QUANTIFYING PARKINSON'S DISEASE SYMPTOMS USING MOBILE DEVICES

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ABSTRACT

Quantifying Parkinson's Disease Symptoms Using Mobile Devices

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Current assessments for evaluating the progression of Parkinson's Disease are largely qualitative and based on small sets of data obtained from occasional doctor-patient interactions. There is a clinical need to improve the techniques used for mitigating common Parkinson's Disease symptoms. Available data sets for researching the disease are minimal, hindering advancement toward understanding the underlying causes and effectiveness of treatment and therapies. Mobile devices present an opportunity to continuously monitor Parkinson's Disease patients and collect important information regarding the severity of symptoms. The evolution of digital technology has opened doors for clinical research to extend beyond the clinic by incorporating complex sensors in commonly used devices. Leveraging these sensors to quantify characteristic Parkinson's Disease symptoms may drastically improve patient care and the reliability of symptom assessment.

The goal of this project is to design and develop a system for measuring and analyzing the cardinal symptoms of Parkinson's using mobile devices. An application for the iPhone and Apple Watch is developed, utilizing the sensors on the devices to collect data during the performance of motor tasks. Assessments for tremor, bradykinesia, and postural instability are implemented to mimic UPDRS evaluations normally performed by a neurologist. The application connects to a cloud-based server to transfer the collected data for remote access and analysis. Example MatLab analysis demonstrates potential approaches for extracting meaningful data to be used for monitoring the progression of Parkinson's Disease and the effectiveness of treatment and therapies. High-level verification testing is performed to show general efficacy of the assessment tasks. The system design successfully lays the groundwork for a mobile device-based assessment tool to objectively measure Parkinson's Disease symptoms.

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LIST OF ABBREVIATIONS

PD = Parkinson's Disease
UPDRS = Unified Parkinson's Disease Rating Scale
HY = Hoehn and Yahr
TOM= technology-based objective measurement
ADL = activities of daily living
OS = operating system
UI = user interface
L-Dopa = levodopa
DBS = Deep Brain Stimulation
NIH = National Institute of Health
NINDS = National Institute of Neurological Disorders and Stroke
BD2K = Big Data to Knowledge
IT = Information Technology
AWS = Amazon Web Services
IDE = integrated development environment
API = application program interface
S3 = Simple Storage Service
PHI = protected health information
GPS = global positioning system
FFT = Fast Fourier Transform
HIPAA = Health Insurance Portability and Accountability Act

CHAPTER 1

BACKGROUND

1.1 INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the manifestation of motor and non-motor dysfunction [1]. While research has shown the disease results from a complicated interplay of genetic and environmental factors, the cause of the disease remains unknown [2]. Further complexity arises from clinical challenges with the disease, including difficulty in making a definitive diagnosis at the early stages and management of symptoms at later stages [2]. The disease is assessed based on clinical criteria with no universally established test dictating proper evaluation [1]. A number of rating scales are used to measure motor impairment, but most of them have not been fully evaluated for validity and reliability [1]. Current treatments reduce symptoms but do not slow the neurodegenerative behavior of the disease.

1.2 HISTORY

In 1817, James Parkinson published "An Essay on the Shaking Palsy" in which he describes six cases of people with a condition Parkinson called *paralysis agitans*, or shaking palsy. He details the progression of disability characterized by increasing tremor severity, deteriorating muscle strength, and hunched over posture in his publication:

> Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured.[1]

[1] James Parkinson, An Essay on the Shaking Palsy

Parkinson notably distinguishes the tremor symptoms he observed from tremors experienced in cases of epilepsy, alcoholism, or stroke. He observed gradual onset of the symptoms with motor impairment beginning in the limbs before moving to the rest of the body. Parkinson concluded from the symptoms he observed that *paralysis agitans*, as he labelled the syndrome, resulted from lesions in the cervical spinal cord but failed to find evidence in post-mortem studies. Four decades later, French doctor Jean-Martin Charcot, known as "the father of clinical neurology", added symptoms to the syndrome and labelled it Parkinson's Disease to honor the work of James Parkinson.

1.3 CARDINAL FEATURES

There are four cardinal features of PD often described using the abbreviation TRAP: tremor, rigidity, akinesia (or bradykinesia), and postural instability [3]. Motor symptoms usually begin gradually and worsen over time, creating difficulties in walking, talking, and other simple tasks. While motor symptoms are often used to gauge the severity of the disease, non-motor symptoms are also impacted. Non-motor symptoms may include mental and behavioral changes, sleep problems, depression, memory loss, and fatigue [4].

1.3.1 Causes of PD

A combination of environmental and genetic factors is believed to cause the neurodegeneration associated with PD [20]. Scientists have identified several genetic mutations linked to PD, most notably the alpha-synuclein gene [4]. While researchers recognize genetic factors are closely tied to PD, most believe environmental exposures increase a person's risk of developing the disease [4]. The same genes and proteins that are altered in inherited cases may also be altered in sporadic cases resulting from toxins or other factors [4]. PD symptoms begin to arise following the gradual death of nerve cells in a small portion of the lower brain called the

substantia nigra [11]. These cells normally connect to the striatum in the brain's basal ganglia under the cerebral cortex and release the neurotransmitter dopamine to produce smooth, purposeful movement [4, 11]. Insufficient dopamine in this circuit results in abnormal nerve-firing patterns causing impaired movement [4]. The cardinal motor impairments associated with PD manifest when roughly 80% of dopamine has been depleted from the basal ganglia [3, 11].

1.3.2 Tremor

Tremor, or shaking, is often the first symptom of affected patients and is the most common and easily recognizable among those impacted by the disease. Tremor usually begins in the arm or hand and progresses to other parts of the body, though not typically to the same extent as the initial location [5]. In some cases, tremor may only affect one side of the body and may also affect the chin, tongue, and lips [5]. Tremor motor symptoms are not unique to Parkinson's Disease. Another condition often confused with Parkinsonian tremor is Essential Tremor, which induces similar dysfunction but subtle differences make it distinguishable from PD. Essential Tremor symptoms increase with motion and are more symmetric than seen in PD patients [21]. Essential Tremor patients do not respond to PD medications making it clear the symptoms do not share a root cause [21]. Parkinsonian tremor has an oscillation frequency of 4-6Hz at the distal end of the affected limb and occurs with a supination-pronation motion, also referred to as "pill rolling" [1]. Parkinsonian tremor is most present at rest and usually decreases with motion, mental concentration, and during sleep [1]. Some PD patients have also reported an "internal" shaking not associated with visible tremor [1]. PD patients may also experience a postural tremor, known as "re-emergent tremor", identified by outstretching the arms in a horizontal plane [3]. The term "re-emergent" refers to the delay of one to several seconds for the tremor to occur after extending the arms [42]. Postural tremor and resting tremor occur at the same frequency and are reduced by the same therapy, indicating a shared root cause. PD patients may also experience

tremor during voluntary movement, known as kinetic tremor, which is often assessed during a writing task or finger-to-nose motion [42]. Tremors symptoms are not present among all PD patients and severity fluctuates as the disease progresses [1].

1.3.3 Rigidity

Rigidity associated with PD is characterized by uniform resistance to movement present in both agonist and antagonist muscles recruited for the movement [3]. Increased stiffness can affect the neck, shoulders, hips, trunk, ankles and wrists [3]. Normal muscle control involves a relaxed state at rest, and a flexed state when moved. In Parkinsonian rigidity, the affected muscles are constantly flexed, often leading to a decreased range of motion [3]. The presence of rigidity is commonly identified while the affected person is walking with little to no swing of the arms [6]. A neurologist often identifies the symptom by moving the patient's arm and observing a ratchet-like motion with short, jerky movement referred to as the "cogwheel phenomenon" [3]. Pain is often associated with rigidity in PD patients, commonly misdiagnosed as other forms of rheumatology or skeletomuscular injury [3]. Postural deformities may arise from rigidity symptoms among PD patients [3]. Some cases of axial postures (i.e. scoliosis or anterocollis) have manifested through rigidity in the neck and trunk late in the disease [3].

1.3.4 Akinesia and Bradykinesia

Often considered the most debilitating symptom of PD is a general lack or slowness of voluntary movement [23]. Akinesia specifically refers to a slowness or inability in the initiation of movement while bradykinesia refers to a slowness in the execution of movement [23]. Bradykinesia is the most characteristic motor symptom of Parkinson's Disease and encompasses difficulties in planning, initiating, and executing movement [1]. Bradykinesia causes difficulty in performing repetitive movements, such as finger tapping, and simultaneous movement [4]. An

inability to perform simple tasks due to bradykinesia creates frustration among PD patients as activities once performed quickly and easily, such as getting dressed or washing the dishes, may take several hours [4]. bradykinesia may cause other discomforts including impaired swallowing, impaired speech, loss of facial expression, and decreased blinking [3]. With its many secondary symptoms, bradykinesia is often regarded as the most debilitating of the PD symptoms [3]. Assessment of bradykinesia symptoms usually involves observing cadence and amplitude while the patient performs rapid, repetitive, alternating movements such as finger tapping, heel tapping, hand gripping, and hand pronation-supination [1].

1.3.5 Postural Instability

Toward the late stages of the disease, following the onset of other clinical features, patients begin to experience postural instability and a loss of postural reflexes [3]. Postural instability refers to an instability while standing upright and a loss of reflexes to maintain an upright posture, often leading to balance issues [6]. The primary danger PD patients face due to postural instability is retropulsion, or a tendency to fall backward, leading to a predisposition to hip fractures [6]. Doctors test this using a "pull test", in which the patient is pulled backward from the shoulders and their recovery is observed [6]. A normal recovery involves a quick step backwards to prevent falling, while those affected by postural instability would tumble backwards without assistance from the doctor [6].

1.3.6 Non-motor Symptoms

The onset of non-motor symptoms may identify PD in some patients. Autonomic dysfunction, while more typically associated with other neurological disorders, affects many PD patients [1]. Examples include orthostatic hypotension, sweating dysfunction, sphincter dysfunction and erectile dysfunction [1]. PD patients may also experience cognitive and

neurobehavioral abnormalities with an increased risk for dementia, depression, apathy, anxiety, and hallucinations [1]. Other non-motor symptoms include sensory abnormalities and sleep disorders [1]. Measurement of non-motor symptoms provides insight on disease severity and is an ongoing research area for PD evaluation [22].

1.4 EVALUATION

Several assessments are used to evaluate the symptoms and severity of Parkinson's Disease with ranging focuses reflecting functional fluctuations and general level of function [3]. The need for a metric to assess the effectiveness of therapeutic intervention was a driving force for creating rating scales [3]. As the disease progresses during treatment, evaluations can determine whether or not the treatment is effective. Often during the course of treatment, patients experience what doctors refer to as an ON/OFF phenomenon. Patients are considered ON when medication is working and OFF when the benefit subsides [3]. The patient's ability to perform tasks can change dramatically between states, so far as being able to run across the room versus an inability to rise from a chair [3]. The following sections detail evaluation techniques used.

1.4.1 Hoehn and Yahr

In 1967, Melvin Yahr and Margaret Hoehn published a system for evaluating the progression of Parkinson's Disease in the journal *Neurology* [8]. The Hoehn and Yahr (HY) system utilizes 5 stages to describe and classify the severity of motor symptoms [8]. The system has since been modified to include steps 1.5 and 2.5 to account for intermediate stages [8]. The HY scale provides a simple method to categorize the severity of the disease to reflect the degree of progression [8]. However, the scale is not linear, and the ranking of stages does not always reflect progression as expected; in some cases, patients have more difficulty performing the stage 2 assessment tasks than those in stage 3 [8]. The advantages of this scale are its popularity and

simplicity to carry out. However, the categorical scale and inaccurate rank-progression correlation has led the scale to be largely supplanted by the Unified Parkinson's Disease Rating Scale [8]. The HY scale is shown in Table 1.

Table 1. Modified Hoehn and Yahr scale [8]

1.0	Unilateral involvement only
1.5	Unilateral and axial involvement
2.0	Bilateral involvement without impairment of balance
2.5	Mild bilateral disease with recover on pull test
3.0	Mild to moderate bilateral disease; some postural instability, physically independent
4.0	Severe disability; still able to walk or stand unassisted
5.0	Wheelchair bound or bedridden unless aided

1.4.2 Schwab and England Activities of Daily Living

Developed by R. S. Schwab and A. C. England Jr., the Schwab and England activities of daily living (ADL) rating scale is frequently used to provide an estimate of severity based on the patient's ability to perform common tasks [7]. The examination involves an interview with the patient and often includes a collateral source, such as a spouse [7]. The examiner will ask about the patient's ability to perform common household chores and whether assistance is needed. The scale uses percentages to rank severity with 5% increments between 0%-100% [7]. Table 2 shows the sections of the Schwab and England ADL assessment.

Table 2. Schwab and England ADL scale [7]

100%	Completely independent. Able to do all chores without slowness, difficulty or impairment. Essentially normal. Unaware of any difficulty.
90%	Completely independent. Able to do all chores with some degree of slowness, difficulty and impairment. Might take twice as long. Beginning to be aware of difficulty.
80%	Completely independent in most chores. Takes twice as long. Conscious of difficulty and slowness
70%	Not completely independent. More difficulty with some chores. Three to four times as long in some. Must spend a large part of the day with chores.
60%	Some dependency. Can do most chores, but exceedingly slowly and with much effort. Errors; some impossible.
50%	More dependent. Help with half, slower, etc. Difficulty with everything.
40%	Very dependent. Can assist with all chores, but few alone.
30%	With effort, now and then does a few chores alone or begins alone. Much help needed
20%	Nothing alone. Can be a slight help with some chores. Severe invalid.
10%	Totally dependent, helpless. Complete invalid.
0%	Vegetative functions such as swallowing, bladder and bowel functions are not functioning. Bedridden.

1.4.3 Unified Parkinson's Disease Rating Scale (UPDRS)

The global "gold standard" rating scale for PD assessment is the Unified Parkinson's Disease Rating Scale (UPDRS), owned and licensed by the International Parkinson and Movement Disorder Society [7]. The UPDRS was developed in an effort to incorporate elements from existing scales into a single comprehensive assessment [24]. However, the UPDRS has important limitations and has undergone several revisions since its development [7].

In 1987, the official UPDRS was published by Stanley Fahn and the UPDRS Development Committee. The UPDRS includes four subscales covering behavioral features, activities of daily living, motor symptom ratings, and therapeutic complications [7]. Part I of the UPDRS covers

mentation, behavior, and mood and examines for intellectual impairments, thought disorders, depression, and changes in motivation [25]. Part II includes a 13 items that directly relate to daily activities such as dressing and eating while also examining patient perceptions of primary disease manifestations like tremor and salivation [24, 25]. Part III evaluates motor impairment including speech, facial expression, rest and postural tremor, rigidity, bradykinesia, posture, gait, and postural stability [25].

In 2001, the International Movement Disorder Society (MDS) created a UPDRS task force with three main objectives: critique existing scales, identify clinical areas that are not adequately rated, and make recommendations on maintaining or modifying currently available scales [24]. The task force unanimously considered the concept of a single clinical rating scale to be an important tool for clear and consistent communication among movement disorder colleagues [24]. In 2003, the conclusions of the task force were published. They agreed the UPDRS has many strengths and provides an effective comprehensive assessment of motor symptoms associated with PD [24]. However, the weaknesses were substantial in the assessment of non-motor symptoms, leading the task force to develop a list of recommended improvements [25]. In 2008, based on the recommendations laid out by the task force, the MDS published an MDS-sponsored revision of the UPDRS (MDS-UPDRS) [26]. The four component design was retained with a shifted focus for each of the sections [26]. Part I of the MDS-UPDRS concerns "non-motor experiences of daily living", Part II concerns "motor experiences of daily living", Part III remains focused on motor symptom examination, and Part IV concerns "motor complications" [26]. In practice, the UPDRS test is combined with the HY and the Schwan and England ADL assessments [27]. Details for each part of the MDS-UPDRS assessment are shown in Table 3.

Table 3. MDS-UPDRS sections [26]

Part I: Nonmotor Aspects of Experiences of Daily Living
1.1 Cognitive impairment
1.2 Hallucinations and psychosis
1.3 Depressed mood
1.4 Anxious mood
1.5 Apathy Features of dopamine dysregulation syndrome
1.6 Sleep problems
1.7 Daytime sleepiness
1.8 Pain and other sensations
1.9 Urinary problems
1.10 Constipation problems
1.11 Lightheadedness on standing
1.12 Fatigue
Part II: Motor Experiences of Daily Living
2.1 Speech
2.2 Saliva and drooling
2.3 Chewing and swallowing
2.4 Eating tasks
2.5 Dressing
2.6 Hygiene
2.7 Handwriting
2.8 Doing hobbies and other activities
2.9 Turning in bed
2.10 Tremor impact on activities
2.11 Getting in and out of bed
2.12 Walking and balance
2.13 Freezing
Part III: Motor Examination
3.1 Speech
3.2 Facial expression
3.3 Rigidity
3.4 Finger tapping
3.5 Hand movements
3.6 Pronation–supination movements of hands
3.7 Toe tapping
3.8 Leg agility
3.9 Arising from chair
3.10 Gait
3.11 Freezing of gait
3.12 Postural stability
3.13 Posture
3.14 Global spontaneity of movement (body bradykinesia)
3.15 Postural tremor of hands
3.16 Kinetic tremor of hands
3.17 Rest tremor amplitude
3.18 Constancy of rest tremor
Part IV: Motor Complications
4.1 Dyskinesias: time spent with dyskinesias
4.2 Dyskinesias: functional impact of dyskinesias
4.3 Dyskinesias: painful off state dystonia
4.4 Motor fluctuations: time spent in the off state
4.5 Motor fluctuations: functional impact of fluctuations
4.6 Motor fluctuations: complexity of motor fluctuations

1.5 PATIENT POPULATION

Parkinson's Disease is one of the most common neurological disorders with an estimated one in every 1,000 people affected by the condition [10]. A widely accepted figure for the approximate prevalence of PD globally is 200 for every 100,000 individuals [10]. In the U.S., an estimated 750,000 to 1.5 million individuals are affected [10]. In the U.K., there are 120,000 to 130,000 diagnosed individuals, but many more are affected that remain undiagnosed [10]. Men are 1.5 times more likely to than women to develop the condition and symptoms generally surface at age 60 [10]. The risk increases to one in 100 for those aged between 60 and 80 years of age, and one in 50 at age 80 [9]. There have been cases of the disorder in individuals under the age of 20, known as juvenile parkinsonism [9]. While the disease prevalence is skewed toward later ages and occurs more frequently in men, there is no boundary in age, race, or gender [9]. A study by Hoehn and Yahr in 1967 observed mortality rates related to the condition. They found 61% of patients were dead or severely disabled 5-9 years after diagnosis, increasing to 80% after 10 years [10]. This rate has since been reduced with the advent of treatments such as Levodopa, a mainstay pharmacological treatment to supplement the loss of dopamine with PD, making it possible for PD patients to live out a normal length life [10, 11].

1.6 TREATMENTS

There is currently no cure for PD, but symptoms can be relieved with surgeries or medication [28]. The primary objective of medical management is to maximize control over the target signs and symptoms by selecting the appropriate drug, dosage, and frequency [25]. Symptoms and response to medication are highly variable from patient to patient and require a very individualized approach [25]. Drug therapies target motor symptoms by increasing dopamine levels in the brain or targeting neurotransmitters in the body and non-motor therapies focus on symptoms like depression [28]. The mainstay drug is levodopa (L-dopa) which provides

a dopamine precursor to nerve cells helping to replenish the brain's reduced supply of dopamine [23]. Patients cannot simply take a dopamine pill because dopamine does not easily pass through the blood-brain barrier, a protective lining of cells inside blood vessels that regulate the transport of nutrients and substances in the brain [23]. Levodopa has a high rate of success with reducing or eliminating motor symptoms during the early stages of PD, allowing a majority of patients to extend the period in which they can lead active, productive lives [23].

When drug therapies are no longer sufficient, surgical approaches are used to relieve symptoms [23]. The earliest types of surgical techniques involved selectively destroying specific parts of the brain that contribute to symptoms [23]. These risky techniques have been largely replaced by deep brain stimulation (DBS), a technique in which an electrode is implanted into part of the brain and connected to a pulse generator implanted in the chest area [23]. When turned on, the pulse generator and electrode stimulate the brain painlessly to block signals that cause many of the motor symptoms of PD [23]. DBS is generally appropriate for patients who have levodopa-responsive PD and do not have memory problems, hallucinations, or severe depression [23]. As with any brain surgery, DBS surgery has potential complications like stroke or brain hemorrhage [23].

1.7 NEED FOR RESEARCH

Recent developments in Parkinson's Disease research are giving researchers optimism that the disease can be defeated. PD is a complex neurodegenerative disease resulting from the death of dopamine producing cells in the substantia nigra [11]. What triggers the death of these cells remains unknown [11]. Studying genetics, epidemiology, and environmental factors all contribute to finding a cure. Identifying genes linked to PD fuels growth in understanding the disease process, revealing drug targets, improving early diagnosis, and developing animal models to mimic the nerve death in humans [11]. The National Institute of Health (NIH) released a

formal Parkinson's Disease research agenda in 2000 stating that new technologies and discoveries in neuroscience are opening new doors to potential cures [11]. Halting the progression of PD, restoring lost function and even preventing the disease are becoming more realistic possibilities through advances in neuroimaging, gene array technologies, animal models, biomarkers and other modern scientific tools [11]. The National Institute of Neurological Disorders and Stroke (NINDS) is currently leading an initiative to better understand and diagnose PD, develop new treatments, and ultimately prevent PD [29]. In 2014, the NNIDS held a conference, labelled "PD2014", bringing neuroscientists, physicians, public and private organization representatives, and PD patients together to develop a set of recommendations addressing the highest priorities for advancing research on PD [29]. In the topic of clinical research, one of the recommendations involves the use of "innovative outcome measures to evaluate motor and non-motor features, including patient- and clinician- reported outcomes that leverage emerging information technology (IT) opportunities, enhance sensitivity and specificity of measurement, and facilitate long-term follow-up of well-characterized cohorts" [30]. One of the approaches to address this research is an investigation of the feasibility and validity of "diverse methods of data collection including computerized tablet, smartphone, remote monitoring, and computerized adaptive testing" [30].

1.8 MOBILE TECHNOLOGY

Difficulties remain in the reliability of clinically evaluated PD symptoms involving functioning in everyday life, long periods of time, and observing critical milestones throughout the course of the disease [12]. Fluctuating events like responses to medicine and incidents like falling are difficult for doctors to track and react to without constant monitoring. The evolving miniaturization, sophistication, proliferation, and accessibility of sensing technologies opens a new door to data collection beyond the doctor's office by introducing novel methods for patient

monitoring [12]. Modern sensors embedded in every day devices can track and send important health information like motion, sleep patterns and heart rate to health professionals within minutes [12]. This can enhance treatment methods, preventative care, and drastically reduce the number of trips taken to the doctor's office. With the rapid growth of these new technologies, the questions now faced are how to properly deploy them, what are the clinical needs, and how to leverage them to replace or enhance current clinical assessment tools. The ability to remotely capture symptom data and use it to optimize treatment strategies introduces a possibility to create closed loop treatment systems while producing valuable information for research [12]. For example, a wearable system may detect a change in step cadence associated with stride length, triggering a device designed to deliver proprioceptive cues for changing postural control and stepping pattern which could in turn prevent a fall [12]. Continuously monitoring PD symptoms may also be used to track and optimize the effectiveness of therapies, such as deep brain stimulation.

1.8.1 Sensor Technology

Modern mobile devices commonly contain sensors for interaction with the device and installed software applications. Evolving sensor technology has led to decreasing sensor sizes allowing for several sensors to be embedded in digital devices like smart phones and wearable technology. Smart devices like mobile phones, tables, and smart watches contain inertial sensors (accelerometer, gyroscope), GPS, and pedometers with high levels of accuracy for motion tracking. Other advanced wearable technologies contain sensors for monitoring respiratory rate, skin conductance, blood pressure, oximetry, and electrocardiography [12]. In addition to the high level of accuracy and wide range of capabilities, the sensors are low power enabling them to poll data for long periods of time. For instance, sleep medicine research has begun utilizing actigraphy (monitoring human rest/activity cycles) to supplant traditional methods like polysomnography

due to its validity, low cost, and ability to monitor patients at home [12]. Accelerometers and gyroscopes are well suited for the detection of PD motor symptoms such as tremor, bradykinesia, gait impairment, and motor complications, such as dyskinesia [12].

1.8.2 Big Data Collection

The health care industry generates large amounts of data, primarily due to regulatory requirements, record keeping, and patient care [16] and biomedical research data is stored in varying formats, increasing the need to organize and understand the data to foster new discovery [31]. While most health care data are stored in hard copy form, the current trend is toward rapid digitization [16]. By definition, big data in health care refers to health data sets so large and complex that traditional data management tools and methods cannot easily manage the data, overwhelmed by the volume and diversity of data types [16]. However, recent technological advances are improving on the compilation, storage, and secured sharing of big data [32]. For instance, electronic medical record (EMR) systems are becoming more affordable and allow data to be exchanged more easily [32]. In 2014, the NIH published a Big Data to Knowledge (BD2K) initiative to maximize the use of big data in health care by defining how to extract value from data and create analytic tools needed to enhance the utility of the data [31]. A recommended approach from the NINDS PD2014 conference for progressing clinical research in PD is to "develop improved informatics capability to include investigation of how 'big data' may contribute to a fuller understanding of PD, a central repository for PD trial data, [and] a resource for trial design simulations" [30]. The medical experts and PD patients in attendance noted that making use of existing data sets is an efficient way to address questions related to the characterization of PD symptoms and progression [30]. They stressed the importance for a central body to manage the standardization of datasets, uniformly archive existing data, and provide a user-friendly end product [30]. Development of an information system for health data must

overcome barriers to use including access to data, ethical challenges, and de-identification of data [30]. Implementing data security measures to protect sensitive patient information is important to comply with HIPAA regulations. Many private-sector companies are developing applications and analytical tools that help patients, physicians, and other health care stakeholders identify value and opportunities with big data [32]. An evaluation of the marketplace in 2013 revealed over 200 businesses created since 2010 are developing such tools to make better use of available health information [32]. Many research groups are in the process of assessing methods to probe individual motor and non-motor symptoms [12]. An opportunity exists to identify technologies and approaches with the most versatility, greatest ease of deployment, least patient and physician encumbrance, and lowest cost [12]. Choosing a platform for technology-based objective measurements (TOM) behind which developers and end-users can coalesce is key for developing applications for big data collection and analysis [12].

1.9 RELATED WORK

The evolution of digital technology has resulted in a surging interdisciplinary effort to explore novel applications in medical research. Researchers from electrical, computer, mechanical and biomedical backgrounds are working cohesively to design, build, and test systems intended to meet an abundance of clinical needs. The need for enhancing assessment tools for Parkinson's Disease is no exception. Within the last 5 years, several methods have been proposed by researchers around the world to enhance PD research efforts by utilizing mobile technology and small sensors. The following examples demonstrate recent developments but only provide a small snippet of the many global research efforts.

1.9.1 mPower

In 2015, Sage Bionetworks launched an observational study using Apple's ResearchKit library on iPhones to evaluate the feasibility of remotely collecting frequent information about

PD symptom severity on a daily basis [37]. Since the release of the iPhone application dubbed "mPower", over 12,000 participants have enrolled [38]. The study is intended to gather data from any population, healthy patients and those affected by PD, to create a large database accessible to researchers interested in the data [37].

1.9.2 Kinesia 360

In January 2016, Great Lakes Neurotechnologies began clinical trials using their Kinesia 360 product, a wearable technology-based device to objectively assess PD symptoms [39]. There are 45 PD patients enrolled in the clinical trial aimed to investigate the efficacy of the product to measure symptoms [39]. Kinesia 36 features a mobile app and wireless motion sensors worn on the wrist and ankle to measure tremor, dykinesias, and mobility during normal daily activities. The data collected is transferred to a cloud server where data reports are generated for clinician review [39].

1.9.3 Academic Research

In addition to interested research organizations, quantification of motor symptoms is a trending topic among academic researchers. A Master's thesis produced by Michelle Vos at the University of Twente in the Netherlands involves the use of a glove containing inertial sensors to quantify tremor, bradykinesia and rigidity in PD patients by observing wrist angle, arm orientation, and movement [41]. The conclusion of the thesis showed promising results with the gloves ability to measure bradykinesia and rigidity symptoms [41]. Another study done by researchers at several universities in China [40] succeeded in creating a wrist worn device with a finger sensor attachment that has very a high correlation with the UPDRS evaluation performed by neurologists for bradykinesia tasks. Both studies were published in 2015 from universities in Europe and Asia, indicating the current global trend toward implementing mobile technology in medical research.

CHAPTER 2

OBJECTIVES

Research groups around the world are attempting to tackle the challenge of leveraging mobile technology to enhance medical care. Difficulties arise when device engineers must take into consideration regulations not normally seen outside of the medical industry. This requires engineers and medical professionals working together to build a cohesive system optimized to meet medical needs and stay within FDA regulations while considering the boundaries of device capabilities. With the current treatment methods and medical care provided for those with Parkinson's Disease, an opportunity exists to harness mobile device technology to provide much improved care. Sensor technology in common devices found in the everyday pockets of people across the nation have the potential to provide valuable insight regarding the progression of the disease and information normally unobtainable for clinicians.

2.1 PROJECT GOAL

The goal of this thesis is to design and develop a working prototype of a mobile application to be used for measuring the cardinal features of Parkinson's Disease. The application should demonstrate the potential for sensors in commonly used consumer electronics to produce valuable clinical data for evaluating Parkinson's Disease symptoms outside of a doctor's office. By harnessing mobile technology already largely integrated into society, gathering large amounts of data for improved analysis becomes feasible. The clinical need for a quantitative assessment of PD motor symptom progression is clear. Designing a system to address this need and accomplish the project goal requires a set of comprehensive functional requirements and system specifications as listed below.

Functional Requirements

- Record patient information (demographics, PD characteristics, etc.)

- Provide a means for measuring tremor symptoms
- Provide a means for measuring gait symptoms
- Provide a means for measuring bradykinesia symptoms
- Store data on cloud server
- Perform analysis on measurements
- User friendly interface
- Secure data by requiring authentication to access
- Include a sign up process with eligibility requirements

System Specifications

- iOS/watchOS application
- iPhone 6 (iOS 9.5.3/10)
- Apple Watch (watchOS 2.3.2/3)
- ResearchKit framework
- Amazon Web Services (AWS) S3 cloud storage
- Matlab 2015a for analysis
- CoreMotion framework to access hardware (sensors, touch screen)
- CoreData framework for data management and persistence
- SQLite Studio for accessing database file on computer

CHAPTER 3

DESIGN OVERVIEW

3.1 SYSTEM OVERVIEW

Designing a digital system for clinical purposes requires consideration of the patient, doctor, and protection of health information. Development of the user interface should ensure ease of use, especially when considering a target audience that is less adaptive to new technology. The front-end system design considers usability, aesthetics, and instruction deliverance to assist in proper use and comfort while using the application. Back-end design focuses on data persistence, speed, security, and data formatting to ensure the necessary precautions are taken with the transportation of digital health information while keeping the data in a format readily used for analysis.

The devices used for development of the application are the iPhone 6 and the Apple Watch. Selection of the hardware was influenced by ease of integration into St. Jude Medical's existing patient care technology, ease of use, and device prevalence among smart device consumers. The iPhone provides data persistence, sensor recordings, and central processing while the Apple Watch provides a secondary wearable source for sensor recordings.

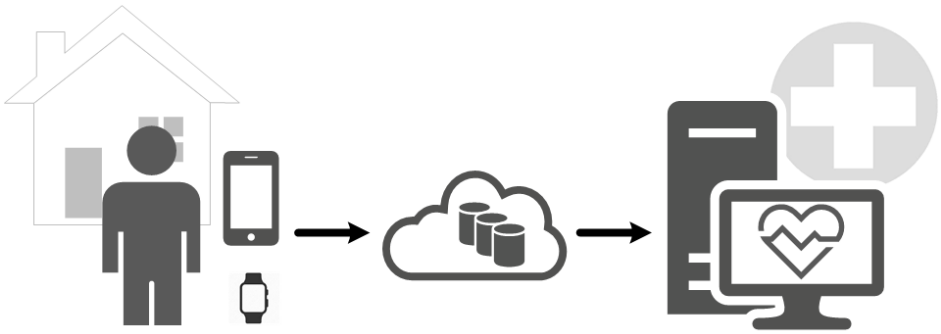

Figure 1. High level system overview

Figure 1 shows the overview of system operation from the user at home with the Apple Watch and iPhone to collect data related to PD symptoms, uploading the data to a cloud database server, and the downloading of data by doctors and clinicians for analysis. The Apple Watch is worn by the user to collect motion data from the arm and transfers that data to the iPhone via Bluetooth. The iPhone provides both data collection and data management by uploading the collected data to a secure cloud server via an internet connection through WiFi or mobile broadband. Once uploaded, the data may be downloaded by an authenticated user, typically a clinician or doctor, and manipulated using data analysis tools to extract valuable parameters.

3.1.1 Design Workflow

The design workflow centers around the flow of data, beginning with collection from the patient and ending with deliverance to the doctor, clinic, or data analyzer. Initial steps of data collection involve instructing the user to navigate through the application, starting and stopping sensor input, and storing sensor output. Deliverance of data involves moving the data from the local device to a remote location while maintaining data integrity. The application design begins with creating a user-friendly interface easily understood to new users. Instructions guide the user through all sections of the application from the signup process to the performance of tasks. During each task, sensors in the iPhone and Apple Watch are turned on to collect motor-related symptoms data and store the data locally on the iPhone. Sensory data may be uploaded to an Amazon Web Services (AWS) server cloud server by pressing an “Upload Data” button easily found in the application. Once the data has been uploaded to AWS cloud storage, the data may be accessed by an authenticated user from a computer and downloaded for analysis.

3.1.2 Sensors

The sensors used in the application focus on collecting motion data related to the cardinal features of PD. The accelerometer, gyroscope, magnometer, and touch screen sensors are used during instructed tasks similar to those performed in the UPDRS assessment. The iPhone 6 features a 6-axis gyroscope-accelerometer combo unit, an additional 3-axis accelerometer, touchscreen controller, magnometer, and GPS. The Apple Watch features a 6-axis gyroscope-accelerometer combo unit, pressure-sensitive touchscreen controller, and heart rate monitor. A full list of sensors found in the Apple Watch and iPhone 6 is shown in Table 4.

Table 4. Sensors in the Apple Watch and iPhone 6

	Apple Watch	**iPhone 6**
Accelerometer	X	X
Gyroscope	X	X
Microphone	X	X
Heart Rate Sensor	X	
GPS		X
Touch ID (Biometric sensor)		X
Proximity Sensor (i.e. phone near ear)		X
Ambient Light Sensor	X	X
Camera/Video Camera		X
Magnetometer		X
Touch Sensor	X	X

The symptoms targeted in this application are primarily motion-based making the motion-related sensors most useful. The accelerometer and gyroscope of the Apple Watch or iPhone 6 are used during the gait and tremor tasks. Continuous data samples from these sensors reveal important information regarding the amplitude and oscillation frequency normally observed visually by a neurologist while performing a clinical assessment. Figure 2 shows the axes of rotation and movement for the gyroscope and accelerometer. Oscillation patterns on each axis are recorded to be analyzed and compared to oscillation frequencies characteristic to PD.

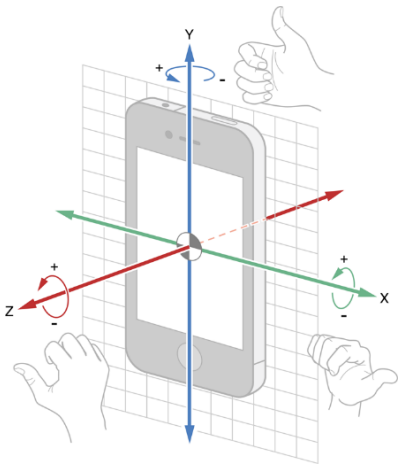

Figure 2. iPhone axes for the gyroscope and accelerometer [19]

The accelerometer and gyroscope in the Apple Watch and iPhone offer high accuracy and sensitivity. Apple does not openly release specifications for their devices, leaving it up to reverse-engineering companies to find out embedded chip specifications used in the devices such as the accelerometer. Device teardowns performed by iFixit [17] and Chipworks [18] reveal the accelerometer and gyroscope part numbers used in the devices to learn about the specifications. The specifications for the accelerometers and gyroscope in the iPhone 6 are listed in Table 5.

Table 5. Accelerometer/Gyroscope specifications for iPhone 6 [36]

Parameter	**Bosch BMA280**	**InvenSense MPU-6500**	**Units**
Sensor type	Accelerometer	Accel/Gyro Combo	-
ADC range	14	16	bit
Acceleration range	±2, ±4, ±8, ±16	±2, ±4, ±8, ±16	g
Maximum sensitivity	4096	16684	LSB/g
Temperature sensitivity	0.015	0.026	%/K
Cross axis sensitivity	1	2	%
Nonlinearity	0.5	0.5	%
Output data rate	2000	4000	Hz
Cold start up time	3	30	ms
Sleep mode start up time	1	20	ms
Accelerometer start up time from sleep mode	1.3	20	ms
Accelerometer supply current in normal mode	130	450	µA
Accelerometer supply current in low power mode 1	6.5	7.27	µA
Accelerometer supply current in low power mode 2	66	18.65	µA
Sleep mode current	2.1	6	µA

The iPhone 6 and Apple Watch both feature touch screen displays capable of accurately measuring tapping motion as related to PD. The iPhone 6 has a capacitive multi-touch touch screen with excellent touch-display response time. While the touch screen primarily serves as the navigation utility, it also provides a valuable sensor for recording PD motor symptoms related to bradykinesia. The 4.7" touch screen on the iPhone 6 is appropriately sized for interaction during the performance of an activity intended to measure **b**radykinesia symptoms. Figure 3 shows the touch screen sensor on the iPhone.

Figure 3. iPhone touch screen sensor [36]

3.1.3 Software

The software used for the application is largely dependent on the hardware. The application runs on Apple's iOS mobile device operating system (OS) for the iPhone and the watchOS software dedicated for the Apple Watch. Apple devices require the use of the proprietary device OS eliminating the need for a software comparison process. The application was built for iOS 9.5.3 on the iPhone 6 and watchOS 2.3.2 on the Apple Watch. In order to maintain compatibility with future iterations of iOS and watchOS, the application has been converted to provide compatibility for iOS 10 and watchOS 3.0. The cloud storage utilized is the

AWS Simple Storage Service (S3). Amazon S3 provides easy to use object storage for developers and offers HIPAA compliance for securely storing protected health information (PHI).

3.2 APPLICATION DESIGN

Development of the application required the use of Apple's proprietary integrated development environment (IDE) Xcode compatible only on Mac OS X. In addition to providing the environment for code editing, Xcode is used for debugging, project file management, compiling, and version control. Developing code for apple devices requires the use of Apple's proprietary coding languages. Objective-C was the standard language used for Apple development until the release of Swift in 2014. Most long-standing applications seen on Apple devices are written in Objective-C. Only recently has Swift gained traction with new applications being written in Swift and old applications beginning to convert. The language used for development of the application discussed here is Swift with frameworks included in the build written in Objective-C. The included frameworks provide application program interfaces (API) enabling the use of hardware and software packages by the application. Accessing sensors, saving data to local storage, uploading data to cloud servers, and manipulating data formats are all examples of functions that may be supplemented using an associated framework. The frameworks used in the application and their corresponding languages are listed in Table 6.

Table 6. Frameworks included in the application

Framework	**Language**
WatchKit	Swift
HealthKit	Swift
ResearchKit	Objective-C
SwiftyJSON	Objective-C/Swift
CoreData	Swift
CoreMotion	Swift
AWS	Objective-C/Swift

In 2015, Apple released ResearchKit, an open source framework intended to provide medical researchers with a platform to conduct studies using Apple technology [33]. The ResearchKit framework provides a model for instructing users through various tasks accessing the sensors on the mobile device, making it a valuable tool for the development of this application. ResearchKit also works seamlessly with HealthKit, a framework connected to the Health app integrated into iOS, providing health-related patient data potentially relevant to the medical topic focused on by a ResearchKit application such as height, weight, age, or skin tone [33].

The WatchKit framework is required for the use of the Apple Watch with an iPhone application. Currently, standalone Apple Watch applications cannot be developed. Instead, a watch "extension" application is installed on the Apple Watch "paired" to the iPhone on which the main application is installed. The WatchKit framework provides functions for initiating and maintaining communication between the Apple Watch and the iPhone while the application is open. This is important for relaying sensor information collected on the watch to the iPhone after completion of the motor tasks performed using the watch.

The CoreMotion framework allows the application to receive motion data from the hardware and process that data. Pre-defined classes and objects provide the means for pulling the hardware output into the software for manipulation in the application. CoreMotion restrictions allows for sampling from the motion sensors at a rate of up to 100Hz.

The CoreData and AWS frameworks are both used for the storage of data. CoreData is used for local storage on the iPhone where sensor samples are stored after task completion before uploading to the cloud server. The AWS framework provides the API needed to pass information stored using CoreData onto the AWS cloud servers.

3.2.1 Key Components

The user-facing portion of the application consists of 3 key components: tasks, patient information, and data analysis. Upon opening the application, the user is presented with a welcome page and the option to sign up to participate in the study affiliated with the application. After signing up, the user interface (UI) consists of 3 main tabs for each of the 3 components. At any time, the user may choose to opt out of the study.

The sign up process for the application involves inputting personal information and health information related to the user's current PD treatment. An eligibility form is completed to determine if the user meets the inclusion criteria for participation in the application. The following criteria must be met to be eligible:

- Over 18 years of age
- Diagnosed with Parkinson's Disease
- Neurologically stable
- Able to understand the study and informed consent form
- Not participating in a clinical investigation that includes an active arm treatment
- Able to perform the motor tasks required for the study
- Able to use the iPhone and Apple Watch apps.

If the user meets the eligibility criteria, demographic and PD characteristic information is collected as shown in Figure 4. This data is stored securely and presented to the user on the profile tab of the UI shown in Figure 5. This provides a visual confirmation for the user to ensure the information input during the signup process is correct. The profile page also includes a button for uploading data collected during the tasks to a secure cloud server.

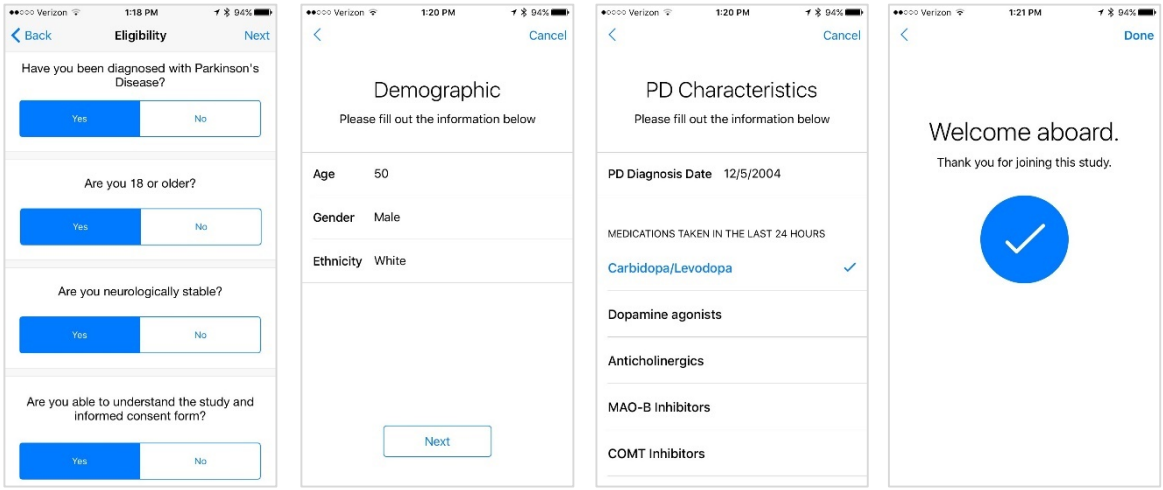

Figure 4. Application signup process

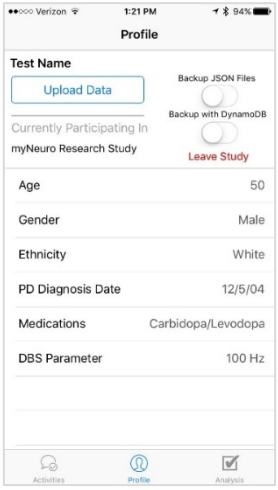

Figure 5. Profile tab of the application

A list of the available tasks is presented after navigating to the activities tab as seen in Figure 6. Tasks may be selected by tapping on the respective list button, after which instructions are presented to guide the user through the completion of the task. Each task takes no longer than 5 minutes to complete with the shortest task taking approximately 10 seconds. Tasks intended to collect motor symptom related data contain visual instruction steps indicating proper performance of the selected task. After navigating through the instructional steps, an audible countdown precedes the initiation of the sensors. The “active step” is the portion of each task dedicated to

collecting data from the sensors while the user performs an indicated motion. The last step of each tasks presents a confirmation of completion and allows the user to return back to the main screen.

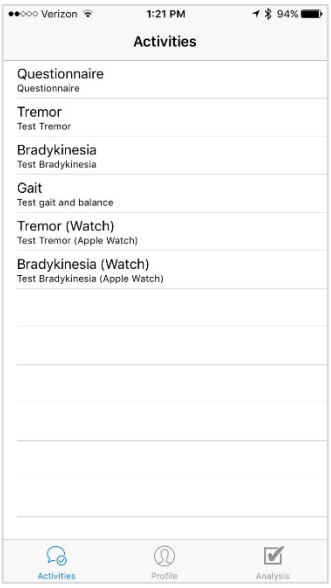

Figure 6. Activities tab of the application

Following completion of each of the motor tasks, the immediate results of low level analysis are displayed on the analysis tab as shown in Figure 7. Data collected from the sensors is processed on the iPhone to be translated into an estimated UPDRS score for each task. In order to estimate the UPDRS score, a correlation between the sensor output and neurologist-based scores will need to be developed through validation testing. After the data has been processed locally, the option to upload to the cloud server becomes available via a button on the profile tab. Once uploaded, the data may be accessed for viewing and further analysis by an authenticated user on a computer.

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5.1.2 Clinical Trials

With a refined user interface and verified sensor efficacy, a clinical study incorporating PD patients should be performed to develop algorithms to calculate UPDRS scores relative to those given by neurologists. A clinical study with PD patients may also provide valuable feedback regarding the ease of use of the application.

5.1.3 Application Improvements

As research progresses in the use of mobile devices for PD symptom assessment, new methods may prove to be more effective for providing insight on the progression of the disease. With this in mind, the application presented here is designed to simplify improvements with content and methods for data analysis. Three tasks were incorporated in the application to demonstrate how the sensors in the mobile devices can be utilized to gather motor related symptom data. This included leveraging the inertial sensors, touch screen, and GPS for tremor, bradykinesia, and postural stability assessment. Other sensors and additional tasks may be seamlessly integrated due to the modular design of the application. For example, to provide insight on vocal symptoms characteristic to PD, a new task may direct the user to speak into the microphone to gather voice data to be analyzed.

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APPENDIX A: USER MANUAL

USER MANUAL

myNeuro

Table of contents

1.0 GENERAL INFORMATION

1.1 Introduction

The myNeuro application is intended for use in a clinical environment by Parkinson's Disease patients under the supervision of a neurologist. The application is not intended to provide diagnostic information. Data gathered by the application is intended for research purposes only.

1.2 Requirements

Hardware Requirements:
- iPod Touch 5/iPhone 5 or greater
- Apple computer (MacBook Pro, MacBook Air, iMac, etc.)
- Apple Watch (optional)

Software Requirements:
- Xcode 7.3.1 or greater
- iOS 9.3.5 or greater
- watchOS 2.2.2 or greater
- OS X 10.11.6 or greater

Other Requirements:
- Apple developer's license
- Amazon Web Services (AWS) account

1.3 Eligibility

The myNeuro app is only intended for use with users who meet the following inclusion criteria:

- Over 18 years of age
- Diagnosed with Parkinson's Disease
- Neurologically stable
- Able to understand the study and informed consent form
- Not participating in a clinical investigation that includes an active arm treatment
- Able to perform the motor tasks required for the study
- Able to use the iPhone and Apple Watch apps

2.0 INSTALLATION

2.1 Installing the App

The myNeuro application is currently in a development phase and is not available to consumers on the App Store. A development version of the app can be installed on a compatible device using Xcode on an Apple computer. There are 2 methods to install the app:

Method 1: Build the app and install

1. Download the source code for the application here.
2. After downloading, unzip the archive and open the ".xcodeproj" file in Xcode.
3. In the Xcode top menu bar, go to Xcode > Preferences and navigate to the Accounts Tab. Add your Apple ID by clicking the plus sign in the lower left corner and choose "Add Apple ID…" and login to your account.
4. With the myNeuro project file selected in the left pane, select each of the Targets (myNeuro, neuroWatch, neuroWatch Extension), go to the General tab, and change the Team to your developer account in the Identity section. Do this for the ResearchKit project file and target as well.
5. Change the bundle identifiers in the following locations:
    a. myNeuro > Targets > myNeuro > General > Bundle Identifier
    com.SJM.myNeuro.[YOURNAME]
    b. myNeuro > Targets > neuroWatch > General > Bundle Identifier
    com.SJM.myNeuro.[YOURNAME].watchkitapp
    c. myNeuro > Targets > neuroWatch Extension > General > Bundle Identifier
    com.SJM.myNeuro.[YOURNAME].watchkitapp.watchkitextension
    d. myNeuro > neuroWatch > Info.plist > WKCompanionAppBundleIdentifier
    com.SJM.myNeuro.[YOURNAME]
    e. myNeuro > neuroWatch Extension> Info.plist > NSExtension > NSExtensionAttributes > WKAppBundleIdentifier
    com.SJM.myNeuro.[YOURNAME].watchkitapp
6. Plug in your device and select it as the build destination by going to Product > Destination and selecting your device.
7. Ensure the myNeuro app is selected if using the app without an Apple Watch. Select the neuroWatch app if an Apple Watch is being used.
8. Select the myNeuro project file in the left panel and click the "Fix Issue" button by the alert under the Team tab. This will generate a code signing signature for the app.
9. Click the "Run" button to build and install the app. This will run the app in debug mode while the device is plugged in. Stop debug mode by clicking the stop button before unplugging the device.

Method 2: Install using the ".ipa" application file

NOTE: The device ID must be entered on the Apple Developer account linked to the myNeuro application at the application build time. Failing to do so will prevent the app from installing on the device. Instructions for finding the device ID can be found here.

The application can be downloaded here by choosing the most recent myNeuro app or neuroWatch app and downloading the ".ipa" application file. Once downloaded, follow these instructions to install the application:

1. Plug in a compatible device into the Apple Computer with Xcode installed.
2. When prompted on the device to trust the computer, choose "Trust".
3. Open Xcode and ensure your device has been connected.
4. With Xcode open, go to Window > Devices. Ensure your connected device is listed on the left panel.
5. Select the desired device. Under the Installed Applications section, click the "+" symbol and open the ".ipa" application file.
6. Xcode will validate and install the application on the device.

3.0 USING THE APP

3.1 Starting the Application

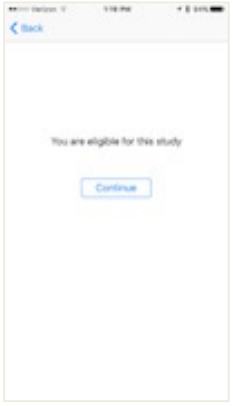
myNeuro app installed on iPhone. Press the app icon to start the app.

myNeuro splash screen after app has started. App contents are loading.

Starting page of the app. Slider style pages with information about the app and a Join Study button.

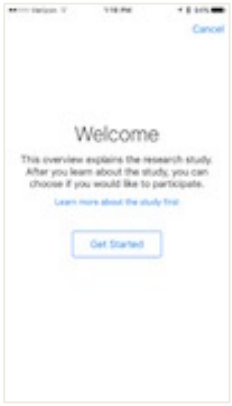
3.2 Joining the Study

Eligibility screen to determine if the user meets the inclusion criteria.

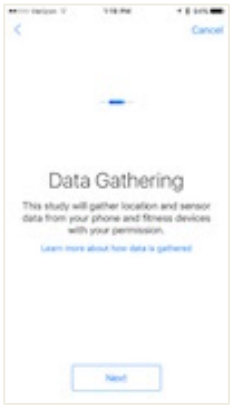


Screen displayed if user meets eligibility requirements. Button to continue on to study.

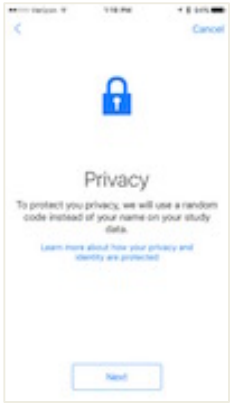
Screen displayed if user does not meet eligibility requirements.



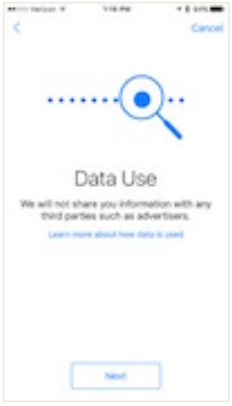
Welcome information during the visual consent process.



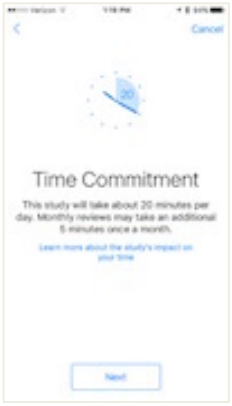
Data Gathering information during the visual consent process.



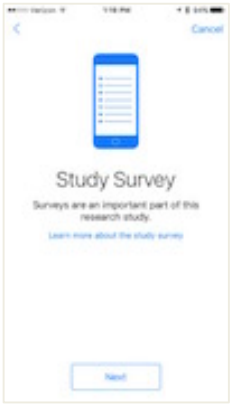
Privacy information during the visual consent process.



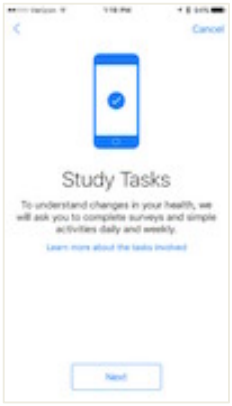
Data use information during the visual consent process.



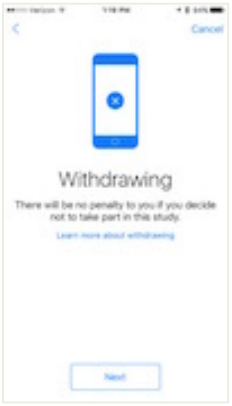
Time commitment information during the visual consent process.



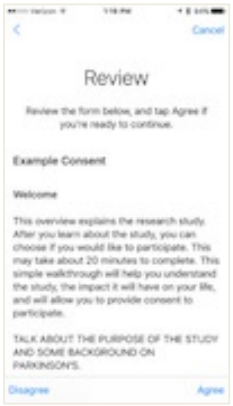
Study survey information during the visual consent process.



Study task information during the visual consent process.

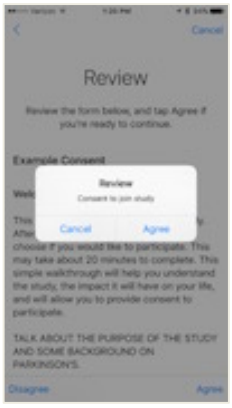


Withdrawing information during the visual consent process.

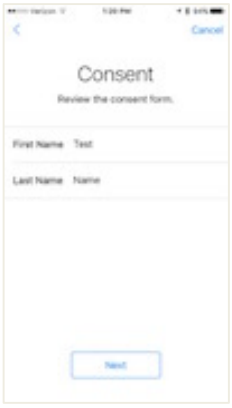


Review consent form. User must agree to the consent form to participate.

Screen displayed if user disagrees to the consent form.



Prompt displayed to confirm user agrees to consent form.

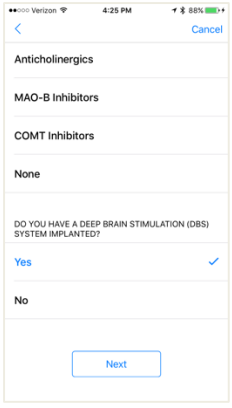


Gather user's full name after they've agreed to the consent form.

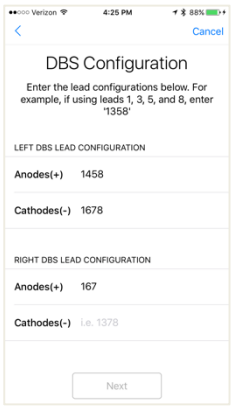
Gather user's signature to confirm they've reviewed the consent form.

Gather patient demographic information.

Gather patient Parkinson's Disease characteristics. (top)

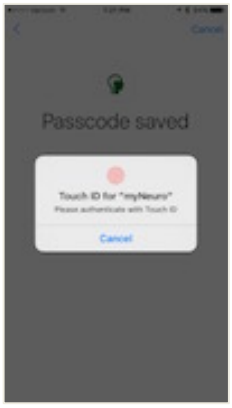


Gather patient Parkinson's Disease characteristics.

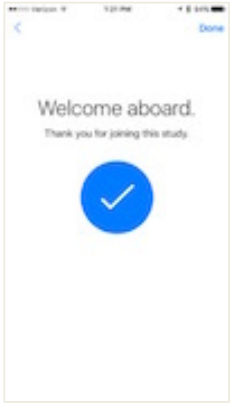


Gather DBS configuration info if DBS implanted.

Enter passcode to protect patient information. Passcode will need to be entered to open the app.

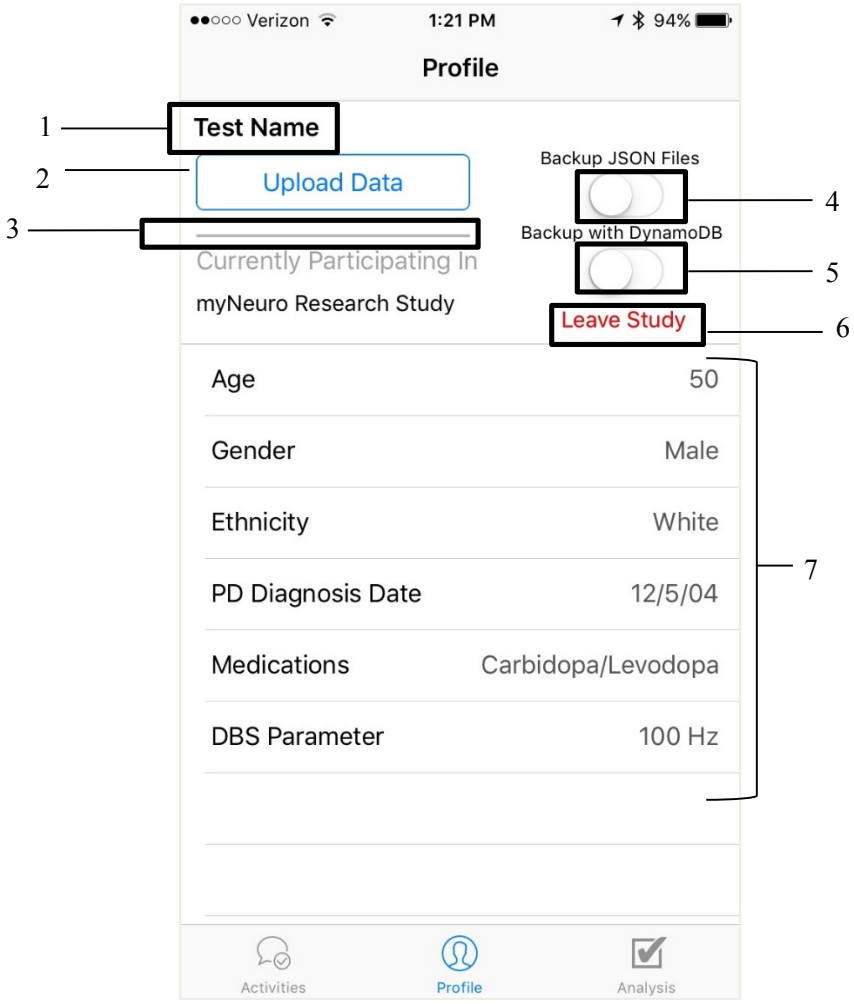


If device has TouchID capabilities, gather a fingerprint.



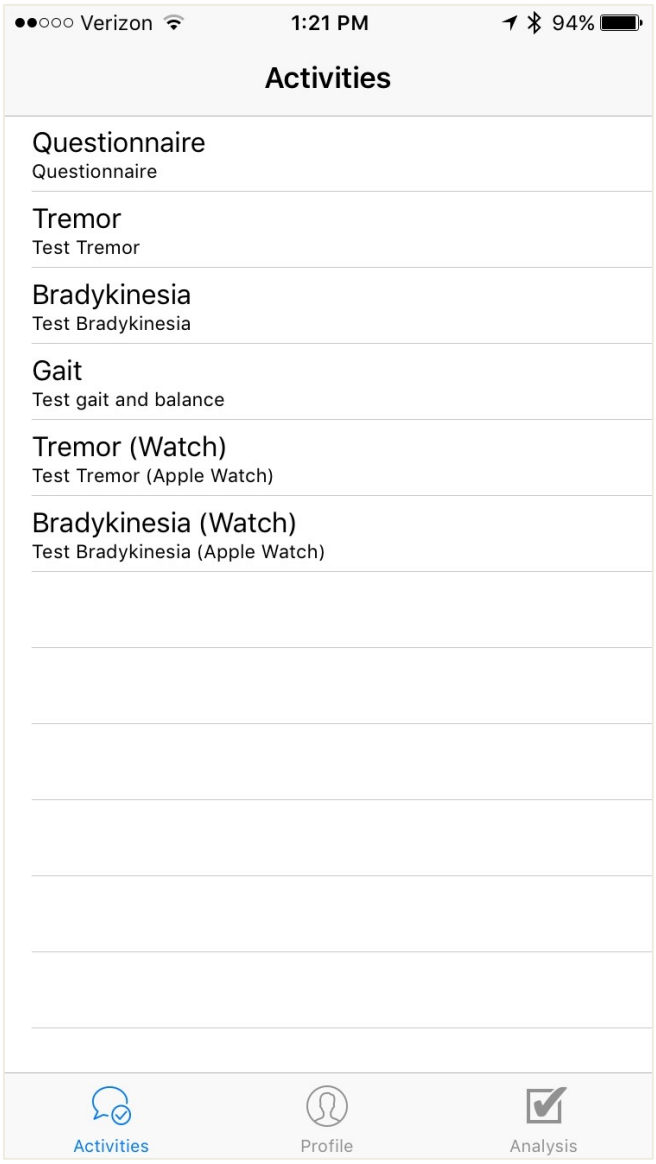
Patient has completed the consent review process.

3.3 Patient Profile



1. *Patient full name*: Displays the full name of the patient.
2. *Upload Data button*: Uploads the Core Data data store to a secure Amazon S3 bucket. Additional data is uploaded if the switches are on (see 4 and 5).
3. *Progress Bar*: Shows the status of the current data upload.
4. *Backup JSON Files switch*: When on, data uploads will include individual JSON files from task results (i.e. accelerometer, device motion, etc.)
5. *Backup with DynamoDB switch*: When on, data uploads will also upload Core Data table entries to a secure Amazon DynamoDB database. Note that this will require much longer to complete the upload and the upload status will not be reflected by the progress bar.
6. *Leave Study button*: Withdraws the current participant from the study. Any data gathered will remain stored on the device. Use this to reset the study for a new patient.
7. *Patient Demographic information and PD Characteristics*: Displayed the demographic information and PD Characteristics gathered during the onboarding process.

3.4 Activities

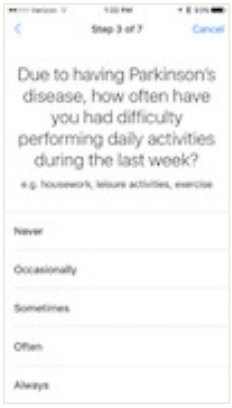


1. *Questionnaire*: Gathers information regarding the patient's Parkinson's Disease symptoms and the impact they have on their daily life.
2. *Tremor*: User performs several motions tasks relating to resting, kinetic, and postural tremor.
3. *Bradykinesia*: User performs a tapping task relating to bradykinesia symptoms.
4. *Gait*: User performs a gait and balance task relating to gait symptoms.
5. *Tremor (Watch)*: User performs several motion tasks relating to resting, kinetic and postural tremor using the Apple Watch.
6. *Bradykinesia*: User performs a tapping task relating to bradykinesia symptoms on the Apple Watch.

3.4.1 Questionnaire

Questionnaire initial screen.

Queston1

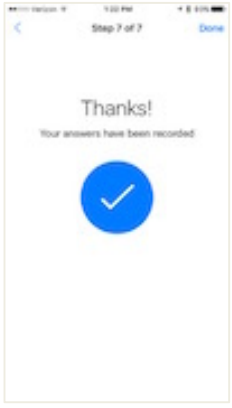


Question 2

Question 3

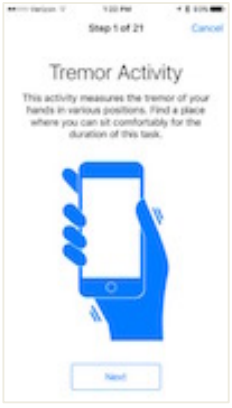
Question 4

Question 5



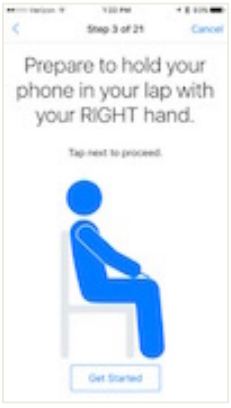
Completion screen.

3.4.2 **Tremor**

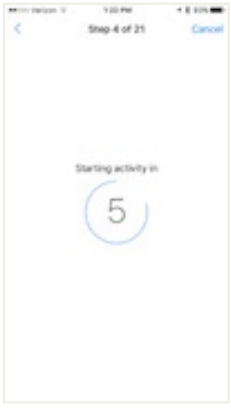


Tremor task introduction screen.

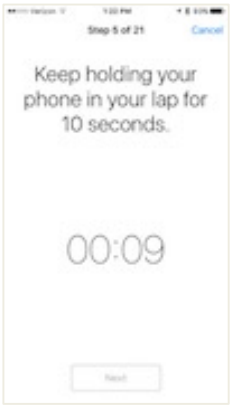
Tremor task description screen.



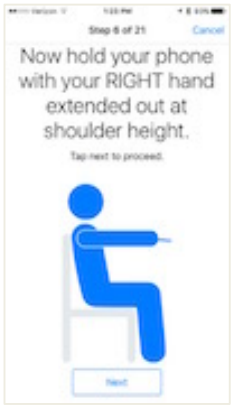
Step 1



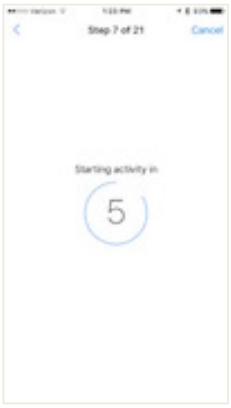
Step 2



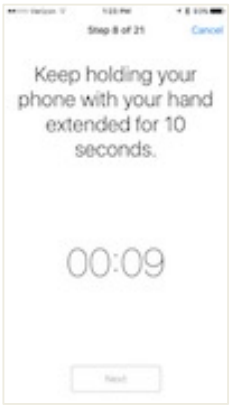
Step 3



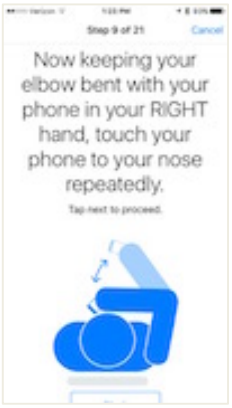
Step 4



Step 5



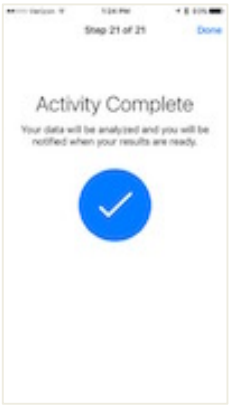
Step 6



Step 7

Step 8

Step 9

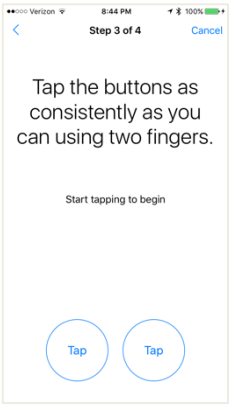


Completion screen.

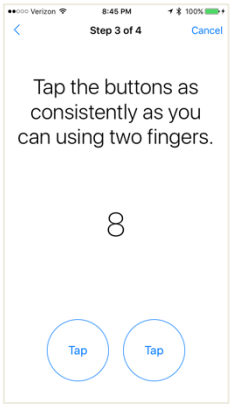
3.4.3 Bradykinesia

Bradykinesia task introduction screen.

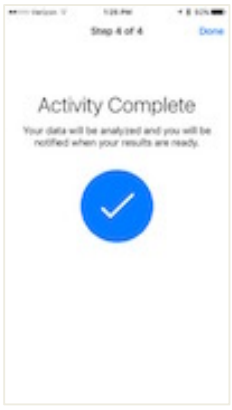
Bradykinesia task description screen.



Step 1

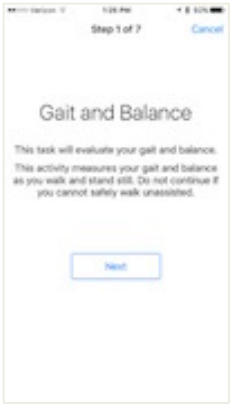


Step 2



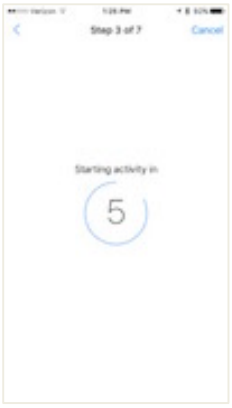
Completion screen.

3.4.4 Gait



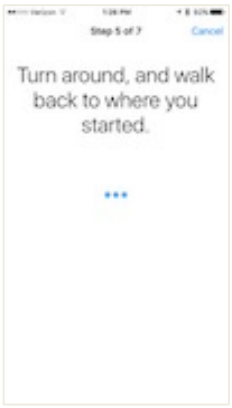
Gait and balance task introduction screen.

Gait and Balance task description screen.

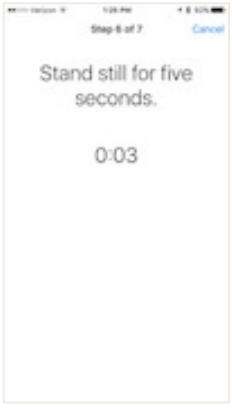


Countdown

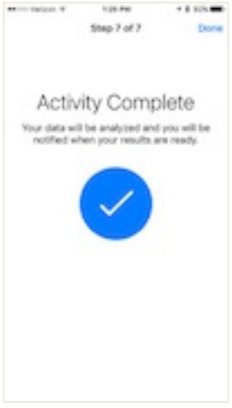
Step 1



Step 2



Step 3

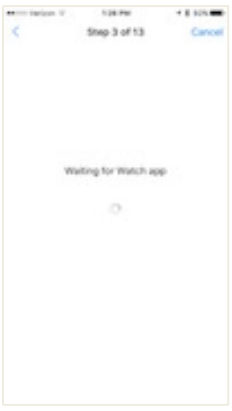


Completion screen.

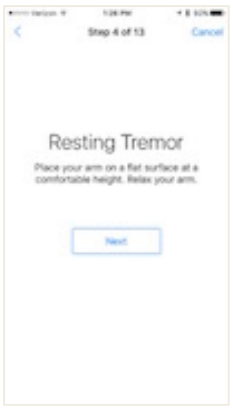
3.4.5 Tremor (Watch)

Tremor Watch task introduction screen.

Tremor Watch task description screen.

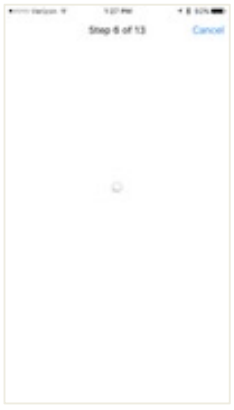


Step 1

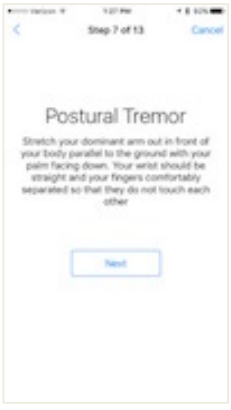


Step 2

Step 3

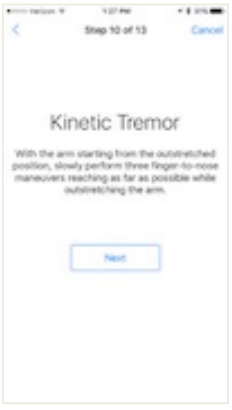


Step 4

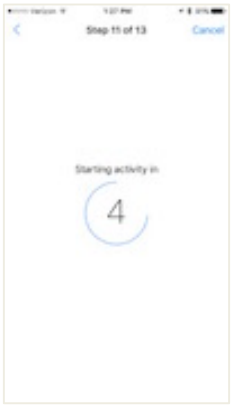


Step 5

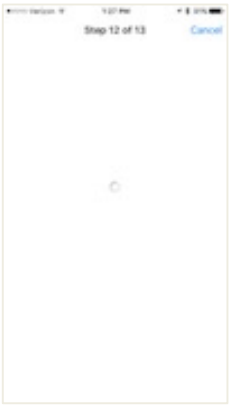
Step 6



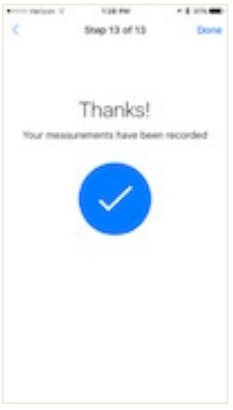
Step 7



Step 8

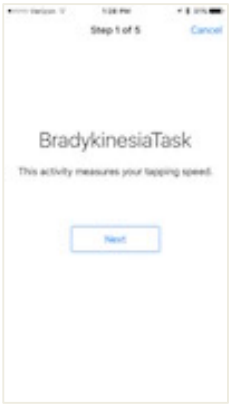


Step 9



Completion screen.

3.4.6 Bradykinesia (Watch)

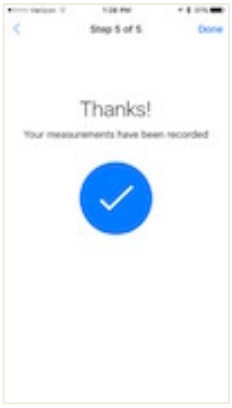


Bradykinesia Watch task introduction screen.

Bradykinesia Watch task description.

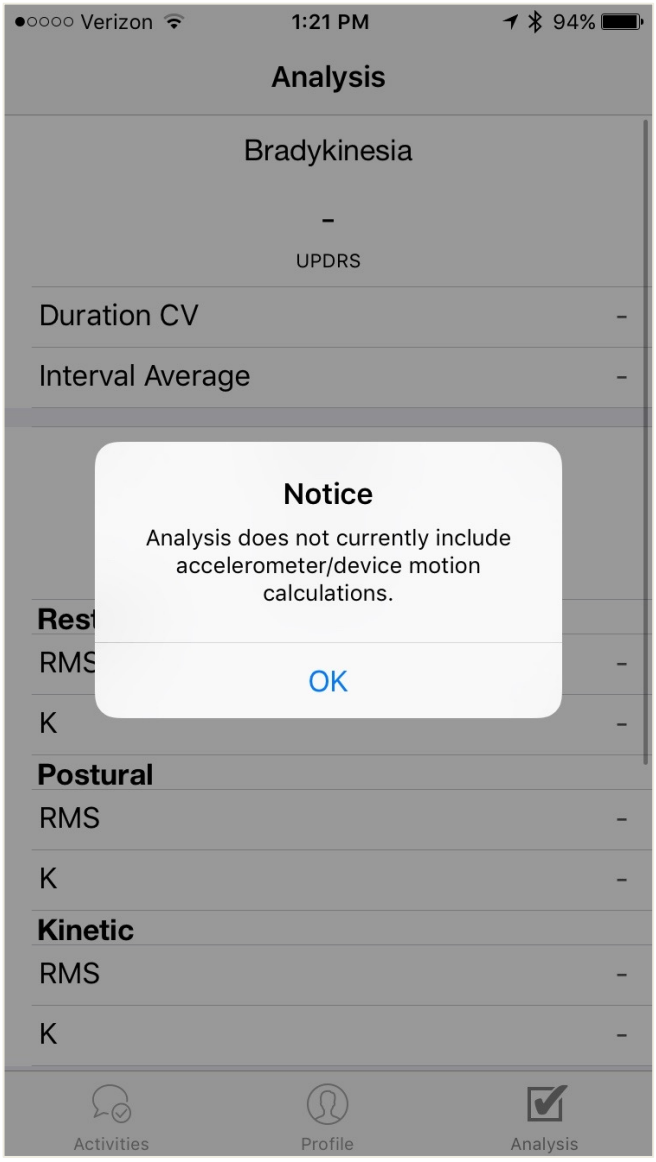
Watch connect screen

Waiting for task to finish screen.



Completion screen.

3.5 Analysis (Under Development)

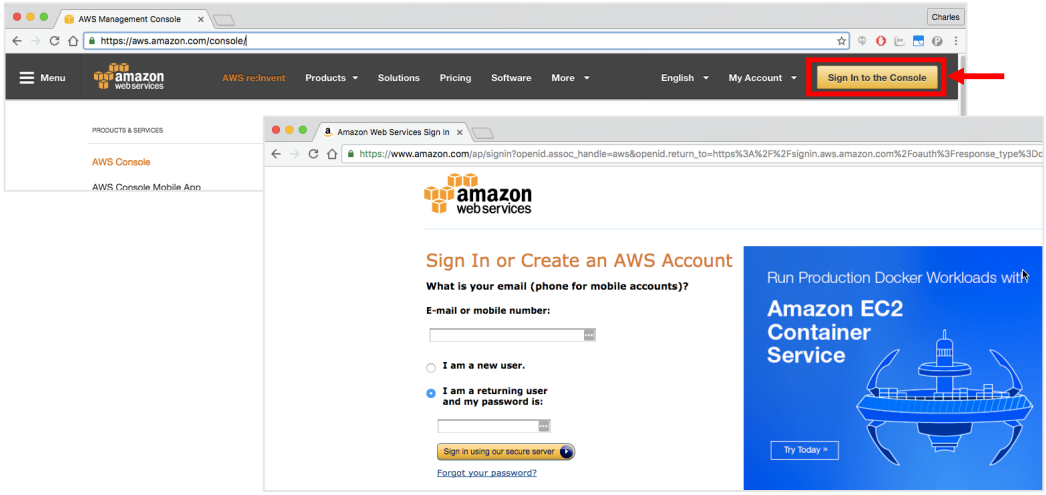


4.0 ACCESSING DATA

4.1 Amazon Web Services (AWS)

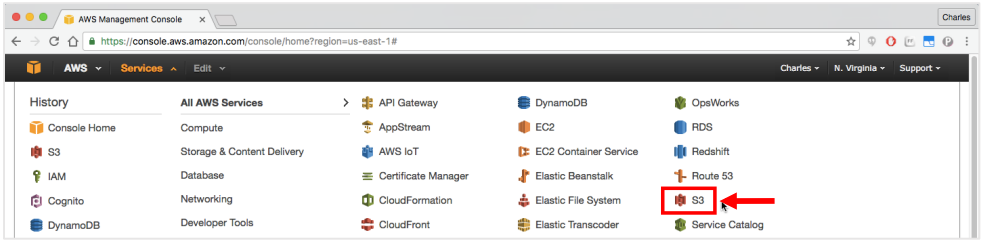
Data from the study may be uploaded to AWS (Amazon Web Services) storage either via files to an S3 bucket or individual table rows to a DynamoDB database. After pressing the *Upload Data* button in the Profile tab, the Core Data data store (SQLite database) is uploaded to the AWS S3 bucket. Switches in the Profile tab also enable/disable individual JSON files from task results and DynamoDB backing in addition to the Core Data data store upload. Any uploaded data can be accessed by following these instructions:

1. Login to the AWS console (https://aws.amazon.com/console/) using the AWS account.

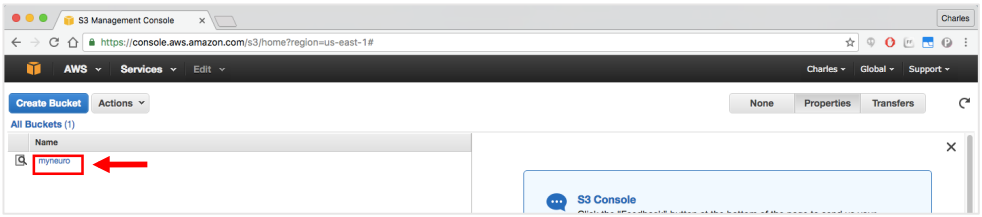


Amazon S3:

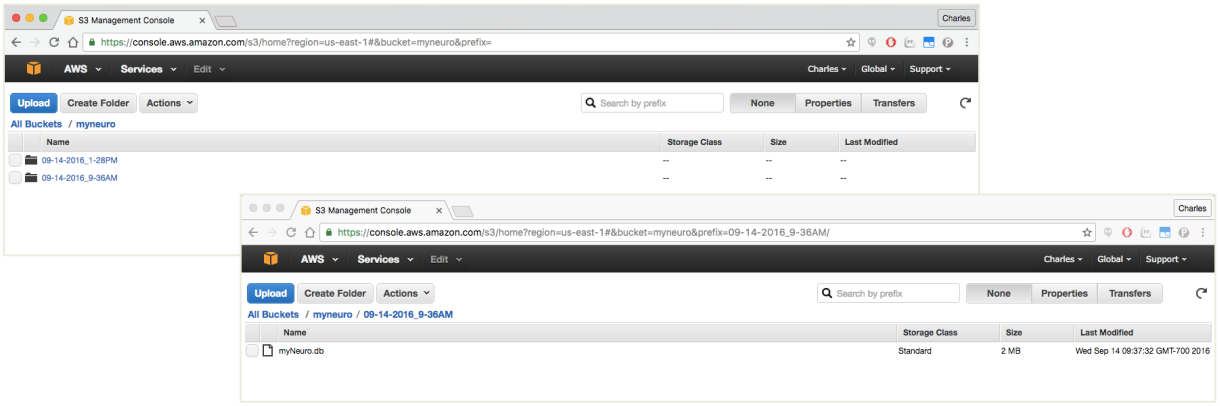
1. On the top menu bar, navigate to Services > S3



2. Click the “myneuro” bucket



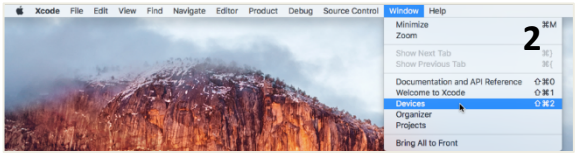
3. Core Data data stored are uploaded to a folder titled with the date and time of the upload. Select the folder containing the file you want to download to your computer. Then double click the file to download.

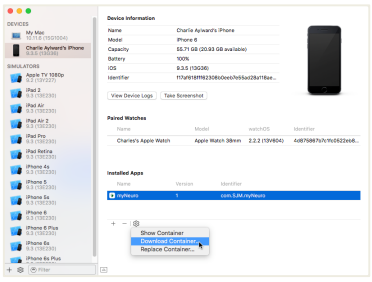


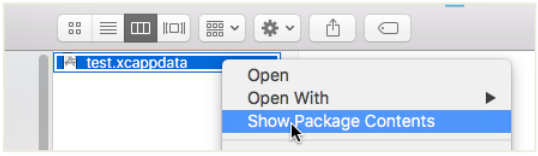
NOTE: ".db" files can be opened using the SQLiteStudio program downloadable for free from http://sqlitestudio.pl/. This program can also export individual table as other file formats (i.e. CSV) for processing with data analysis programs.

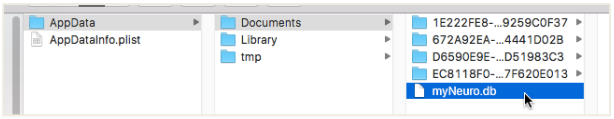
4.2 Offline

1. Plug in the device and open Xcode.
2. In the top menu bar, go to Window > Devices
3. Select the device on the left panel
4. In the "Installed Apps" section, select the myNeuro application
5. Click the gear icon below and choose "Download container". Choose a location to save. This will save the app data to a ".xcappdata" file.
6. A finder window containing the file should open automatically. If not, navigate to the folder containing the container.
7. Right click the file and choose "Show Package Contents".
8. The ".db" file containing the results is located in the AppData/Documents folder. Open this file using SQLite Studio





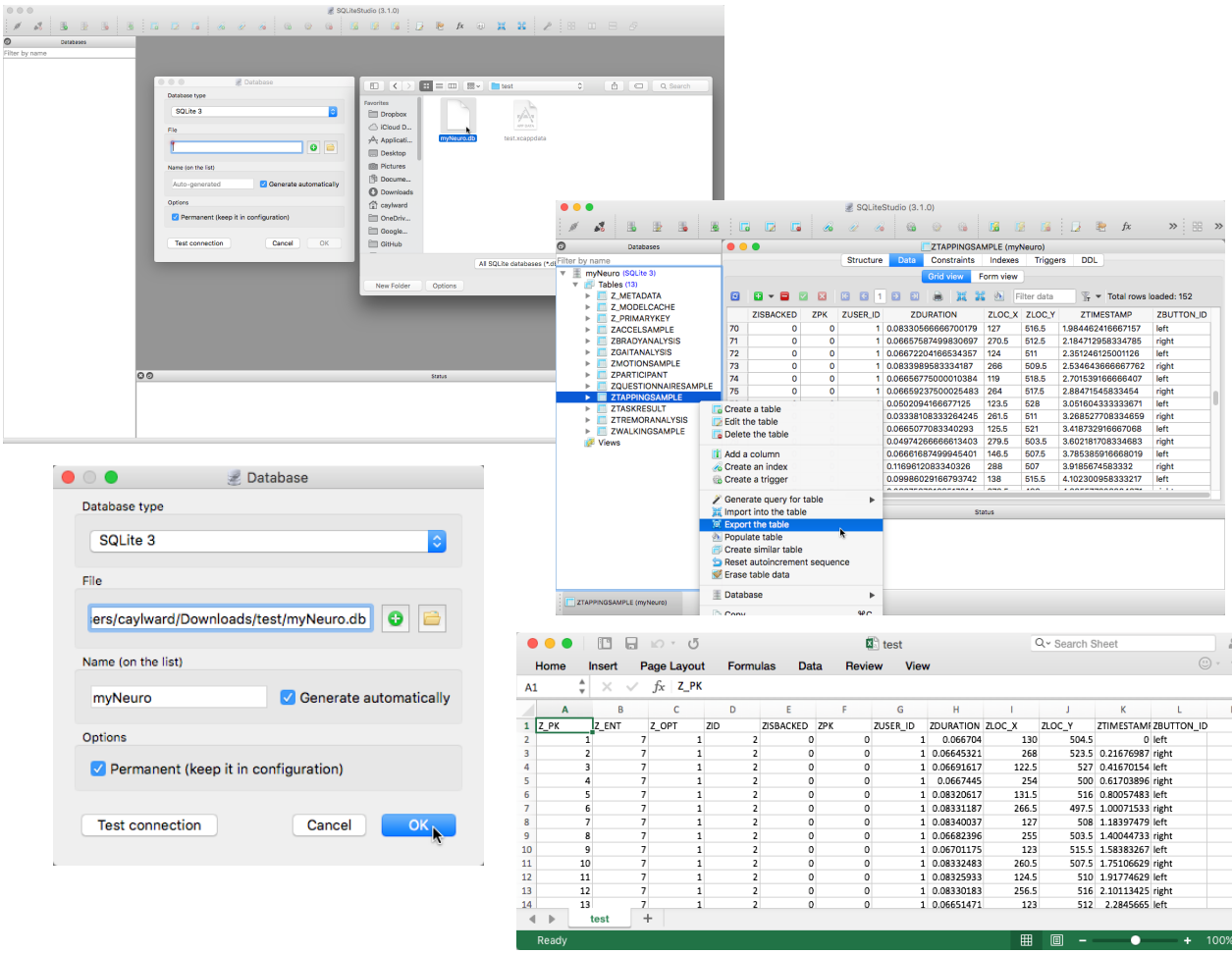




4.3 SQLiteStudio

In order to access the ".db" files containing the data gathered through the app, SQLiteStudio is a great resource. This program is available for free from http://sqlitestudio.pl/ . After opening the ".db" files in SQLiteStudio, we can export the data in other formats like .csv for processing in data analysis programs like MatLab.

1. Open SQLiteStudio
2. In the top menu bar, go to Database > Add a database. Select "SQLite 3" for the database type. Click the folder icon to browse for the myNuero.db file. You may need to copy/paste the ".db" file from within the ".xcappdata" package contents to an outside folder to navigate to the file.
3. Select the myNeuro.db file and press Ok.
4. Double click on the database to connect to it or use the connect button in the upper left of the window.
5. Data tables are displayed. Use the "Data" tab to see the contents of the tables.
6. To export data, right click on a table and select "Export the table".
7. Navigate through the export settings changing them as you'd like.



These pages have been redacted per request of the author.