**COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY**

**YALE UNIVERSITY SCHOOL OF MEDICINE**

**Study Title:** Effects of Cognitive Training on Everyday Cognitive and Brain Function in Parkinson's Disease.

**Principal Investigator (the person who is responsible for this research):** Dr. Sule Tinaz, Yale University, Department of Neurology, 15 York Street, PO Box 208018, New Haven, CT 06520-8018.

**Phone Number**: 203-737-6158

**Research Study Summary:**

- We are asking you to join a research study.
- The purpose of this research study is to determine whether cognitive training will improve cognitive and brain functions in people with Parkinson's Disease (PD) during activities of daily living using cognitive evaluations and magnetic resonance imaging (MRI).
- Study procedures will include: A phone call and videoconference (Zoom) for screening and 4 separate in-person visits to the Yale Magnetic Resonance Research Center (MRRC) in The Anlyan Center (TAC). Some of these visits may also take place at the Yale Center for Clinical Investigation (YCCI). You will be asked to complete neurological exams, standardized cognitive tests, surveys, cognitive training, and a total of three MRI scans. You will also be assigned homework to assess your progress.
- Four visits are required.
- These visits will take 11 hours total over a period of 22 weeks.
- There are some risks from participating in this study. Potential risks are from 1) MRI scanning, 2) Loss of confidentiality, and 3) Unanticipated events
- The study may have benefits to you. You may benefit from the cognitive training in terms of improvement in cognitive functioning during activities of daily living. Additionally, the knowledge gained from this study will facilitate future research. Through this research, it is possible that cognitive training will be incorporated into rehabilitation programs and will lead to improvements in the treatment of cognitive problems for people with PD.
- There are other choices available to you outside of this research. For example, you can enroll in a variety of different cognitive rehabilitation and brain training programs both online and in-person.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

**Why is this study being offered to me?**

We are asking you to take part in a research study because you are age 40 or above, are physically independent, and have PD. We are looking for approximately 120 participants to be part of this research study.

**Who is paying for the study?**

This study is currently funded by the National Institutes of Health-National Institute of Neurological Disorders and Stroke (NIH-NINDS).

**Who is providing other support for the study?**
No one.

**What is the study about?**
The purpose of this study is to determine whether cognitive training will improve cognitive and brain function in people with PD during activities of daily living using cognitive evaluations and MRI scans.

**What are you asking me to do and how long will it take?**
If you agree to take part in this study, this is what will happen:
This study will use two types of cognitive training: 1) Mental imagery training or 2) Psychoeducation. Mental imagery means forming mental pictures in the mind. Various forms of mental imagery have been used in psychology for health or performance benefits. Psychoeducation refers to an educational model that informs learners of the cognitive impact of their condition (in this case PD). You will be randomly assigned to one of these groups. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researchers will choose the group. You will have an equal chance of being placed in any group.

You will also perform tasks in the MRI scanner: 1) You will perform mental imagery of everyday tasks (for example, preparing a meal, planning an event), 2) You will watch video footage of everyday tasks. MRI is a medical imaging technique that uses magnetic fields to take pictures of structures inside the body. In this case, it will show us how your brain behaves during mental imagery and video watching.

If you agree to take part in this study, you will be asked to complete a screening assessment, online surveys, cognitive training, homework assignments, and four in-person research visits which will include neurological exams, standardized cognitive tests, surveys, and three MRI scan sessions. The total time commitment of all procedures is approximately 13 hours. You will continue to take your PD medications as scheduled throughout the study. The details of the procedures are described below.

Summary of procedures

| **Study Procedure** | **When/where** |
|---|---|
| Initial phone screening (MRI safety, health questionnaires) | Where: phone call<br>When: during initial screening session |
| Video screening (Consent, and cognitive evaluations) | Where: videoconference (Zoom)<br>When: during follow-up video screening session |
| In-person clinical and cognitive evaluations | Where: Yale MRRC or YCCI<br>When: visits 1 & 3 & 4 |
| Cognitive training (mental imagery or psychoeducation) and homework assignments | Where: videoconference (Zoom) and online<br>When: following visit 2 over the course of 6 weeks |

| | |
|---|---|
| 3 MRI scans:<br>1. Baseline<br>2. After 6 weeks<br>3. After 12 weeks | Where: Yale MRRC<br>When: visit 2 & 3 & 4 |

Description of Procedures and Estimated Durations

**Phone Call:** MRI safety screening and health questionnaires (15 min)

**Videoconferencing (Zoom**): Consent and brief cognitive evaluations (45 min)

**Online Surveys**: Brief questionnaires on emotions, fatigue, sleep, and quality of life (30 min)

**Visit 1:** Clinical and cognitive evaluations (3 hrs)

**Visit 2:** Practice of tasks outside the MRI scanner and subsequent MRI scans (2 hrs)

**Training and Homework:** Cognitive training (mental imagery or psychoeducation) via Zoom and online homework assignments (6 weeks).

**Visit 3:** Clinical and cognitive evaluations, and MRI scans after 6-week training (3 hrs)

**Visit 4:** Clinical and cognitive evaluations, and MRI scans 12 weeks after Visit 3 (3 hrs)

The visits and procedures are described in detail below.

Consent and Initial Screening

First, you will be contacted by a member of the research team via phone call to screen for MRI safety and medical history. If you are still eligible for the study, you will meet with a member of the research team on a videoconference via Zoom. The researcher will describe in detail the purpose of this study, the research procedures that will be used, any risk that these procedures might entail, as well as any possible benefits. You will be encouraged to ask questions and you will be given enough time to discuss any aspect of the study you wish to know more about. Subsequently, you will have to demonstrate understanding of the study procedures and what is expected of them. Once a clear understanding is demonstrated, you will be asked to electronically sign the consent form.

If you consent to the study, you will be screened for demographic data and cognitive functional abilities. The cognitive tests will evaluate skills such as memory, attention, and language. In total, the screening process will take approximately 15 minutes via phone and 45 minutes via Zoom.

If you pass the initial screening, you will be asked to fill out brief surveys with questions about your emotions, levels of fatigue and sleepiness, and quality of life. The online surveys will take approximately 30 min to complete. You will then be invited to come to Visit 1.

Visit 1: Clinical and Cognitive Evaluations

Within two weeks of the screening, you will come to Yale for Visit 1. During Visit 1, a standard neurological exam will be performed by one of the neurologists working on this study. Your motor

function will be evaluated using the standard PD rating scale. During this evaluation, you will be asked to perform simple tasks, such as tapping your fingers, holding your arms stretched out in front of you, or stomping your foot on the ground. Additional cognitive tests will be administered during Visit 1 for a more comprehensive evaluation of skills such as memory, attention, and language. These tests will include tasks like basic arithmetic, picture naming, and dictation. You will also be asked to answer questions about your day-to-day life to assess your cognitive functioning. If you pass the cognitive tests, you will be randomly assigned to either the mental imagery group or psychoeducation group. In total, Visit 1 will take approximately 3 hours.

Visit 2: MRI Scans, Training Instructions, and Homework Assignments

MRI Scans

A member of the research team will accompany you to the MRRC and will stay with you for the duration of the MR study.

Within two weeks of Visit 1, you will return to Yale for Visit 2. During Visit 2, you will complete a questionnaire that assess the quality of your mental imagery skills. You will then receive instructions for the mental imagery and video-watching tasks that you will complete in the MRI scanner. The MRI session will include both structural imaging, which shows us what your brain looks like, and functional imaging, which shows us how your brain behaves during tasks.

Inside the scanner, you will first complete tasks during which you will imagine yourself in various scenarios of everyday living. After each imagery scan you will answer a series of short questions about the content and overall quality of your experience. In total, there will be four imagery scans each lasting approximately 5 minutes.

Subsequently, you will watch four different videos of day-to-day activities while inside the scanner and answer a series of short questions about the content of the videos. In total, there will be four video-watching scans each lasting approximately 5 minutes.

The entire MRI scan session will last not more than 1 hour.

A debriefing session will take place after the scanning to assess other aspects of your experience. In total, Visit 2 will take approximately 2 hours.

Training and Homework Assignments

Following Visit 2, both the mental imagery group and the psychoeducation group will complete **six weeks** of training and homework assignments.

**If you are assigned to the mental imagery group:** You will receive personalized training during one-on-one sessions through Zoom 3 times a week for the first 4 weeks. You will be guided to mentally simulate the planning and implementation of everyday tasks (for example, going grocery shopping). The training sessions will last about 15-20 min. We will also record mental imagery scripts for you to use as self-practice on non-training days in the first 4 weeks and for daily self-practice that will take place in the subsequent 2-week period. After each self-practice, you will be asked to submit a daily mental imagery diary via an online survey platform. You will be asked to report on key elements of your mental imagery content and experience including the setting, objects, sensations, movements, emotions, and vividness. A member of the research team will call you once a week in the last 2 weeks to check in.

**If you are assigned to the psychoeducation group:** You will receive psychoeducation 3 times a week for 4 weeks regarding cognitive functioning and brain health in PD. You will receive private video links with pre-recorded PowerPoint lectures covering topics such as basic brain anatomy, physical activity, diet, and more. The lectures will last about 15-20 min. On no-lecture days in the first 4 weeks and in the subsequent 2-week period, you will be assigned quizzes through an online survey platform that cover the lecture topics you received. A member of the research team will call you once a week in the last 2 weeks to check in.

Visit 3: 6-week Cognitive Evaluations and MRI Scans

Six weeks following Visit 2, you will be asked to return in-person to Yale to assess the short-term benefits of your assigned cognitive training. Visit 3 will begin with you completing a questionnaire that evaluates the quality of your mental imagery skills. You will also undergo cognitive testing to evaluate skills such as memory, attention, or language. Lastly, you will enter the MRI scanner and be assigned mental imagery and video-watching tasks followed by short questions similar to those that you completed during Visit 2. Each scan will last approximately 5 minutes. The entire MRI scan session will last not more than 1 hour. In total, Visit 3 will take approximately 3 hours to complete.

After Visit 3, there will be no formal homework or training assignments. However, if you are in the mental imagery group, you will be encouraged to incorporate mental imagery into your daily life, and if you are in the psychoeducation group, you will be encouraged to retain the psychoeducational information you learnt. Following these guidelines will help us measure the sustained effects of your assigned cognitive training over the following 12-week period.

Visit 4: 12-week Cognitive Evaluations and MRI Scans

Visit 4 will be scheduled 12 weeks following Visit 3 to assess the sustained benefits of your assigned cognitive training. It will be a repeat of all the procedures previously performed during Visit 3 including assessing the quality of mental imagery, evaluating your cognition through testing, and having you complete 4 mental imagery and 4 video-watching tasks followed by short questions after each in the MRI scanner. Once again, each scan will last approximately 5 minutes. The entire MRI scan session will last not more than 1 hour. In total, Visit 4 will take approximately 3 hours to complete.

**What are the risks and discomforts of participating?**

Possible risks from participation in this study include risks from 1) MRI scanning, 2) Loss of confidentiality, 3) Unanticipated Events, and 4) Risks to pregnancy

MR Scanning*:* Magnetic resonance (MR) is a technique that uses magnetism and radio waves, not x-rays, to take pictures and measure chemicals of different parts of the body. The United States Food and Drug Administration (FDA) has set guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines. You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them. There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MR scanner might harm you. Another risk is the possibility of metal

objects being pulled into the magnet and hitting you. To lower this risk, all people involved with the study must remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet. We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety Questionnaire and be sure to tell us any information you think might be important.

This MR study is for research purposes only and is not in any way a complete health care imaging examination. The scans performed in this study are not designed to find abnormalities. The principal investigator, the lab, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a health care evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will be asked to review the relevant images. Based on his or her recommendation (if any), the principal investigator or consulting physician will contact you, inform you of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie only with you and your physician. The investigators, the consulting physician, the Magnetic Resonance Research Center, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a health care MR exam and for that reason, they will not be routinely made available for health care purposes.

Loss of Confidentiality*:* The clinical and cognitive testing components of this study are not associated with any physical risks. However, some questions may make you uncomfortable, and there is a rare chance for a possible risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Unanticipated Events: Your health and safety will always be the primary concern of the doctors and staff performing the study. In the event of an unanticipated event, all necessary medical action will be taken according to Yale University IRB guidelines for human subject protection in the setting of the Yale School of Medicine campus including the Yale MRRC and YCCI outpatient facilities, where – in addition to the medically credentialed principal investigator, Dr. Tinaz– physicians, nurses and code teams are on call to assist in any kind of unforeseen medical emergency.

Risk to Pregnancy*:* If you are a woman younger than 50 years of age and have your menses, you will receive a urine pregnancy test at each study visit. You may not participate in this study if you are currently pregnant, if you might become pregnant during the study, or if you are breastfeeding an infant. If the test is positive, you will not be included in the study.

**How will I know about new risks or important information about the study?**

We will tell you if we learn any new information that could change your mind about taking part in this study. Discovery of any clinically relevant results (for example, improvements in cognitive testing) will be disclosed to you. Furthermore, during the clinical evaluation if your answers to the questionnaires that assess your emotional wellbeing indicate feeling quite down and blue, we will provide you with information about mental health counseling services and referrals. If your answers to this questionnaire indicate imminent risk of self-harm, we will refer you to the Yale New Haven Hospital Emergency Department on the same day for further evaluation.

**How can the study possibly benefit me?**
You may experience a direct benefit from the cognitive training in terms of improvement in goal-directed behavior and cognitive functioning during activities of daily living.

**How can the study possibly benefit other people?**
The benefits to science and other people may include a better understanding of cognitive training that could be incorporated into rehabilitation programs for the treatment of cognitive problems in people with PD.

**Are there any costs to participation?**
If you take part in this study, you will not have to pay for any services, supplies, study procedures, or care that are provided for this research only (they are NOT part of your routine medical care). However, there may be additional costs to you. These can include costs of transportation and your time to come to the study visits. You or your health insurance must pay for services, supplies, procedures, and care that are part of your routine medical care. You will be responsible for any co-payments required by your insurance.

**Will I be paid for participation?**
You will be paid for taking part in this study. You will be compensated for your participation as followed:

$100 for each completed in-person visit (4 total).
$50 for the completion of each weekly training session (4 total).
$50 for the cost of parking at Yale.

The total possible compensation for this study will be $650. We will use a Bank of America pre-paid debit card to provide the payment for taking part in the study. We will have to share your name, address, and telephone number with Bank of America for ePayments. You will receive a card in the mail with the first payment. You will need to activate the card over the phone. Each additional payment will be automatically added to your card**.** You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

**What are my choices if I decide not to take part in this study?**
Instead of participating in this study, you have some other choices.
You could:

- Get treatment without being in a study. For example, you can enroll in a cognitive rehabilitation or online brain training program.
- Take part in another study.

**How will you keep my data safe and private?**
We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information such as your name, date of birth and address. Any forms with personal identifiers will be kept in a locked filing cabinet. All study data will be coded, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the principal investigator.

Electronic records will be kept on password-protected research computers and servers provided by the Yale University. The imaging data will be stored on secure and HIPAA compliant servers in the MRRC. We will use computers that are password-protected, in locked areas, and encrypted.

Upon completion of the study, study binders will be stored in a locked facility for the amount of time required by law. After this time, the study binders will be destroyed by shredding. The electronic databases will stay on the computers and servers until the study closes. The link to your personal information will be kept until the end of the study, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

The username- and password-protected Yale REDCap platform will be used for the online surveys. You will be emailed survey links individually that will generate a unique subject code linked to your records.

Password-protected Zoom conferences will be conducted using an encrypted computer connected to the Yale secure network. To ensure security, each time a different invitation link with a unique meeting ID and password will be emailed to you. As soon as you join, the meeting will be locked to prevent others from joining. The Zoom meetings will be recorded by the research team to facilitate data collection of mental imagery content and you will be permitted to record the meetings as well. Once data transcription is complete, the video recordings will be deleted. Zoom software will be updated regularly to ensure that new security features are incorporated.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission. We may also share information about you with other researchers for future research, but we will not use your name or other identifiers. We will not ask you for any additional permission.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

**What Information Will You Collect About Me in this Study?**

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Demographic information

- MRI safety screening and health questionnaires
- Neurological exam
- Cognitive test results
- Survey responses
- Homework assignments (diaries, quizzes)
- Structural and functional MRI imaging results
- Records about your study visits
- Records about phone calls made as part of this research

**How will you use and share my information?**

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- National Institutes of Health-National Institute of Neurological Disorders and Stroke (NIH-NINDS)
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Yale University MRRC where your MRI scans will occur.
- Principal Investigator of the study Dr. Sule Tinaz
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

**Why must I sign this document?**

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

**What if I change my mind?**

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to Dr. Sule Tinaz, at the Yale University, Department of Neurology, 15 York Street, PO Box 208018, New Haven, CT 06520-8018.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

**Who will pay for treatment if I am injured or become ill due to participation in the study?**

If you sustain an injury during your research visit that requires more than basic medical care, then you may choose to seek treatment through the Yale New Haven Hospital emergency room or at any other healthcare facility that you deem appropriate. If you are injured while on study, seek treatment and contact the study doctor, Dr. Sule Tinaz, as soon as you are able.
Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.
You do not give up any of your legal rights by signing this form.

**What if I want to refuse or end participation before the study is over?**
Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.
To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.
The researchers may withdraw you from participating in the research if necessary. This might happen, for example if you are found to have or develop a medical condition for which it is important that you be treated, and such diagnosis and treatment might interfere with your participation in the study or might contribute results to the study that could make it more difficult to draw accurate scientific conclusions from the research. You may also be withdrawn from the study if you are unable to comply with any of the study procedures.

**What will happen with my data if I stop participating?**
You have the ability to stop participating at any time. When your participation is terminated, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to ensure the integrity of the study and/or study oversight.

**Who should I contact if I have questions?**
Please feel free to ask about anything you don't understand.
If you have questions later or if you have a research-related problem, you can call the Principal Investigator. Dr. Sule Tinaz, at 203-737-6158.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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

**Authorization and Permission**

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

| Participant Printed Name | Participant Signature | Date |
|---|---|---|

| Person Obtaining Consent Printed Name | Person Obtaining Consent Signature | Date |
|---|---|---|