Moving Mindfully for Freezing in Parkinsons

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Moving Mindfully: AIM 1/AIM 2 Protocol/SAP

RESEARCH DESIGN AND METHODS

Aim 1: Create a Mindfulness-Based Walking Therapy (MBWT) program by modifying the MBSR standard protocol based upon feedback from an advisory group. An advisory group consisting of physical therapists, mindfulness instructors, research team members, 3-5 people with PD+FOG and their care partners will provide input regarding adaptations needed to make the standard MBSR program acceptable and feasible for people with PD+FOG and to shift the focus from sitting, standing, or lying meditations to walking mediations.

RATIONALE

The use of an advisory group is a collaborative and valuable research tool that will provide integrated insight to modify the standardized MBSR protocol.

DESIGN

We will recruit 3-5 people with PD+FOG and their care partners and schedule a series of collaborative meetings with team members including the research physical therapist and mindfulness instructors to: 1) modify the MBSR program by replacing sitting, lying, and standing meditations with walking mediations and ensuring the content is appropriate and clear for people who have PD+FOG; and 2) finalize a protocol that will include the MBSR Standards of Practice (SOP). To facilitate these goals, the advisory group will convene once a week for eight weeks that will include discussions about FOG knowledge, existing mindfulness training in PD and older adult literature, inclusion/exclusion criteria, outcome and feasibility measures, and technology usage for tracking adherence. An outline for these objectives is included in the Narrative Study Description.

People with PD+FOG will also be asked to participate in phone interviews to ask questions about their history with FOG and anxiety using questions on the FOG and Anxiety Questionnaire. Information from this interview will provide information about how participants describe and experience FOG and anxiety in their own words and what different scenarios or environments tend to elicit FOG.

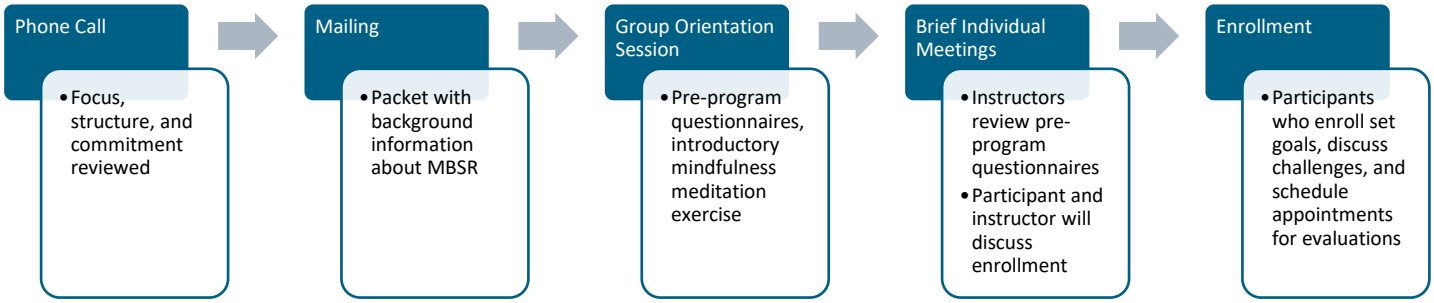
A Mindfulness-Based Stress Reduction Workbook. We will use the MBSR Workbook to facilitate the program. The MBSR Workbook follows the teachings and SOP written by Jon Kabat-Zinn and includes both formal and informal practices to better understand and learn mindfulness. There are places to journal, self-reflect, and schedule time to practice mindfulness. Members of the advisory group will receive a copy of the workbook to review for two main purposes: 1) exchange meditations that include sitting, lying, or standing mindfulness practices with walking meditations; and 2) ensure the meditations are appropriate and clear for our population. We will follow the recommendations on how to use the MBSR workbook and include the majority of the current mindfulness practices that are included to ensure adequate mindfulness training. The MBSR Workbook currently includes one walking meditation and the advisory group will create additional walking meditations that address situations that are difficult for people living with PD+FOG. For instance, turning is a frequent occurrence in our daily lives. Additional walking meditations to be proposed will include using mindfulness for complex walking scenarios such as places with large crowds, places that require quick movements such as getting on or off an elevator, walking through narrow spaces and doorways, and surfaces that change (i.e., tile to carpet). Walking mediations that require stopping and starting frequently could address freezing that occurs at gait initiation.

MBSR Standards of Practice (SOP). The MBSR SOP was written by Jon Kabat-Zinn at the Center for Mindfulness in Medicine, Health Care & Society and the University of Massachusetts's Medical School. The SOP includes three main sections that outline the minimum standards required to be considered a MBSR program:

Background and Overview: Presents the fundamental values of MBSR and reflects the methodical, yet flexible, approach of mindfulness training. These values include embracing mindfulness as a positive and educational lifestyle change, incorporating it into daily practice, and the importance of living in the present moment.

Structure and Methods: Presents the outline of successful MBSR programs which includes a pre-program orientation session, eight weekly classes 2.5 hours in duration, an all-day silent retreat during the sixth week of the program (7.5 hours), specified mindfulness mediations methods (i.e., body scan, gentle hatha yoga, sitting mediation, and walking mediation) and practices (e.g., deliberate awareness during routine activities and events such as eating or walking), daily home assignments (e.g., journaling, reading), individual and group dialogue, and exit assessments including a participant self-evaluation. The total in-class contact is 30 hours and total home assignments is a minimum of 42 hours.

Program Standards: The MBSR SOP includes the following pre-program initiatives to ensure participants are familiar with their upcoming involvement. The Program Standards also reviews screening criteria, learning contract, and curriculum guidelines.



Participants are given a Session Evaluation form after each session and the Client Satisfaction Questionnaire (CSQ)[83] to complete at the end of the program, both of which provide Likert-scale questions to be used in the feasibility benchmarks and open-ended questions to provide qualitative data to evaluate and refine the meditations, instructions, and study procedures.[82,84] Insights from these questionnaires and the exit interview will also be used to explore response distributions such as skewness, floor/ceiling effects, or missing data.

The advisory group will be employed to address each of these sections in the MBSR SOP and determine which areas may need modification. Based on our knowledge of working with people with PD+FOG and preliminary studies of MBSR with older adults or people with Parkinson disease, we anticipate changing the all-day silent retreat (7.5 hours) to a half-day retreat (3.5 hours).

Review outcome measures for clarity and burden. We will present the following outcome measures to the advisory group for review.

Functional Measures. The New Freezing of Gait Questionnaire (NFOG-Q) assesses types of freezing and severity for the past month.[86] The StepWatch™ Activity Monitor (SAM)[87] will be worn on the ankle by participants 24 hours per day for seven consecutive days after each evaluation to record number of daily steps. Motor systems will be assessed using the Movement Disorders Society Unified Parkinson's Disease Rating Scale-III (MDS-UPDRS-III), an 18-item questionnaire that provides an index of motor severity.[88] Balance will be assessed with the Mini-Balance Evaluations Systems Test (Mini-BEST).[89] Participants are asked to stand on one leg, stand on the ground and foam surfaces, and walk while performing different tasks. During the in-person assessments, participants will also wear APDM's Mobility Lab sensors[90] and perform several tests including the Timed Up and Go and the two-minute walk test. These inertial sensors provide detailed spatiotemporal data regarding gait.

Mindfulness Measures. The Revised Cognitive Affective Mindfulness Scale (CAMS-R) has 12 items to assess how participants relate to their thoughts and feelings in relation to attention, awareness, present-focus, and acceptance/nonjudgment in order to achieve an overall mindful state.[91]

Psychological Measures. The Hamilton Anxiety Scale (HAM-A) is a 14-item questionnaire to analyze the symptoms and severity of psychic and somatic anxiety.[92] The Hamilton Depression Scale (HAM-D) is a 21-item questionnaire to analyze symptoms such as depressed mood, feelings of guilt, suicidal tendencies, and insomnia.[93] The Penn State Worry Questionnaire is a self-reporting measure with 16 items to index the amount of worry a person experiences.[94] The Parkinson Disease Questionnaire-39 (PDQ-39) is a 39-item self-report survey that provides information on the impact Parkinson disease has on the participant's quality of life.[95] Overall

physical, mental, and social health will be measured using the Neuro-QOL Battery, a self-reported assessment to analyze several domains including anxiety, stigma, depression, social interactions and the ability to do physical tasks while living with a neurological condition.[96] The Hamilton Anxiety Scale (HAM-A) is a 14-item questionnaire to analyze the symptoms and severity of psychic and somatic anxiety. The Hamilton Depression Scale (HAM-D) is a 21-item questionnaire to analyze symptoms such as depressed mood, feelings of guilt, suicidal tendencies, and insomnia.

Sense of Agency Measure. The Sense of Agency scale is a tool used to measure one's core agency by analyzing the extent to which someone believe to have control over their own body, thoughts, and the environment in order to become more aware of internal and external experiences.[67]

Cognitive Measures. To measure cognition, the NIH Toolbox will be used. Tests include 1) episodic memory with the Picture Sequence Memory Test; 2) working memory via the List Sorting Working Memory Test; 3) the Picture Vocabulary Test and Oral Reading Recognition Test to test language processing; 4) executive functioning via the Dimensional Change Card Sort Test; 5) processing speed using the Pattern Comparison Processing Speed Test and Oral Symbol Digit Test; and 6) the Auditory Verbal Learning Test (Rey) to assess immediate recall.

KEY FEASIBILITY ELEMENTS, EXPECTED OUTCOMES, AND BENCHMARKS

For this first aim, our expected outcomes include demonstrating successful start-up procedures including regulatory approvals, formation of the advisory group, modifications of the MBSR protocol, and standardization of the protocol to use in Aim 2.

For feasibility, we will monitor and track: 1) difficulties that arise during the start-up phase; 2) challenges with formation and meetings with the advisory group; 3) discussions and outcomes during each of the advisory group meetings to ensure objectives are met; 4) challenges that present as a result of modifying the MBSR protocol to focus on walking mediations; 5) comments from the advisory group regarding the outcome measures; and 6) comments regarding clarity of content in the MBSR workbook.

Benchmarks for Aim 1 include: 1) identification and recruitment of the full advisory committee with an initial meeting held within the first three months of the award; 2) complete initial review of all required elements (SOP, Workbook, Literature, Inclusion/Exclusion Criteria, Technology) within five months of initial meeting; and 3) have a final draft of the initial mindfulness-based walking training protocol for rollout in Aim 2 within twelve months of the first advisory committee meeting.

INCLUSION/EXCLUSION CRITERIA

Participants with PD will meet the following inclusion criteria:

- diagnosed by a neurologist with idiopathic PD;
- age 50 and older;
- history of freezing of gait;
- able to provide informed consent;
- able to walk independently with or without an assistive device for at least five minutes; and
- experience fear and/or worry in relation to their FOG.

Care partners of people with PD+FOG will meet the following inclusion criteria:

- able to provide informed consent; and
- able to walk independently with or without an assistive device for at least five minutes.

Participants with PD will be excluded if they have any of the following:

- evidence of dementia (Mini-Mental Status Examination < 24) to ensure understanding of materials;
- are under consideration for deep brain stimulation surgery within the next three months;
- neurologic condition other than PD;
- inability to cooperate with the protocol;

- history of orthopedic or other medical problems that limit ability to participate safely in the practice sessions; or
- language, visual, or hearing barriers to participation.

Care partners of people with PD+FOG will be excluded if they have any of the following:

- evidence of dementia (Mini-Mental Status Examination < 24);
- inability to cooperate with the protocol;
- language, visual, or hearing barriers to participation; or
- history of orthopedic or other medical problems that limit ability to participate safely in the practice sessions.

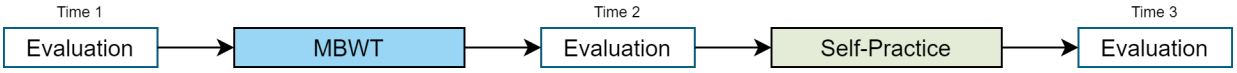
Aim 2: Refine and standardize the MBWT protocol to ensure feasibility and acceptability through open pilot testing. Twelve people with PD+FOG will participate in the open pilot MBWT program designed in Aim 1. After this open pilot the protocol will be modified based on participant feedback, safety, and satisfaction. Feasibility elements include meeting benchmarks for: recruitment and randomization; retention and satisfaction; delivery of the intervention; participant adherence using technology; evaluating clarity and burden of outcome assessments; and monitoring adverse events.

RATIONALE

Open piloting the MBWT will provide a better standardized MBWT intervention for use in Aim 3. We will be able to monitor the group of participants (n = 12) who receive the MBWT intervention and receive their feedback as well as input from the mindfulness instructors on how to ensure this intervention is prepared for the randomized controlled pilot in Aim 3 and for potential future effectiveness trials.

DESIGN

The new twelve-week MBWT group intervention will be tested in this aim, with modifications of the MBWT program and protocol from the advisory team.



After the participants are deemed eligible via the phone screen, they will be scheduled for their first evaluation (Time 1). Participants will then attend the pre-program orientation session, followed by the twelve-week MBWT program. There will also be a half-day retreat around week nine. Participants will be encouraged to attend all classes in-person in our lab space. However, in case of illness or other circumstances that prevent in-person attendance, the mindfulness instructor and research team member may speak to the participant to see if participating via a video conference platform is feasible, and if the participant is willing and able to do so. Participants will then be asked to complete the post-program evaluation (Time 2) and be encouraged to continue practicing mindfulness on their own, record practice time, and journal their usual care regimes during a second fourteen-week period (the fourteen weeks is to match the time they were in the intervention (pre-program orientation + twelve-week program + half-day retreat). They will then return for a follow-up evaluation (Time 3). There is not any standardized treatment for FOG, thus having participants record their usual care (i.e., health care visits and changes in medications) will provide information for future comparator conditions.

EXPECTED OUTCOMES AND BENCHMARKS – STATISTICAL ANALYSIS PLAN FOR FEASIBILITY STUDY

In addition to having a standardized version of the MBWT intervention and protocol by the end of year two to use in Aim 3, our feasibility aims and benchmarks include:

Ability to recruit our target sample. We estimate screening approximately 70 participants by phone to find 12 participants who meet inclusion criteria and agree to participate. These 12 participants will participate in the pre-program orientation. This anticipated screening rate of 35% is based on our recent interventions. We anticipate two people will decide not to participate after attending the pre-program orientation or Time 1 evaluation, leaving ten participants. We will track reasons for not continuing during the phone screens. *Benchmark:* (1) Recruit one person for every eight screened. (2) Recruitment of 12 participants.

Retention of participants and satisfaction with the intervention. We will collect data on why classes are missed and reasons for drop-outs, if any. Make up classes may need to be scheduled. The Session Evaluation form will provide data for the acceptability and satisfaction of each session. The CSQ will provide acceptability and satisfaction data on the program as a whole. Modifications to the protocol will be informed by these two measures as well as open-ended questions and exit interviews. *Benchmarks:* (3) Attendance and retention of participants, defined as at least 80% participants attending 80% of the sessions; (4) Session satisfaction defined as a minimum average rating of >0.5 on the Session Evaluation Form; and (5) Program satisfaction as a minimum average rating of >1.5 on Client Satisfaction Questionnaire (CSQ).

Participant adherence. Adherence for home practice will be monitored using a tablet (iPad mini) that will prompt the participants daily. The prompts will ask how many minutes they practiced mindfulness today. *Benchmark:* (6) Home practice adherence, at least 70% of participants will complete at least 70% of the daily home assignments during the active intervention period. Number of home practice hours is 20 hours over the course of the mindfulness intervention. (7) Maintenance of practice, at least 50% of participants will report continued engagement in mindfulness practices during the fourteen-week follow-up period.

INCLUSION/EXCLUSION CRITERIA

Participants with PD will meet the following inclusion criteria:

- diagnosed by a neurologist with idiopathic PD;
- age 50 and older;
- a score on the Hoehn & Yahr (H&Y) scale between I-IV;
- history of freezing of gait;
- able to provide informed consent;
- able to walk independently with or without an assistive device for at least five minutes;
- experience fear of falling, frustration, irritation, anxiety, and/or worry in relation to their FOG; and
- stable medication regimen for one month prior to enrollment.

Participants with PD will be excluded if they have any of the following:

- evidence of dementia (Montreal Cognitive Assessment-T < 13) to ensure understanding of materials;
- are under consideration for deep brain stimulation surgery within the next six months or have had DBS surgery within the past six months;
- major depression disorder or post-traumatic stress disorder without permission from health provider to participate;
- neurologic condition other than PD;
- inability to cooperate with the protocol;
- language, visual, or hearing barriers to participation; or
- history of orthopedic or other medical problems that limit ability to participate safely in the intervention.

DATA MANAGEMENT AND POWER ANALYSIS

Data management resources will include developing forms to use for the feasibility aims and entering data into REDCap. Dr. Rawson has experience with development of REDCap databases for multiple studies, enforcing standard operating procedures, and data monitoring. She has excellent methods for reducing the potential for data errors through smart design of measures and data entry procedures. As this is a feasibility study, a formal power analysis was not conducted. We have adopted statistically efficient designs that control for baseline status (Aims 2 and 3) and selected measures that are reliable and valid among people with PD. We elaborate on this choice in the Statistical Design and Power document. We have a target sample size of 12 people per group (allowing for attrition to n = 10) based on previous studies delivering the mindfulness intervention, discussion with the mindfulness instructors, recommendations in the MBSR standard operating procedures, as well as our knowledge of delivering group-based interventions for people living with PD.

STUDY TIMELINE

Study Milestones	Year 1	Year 2	Year 3
Obtain IRB Approval	X		
Recruit 3-5 Participants to form Advisory Group	X		

Advisory Group Committee Meetings	X		
Finalize Study Procedures/MBWT Protocol	X		
Obtain IRB Approvals on updated Protocol	X		
Aim 2: Participant Recruitment for Wave 1 and 2	X		
Aim 2: Participant Assessments		X	
Aim 2: MBWT Intervention Wave 1 and 2		X	
Aim 2: MBWT Modifications after Wave 1 and 2		X	
Aim 3: Participant Recruitment (MBWT & UC)		X	
Aim 3: Participant Assessments (MBWT & UC)			X
Aim 3: MBWT Intervention and UC			X
Aim 3: MBWT Modifications			X
Feasibility Reports			X
Dissemination via Manuscript Submission			X
Submission of Subsequent Grant Application			X

Abbreviations: MBWT, Mindfulness Based Walking Therapy; UC, Usual Care

STUDY TIMELINE JUSTIFICATION

The first year of the study will be devoted to obtaining IRB approval, forming the advisory committee, and creating the first draft of a MBWT program by modifying the standard MBSR protocol to focus more specifically on walking (Aim 1). In the second year, we will conduct the open pilot study (Aim 2), allowing time between waves to evaluate results and make adjustments to the MBWT intervention after each iteration. The final year will be devoted to piloting of the finalized MBWT intervention and comparing it to usual care in a randomized controlled pilot study (Aim 3). We will utilize results obtained to inform future effectiveness trials and mechanistic studies and plan to submit a grant to support the next steps in this line of research by the end of the third year.