Design of a Neurocognitive Digital Health System (NDHS) for Neurodegenerative Diseases

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ABSTRACT

Digital health technology is becoming more ubiquitous in monitoring individuals' health as both device functionality and overall prevalence increase. However, as individuals age, challenges arise with using this technology particularly when it involves neurodegenerative issues (e.g., for individuals with Parkinson's disease, Alzheimer's disease, and ALS). Traditionally, neurodegenerative diseases have been assessed in clinical settings using pen-and-paper style assessments; however, digital health systems allow for the collection of far more data than we ever could achieve using traditional methods. The objective of this work is the formation and implementation of a neurocognitive digital health system designed to go beyond what pen-and-paper based solutions can do through the collection of (a) objective, (b) longitudinal, and (c) symptom-specific data, for use in (d) personalized intervention protocols. This system supports the monitoring of all neurocognitive functions (e.g., motor, memory, speech, executive function, sensory, language, behavioral and psychological function, sleep, and autonomic function), while also providing methodologies for personalized intervention protocols. The use of specifically designed tablet-based assessments and wearable devices allows for the collection of objective digital biomarkers that aid in accurate diagnosis and longitudinal monitoring, while patient reported outcomes (e.g., by the diagnosed individual and caregivers) give additional insights for use in the formation of personalized interventions. As many interventions are a one-size-fits-all concept, digital health systems should be used to provide a far more comprehensive understanding of neurodegenerative conditions, to objectively evaluate patients, and form personalized intervention protocols to create a higher quality of life for individuals diagnosed with neurodegenerative diseases.

CCS CONCEPTS

• **Applied computing → Health care information systems**; • **Information systems** → *Information systems applications*; • **Human-centered computing** → *Interaction devices.*

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KEYWORDS

digital biomarker, mobile app, neurodegenerative disease

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1 INTRODUCTION

Digital health technology is becoming more pervasive in the monitoring of individuals' health as device functionalities increase as does their overall prevalence [12]. As individuals age, challenges can arise with using digital health technology primarily due to the progressive decline of many physiological (e.g., sight or hearing) and neurocognitive functions (e.g., memory, executive function, and motor issues), in addition to an increased susceptibility to certain neurodegenerative diseases (e.g., Parkinson's disease (PD), Alzheimer's disease, and ALS) [40, 53, 54, 57]. Traditionally, neurocognitive functions of interest have been assessed in clinical settings using various accepted pen-and-paper style assessments (e.g., Montreal Cognitive Assessment (MoCA) [31], Mini Mental State Examination (MMSE) [49], and the Menu Task Assessment (MT) [1]) [52]. However, these assessments only evaluate a subset of relevant neurocognitive functions [47]. Neurocognitive functions of motor, memory, speech, language, executive function, sensory, behavioral and psychological function, sleep, and autonomic functions should all be evaluated as each of them may be difficult for individuals with neurodegenerative diseases [3, 7, 9, 11, 15, 21, 23, 29, 33]. The use of digital health technology and its capabilities (e.g., device configurations, inherent device sensors, and human-device interactions) allows for the collection of far more information and objective metrics than we ever could achieve using pen-and-paper style tests, while also assessing all functional areas of neurocognition [10, 47]. Further, digital health systems can also support continuous and objective health monitoring, encourage healthy behavior, support chronic disease self-management, enhance clinician knowledge, and aid in the personalization of interventions [20].

The objective of this paper is the formation and implementation of a neurocognitive digital health system (NDHS) that provides objective, longitudinal, and symptom-specific data for individuals with neurodegenerative diseases for use in personalized intervention protocols. The NDHS uses specifically designed tablet-based assessments and wearable devices to collect objective digital biomarkers, while also collecting patient reported outcomes (e.g., by both the individual and their caregivers) for additional insights on their condition. This system was created to aid in accurate diagnosis, longitudinal monitoring of all neurocognitive functions (e.g., motor, memory, speech, executive function, sensory, language, behavioral and psychological function, sleep, and autonomic function), and formation of personalized intervention protocols. The preliminary analysis in this paper focuses on individuals with PD as they demonstrate impaired functionality across all areas of neurocognition. However, this work is intended to be applied to all neurodegenerative conditions to aid in the monitoring of diagnosed individuals and the formation of personalized interventions.

2 RELATED WORK

2.1 Device Capabilities

As digital health technology is becoming more commonplace in the healthcare arena, integration of device sensors and capabilities for the collection of relevant and objective data increases [47]. Previous work has identified sensor-based digital assessments (e.g., accelerometry based gait assessments or speech recognition systems for healthcare) which provide promising user-device interactions for the collection of objective digital biomarkers across functional areas of neurocognition [5, 17, 28, 41, 50, 55]. Inherent device sensors (e.g., accelerometers, gyroscopes, cameras, microphones, and timers), along with human device interactions (e.g., screen taps or device manipulation) can enhance the monitoring of neurocognitive functions (e.g., motor, memory, speech, and executive function) for individuals with neurodegenerative conditions [5, 19, 50, 55]. Further, wearables and other functional sensing devices can allow for even more vital data to be collected [26, 35]. Using device-based sensors and/or interactions in the formation and configuration of functional tasks enhances the utility and quality of collected data. Additionally, with increased opportunity for user participation on their own devices and the ability of clinicians to collect and analyze enhanced objective datasets, digital health systems become a robust modality for the administration of neurocognitive assessments [47].

2.2 Patient Reported Outcomes

Although digital health technology can provide objective measurements of physiological and neurocognitive data of patients; another important aspect of personal health is information obtained from the patient themselves [13]. Patient reported outcomes (PROs) are a commonly utilized way to monitor a patient's thoughts or opinions with respect to short-term (e.g., day to day) changes, and can also lead to improved disease management by allowing the individual to recognize and understand their condition and to be aware of their symptoms and triggers [13, 51]. Exploratory analyses show that high PROs for physical activity is associated with less disease progression for individuals with neurodegenerative diseases [2]. However, the aim of digital health systems should be to increase the reliability and accuracy of this patient reported data by combining it with objective data from mobile devices, as there may be individual variability and/or bias [32, 37, 39].

2.3 Interventions

Currently there are both pharmacological and nonpharmacological therapies for individuals with neurodegenerative diseases. Nonpharmacological therapies include physical interventions (e.g., functional strength activities, boxing, and yoga) and speech, occupational, psychological, and music therapies [16, 24]. Previous work suggests that physical activity during the critical window of early- to mid-stage of muscular neurodegenerative diseases is vital to the management of symptoms and disease progression [8, 22]. These activities encompass both routine activities of daily living (ADLs) (e.g., household activities, walking) and dedicated exercise (e.g., aerobics, strength training) [27]. Further, supervised and structured exercise is noted to be effective at improving functional performance outcomes (e.g., balance and functional ambulation) in individuals with neurodegenerative diseases [38, 46]. However, many studies evaluate interventions as a one-size-fits-all concept as current evidence is not sufficient to develop personalized rehabilitation programs [34]. To gain further insights for personalized rehabilitation programs, it is imperative to administer precise and objective assessments for the understanding of current intervention approaches [42].

3 NEUROCOGNITIVE DIGITAL HEALTH SYSTEM DESIGN

The designed NDHS was created to collect longitudinal information from a variety of sources (e.g., personal health information, patient reported outcomes, specifically designed tablet-based neurocognitive functional assessments, wearable devices, and caretaker surveys) for the comprehensive assessment and monitoring of the symptoms associated with neurodegenerative diseases and provide individualized intervention recommendations. Given different devices and collection methodologies, both objective (e.g., clinical diagnoses, numerical physiologic data, neurocognitive assessment scores) and subjective (e.g., patient or caretaker reported outcomes) information is collected. This objective and subjective data is necessary for disease classification in addition to the comprehensive monitoring and rehabilitation of said condition [25, 30, 47]. The information collected from each NDHS component, across functional areas of motor (e.g., fine and gross motor), memory (e.g., long and short term), speech (e.g., frequency, variations, and repeatability), executive function (e.g., judgement and planning), sensory (e.g., visual, tactile, and aural), language (e.g., semantics, syntax, and pragmatics), behavioral and psychological function (e.g., emotion), sleep (e.g., quality and duration), and autonomic function (e.g., heart rate, blood oxygen saturation), are seen in Table 1. Both objective (e.g., diagnoses of conditions represented in personal health information, or quantitative measures collected from tablet-based assessments and wearables) and subjective (e.g., Patient Reported Outcomes and Caretaker Surveys) measures are also represented in Table 1. All neurocognitive functions of interest should be monitored by both objective (e.g., tablet-based assessments, wearable devices, or both) and subjective reported outcomes for a comprehensive understanding of each function. A further breakdown of each NDHS component is seen in Subsections 3.1-3.6.

3.1 Personal Health Information

A collection of an individual's personal health information is necessary for the classification of their neurodegenerative disease [44]. Personal health information regarding an individual's medical history including their age, gender, diagnosis (e.g., date and current stage), comorbidities, medication and medication cycles, therapies and interventions, initial presenting symptoms and current symptoms are all necessary to this classification. There are different

Table 1: Neurocognitive function data collected from NDHS components

	Neurocognitive Functions								
Data Sources	***Motor***	***Memory***	***Speech***	***Executive***	***Sensory***	***Language***	***Behavior***	***Sleep***	***Autonomic***
Objective									
Personal Health Info	X	X	X	X	X	X	X	X	X
Functional Assessment	X	X	X	X					
Wearables	X							X	X
Subjective									
PROs	X	X	X	X	X	X	X	X	X
Caretaker Survey	X	X	X	X			X	X	

sources for such personal health information, such as electronic health records (EHRs); however, they can also be provided by clinicians or patients during initial assessments. Further, this personal health information is intended to interoperate with sensors and performance testing systems to allow for better and more personalized care [18]. Figure 1 is a sample depiction of the tablet-based questionnaire regarding an individuals personal health information and medical history.

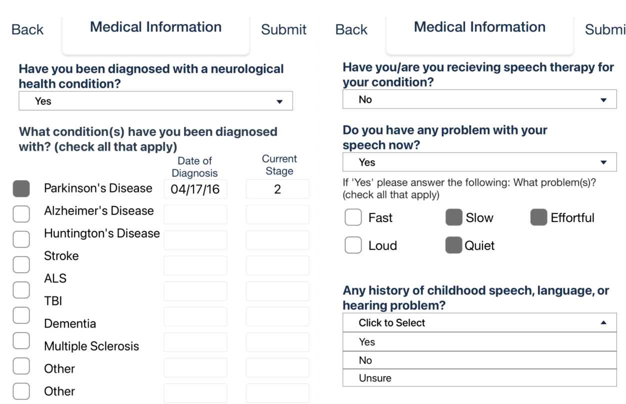

Figure 1: Sample views of 'Personal Health Information' including diagnosis and symptoms.

3.2 Patient Reported Outcomes

In addition to collecting the individual's medical history, gathering PROs over time is necessary for the understanding of how a neurodegenerative disease can affect an individual [30]. As this preliminary work focuses on individuals with Parkinson's disease, patient reported outcomes were determined using the Parkinson's Disease Questionnaire-39 (PDQ-39) where higher denoted scores give an indication of poorer quality of life [56]. The collected information in this part of the NDHS is a subjective evaluation based on a Likert Scale of 1-5, with 1 indicating having zero difficulty or zero experience of the prompted symptom and 5 indicating always having difficulty or always experiencing the prompted symptom. Figure 2 depicts sample views of the tablet-based questionnaire for the collection of information on how the individual feels and interprets their health, their comfort levels, and their ability to participate in and enjoy life events.

Figure 2: Sample views of 'Patient Reported Outcome Survey' utilizing PDQ-39 [56].

3.3 Functional Assessment

Digital assessments have the capability and promise to expand traditional functional assessments by allowing for both objective scoring and/or the interpretation of results relating to the initial diagnosis and monitoring of disease progression [25]. The transition of these assessments to mobile devices also allows for standardized administration which is unaffected by examiner bias [58].

The developed functional assessment of the NDHS is comprised of 14 tablet-based tasks, collecting 140 digital biomarkers (e.g., objective, quantifiable physiological and behavioral data that are collected and measured by means of digital devices), with a focus on the neurocognitive areas of motor, memory, executive function, and speech (e.g., tracing shapes, apraxia tests, reflex tasks, card matching, trail making, speech based assessments, and multi-functional tasks). These implemented tasks are versions of administered tasks from commonly used screening assessments (e.g., MoCA [31] or MMSE [49]) which are usually given whenever a neurodegenerative condition is suspected. Figure 3 gives a depiction of the tablet-based neurological assessment tool (e.g., from the task menu, the instructions of a functional task, and interactive view of that task) [48]. These tablet-based versions allow for the collection of objective digital biomarkers with the use of inherent device sensors (e.g., accelerometer, gyroscope, microphone, and timer) and human-device interactions (e.g., screen taps, drawing, and device manipulation). Instructions of the administered tasks are included.

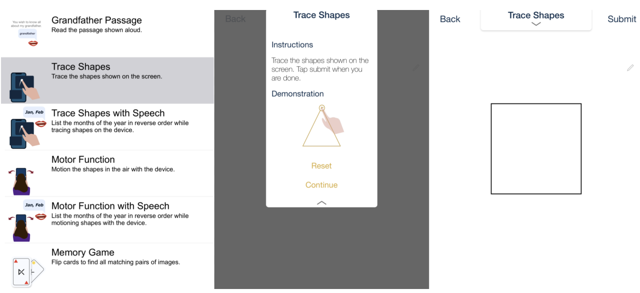

Figure 3: Sample views of the tablet-based 'Functional Assessment' including Task Selection, Task Instruction, and User Execution.

For a fine-motor tracing task the individual is instructed to use their index finger to trace a depicted shape. In a gross-motor task the user is to manipulate the tablet to "air"-trace a prompted shape (e.g., a square). For reflex tasks, the user is intended to tap on the screen to interact with a set of targets. For a memory task the user is to tap on depicted cards until all cards have been matched in pairs. In a trail making task the user is intended to draw a line using their index finger to connect the shapes in increasing numerical order. For a set of speech based tasks, the user is instructed to read a sentence or passage out loud or name prompted objects. Finally, a set of tasks also implements dual task interference for the understanding of how these individuals interact in multifunctional task approaches. Examples of dual tasks include both fine (e.g., tracing an object) and gross (e.g., manipulating the tablet) motor tasks paired with a non-automatic speech task (e.g., listing the months of the year, aloud, in reverse order; December to January). Additionally, executive functional tasks are also dual task by nature as the individual must "put into action" their necessary 'executive functions'. This is seen in the Stroop Word Color Test (SWCT) [45] as the user is required to discern the difference between prompted colors and words and then speak the correct response.

The collected digital biomarkers were systematically distributed across all functional tasks (e.g., tasks assessing a singular function received proportionally half the number of biomarkers compared to a dual-functional received). Metrics included both temporal (e.g., time to interact with the tablet following a prompt, or total time to complete the task) and accuracy measures (e.g., number of correct screen interactions or overall distance from true value points).

3.4 Wearable Integration

Implementing wearable devices into the NDHS can allow for even more vital data to be collected [47]. The wearable component of this system allows for the objective monitoring of additional neurocognitive functions that the functional assessment element of the system cannot. These functional areas are autonomic function and sleep. Digital biomarker collection from wearables relates to the additional health-related monitoring capabilities on these devices (e.g., heart rate, blood oxygen saturation, and electrodermal activity [4]), in addition to using on-device accelerometers and gyroscopes. Further, these wearable sensors can also allow for the collection of this objective data throughout the day, enhancing the NDHS with more opportunistic collections. The following implementations, a labeled event/activity and an opportunistic collection model, are seen in Figure 4.

Figure 4: Sample views of wearable device integration for a labeled event or activity.

3.5 Caretaker Survey

All aforementioned components of the NDHS involve the collection of information from an individual diagnosed with a neurodegenerative disease. However, the collection of supplementary information from a caretaker who plays a critical role in the aid and well-being of the diagnosed individual is highly beneficial [14]. Similar to the PROs questionnaire listed prior, a set of questions based on a Likert Scale of 1-5 is asked to the caretaker regarding the diagnosed individual's symptoms. Figure 5 depicts sample views of the tablet-based questionnaire given to caretakers regarding the individual they care for.

3.6 Intervention Recommendation

The final part of the NDHS is intended to gather all objective, subjective, longitudinal, and symptom-specific information to aid in the recommendation of interventions. Many different recommendations are advocated for with respect to neurodegenerative diseases; however, many studies evaluate some interventions as a one-size-fits-all concept as current evidence is not sufficient to develop personalized intervention programs [34]. The intervention recommendation aspect of this system is beneficial for finding therapies that should be recommended for newly diagnosed individuals (e.g., activities that positively affect the most areas of neurocognitition to the highest extent), but also in an individualized manner (e.g., in the formation of a personalized symptom-specific report card with respect to different interventions). Comparing all collected data in conjunction with administered intervention protocols for these

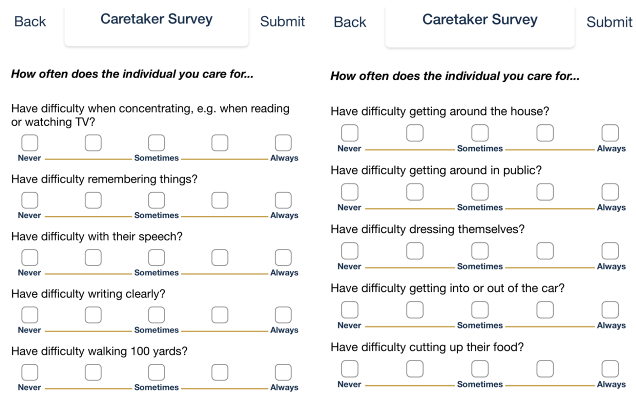

Figure 5: Sample views of 'Caretaker Survey' using modified version of PDQ-39 [56].

approaches is necessary for the improvement of exercise counseling and the design of appropriate interventions [27, 34]. Preliminary work with the NDHS is intended to depict how different physical activities (e.g., boxing, functional strength, yoga, and agility) affect neurocognitive functions through the collection of objective digital biomarker sets (e.g., from functional assessments) with relation to each activity. However, this concept can be extended to other rehabilitative intervention protocols (e.g., speech, occupational, music, or pharmacological interventions) and by using expanded digital biomarker sets (e.g., collected utilizing wearable devices).

4 METHODS

Participants in this preliminary study were 25 adults between the ages of 52 and 84, all with a confirmed diagnosis of Parkinson's disease (stages 1-3). All individuals participated regularly (e.g., at least twice a week) in structured, in-person, physical intervention programs led by certified fitness instructors. These in-person intervention programs are formed specifically for individuals with PD and they occur at local health and fitness centers with access to a variety of training and exercise equipment. A subset of these individuals also completed physical exercise either at home or outside these structured intervention programs. Individuals were recruited to participate in this IRB approved study via advertisement through the structured intervention programs, physician and clinician referrals, and prior studies from our laboratory. Given the mean age of onset for PD in the Western world is early-to-mid 60's [36], our recruitment efforts were limited to diagnosed individuals age 50 years or older. 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 instructions of the functional task assessment were formatted in English).

All participants were required to fill out questionnaires regarding their personal health information and medical history, and patient reported outcomes. Subsequently, all participants were required to take the tablet-based functional assessment prior to and following their in-person intervention program sessions. This testing protocol was included to assess the positive affects of the intervention protocol (e.g., different activities including boxing, functional strength, or yoga) on the individual's neurocognitive functions. Intervention specific protocol spanned 2 hours; allocating 15 minutes for the tablet-based functional assessment, 10 minutes of warm up activities (e.g. stretching), 45-60 minutes of main activity (e.g., boxing, yoga, etc.), 10 minutes of cool down activities (e.g., stretching), 15 minutes for the tablet-based functional assessment, and remaining time for rest and transitions between each component. Improvement during the intervention specific protocol was measured via calculated deltas of each metric between assessments (e.g., increased count and accuracy in a reflex test or decreased time to complete the matching of all pairs in a memory task). As participants were required to take the functional assessment twice within a period of 2 hours, internal randomization was included in the functional assessment 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).

5 RESULTS

Intervention recommendations were formed using objective, symptom-specific digital biomarkers collected from the functional assessments, across all participants (e.g., given prior to and following different physical interventions). 140 digital biomarker metrics were collected using different inherent device sensors (e.g., accelerometers, gyroscopes, microphones, and timers) and human device interactions (e.g., screen taps, drawing, and device manipulation). The changes in these metrics following interventions were categorized as either being improved (e.g., better following the intervention) or staying the same/worsening.

The collected categorized information across different functional areas of neurocognition (e.g., motor, memory, speech, executive function, and dual task) generated the following heat map in Figure 6. Scores indicate the level of improvement that each activity yields to individuals with PD across different functional areas of neurocognition on a scale of 0-1. Values closer to 1 denote a higher number of individuals with a higher proportion of digital biomarkers per functional area (e.g, motor, speech, memory, or executive function) that improved due to the respective intervention (e.g, boxing, agility, yoga, or walking). Given the sample population and interventions listed, yoga had the highest overall improvement of neurocognition with 62% of digital biomarkers being categorized as improving following the intervention. Walking showed a high overall improvement of neurocognition while also having a relatively even distribution of digital biomarkers that improved following the intervention.

6 DISCUSSION

Following the generation of the aforementioned heat maps, with respect to both intervention types and neurocognitive functions, personalized intervention recommendations can be formed. The information collected from personal medical information, patient reported outcomes, and caretaker surveys give insights to which functional areas of neurocognition that a individual diagnosed with a neurodegenerative disease struggles with (e.g., motor function, memory, or speech). The generated heat map is intended to give insights to which functional areas of neurocognition are positively affected by different interventions. The preliminary work displays structured physical interventions like boxing, agility, functional

Figure 6: Relation between interventions and neurocognitive functions to aid in 'Intervention Recommendation'.

strength, and yoga; however, this process can be applied to other intervention programs including speech therapy, music therapy, or occupational therapy and across more areas of neurocognition (e.g., autonomic function, sleep, language, sensory, and behavioral or psychological function). Further, this preliminary work focuses on a group based approach for the formation of heat maps. This is beneficial for finding activities that should be recommended for newly diagnosed individuals (e.g., activities that positively affect the most areas of neurocognitition to the highest extent). However, in the use case of Parkinson's disease (e.g., a "designer disease", with no two diagnosed individuals manifesting the exact same symptoms [6, 43]), this process should also be implemented in an individualized manner. As an individual interacts with new therapies over time, the collection of their digital biomarkers (e.g., both prior to and following interventions) will give insights on how that participant fares with respect to a specific intervention. Thus, generated heat maps given objective, longitudinal, and symptom-specific data can be created for an individual with specific recommendations given their symptoms and response to interventions.

The implementation of wearable devices into the NDHS allows for the collection of objective digital biomarkers for autonomic function, motion, and sleep. This expands what is depicted by the presented heat map. Further, these wearable devices give the ability for new labeling capabilities and opportunistic data collections. Although the presented data shown above does not represent the implementation of the wearable device, the corresponding application for the wearable has been created for integration in future work. Future work is also intended to validate the efficacy of the collected digital biomarkers from this portion of the system.

As digital health systems for neurocognitive assessments become more readily available, it is also important to maintain clinical expertise [47]. Subjective biases are reduced with the implementation of these new objective digital health systems with the collection of digital biomarkers. With the increased opportunity for user participation on their own devices and the ability of the clinician to collect and analyze enhanced objective datasets, this becomes a robust modality for the administration of neurocognitive assessments. Additionally, although this version of the digital assessment [48] was created for individuals to perform tasks by themselves without help, clinician interactions should be maintained for both onboarding and overall recommendations (e.g., nonpharmacological therapies).

A limitation of this work is that all participants in this study participated in intervention protocols. Individuals with neurodegenerative diseases who do not participate in any structured programs as well as age-matched control populations were not represented in this work. A further understanding of how individuals with neurodegenerative conditions fare given no or limited interventions is necessary to see the benefit of various interventions overall. Further, analysis of how different interventions help individuals in different stages of their condition in comparison to age-matched control populations is necessary to assess. Additional work should also be completed to understand how individuals with different neurodegenerative conditions (e.g., Alzheimer's disease, ALS, and dementia) and stages are affected given no, limited, or various structured interventions. This system could also be utilized for routine examinations of at-risk populations for the monitoring of their neurocognitive functions over time. Finally, future work includes the provision of revised versions as needed to accommodate individuals with other conditions and at different stages.

7 CONCLUSION

Using a digital health system approach for the monitoring of individuals with neurodegenerative diseases allows for a more comprehensive understanding of how neurological conditions manifest while also providing methodologies for more personalized intervention protocols. The collection of both digital biomarkers and patient reported outcomes across all areas of neurocognition is imperative to a comprehensive digital health system. With the influx of quality data from digital health systems, further efforts should be directed into evaluation and development of personalized rehabilitation programs to create a higher quality of life of the participants. Ultimately, the formation of usable digital health systems, for the monitoring of neurocognitive functions, can aid clinicians, diagnosed populations, and caretakers in the monitoring of individuals with neurodegenerative diseases while also allowing for the increased accuracy for both diagnostic and rehabilitative purposes.

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