Title: KICK OUT PD: Karate Intervention to Change Kinematic Outcomes in Parkinson's Disease
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ABBREVIATIONS

DST	Digit Span Test
FRT	Functional Reach Test
HADS	Hospital Anxiety and Depression Scale
HY	Hoehn and Yahr Scale
PD	Parkinson's Disease
PDQ-8	Parkinson's Disease Questionnaire – Short Form
PGIC	Patient Global Impression of Change
PHI	Personal History Information
PI	Principal Investigator
REDCap	Research Electronic Data Capture
SDMT	Symbol Digit Modalities Test
TMT	Tinetti Mobility Test
TUG	Timed Up & Go test
UPDRS	Unified Parkinson's Disease Rating Scale

I. Project Rationale and Description

I.a. Purpose of the Study

The aim of this study is to test whether and to what degree a community-based karate class tailored for individuals with early- to middle-stage Parkinson's Disease (PD) 1) is feasible; and 2) improves objective and patient-reported outcomes. The benefits of exercise for general health and wellbeing in older adults are well-established. Balance exercises such as tai chi and yoga, along with resistance training, can improve or maintain physical function in older adults and enhance muscle strength. Furthermore, aerobic activity is critical for maintaining and improving cardiovascular and functional health. Non-contact boxing has recently seen a surge in popularity among individuals with PD, with components of both aerobic and balance exercise. While participants anecdotally note improvements in stress and physical function, this has only been minimally studied. However, drawing on this experience and the combined aerobic, balance, and mindfulness practices that comprise karate, we hypothesize that participation in structured karate programs may offer similar or greater benefits. In particular, the aerobic, resistance, and balance aspects of karate may be beneficial for physical and cognitive wellbeing, and the mindfulness exercise may improve overall wellbeing. Therefore, we propose a pilot, 10 week-long study of a structured karate exercise program for people with early to middle PD, with pre- and post-intervention assessment of mobility, gait, balance, falls, attention, quality of life, patient-reported global impression of change, and mood. We will assess feasibility with measurement of attendance at each class, and will assess preliminary sustainability with a six-month follow-up phone call to assess continued engagement in karate classes or other regular exercise. We will gather qualitative data on expectations and experience with the classes through pre-intervention and post-intervention focus groups.

We hypothesize: 1) Subjects will show improved mobility after 10 weeks of twice weekly karate classes, as measured by change in Timed Up & Go (TUG)[1]; 2) The majority of subjects will report a positive change from baseline in their overall wellbeing, as measured by a response of "very much improved", "much improved" or "minimally improved" on the Patient Global Impression of Change Scale (PGIC)[2] following 10 weeks of classes; 3) Feasibility will be high, as measured by $\geq$75% attendance rate and a response of "yes" to either "Would you recommend this program to someone else with PD?" *or* "If available, would you continue to participate in this or a similar karate class?" Exploratory outcomes will include measures of gait and balance, including change in functional reach test (FRT)[3] and change in Tinetti Mobility Test (TMT)[4,5], along with change in anxiety and depression, as measured by the Hospital Anxiety and Depression Scale (HADS), and measures of attention such as the Symbol Digit Modalities Test (SDMT) and the Digit Span Test (DST)[6]

I.b. Background

Parkinson's Disease, the second most common neurodegenerative condition[7] presents a significant health concern and the progressive, incurable course of the disease impacts functional abilities of the patient and quality of life for both the patient and caregivers. Exercise is an established supplement to pharmacologic PD treatment and various modalities have demonstrated benefits in gait, balance, PD symptoms, and quality of life measurements.[8,9,10] Research has encompassed many forms of exercise, including aerobic activities and mindfulness-based practices. Vigorous, aerobic activity has been repeatedly shown to have disease-modifying effects ranging from quality of life to overall cognitive and physical improvement.[10] Mindfulness-based practices, such as tai chi, have seen a recent surge in interest and an overall beneficial effect for participants.[11,12] A notable trial compared resistance training,

stretching and tai chi interventions among Parkinson's patients and while both the resistance and tai chi arms showed improvements on multiple measures of physical ability, tai chi demonstrated a significantly greater impact in measures of balance and postural stability.[13] Furthermore, resistance training and tai chi were both correlated with improved patient-reported outcomes and participants in the tai chi group who reported benefits were more likely to continue their exercise programs.[14]

In addition to scholarly efforts, efforts to incorporate various forms of activity into PD care have gained popularity in the community at large, with notable examples including Rock Steady Boxing, a non-contact, PD-focused boxing class that has garnered national media attention. Anecdotal reports of the benefits of these vigorous, goal oriented, exercise classes are numerous; however, it has been minimally studied from the academic perspective. A case series describing six patients attending Rock Steady boxing classes reported at least some improvement in gait, balance, activities of daily living, and quality of life.[15] A randomized trial with 31 patients comparing traditional exercise and boxing demonstrated significant improvements in balance, movement, and quality of life measures among both interventions, with greater gains in gait among the boxing group.[16] Similar to boxing, karate for patients with PD has received some popular attention and media coverage both within the United States and internationally.

Karate is a martial art that incorporates the vigorous activity of aerobic and resistance exercise, mindful practice similar to tai chi, and is taught as large, directed movements in a class-based, communal environment. Karate as an adjunct therapy in PD has not yet been investigated, although one study reports improvements in cognitive speed and subjective mental health among healthy older adults participating in karate training compared to others in a mindfulness intervention without exercise.[17] The combined benefits of exercise, mindfulness-based practice, and the popularity and promise of these types of interventions lead us to believe that karate is a promising exercise modality for PD patients and warrants further investigation. There is significant opportunity to document the potential benefits of the physical activity and mindfulness components of karate training and begin filling in this gap in the PD and exercise literature.

I.c. Study Design

This is a non-randomized, open-label, non-blinded, 10-week pilot study of a novel intervention, namely, non-contact karate, for early to middle stage PD. The intervention—namely, karate classes—are developed for and will include only patients with Parkinson's disease. Eligible subjects will engage in twice-weekly karate classes for 10 weeks, specifically designed for individuals with early to middle stage PD, focused on incorporating upper and lower limb movements in multiple directions, increasing awareness throughout the body, shifting body weight and rotation, relaxation of the muscles, improving reaction time, using complex repetitive actions to improve coordination, footwork training and centered weight shifts to help with fall prevention, and striking shields for self-defense and stress relief.

Each subject will attend a pre-intervention focus group, at which time the study logistics will be reviewed, informed consent process will occur, the subject will complete a brief, individual pre-intervention assessment focused on overall mobility, gait, balance, attention, mood, and quality of life, and the subjects will be prompted to share aloud their thoughts on exercise, balance, and mindfulness practices in general and in PD specifically, and any expectations or preconceptions that they have regarding karate classes for PD. The focus group sessions will be audiotaped. After the sessions the information recorded will be transcribed into electronic documentation for later review and analysis. At the end of the study, the audiotapes will be destroyed.

Following 10 weeks of twice weekly classes, the subjects will have a post-intervention assessment and focus group, in which the pre-intervention assessments (TUG, FRT, TMT, PDQ-8, HADS, SDMT, DST) will be re-administered, along with the PGIC for the subject's global impression of change. Subjects will be prompted to share their thoughts on how the intervention impacted their overall wellbeing, balance, and mindfulness; whether the intervention achieved their expectations; and they will be asked to provide feedback for improvements. Finally, the study team will contact subjects 6 months post-intervention to assess continued engagement in karate or related activities and again, the subject's quality of life and global impression of change.

The PI and research team will collaborate with a professor of Cinema and Television Arts from Columbia College Chicago, IL to develop a documentary to educate others about karate as an interactive form of exercise and its potential benefits on the symptoms and quality of life of people with PD. To capture the groups' journey over 10-weeks, portions of the pre-intervention focus group, the karate classes, and the post-intervention focus group will be videotaped. For a more in-depth look, two to three subjects will be followed during the entire study and interviewed to provide a personal narrative of their experiences with the karate classes and living with PD. The interviews will be videotaped.

We will recruit 30 individuals with PD diagnosed by a neurologist, ages 30-90, living in Chicago, and with Hoehn & Yahr (HY) stage 1 (unilateral symptoms, no balance issues), stage 2 (bilateral symptoms, no balance issues), or stage 3 (bilateral symptoms, some postural or balance involvement). Subjects will be assigned to one of two cohorts of 15 subjects each, based on dojo location and class schedule. For example, one cohort may take classes Tuesday and Thursday nights at the Wilmette dojo, and the second cohort may take classes Wednesday and Saturday mornings at the Glenview dojo, however class times and locations are to be determined.

II. Characteristics of the Research Population

II.a. Number of Subjects

Total Number of Subjects: 30

This is a pilot study; our power analysis (see table below) is based on the TUG, with the following assumptions: mean TUG score for individuals with PD is 14.8 seconds with standard deviation of 5.8 seconds, alpha of 0.05, and correlation between baseline and follow-up assessments of 0.5. We calculated sample sizes necessary with various minimum clinically important difference values for the TUG, which ranges from 2 seconds to 5 seconds in various studies[1,18], and varying for power between 80-90%. With a sample size of 30, we will have 80% power to detect a change of 3 seconds in the TUG, and will be more than 90% powered to detect a change of 4 seconds or greater.

Baseline mean TUG	Baseline SD TUG	Min. clin. Important difference	Correlation b/w baseline, follow-up	Power	Sample size
14.8s	5.8	2s	0.5	.9	89
			0.5	.8	67
14.8	5.8	3s	0.5	.9	40
			0.5	**.8**	**30**

14.8	5.8	4s	0.5	.9	23
			0.5	.8	17
14.8	5.8	5s	0.5	.9	15
			0.5	.8	11

II.b. Gender of Subjects

There will be no exclusion of subjects based on gender.

II.c. Age of Subjects

Subjects will be 30-90 years of age.

II.d. Racial and Ethnic Origin

There will be no exclusion of subjects based on racial or ethnic characteristics. However, subjects must be fluent in English to participate in the karate classes, as that is the language of instruction, and due to the general lack of appropriately translated neurological and neuropsychological assessments and appropriate normative comparison samples. These factors are critical for accurate administration, scoring, and interpretation of neurological and neuropsychological test data.

II.e. Inclusion Criteria for All Subjects:

1. Each subject must be between 30-90 years of age. A subject may be of either gender, any race/ethnicity.
2. Subjects will be those diagnosed with Parkinson's Disease by a treating neurologist; if the subject is seen at Rush University Medical Center, this will be verified via chart review. If the subject is seen elsewhere, he or she will be asked to have their neurologist sign a form confirming the diagnosis of Parkinson's Disease and indicating the subject's HY stage (with definitions of each stage provided on the form for providers who may not be familiar with HY staging) at the most recent visit, to be sent back to the study coordinator for eligibility verification.
3. English speaking.
4. Living within the Chicago area.
5. Subjects may be untreated for Parkinson's Disease, or may be taking any individual PD medication or combination thereof. Subjects may or may not have had Deep Brain Stimulation. Subjects may or may not be receiving physical or occupational therapy. Subjects will be encouraged to maintain their same medication regimen throughout the duration of the 10-week study, however if emergent issues arise requiring medication changes, the subject will not be disqualified.

II.f. Exclusion Criteria for All Subjects

1. Subjects requiring an assistive device (cane, walker, wheelchair) or the assistance of another person in order to ambulate.
2. Subjects with active psychosis or exhibiting symptoms of a severe psychiatric disorder.
3. Subjects unable to commit to attending, or to travel to, two classes weekly for 10 weeks.
4. Subjects previously participating in a karate or other martial arts program, including boxing programs for PD, in the past 30 days.

5. Subjects with atypical parkinsonism, including Progressive Supranuclear Palsy, Multiple System Atrophy, Dementia with Lewy Bodies, Corticobasal Syndrome, drug-induced parkinsonism, vascular parkinsonism, or atypical parkinsonism not otherwise specified, according to the referring neurologist.

II.g. Vulnerable Subjects – This study will not include children, prisoners, and homeless persons. The consent form will state that participation in our study will **not** affect their clinical care.

III. Methods and Procedures

Study Visits

Screening Phone Call

Subjects who are interested in participating based on review of printed or electronic recruitment materials will be directed to contact the study coordinator by phone, who will provide them with information about the study and the opportunity to ask questions about it in detail; those who express continued interest in participation will be screened for eligibility and ability to attend the scheduled classes, held at one of the five Fonseca Martial Arts Dojos in Glenview, Wilmette, Park Ridge, Evanston and/or Roscoe Village. Classes will occur twice weekly for ten weeks, between June through August 2018, and subjects can select from participating in either a weekend/weekday daytime class, or a weekday/weekday evening class, depending on their availability and proximity to each dojo's geographic location. Screening will occur on a rolling basis until the 15 slots in each class are filled.

Pre-Intervention Focus Group

Prior to the first class, subjects will attend a pre-intervention focus group, at which time the study team, including Principal Investigator, Research Coordinator, and research assistants, will review the study design and flow, informed consent process, and each subject will be individually visited by a member of the study team to review and sign the informed consent form (ICF).

Subjects will then complete a brief demographic questionnaire, including duration of PD diagnosis in years, baseline activity level, prior involvement with karate or other martial arts, number of falls in the past 12 months, and subjects will complete the Parkinson's Disease Questionnaire-8 (PDQ-8)[19], a brief, validated, PD-specific 8-item measure of quality of life. Subjects will complete the Hospital Anxiety and Depression Scale (HADS). Subjects will also write their response to the open-ended prompt, "What do you hope to achieve in this class?"

Subjects will then meet with a study team member to complete the TUG (see description below), FRT, and TMT. Next, the subject will meet with the PI or another study team member in a private room for a brief assessment of bradykinesia, tremor, rigidity, and postural stability in order to determine baseline HY stage. Lastly, subjects will meet with a study team member to complete short attention assessments with a SDMT and DST. Once all subjects have completed the pre-intervention written and physical assessments, the focus group will commence.

Subjects will be prompted to share aloud their thoughts on exercise, balance, and mindfulness practices in general and in PD specifically, and any expectations or preconceptions that they have regarding karate classes for PD.

Intervention
Each karate class will follow a structured curriculum, as shown in Appendix 1, with complexity of movements and movement patterns increasing over the 10-week study period. Classes will take place twice weekly, and subjects will be required to attend their assigned class time/location. Each class will last approximately 45-60 minutes. Attendance will be recorded in hard copy by the instructors at each class, with recordings only of the subject's name, not linked to their unique study ID; the attendance log will be shared with the study coordinator following the final class. A member of the study staff will be present at each class in order to answer questions and to support participants and instructors should any questions about protocol or PD safety arise.

Post-intervention focus group
In the week prior to the 10th class, the study team will contact subjects to remind them of the date and time of the final class and the post-intervention focus group. The post-intervention assessment will consist of a repeated TUG, FRT, TMT, HADS, PDQ-8, SDMT, DST, brief question about falls in the past 10 weeks, and PGIC. Each subject will receive their initial response to the "What do you hope to achieve in this class?" prompt, and will be asked to reflect in a written, open-ended manner on whether they feel that they achieved their goal. In addition, subjects will indicate their response to the following questions regarding feasibility: "Would you recommend this program to someone else with PD?" and "If available, would you continue to participate in this or a similar karate class?"

Subjects will then participate in a focus group, similar to the pre-intervention focus group, in which they be asked to share and reflect on how the intervention affected their overall attitude towards exercise; how it affected their balance and falls; how it affected their mindfulness; any other positive or negative benefits; any impact on their care partner(s) (if applicable); and suggestions for changes to the intervention for the future. Depending on availability of space, the post-intervention focus group may take place at Rush University, or may take place immediately following the last class at the respective dojo.

Documentary
Portions of the focus groups and karate classes, and the entire in-depth interview will be videotaped by the Columbia filmmakers using personal equipment. Subjects may choose to not participate in the documentary project which means subjects will not participate in the in-depth video interviews, and they will not be included in individual or group video shots during the focus groups and karate classes. To ensure confidentiality, subjects will be placed in one of two groups, Group A or Group B, depending on whether they decide to participate in the documentary or not. Subjects who agree to be videotaped and possibly interviewed will be part of Group A while subjects who choose not to be videotaped or interviewed will be in Group B. Subjects may not switch groups after the study begins with the pre-intervention focus group. Participation in the karate classes and focus groups will not be affected if a subject does not wish to be videotaped or interviewed. Subjects will not be penalized if they decide to not take part in the documentary

Six month follow-up phone call
The study team will contact the subjects by phone six months after the final class to ask whether the subject has continued to participate in any structured karate or martial arts classes; if yes, frequency and location will be asked. If no, reasons for lack of participation will be asked. Finally, PGIC will be administered a final time.

Assessments: Subjects who agree to be part of the study and sign the Informed Consent Form will be asked to complete a series of assessments to assess their current neurological status and overall wellbeing. There is no known risk associated with participation in these assessments, and they are a part of routine clinical care for these conditions. These tests are typically experienced as interesting to subjects. Administration of these assessments should take 15 minutes per subject immediately prior to the first class, and 15 minutes per subject immediately after the final class. All or some of the following assessments and self-report measures may be administered but are not limited to:

- *Demographic/disease questionnaire:* This brief, one-page questionnaire will ask for the subject's name, phone number (for 6-month follow-up call), age, gender, race, ethnicity, PD duration in years, prior exposure to karate or martial arts classes, baseline activity level, and number of falls in the past 12 months. There will be one open-ended question asking, "What do you hope to achieve in this class?"

- *Hoehn and Yahr Scale (HY):* A system used for describing how Parkinson's symptoms progress and the relative level of disability. There are five stages: Stage 0 – No signs of disease; Stage 1 – Unilateral disease; Stage 1.5 – Unilateral plus axial involvement; Stage 2 – Bilateral disease, without impairment of balance; Stage 2.5 – Mild bilateral disease with recovery on pull test; Stage 3 – Mild to moderate bilateral disease; some postural instability; physically independent; Stage 4 – Severe disability; still able to walk or stand unassisted; Stage 5 – Wheelchair bound or bedridden unless aided.[20]

- *Timed Up and Go (TUG)*: A well-validated, brief measure of mobility. Administered by a study team member with a stopwatch who has previously measured out the distance between a standard arm chair and a taped line on the ground 10 feet (3 meters) away, subjects sit in a standard arm chair and are instructed that when the team member says "Go", they should stand up from the chair, walk at their normal pace to the line, turn, walk back to their chair at a normal pace, and sit down again. The study team member will record the TUG results in seconds using a stopwatch. This is a recommended test of balance in PD.[21]

- *Functional Reach Test (FRT)*: This brief, valid, reliable, and practical assessment of balance involves a yardstick being mounted on a wall at shoulder height. The subject is asked to stand next to the yardstick, extend the arm closest to the wall at 90 degrees of shoulder flexion, and the distance is recorded. The subject is then asked to reach as far as he or she can forward without taking a step, and the distance is recorded again. The difference between start and end position is the reach distance.[3] This is a recommended test of balance in PD.[21]

- *Tinetti Mobility Test (TMT):* This balance scale has strong psychometric properties and consists of 2 subscales: balance tests (9 items, scored from 0-16) and gait tests (7 items, scored from 0-12), where higher scores reflect better performance.[5] This meets criteria for a "suggested" scale in PD. This is a recommended test of balance in PD.[21]

- *Hospital Anxiety and Depression Scale (HADS):* Brief, 14-item highly validated scale for measuring anxiety (7 items) and depression (7 items), where scores of >8 for either anxiety or depression indicate probable symptoms.[6] The HADS was selected due to its use in prior peer mentoring studies and strong psychometric profile

- *Modified Unified Parkinson's Disease Rating Scale (UPDRS)*: A shortened version of the UPDRS motor subscale will be conducted by the PI or study staff, assessing only rigidity, resting tremor, and bradykinesia in all four extremities and the head/neck, as well as postural stability, in order to determine the subject's HY stage.

- *Patient Global Impression of Change (PGIC)*: This single-item rating scale administered only at the post-intervention assessment asks subjects to rate their overall response to the intervention using a 7-point rating scale, with the options of "very much improved", "much improved", "minimally improved", "no change", "minimally worse", "much worse" and "very much worse". Recommendations for assessing importance of this scale include reporting the percentages of subjects endorsing each of the 7 response options.

- *Parkinson's Disease Questionnaire- Short Form (PDQ-8):* A validated and shortened version of the PDQ-39, with 8 items each representing one domain of the PDQ-39, also with a summary index score standardized to a scale of 0-100, with higher scores signifying worse quality of life; this scale is recommended for use in PD by the Movement Disorder Society.

- *Symbol Digit Modalities Test:* This uses a reference key while the examinee has 90 seconds to pair specific numbers with given geometric figures. Responses can be written or oral, and for either response mode, administration time is 5 minutes. The WPS AutoScore Test Form simplifies scoring. SDMT allows the opportunity to compare written and spoken responses from the same individual. The Manual provides separate norms for written and oral administrations of the test. Norms for adults are separated by age group and level of education.

- *Digit Span Test:* This tests the number of digits a person can absorb and recall in correct serial order after hearing them or seeing them. Here the person has to remember a small amount of information for a relatively short time, and the order of recall is important. To test the auditory digit span of a person, the administer says numbers slowly in one second intervals, in a monotone voice. For example, the administer will say 6-1-5-8 and have the person repeat it back in the order it was given or the reverse order. If the person is able to say a 4 digit sequence back correctly 75% of the time on the first try, it will be considered a short term memory of 4, and is the same for each higher digit. The average in our society for a seven-year old to adult is 7.

III.b. Data Analysis and Data Monitoring

Oversight of the Data: Karate for PD will be maintained by the Principal Investigator. The Principal Investigator will review study procedures annually and report any concerns in the IRB continuation application. This is a Level I, Low, Minimal Risk study; therefore, there is minimal risk of unanticipated problems with the exception of breaches in confidentiality. The quantitative data for the study will be entered into a secured database using an electronic data capture program, Research Electronic Data Capture (REDCap).[22] The database will be stored on a secure password-protected server and not on individual desktop computers. The code sheet will be password protected and the password will be updated annually. Breaches of confidentiality will be reported to the IRB immediately with the "Reportable Event/Unanticipated Problem Form."

Data will be exported from REDCap in de-identified format for statistical analysis, with all PHI stripped from the dataset prior to analysis by statisticians. We will summarize categorical variables by

frequencies and percentages and will assess continuous variables for normality, summarized by mean/standard deviation, or median/interquartile range. We will report the basic descriptive statistics of the cohort, including baseline TUG, FRT, TMT, HADS, PDQ-8, SDMT, and DST, stratified by HY stage. We will report on attendance, defined as the percentage of classes attended, where 20 is the denominator. We will analyze the change in TUG, FRT, TMT, HADS, PDQ-8, SDMT, and DST, respectively, from pre- to post-intervention, using paired *t*-tests or nonparametric Wilcoxon sign rank tests, as appropriate, stratifying for HY stage. We will report on the percentage of subjects endorsing each of the 7 PGIC response options, stratifying for HY stage. We will report the descriptive statistics concerning whether subjects' individual predefined goal for the class was achieved (binary outcome), and will present de-identified qualitative comments noted in the feedback at the post-intervention assessment. We will report descriptive statistics on continued interest and likelihood of recommending the program to someone else with PD. After the 6-month follow-up call, we will analyze descriptive statistics on continued involvement in karate/martial arts, and will again report the percentage of subjects endorsing each PGIC response option.

The qualitative data from the focus groups will be audio-recorded and transcribed, with all identifying information stripped from the transcripts. Once transcribed, the audio recordings will be destroyed. The qualitative data will be analyzed using a grounded theory approach to identify pertinent themes, with data stored as password-protected files behind the Rush firewall, accessible only to study staff.

All video footage will be the sole property of the PI. Videos will have identifying information (i.e. image of patient's face, first name). Video files will be stored and password-protected behind the Rush and the Columbia firewall. The video along with the data collected from the focus groups and karate classes may be used as part of the dissemination of the study results and for educational purposes.

The PI, co-investigators, and/or study staff will review all data collection forms on an ongoing basis for data completeness and accuracy as well as protocol compliance. The data will be reviewed on a quarterly basis:

- Subject accrual (including compliance with enrollment criteria)
- Status of all enrolled subjects
- Adherence data regarding study visits and procedures

Safety data (AEs and SAEs) will be reported to the Principal Investigator and reviewed per occurrence and in accordance with the IRB's regulations. Any significant findings (i.e. protocol deviations) will be reported to the IRB in accordance with requirements and will be documented accordingly.

III.c. Data Storage and Confidentiality

All subjects will be assigned unique ID numbers. All research data files will be stored at the Rush University Parkinson's Disease and Movement Disorders Program in secured file cabinets, including hard copies of case report forms, informed consent forms and informed consent documentation checklists. Data will be entered into a secured database (REDCap). The database will be stored on a secure password-protected server and not on individual desktop computers. The code sheet will be password protected and the password will be updated annually. Hard copies of case report forms and informed consent documentation checklists will be labeled with the study ID only and maintained in individual files by study ID number. Signed informed consent forms, containing subject names, will be stored separately in the regulatory binder, which will be stored in a locked file cabinet in the PI's office. Class

attendance records will be maintained using name only, not subject ID, by the class instructors. These records will then be given to the study coordinator following the final class, who will then link the attendance information with the subjects' data using the code sheet. Attendance information will be entered into REDCap, after which time, the hard copies of the attendance information will be destroyed.

Before videotaping begins, subjects who agree to participate in the documentary must sign their name on the informed consent form. Participating in the documentary is voluntary. Informed consent forms will be stored in the regulatory binder, which will be stored in a locked file cabinet in the PI's office. The PI and the Columbia Cinema and Television Arts filmmakers will have access to the video files to perform activities only related to the study.

Only the PI and research staff will have access to the database and hard copies of study documents. Data will be stored in a format suitable for research inquiries by the PI who might make use of the data in a retrospective manner for other Rush-based research studies. If a particular researcher/collaborator has an interest in a study population, then the PI will review the database to identify eligible subjects that meet the study inclusion criterion and the potential participant(s) will then be contacted by a member of this study team whom the subject has already met to see if they are interested in participating in the particular study. If a participant is interested, he or she will be referred to that Rush study team and will be scheduled for a separate consent procedure with the individual Rush researcher for that particular study and at that point the participant can choose whether to participate or not in that particular study. The results of the Karate for PD study may be published in a book, journal, and other media or used for teaching purposes. However, all published data will be made anonymous.

IV. Risk/Benefit Assessment

IV.a. Risk

There are no known risks from participating in neurological or neuropsychological tests. Subjects may experience mild boredom or cognitive fatigue; however, most individuals with like symptoms find the tests interesting and are able to tolerate up to two-hour duration of testing well. There is, however, a risk of falls or injury associated with participation in any exercise, including karate, for which subjects will sign a liability waiver used for all karate class participants at the Fonseca Martial Arts dojos. The risks will be minimized to the extent possible by 1) having all instructors undergo basic instruction in principles of PD by the PI prior to the first class; 2) having all classes held at quieter times in the dojo, so as to avoid overcrowding and risks of falls or freezing of gait in crowded, busy situations; 3) having small instructor to subject ratios (2 instructors per 15 subjects) to allow for maximal supervision and guidance; 4) having study staff present to assist with mobility issues at as many classes as possible.

Another possible risk is the loss of confidentiality by participating in the video because the subject's image may be captured. However full names will not be used during interviews with the two or three subjects who agree to answer questions about their experiences with the karate classes.

IV.b. Potential Benefit to Subjects

Potential benefits to subjects include the following: 1) cognitive and physical improvements in PD symptoms related to both vigorous physical activity and mindful exercise; 2) benefits of mindful exercise on quality of life; 3) the enjoyment of participating in a new activity in a social environment with other individuals with PD; 3) the satisfaction of learning a new skill; 4) the knowledge that by participating,

subjects are contributing to the understanding of how karate impacts individuals with PD; 5) the altruistic benefit of contributing to the development of a fun, novel intervention for themselves and potentially others. Additional benefits include the opportunity to be active in the community and form relationships with peers. The positive effects on subjects with PD also have the potential to impact the wellbeing of their families and caregivers, as this karate class offers a new option for fun, therapeutic activity. The potential benefits to society include furthering the involvement of individuals with chronic diseases in community activities and the potential physical benefits may help modify the disease progress for the many affected by PD.

V. Subject Identification, Recruitment, and Consent/Assent

V.a. Method of Subject Identification and Recruitment

Individuals will be recruited via posted fliers, print and electronic newsletter postings, and social media postings from the Rush University Parkinson's Disease and Movement Disorders Program, electronic newsletter postings in the Rush University Medical Center Research Newsletter, Rush clinical trials website, via electronic and printed copies of fliers sent to Rush University Medical Center (1725 W Harrison St Ste 755 Chicago, IL 60612), Rush Oak Park Hospital (520 S Maple Ave Oak Park, IL 60304), Northwestern University (710 N Lake Shore Dr Abbott Hall, 11th Fl Chicago, IL 60611), University of Chicago (5841 S Maryland Ave MC 2030 Chicago, IL 60637), University of Illinois-Chicago (1801 W Taylor St Ste 4E Chicago, IL 60612), Jesse Brown Veterans Affairs Hospital (820 S Damen Ave Chicago, IL 60612), Captain James A. Lovell Federal Health Care Center (3001 Green Bay Rd North Chicago, IL 60064), Edward Hines Jr. VA Hospital (5000 5th Ave Hines, IL 60141), Evanston Hospital (2650 Ridge Ave. Evanston, IL 60201), Glenbrook Hospital (2100 Pfingsten Road, Glenview, IL 60026), Highland Park Hospital (777 Park Ave. West, Highland Park, IL 60035), Skokie Hospital (9600 Gross Point Road, Skokie, IL 60076) general neurologists and movement disorder specialists. Information will be disseminated to PD patients at monthly support group meetings and other educational and research fairs, as they arise. If possible, the IRB-approved recruitment fliers will be shared with the Parkinson Foundation for possible distribution through their electronic newsletters and social media avenues to increase reach to other potential subjects throughout the Chicago area. We will also post to clinicaltrials.gov within 30 days of starting enrollment.

V.b. Process of Consent

At the time of the pre-intervention focus group, the study team, including Principal Investigator, Research Coordinator, and research assistants, will review the study design and flow, informed consent process, and each subject will be individually visited by a member of the study team to review the informed consent form (ICF), engage in capacity assessment as described below, and assuming capacity, sign the ICF, witnessed by the study team member. The study team member will complete an ICF documentation checklist, as well.

V.c. Subject Capacity

Capacity to consent will be assessed by the designated trained research staff member and/or the PI. Throughout the consent process, the study staff member will assess the participant's comprehension by asking the participant to verbally summarize key elements of the consent form particularly the sections

of the consent form that explains that they are being asked whether they agree to be contacted for other studies, as well as aspects of the consent form that explain the inclusion of PHI in the database, how their confidentiality will be protected, and how their data will be stored for future use. Subject's capacity is not expected to fluctuate significantly during the 10 weeks of the study, and would not be expected to be significantly impaired in early to middle stage PD.

During the consent process, subjects will have the opportunity to indicate whether they wish to be contacted for participation in future studies conducted by researchers at Rush and their collaborators. Subjects who agree to participate in the program will also have an opportunity to authorize having their Personal History Information (PHI) shared with our collaborators. PHI data will **NOT** be shared unless written authorization is obtained from the subject. Subjects will be given a copy of the signed IRB approved Informed Consent Form for their future reference. Signed consent forms will be stored in a locked cabinet in the PI's office at Rush, separate from the study data.

V.d. Debriefing Procedures

Subjects will be debriefed about the aims and study hypotheses following administration of all study procedures; this will occur at the end of the six-month follow-up phone call in order to avoid introducing bias into subjects' responses to questions.

V.e. Documentation of Consent

A Consent Process Documentation Form will be included in the subjects' research chart that will document the informed consent process that took place.

V.f. Costs to the Subject

Subjects will not receive any inducements before, or rewards or compensation (i.e. cash, taxi fares, medical care, gifts, etc.) after the study. There will be no cost to subjects associated with participation in this study. Subjects will wear their own comfortable workout clothing; they will not need to purchase traditional uniforms for this karate class.

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Appendix 1: Sample Karate Class Curriculum

Curriculum Sample:

Warm-ups:

Single knee ups
Double knee ups
Alternating knee ups
Knee swings (inside-out)
Knee rotations
One leg squat, with other leg doing toe taps (forward, backward, side)
Squats with arms extended
Hip circles
Body rotation
Arm side swings
Arm circles
Rotator cuff

Strikes from Ready Stance (feet shoulder width apart, knees slightly bent):

Deep breathing with palms extended
Double palm strike
Single palm strike (alternate arms)
Single punching (alternate arms)
Rising block (two count)
Rising block (one count)
Downward block (same arm with other hand on hip)
Downward block (alternating arms)
Knee strike (alternate legs)
Front snap kick (same leg)
Front snap kick (alternating)

Strikes from Fighting Stance (switch feet and repeat):

Jab (stationary)
Reverse (stationary)
Jab-Reverse (stationary)
Jab with front foot step
Reverse with front foot step
Jab-Reverse with single front foot step

Stance Work:

Front stance (moving forward)
Front stance (moving backward)
Double palm strike slowly (two count, then one count)
Front punch (two count, then one count)
Rising block (two count, then one count)
Downward block (two count, then one count)
Knee strike (forward only)
Front snap kick (forward only)

Mitt/Paddle Work:
Jab (mitt stationary and flashing for reaction)
Reverse (mitt stationary and flashing for reaction)
Jab-Reverse (mitt stationary and flashing for reaction)