The Case for Symptom-Specific Neurological Digital Biomarkers

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Abstract. Digital biomarkers provide novel and objective assessment of neurodegenerative diseases, such as Parkinson's Disease (PD). This paper demonstrates that objective digital biomarkers, obtained from mobile-based functional assessments, can be used for symptom-specific insights on neurological deficiencies. These digital biomarkers were found to be sensitive to change in relation to structured physical interventions. In this pilot study, 54 participants (n = 36 PD; n = 18 control) completed 13 neurocognitive functional tasks with 115 digital biomarkers being identified and compared between groups for objective assessment, evaluation, and monitoring of disease progression. 36 (31.30%) of these biomarkers were significant ($p < 0.10$) between groups. Of the 36 significant biomarkers, 10 were motor, 6 were memory, 1 was speech, 6 were executive function, and 13 were multi-functional. 8 biomarkers were significant ($p < 0.10$) between groups regardless of intervention, which may indicate strong biomarkers to assess PD. Further, 15 (13.04%) digital biomarkers showed significance ($p < 0.10$) in relation to structured physical intervention. Overall, mobile-based digital biomarkers provide promising measures and sensitivity to functional change that can be used in assessment and monitoring of Parkinson's Disease. Further integration of mobile device capabilities can enhance the understanding of how neurodegenerative diseases present and aid clinicians in the diagnosis and monitoring of conditions.

Keywords: Digital biomarkers · Neurocognitive assessment · Mobile app · Parkinson's disease

1 Introduction

Mobile devices are becoming increasingly prevalent in the area of neurocognitive assessments as their capabilities allow for the collection of more objective information than is currently achievable using pen-and-paper style tests (e.g., the Montreal Cognitive Assessment (MoCA) [1] or Mini Mental State Examination

X. Gao et al. (Eds.): MobiHealth 2021, LNICST 440, pp. 235–255, 2022.
https://doi.org/10.1007/978-3-031-06368-8_16

(MMSE) [2]) [3,4]. These pen-and-paper assessment instruments are administered by clinicians to 'score' neurological and cognitive functional tasks (e.g., motor, speech, memory, and executive function). These tasks are often difficult for individuals with neurodegenerative conditions including Parkinson's Disease (PD) [5–9]. This paper focuses on individuals with Parkinson's Disease as they demonstrate impaired functionality in both motor and cognitive areas [10].

The transition to mobile-based versions of neurocognitive assessments has become increasingly popular within the healthcare sector for the administration of functional tasks, objective scoring, and the interpretation of symptoms relating to neurological health or illness [11]. This transition also allows for the collection of additional unique digital biomarkers for specific functional tasks of interest (e.g., a Trail Making Task), and allows for the creation of multi-functional assessments with more expansive digital biomarker sets [12,13]. As Parkinson's Disease is often described as a "designer disease", meaning no two diagnosed individuals manifest the exact same symptoms, personalized medicine should be the goal and is required to optimize care and individuals' quality of life [14,15]. However, to reach personalized medicine for individuals with PD (e.g., the formation of individualized intervention protocols in an evidence-based manner), clinicians need further knowledge on specific patient characteristics to develop personalized rehabilitation programs [16].

The objective of this pilot study was to demonstrate that objective digital biomarkers, collected from mobile-based functional assessments, can be used to provide symptom-specific insights on neurological deficiencies of individuals with PD. Further, this work was to demonstrate that these digital biomarkers are sensitive to functional change in relation to structured physical interventions. This was completed by comparing subjects with Parkinson's Disease to age-matched controls across 13 mobile-based neurocognitive functional tasks, in addition to monitoring digital biomarkers for the PD group in relation to structured physical interventions.

2 Related Work

Neurodegenerative diseases, such as PD, present with progressive degeneration which can involve both movement disorders and neurological and/or cognitive deficits [17]. Neurocognitive assessments that evaluate this degeneration consist of functional tasks involving motor, speech, memory, and executive functions [7–9]. Previous works have identified sensor-based digital assessments (e.g., accelerometry based gait assessments or speech recognition systems for healthcare) which provide promising applications and user-device interactions for the collection of objective digital biomarkers across functional areas of neurocognition [5,13,18–22]. This pilot study further assesses mobile device capabilities by implementing mobile-based neurocognitive tasks that use device sensors to objectively collect information (e.g., digital biomarkers) that will provide clinicians with symptom-specific information that can assist with diagnosis, monitoring, and rehabilitation of individuals with PD [5,13].

2.1 Functional Assessments

Currently the assessment and monitoring of individuals with PD is primarily based on a set of clinical criteria from functional assessments, as physical biomarkers alone (e.g., blood based) are not able to reliably confirm the presence of the disease [23]. Mobile-based neurocognitive assessments have the capability and promise to expand functional assessments to allow for objective scoring, the interpretation of results relating to the initial diagnosis, and monitoring of disease progression [6,24]. Inherent device sensors (e.g., accelerometers, gyroscopes, cameras, microphones, and timers), along with human device interactions, can enhance the monitoring of neurocognitive functions (e.g., motor, memory, speech, and executive function) for individuals with neurodegenerative conditions such as PD [13,18,20,21,25]. The transition of these assessments to mobile devices also allows for standardized administration which is unaffected by examiner bias [26].

2.2 Physical Interventions

Currently there are both pharmacological and physical therapeutic interventions available for individuals diagnosed with PD. Previous work suggests that physical activity during the critical window of early- and mid-stage of the disease is vital to the management of PD symptoms and disease progression [27,28]. These activities encompass both routine activities of daily living (ADLs) (e.g., household activity, walking) and dedicated exercise (e.g., aerobics, strength training) [29]. Further, supervised and structured exercise is noted to be effective at improving functional performance outcomes (e.g., balance and functional ambulation) in individuals with PD [30,31]. However, many studies evaluate physical interventions as a one-size-fits-all concept as current evidence is not sufficient to develop personalized rehabilitation programs [16]. To gain further insights for intended personalized rehabilitation programs, it is imperative to administer precise and objective assessments providing symptom-specific information on physical rehabilitative efforts and for the understanding of various intervention approaches [32].

3 Methodology

Fifty four adults between the ages of 52 and 84 were divided into two groups-those with a confirmed diagnosis of Parkinson's Disease and age-matched healthy controls participated in this pilot study. Of those, the PD population included 36 individuals; with slightly less than half of the population being female (n = 17 or 47.22%). The age-matched control population included 18 individuals; more than half (n = 10 or 55.56%) being female. Participants were recruited through advertisements, physician and clinician referrals, spouses or caretakers of the diagnosed population, and prior studies from our laboratory. The inclusion criteria for this study consisted of being age 50 years or older. As the mean onset age for PD in the Western world is early-to-mid 60s [33], recruitment efforts for this pilot study were limited to diagnosed individuals age 50 years or older and appropriate age-matched controls. Participants were excluded from the current study if they were unable to provide informed consent or if their native language was not English (as all tasks were formatted in English).

3.1 Mobile Application Testing

All participants were administered a tablet-based neurocognitive assessment designed for individuals with Parkinson's Disease that focused on user-device interactions for the collection of objective measures [34]. Each participant completed mobile versions of 13 neurocognitive functional tasks across the areas of motor, memory, speech, and executive function. Functional tasks included single functional tasks (e.g., having focus on only one area of neurocognition; motor or memory) and multi-functional tasks (e.g., combining two or more single functional tasks into a functional task). The 13 administered neurocognitive tasks collected 74 objective mobile-based digital biomarkers for all participants. All task descriptions are listed below. For a fine-motor tracing task the individual was instructed to use their index finger to trace a depicted shape. For a gross-motor task the user was instructed to manipulate the mobile device to "air"-trace a depicted shape. For reflex tasks, the user was to tap on the screen to interact with a set of targets. For a memory task the user was to tap on depicted cards, in pairs, until all cards have been matched. For a trail making task the user was instructed to draw a line using their index finger connecting all shapes in increasing numerical order. For a set of speech based tasks, the user was prompted to read a sentence out loud or name prompted objects. Examples of multi-functional tasks include both fine (e.g., tracing an object) and gross (e.g., manipulating the mobile device) motor tasks paired with either an automatic (e.g., listing the months of the year in order from January to December) or non-automatic speech task (e.g., listing the months of the year, aloud, in reverse order; December to January). For an executive function/multi-functional task a digital version of the Stroop Word Color Test (SWCT) [35] was utilized where the user was required to discern the difference between prompted colors and words and then speak the correct response. For an expanded multi-functional task approach (e.g., Narration Writer), the user was instructed to narrate a sentence while also writing the sentence word by word (e.g., writing the same word being said aloud) in the space provided.

A subset of both PD and age-matched control populations ($n = 12$ and $n = 8$ respectively) were given an updated version of this neurocognitive assessment containing an expanded set of objective digital biomarkers ($n = 115$). All digital biomarkers collected in this expanded set made use of additional inherent device capabilities (e.g., device timers between instances of screen interactions, speech recognizers/dictionaries, and user interactions with relative positions on the device screen). This expanded digital biomarker set was implemented to give further monitoring of neurological and cognitive deficits.

3.2 Physical Interventions

All individuals with PD participated regularly (e.g., at least twice a week) in structured rehabilitation/intervention programs designed for PD. The supervised physical intervention activities included, but were not limited to, non-contact boxing, functional strength, yoga, dancing, and cycling. Each intervention training session lasted between 45 and 60 min and consisted of guided warm-up, main, and cool-down activities. All sessions were led by certified personal trainers. Individuals were given a mobile device assessment, consisting of the functional tasks discussed above, both prior to and directly after these supervised physical intervention programs. This testing protocol was included to see if the collected mobile-based digital biomarkers showed sensitivity to functional changes seen as a direct response to the intervention programs. In addition, the participants were required to take the functional assessment twice within a period of 2 h. Therefore, the tasks included in this assessment were internally randomized to avoid the test-retest phenomena (e.g., for a memory task, the location of matching card pairs; or in the Stroop Word Color Test, the order of colors and word combinations).

3.3 Statistical Analysis

All collected digital biomarker scores were compared for individuals with PD prior to a structured physical intervention (e.g., 'Before'), following a structured physical intervention (e.g., 'After'), and healthy age-matched controls (e.g., 'Control') using statistical methods (e.g., ANOVA and post hoc t-tests).

4 Results

4.1 Mobile Application Testing

The results from this work are discussed in two parts- Symptom-Specific Digital Biomarkers (i.e., to demonstrate that objective digital biomarkers can be used to provide symptom-specific insights on neurological deficiencies of individuals with PD), and Digital Biomarker Sensitivity (i.e., to demonstrate that these digital biomarkers are sensitive to functional change in relation to structured physical interventions).

The average scores for each digital biomarker for individuals with PD prior to a structured physical intervention (e.g., 'Before'), following a structured physical intervention (e.g., 'After'), and healthy age-matched controls (e.g., 'Control') are shown in supplemental Tables 5, 6, 7, 8 and 9 (Sect. A). The significance between groups for all digital biomarker scores ($p < 0.05$) is denoted by the following symbols: diagnosed PD populations prior to a physical intervention versus age-matched controls ($*$), diagnosed PD populations following a physical intervention versus age-matched controls (†), and diagnosed PD populations prior to a structured physical intervention versus directly following physical intervention (‡).

4.2 Symptom-Specific Digital Biomarkers

74 device-calculated, objective digital biomarkers were collected from all individuals (36 PD and 18 Control). Of the 74 digital biomarkers, 28 were collected from single functional tasks and the remaining 46 were collected from multi-functional tasks. Assessment results are seen in Table 1, Fig. 1, and supplemental Tables 5, 6 (Sect. A).

Table 1. Significant digital biomarker summary ($n = 74$ digital biomarkers).

Digital Biomarkers	Before/Control(∗)	After/Control(†)	Before/After(‡)
Significant Digital Biomarkers ($p < 0.05$)	17 (22.97%)	7 (9.46%)	7 (9.46%)
Single Functional Task	8 (10.81%)	4 (5.41%)	2 (2.70%)
Motor	*7 (9.46%)*	*4 (5.41%)*	*2 (2.70%)*
Memory	*1 (1.35%)*	*0 (-)*	*0 (-)*
Speech	*0 (-)*	*0 (-)*	*0 (-)*
Multi-Functional Task	9 (12.16%)	3 (4.05%)	5 (6.76%)
Executive Funciton	*5 (5.41%)*	*2 (2.70%)*	*3 (4.05%)*

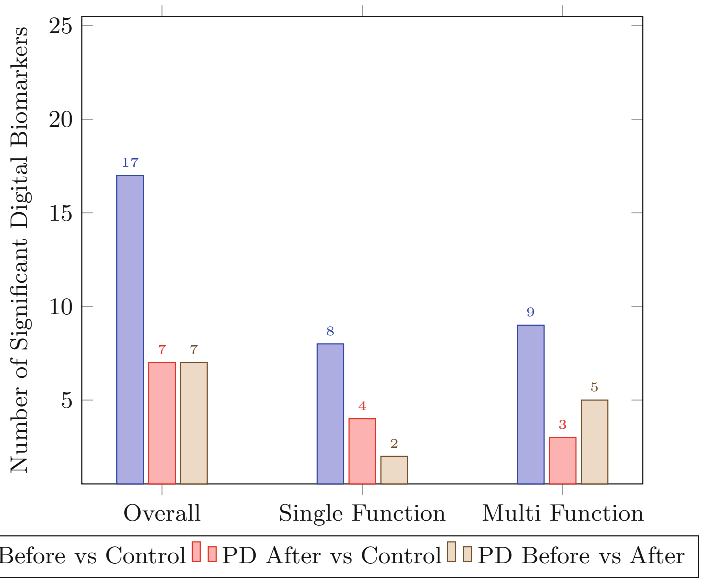

Fig. 1. Preliminary Assessment's Significant Digital Biomarkers. ($n = 74$) for the Total Number of Collected Biomarkers in the Preliminary Assessment.

Table 1 and Fig. 1 give a summary of the number of significant digital biomarkers between groups ($p < 0.05$) across task type (e.g., single or multi-functional tasks) and symptoms (e.g., motor or memory). Of the 74 collected digital biomarkers, 17 or 22.97% were significant ($p < 0.05$) when comparing individuals with PD prior to physical interventions, and age-matched controls.

A representative subset of the overall population (e.g., $n = 20$ individuals; $n = 12$ PD and $n = 8$ Control) interacted with an expanded version of the digital biomarker assessment. Of the 115 device-calculated, objective digital biomarkers, 41 were collected from single functional tasks and the remaining 74 were collected from multi-functional tasks. The expanded digital biomarker set results are seen in Table 2, Fig. 2, and supplemental Tables 7, 8 and 9 (Sect. A).

Table 2 and Fig. 2 give a summary of the number of significant digital biomarkers between groups ($p < 0.05$), across task types (e.g., single or multi-functional tasks) and symptoms (e.g., motor or memory) for the expanded digital biomarker assessment. Of the 115 digital biomarkers from the expanded set assessment, 20 were significant ($p < 0.05$) when comparing individuals with PD prior to physical interventions, and age-matched controls.

Table 2. Significant digital biomarker summary ($p < 0.05$) ($n = 115$ digital biomarkers).

Digital Biomarkers	Before/Control∗)	After/Control(†)	Before/After(‡)
Significant Digital Biomarkers ($p < 0.05$)	20 (17.39%)	15 (13.04%)	8 (6.96%)
Single Functional Task	10 (8.70%)	9 (7.83%)	2 (1.73%)
Motor	*7 (6.09%)*	*4 (3.48%)*	*2 (1.74%)*
Memory	*3 (2.61%)*	*4 (3.48%)*	*0 (-)*
Speech	*0 (-)*	*1 (0.87%)*	*0 (-)*
Multi-Functional Task	10 (8.70%)	6 (5.22%)	6 (5.22%)
Executive Function	*5 (4.35%)*	*2 (1.74%)*	*4 (3.48%)*

Given the sample size of this pilot study, the definition of significant digital biomarkers was expanded to $p < 0.10$. Increasing the p-value to $p < 0.10$ allows for a better understanding of PD given the nature of the condition; as individuals with PD do not always manifest the same symptoms [14]. Digital biomarkers with a p-value of less than $p < 0.10$ indicate functional biometrics that should be included in future functional assessments with a larger sample size as they have a higher likelihood of being significant within a p-value of $p < 0.05$. Table 3 and Fig. 3 depicts the number of significant digital biomarkers ($p < 0.10$) needed for inclusion in mobile-based neurocognitive assessments containing the aforementioned tasks. Out of 115 collected digital biomarkers in the expanded test set, 36 digital biomarkers (31.30%) were significant ($p < 0.10$). A breakdown of single and multi-functional tasks is also seen in Table 3 and Fig. 3. Of the 41 collected single functional task digital biomarkers, 17 (41.46%) were significant ($p < 0.10$) between individuals with PD and control groups. However, only 19

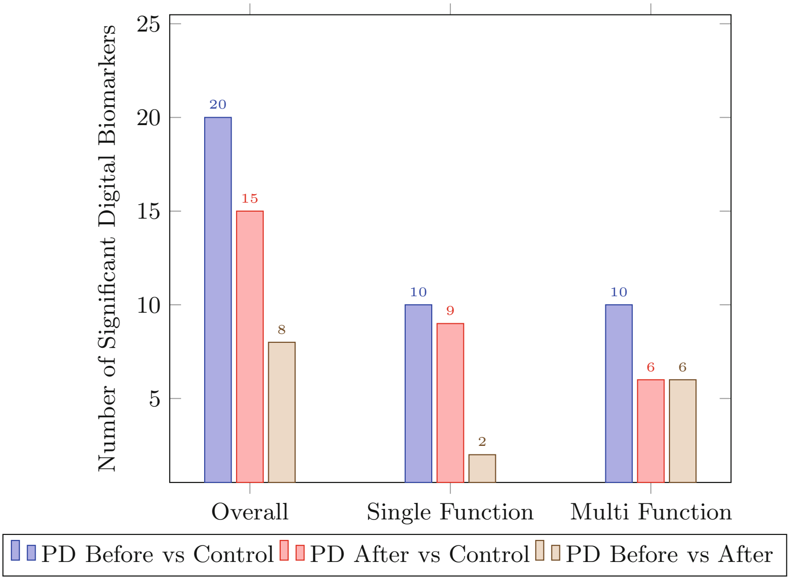

Fig. 2. Expanded Assessment's Significant Digital Biomarkers. ($n = 115$) for the Total Number of Collected Biomarkers in the Expanded Assessment.

of 74 (25.68%) digital biomarkers from multi-functional tasks were significant ($p < 0.10$) between groups.

For a more in depth understanding of how individuals with PD exhibit different neurocognitive functions of interest in a symptom-specific manner, a breakdown of the digital biomarkers by functional area was included in Fig. 4. A total of 36 (31.30%) mobile-based digital biomarkers were significant ($p < 0.10$) when comparing individuals with PD (e.g., before or after physical intervention) to age-matched controls. Further, Fig. 4 shows the number of collected digital biomarkers and the number of significant digital biomarkers ($p < 0.10$) for the categories of motor, memory, speech, executive function, and multi-functional tasks. The multi-functional task category includes all tasks that involve two or more areas of neurocognition in a single task. It should be noted that all executive function tasks are inherently multi-functional in nature (e.g., an individual needs to move or speak to carry out the executive function) and therefore are a subset of the multi-functional task digital biomarker set (e.g., denoted by an * in Fig. 4). Of the single functional tasks, 10 of 26 (38.46%) motor digital biomarkers, 6 of 10 (60.00%) memory digital biomarkers, and 1 of 5 speech digital biomarkers (20.00%) were significant ($p < 0.10$). 19 multi-functional digital biomarkers were also significant ($p < 0.10$); with 6 executive function digital biomarkers being included in this group. Lastly, all remaining significant multi-functional digital biomarkers (13; 17.57%) relate to both speech and motor function as the main components of the configured tasks (e.g., completing a motor task paired with an automatic or non-automatic speech task).

Table 3. Significant digital biomarker summary ($p < 0.10$) ($n = 115$ digital biomarkers).

Digital Biomarkers	Before/Control(∗)	After/Control(†)	Before/After(‡)
Significant Digital Biomarkers ($p < 0.10$)	30 (26.09%)	21 (18.26%)	15 (13.04%)
Single Functional Task	16 (13.91%)	12 (10.43%)	4 (3.48%)
Motor	*10 (8.70%)*	*7 (6.10%)*	*4 (3.48%)*
Memory	*6 (5.22%)*	*4 (3.48%)*	*0 (-)*
Speech	*0 (-)*	*1 (0.87%)*	*0 (-)*
Multi-Functional Task	14 (12.17%)	9 (7.83%)	11 (9.57%)
Executive Function	*5 (4.35%)*	*4 (3.48%)*	*6 (5.22%)*

4.3 Digital Biomarker Sensitivity

Of the 74 device-calculated, objective digital biomarkers collected from all individuals ($n = 36$ PD; $n = 18$ Control) 7 digital biomarkers were significant ($p < 0.05$) between individuals with PD following a physical intervention compared to controls (Table 1 and Fig. 1). 7 digital biomarkers were also significant ($p < 0.05$) when comparing those individuals with PD before and after physical intervention.

Of the 115 device-calculated digital biomarkers in the expanded set for a representative subset of the overall population (e.g., $n = 20$ individuals; $n = 12$ PD and $n = 8$ Control), 15 digital biomarkers were significant ($p < 0.05$) between individuals with PD following a physical intervention compared to controls (Table 2 and Fig. 2). Further, 8 digital biomarkers were significant ($p < 0.05$) when comparing individuals with PD before and after physical intervention in the expanded set. Given the expanded definition of significant digital biomarkers ($p < 0.10$), 21 digital biomarkers were significant between individuals with PD following a physical intervention compared to controls (Table 3 and Fig. 3). Finally, 15 digital biomarkers were significant ($p < 0.10$) when comparing those with PD before and after physical intervention in the expanded set.

5 Discussion

This pilot study implemented an assessment tool specifically designed for individuals with Parkinson's Disease that focused on tablet-based user-device interactions for the collection of function-specific digital biomarkers [34]. Mobile-based neurocognitive assessments allow for objective scoring of novel and relevant digital biomarkers with the use of device sensors and human device interactions to provide insights on neurological deficiencies specific to individuals with PD [13,24]. Following acquisition and analysis, objective digital biomarkers were found to provide symptom-specific insights on neurological deficiencies of individuals with PD. Further, these digital biomarkers were found to be sensitive to functional change in relation to structured physical interventions for individuals with PD. A task-specific list of these metrics is depicted in Table 4 which gives rise to symptom-specific digital biomarkers. Of the 36 digital biomarkers that were significant ($p < 0.10$), 10 were motor, 6 were memory, 1 was speech, 6 were executive function, and 13 involved multi-functional tasks. Additionally, 8 of the 36 digital biomarkers were found to be significant regardless of intervention which may indicate strong biomarkers for PD. These 8 digital biomarkers are denoted by (∗) in Table 4. The 36 significant digital biomarkers ($p < 0.10$) are listed in Table 4. Each of these biomarkers were found to be important in the configuration of mobile-based neurocognitive assessments as they provide insights regardless of physical intervention when comparing outcomes of PD populations to age-matched controls.

Future work should involve analyzing digital biomarkers across larger populations (e.g., PD populations in different stages of disease progression and other populations with other neurodegenerative diseases) and across the different stages of diagnoses. The analysis of different neurodegenerative diseases (e.g., Alzheimer's Disease, dementia) and their stages would help in extracting significant disease-specific digital biomarkers and aid in the prediction and monitoring of these various conditions over time. Additionally, a larger sample size would allow for adjusted statistical analyses and confidence intervals. Next, further exploration and expansion of all digital biomarkers, but particularly single functional digital biomarkers (e.g., memory and speech) should occur. Although individuals with PD exhibit difficulty in performing multi-functional tasks [36], single functional task digital biomarkers are still highly necessary in the understanding of how PD symptoms manifest. Similarly, while Parkinson's Disease is a progressive neurodegenerative disease primarily characterized by the hallmarks of motor symptoms (e.g., akinesia, rigidity, and tremor) [9,37] memory task digital biomarkers were shown to be important in the understanding of Parkinson's Disease with 60% of collected memory metrics being significant. The number of single functional memory and speech based digital biomarkers should also be increased for a more even distribution across all neurocognitive functions of interest. This expansion should include digital biomarkers collected using different device sensors (e.g., speech frequency, amplitude, timing using audio samples; or gait, using accelerometers, gyroscopes, and/or device cameras) or comprehensive systems (e.g., IoT or wearable devices).

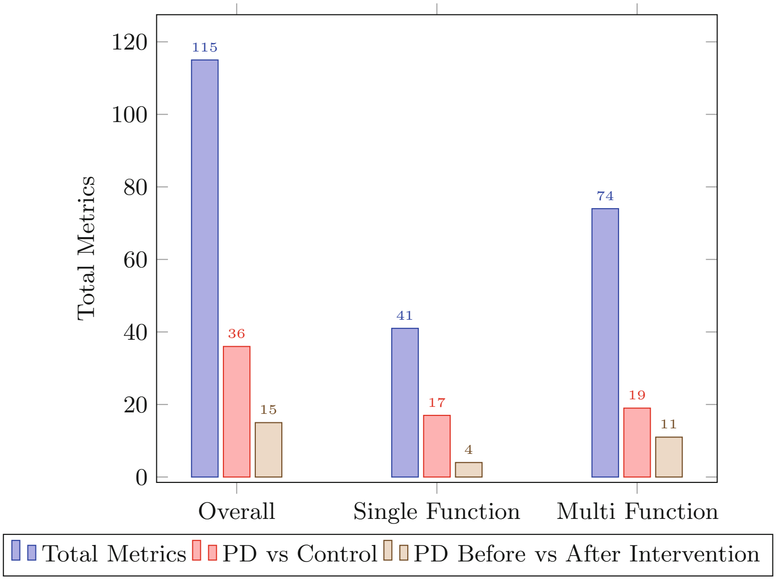

Fig. 3. Metrics Needed in Mobile-based Neurocognitive Assessments for Individuals with PD.

This study found that the number of significant digital biomarkers of the PD group following structured physical interventions decreased compared to the age-matched control group. Future work should include an investigation on how different activities (e.g., non-contact boxing, functional strength, yoga, dancing, and cycling) affect neurocognitive functions of interest through the collection of objective digital biomarker sets with relation to each activity [16,29]. Future work should also explore the extent to which these digital biomarkers are affected by different intervention types, across different stages, and populations. The knowledge gained through the use of objective and comprehensive digital assessments would aid clinicians and healthcare workers in the formation of specific recommendations for personalized therapeutic programs based on the

Table 4. Significant Digital Biomarkers ($p < 0.10$) by Task and Category

Category	Task		Digital Biomarker
Motor	Fine Motor Tracing	Circle	Average Distance Total Distance*
		Square	Average Distance Total Distance
	Gross Motor Emulation	Circle	Time
		Square	Time Min Magnitude of Acceleration
	Reflex Target Tapping		Num small tapped* Total tapped* Avg. prompt to hit time
Memory	Card Matching	Unique Shapes	Avg Times Flipped Avg Match Pair Time*
		Unique Shapes and Colors	Time Max Times Flipped Avg Times Flipped Avg Match Pair Time
Speech	Narration		Prompt to First Word Time
Executive Function	Visuospatial	Connect the Dots	Avg Closest Distance* Total Distance Drawn Time
		Connect the Shapes	Total Distance Drawn* Time
	Stroop Word Color		Avg Response Time (Correct)
Multi-Functional	Fine Motor Tracing (speech)	Circle	Writing Time Avg Distance Total Distance *Outline Crossings* Num of Additional Words Max Time Between Words Speaking Time
		Square	Writing Time Outline Crossings
	Gross Motor Emulation (Speech)	Circle	Num of Additional Words
		Square	Max Mag of Acceleration* Min Mag of Acceleration Num of Additional Words

functional deficits of each diagnosed individual [32]. Additionally, the inclusion of individuals with PD who do not interact with physical interventions should be completed to gain further insights on PD in addition to demonstrating quantifiable benefits of structured physical interventions. Finally, the expansion of these functional assessments for other neurodegenerative diseases (e.g., Alzheimer's disease, ALS, or dementia) should be completed.

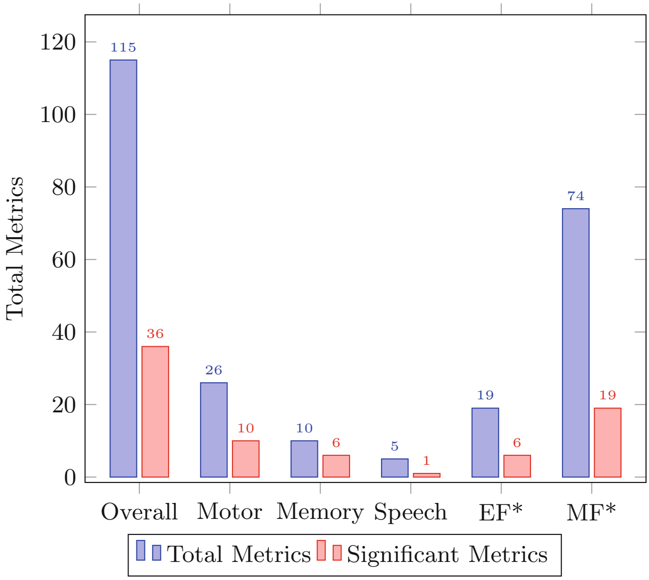

Fig. 4. Number of Significant Metrics ($p < 0.10$) by Neurocognitive Function Category.

6 Conclusions

Mobile-based digital biomarkers provide promising measures that can be useful in the diagnostic and monitoring processes that currently rely on subjective clinical judgements and self-reported information. Further integration of these mobile capabilities for the collection of objective measures can enhance the understanding of how neurodegenerative diseases present, and provide necessary personalized diagnostic and monitoring information.

This pilot study gives both an understanding of digital biomarkers specific to Parkinson's Disease that should be included in mobile-based neurocognitive assessment systems while also yielding further updates to be considered when expanding data collection efforts. Collected digital biomarkers in this work were used to (1) demonstrate that objective digital biomarkers, collected from mobile-based functional assessments, can be used to provide symptom-specific insights on neurological deficiencies of individuals with PD and (2) demonstrate that these digital biomarkers are sensitive to functional change in relation to structured physical interventions for individuals with PD.

A Appendix

Table 5. List of collected digital biomarkers from single functional tasks ($n = 54; PD = 36; Control = 18$). (* = Sig. BvC) († = Sig. AvC) (‡ = Sig. BvA); ($p < 0.05$)

Digital Biomarker	Before	After	Control
Fine Motor Tracing - Circle			
Time	7.95	6.59	7.29
Average Distance	**14.21***	14.39	**9.45***
Total Distance	**5687.01***	**4957.74†**	**2867.15*†**
Outline Crossings	5.89	5.71	5.17
First Point Distance to Shape	109.89	118.71	96.11
First Point Distance to Last Point	285.31	309.14	240.27
Fine Motor Tracing - Square			
Time	6.45	6.42	5.84
Average Distance	9.98	**11.85†**	**7.24†**
Total Distance	5086.28	5186.20	3012.72
Outline Crossings	6.87	6.56	4.56
First Point Distance to Shape	19.98	22.48	7.47
First Point Distance to Last Point	121.52	169.83	66.06
Gross Motor Emulation - Circle			
Time	**7.02*‡**	**5.266‡**	**4.70***
Average Magnitude of Acceleration	1.01	1.01	1.00
Maximum Magnitude of Acceleration	1.22	1.24	1.20
Minimum Magnitude of Acceleration	0.82	0.81	0.79
Gross Motor Emulation - Square			
Time	**7.82*‡**	**5.92‡**	**4.97***
Average Magnitude of Acceleration	1.00	1.01	1.01
Maximum Magnitude of Acceleration	1.26	1.30	1.34
Minimum Magnitude of Acceleration	**0.79***	0.75	**0.68***
Reflex - Target Tapping			
Number of Small Tapped	**21.24***	**21.74†**	**34.83*†**
Number of Large Tapped	15.02	16.67	16.58
Number of Total Tapped	**36.26***	**38.41†**	**51.42*†**
Memory - Card Matching - Unique Colors & Shapes			
Time	**52.21***	45.75	**36.91***
Memory - Card Matching - Unique Shapes			
Time	53.34	45.97	36.95
Speech - Narration			
Time	4.48	4.30	4.81
Missed Words	2.00	0.50	0.50
Additional Words	0.50	0.167	0.00

Table 6. List of collected digital biomarkers from multi-functional tasks ($n = 54; PD = 36; Control = 18$). (* = Sig. BvC) († = Sig. AvC) (‡ = Sig. BvA); ($p < 0.05$)

Digital Biomarker	Before	After	Control
Fine Motor Tracing with Speech - Circle			
Writing Time	**13.42‡**	**9.71‡**	9.51
Average Distance	**11.97***	10.73	**6.56***
Total Distance	12939.79	8758.14	4857.14
Outline Crossings	9.12	8.79	11.00
First Point Distance to Shape	89.40	97.94	92.43
First Point Distance to Last Point	226.24	247.87	407.05
Number of Missing Months	1.50	0.00	0.25
Number of Additional Words	2.62	0.375	0.25
Speaking Time	14.643	10.87	9.19
Fine Motor Tracing with Speech - Square			
Writing Time	**10.08*‡**	**8.54‡**	**7.92***
Average Distance	10.87	10.54	7.13
Total Distance	9842.72	8272.29	5073.25
Outline Crossings	8.02	7.88	10.17
First Point Distance to Shape	8.41	23.60	5.90
First Point Distance to Last Point	208.91	174.42	297.80
Number of Missing Months	1.50	0.00	0.25
Number of Additional Words	2.62	0.375	0.25
Speaking Time	14.875	10.88	9.25
Gross Motor Emulation with Speech - Circle			
Movement Time	8.72	7.97	6.85
Average Magnitude of Acceleration	1.00	1.01	1.01
Maximum Magnitude of Acceleration	1.17	1.20	1.18
Minimum Magnitude of Acceleration	0.87	0.84	0.82
Number of Missing Months	0.50	0.25	0.00
Number of Additional Words	1.50	0.00	0.50
Speaking Time	14.82	11.56	11.73
Gross Motor Emulation with Speech - Square			
Movement Time	10.15	8.24	7.98
Average Magnitude of Acceleration	1.00	1.00	1.00
Maximum Magnitude of Acceleration	**1.17***	**1.20†**	**1.31*†**
Minimum Magnitude of Acceleration	**0.83***	0.81	**0.731***
Number of Missing Months	0.25	0.00	0.50
Number of Additional Words	0.75	0.00	0.75
Speaking Time	13.97	11.41	11.58
Visuospatial Task - Connect the Dots			
Average Closest Distance	**12.56***	**13.20†**	**9.66*†**
Total Distance Drawn	**394.52*‡**	**333.09‡**	**293.67***
Time	**15.43*‡**	**12.39‡**	**11.32***

(*continued*)

Table 6. (*continued*)

Digital Biomarker	Before	After	Control
Visuospatial Task - Connect the Shapes			
Average Closest Distance	12.26	12.02	11.90
Total Distance Drawn	**368.28***	**336.11**†	**252.58***†
Time	**15.53***‡	**13.07**‡	**10.84***
Stroop Word Color Task			
Total Generated	8.50	9.83	7.5
Total Correct	6.00	8.83	6.00
Object Naming			
Total Generated	14.5	14.83	14.33
Total Correct	12.83	13.16	14.00
Narration Writer			
Writing Time	31.872	29.66	26.81
Speaking Time	22.96	24.30	21.54
Missed Words	1.667	1.667	1
Additional Words	3.167	0.833	0.00

Table 7. Expanded list of collected digital biomarkers from single functional tasks ($n = 20; PD = 12; Control = 8$). (* = Sig. BvC) († = Sig. AvC) (‡ = Sig. BvA); ($p < 0.05$)

Digital Biomarker	Before	After	Control
Reflex - Target Tapping			
Number of Missed Targets	2.0	2.25	1.67
Average Miss Distance	140.55	65.72	99.12
Average Time between Prompt and Hit	0.74	**0.77**†	**0.58**†
Memory - Card Matching - Unique Colors & Shapes			
Maximum Flipped	4.00	**4.82**†	**3.25**†
Average Times Flipped	2.23	**2.53**†	**1.90**†
Average Time for Match Pair	1.29	**1.39**†	**1.07**†
Average Time of Non-Match Pair	1.49	1.43	1.49
Memory - Card Matching - Unique Shapes			
Maximum Flipped	4.55	4.91	3.63
Average Times Flipped	**2.46***	2.59	**1.98***
Average Time for Match Pair	**1.38***	**1.30**†	**1.06***†
Average Time of Non-Match Pair	1.51	1.43	1.28
Speech - Narration			
Time Between Prompt and First Word Spoken	2.58	**2.15**†	**3.14**†
Average Time Between Words	0.32	0.31	0.25

Table 8. Expanded list of collected digital biomarkers from multi-functional tasks ($n = 20; PD = 12; Control = 8$). (* = Sig. BvC) († = Sig. AvC) (‡ = Sig. BvA); ($p < 0.05$)

Digital Biomarker	Before	After	Control
Fine Motor Tracing with Speech - Circle			
Writing Time	**21.84‡**	**16.06‡**	16.08
Average Distance	**12.90***	10.98	**9.12***
Total Distance	**24402.72***	16995.06	**12778.22***
Outline Crossings	**20.00***	**14.46†**	**8.29*†**
First Point Distance to Shape	106.36	97.58	103.31
First Point Distance to Last Point	308.60	284.58	334.38
Number of Missing Months	3.73	3.27	4.43
Number of Additional Words	**2.82***	1.73	**0.43***
Start Time to First Word	5.41	4.64	3.53
Average Time Between Words	1.31	1.12	1.32
Maximum Time Between Words	4.24	**2.87†**	**7.55†**
Speaking Time	**21.30‡**	**14.83‡**	18.95
Fine Motor Tracing with Speech - Square			
Writing Time	22.58	18.60	15.17
Average Distance	13.62	9.30	9.09
Total Distance	22669.22	16074.48	12681.91
Outline Crossings	8.024	**15.27†**	**8.86†**
First Point Distance to Shape	20.25	38.67	7
First Point Distance to Last Point	312.38	235.26	209.48
Number of Missing Months	4.55	3.46	5.27
Number of Additional Words	2.55	1.82	0.57
Start Time to First Word	3.66	2.72	1.50
Average Time Between Words	1.91	2.76	1.79
Maximum Time Between Words	5.56	5.64	6.02
Speaking Time	21.13	19.23	18.90
Gross Motor Emulation with Speech - Circle			
Movement Time	14.87	13.62	15.65
Average Magnitude of Acceleration	1.01	1.01	1.00
Maximum Magnitude of Acceleration	1.14	1.20	1.15
Minimum Magnitude of Acceleration	0.88	0.83	0.85
Speaking Time	14.78	13.86	14.98
Number of Missing Months	1.75	0.75	0.00
Number of Additional Words	**2.25***	1.75	**0.67***
Average Time Between Words	1.20	0.96	1.02
Maximum Time Between Words	2.69	1.60	1.92

(*continued*)

Table 8. (*continued*)

Digital Biomarker	Before	After	Control
Gross Motor Emulation with Speech - Square			
Movement Time	21.26	16.60	15.63
Average Magnitude of Acceleration	1.01	1.01	1.01
Maximum Magnitude of Acceleration	1.24	1.26	1.36
Minimum Magnitude of Acceleration	0.79	0.78	0.75
Speaking Time	23.69	16.03	15.36
Number of Missing Months	1.00	0.75	0.33
Number of Additional Words	2.25	**2.75**†	**0.33**†
Average Time Between Words	1.62	1.08	1.10
Maximum Time Between Words	4.47	2.59	2.04

Table 9. Expanded list of collected digital biomarkers from multi-functional tasks continued ($n = 20; PD = 12; Control = 8$). (* = Sig. BvC)(† = Sig. AvC) (‡ = Sig. BvA); ($p < 0.05$)

Digital Biomarker	Before	After	Control
Visuospatial Task - Connect the Dots			
Number of Hits	9.83	9.00	9.00
Number of Misses	0.167	1.00	1.00
Average Time Between Correct Dots	0.96	0.51	0.43
Max Time Between Correct Dots	2.46	0.89	0.91
Visuospatial Task - Connect the Shapes			
Number of Hits	9.83	9.33	10.00
Number of Misses	0.17	0.67	0.00
Average Time Between Correct Shapes	0.88	0.71	0.50
Max Time Between Correct Shapes	2.73	1.27	1.58
Stroop Word Color Task			
Average Response Time - Correct	**2.57**‡	**2.20**‡	2.78
Average Response Time - Incorrect	3.23	3.29	1.29
Max Response Time	5.67	2.76	4.39
Object Naming			
Average Response Time - Correct	2.34	2.23	2.35
Narration Writer			
Total Number of Points	836.33	8.13.67	717.00
Total Number of Strokes	28.50	26.33	33.00
Average Stroke Time	0.66	0.70	0.40
Average Time Between Strokes	0.27	0.27	0.21
Time from Start to First Word	3.91	4.23	4.61
Average Time Between Words	3.59	2.96	3.05

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