Official Title: Cognitive Rehabilitation for Individuals with Parkinson's Disease and MCI

Date: Most Recent Version Last Approved on 1/17/2020

Human Protocol (Version 1.33)

General Information

***Please enter the full title of your protocol:**

Cognitive Rehabilitation for Individuals with Parkinson's Disease and MCI

***Please provide a short name (nickname) to reference this protocol:**

CogSMART-PD-II
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

Add Site(s)

VA Site (******** DO NOT ADD OR CHANGE, just save and continue **********):**

Primary Dept?	Department Name
◆	**VASDHS** - VASDHS

Identify protocol staff members

***Please add a Principal Investigator for the study:**

Schiehser, Dawn M., PhD

3.1 Add all other VA research staff personnel (if name is not in the list, please contact Research Staffing to confirm appointment status)

A) Additional Investigators

Filoteo, J. Vincent, PhD
Co-Investigator
Harrington, Deborah L., PhD
Co-Investigator
Simmons, Alan N., PhD
Co-Investigator
Twamley, Elizabeth W., PhD
Co-Investigator

B) Research Support Staff

Almklov, Erin L., PhD
Research Associate
Bashor, Kaylee
Research Associate

Bayram, Ece, PhD
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Cabrera Tuazon, Angelie
Study Coordinator
Clark, Alexandra Leigh
Research Associate
Das, Aishee
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Holiday, Kelsey Anne, BS
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Lessig, Stephanie L., MD
Participating Clinician
McMann, Tiana
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Ton Loy, Adan F
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Vannini, Maya Bina Najmi
Research Associate
Walsh, Michael J.
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White, Beatrice M.
Research Associate
Whiteley, Nicole M.
Research Associate

***Please select the Research Contact(s)**

Cabrera Tuazon, Angelie
Schiehser, Dawn M., PhD

The Research Contact(s) will receive all important system notifications along with the Principal Investigator. (Research Contacts are typically Study Coordinators or the Principal Investigator themselves).

VASDHS IRB
Human Subjects Protocol

v20190121

Section 1 - Preliminaries

Principal Investigator:

Dawn M. Schiehser, PhD

Protocol Title:

Cognitive Rehabilitation for Individuals with Parkinson's Disease and MCI

IRB Protocol Number:

H130022

Protocol Nickname:

CogSMART-PD-II

Form Template Version:

Date Prepared:

01/15/2020

Please be advised that this protocol application form has changed as a result of the 2018 Common Rule. There are new questions and sections, and you may be required to provide additional information to previous sections.

1a) Is this study considered human research?

- (•) Yes
- ( ) No
- ( ) I don't know

1b) Please select:

- ( ) This is an application for a NEW human subject research protocol
- (•) This is a revision of an existing protocol

Was this study initially approved prior to January 21, 2019?

(•) Yes ( ) No

Were you instructed to convert to the 2018 Common Rule Requirements?

( ) Yes (•) No

Section 2 - Research Subjects

2a) What is the total planned number of VA-consented subjects?

Include the total number of subjects who will prospectively agree to participate in the study (e.g., documented consent, oral consent, or other).

350

2b) What is the total number of VA subjects who WILL NOT be consented?

Include the total number of subjects that will be included without consent (e.g., chart review). *Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still should enter the number of charts as your "planned subjects."*

0

Section 2.1 Consented Subject Groups

2.1) For each of the subject categories listed below, indicate whether or not these subject groups will participate in the study:

2.1a) Children under the age of 18
Note: If neonates or children will be involved in this study, certification by the Medical Center Director will be required. Only minimal risk research may be performed with children. Only non-invasive monitoring and/or prospective observational and retrospective record review studies that are minimal risk can be conducted in VA involving neonates.

( ) Yes (•) No

2.1b) Pregnant women

( ) Yes (•) No

2.1c) Individuals with cognitive/decisional impairment

(•) Yes ( ) No

2.1d) Non-English-speaking individuals

○ Yes ◉ No

2.1e) Prisoners of War (explicitly targeting this group)

○ Yes ◉ No

2.1f) Non-Veterans (Note: Justification for inclusion of non-Veterans will be required)

◉ Yes ○ No

2.1g) Incarcerated individuals (Note: VA CRADO approval will be required)

○ Yes ◉ No

2.1h) VA employees - including VA paid, IPA, or WOC (Note: Union review and authorization may be required)

○ Yes ◉ No

2.1i) Students of the institution (e.g., resident trainees) or of the investigator

○ Yes ◉ No

2.1j) Patients with cancer (or high cancer risk) [explicitly targeting this group]

○ Yes ◉ No

Section 3 - Study Features (these items default to "No" for convenience)

3) This section consists of several Yes/No questions addressing protocol characteristics. Click on *Save and Continue.*

Section 3.1 Protocol Basics

Select all that apply

3.1a) The research **intends to change** the participant.

◉ Yes ○ No

3.1b) **Interactions** with living participants to collect data or specimens with no intent to change them.

○ Yes ◉ No

3.1c) This is a study that **never** has any **subject contact and does not collect subject identifiers**

○ Yes ◉ No

3.1d) This is a **chart review** study involving retrospective or prospective medical records.

○ Yes ◉ No

3.1e) This is a **multi-site** study occurring in-part or in-full at other locations.

○ Yes ◉ No

3.1f) There is an **international** component to this research. *International research includes sending or receiving human derived data or specimens (identifiable, limited data set, coded, or deidentified) to or from an international source. International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator.*

○ Yes ◉ No

3.1g) This study includes **off-station activity** (not including VA-leased space or CBOC clinics) conducted under VASDHS IRB approval. *Note: this does not include research conducted by a collaborator at their home institution under their institutional approval.*

(●) Yes ( ) No

3.1h) VA subjects will **participate** in part or in full **at other locations** (not including VA-leased space or clinics) under VASDHS IRB approval.

(●) Yes ( ) No

Section 3.2 Specimen Use and Data Repository

Indicate whether or not each of the following applies to this protocol

3.2a) Involves specimens that are left over from pathological or diagnostic testing (**non-research specimens**)

( ) Yes (●) No

3.2b) Involves **specimens collected for research** purposes **only**

(●) Yes ( ) No

3.2c) This study includes **specimen banking** (specimens are retained for use outside of the purposes of this protocol)

( ) Yes (●) No

3.2d) The study involves **DNA** genotyping or other **genetic analysis**

(●) Yes ( ) No

Does this include whole genome sequencing?

( ) Yes ( ) No

Will participants be informed of the results of any DNA testing?

( ) Yes ( ) No

3.2e) Biological **specimens/material** will be sent outside of the VA.

( ) Yes (●) No

3.2f) A **data repository** is maintained (data are retained after completion of the protocol for other uses, IMPORTANT: see **?** before checking "yes")

( ) Yes (●) No

3.2g) **Data will be shared outside** of the VA (identifiable, coded, limited data set, or deidentified)

(●) Yes ( ) No

Section 3.3 Treatment and Clinical Trials

Indicate whether or not each of the following applies to this protocol

3.3a) Includes a **treatment** component (a research treatment)

(●) Yes ( ) No

3.3b) Study is a **clinical trial.** *Note: A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.*

( ) Yes (●) No

3.3c) Has a data safety monitoring board (**DSMB)** or data safety monitoring committee.

○ Yes ◉ No

3.3d) Has a **data safety monitoring plan** (but not a DSMB) (this is not the data security plan, it is a safety plan).

○ Yes ◉ No

Section 3.4 Drugs and Devices

Indicate whether or not each of the following applies to this protocol

3.4a) **Drugs** that require **FDA** action such as an Investigational New Drug (IND) approval or exemption or 510(k) approval.

○ Yes ◉ No

3.4b) Other drugs, supplement, etc. that **do not require FDA** action for inclusion in the study.

○ Yes ◉ No

3.4c) Medical **devices requiring FDA** IDE approval or waiver

○ Yes ◉ No

3.4d) **Other** medical **devices**

○ Yes ◉ No

Section 3.5 Risk and Hazards

Indicate whether or not each of the following applies to this protocol

3.5a) Study places subjects at **greater than minimal risk** (do not include risks that are due to standard care)

○ Yes ◉ No

3.5b) Human subjects are exposed to **radioisotopes** (do not include standard care).

○ Yes ◉ No

3.5c) Subjects have other **radiation exposure** (e.g., x-rays) (do not include standard clinical use).

○ Yes ◉ No

3.5d) Target population has psychiatric diagnosis or behavioral complaint.

◉ Yes ○ No

Section 3.6 Clinical Facilities and Standard Care

Indicate whether or not each of the following applies to this protocol

3.6a) Study **uses VA clinical services** (e.g., adds required tests run in the VA lab for study purposes; research procedures concurrent with clinical care)

○ Yes ◉ No

3.6b) Includes procedures or drugs that will be considered **part of standard care.**

○ Yes ◉ No

3.6c) Involves **lab tests done for research** purposes.

○ Yes ◉ No

Section 3.7 Subject Expenses and Compensation

Indicate whether or not each of the following applies to this protocol

3.7a) There may be expense or added **costs to the subject** or the subject's insurance.

○ Yes ◉ No

3.7b) This is a **qualifying cancer treatment trial** and subjects may be billed for study drugs or procedures.

○ Yes ◉ No

3.7c) This is a cancer treatment trial but **subjects will not be billed** for study drugs or procedures.

○ Yes ◉ No

3.7d) Subjects will be **compensated** (either in cash or other means such as a gift certificate).

◉ Yes ○ No

Section 3.8 Subject Activities

Indicate whether or not each of the following applies to this protocol

3.8a) Involves **surveys or questionnaires** completed by subjects

◉ Yes ○ No

3.8b) Includes the use of **recruitment materials** such as flyers, advertisements, or letters

◉ Yes ○ No

3.8c) Involves facial **photographs** or audio or video **recordings** of **patients**

◉ Yes ○ No

Section 3.9 Sponsors and Collaboration

Indicate whether or not each of the following applies to this protocol

3.9a) This research is a funded research project **(commercial (industry) sponsor, NIH, VA, other).**

○ Yes ◉ No

3.9b) Other **commercial (industry) non-financial support** is provided (e.g., drugs or supplies).

○ Yes ◉ No

3.9d) The protocol has **Department of Defense** involvement (e.g., subjects or funding).

○ Yes ◉ No

3.9c) The PI or other study staff member has a financial interest or other **real or potential conflict** related to this study.

○ Yes ◉ No

3.9e) This study involves **collaborative** research activities (research conducted at other institutions under the authorities or approvals of the other institution/s). *Note: this may include other VA and/or non-VA institutions, but does not include off-site VA research.*

(•) Yes ( ) No

Section 4 - Estimated Duration

4) What is the estimated duration of the entire study? (From IRB approval to IRB closure)

10 years

Section 5 - Lay Language Summary

5) Provide a summary or synopsis of the proposed study using non-technical language (not more than 1 paragraph)

Dr. Dawn Schiehser and associates are conducting a research study to find out more about the effectiveness of a cognitive training group intervention that provides education about cognitive, physical, and emotional changes associated with Parkinson's Disease and teaches strategies to improve cognitive skills, including attention, learning and memory, and problem-solving. The purpose of this study is to see how a cognitive training course (CogSMART) impacts thinking, mood, and quality of life in individuals who have Parkinson's disease with cognitive impairment. A subset of individuals will also participate in a pre- and post-intervention cognitive task while undergoing fMRI to assess neural changes associated with cognitive training. Additionally, some individuals will be asked to complete an adjunct exercise program either using the Wii or by participating in the Odoroki program (performing physical activity to music using a computer system). Some individuals will also be asked to provide a saliva sample (via buccal swab and/or a passive drool test) for analysis of neuroinflammatory biomarkers (e.g., cortisol, CRP, DHEA, and alpha-amylase) pre- and post-treatment, as well as DNA.

Section 6 - Specific Aims

6) Provide a statement of specific aims and hypotheses that serve as the basis for this protocol. Emphasize those aspects that justify the use of human subjects.

Phase I:
This study will investigate the effectiveness of a cognitive rehabilitation and psychoeducation program on the neuropsychological functioning of individuals with Parkinson's Disease (PD) who have cognitive impairment. The study will employ the Cognitive Symptom Management and Rehabilitation Therapy (CogSMART), a group cognitive training intervention that provides education about cognitive, physical, and emotional changes associated with PD and teaches compensatory cognitive skills (attention, learning and memory, and problem-solving) that are affected by PD.

Aim 1. To investigate the efficacy of a cognitive rehabilitation program, CogSMART, in a population of individuals with Parkinson's disease who have cognitive impairment.

Hypothesis 1a: Compared to wait-list controls, CogSMART participants will have improved cognitive functioning, functional skills and quality of life immediately following treatment.

Hypothesis 1b: CogSMART participants will maintain their improvements at 6 months (3 months post-treatment).

Hypothesis 1c: CogSMART participants will maintain their improvements at 12 months (9 months post-treatment).

Aim 2. To investigate the vicarious effects of a cognitive rehabilitation program, CogSMART, on the caregivers of the participants.

Hypothesis 2: Compared to wait-list control caregivers, caregivers of CogSMART participants will report increased quality of life and mood immediately following their participant's treatment and 3- and 9-months post-treatment.

Exploratory Aim 1: To examine neural changes associated with the performance on an fMRI executive

function task following participation in CogSMART.

Exploratory Hypothesis 1: Compared to the non-intervention/waitlist PD participants, CogSMART completers will evidence a reduction in the dorsolateral prefrontal gyrus (due to increased cognitive efficiency) during an fMRI task of executive functioning.

Exploratory Aim 2: To investigate the feasibility and efficacy of improving visual-spatial cognition by using the Wii as an adjunct to CogSMART.

Exploratory Hypothesis 2: Compared to CogSMART (without Wii) completers, participants who use Wii as an adjunct to CogSMART (CogSMART+Wii) will demonstrate greater gains in visual spatial cognition.

Phase II:

Aim 1. Establish the efficacy of a cognitive rehabilitation program (CogSMART-PD) to improve cognition in individuals with PD-MCI.

Hypothesis 1: Compared with the supportive care control group, CogSMART-PD participants will demonstrate greater improvements in cognition at the 10-week assessment. We will examine executive function (Matrix Reasoning Test) as our primary outcome, as it is the test most sensitive to the earliest cognitive deficits in PD, impacts other cognitive functions in PD, and is a main focus of the intervention. We will examine the effects of the intervention on memory, subjective cognition, and cognitive strategy use in secondary analyses.

Aim 2. Examine the efficacy of CogSMART-PD in reducing neuropsychiatric symptoms and improving quality of life/ health status in individuals with PD-MCI.

Hypothesis 2: Compared with the supportive care control group, CogSMART-PD participants will demonstrate greater improvement in QoL/HS, and neuropsychiatric symptoms at the 10-week assessment.

Aim 3. Investigate the longitudinal effects of CogSMART-PD on cognition, neuropsychiatric symptoms and quality of life / health status in individuals with PD-MCI.

Hypothesis 3: Compared with the supportive care control group, CogSMART-PD participants will demonstrate less cognitive decline, fewer neuropsychiatric symptoms, and better QoL/HS at the 6- and 12-month follow-up assessments.

Exploratory Aim 1: To examine neural changes associated with the performance on an fMRI executive function task following participation in CogSMART.

Exploratory Hypothesis 1: Compared to the non-intervention/waitlist PD participants, CogSMART completers will evidence a reduction in the dorsolateral prefrontal gyrus (due to increased cognitive efficiency) during an fMRI task of executive functioning.

Exploratory Aim 2: To investigate the feasibility and efficacy of improving visual-spatial cognition by using the Wii as an adjunct to CogSMART.

Exploratory Hypothesis 2: Compared to CogSMART (without Wii) completers, participants who use Wii as an adjunct to CogSMART (CogSMART+Wii) will demonstrate greater gains in visual spatial cognition.

Exploratory Aim 3: To investigate the feasibility and efficacy of improving visual-spatial cognition and motor skills by participating in Odoroki (computer program performing physical activity to music) as an adjunct to CogSMART.

Exploratory Hypothesis 3: Compared to CogSMART (without Odoroki) completers, participants who practice Odoroki as an adjunct to CogSMART (CogSMART+Odoroki) will demonstrate greater gains in visual spatial cognition and motor skills.

Exploratory Aim 4: To investigate changes in neuroinflammatory biomarker (cortisol, CRP, DHEA, and alpha-amylase) levels pre- and post-treatment for intervention and control participants.

Exploratory Hypothesis 4: Compared to the supportive care control group, CogSMART-PD participants will show a reduction in in neuroinflammatory biomarker levels and this reduction will be associated with cognitive improvement.

Exploratory Aim 5: To investigate in the association between Brain-derived Neurotrophic Factor (BDNF) gene expression levels and cognitive change pre- to post- intervention.

Exploratory Hypothesis 5: BDNF gene expression levels will be associated with greater cognitive improvement following the CogSMART-PD intervention compared to the control condition.

Exploratory Aim 6: Investigate mediators of CogSMART-PD treatment effects.

Section 7 - Background and Significance

7) Provide a succinct discussion of relevant background information to justify performing the proposed study.

Phase I

Cognitive impairment is commonly seen in individuals with PD and includes those with mild cognitive impairment (MCI) or dementia (2003b; Janvin et al., 2006a; Janvin et al., 2006b; Williams-Gray et al., 2007). It is estimated that 30-80% of individuals with PD meet criteria for dementia (Aarsland et al., 2001; Aarsland et al., 2003b; Aarsland et al., 2005), whereas 31-42% meet criteria for MCI (Caviness et al., 2007; Tedrus et al., 2009). In non-demented PD samples, estimates of MCI range from 40-53% (Janvin et al., 2006a; Caviness et al., 2007; Kim et al., 2009; Sollinger et al., 2009). Cognitive deficits in PD are most frequently seen in the areas of attention, executive function and memory (Muslimovic et al., 2005; Caviness et al., 2007). Cognition in PD tends to deteriorate over time, with average annual decreases on the MMSE of 2.3-2.4 points in non-demented PD (Kandiah et al., 2009). In an unpublished study, Dr. Filoteo and colleagues found that their sample of non-demented PD patients declined from a mean of 139.0 to 134.2 on the Mattis Dementia Rating Scale (MDRS; Mattis, 1988), a scale of global cognitive functioning. In a meta-analysis conducted by Muslimovic et al. (2007)declines in global cognitive function, visuoconstruction, and memory were evident in non-demented PD over a mean of 29 months. Dementia in PD, most commonly referred to as Parkinson's disease dementia (PDD), is characterized predominantly by a progressive dysexecutive syndrome in the absence of prominent aphasia, apraxia or agnosia (Emre, 2003). The conversion to dementia is greater in PD compared to normal age-matched controls (Aarsland et al., 2003b). In a longitudinal study conducted over 8 years by Aarsland et al. (2003), 26% of individuals with PD met criteria at baseline (average duration of symptoms = 11 years), 52% met criteria for dementia after 4 years, and 78% met criteria for dementia after 8 years. As evidenced these aforementioned studies, those with PD and cognitive impairment are at high risk for further cognitive decline and progression to dementia. The ability to improve cognition in those who have cognitive impairment and possibly slow the progression of cognitive decline would be extremely beneficial to individuals with PD and their caregivers. Improvements in cognition could enable individuals with PD to become more independent and improve the quality of their life as well as the quality of life of their caregivers.

Most interventions for cognitive impairment in PD to date have been pharmacologic and although positive results have been found with cholinesterase inhibitors rivastigmine (Emre et al., 2004), galantamine (Aarsland et al., 2003a), and donepezil (Fabbrini et al., 2002), side effects, including increased in motor symptoms, have weakened enthusiasm for this method of treatment. Cognitive rehabilitation has been well documented to successfully provide cognitive improvements in non-progressive conditions such as traumatic brain injury and stroke (Cicerone, 2005); yet only recently have cognitive rehabilitation techniques been explored in individuals with PD. While the literature in this area is still limited, there is emerging evidence that cognitive rehabilitation techniques may be effective with a PD population. In a study by Sinforiani et al. (2004), cognitive rehabilitation via computerized neuropsychological training was found to be effective at improving cognition in story memory, phonemic fluency, and visuospatial executive functioning (Raven's matrices) in 20 early PD patients with mild cognitive deficits. Improvements remained after 6 months, suggesting that cognitive rehabilitation was effective at improving cognition long-term (Sinforiani et al., 2004). Sammer et al. (2006)found that following executive function skills training, 24 PD patients demonstrated improvement on similar measures of executive function compared to baseline. While these studies are promising and provide data that cognitive training can be effective at improving measurable cognitive skills, no literature exists as to whether cognitive rehabilitation can improve functional capacity outside of the testing environment or quality of life of the patients or caregivers. It is our desire to include these assessments to better ascertain the benefits, if they exist, to cognitive rehabilitation for individuals with PD and cognitive impairment.

Results of this study will provide essential information about non-pharmacologic (i.e., cognitive rehabilitation) interventions for individuals with PD and cognitive impairment that may improve cognitive abilities of affected individuals as well as their functional capacity, their quality of life and the quality of life of their caregivers. Moreover, these results may provide the first evidence of preventing or extending cognitive decline over time in PD.

As an exploratory aim, this study will also provide information regarding the neural changes associated with cognitive training in PD. To our knowledge, only one study has attempted to use fMRI to assess changes in brain function following cognitive training. Nombela and colleagues (2011) compared the performance of 5 PD patients trained on Sodoku puzzles to 5 untrained PD patients on an fMRI executive

function task. Trained individuals demonstrated improved executive function on the task as well as reduced cortical activation patterns (Nombela et al.). The authors reported that since previous studies have linked cortical over-activation in PD to the depletion of neuro-transmitters, including dopamine and their metabolites, a reduction in *overall* brain activation patterns suggest *improvement* in brain functioning. However, further study is needed to verify these findings.

As an additional exploratory aim, we will investigate the feasibility and efficacy of improving visual-spatial cognition by using the Wii as an adjunct to CogSMART. CogSMART teaches compensatory strategies for many of the relevant cognitive deficits (i.e., attention, memory, executive function) observed in PD patients. However, the program is limited by the lack of strategies for improving visual-spatial function. Visual-spatial functions are often impaired in PD patients and can cause problems in everyday activities of living (e.g., driving). Therefore, a program that can ameliorate this vital function would be advantageous to improving the quality of lives in these patients. Recent evidence supports the use of the Wii in improving motor functions in PD patients (Mhatre et al., 2013), but it is currently unknown how participation in such a program may impact visual-spatial functions. As the Wii games involve not only coordination of movements, but also visual-spatial function, it is plausible that Wii participation could improve these functions.

Phase II:

In addition to cognitive deficits, individuals with PD experience neuropsychiatric symptoms, such as depression, anxiety, fatigue and sleep disturbance, all of which are more common in individuals with PD-MCI compared to PD patients with normal cognition[18]. Neuropsychiatric symptoms impact QoL to a greater extent than motor symptoms[19] and may interfere with cognitive functioning as well complicate traditional treatment approaches. **Therefore, interventions that also target neuropsychiatric symptoms in PD-MCI may be the most efficacious to improve cognition and QoL.**

Cognitive rehabilitation is a structured, non-pharmacological intervention that aims to improve, maintain, or delay the decline of cognitive skills with the ultimate goal of improving the ability to function in everyday life[22]. Data on the efficacy of cognitive rehabilitation in individuals with PD is tremendously limited. Based on our review of the literature (*Schiehser et al., in press*[26]) and a recent review paper on non-pharmacological interventions for cognitive impairment in PD[27], only a handful of studies have evaluated cognitive rehabilitation in PD. The majority of these studies used computerized drill-training with the focus on one or more cognitive deficits (commonly called restorative rehabilitation).
In their recent review paper, Hindle and colleagues (2013) concluded that there was only one randomized controlled study with a low risk of bias[27]. This study, conducted by Paris et al.[31], demonstrated that after 4 weeks of comprehensive cognitive skills training (three 45-minute sessions per week),16 nondemented PD patients (50% PD-MCI) showed significant improvements in attention, processing speed, memory, visuospatial abilities, and executive function[31]. Despite these promising findings, this study and the majority of other related studies have been limited by small sample sizes, minimal use of control groups, lack of using a standard MCI diagnosis, and inadequate assessment of treatment impact on everyday cognition and QoL[27]. As a final statement, Hindle[27] emphasized that "There is an urgent need for rigorous randomized controlled trials of non-pharmacological, noninvasive treatments for cognitive impairment in PD "p.1048.

There are two main approaches to cognitive rehabilitation: 1) Restorative, which focuses on re-training patients on specific cognitive skills lost due to trauma or disease, and 2) Compensatory, which focuses on teaching patients compensatory strategies to work around their cognitive deficits. While restorative approaches have been the type of rehabilitation most studied in PD to date, there have been no studies of compensatory approaches in PD. The focus of this project will be to examine the impact of a compensatory cognitive rehabilitation program in PD-MCI. Our decision to examine this approach (as opposed to restorative approaches or a comparison of the two) was made for several reasons. First, past meta-analytic studies strongly suggest that cognitive deficits in other progressive neurocognitive disorders are best targeted by compensatory strategies[32 p. 526]. Second, there currently are no evidenced-based studies showing the efficacy of a compensatory strategy in treating cognitive deficits in PD-MCI. Third, until there is strong evidence for the use of compensatory approaches to cognitive rehabilitation in PD-MCI, it would be premature to contrast this approach with other approaches (see Huckans et al.[33] for a similar argument in MCI). Fourth, our years of experience in researching cognitive functioning in PD (e.g., Schiehser et al.[14, 34]; Filoteo et al.[35-37]) and cognitive rehabilitation using compensatory approaches (e. g., Twamley et al.[38, 39]) has placed our group in a very unique position to develop and provide empirical evidence for a novel compensatory approach to treat cognitive impairment in PD-MCI.

Relevance to Veterans' Health

PD is a progressive degenerative disorder with an estimated 80,000 current Veterans diagnosed with PD who receive care at the Department of Veterans Affairs (VA)[1]. It is projected that the number of VA patients over the age of 65 will increase, indicating that the number of Veterans with PD will be even larger in years to come. Given that a large proportion of these Veteran PD patients will develop cognitive

deficits, it is imperative to develop an empirically-validated cognitive rehabilitation program that can slow or even reverse cognitive decline and improve quality of life for people with PD.

Development of CogSMART-PD
The general framework of CogSMART-PD is predicated on the versions that were initially designed for other neurologically impaired groups (e.g., psychosis, traumatic brain injury [TBI]). However, as PD represents a progressive disorder with its own unique set of cognitive deficits and neuropsychiatric symptoms, the program was modified substantially and tailored for use in PD. Specifically, the program includes information on cognitive and non-motor symptoms most impacted in PD as well as psychoeducation regarding the progressive nature of cognitive deficits. Likewise, strategies to improve neuropsychiatric symptoms, such as sleep, fatigue, and mood are also incorporated.

As an exploratory aim, this study will also provide information regarding the neural changes associated with cognitive training in PD. To our knowledge, only one study has attempted to use fMRI to assess changes in brain function following cognitive training. Nombela and colleagues (2011) compared the performance of 5 PD patients trained on Sodoku puzzles to 5 untrained PD patients on an fMRI executive function task. Trained individuals demonstrated improved executive function on the task as well as reduced cortical activation patterns (Nombela et al.). The authors reported that since previous studies have linked cortical over-activation in PD to the depletion of neuro-transmitters, including dopamine and their metabolites, a reduction in *overall* brain activation patterns suggest *improvement* in brain functioning. However, further study is needed to verify these findings.

As an second exploratory aim, we will investigate the feasibility and efficacy of improving visual-spatial cognition by using the Wii and/or a program called Odoroki (a prototype system which engages the visual, vestibular, proprioception, motor, and auditory systems of an individual or small group of users in simultaneous physical and mental activity) as an adjunct to CogSMART. CogSMART teaches compensatory strategies for many of the relevant cognitive deficits (i.e., attention, memory, executive function) observed in PD patients. However, the program is limited by the lack of strategies for improving visual-spatial function. Visual-spatial functions are often impaired in PD patients and can cause problems in everyday activities of living (e.g., driving). Therefore, a program that can ameliorate this vital function would be advantageous to improving the quality of lives in these patients. Recent evidence supports the use of the Wii in improving motor functions in PD patients (Mhatre et al., 2013), but it is currently unknown how participation in such a program may impact visual-spatial functions, or how participation in Odoroki can improve visual spatial functioning or motor symptoms.. As the Wii games and Odoroki involve not only coordination of movements, but also visual-spatial function, it is plausible that Wii participation and/or Odoroki could improve these functions.

As an additional exploratory aim, we will investigate salivary brain-derived neurotrophic factor (BDNF) and salivary cortisol levels (post-intervention compared to pre-intervention) in both groups.
Animal and human evidence demonstrates that glucocorticoids (mainly cortisol in humans), the main class of stress hormones, are found in greater density in the prefrontal cortex and limbic system structures (e.g., amygdala, ACC) (Herman et al, 2012; Lucassen et al., 2014), and are strongly linked to memory performance, such that elevated levels of cortisol are associated with memory decline in normal and pathological cognitive aging (Souza-Talarico, 2011). In PD, cortisol levels are abnormally elevated compared to healthy controls (Charlett et al., 1998; Hartmann et al., 1997), indicating that cortisol may be more detrimental to cognition in this vulnerable subset of the population. Empirical research has demonstrated that behavioral interventions promote cognitive function and may inhibit the production of cortisol in the HPA axis (Holdevici and Crăciun, 2015). However, the interaction between cognitive remediation and the glucocorticoid response in PD is unclear. It is hypothesized that cognitive rehabilitation (CogSMART-PD) will promote better cognitive functioning and correspond to a reduction in cortisol in PD-MCI.

BDNF plays a critical role in synaptic plasticity and dopaminergic neural growth (Gómez-Palacio-Schjetnan and Escobar, 2013). In PD, BDNF is reduced (Scalzo et al., 2010) and this reduction has been linked to cognitive deficits observed in this population (Kahlil et al., 2016). A recent pilot study (n=8) supports BDNF as a biomarker of the effects of cognitive rehabilitation in PD (Angelucci et al., 2015). Thus, it is hypothesized that BDNF gene expression levels will be associated with cognitive change following CogSMART-PD.

Section 9 - Design and Methods

9) Describe the research design and the procedures to be used to accomplish the specific aims of the project. Provide a precise description of the planned data collection (include what systems or databases will be used/accessed to gather data), analysis and interpretation. For chart review studies, include the timeframe of collection. Address sample size, inclusion of women and minorities. Define in clear terms exactly what will be done to the human subjects.

Phase I:

Participants: We will recruit approximately 80 individuals who have PD and documented cognitive impairment and 80 caregivers from ongoing studies of neuropsychological functioning in PD (PI: Filoteo). Over-recruitment by 10% will also be instituted to account for subject attrition or unusable data and to ensure a final sample size of 20 participants (10 x 2 CogSMART groups) for Aims 1 and 2 and 60 for the Exploratory Aim. All participants will be screened and excluded if they have a history of significant head trauma, other neurologic or major psychiatric disorders, history of developmental learning disorder, substance dependence, or any contraindication to participating in the cognitive treatment. The participants' diagnosis of Parkinson's disease will be confirmed by participating neurologists and cognitive impairment (i. e., MCI or dementia) will be confirmed via neuropsychological testing and the consensus of the neuropsychologist investigators (Drs. Schiehser and Filoteo). We will also recruit any identified and consistent caregivers of the participants to complete several questionnaires regarding the participant's quality of life and daily functioning prior to and following (immediately, 3- and 9-months) the intervention. All caregivers will be asked to participate if they do not have any known memory impairment, dementia, or another condition which would prevent them from accurately completing the questionnaires.

Procedures: PD participants: Appropriate individuals will be provided information about the study and study staff will contact those who agree. After receiving detailed information about the study, those who wish to participate will provide informed consent prior to participating in the study. Although participants will be screened for inclusion/exclusion criteria prior to study entry, if, during the course of any of the following assessments exclusionary information becomes available, that participant's data will not be analyzed for the present study. Those passing basic screening procedures will come to the VA to consent to the study. If they consent to participate, PD participants will undergo neuropsychological baseline testing in the same visit. Research assistants trained in neuropsychological testing will administered the neuropsychological assessments to the subjects. Their VA chart, if applicable, will not be reviewed until after the participant has consented to participate. Further, all PD participants will be able to continue with any standard clinical care that they have been participating in or may be recommended by their doctor during the course of their participation in the study. After testing, PD participants will be randomized to either the treatment group or a wait-list control group upon consent and prior to any assessment or treatment by a research assisant. Individuals will be randomized into the treatment vs. waitlist groups by alternating the assignments serially per each qualifying subjects' ID number that is assigned upon study entry. In other words, subjects #s 1100, 1102, 1104, etc will be assigned to the treatment group and subjects 1101, 1103, 1105, etc will be assigned to the waitlist group. Those randomized to receive treatment will attend a group cognitive rehabilitation psychoeducation program, which will meet once per week for 10 weeks. Groups will consist of 8-10 individuals and will be lead by a postdoctoral fellow and/or an appropriately trained individual who is blinded to the participants' neuropsychological test results.

Wait-list control PD participants will continue to participate in any clinical treatment-as-usual and will receive neuropsychological assessments on the same schedule as the intervention group, though will not be receiving the treatment. At the completion of the intervention, those in the wait-list group will be invited to enter treatment if they choose. Three and nine months post-intervention (i.e., 6 and12 months post-initiation of treatment, respectively) participants will be tested again to determine maintenance of any cognitive gains and delay of cognitive decline.

	Baseline (0 months)	0-3 months	3 months	3-6 months	6 months	12 months
CogSMART group (N=8-10)	Consent and Assessment 1 + Home Visit	CogSMART intervention	Assessment 2	No CogSMART intervention	Assessment 3	Assessment 4
Wait-list group (N=8-10)	Consent and Assessment 1 + Home Visit	No CogSMART intervention	Assessment 2	CogSMART intervention (if desired)	Assessment 3	Assessment 4

The intervention is the Cognitive Symptom Management and Rehabilitation Therapy (CogSMART), a manualized group course, predicated on a compensatory approach to cognitive difficulties where participants learn strategies to help accommodate for any cognitive weaknesses. This is a psychoeducation program, not a therapy intervention. A trained clinician(s) leads the program one time per week and each session is approximately 2 hours long. Given that this is a manualized psychoeducation program, individuals with a Bachelor's degree with training and supervision, are appropriate to lead the group class. Groups will be lead by a postdoctoral fellow and/or an appropriately trained individual who is blinded to the participants neuropsychological test results. During the first hour, psychoeducation and techniques are provided in a specific cognitive domain, and during the second hour, the skills are practiced and individualized to each participant's own situation. In this way, the intervention can be conducted in groups, allowing for participants to share strategies with each other, but the content can be individually tailored. The skills taught during the program are then generalizable to each patient's unique situation. The four targeted cognitive domains (see table below) were chosen for their relevance to everyday functioning skills and because they have been shown to be modifiable. The program will focus

on: education regarding cognitive and motor changes with PD, *prospective memory*, *attention and concentration*, *learning and memory, and problem-solving and cognitive flexibility*. The program is further detailed in the table below:

Targeted Domain	**Examples of Importance of Domain at Work /School or for Independent Living**	**Specific Compensatory Strategies and Habits in CogSMART Cognitive Training**
Prospective Memory	• Remembering to go to appointments • Remembering to take medications • Remembering to send in bills or requested paperwork • Remembering to do tasks/chores in response to cues	1. Daily calendar use 2. To-do lists and prioritizing tasks 3. Linking tasks or using "can't miss reminders" to remember tasks
Attention and Concentration	• Paying attention to communications from family and friends • Maintaining focus during medical appointments • Maintaining attention to tasks or household projects without getting distracted	1. Conversational vigilance skills (reduce distractions, eye contact, paraphrasing, and asking questions) 2. Task vigilance skills (paraphrase instructions, use self-talk during tasks to maintain focus)
Learning and Memory	• Learning and remembering tasks • Learning novel information in books, community lectures, or programs. • Learning and remembering names of new people	1. Encoding strategies (write things down, paraphrasing/repetition, association, chunking, categorizing, acronyms, rhymes, visual imagery, name-learning strategies) 2. Retrieval strategies (systematic searching) and organizational strategies for general learning and memory
Executive Functioning (Problem Solving and Cognitive Flexibility)	• Problem solving and coping with unexpected situations • Thinking flexibly and self-monitoring performance on daily activities	1. 6-step problem solving method (define problem, brainstorm solutions, evaluate solutions systematically, select a solution, try it, evaluate how it worked) 2. Self-talk while solving problems 3. Hypothesis testing 4. Self-monitoring

Previous work with this intervention in a psychiatric population has been well received by participants, and demonstrated medium effect sizes for verbal memory, learning and executive functioning, a large effect size for attention/concentration, and a medium effect on self-reported cognitive problems (Twamley et al., 2008). Many of these gains were maintained at three months post-intervention.

Caregivers: If the participant has an identified consistent caregiver (e.g., spouse), this individual will be asked to complete several questionnaires related to their assessment of the patient's functioning at the time of the participants baseline assessment and again immediately following the intervention, and at 3- and 9-months post-intervention. The caregivers to the participants will be invited to attend the CogSMART class solely as observers. They will not be allowed to participate, but they will be able to sit in to have a better understanding of what the patient is learning.

Assessments: To document changes over time in both the intervention and wait-list groups, all participants will undergo neuropsychological assessment at baseline (pre-treatment), after the three month intervention period, six-months after baseline (three months from the end of the intervention), and 12 months after baseline (nine months from the end of the intervention) to determine persistence of results. The baseline assessment will entail a comprehensive neuropsychological exam consisting of measures of global cognitive functioning [Mattis Dementia Rating Scale (MDRS; Mattis, 1988), memory [California Verbal Learning Test (CVLT-II; Delis et al., 2000); Visual Reproduction Test (VRT) from the *Wechsler Memory* Scale-*Fourth Edition* (Wechsler, 2008a)], attention/concentration (Digit Span and Digit Symbol Coding from the *Wechsler Adult Intelligence Scale-IV* (Wechsler, 2008b)], language [Wide Range Achievement Test- Reading (WRAT-4; Wilkinson, 1993)], visuospatial skills [Judgment of Line Orientation Test (Benton et al., 1983)], executive functioning [Wisconsin Card Sorting Test-64 (WCST-64; Kongs et al., 2000); Verbal Fluency Test and Color-Word Interference Test from the Delis Kaplan Executive Functioning System (DKEFS; Delis et al., 2001); Matrix Reasoning from the WAIS-IV], mood/anxiety [Hamilton Rating Scale for Depression 17-Item (HAMD-17; Hamilton, 1960); Geriatric Depression Scale (GDS; Yesavage e
t al., 1982); Neuropsychiatric Inventory 14-Item version (NPI; Cummings et al., 1994); State Trait Anxiety Inventory (STAI; Spielberger et al., 1983)], functional skills [Unified Parkinson's Disease Rating Scale (UPDRS; Fahn, 1987); The Physical and Instrumental scales of the Activities of Daily living Questionnaire (IADL; Lawton and Brody, 1969)], and quality of life [Parkinson's Disease Questionnaire-39 (PDQ-39; Peto et al., 1995)]. Motor functioning will be assessed by a neurologist using the UPDRS-Part 3. The entire pre-treatment cognitive/motor assessment will take approximately three hours to complete. If participants have recently been tested clinically or as part of participation in an existing cognitive aging study, this data may be used for the baseline assessment, to reduce any unnecessary burden to the participant. In addition, all participants who consent and agree will undergo a 30-minute home evaluation. This evaluation will assess impediments to ideal cognitive and motoric functioning (e.g., organization of home) and offer strategies to improve motoric and cognitive function (e.g., use of mats/runners through doorways for cues to prevent freezing). If the participant has an identified consistent caregiver (e.g., spouse), this individual will be asked to complete several questionnaires related to their assessment of the patient's functioning (Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm and Jacomb, 1989); The Physical and Instrumental scales of the Activities of Daily living Questionnaire (IADL; Lawton and Brody, 1969), NPI – informant version) and quality of life (PDQ-39 proxy form), their ratings of their own level of burden regarding caregiving [Caregiver Burden Inventory; (CBI; Novak and Guest, 1989)], and their self-reported mood [HAMD-17, GDS; and STAI]. The caregiver questionnaires are estimated to take approximately 30-40 minutes to complete.

At post-treatment and 6-month (3 months post-intervention) follow-up, participants will be administered the Mattis Dementia Rating Scale (MDRS; Mattis, 1988), California Verbal Learning Test – II (CVLT-II; Delis et al., 2000), Digit Span and Digit Symbol Coding from the WAIS-IV (Wechsler, 2003), Verbal Fluency and the Color-Word Interference tests from the Delis Kaplan Executive Functioning System (Delis et al., 2001), Matrix Reasoning from the WAIS-IV, the Geriatric Depression Scale (Yesavage et al., 1982), Hamilton Rating Scale for Depression 17-Item (HAMD-17; Hamilton, 1960), Neuropsychiatric Inventory 14-Item version (NPI; Cummings et al., 1994); State Trait Anxiety Inventory (STAI; Spielberger et al., 1983), The Physical and Instrumental scales of the Activities of Daily living Questionnaire (IADL; Lawton and Brody, 1969), and the Parkinson's Disease Questionnaire-39 (PDQ-39; Peto et al., 1995). These follow-up assessments will take approximately 2 hours to complete. Caregivers will be asked to complete the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm and Jacomb, 1989), the PADL and IADL scales – informant version, the PDQ-39 proxy form, the Caregiver Burden Inventory (CBI; Novak and Guest, 1989), and the Hamilton Rating Scale for Depression 17-Item (HAMD-17; Hamilton, 1960), Geriatric Depression Scale (GDS; Yesavage et al., 1982), and the State Trait Anxiety Inventory (STAI; Spielberger et al., 1983). We will use counterbalanced alternate forms of the tests included in the neuropsychological assessment, when available, to partially address practice effects. At 12 months (9 months post-intervention), participants will be given the entirety of the battery they completed at baseline. Standardized alternative forms that measure the same or similar cognitive abilities may be substituted for the aforementioned tests if warranted to prevent practice effects, fatigue, or participant attrition.

All data will have quality control measures applied. All neuropsychological assessments will be double-scored to ensure accuracy. Data will be compiled in a database and all data will be double entered to preserve the integrity of the database. The subjects' confidentiality will be strictly maintained in data storage, analysis, and presentation.

Our projected sample size is consistent with the sample reported on in the preliminary data section (Twamley et al., 2008). As we propose to use a similar sample size and the same cognitive rehabilitation program, we anticipate achieving similar medium to large effect sizes in the proposed study. To determine whether CogSMART will improve cognition in PD, we will employ statistical analyses including reliable change indexes to take into account change in neuropsychological test scores over the course of the intervention while also accounting for predicted practice effects. We will compare the treatment and control groups on baseline and three-month change scores. Group comparisons of differences and

changes in neuropsychological test scores between as well as within groups will also be determined via repeated measures (RM) ANCOVAs. Cognitive, functional, and quality of life indices of both participants and caregivers will be of interest in determining efficacy of treatment.

As an exploratory aim, we will recruit 60 additional individuals to complete the protocol as described above and in addition, participate in two (pre/post) hour-long brain imaging (fMRI) sessions. The imaging sessions will consist of a structural brain scanning and participation in an fMRI cognitive task (please see below). Following the baseline evaluation, half of the participants will be randomly assigned to the intervention group (n = 30) and participate in the CogSMART program. The groups will be broken up to consist of 8-10 individuals. The remaining participants (n = 30) will be assigned to the non-intervention /waitlist ("care-as-usual") group. This group will also be broken down into groups of 8-10 when enrolled in the intervention. Participants will be retested by a group assignment-blinded examiner on the clinical and cognitive battery and imaging protocol following the intervention or waitlist.

fMRI task and analysis: Participants will undergo fMRI while performing the Matrix Reasoning task (f-MRT), a well-developed and normed test of executive functioning for fMRI (Allen & Fong, 2008). Within the scanner, participants will be presented with 4 practice items followed by 24 test stimulus items and 24 alternative stimuli, conceptually modeled after problems found on the Raven's Progressive Matrices test, as well as items from the matrix reasoning subtest of the WAIS-III, collectively called the f-MRT (Allen and Fong, 2008). Each stimulus consists of a 3 × 3 matrix of complex visual figures, with one figure missing. For each matrix problem, participants will be instructed to "indicate what the missing figure should be," and to then select it from among the four choice alternatives presented on the right side of the matrix. Participants will also be told to place more importance on response accuracy than on response speed. Accuracy (% correct) and reaction time will be measured.

Each participant's scanning session will last approximately one hour, during which an anatomical scan and two functional scans will be run while performing the tasks. An 8-channel brain array coil during a series of T2* weighted EPI scans acquired to measure BOLD functional activity will be used. The parameters for the EPI scans will be: 64x64 matrix, 3.43 x 3.43 x 2.6 mm voxels with 1.4 mm gap, TR = 2 seconds, TE = 32 ms, flip angle of 90 degrees, and 30 slices. These parameters will cover the entire brain. The acquisition of the EPI scans will be performed in the axial plane. Tasks are synchronized with the scanner using a TTL pulse sent to a laptop computer.

As secondary exploratory aim, we will recruit 8-10 additional individuals to participate in 30-minutes of Wii training (tennis, golf, and ping pong games) in addition to the CogSMART program. These individuals will be assessed with the same procedures as described for the CogSMART (without Wii) participants.

All procedures are performed for research purposes.

Phase II:

Participants: 110 patients (55 per group) with PD-MCI will be recruited for this study as well as 110 identified and consistent caregivers of the participants. All caregivers will be asked to complete several questionnaires regarding the participant's quality of life and daily functioning prior to the intervention, at follow-up visits, and after the intervention. Although attrition did not occur in Phase I, over-recruitment by 20% will be instituted to account for possible subject attrition or unusable data. Participants will receive a payment of $40 for each of the four assessments they complete (pre- and post-intervention/support and 6- and 12-month follow-ups).

Procedures: We will primarily recruit Veterans with PD from the VASDHS Neurology and Neuropsychology Clinics. While we will attempt to exhaust recruitment at VA clinics first, recruitment of women may be limited at the VA, and therefore, we will likely need to recruit from outside clinics to obtain a PD-epidemiologically accurate gender ratio of 60 (men)/40 (women). In this regard, we will primarily recruit from the University of California, San Diego (UCSD) Movement Disorders Center. Referred participants will be screened for inclusion/exclusion criteria (please see above) and consented if appropriate. All participants will have Level II MDS-criteria based diagnosis of MCI derived from a formal neuropsychological evaluation within the past 12 months. As most participants will be referred from the VASDHS and UCSD Movement Disorder Center, the majority will have MDS-criteria MCI diagnoses prior to referral. However, should a PD patient be referred for this study who has not had formal neuropsychological testing or if testing is outdated (>12 months), pre-inclusion neuropsychological testing will be performed through Dr. Filoteo's lab, which follows patients neuropsychologically. Likewise, if the WRAT-4 Reading scale has not been administered within the past year, this 2-5 minute measure will also be administered to ensure adequate reading level. To avoid confounds, no test proposed as outcome measures in this study will be used to determine the PD-MCI diagnosis.

Upon meeting study criteria, participants will be randomized to one of two 10-week conditions (CogSMART-PD or Supportive Care). Randomization will occur in blocks (i.e., first 5 people enrolled will be assigned to the intervention group, next 5 will be assigned to control group, next 5 will be assigned to the intervention group, and so on until the sample size of 55 per group is met). Within one to 1.5 weeks prior to beginning the group, participants will be tested by a research assistant blinded to group assignment on a 2-2.5 hour

battery of cognitive, neuropsychiatric, health status/QoL, and strategy use measures as well as a motor assessment (UPDRS-Part III), which will immediately precede the cognitive assessment (please see Assessment/Materials). Participants will be tested in the "on-state" of parkinsonian medications to limit confounding variability (e.g., of motor symptoms, such as tremor) on test results. All participants will be tested at the same time, preferably in the morning, if possible. Breaks will be given during the assessment as needed. Groups will consist of 5 individuals with PD-MCI and be led by a trained clinician (who is not involved in the clinical care or assessment of these participants). Following the intervention and 6- and 12-months post-intervention, PD-MCI participants will be re-tested by a group-blinded research assistant. 24 months post-intervention, participants will be asked to complete a brief (15 minute) telephone interview regarding changes in health status or living situation since the 12-month follow up. Following the 12-month follow-up, the control (support) group will be permitted to join CogSMART-PD.

Assessment/Materials: Outcome measures were carefully selected so that they: 1) represent areas that are frequently impaired, dysfunctional, or problematic for individuals with PD-MCI; 2) correspond to domains that are targeted for improvement by the CogSMART-PD intervention; 3) have adequate psychometric properties for use in PD; and 4) have shown utility and applicability based on the pilot and preliminary studies. Total neuropsychological and motor testing time is estimated to be 2-2.5 hours.

Cognitive Function and Cognitive Strategy Assessment:

1. Matrix Reasoning subtest (MRT) from the Wechsler Adult Intelligence Scale-IV [WAIS-IV] is a 15-minute valid, reliable, and widely-used standardized neuropsychological test that is considered one of the gold standards of executive function[28]. The MRT is commonly used to assess executive function in individuals with PD, as it does rely on motor function.

2. Memory for Intentions Screening Test (MIST)[62]. The MIST is an 8-trial and 30-minute performance-based prospective memory test with a minimal motor component. Scores range from 0 to 48, with higher scores representing better performance. The MIST entails participants performing prospective memory-based tasks based on time cues (e.g., "In 15 minutes, tell me that it is time to take a break") or event cues (e.g., "When I show you a post card, self-address it") while performing word search puzzles (distracter task). There are four trials each of the time and event cues, with each item scored from 0-2 points; thus, the separate event-based and time-based scales have scores ranging from 0 to 8. The time- and event-based trials are balanced for delay interval (i.e., 2- and 15-min delay periods) and response modality (i.e., verbal and action responses). The "event cues" task score is considered particularly ecologically relevant, in the required response is related to the actual task (e.g., "When I hand you a request for records form, please write your doctors' names on it.") and therefore, represents natural cuing that is often encountered in everyday life [63]. Thus, this measure will be the primary variable studied in this study. Other indices (e.g., summary score and time-based score) will be explored as well. The MIST has been studied in PD[63, 64] and studies support its adequate reliability and construct validity[43, 65].

3. Memory Assessment Scales (MAS) Names-Faces subtest is a 10-minute valid, reliable, standardized neuropsychological test of verbal (name)-visual (face) memory[42], which has been characterized as "a more ecologically valid memory test than the other laboratory analogues of everyday memory functions"[66, p.356]. Moreover, face-name memory is a common concern of individuals with PD and is directly relevant to the intervention (i.e., name learning strategy), as well as not reliant on motor functioning, thus suitable for PD.

4. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[39]. The IQCODE is a 26-item, 5-minute informant-based questionnaire used to assess the patient's everyday functional-based measure of cognition (e.g., recognizing familiar faces, remember things in general, handling financial matters) on a 5-point scale (1=much improved to 5=much worse). The IQCODE has been used fairly extensively in individuals with cognitive impairment and has been found to have high reliability and good validity[52]. In addition, we will also administer the self-report version the IQCODE (IQCODE-SR) to the patients. A psychometric study of the IQCODE-SR found it to have good feasibility, homogeneity, and construct validity [67]. The IQCODE has been used as an outcome in several seminal PD studies (e.g., Aarsland et al., 2009[68]). We conducted a validation study (manuscript in preparation), of the IQCODE in 100 PD patients and found it to have adequate convergent validity with a clinician-measure of cognition (UPDRS Item 1; $r = .39$, $p < .001$) and excellent discriminant validity from measures of motor symptoms (UPDRS-Part III Total; $r = .08$, $p = .41$) and disease severity (Hoehn and Yahr; $r = .11$, $p = .26$).

5. The Montreal Cognitive Assessment (MoCA) will be administered at the baseline (pre-intervention) assessment as a measure of general cognition and will be used as a covariate in the statistical analyses (please see Data Analysis section below). The MoCA is a suitably accurate, brief (10-minute) test of cognitive impairment in PD and has established cut-offs for both PD-MCI and PDD.[69]

6. Cognitive Problems and Strategies Assessment (CPSA)[38]. The Strategies Assessment section of the CPSA will be used as an assessment of compensatory strategies used by the individual. This questionnaire was found to be sensitive to the use of cognitive strategies after cognitive rehabilitation (CogSMART) participation[38]. The CPSA takes 8-10 minutes to complete.

7. Parkinson's disease Cognitive Rating Scale (PD-CRS; Pagonabarraga et al., 2008). This is a cognitive scale specifically designed for individuals with Parkinson's disease. The assessment has a total of 9 tasks meant to assess attention, working memory, alternating and action verbal fluency, clock drawing, and verbal memory and takes approximately 15 minutes to administer.

Quality of Life, Health Status, and Neuropsychiatric Symptom Assessment:
1. World Health Organization Quality of Life-BREF (WHOQOL-BREF[45]). The WHOLQOL-BREF is a 26-item, 5-10 minute measure of general QoL (i.e., an individual's perception of their position in life[57]), which contains 4 subscales (physical, psychological, social, and environmental) and has been recommended[70] and "suggested" for use in the PD by a 2011 MDS Task Force[71]. The MDS did not give it is highest rating only due to limited evidence in PD. Yet, additional validation studies of the WHOQoL-BREF in PD have been published since the MDS report, indicating that the WHOQoL-BREF has excellent internal consistency (Cronbach's alpha = 0.91) and adequate to excellent convergent and discriminant validity in PD[72, 73]
2. Parkinson's Disease Questionnaire-39 (PDQ-39)[44]. The PDQ-39 is a self-report measure of health status (HS), which is considered different than QoL, in that it does not ask for perceptions, judgments or reactions [71]. For example, while the WHOQOL-BREF asks, "how satisfied are you with your ability to perform daily living activities?", the PDQ-39 asks, "how often do you have difficulty with [daily living activities]?". The PDQ-39 has been well-validated in PD[44] and is recommended for use by the MDS.
3. Neuropsychiatric Inventory 12-Item version (NPI-Q)[53]. The NPI-Q is a 12-item, 5-10 minute, clinician-administered questionnaire that assesses various neuropsychiatric symptoms (e.g., depression, anxiety, apathy, and sleep disturbance). Psychiatric symptoms are identified using structured screening questions and positive responses are probed with structured follow-up questions. Follow-up questions are rated in terms of frequency on a scale of 1 to 4 and severity on a scale of 1 to 3. A composite score for each item is then devised based on the product of the frequency and severity for each item, thus resulting in a range of 1 to 12 for each item and a maximum score of 120, with higher scores indicating greater frequency /severity of psychiatric symptoms. The NPI-Q has been used successfully in previous work to characterize psychiatric symptoms in both demented and nondemented PD patients[74].

PD Motor and Disease Severity Assessment:
The Unified Parkinson's disease Rating Scale - Part III (UPDRS-Part III)[75, 76] and the modified Hoehn and Yahr Rating Scale (HYRS)[77, 78] will be used to assess level of motor impairment and disease severity. For this assessment participants go through a series of tasks designed to assess various motor characteristics such as speech, facial expression, rigidity, finger tapping, hand movements, toe tapping, freezing of gait, balance, etc. We will also use UPDRS item #13 to assess fall risk (please see Monitoring Plan below). These are standard instruments for measuring the motor symptoms and disease severity in patients with PD and have been used extensively in both research and clinical settings. VASDHS/UCSD neurologists will perform these assessments immediately prior to the cognitive assessment at the pre and 12-month follow up evaluations.

Adjunct Performance Measures:

Motor Skill Fitness measures will be carried out by a trained research assistant at the VA Medical Center

Subjects will undergo body mass index analysis at the VA Medical Center

De-identified data from these Motor Skill Fitness measures will be analyzed in the Smart Lab at UC San Diego. No participant data will be collected there.

Client Satisfaction with the intervention will be assessed at the end of the intervention with the Client Satisfaction Questionnaire (CSQ-8)[79]. The CSQ-8 is an 8-item, 2-3 minute measure that yields a single score, ranging from 8 to 32 (each item rated on a 4-point Likert scale), with higher scores indicating greater satisfaction. The CSQ-8 has been widely used in clinical research trials and is reported to have excellent reliability and internal consistency, acceptability to clients and service providers, and sensitivity to different levels of program quality.

Intervention: The treatment intervention is CogSMART-PD. Participants will meet in groups of 5 individuals per group for 1.5 hours once per week for 10 weeks.
Control Group: The supportive care (control) group will entail having groups of 5 individuals with PD-MCI meet for peer-support for 1.5 hours once per week for 10 weeks. A trained clinician will serve as the facilitator of this group and will be instructed to not provide any treatment or intervention strategies. The main role of the facilitator will be to create a safe and respectful environment where members feel comfortable sharing their knowledge and insight with each other.

Monitoring Plan. As individuals with PD are at high risk for falls, we will carefully screen all individuals for history of falls upon recruitment. We will use the baseline UPDRS falling item (#13) in which a history of falls is categorized on a likert scale from 0 (none) to 4 (falls >once per day). A history of falls as assessed by the UPDRS appears to be one of the best predictive methods of subsequent falls at this time[80]. Those individuals who endorse a history of falling or score >0 on the UPDRS falling item, will be closely monitored. This includes ensuring that they are escorted to and from the intervention room from their vehicle as well as to and from the bathroom, as needed. Should a patient need help within the bathroom,

a caregiver will be requested to assist. If needed, we will utilize the VA escort service. Although not common in PD, all participants will also be assessed for suicidal ideation/intent at baseline, as standard of care for psychological/behavioural interventions. If suicidal ideation is acknowledged, indicated by a score of 2 or greater on item 9 of the Beck Depression Inventory-II (BDI-II), research participants will be referred directly to a VA-privileged clinician for further evaluation. These participants will be monitored for changes in mood during the intervention.

Data Analysis: Preliminary analyses will begin with an examination of the distribution of variables to assess their characteristics (means, standard deviations, skewness), to provide descriptive statistics of the study population, and to allow assessment of randomization. Continuous measures will be tested for normality and homogeneity of variance. Non-normally distributed variables will be transformed to meet the normal distribution assumption for linear effects models. Analyses will include tests of randomization and comparability across conditions. Randomization will be tested by performing a series of t-tests and chi-square tests to compare the groups on demographic and initial clinical variables. Pre-specified baseline variables including age, education, gender, severity and duration of illness, and motor symptoms will be considered as potential covariates (as fixed effects) in the multivariate analyses. Any other variables (e.g., baseline cognition as assessed by the MoCA, medications) on which the groups differ initially will also be explored as covariates in subsequent analyses, as described below. In the case of missing data, appropriate data analytic techniques will be used, which may include deletion, imputation, inclusion of an indicator of missing values, or pattern-mixture modeling. Outcomes will be analyzed using SPSS release 16 (SPSS, 2007), and open source statistical software R[81].

As an exploratory aim, we will recruit 60 additional individuals to complete the protocol as described above and in addition, participate in two (pre/post) hour-long brain imaging (fMRI) sessions. The imaging sessions will consist of a structural brain scanning and participation in an fMRI cognitive task (please see below). Following the baseline evaluation, half of the participants will be randomly assigned to the intervention group (n = 30) and participate in the CogSMART program. The groups will be broken up to consist of approximately 5 individuals. The remaining participants (n = 30) will be assigned to the non-intervention/control ("supportive care") group. This group will also be broken down into groups of 5 when enrolled in the intervention. Participants will be retested by a group assignment-blinded examiner on the clinical and cognitive battery and imaging protocol following the intervention or waitlist.

fMRI task and analysis: Participants will undergo fMRI while performing the Matrix Reasoning task (f-MRT), a well-developed and normed test of executive functioning for fMRI (Allen & Fong, 2008). Within the scanner, participants will be presented with 4 practice items followed by 24 test stimulus items and 24 alternative stimuli, conceptually modeled after problems found on the Raven's Progressive Matrices test, as well as items from the matrix reasoning subtest of the WAIS-III, collectively called the f-MRT (Allen and Fong, 2008). Each stimulus consists of a 3 × 3 matrix of complex visual figures, with one figure missing. For each matrix problem, participants will be instructed to "indicate what the missing figure should be," and to then select it from among the four choice alternatives presented on the right side of the matrix. Participants will also be told to place more importance on response accuracy than on response speed. Accuracy (% correct) and reaction time will be measured.

Each participant's scanning session will last approximately one hour, during which an anatomical scan and two functional scans will be run while performing the tasks. An 8-channel brain array coil during a series of T2* weighted EPI scans acquired to measure BOLD functional activity will be used. The parameters for the EPI scans will be: 64x64 matrix, 3.43 x 3.43 x 2.6 mm voxels with 1.4 mm gap, TR = 2 seconds, TE = 32 ms, flip angle of 90 degrees, and 30 slices. These parameters will cover the entire brain. The acquisition of the EPI scans will be performed in the axial plane. Tasks are synchronized with the scanner using a TTL pulse sent to a laptop computer.

As secondary exploratory aim, we will recruit 8-10 additional individuals to participate in 10, 30-minutes of Wii training (tennis, golf, and ping pong games) in addition to the CogSMART program. These individuals will be assessed with the same procedures as described for the CogSMART (without Wii) participants.

As an additional exploratory aim, we will recruit 8-10 individuals to participate in 20, 1 hour-long Odoroki sessions where the individuals will perform physical activities to music by using a computer program. These individuals will be assessed with the same procedures as described for the CogSMART participants without an adjunct exercise program.

As a final exploratory aim, we will recruit 8-10 individuals to complete saliva sample collections (pre- and post-intervention) for salivary analysis of neuroinflammatory biomarkers (e.g., cortisol) before and after treatment.

All procedures are done for research purposes.

Section 9.6 Specimens

9.6) Identify the biological materials, procedures for obtaining material, and the sources of the specimens. ***Effective 12/01/2019: Specify whether research or clinical staff (from which service) will be collecting the specimens and describe "hand-off" procedures to ensure that release of the specimens has been authorized by Pathology and Laboratory Medicine Service (PALMS).***

Pre- Intervention Buccal Swab:
Participants will be given 3 oral swab collection kits at their pre-assessment. On the day before the first session, participants will swab their own cheek at home once before going to bed, once upon waking in the morning, and once 30 minutes after waking. Participants will bring kits back on the first day of group.

Post- Intervention Buccal Swab:
Participants will be give 3 oral swab collection kits on the last session. After the last session, participants will swab their own cheek at home once before going to bed, once upon waking in the morning, and once 30 minutes after waking. Participants will bring kits back to their post-assessment.

Pre and Post- Intervention Passive Drool Test:
Participants will be asked to split or drool into a tube which has a funnel on top. If participants experience difficulty producing saliva, suggestions for improving saliva generation will be made.

Samples will be stored at and analyzed by the UCSD Integrative Health and Mind-Body Biomarker Laboratory. Samples will be labeled with subject ID numbers and will not have identifiable information (i. e., name, SSN, or date of birth) on the labels; the de-identified sample will be walked over to the UCSD Integrative Health and Mind-Body Biomarker Laboratory in a locked briefcase by study personnel. Samples will be destroyed after analysis.

Section 9.8 Questionnaires & Surveys

9.8) Provide the name and a reference for questionnaires/surveys that are standard or identify them here and attach a copy of the questionnaire/survey. ***Questionnaires or surveys that are not clinical standard references must be uploaded. Reference the help link for additional information related to surveys administered to VA personnel and approved platforms for web-based surveys.***

Geriatric Depression Scale
Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., et al. (1982). Development and validation of a geriatric depression screening scale: A preliminary report. J Psychiatr Res, 17(1), 37-49.

Beck Depression Inventory (BDI-II)
Beck, A., Steer, R., &Brown, G. (1996). Manual for the BDI-II.

State/Trait
Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., &Jacobs, G. A. (1983). Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press.

The Parkinson's Disease Questionnaire
C. Jenkinson, R. Fitzpatrick, V. Peto, R. Greenhall, and N. Hyman, "The Parkinson's disease questionnaire (PDQ-39): development and validation of a Parkinson's disease summary index score," Age and Ageing, vol. 26, no. 5, pp. 353–357, 1997.

Parkinson's Disease Sleep Scale
Chaudhuri KR, Pal S, DiMarco A, et al. The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. J Neurol Neurosurg Psychiatry. 2002;73(6): 629–635.

Modified Fatigue Impact Scale
Fisk, John D., et al. "Measuring the functional impact of fatigue: initial validation of the fatigue impact scale." Clinical Infectious Diseases 18.Supplement 1 (1994): S79-S83.

Frontal Systems Behavior Scale
Malloy, Paul, et al. "The Frontal Systems Behavior Scale discriminates frontotemporal dementia from Alzheimer's disease." Alzheimer's and Dementia 3.3 (2007): 200-203.

Informant Questionnaire on Cognitive Decline in the Elderly
A. F. Jorm and P. A. Jacomb (1989). The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. Psychological Medicine, 19, pp 1015-1022.

Activities of Daily Living

Lawton, M.P., &Brody, E.M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. The Gerontologist , 9 (3), 179-186.

Caregiver Burden Scale
Elmstahl, S., Malmberg, B., &Annerstedt, L. (1996). Caregiver's burden of patients 3 years after stroke assessed by a novel caregiver burden scale. Archives of physical medicine and rehabilitation, 77(2), 177-182.

Short Form-12 Health Survey
Gandek, Barbara, et al. "Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment." Journal of clinical epidemiology 51.11 (1998).

The WHOQOL Group, Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med, 1998. 28(3)(3): p. 551-8.

Neuropsychiatric Inventory 12-Item version (NPI-Q)
Kaufer, D.I., J.L. Cummings, P. Ketchel, V. Smith, A. MacMillan, T. Shelley, O.L. Lopez, and S.T. DeKosky, Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. J Neuropsychiatry Clin Neurosci, 2000. 12(2): p. 233-9.

14-item Modified Falls Efficacy Scale (MFES)
Hill, K. D., Schwarz, J. A., Kalogeropoulos, A. J., & Gibson, S. J. (1996). Fear of falling revisited. Archives of physical medicine and rehabilitation, 77(10), 1025-1029.

Section 9.11 Pictures and Audio/Video Recordings of Patients

9.11) Describe the purpose of photographs (facial), or audio, or video recordings of patients. Describe whether the recordings will contain, or potentially contain, identifiers. ***Note: use of photographs or recordings must be covered in the informed consent process and documented consent documents (e.g., consent form, information sheets, telephone screen scripts).***

We will follow accepted standards for establishing and assessing treatment integrity and fidelity. This includes: a) treatment manual with weekly objectives, outcomes, and agendas, b) clinician training, and c) ongoing evaluation of treatment integrity through audio-rating of therapy sessions and supervision and weekly participant and clinician evaluations. All group sessions will be audio-recorded and available for rating. Supervisors (Drs. Schiehser and Twamley) will review all of the audio recordings for the first CogSMART-PD group and then will randomly select 10% of sessions thereafter for review. The supervisors will provide corrective feedback to the clinician, if needed. Audio recordings will be destroyed at the end of the study, and participants may refuse to be audio-recorded. Audio recordings transferred into a computer system will be assigned group numbers and will not be individually identifiable. The key that relates the group numbers to the individuals will be stored separately, protected by strong passwords, and accessible only by approved study personnel. On these recordings group members refer to each other by first name only, to ensure that they remain unidentifiable.

Section 9.12 Off Station Activities

9.12) Describe each off-station activity including where it occurs, subject involvement, and any additional required protections. ***Note: if the off-station activity is being conducted under the approval authority of another institution, this is not VA offsite research and should be described as collaborative research effort. Please contact the HRPP office if you have any questions***

Phase I:
100 participants will be scanned at the UCSD Keck Center for fMRI.

Participants who consent to do so will participate in a home evaluation conducted within their home. One form which assess the home environment will be used for this assessment (please see appended form). All data collected during the home visits will only be identified by a subject ID number that is assigned during the consent process.

Phase II:
Up to 60 individuals may be scanned at the UCSD Keck Center for fMRI.
De-identified data from Motor Skills Assessments will be analyzed by collaborators in UC San Diego's Smart Lab, located in Atkinson Hall, 5202. No participant data will be collected at the Smart Lab.

De-identified saliva samples will be stored and analyzed by the UCSD Integrative Health and Mind-Body Biomarker Laboratory, located at the Medical Teaching Facility, Room 431. Samples are destroyed after analysis.

Section 10 - Human Subjects

10) Describe the characteristics of the proposed subject population. Include age, gender, ethnicity, and health status as appropriate. ***Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still describe the characteristics related to the subjects whose charts you will review.***

- **Provide inclusion and exclusion criteria as appropriate. Provide a statement how non pregnancy is confirmed if pregnancy is an exclusion criteria.**
- **For multisite studies, provide the total number of subjects from all sites and include description of the local site's role as a coordinating center if applicable.**
- **Indicate the number of VA participants to be studied.**
- **Indicate the estimated number of consented subjects that will fail the screening process, if any.**

Phase I:
Approximately 240 subjects in total will be recruited for this study: 20 PD patients to participate in CogSMART only (no imaging), up to 100 PD patients to participate in CogSMART and the imaging protocol, and 120 caregivers. The PD patients will range in age from 55-95. No patients under 55 will be imaged.

One hundred twenty individuals who have PD and documented cognitive impairment will be recruited from ongoing studies of neuropsychological functioning in PD (PI Filoteo). Over-recruitment by 10% will also be instituted to account for subject attrition or unusable data and to ensure a final sample size of 20 participants (10 per treatment and 10 per wait list group) for Aims 1 and 2 and up to 100 participants for the Exploratory Aim. All PD participants will be screened and excluded if they have a history of significant head trauma, other neurologic or major psychiatric disorders, history of developmental learning disorder, substance dependence, or any contraindication to participating in the cognitive treatment. PD patients must be medically/clinically stable in order to be included in this study. The participant's Parkinson's disease diagnosis will be confirmed by the participating neurologists, and cognitive impairment (i.e., MCI or dementia) will be confirmed via neuropsychological testing and the consensus of the neuropsychologist investigators (Drs. Schiehser and Filoteo). We will also recruit any identified and consistent caregivers (e.g., spouse, friend, relative) of the participants to complete several questionnaires regarding the participant's quality of life and daily functioning prior to and following (immediately, 3- and 9-months) the intervention. All caregivers will be asked to participate if they do not have any known memory impairment, dementia, or another condition which would prevent them from accurately completing the questionnaires.

PD participants may gain cognitive improvement and/or a delay in cognitive decline over time resultant from participating in this study with the additional scientific benefit of understanding the kinds of non-pharmacologic interventions that may aid cognition in PD with cognitive impairment and/or dementia. Study participants will be provided with a CogSMART manual. Those individuals in the wait-list control group will be offered the cognitive treatment at the completion of the intervention period if they are interested. There will not be any direct benefit to the caregivers, however, the investigator and associates may learn more about how participation in a cognitive skills training course impacts the function and quality of life of individuals with Parkinson's disease. Additionally, we may learn if caregivers of individuals with Parkinson's disease may benefit indirectly (e.g., improvement in caregiver's quality of life) from the group participant's (e.g., spouse, relative, friend's) participation in the intervention.

Inclusion of Women and Minorities: No exclusions will be made based on gender, race or ethnic background. Gender and ethnic composition of the samples will reflect that of the population of eligible patients presenting from the recruitment sources.

Phase II:
We will recruit 110 individuals with Parkinson's disease (PD) and Mild Cognitive Impairment (PD-MCI) primarily from the VA San Diego Healthcare System (VASDHS) Neurology and Neuropsychology Clinics, as well as 110 identified and consistent caregivers (e.g., spouse, friend, relative) of the participants to complete several questionnaires regarding the participant's quality of life and daily functioning prior to the intervention, during follow-up visits, and after the intervention. However, as recruitment of women may be limited at the VA, we may need to recruit women outside of the VA to obtain a PD-epidemiologically accurate gender ratio of 60 (men)/40 (women). We will plan to recruit from the University of California,

San Diego (UCSD) Movement Disorders Center as well as from additional sites (e.g., PD Association of San Diego, San Diego hospitals, private clinics, and the community). Participants will be included who are > 40 years of age, as < 40 years of age may represent a different form of PD. Participants will generally fall within the age range of 60-80 due to the prevalence of PD in these groups; however, no upper age limit or gender restrictions will be applied for this study.

Inclusion criteria: (1) Clinical diagnosis of PD based on the UK Brain Bank Criteria59 (2) Clinical diagnosis of MCI based on formal criteria set forth by the Movement Disorders Society (MDS) Task Force5, and 3) >40 years of age (due to likelihood that individuals <40 may represent a different form of PD than idiopathic PD). The PD diagnosis will be confirmed by one of the VASDHS/UCSD neurologists. The MCI diagnosis will be confirmed by a licensed clinical neuropsychologist (Drs. Schiehser or Filoteo). Level II MDS Task Force criteria is as follows: (1) cognitive decline reported by the patient or caregiver or observed by a clinician, (2) cognitive deficits not severe enough to significantly interfere with functional independence, and (3) cognitive deficits on formal neuropsychological testing including two tests for each of five domains: Attention, Language, Memory, Executive Function, and Visuospatial Ability5. As per MDS criteria, cognitive deficits will be determined by impairment (i.e., 1.5 standard deviations below appropriate norms) on either two tests in one cognitive domain or on one test in two different cognitive domains.
Exclusion criteria: (1) Secondary causes of Parkinsonism (e.g., corticobasal degeneration, progressive supranuclear palsy, multiple systems atrophy, drug-induced parkinsonism, etc.); (2) other neurological conditions (e.g., stroke); (3) normal or dementia diagnosis via neuropsychological testing and based on the MDS criteria for PD dementia; (4) psychosis, antipsychotic treatment or treatment for substance abuse; (5) untreated current major depression disorder or anxiety disorder; (6) uncorrected vision or hearing to adequately read the manual and hear intervention facilitator; and (7) reading level below an eighth grade level determined by a standardized reading test (Wide Range Achievement Test 4 - Reading [WRAT-4]60), as the intervention involves reading. In order not to overly restrict our sample and as almost all PD patients will be on some form of dopaminergic replacement therapy and various other medications for cognitive and mood symptoms (e.g., SSRIs), we will not exclude patients based on medications. However, we will ensure that participants are stabilized on medications by recruiting those patients who have not had any major changes in medications (i.e., PD medication regimen or antidepressant dosages) within 30 days of baseline testing and not including data in our analyses from any patient who had medication changes during the course of the treatment. We recognize that certain medications can worsen cognition, such as anticholinergic agents, amantadine, dopamine agonists and benzodiazepines61. Therefore, we will carefully document all medication types and dosages at each testing session and control for these in statistical analyses as needed. It is also recognized that medication changes may occur during and after the intervention. We will diligently record this changes and account for them in the analyses accordingly (e.g., as covariates).

There will not be any direct benefit to the caregivers, however, the investigator and associates may learn more about how participation in a cognitive skills training course impacts the function and quality of life of individuals with Parkinson's disease. Additionally, we may learn if caregivers of individuals with Parkinson's disease may benefit indirectly (e.g., improvement in caregiver's quality of life) from the group participant's (e.g., spouse, relative, friend's) participation in the intervention.

We expect no subjects once consented to fail the screening process.

Section 10.1 Non-Veteran Subjects

10.1a) Recruitment of non-Veterans cannot be for the sake of convenience for this study. Provide the objective and justification for the inclusion of non-Veteran subjects. Identify how the research results will be generalizable to the Veteran population. Identify the approximate number of non-Veterans who will be enrolled.

Phase I:

Most participants will be recruited from ongoing studies of neuropsychological functioning in PD (PI Filoteo) which recruits both veteran and non-veteran participants.

In addition to recruiting patients within the VASDHS, subjects will also be referred to us through clinics at UCSD because the number of patients at the VASDHS is not sufficient alone to meet our enrollment requirement. Currently there are over 350 PD patients being followed clinically in the Neurology Service at the VASDHS and the UCSD Movement Disorders Clinics. VA neurologists follow approximately 150 PD patients at the VASDHS and, approximately 200 patients at UCSD. Roughly two-thirds of their new patient evaluations are for PD patients at varying stages of the disease. For both the VASDHS and UCSD clinics, about 40% of the patients currently being followed would likely meet the inclusion criteria for the proposed project, which would result in about 140 patients being eligible for the study, of those 140 about 50% will have the necessary availability and schedule that can allow them to come to the VA weekly for

12 weeks and undergo two fMRIs. There is also a 5%-10% exclusion for participants unwilling and/or unable to undergo MRIs for various reasons (claustrophobia, metal in eyes/head, physicals restrictions). Thus, in total, there are roughly 60-70 potential patients being followed continuously by the Movement Disorder specialists at the VA and UCSD (note this figure does not take into account potential new patient evaluations that will occur during the first year of recruitment).

PD patients will be referred from outside of the VA to meet enrollment criteria within the study period. It is often the case that PD patients within the VA have multiple other risk factors associated with cognitive decline including histories of substance abuse, head injury, and psychiatric conditions that would preclude them from participating in our study. They also fMRI limiting factors, such as shrapnel in their bodies that exclude them from participation in fMRI. Thus, additional non-veteran subjects from UCSD will be studied as needed.

Caregiver participation is necessary to measure the Parkinson's disease participant's quality of life. The caregivers enrolled in the study may be non-Veterans.

Phase II:

We will primarily recruit Veterans with PD from the VASDHS Neurology and Neuropsychology Clinics. While we will attempt to exhaust recruitment at VA clinics first, recruitment of women may be limited at the VA, and therefore, we will receive referrals from outside clinics to obtain an epidemiologically accurate gender ratio of 60 (men)/40 (women). In this regard, we will primarily recruit from the University of California, San Diego (UCSD) Movement Disorders Center. The VASDHS/UCSD neurologists follow approximately 600 PD patients in the VASDHS clinics and approximately 600 PD patients within the UCSD Movement Disorders Clinic. Should it be necessary, we will recruit outside of the VA and UCSD, including recruiting from the Parkinson's Association, San Diego area hospitals and clinics (e.g., Scripps and Sharp Healthcare Systems) who serve PD patients, private practices, and the community. It is estimated that there are 16,000-19,000 individuals living with PD in the San Diego area, of whom half are members of PASD. Our study team has ample experience recruiting from the community, including the use of flyers, tables at community-based events (e.g., PD Walks), and participation in PD-associated speaking engagements. San Diego contains a tight-knit community of professionals who work together to better serve individuals with PD and numerous people have expressed their support of this study.

10.1b) Non-Veterans must be given a copy of the VA Notice of Privacy Practices (NOPP) and sign the acknowledgement form. The Privacy Officer must be notified when a non-Veteran is enrolled in the study and be provided with a copy of the signed NOPP. If CPRS notes are entered, and the acknowledgement must also be scanned into CPRS. ***The NOPP, Acknowledgement form, and instructions to provide the completed form to the PO are available under the ? at the top right corner of this page.***

(•) Agree ( ) Disagree

Section 10.5 Individuals with Cognitive/Decisional Impairment

10.5) Provide the rationale and additional study procedures that will be required for including individuals with known cognitive impairment or institutionalized individuals. ***Address Decisional Capacity Assessment and Surrogate Consent Sections 12.6 and 12.7.***

Phase I:

If participant lacks capacity to complete neuropsychological assessments, they will be thanked for their time and excused from the research study.

Phase II:

If a subject meets criteria for our study and is interested in participating, an appointment will be made to enroll the individuals in the study. Informed consent will be obtained at the time of visit. When the subject arrives for the appointment, a verbal explanation of the protocol will be given by the Principal Investigator or a member of the research team. A post-consent quiz will also be administered to ensure adequate understanding of the key elements of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and

excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent.

Similarly, for individuals participating in the adjunct programs, informed consent will be obtained at the time of visit. When the subject arrives for the appointment, a verbal explanation of the adjunct programs will be given by the Principal Investigator or a member of the research team. A post-consent quiz will also be administered to ensure adequate understanding of the key elements of this portion of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent.

Section 11 - Recruitment

11) Describe, step-by-step, the plans for recruitment of subjects (or selection of subjects as in record review). This description must include how, when, and where potential subjects are approached as well as procedures for identifying potential participants (through medical records, physician referral, third-party sources, etc.). Include how selection is equitable. Indicate if vulnerability to coercion may be present and if so plans to ensure voluntary participation.

Phase I:

At the time of their clinical or research visit in which they are identified as having PD with cognitive impairment and/or dementia, participants meeting inclusion criteria for this study will be approached about their interest in participating in the study. Potential participants will be informed of the study via a flyer (appended) and, if requested, study coordinators (e.g., Dawn Schiehser, Ph.D. or any co-investigator affiliated with the study) will contact the individual to explain the study procedures and answer any questions the potential participant may have.

We will also recruit patients by placing announcements in local newsletters sent out by various Parkinson's disease support groups (e.g., the Parkinson's Disease Association of San Diego) and advertisements in the local media calling for potential research participants. The same wording as in the handout will be used for these announcements, except the phrase "You have been given this handout because you may be interested in participating in this study" will be removed.

Approximately 60 PD patients (30 patients assigned to the intervention group and 30 patients assigned to the waitlist group)who meet the inclusion criteria to participate in the study will be asked if they would like to participate in the imaging protocol. Should they decline, they will participate in the non-imaging component of the study.

Each participant will be asked if they have an identified consistent caregiver (e.g., spouse) who would like to participate in the study. If they answer in the affirmative, the caregiver will be contacted and informed of the study. If they agree to participate, the caregiver will be consented and asked to complete several questionnaires related to their assessment of the patient's functioning at the time of the participants baseline assessment and again immediately following the intervention, and at 3- and 9-months post-intervention. The caregivers participants will be invited to attend the CogSMART class solely as observers.

Phase II:

Potential subjects may be referred from the VASDHS Neurology clinics of (or UCSD if needed). If the VASDHS neurologists feel that the patient is appropriate for the study, they will inform the patient about the study and provide a handout that briefly describes the study as well as appropriate contact numbers where the potential subject can call to obtain more information about the study. Potential subjects may also be referred from the Neuropsychology, Neurology, and/or other relevant clinics (such as Occupational Therapy or Physical Therapy) at VASDHS. If the patient is interested and willing, the treating provider will have the patient sign a Research Candidate Form on which they will provide a contact number. Alternatively, if the patient is interested and willing, the clinician will contact research study staff, who if available, will meet with the patient at the clinic to describe the study. In addition, the clinician will inform the research team of a potential research participant if they give verbal consent to the clinician to do so. In turn, the research team will send a letter to the patient informing them that study staff will be contacting them about the research study. If needed, we will recruit through other organizations (Parkinson's Association, community) by use of flyers, brochures, and attendance at community events.

Potential subjects may also be recruited by a search of ICD codes for Parkinson's disease and/or cognitive impairment in CPRS. Any patients not previously referred to our study from VASDHS clinics aforementioned, who may be eligible for the study, will be notified via the uploaded Recruitment Letter that a research assistant on this protocol will be contacting them approximately 2 weeks from the day the

letter is sent. A research assistant will then call the patient to explain the study and gauge interest in participating. If the patient indicates that they are not interested, the research assistant will thank them for their time and will not contact them again regarding the study. Similarly, potential subjects may be recruited from co-investigators' research studies previously completed (e.g., Dr. Filoteo's research study). If a research participant who is potentially eligible for our study indicated in the previously completed research study that they would like to be contacted for future research opportunities, he or she will be informed of our research opportunities via the uploaded Previously Enrolled Subject Letter. A research assistant will then call the potential subject to explain the study and gauge interest in participating. If the patient indicates that they are not interested, the research assistant will thank them for their time and will not contact them again regarding the study.

If the individual continues to show an interest in participating, he or she will be informed that they will need to be asked a series of screening questions related to their medical and psychiatric history. The potential subject will be informed that the information will be used solely to determine their potential eligibility for our study. They will be told that, if they agree to answer the questions, their information will be kept under lock and key in our laboratory and will not be available to any other individual outside of our research group.

If a subject meets criteria for our study and is interested in participating, an appointment will be made to enroll the individuals in the study. Informed consent will be obtained at the time of visit. When the subject arrives for the appointment, a verbal explanation of the protocol will be given by the Principal Investigator or a member of the research team. A post-consent quiz will also be administered to ensure adequate understanding of the key elements of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent. A copy of the signed consent form and the Experimental Subject's Bill of Rights is always provided to the subject. Participants will also provide written informed consent (HIPAA authorization) for their medical records to be viewed.

Section 11.1 Recruitment Materials

11.1) Identify all recruitment materials (flyers, advertisements, letters, etc.) that will be used; include the web address for any web-based advertisements. The text of all communications with prospective participants must be reviewed and approved by the IRB before it can be used. You will be reminded to attach copies of recruitment materials to the initial submission packet.
Note: Posting of flyers with pull tabs is not permitted within VASDHS (including the VMRF building).

Phase I:

We will also recruit patients by placing announcements in local newsletters sent out by various Parkinson's disease support groups (e.g., the Parkinson's Disease Association of San Diego) and advertisements in the local media calling for potential research participants. The same wording as in the handout will be used for these announcements, except the phrase "You have been given this handout because you may be interested in participating in this study" will be removed.

Phase II:

We will also recruit patients by placing announcements in local newsletters sent out by various Parkinson's disease support groups (e.g., the Parkinson's Association) and advertisements in the local media calling for potential research participants. The same wording as in the handout will be used for these announcements, except the phrase "You have been given this handout because you may be interested in participating in this study" will be removed.

Patients will also be recruited from other studies completed if they had indicated they would like to be contacted for future research opportunities. Patients may be made aware of this research opportunity via the uploaded Previously Enrolled Subject Letter, and will be called after the letter has been sent as outlined in the letter (~2 weeks after the letter is sent).

Section 12 - Informed Consent

12) Indicate whether or not each category of consent is involved in this study:

12a) Will the study team obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without (or prior to) obtaining informed consent of the prospective subject or the prospective subject's LAR?

○ Yes ◉ No

12b) **Signed** informed consent

◉ Yes ○ No

12c) Waiver of documented consent (e.g., **oral** consent) for all or part of the study.

◉ Yes ○ No

12d) Request for a **waiver** of consent for all or some study activities.

○ Yes ◉ No

12e) Alteration of **other required elements** of consent.

○ Yes ◉ No

12f) **Child** assent to participate (Director approval will be required)

○ Yes ◉ No

12g) Will any language **other than English** be used by those obtaining consent and understood by the prospective participant or the legally authorized representative?

○ Yes ◉ No

12h) **Decisional Capacity Assessment** to determine if participants have the capacity to consent for themselves.

◉ Yes ○ No

12i) **Surrogate** consent (legally authorized representative)

◉ Yes ○ No

Section 12.1 Informed Consent Process

12.1a) Will consent be obtained before any study procedures are performed (including screening procedures except screening procedures with Consent/HIPAA waiver approval)?

◉ Yes ○ No

12.1b) Will the information being communicated to the participant or legally authorized representative during the consent process include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the VA or its agents from liability for negligence.

○ Yes ◉ No

12.1c) A master list of all VA subjects consented (written or not) under this protocol will be maintained.

◉ Agree ○ Disagree

12.1d) Identify the circumstances under which consent will be obtained including where the process will take place; any waiting period between describing the research and obtaining consent including sufficient time for the prospective participant to consider participation, and any steps taken to minimize the possibility of coercion or undue influence.

Phase I:

Informed consent will be obtained at initial visit. When the participant arrives for the appointment, Dr. Schiehser or a senior research assistant will discuss the consent form and administer a post-consent questionnaire to determine capacity to sign the consent form. If the participant performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the participant is unable to demonstrate capacity to sign the consent form, the procedure for surrogate consent and decisional capacity will be enacted. If surrogate consent cannot be provided in this situation, the subject will no longer be included in the study. Copies of the Informed Consent and Informed Consent Exit Questionnaire (Evaluation of Decision-Making Capacity) forms have been attached.

The informed consent procedure will adhere to the HIPAA Privacy Rule and all subjects will be given a VA-specific HIPAA authorization form.

Phase II:

Informed consent will be obtained at the time of initial visit. When the subject arrives for the appointment, a verbal explanation of the protocol will be given by the Principal Investigator or a member of the research team. A post-consent quiz will also be administered to ensure adequate understanding of the key elements of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Copies of the Informed Consent and Informed Consent Exit Questionnaire (Evaluation of Decision-Making Capacity) forms have been attached.

Similarly, for individuals participating in the adjunct programs, informed consent will be obtained at the time of visit. When the subject arrives for the appointment, a verbal explanation of the adjunct programs will be given by the Principal Investigator or a member of the research team. A post-consent quiz will also be administered to ensure adequate understanding of the key elements of this portion of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent.

The informed consent procedure will adhere to the HIPAA Privacy Rule and all subjects will be given a VA-specific HIPAA authorization form.

Section 12.3 Waiver of Documented Consent

12.3a) Select one of the following situations permitting waiver of documented consent:

12.3a1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. *Note: This criterion cannot be used for FDA-regulated studies.*

○ Yes ◉ No

12.3a2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

◉ Yes ○ No

12.3b) Is a waiver of the requirement to enter the consented subjects' names on a master list requested and appropriate in order to protect the subject's privacy and the confidentiality of the data?

○ Yes ◉ No

Section 12.6 Decisional Capacity Assessment

12.6a) Describe the method(s) for determination of decisional capacity: (see ? for guidance) ***Please note that documentation of the assessement is required.***

Phase I:

Identifying Persons to Provide Surrogate Consent
In a nonemergency room research environment, surrogate consent will be obtained from any of the following potential surrogates who has reasonable knowledge of the subject, in the following descending order of priority:
1. The person's agent designated by an advance health care directive
2. The conservator or guardian of the person having the authority to make health care decisions for the person
3. The spouse of the person
4. The domestic partner of the person as defined in Section 297 of the Family Code
5. An adult son or daughter of the person
6. A custodial parent of the person
7. Any adult brother or sister of the person
8. Any adult grandchild of the person
9. An available adult relative with the closest degree of kinship to the person
In a nonemergency room research environment, no surrogate consent will be utilized if there is a disagreement whether to consent among the members of the highest available priority class of surrogates (e.g., where two members of persons in the highest of categories, 5-7, disagree and there is no person in categories 1-4 available).
In a nonemergency room research setting, the Investigator or designee will be responsible for ensuring that the surrogate
• Has reasonable knowledge of the subject;
• Is familiar with the subject's degree of impairment;
• Is willing to serve as the substitute decision maker;
• Understands the risks, potential benefits, procedures and available alternatives to research participation; and
• Makes his or her decisions based on the subject's known preferences, and where the subject's preferences are unknown, makes decisions based on the surrogate's judgment of what the subject's preferences would be if different from his or her own.

Phase II:

A post-consent quiz will also be administered to ensure adequate understanding of the key elements of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent. A copy of the post-consent questionnaire is attached.

Similarly, for individuals participating in the adjunct programs, a post-consent quiz will be administered to ensure adequate understanding of the key elements of this portion of the study. If the subject performs adequately on the post-consent questionnaire, they will be asked to sign the consent form. If the subject is unable to demonstrate capacity to sign the consent form, they will be thanked for being a possible subject in the study and excused from the rest of testing. Given that we will be recruiting nondemented PD patients, it is not anticipated that any patients will be unable to consent.

12.6b) If subjects with limited decisional capacity will be enrolled, describe methods for obtaining subject assent or why they are not indicated:

Obtaining Consent from the Surrogate
1. The Investigator or designee will describe to potential surrogates the nature of ongoing decisions during the study regarding the subject's participation, decision to participate in certain procedures, changes to the study, etc., in order to ensure that the surrogate will be willing to undertake these on-going responsibilities.
2. The surrogate will complete the "Self-Certification of Surrogate Decision Makers for Participation in Research" form as an attachment to the informed consent document for the research study, and keep the signed form along with a copy of the consent. In addition, the Investigator will keep a copy of this form in the research records along with the signed consent. The "Self-Certification of Surrogate Decision Makers for Participation in Research" form will verify the willingness of the person to serve as a surrogate, and detail the relationship of the surrogate to the subject and the surrogate's qualifications demonstrating "reasonable knowledge" of the research subject.
3. Potential surrogates will be advised that if a higher-ranking surrogate is identified at any time, the Investigator will defer to the higher-ranking surrogate's decision regarding the subject's participation in the research.
4. For nonemergency room environment research only, if the potential surrogate identifies persons of a higher degree of surrogacy, the Investigator or designee will be responsible for contacting such individuals

to determine if they want to serve as surrogate.
5. Surrogates will be prohibited from receiving any financial compensation for providing consent. This will not prohibit the surrogate from being reimbursed for expenses that he or she may incur related to the participation in the research.
6. Assessment of the decision-making capacity of the surrogate will be implemented only when the Investigator or designee has reason to believe that the surrogate's decision-making capacity may be impaired.
Reconsenting of Research Subjects
Consenting will be an ongoing process. All applicable criteria that would trigger reconsenting a subject in any study will apply to subjects whose consent has been provided by a surrogate. In addition:
• A subject who regains the cognitive ability to consent must be reconsented using standard consenting procedures.
• In the event a subject has been initially consented by a surrogate, and a surrogate of higher priority subsequently notifies the Investigator of that relationship to the subject, the Investigator will defer to the higher-priority surrogate's decision regarding whether the subject will continue to participate or will withdraw from the study.
• The Investigator or designee will describe to potential surrogates the nature of ongoing decisions during the study regarding the subject's participation, decision to participate in certain procedures, changes to the study, etc., in order to ensure that the surrogate is willing to undertake these ongoing responsibilities. In the event that the surrogate dies, the subject will be reconsented subsequently upon any event that would otherwise trigger re-consenting the subject.

Phase II:

Subjects with limited decisional capacity will not be enrolled in phase II of the study.

12.6c) If subjects with limited decisional capacity will be enrolled, describe procedures for respecting subject dissent and any additional safeguards or why these features are not needed:

Phase I:

If the subject expresses resistance or dissent to participation or to the use of surrogate consent by word or gesture, the subject will be excluded from the research study.
· If no resistance or dissent is expressed by the potential research subject, the Investigator or designee will document this fact, and document that the description of the research project was communicated to the subject by placing a note in the medical record and in the research record.
· Proceed with the steps listed above under Identifying Persons to Provide Surrogate Consent

12.6d) If subjects with limited decisional capacity will be enrolled, describe the risk and, if greater than minimal, the relation to potential benefits:

Phase I:

The primary risks in participating in this study are fatigue, test anxiety, and breach of confidentiality. As noted above, there are specific plans in place to lessen the likelihood of any of these potential risks. In contrast, the benefits of the study are much greater in that we could gain a better method of predicting future cognitive impairment in patients with PD. This knowledge has the potential to help patients, family members, and the patients' physicians better prepare for and potentially treat the onset of any cognitive deficits observed as the disease progresses. As such, the risk to benefit ratio is low.

Given that the primary risk to patients is that although there will be no direct benefit to participants for taking part in this study, we have found patients more than willing to participate in our previous studies. The study involves minimal risk and most participants are eager to contribute to an understanding of the cognitive effects of PD.

12.6e) If subjects with limited decisional capacity will be enrolled, describe the justification for the inclusion of any incompetent persons or persons with impaired decision-making capacity:

Phase I:

The primary aim of this study is to examine cognitive deficits in patients with PD and compare the pattern of their deficits with other patient populations who also have cognitive impairment, including patients with Dementia with Lewy Bodies and Alzheimer's Disease, so by its very nature the study will include participants who might have impaired decision-making capacity.

Section 12.7 Consent by Legally Authorized Representative (Surrogate Consent)

12.7a) Where endorsed by the IRB, the following persons may be authorized to consent on behalf of persons who lack decision-making capacity in the indicated order of priority: (a) Health care agent (i.e., an individual named by the individual in a Durable Power of Attorney for Health Care (38 CFR.17.32(a)(iii)); (b) Legal guardian or special guardian; (c) Next of kin in this order: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; (d) A close friend [however, California Health and Safety Code §24178 does NOT include the close friend category]

(●) Agree ( ) Disagree

12.7b) Legally Authorized Representatives (LARs) will be told that their obligation is to try to determine what the subjects would do if able to make an informed decision. If the potential subject's wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects' best interests. LARs generally assume the same rights and responsibilities as the individuals who lack decision-making capacity in the informed consent process.

(●) Agree ( ) Disagree

12.7c) If feasible, the investigator will explain the proposed research to the prospective research subject even when the surrogate gives consent. Although unable to provide informed consent, some persons may resist participating in a research (i.e., if they dissent) protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

(●) Agree ( ) Disagree

12.7d) For subjects with fluctuating decision-making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent will be employed when needed

(●) Agree ( ) Disagree

Section 12.9 HIPAA Authorization

For each category below, indicate whether or not this study involves the indicated process:

12.9a) **Signed** HIPAA Authorization. ***New Template is available in the ? Help section***

(●) Yes ( ) No

12.9b) HIPAA waiver to cover the entire study

( ) Yes (●) No

12.9c) HIPAA waiver for recruitment, screening, and/or for a portion of the study.

(●) Yes ( ) No

12.9d) HIPAA Authorization or waiver is **not required** for some or all of the study subjects (e.g. no health data).

( ) Yes (●) No

Section 12.10 HIPAA Waivers and Alterations

12.10a) Describe the purpose/nature of the HIPAA waiver or alteration and list specifically, what identifiers and health information are being requested under the waiver/alteration and identify whether the waiver is for access, use, and/or collection of this information.

1) The waiver will be used to conduct a brief phone screen on potential patients referred to the study from

outside the VASDHS as referenced in section 10.1. The phone screen will be used to determine eligibility for the study so that potential participants do not waste time traveling to the VASDHS. The data that will be collected under the waiver will include Name, address, phone number, veteran status, neurological diagnosis (if any), and the following 15 questions:

1. Are you 40 years of age or older?
2. Is English your first language?
3. Do you have any other neurological diagnosis besides PD?
4. Do you have any other neurological condition, such as stroke or traumatic brain injury?
5. Have you had DBS (deep brain stimulation) surgery? Other brain surgeries, or planned surgeries?
6. Do you have a history of memory problems, or have you been diagnosed with dementia?
7. Do you have any history of psychosis?
8. Do you have any other psychiatric history (e.g. PTSD, Bipolar Disorder, Schizophrenia, etc.)?
9. Do you have any history of major depression or anxiety (Past or current Dx)?
10. Are you currently taking any antidepressant or antipsychotic medications?
11.Have you ever been treated for substance abuse?
12. Have you ever had an acute medical crisis (major accidents, illnesses, etc.)?
13. Do you have any vision, hearing, or movement problems that could interfere with taking tests, reading, or interacting in a group setting?
14. Have you had any major changes in medications within the last month, or any anticipated within the next month?
15. Do you have a primary caregiver, spouse, relative, or close friend who would be able to answer questions about how you've been doing?

2) The waiver will also be used to recruit potential study participants through the Neuropsychology, Neurology, and other relevant clinics at VASDHS. Patients who may be interested will be asked to sign a Research Candidate Form by their provider, and a research assistant will contact them if they indicate on the form that they agree to be contacted. Additionally, the provider may inform the research team of a potential study participant. At that point, a research assistant will either go speak to the patient in person about the study if the patient expresses interest in meeting with study staff, or will send the patient a letter (uploaded in protocol documents) stating that we will be calling them about a research opportunity.
2b) The Research Candidate form asks for the patient's name, provider name, appointment day/time, and telephone number (if they indicate they would like to be contacted). Sending a letter will require patient's name, mailing address, and telephone number to later be contacted.
2c) Sending the letter and making a follow-up phone call will require the patient's name, mailing address, and telephone number.

3) The waiver will also be used to reach potential study participants through CPRS (using the ICD codes for Parkinson's disease and cognitive impairment). For any patients who may be eligible, who were not previously referred to the research team by the clinician and did not sign a Research Candidate Form, will be sent a letter informing the patient that we will be calling them about a research opportunity. Sending a letter will require patient's name, mailing address, and telephone number to be contacted in the future.
3b) Recruiting by ICD code search requires knowing the patient's medical diagnoses (of Parkinson's disease and mild cognitive impairment). Sending the letter and making a follow-up phone call will require the patient's name, mailing address, and telephone number.

4) Finally, the waiver will also be used to reach potential study participants through previously completed research studies, if they had agreed to be contacted for future research opportunities. Any patients who may be eligible will be sent the uploaded Previously Enrolled Subject Letter informing them of our new research opportunities, and letting them know that we will call to discuss these opportunities further with them. Sending this letter will require the patient's name, mailing address, and telephone number to be contacted in the future.

12.10b) The proposed access, use, and/or disclosure of PHI involves no more than a minimal risk to the privacy of individuals.

(•) Agree ( ) Disagree

12.10c) The plan to protect the identifiers from improper use and disclosure is adequate.

(•) Agree ( ) Disagree

Describe the plan

A Privacy and Security Data Plan has been constructed to ensure confidentiality of all Sensitive Information (SI) and is outlined as follows:
1. This study will collect VA Sensitive Information (SI) (i.e., data, in any format, which requires protection

due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration or destruction) from all participating subjects. SI used in this study will include individually identifiable medical and health data and personal information, such as age, educational level, gender and ethnicity.
2. SI, such as subjects' medical diagnoses, will be used for the purpose of enrollment and subjects' personal information, such as age, gender, and education, will be used to characterize the subject pool utilized in this study. Addresses and telephone numbers will also be collected as a means to contact the subjects for follow-up when indicated. All data used in this study will be de-identified and linked to SI by a subject number.
3. SI will be used by approved study personnel only.
4. In the event of a real or suspected breach of security, the VA Police, the VA Information Security Officer, and the VA Privacy Officer will be notified.
5. Study records entered into a computer system will be assigned code numbers and will not be individually identifiable. The key that relates the code numbers to the individuals will be will be stored in a stand-alone (non-networked) computer system that is maintained in a locked office within the PI's lab space in Building #13 of the VA San Diego, protected by strong passwords, and accessible only by approved study personnel. This system will not leave the protected VA environment unless the data storage components are removed or destroyed. Hardcopy SI will also be stored for backup purposes in the PI's laboratory within Building #13 of the VA San Diego, in a locked cabinet. Code-numbered data will be stored in a separate filing cabinet under lock and key in Building #13. Data collected in other areas (testing rooms) will be brought to the lab and locked away each night. Only approved study personnel will have access to this information.

12.10d) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

◉ Agree ○ Disagree

12.10d2) Describe the plan:

SI, such as subjects' medical diagnoses, will be used for the purpose of enrollment and subjects' personal information, such as age, gender, and education, will be used to characterize the subject pool utilized in this study. Addresses and telephone numbers will also be collected as a means to contact the subjects for follow-up when indicated. All data used in this study will be de-identified and linked to SI by a subject number. Hardcopy SI will also be stored for backup purposes in the PI's laboratory, within Building #13 of the VA San Diego, in a locked cabinet. Code-numbered data will be stored in a separate filing cabinet under lock and key in Building #13. We will need to keep this SI to maintain accurate characterization of our subject pool for subjects in follow-up, as medical diagnoses, addresses, and telephone numbers may change over the course of the study.

12.10e) By signing this protocol for submission, the PI is providing written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Rule. 38 U.S.C. 7332 Information: If the waiver of HIPAA authorization is for the use of 38 USC 7332 information (applicable to drug abuse, alcohol abuse, HIV infection, and sickle cell anemia records), by signing this protocol for submission the PI is providing written assurance that the purpose of the data is to conduct scientific research and that no personnel involved may identify, directly or indirectly, any individual patient or subject in any report of such research or otherwise disclose patient or subject identities in any manner. (Ref: 38 U.S.C. 7332(b)(2)(B))

◉ Agree ○ Disagree

12.10f) The research could not practicably be conducted without the waiver or alteration.

◉ Agree ○ Disagree

12.10f2) Describe how the waiver/alteration enables the research to be conducted

Without the phone screen for contact information and brief exclusionary criteria there would be no feasible way for us to send participants directions and appointment confirmation. There would also be potential for many participants to travel to VASDHS to participate in the study, sign a consent form only to find out they are ineligible for the study and be excused. This would waste the time of the participant as well the VASDHS.
The ability to contact VA patients directly will allow us to recruit more veterans to be enrolled in the study. Additionally, the ability to access medical diagnoses consistent with study inclusion criteria will reduce burden on potential study participants as we will not have to schedule additional appointments or

testing to verify diagnoses of these patients. This will also reduce burden on clinicians who may not have time to recruit patients during busy clinic duties and will expand access to these services for Veterans who may not have any upcoming clinic visits in the near future.

12.10g) The research could not practicably be conducted without access to and use of the PHI.

(•) Agree ( ) Disagree

12.10g2) Describe why it would be impracticable to conduct this research without the PHI described 12.10a. (v3/8/18)

1) The phone screen confirms the potential participant knows they have a diagnosis of Parkinson's disease which is a primary requirement of participation in the study.

2) The research candidate form allows research assistants on this protocol to call the patient and recruit them for the study, if interested and eligible. This form provides the means to contact the patient.
2b) The patient's name and mailing address will be required to send the letter before calling patients who were not presented the opportunity to sign the form (this includes subjects previously enrolled in other studies). The patient's phone number will be required to contact the patient after the letter is sent.

3) Accessing medical diagnoses in CPRS allows the research team to focus recruiting attention on those who are likely eligible (i.e., a veteran with Parkinson's disease and cognitive impairment). Additionally, having access to this information reduces participant burden; Veterans will not be scheduled for multiple testing sessions (through research and clinical services) and we will not have to schedule additional appointments or additional testing to verify diagnoses, as they are already listed on file. Furthermore, this will allow us to expand recruitment to Veterans who may not otherwise be reached within targeted clinics at VASDHS.

Section 13 - Alternatives to Participation

13) Describe the alternatives to participation in this research study (see ? for guidance)

Phase I & II:

The alternative to participating is to not participate.

Section 14 - Potential Risks

14) Describe any potential or known risks or discomforts and assess their likelihood and seriousness (see ? for guidance)

Phase I:

The primary safety issues for this study are those related to mental fatigue, boredom and/or anxiety during the intervention or assessment. To ensure the safety and comfort of all subjects, rest breaks are built into CogSMART as well as the neuropsychological assessments. Participants will also be free to discontinue the intervention or testing at any time for any reason or to ask for additional rest breaks or other accommodations to increase tolerability of CogSMART or the paper-and-pencil testing. Home visits will be offered to the participants to increase functional gains, but further inclusion in the CogSMART program 10-week treatment group will not be denied if the participants and/or the caregivers decline this assessment. In general, the study poses no significant increase in risk than what would normally be present in proper clinical management of PD patients. The intervention is offered in a group format and there may be a somewhat greater risk of social discomfort and confidentiality breach than might be present in a non-group format. All group participants, however, will be strictly instructed on the need for confidentiality related to group membership and group proceedings. A tertiary risk might include unintentional disclosure of confidential test information but confidentiality will be strictly maintained in data storage, manipulation, and presentation. Participant identity will be coded immediately upon entry into the study, and neither the participants' names nor any identifying information will be present in the data set. Presentation of the results will involve group data and the subjects' identity will not be disclosed. Given the age and medical condition (i.e., Parkinson's disease) of the participants, it is possible that individuals may experience medical or psychological changes, unrelated to the study that would necessitate early termination of the study. If the individual situation warrants, participants may be able to rejoin a later group. Because this is a psychoeducation group, not a therapy group, there is no expectation that individuals will divulge mental health related information during the 10-week course. However, should any such information arise that causes study staff to be concerned about that participant'

s psychological well being, appropriate referrals to either VA Geropsychiatry or other appropriate community referrals will be made. All intervention group participants will be provided with the class manual and so if there is a need for early termination with no opportunity to join another group, those individuals will still have the psychoeducation materials.

MRI neuroimaging
The primary safety issues for this study are those related to MRI scanning in general. MRI is a noninvasive procedure and overall, risks for MRI scanning are minimal given appropriate screening, which is done via an initial phone interview and again immediately prior to scanning. It is dangerous to be scanned if one has post-surgical metal clips in the body, metal implants, cardiac pacemakers, or any other possible ferrous-based device as outlined in the consent form. No such known cases will be scanned. MRI may not be appropriate under some of these conditions: a cardiac pacemaker; metal fragments in eyes, skin, body; heart valve replacement; brain clips, venous umbrella; history of being a sheet metal worker or welder; aneurysm surgery, intercranial bypass, renal, aortic clips; prosthetic devices such as middle ear, eye, joint or penile implants, joint replacements; hearing aid; neurostimulator; insulin pump; IUD; shunts /stents; metal mesh/coil implants; metal plate/pin/screw/wire, or any other metal implants; permanent eyeliner, eyebrows. The MR imager makes a loud, banging noise while it takes pictures, but earplugs are provided. Sound pressure levels at the center of a head gradient coil were measured to be in the range from 122-131 dB SPL for a 3T scanner during echo planar imaging (Foster et al., 2000).

Participants may experience vertigo, tinnitus, optic phosphemes or fasciculations during movement in the 3T magnetic field. These symptoms are generally mild and transient, as will be explained to participants. Testing will be stopped at any time upon request. A physiological reaction (nerve or muscle stimulation) can occur in some individuals during certain imaging sequences if their position in the scanner forms a circuit (e.g., connected hands). Therefore, participants will be asked not to cross arms or legs and will be visually monitored to confirm this. Dizziness, excessive warmth, visual flashes, dots, scintillations, or tactile sensations due to rapidly switching gradients may also occur. Some patients undergoing this procedure become anxious or claustrophobic. If this happens, the subject can stop the procedure at any time. Subjects may experience some discomfort and fatigue from lying still in a confined space during imaging (total acquisition time for a particular MR imaging session will not exceed one hour for any study participant). Secondary risks include the possibility of an abnormal finding on the MRI exam, however, this MRI scan is not being done for clinical purposes, and is not sufficient for a clinical diagnosis of any brain disorder. We will notify participants and their physician in the event of any abnormal finding. As this is an experimental procedure, there are no alternative treatments, but subjects are free to discontinue participation at any time for any reason.

Sensitive informaiton is not collected at the Keck Center. Patients are only identified by their subject ID number assigned prior to scanning. The VA Consent form is carried to the Keck Center so that the subject can undergo MRI scanning. The VA Consent form is carried back to the VA inside a locked briefcase and stored inside a locked cabinet inside a locked room 1-2304. The consent is not give or any information recorded at the Keck Center, it is mainly utilized to confirm subjects concurrence to undergo the scanning procedure Then, the subject is assigned a code to identify the scanned images.

Wii participation
For those individuals who participate in the Wii adjunct program, there is an increased risk of physical injury, frustration and/or physical fatigue during the sessions. However, the Wii program is a low-exertion physical activity that only involves upper body (arm) movements. For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the Wii activities. Breaks and water will be frequently offered throughout the 30-minute session to prevent physical fatigue, frustration, and/or dehydration.

Phase II:

The primary safety issues for this study are those related to mental fatigue, boredom and/or anxiety during the intervention (CogSMART-PD) or the pre-, post- and follow-up assessments. To ensure the safety and comfort of all subjects, rest breaks are built into CogSMART-PD as well as the neuropsychological assessments. Participants will also be free to discontinue the intervention or testing at any time for any reason or to ask for additional rest breaks or other accommodations to increase tolerability of CogSMART-PD or the paper-and-pencil testing. The UPDRS motor examination may cause participant discomfort due to making motor movements. Prior to the motor exam, study staff will briefly explain what this exam will entail, and subjects may discontinue this exam at any time. The intervention is offered in a group format and there may be a somewhat greater risk of social discomfort and confidentiality breach than might be present in a non-group format. All group participants, however, will be strictly instructed on the need for confidentiality related to group membership and group proceedings. Given the age and medical condition (i.e., Parkinson’s disease) of the participants, it is possible that individuals may experience medical or psychological changes, unrelated to the study that would necessitate early termination of the study. If the individual situation warrants, participants may be able to rejoin a later group. Because this is a cognitive rehabilitation group, not a therapy group, there is no expectation that individuals will share personal and/or mental-health information. However, should any

such information arise that causes study staff to be concerned about that participant's psychological well being, appropriate referrals to the VASDHS Geropsychiatry Clinic or other appropriate community referrals will be made. As individuals with PD are at a high risk for falls, we will carefully screen all individuals for history of falls upon recruitment. We will use the baseline UPDRS falling item (#13) in which a history of falls is categorized on a likert scale from 0 (none) to 4 (falls >once per day). A history of falls as assessed by the UPDRS appears to be one of the best predictive methods of subsequent falls at this time. Those individuals who endorse a history of falling or score >0 on the UPDRS falling item, will be closely monitored. This includes ensuring that they are escorted to and from the intervention room from their vehicle as well as to and from the bathroom, as needed. Should a patient need help within the bathroom, a caregiver will be requested to assist. If needed, we will utilize the VA escort service. Although suicide is an extremely minimal risk factor for PD patients, suicidal ideation/intent will be assessed at baseline. Any indication of suicidal ideation will be brought to licensed and privileged supervisor's immediate attention. All intervention group participants will be provided with the class manual and so if there is a need for early termination with no opportunity to join another group, those individuals will still have the psychoeducation materials. In general, the study poses no significant increase in risk than what would normally be present in proper clinical management and psychological treatment of PD-MCI patients.

A tertiary risk might include unintentional disclosure of confidential test information, but confidentiality will be strictly maintained in data storage, manipulation, and presentation. Participant identity will be coded immediately upon entry into the study, and neither the participants' names nor any identifying information will be present in the data set. Presentation of the results will involve group data and the subjects' identity will not be disclosed.

MRI neuroimaging
The primary safety issues for this study are those related to MRI scanning in general. MRI is a noninvasive procedure and overall, risks for MRI scanning are minimal given appropriate screening, which is done via an initial phone interview and again immediately prior to scanning. It is dangerous to be scanned if one has post-surgical metal clips in the body, metal implants, cardiac pacemakers, or any other possible ferrous-based device as outlined in the consent form. No such known cases will be scanned. MRI may not be appropriate under some of these conditions: a cardiac pacemaker; metal fragments in eyes, skin, body; heart valve replacement; brain clips, venous umbrella; history of being a sheet metal worker or welder; aneurysm surgery, intercranial bypass, renal, aortic clips; prosthetic devices such as middle ear, eye, joint or penile implants, joint replacements; hearing aid; neurostimulator; insulin pump; IUD; shunts /stents; metal mesh/coil implants; metal plate/pin/screw/wire, or any other metal implants; permanent eyeliner, eyebrows. The MR imager makes a loud, banging noise while it takes pictures, but earplugs are provided. Sound pressure levels at the center of a head gradient coil were measured to be in the range from 122-131 dB SPL for a 3T scanner during echo planar imaging (Foster et al., 2000).

Participants may experience vertigo, tinnitus, optic phosphemes or fasciculations during movement in the 3T magnetic field. These symptoms are generally mild and transient, as will be explained to participants. Testing will be stopped at any time upon request. A physiological reaction (nerve or muscle stimulation) can occur in some individuals during certain imaging sequences if their position in the scanner forms a circuit (e.g., connected hands). Therefore, participants will be asked not to cross arms or legs and will be visually monitored to confirm this. Dizziness, excessive warmth, visual flashes, dots, scintillations, or tactile sensations due to rapidly switching gradients may also occur. Some patients undergoing this procedure become anxious or claustrophobic. If this happens, the subject can stop the procedure at any time. Subjects may experience some discomfort and fatigue from lying still in a confined space during imaging (total acquisition time for a particular MR imaging session will not exceed one hour for any study participant). Secondary risks include the possibility of an abnormal finding on the MRI exam, however, this MRI scan is not being done for clinical purposes, and is not sufficient for a clinical diagnosis of any brain disorder. We will notify participants and their physician in the event of any abnormal finding. As this is an experimental procedure, there are no alternative treatments, but subjects are free to discontinue participation at any time for any reason.

Sensitive information is not collected at the Keck Center. Patients are only identified by their subject ID number assigned prior to scanning. The VA Consent form is carried to the Keck Center so that the subject can undergo MRI scanning. The VA Consent form is carried back to the VA inside a locked briefcase and stored inside a locked cabinet inside a locked room within the PI's lab space in building 13 (rooms 332 and 306B). The consent is not give or any information recorded at the Keck Center, it is mainly utilized to confirm subjects concurrence to undergo the scanning procedure Then, the subject is assigned a code to identify the scanned images.

Wii participation
For those individuals who participate in the Wii adjunct program, there is an increased risk of physical injury, frustration and/or physical fatigue during the sessions. However, the Wii program is a low-exertion physical activity that only involves upper body (arm) movements. For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the Wii activities. Breaks and water will be frequently offered throughout the 30-minute session to prevent physical fatigue, frustration, and/or dehydration.

Odoroki participation
For those individuals who participate in the Odoroki adjunct program, there is an increased risk of physical injury, frustration and/or physical fatigue during the sessions. However, the Odoroki program is a low-exertion physical activity. For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the physical activities. Breaks and water will be frequently offered throughout the 60-minute session to prevent physical fatigue, frustration, and/or dehydration.

Saliva Sample
There is no identifiable bodily risk in taking a saliva sample beyond that of an ordinary medical examination; there is potential of small discomfort a mild scraping with a swab of the inside of the cheek to obtain the sample, and subjects that provide a saliva sample may experience dry mouth or difficulty producing saliva. Suggestions for improving saliva generation will be provided. The saliva sample will not be banked and, instead, the sample will be destroyed after processing.

Section 15 - Risk Management

15) Describe the procedures for protecting against or minimizing any potential risks/discomforts, and the adequacy of resources for conducting the study and resources participants may need as a consequence of the research. When applicable, include detail of the following safety measures: (a) The type of safety information to be collected, including AEs; (b) Frequency of safety data collection; (c) Frequency or periodicity of review of cumulative safety data; (d) Statistical tests for analyzing the safety data to determine if harm is occurring; and (e) Conditions that trigger an immediate suspension of the research. See ? for further requirements.

Phase I:

Test anxiety and fatigue will be minimized by explaining the testing procedures, by supportive assurance, and by taking brief rest periods throughout the evaluation. Pre-treatment evaluations will last approximately 2-3 hours and the home visit (optional) will last approximately 30 minutes for the PD participants. The caregivers' participation will last approximately 30 minutes to 1 hour for completion of the interview and questionnaires and if agreed to, they will be involved in the 30-minute home evaluation. Each participant will be offered a home evaluation as part of the evaluation; however, should the participant or their caregiver decline this evaluation, the individual with PD will still be permitted to participate in the 10 week CogSMART treatment group. Each CogSMART session will last approximately two hours. Evaluations will be performed by examiners experienced in working with geriatric and neurologic populations.

In order to protect individuals from a breach of confidentiality, sensitive information will be kept confidential by using coded numbers instead of names to identify individual protocols. All completed test material will be stored in a locked file cabinet in Dr. Filoteo's laboratory at the VA Medical Center. A Privacy and Security Data Plan has been constructed to ensure confidentiality of all Sensitive Information (SI) and is outlined as follows:

MRI Risk Management Procedures:
The primary safety issues for this study are those related to MRI scanning in general. Overall, risks for MRI scanning are minimal given appropriate screening, which is done via an initial phone interview and again immediately prior to scanning. We will use a standard MRI screening form. This instrument has been used successfully in multiple protocols to exclude patients with suspected or known risk factors. If the screening form elicits any suspected risk factors, the form will be supplemented by review of medical records with the subject's permission. In the case of possible risk related to medical implants, the manufacturer's number of any implant will be cleared for safety with the CFMRI's safety officer or the participant will not be scanned. As an additional precaution, subjects will be screened with a hand-held metal detecting wand immediately before entering the magnet room as a final confirmation that the participant is free of metal on their person. Subjects will be apprised of the risks as part of signing the consent form. Subjects with pacemakers, heart valves, brain clips, venous umbrellas, aneurysm surgery or intercranial bypass, aortic clips, prosthetic devices, neurostimulators, insulin pumps, shunts, metal coil implants, or other contraindications to receiving an MRI will be excluded. For any potential participant of childbearing age, they will assert that they are not currently pregnant or they will be excluded from imaging component of the study. To reduce risk of unwanted physiological reactions, participants will be monitored to ensure their body does not form a circuit (e.g., connected hands). Subjects will be strongly encouraged to move slowly when entering or exiting the magnetic field. The scanner bed has been designed to slowly move the subject so as to minimize the possibility of dizziness. RF-induced local heating is unlikely due to the software requirement that subject's weight is accurately recorded and used in determining the appropriate changes in gradients. The participant will be reminded that he/she can discontinue the MRI portion at any time, before or during the scan. Risk of physical discomfort during imaging sessions will be minimized with attention to cushioning the subject's head, neck, shoulders and knees such that the patient may fully relax and not hold any tension to maintain position within the bore

of the magnet. Rest breaks may be taken anytime; the patient is free to move about except during the approximate 0.50 to 1.0 hours of imaging time. The potential risk of hearing loss associated with the noise generated during MRI is eliminated using ear plugs (rated to reduce noise by 32 dB) and through the use of headphones (rated to reduce noise 30 dB). All participants will be required to wear hearing protection (e.g., ear plugs and headphones). Subjects will be told before being placed in the bore of the magnet that they may experience claustrophobia or other discomfort while in the magnet and that they should report this via the intercom should they experience any discomfort or feel the need to be removed, in which case imaging personnel will remove them immediately. The technician has continuous voice and visual contact with the participant. The technician will discontinue the scan at any time discomfort or excessive anxiety is apparent, and the participant can signal by voice, gesture, or alarm bell to discontinue the scan. Subjects will be told they are free to terminate the study at any time at no detriment to themselves or to any care they may be receiving from the VA.

Discomfort during imaging sessions will be minimized with attention to cushioning the subject's head, neck, shoulders and knees such that the patient may fully relax and not hold any tension to maintain position within the bore of the magnet. The patient is free to move about except during the approximately ¾ hour's imaging time. Subjects will be told before being placed in the bore of the magnet that they may experience claustrophobia or other discomfort while in the magnet and that they should report this via the intercom as soon as they feel the need to be removed, in which case imaging personnel will remove them immediately. Subjects will be told they are free to terminate the study at any time at no detriment to themselves or to any care they may be receiving from the VA. The risk of imaging subjects with metal in their body, or who have pacemakers, will be eliminated by screening using a standard MRI screening form. This instrument has been used successfully in past protocols to exclude patients with suspected or known risk factors. This screening form is administered over the telephone when making the MRI scan appointment and again independently on the day of scanning. If the screening form elicits any suspected risk factors, the form will be supplemented by review of medical records with the subject's permission. Finally, subjects will be asked the screening questions one more time by the MRI technician before being placed in the magnet and will be apprised of the risks as part of signing the consent form.

Wii participation:
Wii games will be restricted to those requiring upper body movements (e.g., tennis, ping pong, and golf). For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the Wii activities. Breaks and water will be frequently offered throughout the 30-minute session to prevent physical fatigue, frustration and/or dehydration.

Phase II:

Test anxiety, boredom and fatigue will be minimized by explaining the testing procedures, by supportive assurance, and by taking brief rest periods throughout the two-2.5 hour evaluation. Evaluations will be performed by examiners experienced in working with geriatric and neurologic populations and will be able to gauge when breaks are needed or when testing may need to be rescheduled or cancelled due to severe fatigue or anxiety. To minimize potential discomfort during the UPDRS motor exam, study staff will briefly explain the nature and purpose of the exam before beginning, and will instruct subjects to ask questions or communicate if they are unsure about or uncomfortable with any portion of the exam. Additionally, subjects will sign and receive a copy of the consent addendum, which has further details about the exam, prior to the exam. Each CogSMART-PD session will last approximately 1.5 hours and breaks are offered throughout the session as well. As individuals with PD are at a high risk for falls, we will carefully screen all individuals for history of falls upon recruitment. We will use the baseline UPDRS falling item (#13) in which a history of falls is categorized on a likert scale from 0 (none) to 4 (falls >once per day). A history of falls as assessed by the UPDRS appears to be one of the best predictive methods of subsequent falls at this time Those individuals who endorse a history of falling or score >0 on the UPDRS falling item, will be closely monitored. This includes ensuring that they are escorted to and from the intervention room from their vehicle as well as to and from the bathroom, as needed. Should a patient need help within the bathroom, a caregiver will be requested to assist. If needed, we will utilize the VA escort service. Although not common in PD, all participants will also be assessed for suicidal ideation/intent at baseline, as standard of care for psychological/behavioural interventions. If suicidal ideation is acknowledged, indicated by a score of 2 or greater on item 9 of the Beck Depression Inventory-II (BDI-II), research participants will be referred directly to a VA-privileged clinician for further evaluation. These participants will be monitored for changes in mood during the intervention.
In order to protect individuals from a breach of confidentiality, sensitive information will be kept confidential by using coded numbers instead of names to identify individual protocols. Sensitive information (SI) will be kept on a secured computer system and a locked filing cabinet (for backup) in the PI's lab. All completed test material will be stored in a locked file cabinet in the PI's laboratory within Building #13 at the VA San Diego Medical Center. A Privacy and Security Data Plan has been constructed to ensure confidentiality of all Sensitive Information (SI) and is outlined as follows:
1. This study will collect VA Sensitive Information (SI) (i.e., data, in any format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration or destruction) from all participating subjects. SI used in this study will include individually identifiable medical and health data and personal information, such as age, educational level, gender and ethnicity.

2. SI, such as subjects' medical diagnoses, will be used for the purpose of enrollment and subjects' personal information, such as age, gender, and education, will be used to characterize the subject pool utilized in this study. Addresses and telephone numbers will also be collected as a means to contact the subjects for follow-up when indicated. All data used in this study will be de-identified and linked to SI by a subject number.
3. SI will be used by approved study personnel only.
4. In the event of a real or suspected breach of security, the VA Police, the VA Information Security Officer, and the VA Privacy Officer will be notified.
5. Study records entered into a computer system will be assigned code numbers and will not be individually identifiable. The key that relates the code numbers to the individuals will be will be stored in a stand-alone (non-networked) computer system that is maintained in a locked office within the PI's lab space in Building #13 of the VA San Diego, protected by strong passwords, and accessible only by approved study personnel. This system will not leave the protected VA environment unless the data storage components are removed or destroyed. Hardcopy SI will also be stored for backup purposes in the PI's laboratory within Building #13 of the VA San Diego, in a locked cabinet. Code-numbered data will be stored in a separate filing cabinet under lock and key in Building #13. Data collected in other areas (testing rooms) will be brought to the lab and locked away each night. Only approved study personnel will have access to this information.

MRI Risk Management Procedures:
The primary safety issues for this study are those related to MRI scanning in general. Overall, risks for MRI scanning are minimal given appropriate screening, which is done via an initial phone interview and again immediately prior to scanning. We will use a standard MRI screening form. This instrument has been used successfully in multiple protocols to exclude patients with suspected or known risk factors. If the screening form elicits any suspected risk factors, the form will be supplemented by review of medical records with the subject's permission. In the case of possible risk related to medical implants, the manufacturer's number of any implant will be cleared for safety with the CFMRI's safety officer or the participant will not be scanned. As an additional precaution, subjects will be screened with a hand-held metal detecting wand immediately before entering the magnet room as a final confirmation that the participant is free of metal on their person. Subjects will be apprised of the risks as part of signing the consent form. Subjects with pacemakers, heart valves, brain clips, venous umbrellas, aneurysm surgery or intercranial bypass, aortic clips, prosthetic devices, neurostimulators, insulin pumps, shunts, metal coil implants, or other contraindications to receiving an MRI will be excluded. For any potential participant of childbearing age, they will assert that they are not currently pregnant or they will be excluded from imaging component of the study. To reduce risk of unwanted physiological reactions, participants will be monitored to ensure their body does not form a circuit (e.g., connected hands). Subjects will be strongly encouraged to move slowly when entering or exiting the magnetic field. The scanner bed has been designed to slowly move the subject so as to minimize the possibility of dizziness. RF-induced local heating is unlikely due to the software requirement that subject's weight is accurately recorded and used in determining the appropriate changes in gradients. The participant will be reminded that he/she can discontinue the MRI portion at any time, before or during the scan. Risk of physical discomfort during imaging sessions will be minimized with attention to cushioning the subject's head, neck, shoulders and knees such that the patient may fully relax and not hold any tension to maintain position within the bore of the magnet. Rest breaks may be taken anytime; the patient is free to move about except during the approximate 0.50 to 1.0 hours of imaging time. The potential risk of hearing loss associated with the noise generated during MRI is eliminated using ear plugs (rated to reduce noise by 32 dB) and through the use of headphones (rated to reduce noise 30 dB). All participants will be required to wear hearing protection (e.g., ear plugs and headphones). Subjects will be told before being placed in the bore of the magnet that they may experience claustrophobia or other discomfort while in the magnet and that they should report this via the intercom should they experience any discomfort or feel the need to be removed, in which case imaging personnel will remove them immediately. The technician has continuous voice and visual contact with the participant. The technician will discontinue the scan at any time discomfort or excessive anxiety is apparent, and the participant can signal by voice, gesture, or alarm bell to discontinue the scan. Subjects will be told they are free to terminate the study at any time at no detriment to themselves or to any care they may be receiving from the VA.

Discomfort during imaging sessions will be minimized with attention to cushioning the subject's head, neck, shoulders and knees such that the patient may fully relax and not hold any tension to maintain position within the bore of the magnet. The patient is free to move about except during the approximately ¾ hour's imaging time. Subjects will be told before being placed in the bore of the magnet that they may experience claustrophobia or other discomfort while in the magnet and that they should report this via the intercom as soon as they feel the need to be removed, in which case imaging personnel will remove them immediately. Subjects will be told they are free to terminate the study at any time at no detriment to themselves or to any care they may be receiving from the VA. The risk of imaging subjects with metal in their body, or who have pacemakers, will be eliminated by screening using a standard MRI screening form. This instrument has been used successfully in past protocols to exclude patients with suspected or known risk factors. This screening form is administered over the telephone when making the MRI scan appointment and again independently on the day of scanning. If the screening form elicits any suspected risk factors, the form will be supplemented by review of medical records with the subject's permission. Finally, subjects will be asked the screening questions one more time by the MRI technician before being

placed in the magnet and will be apprised of the risks as part of signing the consent form.

Wii participation:
Wii games will be restricted to those requiring upper body movements (e.g., tennis, ping pong, and golf). For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the Wii activities. Breaks and water will be frequently offered throughout the 30-minute session to prevent physical fatigue, frustration and/or dehydration.

Odoroki participation:
For those at risk of falling (as indicated by medical chart), we will have these patients sit in a chair while performing the Odoroki activities. Breaks and water will be frequently offered throughout the 60-minute session to prevent physical fatigue, frustration and/or dehydration.

Saliva sample:
Saliva samples will be labeled with participant ID numbers and date of visit only, as outlined in HIPAA authorization. Labels will not contain any other identifiable information (such as name, SSN, or date of birth). Samples will not be banked and will be destroyed after analysis.

Section 17 - Potential Benefits

17) Discuss benefits that may be gained by the subject as well as potential benefits to society in general (see ? for guidance)

Phase I:

The expected outcomes for this program include improvement in cognitive, functional performance, and quality of life of PD patients as determined by neuropsychological and functional outcome measures. It is also hypothesized that caregiver's quality of life will improve. Moreover, it is expected that participation in this program will result in fewer visits to VA or other medical services. That is, if the intervention results in prolonging of cognitive and functional independence, then the participants may utilize fewer medical resources in the long run.

Phase II:

The expected outcomes for this program include improvement in cognitive, neuropsychiatric symptoms, and quality of life in PD-MCI participants. All participants will engage in some type of treatment (cognitive rehabilitation or supportive care), therefore, all participants are expected to benefit from participation in this study. We expect that there may be improvement in mood and quality of life in the control (supportive care) group participants. However, we predict there to be greater improvements and gains in the CogSMART-PD participants, especially as it pertains to cognitive function. In addition, it is possible that participation in the intervention and/or the study overall will result in fewer visits to VA or other medical services. That is, if the intervention results in prolonging of cognitive and functional independence, then the participants may utilize fewer medical resources in the long run.

Section 18 - Risk/Benefit Analysis

18) Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

Phase I:

The study does not pose any major risks that are not commonly involved in the clinical management of PD patients, particularly those delivered in a group format. Given the potential of direct benefit to the CogSMART participants, the minimal risk associated with routine clinical management of PD appears reasonable.

Phase II:

The study does not pose any major risks that are not commonly involved in the clinical, psychological or behavioral treatment of neurological patients. Given the potential of direct benefit to the CogSMART-PD participants and the lack of current treatment options for PD-MCI, the minimal risk associated with this study appears reasonable.

Section 20 - Compensation for Participation

20) Provide all details and justifications of the compensation plan. See ? for detailed requirements.

Participants will receive a payment of $40 for each of the four assessments they complete (pre- and post-intervention/support and 6- and 12-month follow-ups).

Section 21 - Responsibilities and Qualifications

Here are the identified study staff members

Dawn M. Schiehser, PhD

Alan N. Simmons, PhD, Deborah L. Harrington, PhD, Elizabeth W. Twamley, PhD, J. Vincent Filoteo, PhD, Angelie Cabrera Tuazon, Stephanie L. Lessig, MD, Adan F Ton Loy, Aishee Das, Alexandra Leigh Clark, Beatrice M. White, Ece Bayram, PhD, Erin L. Almklov, PhD, Kaylee Bashor, Kelsey Anne Holiday, BS, Maya Bina Najmi Vannini, Michael J. Walsh, Nicole M. Whiteley, Tiana McMann

21) For each staff member listed above, describe their role and qualifications. Also indicate which of the study staff are authorized to obtain consent, when applicable to the study.

The CogSMART groups at the VASDHS will be led by Dr. Raeanne Moore, a Neuropsychologist with expertise in Parkinson's disease and cognitive rehabilitation. All staff will be trained and closely supervised by Dawn Schiehser, Ph.D., Staff Neuropsychologist of the Cognitive Rehabilitation at the VASDHS with appropriate VA clinical privileges and a licensed psychologist in the state of California. Given that the CogSMART intervention is a psychoeducational program and not a therapy program, individuals with a Bachelor's degree and appropriate training and supervision can lead the class.

Dr. Filoteo is a licensed Clinical Psychologist with staff privileges at the San Diego VA and UCSD. Dr. Filoteo has conducted several neuropsychological studies in patients with Parkinson's disease. He is authorized to obtain consent for subjects of VA research.

Dr. Dawn Schiehser is an Assistant Adjunct Professor at UCSD and a licensed Clinical Psychologist with full staff privileges at the VA San Diego who specializes in the cognition of movement disorder patients and individuals with traumatic brain injury. She is authorized to obtain consent for subjects of VA research.

Dr. Stephanie Lessig is a board-certified neurologist with specialty training in movement disorders. She will administer the UPDRS Motor Examination to participants.

Angelie Cabrera Tuazon is the study coordinator and study contact in the lab. She will manage the study and be responsible for subject tracking, scheduling, and also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Nicole Whiteley is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Tiana McMann is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Kaylee Bashor is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Aishee Das is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Beatrice White is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Adan Ton Loy is a research assistant in the lab and will also aid in subject recruitment. He is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Maya Vannini is a research assistant in the lab and will also aid in subject recruitment. She is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Michael Walsh is a research assistant in the lab and will also aid in subject recruitment. He is authorized to obtain consent for subjects of VA research and administer neuropsychological tests involved with the study.

Dr. Ece Bayram is a research associate and post-doc fellow that will aid in administration of the UPDRS.

Dr. Erin Almklov is a licensed Clinical Psychologist with staff privileges at the San Diego VA. Dr. Almklov will be assisting with assessing suicidality.

Alexandra Clark is a post-doc fellow at the San Diego VA. She will be assisting with assessing suicidality.

Kelsey Holiday is a research associate and WOC'd graduate student that will assist with assessing suicidality.

Section 22 - Bibliography

22) List relevant articles that the IRB can use to provide necessary background for the protocol. Do not include an extensive NIH-grant-style bibliography. (Up to 5 recommended, but use more if needed to support the protocol or citations above.)

Aarsland D, Hutchinson M, Larsen JP (2003a) Cognitive, psychiatric and motor response to galantamine in Parkinson's disease with dementia. Int J Geriatr Psychiatry 18:937-941.

Aarsland D, Zaccai J, Brayne C (2005) A systematic review of prevalence studies of dementia in Parkinson's disease. Mov Disord 20:1255-1263.

Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P (2003b) Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol 60:387-392.

Aarsland D, Andersen K, Larsen JP, Lolk A, Nielsen H, Kragh-Sorensen P (2001) Risk of dementia in Parkinson's disease: a community-based, prospective study. Neurology 56:730-736.

Nombela C, Bustillo PJ, Castell PF, Sanchez L, Medina V, Herrero MT Cognitive rehabilitation in Parkinson's disease: evidence from neuroimaging. Front Neurol 2:82.

Section 23 - Sponsors and Collaborators

23) Clarify any industry financial or other support (e.g., NIH funds the study or Company X provides the assay kits). Identify non-VA Research collaborators and their role in this protocol, including whether or not they have access to subjects or identified data.

Coded data from the Odoroki program will be analyzed by UC San Diego's Smart Lab, located in Atkinson Hall, 5202. No participant data will be collected at the Smart Lab.

Saliva samples will be stored at and analyzed by the UCSD Integrative Health and Mind-Body Biomarker Laboratory, located at the Medical Teaching Facility, Room 431. Samples are de-identified, and are destroyed after analysis.

In the submission form, upload a copy of the grant, subaward, CRADA, etc. as appliable to the study.

Section 27 - Privacy, Confidentiality, and Information Security

27a) Provide a brief description of how participant privacy and confidentiality will be protected in this study. Describe the circumstance under which it may be possible for a research team member to identify subjects and any related protections or assurances to prohibit or avoid identification. Describe how the number of people with access to identifiers for research purposes is limited in order to protect a participant's privacy.

All data used in the study will be de-identified and linked to SI by an identifier number. SI will remain in a locked filing cabinet in the PI's lab space in building #13, separate from the de-identified data files, and will only be accessible by approved study personnel.
In the groups, which are audio recorded, subjects are asked to call each other only by first name, to help avoid confidentiality breach.
In the event of a real or suspected breach of security, the VA Police, VA Information Security Officer, and VA Privacy Officer will be notified.
Study records entered into a computer system will be assigned code numbers and will not be individually identifiable.

27.b) Entry of a CPRS Research Informed Consent Note is required when subjects will be admitted as inpatients or treated as an outpatients for research *and* the study involves research medical care or may affect medical care.

- ***If a Research consent Note is required, then a Research Progress Note should also be entered for each procedure or intervention.***
- ***Scanning the Consent and HIPAA Authorization into CPRS is not required. Linking the Consent to the Research Informed Consent Note may be permitted and can be useful for trials involving the Research Pharmacy or when research will be performed in conjunction with clinical procedures.***
- ***For Non-Veterans, if Research Informed Consent Notes are entered, then the NOPP Acknowledgment must be scanned into the record. Otherwise a copy of the signed NOPP must be retained with the Investigator's research records and a copy sent to the Privacy Officer; see the ? Help for more information.***

27.b1) Is entry of CPRS notes required based on the above criteria?

- ○ CPRS notes are needed for ALL subjects
- ◉ CPRS notes are needed for SOME subjects
- ○ CPRS notes are NOT needed for any subjects

Identify for which group or groups CPRS records will be entered and to which groups this requirement does not apply.

CPRS notes will be entered for individuals who are consented and attend the treatment sessions. Caregivers who are enrolled into the study do not need CPRS notes because they do not attend treatment sessions nor receive any treatment. Additionally, there are cases where individuals consent to be in the study and complete neuropsychological assessments to determine eligibility but do not end up enrolling into group due to various reasons such as not being able to commit to the 10-week group, loss of interest, etc. In those cases, they do not attend the first day of group and do not receive any treatment; therefore, CPRS notes would not need to be entered for those individuals.

27c) Select the VA Sensitive Information (VASI) use category

- ○ This study does not collect or use any VASI
- ○ This study uses but does not save, collect, copy, or record VASI
- ◉ This study does collect or record VASI

Section 27.1 VA Sensitive Information (VASI)

27.1a) For each type of VASI, indicate all that apply:

Indicate which of the following will be collected/recorded:

- [x] Protected Health Information (PHI)
- [x] Names
- [ ] Device identifiers and serial numbers
- [ ] E-mail addresses
- [ ] Medical record numbers
- [ ] URLs (Universal Resource Locator)
- [x] All elements of dates (except year) or any age over 89
- [ ] Health plan beneficiary numbers
- [ ] IP Addresses (Internet Protocol)
- [x] Telephone numbers
- [x] Account numbers
- [ ] Biometric Identifiers including finger and voice print
- [ ] Fax numbers
- [ ] Certificate or license numbers
- [ ] Full face photographic images and comparable images
- [ ] All geographic subdivisions smaller than a state
- [ ] Vehicle ID and serial numbers including license plate numbers
- [x] Social security numbers or scrambled SSNs (describe below)
- [ ] Other unique identifying number, characteristic, or code (describe below)

27.1a1) Describe why SSN are needed for this study

SSN are needed for subject payment

27.1b) Consent Forms and/or HIPAA Authorization

(•) Yes ( ) No

27.1c) Images with personal identifiers are used for this study (x-rays, MRI images with patient names, record numbers, dates, etc.)?

( ) Yes (•) No

27.1d) Photos with faces or audio video recordings are used for this study.

(•) Yes ( ) No

27.1d1) Identify the device or devices that will be used to take/make the photographs or recordings.

An audio recorder will be used to record group interventions to assess treatment fidelity.

27.1d2) Identify where images will be stored (e.g., in the medical record, with study hardcopy records, with study electronic VASI records

Audio recordings will be transferred to a computer system and assigned group numbers, and will not be individually identifiable. The key relating group numbers to the individuals will be stored separately, protected by strong passwords, and accessible only by approved study personnel.

27.1e) Biological specimens with identifiers are used for this study.

(•) Yes ( ) No

Section 27.2 Data Collection, Tools, and Resources

27.2a) Will any specially obtained software be used?

( ) Yes (•) No

27.2b) Will any mobile devices (laptop, tablet, portable hard-drive, etc.) be used in support of this study?

( ) Yes (•) No

27.2c) Does the study require use of an electronic data capture system?

( ) Yes (•) No

27.2d) Will any other web-based applications be used (e.g., for recruitment, completing online questionnaires, or processing data)?

( ) Yes (•) No

27.2e) Will coded data that excludes personal identifiers be used? Coded data excludes *all* HIPAA identifiers (per VHA Handbook 1605.1 Appendix B), including dates

( ) Yes (•) No

Section 27.3 Data Sharing and Transportation

27.3a) Does this study involve collecting, sharing or transporting any type of data outside of the local VA?

(•) Yes ( ) No

27.3b) This study collects VASI outside of VA (i.e., at a non-VA location).

( ) Yes (•) No

27.3c) VASI is transported outside of VA for any purpose other than sharing.

( ) Yes (•) No

27.3d) PHI may be disclosed to monitoring/auditing agencies by HIPAA Authorization. ***Note: The Research Office must be notified when monitors come to audit***

○ Yes ◉ No

27.3e) Data may be shared with collaborators or others in the conduct of this protocol.

◉ Yes ○ No

27.3e1) Describe the data to be shared or disclosed, the entities to which the data are to be disclosed, how the data are to be transmitted, and how the transmitted data will be stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data. For PHI and VASI, indicate the authority/ies permitting the sharing or disclosure of data (HIPAA Authorization, Limited Data Set, Data Use Agreement, VA Form 10-5345-Request for and Authorization to Release Health Information., etc.).

De-identified data may be shared to be analyzed by the Smart Lab at UC San Diego. This de-identified data will be sent via encrypted email, and while being analyzed will be stored in a standalone (non-networked), password-protected computer in the Smart Lab at UCSD. No participant data or identifying data will be collected at the Smart Lab, and no identifying data will be stored there.

Section 27.4 Research Record Storage and Retention

For each type of record, indicate whether it is collected for this study

27.4a) Hardcopy records/data (includes paper, pictures, film, etc.)

◉ Yes ○ No

27.4a1) Identify precisely where hardcopy data will be stored to include physical site, building, and room number, etc. For each location identify whether VASI or non-sensitive information is stored at that location. For VASI, identify how the data is secured.

Neuropsychological tests, administered in a pencil-and-paper format, will be administered and recorded answers will be stored in the PI's lab space (rooms 330, 332, and/or 306B) in building 13.

27.4a2) Are all of the above locations at VA?

◉ Yes ○ No

27.4b) Electronic study records (includes computer files, removable disk files, digital files, etc.).

◉ Yes ○ No

27.4b1) Identify precisely where ***non-sensitive*** electronic records/data will be stored to include the full map drive, network location/server name, etc., and a brief description of what data/information is stored at each location.

Audio recordings of the intervention meetings will be transferred to the VA computer R drive so that investigators may assess treatment fidelity, and all audio files will be destroyed at the end of the study.

27.4b2) Identify precisely where ***VASI*** electronic records/data will be stored to include the full map drive, network location /server name, etc., and a brief description of what data/information is stored at each location.

If no VASI is collected or recorded for this study, simply indicate that the "Study does not collect or record VASI".

Study does not collect or record VASI

27.4b3) Are any of the locations described in 27.4b outside of the VA Secure Network? *Note: this includes storage on a computer local hard drive.*

○ Yes ◉ No

27.4c) Record Retention - VHA requires compliance with Records Control Schedule (RCS-10) for retention of electronic and hard copy records. Following study closure, these temporary records must be retained for six years and then destroyed. Longer retention may be permitted if requred by other Federal regulations or requirements. Will RCS-10 requirements be followed (i.e., 6-year retention)?

◉ I will adhere to VHA Records Control Schedule-10 requirements
○ I request an exception to RCS-10 requirements

Section 27.5 Additional Privacy or Information Security Details

Provide any other privacy or information security details here.

Section 27.6 Attestations

In the event of real or suspected breach of security, the Information Security Officer, Privacy Officer, VA Police (if appropriate), and the individual's supervisor will be notified within one hour of learning of the event.

◉ Agree ○ Disagree

Study staff will be up to date on any required VHA Privacy Policy and Information Security training or they will not be allowed access to VA Sensitive Information.

◉ Agree ○ Disagree

Access to research sensitive information, if any, will be removed when study personnel are no longer part of the research team.

◉ Agree ○ Disagree

At least one copy of all study records (whether sensitive or non-sensitive) will be retained under VA control and only destroyed in compliance with the approved Records Control Schedule

◉ Agree ○ Disagree

The VA retains ownership of the research data. Should the investigator leave the VA, custody of the research records will be assigned to another investigator and the Research Service notified in writing, or custody of the research records will be transferred to the Research Service.

(●) Agree ( ) Disagree

Section 28 - Protocol Association to New or Existing Project

28) Is this a new R&D Project? Before you go on to complete the *Initial Review Submission Form* (which is used for attachments), please address the association of this Protocol to an R&D Committee Project. This Protocol may represent a new R&D Project, or it may be an additional Protocol under an existing R&D Project (such as when a single grant supports multiple Protocols). Will this Protocol be submitted to the R&D Committee as a new Project?

( ) Yes (●) No

Section 29 - Existing Project Association

29) The associated R&D Project should already exist in the database. Identify the R&D Project(s) that correspond to this protocol.

Project Status	Proposal Number	Project Title	Principal Investigator
Approved	1154731	1154731	Dawn M. Schiehser, PhD
		Cognitive Rehabilitation in Individuals with Parkinson's Disease and Cognitive Impairment	

The Protocol Application is now complete for a Protocol attached to an existing Project.

Next you will go on to the Initial Review Submission Form. This form is used to collect the Application and any other needed attachments for submission to the IRB for review.

Press *Save and Continue*