Department of Veterans Affairs

VA RESEARCH CONSENT FORM

Subject Name:

Title of Study: Aerobic Exercise in Parkinson's Disease

Principal Investigator: Ergun Uc, MD **VAMC:** Iowa City, Iowa

INFORMED CONSENT DOCUMENT

Project Title: **Long Term Aerobic Exercise in Parkinson's Disease**

Principal Investigator: Ergun Uc

Research Team Contact: Ergun Uc, MD (phone number: [redacted])

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you carry the diagnosis of Parkinson's disease (PD).

The purpose of this research study is to determine if aerobic exercise improves movement, cognition, mood, driving, quality of life, and the health of brain tissue in PD when compared to usual medical care and counseling you receive for your PD. Preliminary studies show that aerobic exercise can be helpful for brain health, movement and cognitive ability, and general well-being in PD, but it remains to be confirmed if long term aerobic exercise truly meets these expectations. The study is designed to test this question in a community setting.

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HOW MANY PEOPLE WILL PARTICIPATE?

Approximately **300** people will take part in this study conducted by investigators at the Iowa City VA Health Care System.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for**:**

- About 13 months: The intervention between the Baseline and Final Visits will be one-year long, with assessments before and after the intervention accounting for the additional month.
- The total number of scheduled in-person visits is 4:
  - Screening Visit to confirm eligibility (5-6 hours)
  - Baseline Visit for eligible participants (8-9 hours) within 2 weeks of the Screening Visit
  - Interim Visit at 6 months after Baseline Visit (1.5-2 hours)
  - "Safety Check" visit to resume the study activities after COVID-19 administrative hold (1-2 hours)
  - Final Visit after the Intervention ends (8-9 hours)
- Phone calls every 2 weeks between Baseline and Final Visits to review compliance, adverse events, concerns, and additional physical activities (15-20 min)

WHAT WILL HAPPEN DURING THIS STUDY?

If you agree to be in this study, you will sign this form before any study procedures are done.

STUDY VISITS AND PROCEDURES:

All visits and procedures will take place in the laboratories and clinics of the University of Iowa (UI). For every visit, you will check in at the Neurology Outpatient Clinic at the University of Iowa Hospitals and Clinics (UIHC), located on the second floor in the Roy Carver Pavilion (RCP) across elevator D. The study staff will meet you there and will take you to specific testing locations. The road test will be conducted on paved roads in and around Iowa City using a specially outfitted vehicle that belongs to the UI. At the end of each visit, the study staff will take you back to the Neurology Outpatient Clinic and help you to return to your vehicle or meet your ride.

We will use your past medical history, your diagnosis, and your past and present physical and mental exam findings from your medical record to determine your eligibility for our study. During the study, we will collect information on your mobility, cognition, mood, sleep, vision, general health, exercise capacity, driving

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performance, brain health, and quality of life. Below is a table that shows the study visits and procedures during each visit, followed by description of each procedure.

		Visits					
Procedures	**Screening**	**Baseline**	**Phone**	**Interim**	**Safety**	**Phone**	**Final**
Driver's license check	+			+			+
History/Physical	+			+	+		+
Questionnaires	+			+	+		+
Cognitive tests	+	+					+
Motor tests	+	+		+	+		+
Bicycle fitness test	+						+
MRI		+					+
OFF period testing		+					+
EEG	+						+
Road test		+					+
Intervention				←	→		
Review of intervention/adverse events/other exercise			+	+	+	+	+
Timing in relation to intervention	-2 weeks	0 months	Every 2 weeks	6 months	anytime	Every 2 weeks	12 months

1) SCREENING VISIT:

The activities during the screening visit will include:

- Medical history and a physical examination by a physician investigator.
- Verification and photocopy of valid US driving license
- Questionnaires to assess mood and driving.
- Tests to assess mobility (e.g., walking) and cognition.
- Lunch
- Cycle ergometry to determine aerobic fitness. Cycle ergometry is like an exercise stress test on a treadmill, but a stationary bicycle is used instead of a treadmill.

- EEG (electroencephalogram)
- Completion of forms for payment (e.g., name, address, SSN, and bank information for direct deposit, etc.)

Cognitive and motor (movement/mobility) testing, questionnaires:

We will use a standardized set of questions and physical examination to collect information about your PD. The questionnaires ask about the effect of PD on your quality of life. We will interview you and collect information about your ability to perform activities of daily life and ask about your cognition, mood, vision, exercise and sleeping habits. There will also be questions about your response to PD medications. The physical examination will measure the speed and ease of your ability to move. You are free to skip any questions that you would prefer not to answer. Then, we will administer a set of tests of your memory and thinking abilities, attention, and vision using paper and pencil, or a computer.

Cycle ergometry:

If you remain eligible after the testing above, you will be asked to ride an exercise bicycle while we measure your heart rate, breathing rate and oxygen use, and blood pressure. Before you begin the exercise, monitors will be taped to your skin to monitor your heart and lung function. You will be instructed to wear a nose clip, and a mouthpiece or a full-face mask. You can wear whichever mouthpiece or face-mask is most comfortable; either device is connected to a monitor that measures airflow in and out of your mouth. We will place a blood pressure cuff on your arm. You will then ride an exercise bicycle. You will warm up for three minutes without any resistance. Then the resistance will steadily increase such that it becomes more difficult to pedal. You will be encouraged to pedal until you feel that you are no longer able to do so. It is anticipated that it will take 10 minutes to reach this point. A physician will be present during all exercise sessions. The physician may end the test early if it appears unsafe to continue. After exercise, you will be monitored until your heart rate and blood pressure return to normal.

For those individuals who participated in [redacted] study 'Mid-frontal delta/theta and cognitive control', we will use your electroencephalogram (EEG) data from that study in our research. All other individuals will complete the following study procedure.

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EEG:

We will attach electroencephalogram (EEG) leads to your scalp that will record your brain activity. This involves the use of gel, glue, and tape. We will also apply modest pressure to your scalp and face to make sure they stay in place. As a result, you may have some minor markings on your face and your hair may be a bit messy or damp afterwards. This will take approximately 45 minutes to complete.

- We will collect EEG data during the resting state (sitting during eyes open/closed) for ~3 mins.

- You will do an interval-timing task in which we measure how well you estimate time.

- You will do an oddball detection task, in which a series of auditory cues are presented and you have to respond when a different cue is presented (e.g. tones vs. birdcalls).

- You will do a stop-signal reaction time task in which you respond to a signal to go or a signal to stop.

- You will press a right- or left button in response to the words "right" or "left" presented to the screen or either ear via headphones.

- You may do a working memory test in which you view a series of faces, letters, or numbers on the screen.

- You may do a task switching task in which you will learn and perform certain keyboard responses to sound cues.

- You may do a multi-source interference task in which you will be identifying and responding to certain number stimuli on the screen.

Each cognitive task will take about 15 minutes. During all cognitive tasks, we will measure your brain activity via electroencephalogram (EEG) leads that we have applied. The recording of brain activity is painless. An experimenter will monitor this closely throughout the entirety of the experiment.

2) BASELINE VISIT:

If you are eligible to *continue*, you will be asked to return for an all day visit within 2 weeks of the Screening Visit. To assess the movement impairment and the brain changes on MRI due to PD more accurately, you will be asked to not to take your Parkinson's medications after 8:00 PM the previous night. However, please take your other medications and have a light breakfast in the morning upon waking up and bring your Parkinson's and other

medications for the day with you to the appointment. You will be asked to report at 8:00 AM to the UIHC Neurology Outpatient Clinic (as above). You will be able to take your PD medications again around 9:30-10:00 AM after the movement and MRI testing is completed (this is called "OFF period" testing). However, if you feel uncomfortable and would like to take your PD medications before these tests are completed, please let us know. Then, we will have you take your medications and resume testing after they start to work and you feel comfortable again (the "ON period"). You will continue taking your Parkinson's and other medications for the rest of the day as usual. All testing after the MRI will be done when your Parkinson's medications are working ("ON period"). The activities of the Baseline Visit will end around 5:00 PM.

The sequence of procedures of the Baseline Visit are as follows:

- Motor testing (15 - 20 minutes)
- MRI (2 sessions of 30 minutes each)
- Taking Parkinson's medications and waiting till they take effect. You will continue taking your Parkinson's and other medications for the rest of the day as usual. All other testing will be done when your Parkinson's medications are working (ON period).
- Cognitive and motor tests (1.5 - 2 hours)
- Lunch
- Road test in the instrumented vehicle after verification of driving license (45 - 60 minutes)
- Randomization
- Instructions on the assigned study intervention (1.5 - 2 hours)

Cognitive and motor (movement/mobility) testing:

These tests will be similar to what you experienced during the Screening Visit; however, this time the tests will be a little longer and more detailed.

Magnetic Resonance Imaging (MRI):

This imaging session involves the use of an MRI scanner which will be used to investigate the characteristics of brain tissue. The images for this study are not being used to evaluate your health. The images obtained for this study are for specific research purposes and are not being used to find medical abnormalities. These images will not be reviewed by a radiology physician to diagnose existing abnormalities.

An MRI scanner takes pictures of the inside of your body by sending out a magnetic field and radio waves. Because the MRI scanner contains a very strong magnet, you may not be able to have the MRI if you have certain

kinds of metal in your body. Someone will ask you questions about this before you have the MRI. You should not participate if you have any of the following:

- pacemaker
- defibrillator
- deep brain or nerve stimulator
- bullets
- shrapnel
- metal slivers

Please inform us if you have ever worked at or near a metal working or construction site. Also tell us if you have had surgery of any kind.

You should also not participate if you have any if the following conditions:

- Anxiety attacks
- Panic disorder
- Claustrophobia
- Pregnant, or trying to become pregnant
- Breast feeding

Many of these conditions would not keep you from having an MRI that was ordered by your doctor but do nevertheless exclude you from this research study.

The MRI scanner is a large machine that contains a hollow tube. You will be asked to lie on your back on a special table that slides into the tube. The sides of the tube will be close to your body and the scanner makes a loud hammering noise while you are inside. You will be able to talk to people in the room through a speaker system. We will monitor you closely while you are inside the scanner.

The following procedures are involved in preparing for the scan. You will be asked to use the restroom prior to beginning the scan, because once the study has started, this is very difficult to do. You will also be asked to remove all metal objects before entering the scan room.

You will then lie on your back on the scanner bed. A sensor that monitors your heart rate and blood oxygen will be placed on a finger on your right hand. An expandable belt will be placed around your lower chest to monitor your breathing. The scanner makes a loud “knocking” or “whooping” noise, so you will be given earplugs or

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insulated headphones to reduce the noise you hear. Padding will be placed around your head to help you hold your head still during the scan. A strip of adhesive tape will be placed across your forehead for the same reason.

A plastic "cage" will slide over your head. This device acts like a radio antenna and receives the signals that produce the pictures of your brain. It has a mirror which allows you to see outside the scanner, toward the control room. A plastic funnel connected to a tube and microphone will be positioned to allow us to record what you say during the study. You will be placed inside the magnet. Your head must be in the center of the magnet for us to obtain the pictures. There are no needles or injections involved.

The imaging will take place in 2 different scanners and you will spend about 30 minutes in each scanner. During imaging, you will be asked to lie quietly in the magnet. In order to gather accurate photo information, it is important that you try your best to hold completely still during the entire time you are in the magnet. You should hold relatively still in between pictures as well.

At all times, we will be in two-way communication with you. Even with earplugs, you will be able to hear us talk to you over the intercom, and you will be able to talk to us in the control room through a speaker system. You can notify us at any time if you become uncomfortable. The study may be stopped at any time. When the scans are completed, you will be taken out of the magnet and all monitoring equipment will be removed.

Will I Be Notified If My Data And Images Result In An Unexpected Finding?

The results from the test data and MRI images we collect in this research study are not the same quality as what you would receive as part of your routine health care. The images obtained for this study are for specific research purposes and are not being used to find medical abnormalities. The test data and MRI images results will not routinely be reviewed by a clinical expert who normally reads such results. Furthermore, the final research review of data and MRI images may not take place until the end of the study when the results are analyzed. Due to this, you might not be informed should any unexpected findings occur. However, if our team notices an unexpected finding during the preliminary review of MRI images, we will show the image to a diagnostic radiologist who will then advise us on how to proceed. If the abnormal image presents a medical concern, a physician will contact you to explain that concern to you. In order to reduce the risk that we unnecessarily upset someone about an abnormal image, we will not allow you or anyone with you to see the pictures at the time of the study. The results of your test data and MRI images will not be placed in your medical record with your primary care physician or otherwise. If you believe you are having symptoms that may require care, you should contact your primary care physician.

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Road test:

This road test takes place on a standard ~20-mile route in and around Iowa City using a specially outfitted vehicle (sedan) that belongs to the University of Iowa. Before the road test, we will verify that you have valid U.S driver's license. You need to show a current and valid U.S.A. driver's license to complete this test. The road test is performed under the supervision of two researchers. The test will take place during daylight hours, in good weather, and on paved roads. This testing may need to be postponed in case of inclement weather. Before the road test, we will check your preparation to drive in an empty parking lot and have you get used to the car. You will be expected to make standard maneuvers like a right turn or a left turn, stopping at a stop sign, and driving on a straight road. In a ~1-mile section of the test, you will be given a route to remember and follow. Along another ~ 1-mile segment, you will be asked to look for and report verbally on traffic signs and restaurants.

Randomization and instructions on the assigned study intervention:

You will be randomly assigned to receive one of the **2** study treatments, either the Aerobic Exercise Program or PD Health Education Program. This means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have a **50/50** chance of receiving any one of the study treatments. Some members of the research team will not know which study treatment you are receiving, but they will be able to get this information quickly if they need it to ensure your safety.

You will receive special written instructions based on your assigned program. These instructions will be reviewed with you at the end of the Baseline Visit.

3) INTERVENTION PERIOD

The time commitment for the intervention program is one year.

Aerobic Exercise Training Program:

The exercise will be in the form of brisk walking that is able to elevate the heart rate (this is how aerobic exercise is defined). You will do your walking sessions in an outdoor or indoor location of your choice in your own community on your own using our instructions (please see separate instruction sheet). Please choose a comfortable and safe exercise route of that provides an even surface and is free obstacles and steep uphill or downhill sections. Before you start your exercises, our team will review possible local exercise location options with you. Please always have your cell phone with you and notify a family member or friend about your whereabouts before you start your exercises session. Please do not engage in other activities such as walking your dog or listening to music

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during these exercises because such activities can distract you and increase the risk of injury.

Your compliance with exercise program will be monitored using a Polar electronic heart rate monitor, which consists of a watch like small wrist computer and a chest strap that picks up heart rate like an ECG and transmits it to the wrist unit. The research team will help to set it up during this visit and instruct you how to use it. You will also be asked to create a personal account with Polar Flow website with guidance from the research team and permit key members of the research team to become your "Follower" so that the research team can monitor exercise data remotely over the internet (please see separate instruction sheet). You will be asked to wear your heart rate monitor watch and heart rate sensor chest strap at the beginning of each exercise session and record the session. You will be asked to synchronize the heart rate monitor with your computer or smartphone after each exercise session.

PD Health Education Program

PD specific health education will be provided by on-line links through a VA web page for education of PD patients. You will receive special written instructions if you are assigned to this program. Please note that all content and media links on this page have been provided for informational purposes only. It is not intended to be a substitute for professional medical advice and should not be relied on as personal health advice. Always seek the guidance of your doctor or other qualified health professional with any questions you may have regarding your Parkinson's disease. Never disregard the advice of a medical professional, or delay in seeking it because of something you have read or watched or heard from the links provided on this page.

The following applies to individuals in either program:

Exercise outside of the study intervention:
The participants in either program will be free to continue their existing exercise habits or to get involved in new programs on their own. We will inquire about exercise outside of the study program during biweekly phone calls.

Care of PD during the study intervention:
The participants in either group continue to receive their medical treatment for Parkinson's disease from their primary neurologist and other healthcare providers as necessary. We will keep track of changes in your treatment for PD throughout the study.

4) FOLLOW-UP PHONE CALLS

The research team will call you every two weeks to check on you and discuss if you have any problems with

intervention, adverse events, changes in health, or physical activity in addition to study intervention. If necessary, a research clinic visit may take place to address emerging issues.

5) INTERIM FOLLOW UP VISIT AT 6 MONTHS

This visit is expected to last 1-1.5 hours and will consist of an interview for review of compliance and adverse events and extra-study physical activities, and a physical examination.

6) "Safety Check" after the administrative hold is lifted

Unless it falls within 2 weeks of a scheduled 6-month Interim Visit, you will be asked to return to the hospital to complete an additional "safety-check" interim visit with Dr. Uc to ensure you can safely continue on with the study when the Administrative Hold on Research by the VA-ORD is lifted. This visit is expected to last 1-2 hours and will consist of an interview and physical examination, questionnaires and walking tests to review your current health status as a safety check after the stay home period due to the COVID-19 pandemic when your usual medical care and lifestyle might have been disrupted.

7) FINAL VISIT:

Within 1 week after completing the intervention, you will be asked to return for a full day visit that is similar to the Baseline Visit. To assess the movement impairment and the brain changes on MRI due to PD more accurately, you will be asked to not to take your Parkinson's medications after 8:00 PM the previous night. However, please take your other medications and have a light breakfast in the morning upon waking up and bring your Parkinson's and other medications for the day with you to the appointment. You will be asked to report at 8:00 AM to the UIHC Neurology Outpatient Clinic (as above). You will be able to take your PD medications again around 9:30-10:00 AM after the movement and MRI testing is completed (this is called "OFF period" testing). However, if you feel uncomfortable and would like to take your PD medications before these tests are completed, please let us know. Then, we will have you take your medications and resume testing after they start to work and you feel comfortable again (the "ON period"). You will continue taking your Parkinson's and other medications for the rest of the day as usual. All testing after the MRI will be done when your Parkinson's medications are working ("ON period"). The activities of the Final Visit will end around 5:00 PM.

The sequence of procedures of the Final Visit are as follows:

- Motor testing (15 - 20 minutes)

- MRI (2 sessions of 30 minutes each)
- Taking Parkinson's medications and waiting until they take effect. You will continue taking your Parkinson's and other medications for the rest of the day as usual.
- Questionnaires, cognitive and motor tests (1.5 - 2 hours)
- Lunch
- Road test in the instrumented vehicle after verification of driving license (45-60 minutes)
- Cycle ergometry (30 minutes)
- EEG (1.5 – 2 hours)

COVID-19 related action regarding delay of Visits:
Due to the pandemic, some time-sensitive visits may not be completed within the time interval required by the study protocol (e.g., Baseline Visit within 2 weeks of Screening Visit). In such cases, we would need to restart the process to abide by the study protocol. For example, if the Baseline Visit cannot be done within 2 weeks of Screening Visit, then we need to restart with the Screening Visit when the pandemic permits.

Data Storage for Future Use

As part of this study, we are obtaining data on how your PD affects your movement ability, cognition, psychology, health, driving, and brain. We would like to study your data on these characteristics in the future, after this study is over.

Your information and data may be placed in a central repository or other national repositories sponsored by the National Institutes of Health or other Federal agencies. If this happens, it may be stripped of identifiers (such as name, date of birth, address, etc.). Other qualified researchers who obtain proper permission may gain access to your sample and/or data for use in approved research studies that may or may not be related to in the purpose of this study.

The tests we might want to use to study your data may not even exist at this time. Therefore, we are asking for your permission to store your data so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding PD, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your data might be used to develop products, tests, or discoveries that could be patented and licensed. In some instances, these may have potential commercial value and may be developed by the Investigators, University of Iowa, commercial companies, organizations funding this

research, or others that may not be working directly with this research team. However, donors of the data do not retain any property rights to the materials. Therefore, there are no plans to provide financial compensation to you should this occur.

Your data will be stored *with a code which may be linked to your name, date of birth, and date of testing* **that would enable us to identify which data are yours**. If you agree now to future use of your data but decide in the future that you would like to have it removed from future research, you should contact the PI, Dr. Ergun Uc (phone: [redacted]). However, if some research with your **data** has already been completed, the information from that research may still be used.

Please place your initials in the blank next to Yes or No for the question below:

My data may be stored/shared for future research for any other purpose.

____ Yes ____ No

My identifiable data may be shared with [redacted], also a member of this research team, for other research purposes.

____ Yes ____ No

Audio Recording/Video Recording/Photographs

One aspect of this study involves making **audio and video recordings** of you. By participating in this study, you consent to such audio and video recordings.

All driving will be recorded using digital video/audio recorders that are placed so that we are able to view the forward and side driving views and yourself (above shoulders). The placement of the cameras will not obscure your view and will allow the researchers to record your response to driving events. We will also collect data about the time, latitude, longitude, speed, heading, brake position, steering angle, and throttle position throughout the drive. These recordings are necessary for the researchers to assess your driving performance. Access to this data will be under the supervision of study investigators. Data analysts assigned to work on this project will also have access to the data. Data gathered during this study will be kept indefinitely.

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Contacting for future studies:

We might contact you again about being in one of our future studies. Therefore, we would like to keep your name, sex, date of birth, and contact information. Please note that agreeing to be in our current study does not obligate you to participate in one of our future studies. A separate Consent Document would be signed for future studies.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

EMOTIONAL OR PSYCHOLOGICAL RISKS:

- Inconvenience in traveling to and from the medical center for evaluations.
- You may become tired during the assessments and will be given rest periods if necessary.
- Withholding Parkinson's medications overnight lead to discomfort due to decreased mobility and emergence of non-motor symptoms such as anxiety and low energy level. This a commonly done procedure when PD patients are evaluated for DBS. Thus, our team is experienced in this procedure and you will be examined by a Parkinson's neurologist in the morning. We will ensure safe and convenient transport while you are off your Parkinson's medications in the morning.
- You may experience frustration during motor and cognitive testing and questionnaires. You may become bored and fatigued, but you will be given frequent rest periods to guard against this.
- You may experience claustrophobia during MRI.

FINANCIAL RISKS:

- Traveling to and from the medical center for evaluations will incur costs, but the study will pay for mileage and parking per institutional guidelines.
- The study visits and exercises may prevent you from engaging in occupational activities.
- Involvement in a car crash during the road test or injury during exercise or testing can lead to medical expenses, loss of earning opportunity, and increase in insurance premiums.

LEGAL OR SOCIAL RISKS:

- Loss of confidentiality is always considered a risk.
- Involvement in a car crash during road test may lead to legal risks.

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PHYSICAL RISKS:

Cognitive and motor testing, questionnaires:

- No physical risks associated with the interview, physical examination, paper-and pencil, and computerized tests. There may be fall risk during walking tests.

Exercise testing on a stationary bicycle:

- Exercising to maximum effort may make one feel uncomfortable and cause muscle strains.
- In individuals with heart or lung disease, exercise may cause changes in heart and lung function that may be life threatening, although this is rare.
- You will be monitored by a physician during the exercise testing and following the testing until your heart rate and blood pressure return to normal.

MRI Scan:

The possible risks from having an MRI for the study are the same as those for a clinical MRI:

- A metal object flying toward the magnet and hitting you comprises the greatest risk associated with MRI. To reduce this risk, we require that all persons who enter the scanner room remove all metal from their clothing and pockets. No metal objects will be brought into the magnet room while you are inside the room. In addition, the door to the room remains closed throughout the entire study so that no one accidentally can bring a metal object into the room.
- You may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time.
- The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of people. You will be given earplugs to reduce this risk.
- There is a risk of loss of confidentiality of your medical information. We will use a study number and not your name to identify any information or images collected for the study. To protect your confidentiality, only the investigators will be able to view your images in the MRI control room.

Exercise Training:

- Engaging in an exercise program, especially if you have been sedentary for a considerable period, creates risk of injury such as falls, strains, sprains, muscle soreness, aggravation of arthritic conditions. There is a risk bodily injury and death. Exercising on level ground and avoiding distractions during exercise may reduce risk of injury.
- Heart and lung problems such as angina, heart attack, asthma attack: Please discontinue the exercise if you have trouble breathing, pain in chest, left neck, shoulder or arm, and immediately seek medical attention.
- Please inform our research team as soon as possible if any of these adverse events occur during training.

Road test:

- You will be asked to drive a vehicle that will travel in a public parking lot and on public roads. Risks associated with driving a motor vehicle during the study are the same as those encountered while driving outside of the study on paved city roads and state/federal highways during non-inclement weather and in daylight. However, risk of car crash with serious injury or death exists as with any road drive. You will be required to wear your seatbelt. Two researchers will be present in the vehicle always.
- All data collection equipment is mounted so that, to the greatest extent possible, it does not pose a hazard in any foreseeable way. None of the data collection equipment interferes with any part of your normal field of view. The addition of the data collection systems to the vehicle will in no way affect the operating or handling characteristics of the vehicle.
- Please note that because your driving is being monitored does not in any way mean that you are safer driving than they are while not being monitored. Should any problem arise, the drive can be interrupted at any time and the study personnel will take over driving.
- If you are involved in a motor vehicle crash while driving as part of this study, the University's automobile insurance will provide coverage for injury or damage to a third party. If it is determined that you are at fault for the crash, the University will not pursue a claim against you or your insurance carrier if the accident occurs while you are performing research-related activities.

EEG:

- Before applying electroencephalogram (EEG) leads on your scalp, we will use a skin prep gel to prep your scalp. The gel is commonly used for electroencephalogram (EEG) studies in epilepsy clinics. Since it is abrasive, there is a risk you may feel uncomfortable.

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WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because the information gained in this study can help develop exercise programs which can improve the mobility, cognition, and quality of life of patients with PD.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your study doctor will discuss the other options that are available to you. You do not have to take part in this study to receive treatment for your Parkinson's disease. You will continue treatment of your PD as determined by your neurologist or other healthcare providers. This study will test the effect of aerobic exercise in Parkinson's disease. Unlike medications or surgery such as deep brain stimulation that have been approved by the Food and Drug Administration, there are no officially approved exercise programs in PD. Instead of being in this study, you could do aerobic or other exercise on your own or participate in one of the programs in the community after consulting with your healthcare providers. Please note, participation in this study will not require you from refraining in participating in any other exercise programs in addition to the exercise program offered by this study.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. We typically make direct deposit payments from the VA to your bank account. Thus, we need your bank account information such as the name of the bank, your account number, and the routing number of the bank. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will earn compensation at a rate of $20 for the group of tests and questionnaires on motor and cognitive function and quality of life; $20 for the MRI; $20 for the exercise test; and $20 for the driving test. Thus, if you complete all procedures, you will be paid $40 for the Screening Visit, $60 for the Baseline Visit, $20 for the

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Interim Visit, and $80 for the Final Visit. There will be no payments for the biweekly phone calls. Your payments will be processed after completion of the Baseline Visit and again at the end of the study. The participants in the aerobic exercise group will keep the electronic heart monitor (about $200 value).

You may also be compensated for meals and travel depending on how long the visit is and the distance traveled. Participants in the local area (e.g., Iowa City, Coralville, and North Liberty) will not be compensated for travel expenses but may qualify for meal compensation depending on the length of the visit. Compensation for travel and meals will be based upon the institutional guidelines.

Total compensation will vary depending on the intervention arm you are assigned to and on the number of study procedures (e.g., MRI, road test, etc.) you participated in. There will be no pro-rating for incomplete procedures. For example, an Iowa City resident who is assigned to aerobic exercise and completed all study procedures would receive a total compensation of $200 + the heart rate monitor.

DO THE RESEARCHERS HAVE PERSONAL FINANCIAL INTEREST IN THIS STUDY?

No.

WHO IS FUNDING THIS STUDY?

This research is funded by the Merit Review program of the Rehabilitation Research and Development Branch of the Department of Veterans Affairs. This means that the Iowa City Veterans Administration is receiving payments from the Department of Veterans Affairs to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from for conducting this study. Dr. Ergun Uc is the principal investigator of this study.

This research study will also use the resources of the Institute for Clinical and Translational Science of the University of Iowa, which is funded by the National Institutes of Health (NIH). This means that the University of Iowa is receiving payments from the NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIH for conducting this study. Discretionary funds from the University of Iowa Department of Neurology may also be used if necessary.

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WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- The US Department of Veterans Affairs (the funding agency)
- Iowa City VA Health Care System
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, records of participation in this research will be maintained in locked files of the Department of Neurology, University of Iowa. The electronic data will be kept on the server in secure shared servers at the University of Iowa; these servers are password protected. The subjects' names will be separated from their data. A coding scheme will be employed to identify the data by subject number only (e.g., Participant No. 3). Results of the research may be used for publication in professional journals, and presentations at professional meetings. If we write a report or article about this study, we will describe the study results in a summarized manner so that you cannot be directly identified.

At the Veterans Administrations Medical Center
A copy of the Informed Consent Document may be placed in your medical record.

At the University of Iowa Hospitals and Clinics
The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

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Data collected from the video recordings and a report of the investigators' findings may be shared with the UI General Counsel Office. The data will include information that could identify you. Under extreme and extraordinary circumstances and under advisement from the General Counsel, law enforcement may be provided information that includes your identity.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate means that the researchers cannot be forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the researcher from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you request in writing that information about you or your participation in the research be released to an insurance company, the researcher may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own privacy. Finally, the researcher is not prevented from taking steps, including reporting to appropriate authorities, to prevent serious harm to yourself or others. You may receive a copy of the Certificate of Confidentiality upon request.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. A copy of the informed consent document will be available on this website. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

There will not be any adverse consequences (physical, social, economic, legal or psychological) of your decision to withdraw from the research.

If you decide to leave the study early, we will ask you for the reasons for dropping out and we will offer you to return for the Final Visit one year after the Baseline Visit. The procedures of the Final Visit are described above. You are not obliged to come for the Final Visit or to complete all procedures during that visit.

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Department of Veterans Affairs

VA RESEARCH CONSENT FORM

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Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because for a variety of different reasons, including because in our judgment it would not be safe for you to continue, because your condition has become worse, because funding for the research study has ended, or because the sponsor has decided to stop the research.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Ergun Uc, M.D., [redacted] If you experience a research-related injury, please contact: Ergun Uc, M.D., [redacted] the UIHC operator and ask to contact Dr. Uc immediately.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, The University of Iowa, Iowa City, Iowa, 52242, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. A copy of the VA brochure 'Volunteering in Research,' (found at http://www.research.va.gov/programs/pride/veterans/Volunteering-in-Research.pdf) has been provided to the prior to signing this informed consent document. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

RESEARCH SUBJECT'S RIGHTS

I have read or have had read to me all of the above. The study team has explained the study to me and answered all my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

Department of Veterans Affairs

VA RESEARCH CONSENT FORM

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I have been told that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The Iowa City VA Health Care System is available to provide necessary medical treatment for any injury resulting from participation in this research study. I have been told that I will not be required to pay for care received as a subject in this study except in accordance with federal law (Title 38 United States Code 1710(f) and 1710(g)) and that certain veterans are required to pay co-payments for medical care and services provided by the VA.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Signature Date

As the subject's Legally Authorized Representative I have been told that my obligation is to try to determine what the subject would do if he/she were competent. If I can't determine what the subject's wishes would be, I have been told that by obligation is to do what I think would be in the subject's best interest.

Signature of Subject's Authorized Representative* Date
*Required only if subject is not competent

Subject's Representative & Relationship (print)

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STATEMENT OF PERSON WHO OBTAINED CONSENT

I have discussed the above points with the subject or, where appropriate, with the subject's authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

Signature of Person who Obtained Consent

Date

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