

Spring 2024 Request for Applications Freezing of Gait (FOG) in Parkinson's disease Research Program

Request for Applications Overview

- This funding program aims to advance knowledge of Freezing of Gait
- Only accepting clinical pre-proposal applications
- Open to multi-centric studies with cross-disciplinary teams



BACKGROUND

Parkinson's disease (PD) affects nearly 1 million people in the US and over 8 million worldwide, and those numbers are expected to rise over the coming decades. PD is highly heterogeneous: individuals experience a wide array of motor and non-motor symptoms, many of which depend on disease severity and duration. Though our understanding of PD and its causes is growing, many questions remain. There are no drugs available for Parkinson's that alter the progression of the disease, and current symptomatic treatments provide limited relief but come with complications and side effects.

The Michael J. Fox Foundation (MJFF) funds research to better define, measure, and treat Parkinson's disease as well as critical tools and other resources to advance related research.

Freezing of gait (FOG) is one of the most debilitating, yet difficult to assess gait impairments in Parkinson's disease. It is defined as "brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk". FOG drastically reduces the quality of life, increases the risk of falls, and results in a loss of independence of people with PD.

The pathophysiology that underlies FOG is not well understood hence the treatment of freezing of gait remains particularly challenging. Multiple theories have been proposed to explain the underlying mechanisms, with motor, sensory, cognitive, and affective impairments all implicated. Laboratory protocols including the use of reported behavioral triggers such as turning, traversing narrow passages, cadence manipulations, and obstacle avoidance have provided important

insights into the variability in the pathophysiology of freezing. Yet, these in-clinic protocols are often simulated and are not representative of everyday situations. Freezing of gait can be classified as responsive, resistant, or induced by dopaminergic medication, suggesting the existence of subtypes. Assessment in everyday conditions and the development of criteria for the identification of subtypes of FOG might lead to better understanding of the problem and treatment for it. Although there is some evidence that FOG can be evaluated and measured ecologically, at least to some degree, the multiplicity of triggers and heterogeneity of presentation of this symptom makes its prediction challenging. In the absence of objective measures and an understanding of the problem, therapy and prevention have been suboptimal.

To this end, MJFF is issuing a Request for Applications (RFA) for clinical studies that can address the critical challenges and foster the understanding of the pathophysiology and biological correlates of FOG and balance disorders in people with PD and identifying suitable therapeutic approaches.



PROGRAM GOAL

The FOG Research Program seeks to support clinical proposals that address FOG and balance disorders on multiple levels.

Funding will support projects that aim to

- Develop and validate new study designs, measurements and outcome assessments for FOG
 - Studies may include but are not limited to: Evaluating new methods to assess/predict FOG; improving/ validating objective clinical assessment of FOG; identification of FOG at home using wearable technology; assessment of gait or behavioral changes alluding to imminent FOG etc. Applications are invited to align with the FDA Patient-Focused Drug Development Guidance on the approaches to collect and use robust and meaningful patient and caregiver input.
- Advance understanding of pathophysiological mechanisms of FOG
 - Studies may include different imaging techniques or electrophysiology to better understand the mechanisms of FOG, neural involvement, and impact. Studies proposing analysis of large available datasets for better understanding and classifying sub-types of FOG will be considered. Animal studies will not be considered in this specific call.
- Conduct interventional studies testing therapeutic strategies to alleviate FOG, improve mobility, and/or reduce falls
 - Studies could include neuromodulation, pharmacological or non-pharmacological (including technological) interventions. Please note that the approach should be

novel (i.e., cueing interventions have been previously funded with moderate success and therefore are not a priority), appropriately powered (pilot studies will not be funded) and reproducible. Studies exploring intensity and dosing of novel or established techniques will be considered.

Relevant projects include hypothesis-driven clinical projects. All projects should be sufficiently powered, thus proposed studies suitable for funding should have compelling data from human pilot studies. For this round, MJFF **will not consider** applications for pre-clinical or animal studies.



PROGRAM PRIORITIES

When considering proposals submitted to this program, MJFF prioritizes those with the strongest potential to advance knowledge of and treatment for FOG. Priority will be given to studies fulfilling the following criteria:

- Multi-centric studies that foster a comprehensive approach or facilitate longitudinal work in function of early detection and prevention
- Cross-disciplinary teams with collaborators from multiple areas of expertise (e.g. clinicians, pathologists, experts in imaging, statisticians/epidemiologists, etc.)
- Funded programs are willing to share data in a pre-competitive manner, to help progress the field (see Additional information section)



FUNDING AVAILABLE

Duration: 2 to 3 years

Award Amount: \$250,000 - \$2,000,000

MJFF research grants aim to de-risk selected therapeutic programs leading to faster progress and results, as well as increased chances of attracting follow-on investment. MJFF prioritizes opportunities to complement and share the costs of therapeutic development with like-minded partners with a current or new commitment to PD. As such we have a flexible approach to funding translational and clinical work that is guided by novelty, the stage of development and the overall priority of the unmet medical need for people with PD. The scope and budget for your study will be discussed with MJFF staff if invited to submit a full proposal and should be commensurate with the ultimate work proposed. In general, award amounts for this program

may range from \$250,000 for smaller, targeted programs to \$2M for larger, multi-centric clinical programs.

These budgets include direct and indirect costs. For academic and for-profit institutions, no more than 15% or 10%, respectively, may go to indirect costs. Additional details about MJFF's indirect cost policy can be found in the [Application Guidelines](#) and [FAQ](#).



DEADLINES & REVIEW SCHEDULE

The Gait Research Program works in **two stages**:

1. Applicants may **submit a pre-proposal** for initial consideration by MJFF. This stage is your first and best opportunity to determine if MJFF is the right partner for you.
 2. Applicants whose pre-proposal is selected for further consideration **will be invited to submit a full proposal**. Invited applicants will have the opportunity to consult with MJFF on proposal development.
- Pre-proposals Due: Sept 26, 2023, 5 p.m. US ET
 - Full Proposal Invitations: Week of November 17, 2023
 - Full Proposals Due (by invite only): January 11, 2024, 5 p.m. US ET
 - Anticipated Award Announcement: April, 2024
 - Anticipated Funding: April, 2024

Applicants are encouraged to apply early to allow adequate time to correct errors found during the submission process.



ELIGIBILITY REQUIREMENTS

Applications may be submitted by researchers or clinicians in:

- U.S. and non-U.S. biotechnology/pharmaceutical companies, or other publicly or privately held for-profit entities; and
- U.S. and non-U.S. public and private non-profit entities, such as universities, colleges, hospitals, laboratories, units of state and local governments and eligible agencies of the federal government.
- Post-doctoral fellows are eligible to apply as co-investigators with the designation of an administrative primary investigator who directs the laboratory in which the fellow will conduct research. The administrative PI will be responsible for assisting in providing all

institutional documents required for the project and will be required to sign any award contract. Training or mentoring-only proposals will not be considered.



DIVERSITY, EQUITY AND INCLUSION (DEI)

In pursuit of our mission to accelerate the development of better treatments and a cure for Parkinson's disease, MJFF aims to support a rigorous research agenda reflecting a wide and diverse range of perspectives on Parkinson's disease and carried out in diverse populations. Diversity may refer to characteristics including, but not limited to, race, religion, ethnicity, sex, gender identity, sexual orientation, socioeconomic circumstance, nationality, geographic background, ability and disability, political ideology and age. Parkinson's is a complex problem; the more angles from which we attack, the greater the chances of finding innovative scientific solutions to benefit everyone living with the disease. As such:

- The Foundation encourages applications from diverse investigators representing groups historically underrepresented in the research enterprise.
- Because research shows that diverse teams outperform homogeneous ones, we urge applicants to share information about the composition of the team that will carry out the funded work.
- Proposed work should seek wherever possible to include relevant diversity, such as inclusion of sex/gender in preclinical studies and inclusive recruitment in clinical studies.



ADDITIONAL INFORMATION

The [Application Guidelines](#) provide general guidance on applying for funding from MJFF, though the Request for Applications always supersedes information contained in the Application Guidelines.

With a long-term goal of standardization and enabling the merge of gait data from different studies, all funded projects will be asked to share their collected data with MJFF and the PD research community. MJFF holds an [open access publication policy](#) requiring articles resulting from MJFF-funded work to be published in a preprint repository, then in an open access forum with free and immediate readership rights.

For any gait study funded by MJFF, the foundation recommends a minimum set of data to accompany gait protocols (including basic demographics and clinical data), and a minimum gait

protocol of at least 1-minute of walking in a straight-line path of 10m with 180 degrees turns to be performed at a comfortable speed. In addition, the committee also recommends adding additional challenging conditions such as fast-paced walking or dual task to enable comprehensive assessment of mobility. Investigators should specify the approach(es) / technology proposed to collect quantitative gait outcomes and provide a detailed explanation for all data collected and the technical and clinical validation of proposed assessments. Gait speed, stride length, variability of stride time and swing time, turning velocity, and a measure of gait symmetry should be, at minimum, reported. These minimum data and protocol recommendations are intended to increase the utility of collected data for reuse by the PD research community and allow for more effective meta-analysis. Applicants are strongly encouraged to describe how they will align with the data and protocol recommendations. The pre-proposal template includes a table with further information.

MJFF requires that the Principal Investigator be the primary applicant (i.e., the person who initiates and takes primary responsibility for the application). All application-related correspondence will be sent to the Principal Investigator.

For questions about the application process or project suitability for this call for applications, please email grants@michaeljfox.org.