Summer 2025 Request for Applications: Personalized Approaches for Understanding, Assessing and Improving Gait in Parkinson's Disease Research Program

Overview

- This funding program aims to advance personalized approaches for understanding, assessing and improving gait in Parkinson's disease
- 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, there are no drugs available that alter the progression of the disease. 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 PD as well as critical tools and other resources to advance related research.

Gait disturbance is a cardinal feature of PD, which is also associated with reduced mobility. Gait impairments can appear as an early clinical sign and typically progress throughout the course of the disease, increasing the likelihood of falls and resulting in higher rates of hospitalization and mortality. People with Parkinson's rank gait impairments as highly important and burdensome with a clear negative impact on their quality of life.

There is a great deal of variance between patients in the presentation and development of gait impairments across the disease continuum. This stems from both the complexity of the neural control and execution of movement, as well as the individual rates and characteristics of disease progression. While gait is mostly automatic, we know that gait in PD is a multifaceted task in which cognitive resources continuously monitor bilateral coordination and dynamic postural control, both necessary for the walking process. Studies have reported interactions between gait disturbances in PD and disease-specific progression, burden of cognitive and other non-motor symptoms and age-related changes, as well as environmental and behavioral aspects. Understanding the complexity and interactions between multiple domains (i.e., motor, cognitive, limbic) that affect the gait pattern of an individual with PD is fundamental for personalized clinical decisions and providing the most suitable treatment.

PD related disturbances in gait and posture are so far partly resistant to drug treatment, highlighting limitations of current dopaminergic therapy and the need to develop pharmacologic and non-pharmacological interventions targeting gait decline. In recent years, it has become increasingly clear that "one size does not fit all" with respect to addressing gait disturbances in PD, specifically due to the large variance between patients and the variance in progression of symptoms. Therefore, interventions should be tailored to a specific phenotype or individual symptoms, encompassing multiple aspects affecting gait. Non-pharmacological interventions, which have shown to improve gait and motor-cognitive functions to a certain degree, may offer unique opportunities for partial personalized prescription.

To this end, MJFF is issuing this Request for Applications (RFA) for clinical studies that promote understanding of gait disturbances in PD toward development of personalized treatments for patients across the continuum of disease.

PROGRAM GOAL

The personalized approaches for understanding, assessing and improving gait in PD Research Program seeks to support clinical research proposals. Preclinical applications will not be considered. Proposals should delineate how the expected results directly contribute to more precise understanding and detection contributions to individualized gait impairment in PD. Proposals evaluating both motor and cognitive contributors to gait disturbances will be prioritized as will proposals with direct applications for development of personalized treatments.
Funding will support projects that aim to:

- **CLEARER DEFINITION** | Advance understanding of the multifaceted pathophysiological mechanisms of gait impairments in PD to help design personalized treatments. Studies may include:
  - Novel imaging or electrophysiological techniques to better understand the interconnectivity of neural mechanisms underlying gait.
  - Understanding the involvement of nonmotor disease features, specifically cognitive and limbic changes, in progressive gait impairment.
  - Studies proposing analysis of large existing longitudinal datasets will be considered if the analysis provides a unique approach to personalization
- **SENSITIVE MEASURES** | Develop or deploy unique assessments to derive metrics to advance development of individualized or on-demand treatment of gait impairments. Studies may include but are not limited to:
  - Develop or validate new study designs/ measurements/ outcome assessments that incorporate multifaceted domains, a holistic approach, to gait impairments that could lead to prescribing personalized treatments.
  - New methods to assess/ predict meaningful declines in gait.

- o Defining outcome measures to assess and understand patient variance in gait, including the impact of non-motor behavioral features of disease that can impact real world gait .
- o Designing and testing a decision tree for physical therapy to address PD gait impairments (i.e., models of signs and symptoms severity reflecting patient variance), which can be used for prescribing / administering treatments, predicting treatment outcomes or defining treatment progression.

- **BETTER TREATMENTS** | Conduct interventional studies testing personalized interventions to reduce or delay gait impairments in PD. Priority will be given to approaches that target both motor and nonmotor contributors to gait disturbance.
  - o Non-pharmacological interventions or neuromodulation techniques, including adaptive interventions (i.e., closed loop).
  - o Approaches to facilitate long-term patient adherence to personalized therapies addressing gait disturbances and impairment.

Applications can cover one or more of the outlined pillars. Please note that the approach should be novel, hypothesis-driven, specifically address personalization, appropriately powered (pilot studies will not be funded) and reproducible.

All projects should include compelling preliminary data from human pilot studies. For this round, MJFF **will not consider** applications for pre-clinical/ animal studies.

PROGRAM PRIORITIES

When considering submitting a proposal to this program, MJFF prioritizes those with the strongest potential to advance knowledge. Priority will be given to studies that are:
- Multi-centric, fostering a comprehensive approach or facilitating longitudinal work
- Cross disciplinary with collaborators from multiple areas of expertise (e.g. clinicians, pathologists, experts in imaging, statisticians/epidemiologists, etc.)
- Willing to share data in a pre-competitive manner to help progress the field.

FUNDING AVAILABLE

Duration: 24 - 36 months
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: **January 14, 2025**
    - Full Proposal Invitations: **March 7, 2025**
    - Full Proposals Due (by invite only): **May 6, 2025**
    - Anticipated Award Announcement: **Week of August 11, 2025**
    - Anticipated Funding: **August 2025**

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. Please see further details in the pre-proposal template. 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.

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.