Digital mobility sub-study in the Parkinson's Progressive Marker Initiative (PPMI) study.

Anat Mirelman[1]; Tanya Simuni[2]; Caroline Tanner[2]; Emily Flagg[4], Ana Lorenzo[4], Jessica Dimos[4], Christopher Coffey[5]; Andrew Siderowf [6]; Kenneth Marek[4] and The Parkinson's Progression Markers Initiative

[1]Tel Aviv Medical Center, Tel Aviv University, Israel; [2]Northwestern University Feinberg School of Medicine, IL, USA; [3]Weill Institute for Neurosciences, UCSF, CA, USA; [4]Institute for Neurodegenerative Disorders; CT, USA; [5]University of Iowa, IA, USA; [6]University of Pennsylvania, PA, USA; and The Michael J Fox Foundation for Parkinson's research.

1 INTRODUCTION

PPMI places great emphasis on identifying prodromal cohorts. Despite the centrality of motor dysfunction in Parkinson's Disease (PD), current motor assessment largely relies on clinical rating scales lacking sensitivity to subtle motor changes in the prodromal stage. Previous work using digital technology and wearable sensors was able to capture subtle gait and mobility changes approximately 3-4 years prior to diagnosis. Building on this work, the digital mobility sub-study will augment the digital platform utilized in PPMI focusing on gait and mobility both in-clinic and in the home environment.

Study objective: To test the feasibility and validity of digital mobility data for enrichment of the prodromal screening and to assess the sensitivity of these measures to early phase progression in prodromal and recently diagnosed patients with Parkinson's disease.

2 METHODS

Two-hundred prodromal subjects enrolled in PPMI will be invited to participate in this longitudinal sub-study. Assessments will be performed annually over 3 years.

During the in-clinic visit, participants will undergo a structured gait assessment while fitted with 3 wireless wearable sensors on both wrists and on the lower back (Opals, APDM Ltd.).

The protocol includes the Timed Up and Go test and two walking trials (preferred speed and dual task) each of 1 minute.

Participants will also receive an additional sensor (Axivity Ltd. AX6) to be worn on their lower back for continuous monitoring (24/7) for one week (Figure 1).

Data obtained from this sensor will include activity, mobility measures collected in the real-world and nocturnal movements.

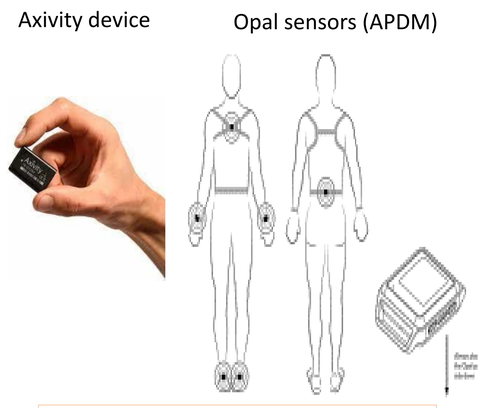
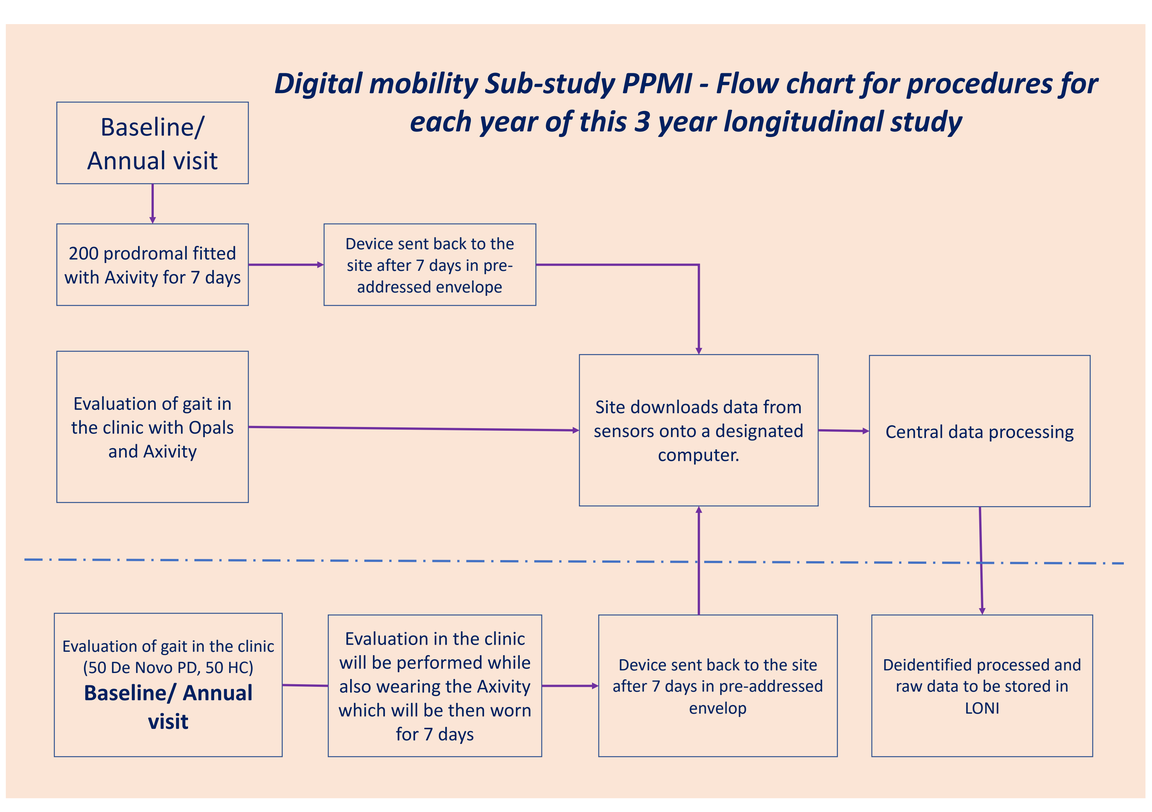


Figure 1: The wearable sensors used in the study.

We will also recruit 50 recently diagnosed patients with PD (<2 yrs.) and 50 healthy controls to undergo the same protocol. These subjects will serve as reference groups for the analysis of gait in the prodromal stage. The study design and procedure flow chart is presented below (Figure 2 below).



3 RESULTS

- The first participant was recruited in March 2023. Recruitment to date includes 21 participants.

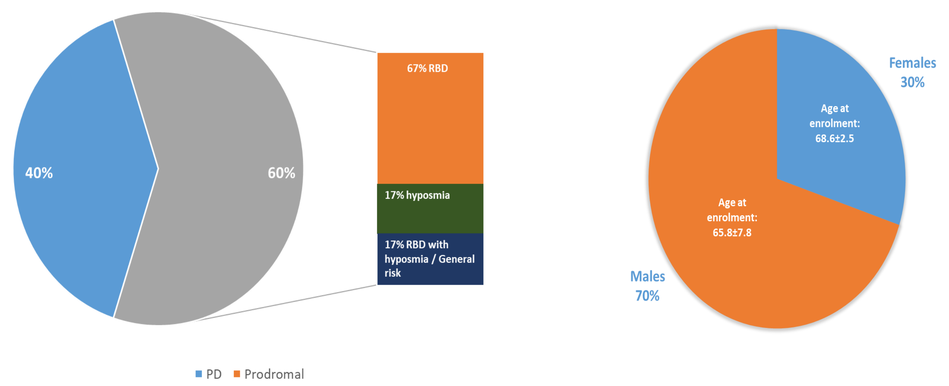
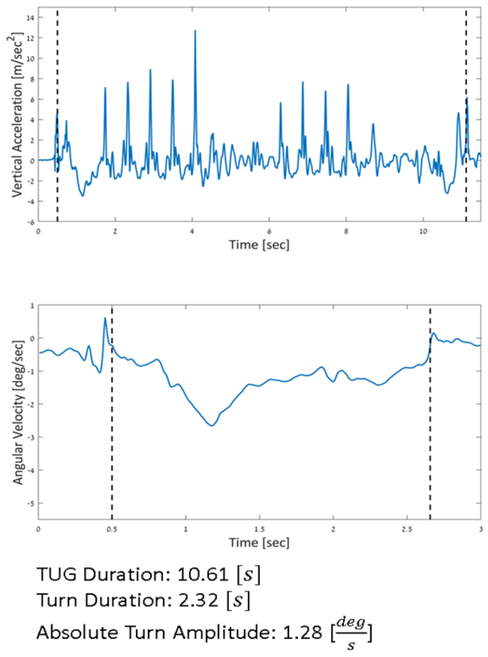


Figure 3: Participants characteristics from available data

- All participants were able to complete the protocol.
- Data collected from real world includes on average 6.2±0.3 days reflecting high adherence and motivation.
- Interim analysis is planned after 50 participants are included. Figure 4 shows an example of data that is extracted from the sensors allowing to observe differences in subtle movement patterns that are not detected using the standard clinical scales.

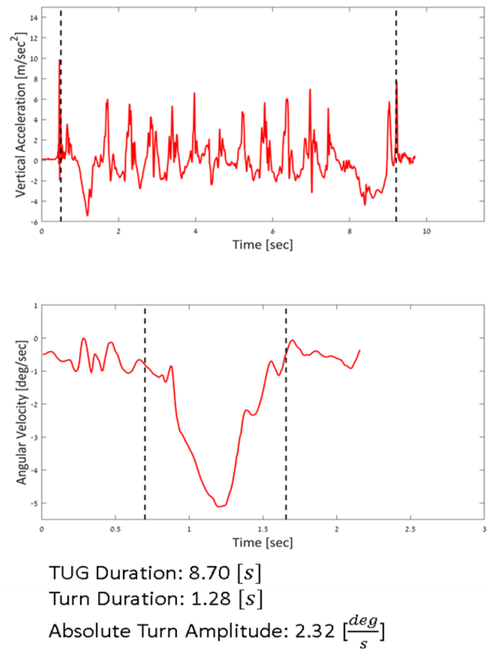
Figure 4: Example of difference in Timed UP and Go collected by the sensors in the in clinic visit

Participant: Male, 65yrs
Genetic status: GBA carrier
MDS-UPDRS III: 0



TUG Duration: 10.61 $[s]$
Turn Duration: 2.32 $[s]$
Absolute Turn Amplitude: 1.28 $[\frac{deg}{s}]$

Participant: Male, 64yrs
Genetic status: Healthy non-carrier
MDS-UPDRS III: 1



TUG Duration: 8.70 $[s]$
Turn Duration: 1.28 $[s]$
Absolute Turn Amplitude: 2.32 $[\frac{deg}{s}]$

4 DISCUSSION

Digital technology is rapidly entering clinical medicine and clinical research as a technology capable of accurately capturing multiple mobility functions. While a number of efforts in this domain are in progress, important gaps remain including validation in prodromal disease, longitudinal progression, variance and modifiers. This sub-study aims to help close some of these gaps.

ACKNOWLEDGMENT

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