while others assess the specific muscular, peripheral and central nervous system impairments leading to impaired neuromuscular performance. In order to grasp a true understanding of fatigability across healthy and clinical populations, it is critical for researchers and clinicians to assess both perceived and performance fatigability and draw parallels between these findings. Therefore, we will evaluate the relationship between performance fatigability and Parkinson's Disease-related fatigue. We will obtain neuromuscular measures (strength, muscle fatigability, power, etc.) and clinical measures that assess Parkinson's disease-related fatigue (questionnaires, and surveys).

How long will it take?

You are being invited to participate in a research study conducted in the Department of Human Health & Nutritional Sciences at the University of Guelph. You will be asked to complete 2 testing visits at the University of Guelph. Visits will take place in the Animal Science and Nutrition building and the Food Sciences building. Please refer to the separate parking handout provided. This should take ~4 hours total over the 2 visits. You will be asked to abstain from caffeine, alcohol, and intense physical activity for 12 hours prior to the second visit.

What will I be asked to do?

We will ask you to wear comfortable exercise clothing. As we outlined in our phone call earlier, we will be taking the following neuromuscular and clinical measurements during the course of 2 visits, including:

1. **Day 1**: Measurement of lean and fat mass using DEXA
2. **Day 2:** Measurement of depression and Parkinson's symptom severity using questionaries. This will ideally occur 7 days after visit 1, however, scheduling can be flexible to work with participants availability. Participants will then undergo neuromuscular testing to assess the strength, power, and fatigability of your legs

Note:

One of the questionnaires will ask you about depression symptoms. This will be completed independently by the participant at home via a Qualtrics form. We will check the results within 3 days of the test. This data is only collected for research purposes.

Am I eligible to be in this study?

To be included in this study you must be between 45-90 years of age and have been diagnosed with Parkinson's disease. You will be excluded if you have a history of any neuromuscular diseases, any lower body injury (< 6 months), history of knee replacement surgery or allergies to adhesive tape. You must also have access to a computer or smartphone to complete the required Qualtrics questionnaires. Participants will be required to provide the research team with their current list of medications. Participation in this study will also require mandatory audio and video recording. We will also recruit age and sex-matched controls with the same exclusion criteria.

The researchers wish to be inclusive in their recruitment process. This project requires interaction one on one with a male or female researchers. If for any reason you may feel uncomfortable taking part, please contact the researcher to discuss possible modifications to the procedure to address your concerns.

Who is conducting this research?

Our research team consists of Faculty and student researchers, each listed below.

Principal Faculty Investigators

Dr. Philip Millar, PhD, Associate Professor, Department of Human Health and Nutritional Sciences, University of Guelph. Contact: pmillar@uoguelph.ca; 519-824-4120 ext. 54818

Dr. Geoffrey Power, PhD, Associate Professor, Department of Human Health and Nutritional Sciences, University of Guelph. Contact: gapower@uoguelph.ca; 519-824-4120 ext. 53752

Student Investigators

Pardeep Khangura, MSc Student, Department of Human Health and Nutritional Sciences, University of Guelph. Contact: pkhang01@uoguelph.ca

Potential risks and discomforts to you if you participate in this study

As all health procedures carry some risk, it is important to disclose these prior to your involvement.

Phone screening: This may pose a moderate psychological risk. Participants may feel upset if they are excluded for any reason. In this population with mobility issues, performing phone screening is most suitable. If a person is excluded, we will continue to provide all the information about the study goals and exercise programs.

Unified Parkinson's Disease Rating Scale (UPDRS): This may pose a minimal psychological risk. Participants may feel upset if they are struggling with cognitive and mental health. They may also feel embarrassed about certain questions that are asked in the UPDRS and in that case, will be allowed to not answer the question if they are uncomfortable. The PIs have worked with individuals living with Parkinson's disease during previous research studies and have experience helping participants work through the questionnaires. All data will be collected as coded information so participants can be at ease knowing their information and scores are confidential.

Anthropometrics: This may pose a minimal psychological risk. Participants may feel uncomfortable when these body measures are taken. The researchers will have age group averages for the anthropometric measures so that the participants can compare their obtained data to group average ranges. A conversation will take place to discuss the results and if participants will be allowed to voice any concerns they may have. At no point will researchers be allowed to advise on how to make changes to any of the anthropometric measures collected, such as weight or BMI, as we aren't certified to give that advice. However, if a participant has a question, we will ask them to refer to their doctor who will better guide them on who they should speak to.

Test results: You may feel embarrassed by your performance on questionnaires or neuromuscular tests. All tests will be completed either independently or with a trained researcher and the results will be confidential.

Electrode adhesives: In rare instances, participants have developed a rash or skin irritation in response to the gel or surface electrodes used in this study. You will be

asked whether you have any skin sensitivities and instructed to contact the researchers if irritation persists.

Dual Energy X-ray Absorptiometry (DEXA): This may pose a minimal physical risk. Participants will be exposed to x-ray radiation. Participants will be screened beforehand to ensure that their avoiding unnecessary exposure to X-ray radiation and only a single scan will be performed. Alternative approaches cannot be used as this is a measure to estimate body/regional limb composition.

Fatigue assessment questionnaires: This may pose a minimal psychological risk. Participants may feel embarrassed or disappointed reporting that they are more fatigued. Researchers will provide an encouraging environment to reduce stress on the participants. It should be noted that many of these questionnaires are common for the Parkinson's population in a clinical setting, so most participants have likely completed these in the past.

Actigraphy: This may pose minimal physical risk as it may feel uncomfortable for some to wear a band around their waist all day for 7 days consistently. Researchers will try to put it on as comfortably as possible for the participant and will also give them instructions on how to adjust it if it becomes too tight/loose.

Muscle strength and fatigue (Neuromuscular testing): There is minimal risk of muscle soreness in the days following maximal voluntary contractions (MVCs). To reduce the risk of soreness, subjects will be asked to hydrate prior to experimentation. If soreness occurs, it will be very mild and dissipate shortly after onset. There is a potential for slight discomfort associated with the electrical current used during the stimulation. Stimulation pads will be placed on your leg to cause (stimulate) a muscle contraction. This will make your leg feel tingly but will not reach a level that is painful.

Dimensional Apathy Scale (DAS): This may pose a minimal psychological risk. Participants may be embarrassed or upset when answering some of the questions. Before being sent the questionnaire, participants will be reminded that all data will be collected as coded information so participants can be at ease knowing their information and scores are confidential. They will also be reminded that there is no right or wrong answer and the questionnaire just helps us better understand their behaviour/feelings. If participants feel uncomfortable answering certain questions, they may skip the question(s).

Benefits to you if you take part in this study

You will help further Parkinson’s disease research and undergo a free DEXA scan that will provide you with information on fat and lean body mass.

Participants will also receive financial compensation. After completing visits 1 and 2, participants will receive $55. For those participating in the longitudinal study (explained on page 7), $15 will be given for months 2, 6, and 10, and $30 for months 4, 8, and 12. An additional $25 will be given to participants who complete all visits in the longitudinal study.

What will happen to the data that are collected?

If you are deemed not eligible to take part in the project, all paper copies of the screening data will be destroyed. Your personal information will be secured using participant ID Codes on all correspondence. Data will be kept on a password- protected computer or in a locked cabinet on site. All de-identified data will be stored indefinitely and may be used in future research involving genetic variations and cardiovascular responses.

All data will be stored electronically in databases with access only granted to investigators named above. Philip Millar, PhD, Associate Professor will be in charge of data stewardship. The master list of data will be secured for the duration of the study and 5 years post study completion. After the 5-year period, this list will be destroyed. Only the principal investigators will have access to the master list. Anonymized data may be made available through Open Access.

Results will be provided to participants upon their request.

What costs are there to you if you enter this study?

No direct costs are required to participate. However, participants will be responsible for travel costs (i.e. gas costs, taxi costs, etc.). Researchers will pay for on-campus parking to anyone driving to the lab.

What to do if you want to withdraw from this study?

You may choose whether to be involved with this study or not. If you volunteer, you may withdraw by notifying the study investigators at any time without consequence. You may exercise the option of removing your data from the study up until January 2026 or one week after study completion. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise that warrant doing so.

Rights of Research Participants

This project has been reviewed by the Research Ethics Board for compliance with federal guidelines for research involving human participants.

If you have any questions regarding your rights and welfare as a research participant in this study (REB *#1256*), please contact: Manager, Research Ethics; University of Guelph; reb@uoguelph.ca; 519-824-4120 ext. 56606.

You do not waive any legal rights by agreeing to take part in this study.

SIGNATURE of RESEARCH PARTICIPANT

I have read the information provided for the study "Investigating the relationship between performance fatigability and Parkinson's disease related fatigue" as described herein. My questions have been answered to my satisfaction, and I agree to participate in this study. I have been given a copy of this form.

_____

Name of Participant (please print)

_____ _____

Signature of Participant Date

Additional information

Please check any of the following and provide your preferred contact information below:

☐ I am interested in receiving feedback from the study results once published.

☐ I am interested in being contacted for future studies.

Email:_____

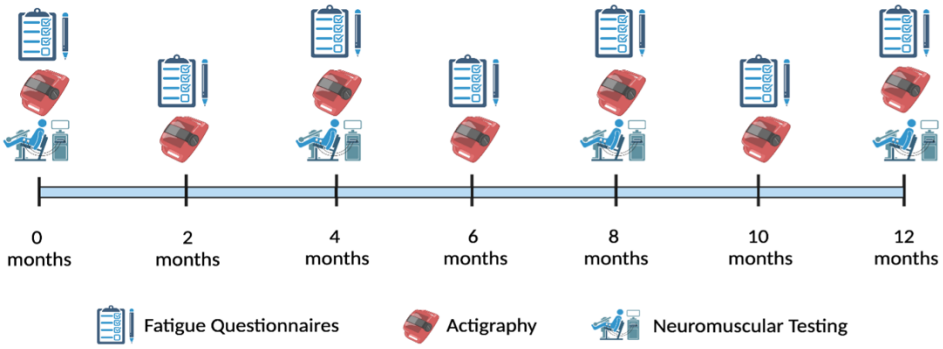
Phone:_____

Address: _____

Additional Consent for Longitudinal Participation

Purpose of Longitudinal Participation:

As part of this research study on perceived fatigue and performance fatigue, we are also interested in understanding how fatigue fluctuates over the course of one year. To gain a more comprehensive understanding, we invite you to participate in this study across multiple time points to assess how changes in sleep, anxiety, depression and physical activity can affect fatigue. This will involve repeating the same study visits at regular 2-month intervals. An experimental timeline is shown below.



Yes, I am interested in participating in the following additional time points.

☐ 2 months ☐ 4 months ☐ 6 months

☐ 8 months ☐ 10 months ☐ 12 months

I understand that I am free to withdraw at any time for any reason.

SIGNATURE of RESEARCH PARTICIPANT

I have read the information provided for the longitudinal portion of the study "Investigating the relationship between performance fatigability and Parkinson's disease related fatigue" as described herein. My questions have been answered to my satisfaction, and I agree to participate in this study. I have been given a copy of this form.

_____
Name of Participant (please print)

_____ _____
Signature of Participant Date

Appendix

Phone Screening *(total time: 15-30 mins)*

If an individual contacts a member of the research team and indicates an in interest in learning more about the study and/or is interested in participating in the study, we will conduct a brief phone screening to ensure eligibility. This will include a review of the inclusion/exclusion criteria for the participants and will also provide instructions for potential participants (e.g. bring shorts and t-shirt to the testing session at the University). If interested and eligible, an appointment to complete their first visit.

DAY 1 *(total time: 30 minutes)*

You will be asked to visit the Animal Science building (ANNU) where one of the researchers will bring you up to ANNU 313 to fill out consent forms and take anthropometric measures. Then you will be walked over to the HHNS Annex building (Annex 279) complete a DEXA scan which will measure fat and lean body mass. Once the scan is complete, participants will be given an Actigraphy monitor to wear around their waist for one week prior to coming in for their second visit.

Dual-energy X-Ray Absorptiometry (DEXA): Dual-energy X-Ray Absorptiometry (DEXA) is used by researchers and clinicians to determine body composition (e.g. bone density, lean & fat mass) and involves exposure of participants to radiation. Each time this procedure is performed the radiation dose to the subject is 0.025mSv. A millisievert is a unit used to measure radiation dose to people. This is less than daily dose of radiation that a person receives from a variety of different sources and is small fraction of the dose received with a single chest x-ray (approximately 10mSv). The scan has also been correlated to spending 2 hours in direct sunlight. One DEXA scan is less radiation than the amount received during an average airplane flight. To put this risk in context, the risk of developing fatal cancer is 400 in 2000 or approximately 20%; following one DEXA examination this risk will increase by a fraction of 1%. *(Cancer risk figures from US Food and Drug Administration Center for Devices and Radiological Health, update 17th April 2002).*

Physical Activity monitoring (Actigraphy): An Actigraphy monitor is a non-invasive method used by researchers to measure physical activity and sleep. The monitor contains an accelerometer which measures waves of movements. It is typically worn on the wrist, ankle or waist. For this study, participants will be asked to wear it on their waist which can be fastened in place with a strap. All participants will wear the monitor for 7 days to get a better sense of each participant's daily physical activity level. The monitor will only be removed if the participant needs to shower, as the actigraphy monitor is not waterproof, or at the end of the 7 days. Participants will also be required to fill out a given sleep and activity log to cross check information from the actigraphy monitor. Actigraphy monitor placement is show below.

Pulse Oximetry: For one night, we will also ask participants to wear a take-home nocturnal pulse oximeter. This device, which is shown below, will help us to accurately measure oxygen saturation levels throughout a night of sleep to assess for obstructive sleep apnea (OSA).

Day 2 *(total time: 120 minutes)*

PD Participants will be brought to ANNU 276 where they will begin by completing the UPDRS. PD and control participants will be required to complete all other fatigue, sleep and depression questionnaires prior to coming in for their second visit. Participants will also be asked to complete measurements of strength and power of the quadriceps using a dynamometer in ANNU 276.

Dimensional Apathy Scale (DAS): Participants will be asked to answer 24 questions about how they've felt over the last month. This will help researchers understand participant's feelings of apathy.

Pittsburgh Sleep Quality Index (PSQI): Participants will be asked to respond to 9

questions about their sleep habits over the past month. This will help gauge an understanding of their recent sleep quality and habits.

Epworth Sleepiness Scale: This scale will provide you 8 situations in which you will be required to rate on a scale of 0-3 to determine how likely you are to fall asleep during those activities. This scale is used to help diagnose sleep disorders.

STOP-Bang: This is a tool used to help assess risk for moderate to severe obstructive sleep apnea (OSA). It will ask 8 questions, four about participant symptoms and four about demographic information.

Patient Health Questionnaire (PHQ-9): It will list 9 statements that you will answer based on how often they have been bothering you in the last 2 weeks. This questionnaire helps to understand the depression severity of an individual.

Generalized Anxiety Disorder 7-Item (GAD-7): It will list 7 statements that you will answer based on how often they have been bothering you in the last 2 weeks. This questionnaire helps to understand how anxious someone may be.

Parkinson's Disease Fatigue Scale (PFS-16): You will be asked to provide responses to 16 written questions that aim to understand your level of fatigue. You will complete this paper survey on your own.

United Parkinson's disease rating scale (UPDRS): You will be asked to provide responses to 50 written questions that aim to understand the severity of motor and non-motor symptoms of Parkinson's disease. You will complete this survey with a researcher whom is trained in administering this test.

Fatigue Assessment Scale (FAS): Participants will be asked to rate on a five point scale from "Never" to "Always" their responses to a 10-item scale evaluating symptoms of chronic fatigue.

Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F): The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) is a 40-item measure that assesses self-reported fatigue and its impact upon daily activities and function.

Multidimensional Fatigue Inventory (MFI): The MFI is a 20-item scale designed to evaluate five dimensions of fatigue: general fatigue, physical fatigue, reduced motivation, reduced activity, and mental fatigue.

Muscle strength and power testing: You will be asked to sit in a Humac Norm Cybex Dynamometer (pictured below). You will be supported around the shoulders and hips, with seat belts immediately when seated to reduce any chance of injury from falling. The dynamometer is used to quantify all the strength measures required throughout the duration of all testing. All contractions are completed while seated and properly harnessed in the dynamometer. All contractions are separated by 3 minutes rest except for the fatigue protocol when you are required to hold/perform a static or dynamic muscle

contraction for as long as you can. Once you voluntarily end the fatigue protocol, we will track your recovery of muscle strength.

Full view of the Cybex dynamometer as set up in ANNU 276.

To test your muscle strength and contractile properties of your muscle we will be using a brief electrical stimulation which produces an involuntary contraction. The stimulation is transmitted through the skin to the nerve that innervates the muscle of interest or through pads which are placed on the muscle. The stimulation resembles a mild to moderate tingling sensation. Surface electromyography is recorded from electrodes (adhesive pads) on the surface of the skin and is not associated with discomfort. The electromyography pads are placed on the belly of the muscle. The measurement of muscle activity through the use of surface electrodes requires the electrodes to be placed directly on bare skin. You will complete a brief 5 second maximal isometric contraction, after which you will perform a series of dynamic contractions at a range of 20% to 100% MVC to measure power output and fatigability. All of these procedures require attire similar to that of an exercise class, therefore we ask you to wear (or bring with you) shorts. If you do not own these, the lab will provide clean clothing for you to wear during your visit.