NEW YORK STATE PSYCHIATRIC INSTITUTE
Participant Consent Form
Cognitive Training and Neuroplasticity in Mild Cognitive Impairment

Principal Investigator (PI): Dr. D.P. Devanand (646[redacted])

Purpose of Study

This study is being conducted to evaluate if systematic cognitive training can improve cognitive performance in participants with memory loss. You have been asked to participate because you reported having difficulty with your memory. This study will evaluate the effects of Computerized Cognitive Training (CCT) for improvement in everyday cognitive and functional status, in addition to long-term changes in brain networks over an 18-month period.

In this study, participants will be randomly assigned to one of two cognitively stimulating exercises: either a crossword puzzle training (CPT) condition or a computerized cognitive training condition (CCT).

This study is supported by a grant from the National Institute on Aging, a division of the National Institutes of Health. Duke University and Queens College are collaborating institutions on this study.

Voluntary

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. Your decision not to participate or stop your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University Irving Medical Center.

Alternative Treatments/Alternatives to Participation

You do not have to join this study to receive treatment for your memory loss. If you decide not to participate, you can review treatment options with your doctor.

Procedures

If you agree to participate, the study will continue for up to 18 months. During this time, you will be asked to come to the Memory Disorders Center at the New York State Psychiatric Institute (NYSPI). After the screening evaluation, you will come for an initial baseline visit, in addition to follow-up visits at Week 12, Week 32, Week 52, and Week 78.

As part of an institutional COVID-19 risk reduction initiative, you will be asked to comply with infection control guidelines while on site for completion of all study assessments and procedures. These include, but are not limited to: allowing staff to take your temperature prior to entering NYSPI, Mind Brain Behavior Institute (MBBI) and Citigroup Biomedical Imaging Center (CBIC) at Weil Cornell Medical Center, wearing a mask at all times, performing frequent hand hygiene and providing the study team with information specific to whether you may have been exposed to or have active COVID-19 infection. Questions specific to COVID-19 exposure and active infection will be posed by the study team via a phone call, 24 hours before your scheduled in-person session. You will be asked again upon your arrival on site and prior to you entering any NYSPI, MBBI or Cornell building. If you report that over the past 14 days you have been exposed to COVID-19, or indicate that you are or have been ill with symptoms consistent with COVID-19, you will not be permitted to come on site or enter any facility for completion of your study assessments or procedures.

At all times while on site for in person assessments and procedures, you will be required to maintain 6 feet of distance between yourself and members of the study team, unless 6 feet or more of distance cannot be maintained, as is the case for some assessments.

Lastly, you will be required to arrive at scheduled at any facility only by private vehicle or Uber/Lyft (reimbursed by the study).

We will perform a screening evaluation. During the screening evaluation, you will be asked about your medical and psychiatric history and we will administer brief memory tests. If we determine from the screening evaluation that you do not qualify for the study, your commitment ends. However, if we find during the screening evaluation that you do qualify, we will ask you to join the study and sign the informed consent.

In order to join the study, you will also need to select an informant who will be available either in person or by phone. An informant may be a family member or friend who will be able to

provide information about you. He/She must be willing to be interviewed, in addition to having the ability to answer questionnaires regarding your memory and daily and social functioning. He/She will be asked to come with you during each of your visits to the clinic. If your informant is unable to come to the clinic, he/she will be contacted by phone by a qualified member of our team. Each interview for the informant may take approximately 30 minutes to complete, and these will be done at every visit.

The initial baseline visit is approximately 2 to 3 hours. During this visit, you can expect to encounter detailed history-taking, a neuropsychological evaluation, and several rating scales. A test of smell will be administered at this visit, which will take approximately 30 minutes. In this test, you will be asked to identify different smells on cards that emit an odor when scratched. The study staff will provide you with specific directions regarding how to complete the test while observing social distancing guidelines, specific to COVID-19 risk reduction and will provide you with the necessary Personal Protective Equipment (PPE) such masks and face shield. You will have almost 2 teaspoons of blood taken as a sample for genetic research. Additional blood samples will be taken: Chemistry (1.2 teaspoons of blood), Complete Blood Count (.8 teaspoons of blood), and Thyroid Function (1.2 teaspoons of blood). You will also receive an MRI scan of the brain, as described below. While you are at the MRI suite you will be required to adhere to the facility's COVID-19 specific infection control guidelines. If you do not adhere to these guidelines, you will not be permitted entry into the facility (MBBI or Cornell).

At the initial baseline visit, you will be given instructions on how to complete the computerized cognitive training over the following 12 weeks. Computerized cognitive training involves cognitive exercises on the computer that target specific abilities/neural networks that may improve cognitive functioning. Computerized cognitive training may include crossword puzzles, matching puzzles, and math puzzles. Computerized cognitive training tasks include Speed Pack, Disillusion, Editor's Choice, Continuum, Familiar Faces, Tidal Treasures, Speed Match, Color Match, Word Bubbles, Train of Thought, Memory Matrix, Lost in Migration, Brain Shift, Trouble Brewing, Ebb and Flow, Masterpiece, River Ranger, and Word Snatchers. Crosswords do not become more difficult over time, since they are very similar to crosswords done in daily newspapers. The goal is for participants to complete 48 at-home cognitive training sessions

during the 12-week intensive training, and 24 at-home booster sessions over the 78-week trial. Four 30-minute sessions will be completed per week and will be accessed by logging into your online account. From the visit at Week 12 and all following visits, you will receive in-clinic booster sessions of computerized cognitive training. At weeks 42 and 64, you will be asked to complete a booster session at home. Each booster session consists of 4 training sessions. It is not required that you complete the computerized cognitive training at a specific time of day. However, it is expected that you complete the computerized cognitive training exercises during a period of time during the day where you are most comfortable and expect the least interruption.

At the initial baseline visit, your study physician will advise you not to make any changes to medications in certain drug classes you may be taking during the first 12 weeks of the study, unless medically necessary. The drug classes are benzodiazepines, narcotics, and anticholinergics. This is because changes in these medications could alter your performance on the computerized training and the in-clinic memory tests.

Genetic Research

Additionally, we want to study genetic factors**,** which are inherited factors passed from parents to their children that may be associated with the risk of developing Alzheimer's disease or other related disorders. The cells of your body contain a molecule called deoxyribonucleic acid, or DNA for short. DNA is passed down from your parents and carries a code, in the form of genes, which determines your physical characteristics, such as the color of your hair and eyes, and risk for some diseases. At the baseline visit, a blood sample of approximately 2 teaspoons will be drawn to assess apolipoproteins that occur naturally in the blood stream; their function is to transport cholesterol and related substances. The presence of some types of apolipoprotein may be associated with an increased risk of developing memory disorders, though this remains to be established. Therefore, the results of the apolipoprotein E genotyping obtained from your blood sample will not be released to you. The blood sample from which the DNA will be extracted for apolipoprotein E genotyping will be stored without any personal identifying information in the Human Genetic Resources Core (HGRC) at the Columbia University Irving Medical Center. The HGRC arranges to have the apolipoprotein E genotype determined from the sample and then sends the results to the Principal Investigator in this study. Participants will not be eligible to

share in any revenue that may result from future potential commercialization of this genetic research.

Your blood sample from which the DNA will be extracted will be labeled with the same number used in the other parts of the trial (your study ID number). The sample will not have your name, initials, or address on it. No one at the HGRC will ever know your identity. If, in the future, you decide that you want your sample destroyed, you must notify Dr. Devanand. The sample will be stored without information linking it directly to you, but Dr. Devanand will have the key to identify your sample.

MRI Brain Scan

The Magnetic Resonance Imaging (MRI) will be performed at the New York State Psychiatric Institute, Columbia University's Mortimer B. Zuckerman Mind Brain Behavior Institute, or Citigroup Biomedical Imaging Center at Weill Cornell Medical College twice: during the initial baseline visit and at the Week 78 visit. MRI involves lying on a table, which slides into a large cylindrical magnet. Radio waves are used to take pictures of the brain. Before beginning the MRI, you will be asked to remove any metal or magnetized objects (such as keys, chains, hairpins, or credit cards). While inside the MRI device, you will lie flat on your back for approximately 30 to 40 minutes. In the scanner, your head will be held in position using tape. You will be asked to breathe quietly and to remain as still as possible. You will not feel anything but will hear a banging noise that is made by the MRI scanner. Your MRI will be interpreted within 1 month of the scan and the results will be shared with you or a physician that you may designate.

Neuropsychological Testing and NCPT

The results of the memory and intellectual tests, and the smell tests, will be shared with you. The results of the apolipoprotein E genotype will not be shared with you.

Neuropsychological testing involving paper and pencil tests of memory and other intellectual functions will be conducted at 6 of your clinic visits, taking 40 minutes to 2 ½ hours on each occasion. The smell test will be given to you at two visits: Baseline and Week 78**.**

The Neurocognitive Performance Test (NCPT) will be completed at Baseline, Week 12, and Week 78. This is a brief, unsupervised, online set of cognitive assessments. It will take approximately 30 minutes to complete.

The total time for most study visits in this part of the study will be approximately 90 to 120 minutes. If you find any questions during the interviews upsetting, you do not have to answer them.

Select neuropsychiatric tests and clinical interviews may be completed remotely over the telephone by a member of the study team (Research staff, Study MD, or Investigator), if the study team believes it is more feasible and safest for you to have testing completed remotely.

Blindness of raters and participants

The main rater administering measures, such as the cognitive testing, will be blind, in other words, unaware to the group to which you have been assigned (CCT group or CPT group). You are instructed not to discuss your online training with the main rater in order to maintain the blindness. However, at your baseline visit, you will be introduced to a second rater, who will help you navigate the online platform for the first time. The second rater will be aware of your assignment; you are free to discuss your training, but only with the second rater. Further, both raters will ensure at the baseline visit that you understand which person is the main rater and which person is the second rater.

Investigator initiated discontinuation of study

There may be times when the investigator decides to stop the study even though you may wish to continue. An example is a medical or psychiatric condition that would interfere with your participation.

Risks

Cognitive Training: There is minimal risk associated with the training. If you find any tasks uncomfortable, you do not have to complete them.

MRI Scan: The Magnetic Resonance Imaging (MRI) scanner uses strong magnetic fields and

radio waves to take measurements in your brain. Some people have reported sensations during MRI scans, such as "tingling" or "twitching" (or, very rarely, a painful sensation), which are caused by the magnetic field that can stimulate nerves in your body. With any MRI, on occasion, some people experience nervousness or discomfort due to the scanner's small space and the need to lie still. Pacemakers, some types of metallic implants, and medication patches may create increased risk with MRI, and this information will be reviewed to ensure your safety before conducting the MRI scan. The MRI scanner produces a loud noise; earplugs will be provided to reduce this discomfort. If you experience any discomfort and wish to stop the scan, you can tell the MRI technologist, so that he or she will stop the scan immediately. In our experience, no one has had sensations from the MRI that did not stop when the scanning ended.

Blood tests: You will have almost 2 teaspoons of blood taken as a sample for genetic research. Additional blood samples will be taken: Chemistry (1.2 teaspoons of blood), Complete Blood Count (.8 teaspoons of blood), and Thyroid Function (1.2 teaspoons of blood). Therefore, the total amount of blood taken will be about 5.2 teaspoons. Some risks that follow these blood draws are discomfort, occasional bruising, and an infection at the needle insertion site, which will disappear in time.

Apolipoprotein blood test: Because we are collecting genetic material (DNA), there are some unique risks involved. These may be associated with unanticipated risks, relating to a breach of confidentiality or discrimination, which would result from concerns related to an increased risk of a genetic disorder. Since this is research, you should not report it as genetic testing if asked. This genetic research is strictly for research purposes; therefore, the results will not be provided to you. The risk of accidental identification is minimized because the blood sample will only be identified by the study ID and without any personal identifying information.

UPSIT: This smell test involves mainly synthetic odors and a few natural odors. If you have allergies that you feel may affect your ability to take the smell test, please inform your study physician in order to reach a decision about whether it is appropriate for you to participate in this study.

Medical and psychiatric history, physical, neuropsychological testing: There is minimal risk associated with these procedures. If you find any questions objectionable, you do not have to answer them.

Study Duration:

Total study duration may exceed 78 weeks should you encounter delays to in-person assessments and/or procedures related to COVID-19 specific pauses to research protocol implementation. A pause to research activity specific to COVID-19 may be put into place as part of institutional risk reduction initiative.

Travel for Research Purposes:

During Stage I re-opening: you will only come on-site if absolutely necessary for completion of study assessments and procedures. While traveling to NYSPI, MBBI, or Cornell facilities to conduct study assessments and procedures, you may be at increased risk of contracting COVID-19. The Principal Investigator and study team will take all precautions necessary to ensure that risk remains minimal, including paying for your transport to site via car service or ride share (utilizing services such as Uber or Lyft).

Research Coordinator will remind you to wear mask and practice frequent hand hygiene while in transport to study visit, during the 24-hour pre-visit reminder call.

In Person Visits and Procedures:

While on site during stage I re-opening, you will adhere to all guidelines and procedures specific to COVID-19 risk reduction in order to reduce the spread of COVID-19 to staff and other study participants at NYSPI/MBBI/Cornell facilities. Any participant unwilling to abide by these guidelines will not be permitted to participate in the study.

Remote Assessments:

Select neuropsychological testing and clinical interviews may be administered remotely throughout stage I re-opening. MRI and majority of neuropsychological testing must be completed in person, on site.

With completion of remote assessments also comes the risk for loss of confidentiality. Remote assessments will be administered exclusively through HIPAA compliant phone calls at a time agreed upon by both you and the member of the study team who will administer the assessment. The individual completing the remote assessments will do so by completing assessments verbally, and recording replies on paper, for later storage in your research subject chart.

Benefits

You may or may not benefit from participating in this study.

Confidentiality

Your participation in this study will be confidential, and if the results are published, your name will not be identified. Your records will be stored in locked files and will be kept confidential to the extent permitted by law. Access will only be allowed to members of the research team or institutional personnel as part of a routine audit. Your name and other personal identifying information will be stored in an electronically secure database at the New York State Psychiatric Institute. Only essential staff will be allowed access to this information. The study could not be completed without this information. There are legal advocacy organizations that have the authority under State law to access otherwise confidential subject records, but they cannot re-disclose this information without your consent. Records will be available to research staff, and to federal, state, and Institutional regulatory personnel (who may review records as part of routine audits).

Research records will be stored in a confidential manner so that your information will be held with the highest confidentiality.

Participants whose history is obtained through the collection of family history information (from the interviewee) are also considered research participants. They are subjected to minimal risk because all information is confidential. There are procedures to safeguard confidentiality of the information gathered about them from other family members, including names or identifying information kept on the family history form or in the records.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena. There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state, or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations. Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality DOES NOT stop you from willingly releasing information about your involvement in this research. It also DOES NOT prevent you from having access to your own information.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. 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.

The investigator or study team may wish to use or share the data obtained in this study with other investigators both inside and outside of Columbia for additional research studies, now or in the future. All data related to you will be de-identified, which means your data will be labeled with a code and will not include your name or any other identifiable information. The list that links your code to your name will be secured in a locked file cabinet separate from the rest of the research data. The data about you may be shared with other researchers. If this information is shared, your name or any other identification will not be included. You have the right to have your unused information kept about you for research purposes destroyed at any time. You can request this at any time by contacting Dr. Devanand at 646[redacted]. This research may involve

collection of biospecimens. Your de-identified biospecimens may be used for commercial profit. You will not share in this commercial profit. This research will not include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Your MRI will be interpreted, and the results will be shared with you or a physician who you may designate. Your MRI report will be maintained as part of the clinical database at the New York State Psychiatric Institute or the Columbia University Medical Center along with your name and will be accessible to clinicians at the Medical Center.

In addition to the confidentiality protections described in this consent form, a federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, long-term care insurance or by adoption agencies. GINA also does not protect you against discrimination based on an already diagnosed genetic condition or disease. If you would like to know more about it, you can discuss this with the Principal Investigator of this study or you can go to the following website: www.genome.gov/10002328

Compensation

Compensation is provided for time, effort and reimbursement of transportation costs. You will receive $50 per MRI scan (Baseline and week 78) and $25 at each of the six major time points: Baseline, Week 12, Week 20, Week 32, Week 52, Week 78. You will also be paid $1 per completed at-home online training session for both training groups. This will be an extra $72 dollars maximum per participant, if you complete all required sessions. Therefore, you will receive a total of $322 for your participation in the study over the course of 18 months. You will receive a check in the mail from Research Foundation of Mental Hygiene within two weeks after the visit in which reimbursement is owed.

In Case of Injury

Federal regulations require that we inform participants about our institution's policy with regard to compensation and payment for treatment of research-related injuries. Please be aware that the Research Foundation for Mental Hygiene, New York State Psychiatric Institute, Columbia University Irving Medical Center and New York Presbyterian Hospital will furnish that emergency medical and psychiatric care determined to be necessary by the medical staff of this hospital. You will be responsible for the cost of such care, either personally or through your medical insurance or other form of medical coverage. No monetary compensation for wages lost as a result of injury will be paid to you by the New York State Psychiatric Institute, Columbia University Irving Medical Center by New York Presbyterian Hospital. By signing this consent form, you are not waiving any of your legal rights to seek compensation through the courts.

Questions

If you have any questions about your rights as a research participant, you can call the New York State Psychiatric Institute-Institutional Review Board (the committee that reviews research studies) at (646[redacted]). You are free to ask any questions to the Principal Investigator, Dr. D.P. Devanand (646[redacted]) and Co-Investigator, Dr. Terry Goldberg (646[redacted]). Dr. Devanand also serves as the study physician in this study. Dr. Devanand or Dr. Goldberg will answer to the best of his ability any questions that the participant may have now or in the future about research procedures, or about the subject's response to the procedures. You have been informed that if you believe that you have sustained injury as a result of participating in a research study, you may contact the Principal Investigator, Dr. D.P. Devanand (646[redacted]) or Co-Investigator, Dr. Terry Goldberg (646[redacted]) so that you can review the matter and identify the medical resources that may be available to you.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of participants in research studies). You may call the IRB Main Office at (646[redacted] during regular office hours.

Documentation of Consent

I voluntarily agree to participate in the research study described above.

Print name: _____

Signed: _____

Date: _____

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____
Person Designated to Obtain Consent

Signed: _____

Date: _____

You will be given a copy of this consent form to take with you.