Repetitive Transcranial Magnetic Stimulation for Dementia

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Title of Study: Repetitive Transcranial Magnetic Stimulation for Dementia	
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Repetitive Transcranial Magnetic Stimulation (rTMS) for Dementia Informed Consent

PURPOSE OF RESEARCH

You are invited to participate in a research study to see if repetitive Transcranial Magnetic Stimulation (rTMS) can help memory and thinking (cognition). You may be a good fit for this study if: 1) you have dementia or mild cognitive impairment; and 2) you are a Veteran.

Researchers at the VA Palo Alto are doing this study. This research study is looking for 62 Veterans who experience cognitive problems and who likely have dementia or mild cognitive impairment.

The primary purpose for this study is to determine if rTMS can improve cognitive function. We will also see if there are measureable biomarkers in the body that change when cognition improves.

VOLUNTARY PARTICIPATION

If you want to be in the study, you would be a volunteer. You can decide to stop at any time. Your decision to volunteer or not will not affect your medical care. You can decide to be in the study now, but change your mind and stop being in the study at any time.

DURATION OF STUDY INVOLVEMENT

This entire research study is expected to be conducted over approximately 2 years; you will be involved for a little over 4 months with the option to extend another 4 months to receive "real" rTMS treatment if you were assigned to the sham group. After the last session of real rTMS treatment session we will keep monitoring for risk of seizure for a year. During that one year, we would like you to contact us if you experience any seizure, lapse of consciousness or any other event that could be related to seizure. If seizure occurs during the follow-up period, we will connect you with the appropriate health care team for a thorough evaluation and proper treatment. At the completion of this follow-up period, we would like to contact you by phone to inquire about your health condition potentially related to seizure.

PROCEDURES

If you choose to join the study, sign this informed consent, and meet the study criteria, you will be enrolled into the study and will be assigned randomly into one of 2 treatment groups: active "real rTMS" or sham (placebo) rTMS. It is important to know that not everyone in this study will get "real" rTMS first. The group getting the sham will be a comparison group. After the 4 month follow-up

people in the sham group will be offered 20 "real" rTMS treatment sessions. Patients who fail screening may be re-screened at a later time at the discretion of the investigator, Dr. Cheng.

If you choose to participate, Dr. Cheng and his research study staff will ask you to participate in the activities described below. All study procedures will be completed by trained professionals and research staff. This study has four phases: screening, baseline, intervention, and follow-up. After the follow-up people who were in the sham group will have the chance to receive 20 "real" rTMS treatments and may have the option to continue assessments

1. SCREENING PHASE (about 2-3 hours)

If you agree to be in this study, you will complete a number of assessments to see if you are eligible and healthy enough to participate. You will read and sign this informed consent form before you begin the screening phase. The on-site screening phase will take approximately 2-3 hours to complete. You may be asked questions in a telephone interview before coming into the clinic. Screening may be done in one day or over several days.

During this phase you will do the following:

- You will be asked general questions about your age, race, ethnicity, and years of education.
- You will be asked to complete a questionnaire about your mood.
- You will have a physical examination.
- Study staff will ask you about all of your medications (prescriptions, "natural food products," supplements, and "over the counter" medications) that you are taking or have taken in the past month. During the study, you will not be able to take any medications known to increase the risk of seizures. Your primary physician may adjust your medications as needed.
- A clinician will ask you about your medical history. If the clinician has concerns about your health a blood or urine sample may be obtained for further assessment.
- We will take measurements using the rTMS machine to find your "motor threshold". This is used to determine the settings that will be used for your study treatments.
- If study staff has concerns that you may be taking illegal drugs, you may be asked to provide a urine sample. Positive results will show up in your CPRS record and may require that you be excluded from this study for your safety. If you are able to stop using these drugs, you may be re-screened later.
- If study staff has concerns that you may be drinking alcohol, you may have a breathalyzer to measure your alcohol level. Positive results may require that you be excluded from this study. If you are able to limit your alcohol consumption to no more than 1 drink a day, you may be re-screened later.
- You will be provided with results of blood, urine, and breathalyzer tests, if you request them.
- If you are a woman capable of becoming pregnant, a urine sample will be used to test for pregnancy. A positive test would exclude you from participation in this study. Additionally, it is important for you to tell us if, to your knowledge, you are pregnant or breast-feeding at the time of this study. The risks of rTMS on a pregnancy are unknown. You will be asked to stop the study if you become pregnant.

2. BASELINE PHASE (about 2 hours)

Upon successful completion of the screening phase, and after careful review of all labs, exams, and assessments to ensure your safety and suitability for the study, you will enter the baseline phase of the study. The baseline phase will take approximately 2 hours to complete. It is usually done on one day.

During the baseline phase, the following will happen:

- You will complete several assessments, including a series of cognitive assessments.
- A blood sample of about 2 teaspoons (10 mL) will be taken and used for assessment of biomarkers that may correlate with the severity of cognitive impairment and/or the effectiveness of the proposed treatment.

3. INTERVENTION PHASE (about 2 to 6 weeks)

If you agree and are eligible to participate in this research study, you will be enrolled in the intervention phase of the study. This phase may last up to 6 weeks. You will come to the clinic for 20 sessions of rTMS treatments. Each session will last approximately 30-60 minutes. You may be able to do multiple sessions a day, Monday through Friday. At the end of your last treatment you will complete several assessments that will take approximately 3 hours and you will have your blood draw for biomarker analysis. These assessments may be done over two days if needed.

During the intervention phase, the following will happen:

- You will be randomized to either active "real rTMS" treatment or to sham treatment. Randomization is a process that is similar to flipping a coin where one side of the coin is active and the other side is sham. There is a 50:50 chance of being randomized to either group. You will have a fifty percent chance of receiving the "real rTMS" treatment. In active treatment "real rTMS", brief pulses of magnetic energy are used to stimulate nerve cells in your brain. In sham treatment, the same machine is used but the magnetic field reaching the brain is reduced so that the nerve cells are not stimulated.
- Neither you nor the study staff will know which treatment you are getting until the end of the 4 month follow-up. This type of study is called a double blind trial and this study type is being used so that your treatment and evaluation won't be affected by someone knowing whether or not you are getting active "real rTMS" or sham treatment. The study machine will know which treatment you are getting so that you will receive the same treatment at each visit. In an emergency the study team can find out which treatment you are getting.
- At the end of the 4 month follow-up, you will be told which study group you were in. If you were randomized to the Sham group, you may choose to receive 20 real rTMS treatment sessions and repeat the procedures in the baseline, treatment and follow-up phase. This will extend your participation in the study for an additional 20 rTMS treatment sessions with another 4 month follow-up visit.
- During treatment you will wear earplugs to protect your hearing from the clicking sound and you will wear headphones that generate white noise. Additionally, you will have electrodes on your scalp and wear a study cap.

- Before each treatment session you will be asked about any changes in your medicines or new medicines you might be taking. You will be asked about any health or behavior changes since you last visit which may or may not be related to the study treatment. You will be asked how much you have slept the night before and if you have taken any drugs or alcohol.
- rTMS treatment takes about 25 minutes when you will need to sit still in the treatment chair. Staff will ensure you are as comfortable as possible during the study treatments.
- You may be asked to provide a urine sample during this phase for drug testing. These results will appear in your VA medical record and results may be disclosed to your primary physician if we think that you are using drugs in a risky manner. You will not be allowed to receive rTMS treatment if you are using drugs in a risky manner.
- You may have a breathalyzer to determine your blood alcohol level during this phase. Your results may be disclosed to your primary physician if we think that you are using alcohol in a risky manner. You may also not be allowed to receive rTMS treatment if you drink more than 1 drink of alcohol per day while in the study.
- End of Treatment Assessments:
- At the end of your last treatment you will complete study assessments over about 2 hours. This will include cognitive assessments and a mood questionnaire.
- At this time you will have a blood draw. About 1 teaspoon will be taken and used for assessment of biomarkers.

The following is a description of the treatment procedure:

- You will be awake and alert throughout the treatment session.
- You will be reclined in a chair. You will be provided with ear plugs and headphones. You will have electrodes placed on your forehead. Your head will be positioned in a holder so that it is correctly positioned. You may close your eyes and rest, but not sleep.
- A metal coil in a plastic case will be held against the scalp on the left side of your head. There is a clicking noise as magnetic pulses are produced, but you will hear white noise through the headphones.
- You may feel a tingling sensation on your head.
- Depending on the treatment group that you have been assigned to, you will receive either active "real rTMS" or sham treatments.
- You may drive yourself to and from treatment sessions and attend to your normal daily tasks.

4. FOLLOW-UP PHASE (about 2 hours)

- During the follow-up phase, you will return to the clinic 4 months after your last study treatment for a final visit. At the end of one year monitoring period the study team will contact you by phone to inquire any events or symptoms that could be related to seizure.
- At the follow-up visit you will :
- Complete several questionnaires about your health and will do a series of cognitive assessments.

5. FOR ALL STUDY PHASES

- It is important for study staff to be aware of any changes in your medications while you are in the study. This includes over-the-counter, medicines you only used once, or herbal medicines. Some medicines are not safe to use while getting rTMS treatments. If there are changes to your medications that might put you at greater risk, study staff may choose to cancel or reschedule your treatment sessions.
- The study takes place at the VA Palo Alto Health Care System (VAPAHCS) during normal business hours, Monday through Friday, 8am to 4:30pm. If asked, we will provide a note for your employer that you were receiving medical treatment. We will not compensate for missed work time.
- You will be asked about adverse events whenever you are seen by study staff for treatment, evaluation, and follow-up visits. An adverse event is any change in your health or behavior or anything bad that has happens to you while you are in the study that may or may not be related to your participation in this study. Please let us know about any changes in your health. An independent committee will be told about all adverse events at least once every six months. If they believe that any aspect of this study is unsafe, they will recommend that changes be made to eliminate the safety problem or they may recommend stopping the study.

Tissue Sampling for Biomarker and Genetic Testing

Genetic tests will be conducted on your blood samples. The tests we plan to do will allow us to study potential predisposition to metabolic, neurological, and/or immunological disease and responses to the study treatment you receive. Research using blood is an important way to try to understand the role genes and/or biomarkers play in the genesis of cognitive impairment and/or how they affect the effectiveness of treatment.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

We will protect the confidentiality of your samples and information about you. Your samples will be stored in a locked area and all information about you will be stored in a locked file cabinet or on a password protected secure computer.

For Women of Child-bearing Potential

For safety reasons, pregnant women will not be allowed to participate in this study. This is because the effects of rTMS on an unborn child are not known. There may be unforeseeable (unanticipated) risks to the participant (or to the fetus) if the participant is pregnant or becomes pregnant during the study.

You will have a urine pregnancy test prior to starting study treatment. Thereafter, you will have a urine pregnancy test every four weeks through the treatment phase of the study to be sure that you are not pregnant.

You must agree to use a medically acceptable form of birth control while participating in the study.

Acceptable forms of birth control are:

- Complete abstinence (not having sexual intercourse with anyone)
- An oral contraceptive (birth control pills)
- Norplant
- Depo-Provera
- A condom with spermicide
- A cervical cap with spermicide
- A diaphragm with spermicide
- An intrauterine device
- Surgical sterilization (having your tubes tied)

If you become pregnant during the intervention phase of the study, you will not be able to continue the study treatments. You will also be referred to a Women's Health Clinic. If you become pregnant during the follow-up phase of the study, you will continue to come in for all remaining follow-up phase visits and will complete all assessments as you normally would.

If you become pregnant at any time during the study, you will be asked to sign a release of information form for study staff to access medical records to obtain information regarding the outcome of your pregnancy. No pediatric records will be reviewed.

There is no likely effect on sperm count or the motility of sperm or other reproductive risks associated with fathering a child, although this has not been formally tested in humans. Likewise, there are no known risks on sperm and ova (eggs).

Tissue Banking for Future Research

As part of this research we would like to save any leftover blood and CSF samples for future research. Your blood and CSF samples will be stored at the Palo Alto VA and will be used for future research on cognition and mental health research. Your samples will be stored until the sample is all used up or until this research study is completed or on December 31, 2075. Your sample and information about you will be labeled with a code that does not contain your name, initials, social security number, date of birth, or other ways that identify who you are. The research we conduct with your blood and/or CSF is being done for research purposes only and we will not tell you or your doctor about the results of the research.

You may withdraw your permission for us to use your blood for future research at any time. Contact the Principal Investigator, Dr. Jauhtai Cheng, MD, at (650) 493-5000 ext. 63617 to withdraw your

permission. If you take back your permission, the research team can continue to use information about you collected before you decided to take back your permission, but they will not collect any information about you going forward and any remaining samples will be destroyed.

The research we conduct using your blood and/or CSF may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. These inventions and discoveries may become financially valuable. You will not receive any money or other benefits from any commercial or other products that are made using your specimens.

Please initial below to indicate if you give permission for the sample to be saved and used for future research.

_____ Yes, I give permission for my samples to be saved for future research, as set-forth above.

_____ No, I do not give permission for my samples to be saved for future research.

Lumbar Puncture (Optional)

Additional information about how rTMS affects cognition may be gained by looking at biomarkers in spinal fluid. Biomarkers may change sooner in the spinal fluid than in the blood. To get spinal fluid we do a procedure called a lumbar puncture. Getting a lumbar puncture will not benefit you but may help us learn more about rTMS and cognition.

If you consent, a lumbar puncture (LP), also known as a "spinal tap" will be performed at the start of the study and at the end of the study treatment phase. You do not have to participate in the optional lumbar puncture to be in the rTMS for dementia study. You can change your mind about getting lumbar punctures at any time during the study.

A lumbar puncture is a procedure that involves inserting a needle in the lower back in order to collect a small amount of the spinal fluid that surrounds the brain and spinal cord.

You will be asked not to eat or drink for 4 hours prior to coming to the clinic for the LP. This means no food or drinks such as coffee, tea, milk and juice (sips of water with your medicine is ok).

During the procedure you will lay on your side curled up into a ball or you will sit on the edge of a chair or bed and lean forward, whichever is easier for you.

The lower part of your back will be cleaned with antiseptic. A local anesthetic will be injected into the skin of your lower back at the area of the lumbar puncture.

When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends. About 5 mL (1 teaspoon) of spinal fluid (CSF) will be removed for analysis and storage. Your body replaces this spinal fluid within 1-2 hours.

After the lumbar puncture is completed, you will remain in the clinic for about 1-2 hours. You will be able to eat and drink before you leave.

You should avoid any strenuous physical activity for the next 24 hours. This includes lifting, bending, doing housework and gardening, or doing exercise such as jogging or bicycle riding.

Lumbar Puncture (LP) Risks
Lumbar puncture (LP) is a way that cerebral spinal fluid (CSF) can be obtained. For most people, a lumbar puncture does not cause any serious problems.

Common risks and complications (more than 5%):
The most common complaint is a bad headache. Less than one third of the people having a lumbar puncture complain about a headache.

Some people also complain about back pain or stiffness, pain at the place where the needle was placed, and neck or shoulder pain. Backache is common especially at the time of the procedure affecting up to two thirds of patients. Shooting pain down the legs at the time of the procedure is less common, up to 10% of patients. Bleeding is more common if you have been taking blood thinning drugs such as Warfarin, Aspirin, Clopidogrel, Prasugrel, Dipyridamole, Ticagrelor, Apixaban, Dabigatran, Rivaroxaban. These complaints are not as common as a headache and can be treated.

Uncommon risks and complications (1 – 5%):
Headache that can be severe and last up to several days, may need further treatment. If the headache does not go away after 1 or 2 days, it may be due to a leak of the spinal fluid. A leak can be treated with a blood "patch". A blood "patch" is made with a small amount of your blood. Your blood is injected into the area where the leak is.

Rare risks and complications (less than 1%):
Rare or very uncommon complaints include low blood pressure and dizziness, bleeding into the spinal canal, or an infection of the spinal fluid (known as meningitis). These rare complaints could be serious. They could require you to be admitted in the hospital. Other neurological problems occur very rarely, such as double vision. Infection may occur at the needle site, and affect the bones of the back or the spinal fluid. It is very rare but death from meningitis can occur. Local problems from needle injury are uncommon and can cause local lumps or tumors (dermoids). Brain Herniation or Coning (Movement of the brain) is an exceedingly rare condition which occurs when the pressure inside the brain is high. Brain herniation can lead to death or severe disability. Death as a result of this procedure is ultra-rare.

You cannot participate in the optional LP if you are taking anticoagulants such as warfarin, dabigatran, or FxA inhibitors, such as endoxaban, apixaban, and rivaroxaban. You cannot participate in the optional LP if you are on dual antiplatelet therapy, with aspirin and an antiplatelet, such as ticragelor, prasugrel,

or clopidogrel. Participants on a single antiplatelet agent, like ASA, will be individually assessed to rule out factors that might increase bleeding risks. Participants on a P2Y12 inhibitor, such as tricragelor, prasugrel, or clopogrel, will be individually assessed to rule out factors that might increase bleeding risks. Assessments will include lab reviews, such as PT, PTT, platelet count, etc.

The procedure is to be performed in a facility with proper equipment and monitoring capability, by a physician with the privilege to perform LP.

Spinal fluid will give us more biomarker information. We will protect your confidentiality and privacy of your Spinal fluid and biomarker results as described above in the section titled "Tissue Sampling for Biomarker and Genetic Testing".

Please initial below to indicate if you give permission for the lumbar puncture and collection of cerebrospinal fluid (CSF).

_____ Yes, I give permission for cerebrospinal fluid to be collected and used in this study.

_____ No, I do not give permission for cerebrospinal fluid to be collected and used in this study.

Functional MRI (Optional)

It is possible to collect an MRI to localize, precisely, the coil placement prior to treatment. By projecting toward the brain in image space it is possible to define a region on the surface of the brain believed to be the target of rTMS. Doing an MRI will not benefit you but may help us learn more about rTMS and cognition.

If you consent, an MRI will be performed at the start of the study. You do not have to participate in the optional MRI to be in the rTMS for dementia study. You can change your mind about getting an MRI at any time.

MRI machines use a strong magnet and radiofrequency magnetic fields to make images of the body interior. The scanning procedure is very much like an X-ray or CT scan.

You will be asked to lie on a long narrow couch for about 60 to 90 minutes while the magnetic resonance imaging machine gathers information. The space within the magnet in which you will lie is somewhat confined; if you feel claustrophobic, you can discontinue the scan at any time.

During scanning, you will be exposed to a large magnet and radiofrequency magnetic fields. You will not feel either. You will hear repetitive tapping noises; you will be required to wear earplugs or some form of hearing protection to reduce the noise.

You may also be fitted for a bite bar in order to keep your head from moving during the scans. A bite bar is a bar made of dental wax which you will hold in your mouth during the scans. This will assist you in keeping your head still.

MRI Risks

The magnetism and radiofrequency magnetic fields do not cause harmful effects at the levels used in the MRI machine. National and Stanford guidelines have been developed for these machines, and these recommendations will be followed.

There are some discomforts. Common ones are feeling nervous from being in an enclosed space and a hearing loud noise from the MRI. Please take note that some subjects have experienced claustrophobia; you may discontinue the scan at any time. Less common discomforts include a localized twitching sensation and nausea. If you feel any burning sensation or any other discomforts, inform the MRI operator or investigator

As metallic objects may experience a strong attraction to the magnet, it is very important that you notify the researcher of any metal objects, devices or implants that are in or on your body before entering the magnet room. This includes biomedical devices such as pacemakers and aneurysm clips, prostheses, and other metallic objects embedded in the body such as bullets, buckshot, shrapnel, and any metal fragments from working around metal. In some cases, having those devices means you should not have an MRI scan performed.

All other metallic objects must also be removed from your person prior to entering the magnet room or approaching the magnet to prevent them from becoming a projectile or being pulled by the magnet. This includes keys, body piercing, jewelry, pocket knives, money clips, paper clips, safety pins, hair pins, and barrettes.

In addition, objects such as watches, credit cards, and hearing aids could be damaged in the presence of the magnetic field. A locker will be provided for you to secure all your items and valuables.

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to arrhythmias), if you are wearing metal braces on your teeth, or (for women) if you could be pregnant, you should not have an MR scan and should notify the operator/investigator. If you are or are trying to get pregnant, the effects of the scan on a fetus are unknown and, therefore, we will not perform the examination at this time.

You should also notify the operator/investigator if you have any tattoos on your body, including eyeliner and other permanent makeup. Tattoos could become warm and irritated during the scan and remain so for several days. If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member.

There is a risk of heating from radiofrequency imaging coils and their cables, button response boxes and their cables, and/or the cables from monitoring devices that record physiologic processes such as heart beats per minute or the electrical activity of the brain. Please report any heating sensation immediately. You may have the scan stopped at any time if this occurs.

Please initial below to indicate if you give permission for the MRI to be conducted and used.

_____ Yes, I give permission for MRI to be done and used in this study.

_____ No, I do not give permission for MRI to be done and used in this study.

PARTICIPANT'S RESPONSIBILITIES

You should:

- Follow the instructions of the investigators and study staff.
- Complete your questionnaires as instructed. You are free to skip any questions that you prefer not to answer.
- Ask questions as you think of them.
- Tell the investigator or research study staff if you stop using birth control or think you might be pregnant.
- Tell the investigator or research staff if you change your mind about staying in the study.
- While participating in this research study, do not take part in any other research study without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing or potential drug interactions. Taking part in other research studies without approval from the investigators may invalidate the results of this research, as well as that of the other studies.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the investigator or study staff to reschedule as soon as you know you will miss the appointment.
- It is important that you not give false, incomplete, or misleading information about your medical history, including past and present drug use, because this could have serious consequences for your well-being.
- The effects of alcohol and substance use while undergoing rTMS are not well known at this time. Alcohol use will be limited to 1 alcoholic beverage, defined as 12 oz. beer, 5 oz. wine, or 1.5 oz. hard liquor, a day. If you drink more than one alcoholic beverage prior to your treatment

session, study staff may reschedule that session. If the study staff is concerned about your drinking you may be asked to stop the study because it would put you at higher risk.

- You cannot use illegal substances, such as marijuana (without a prescription), cocaine, and amphetamines, during your participation in the study. If you begin to use substances during your participation in this trial, you may be asked to stop the study.
- Contact the investigator or research staff if you experience any seizure, lapse of consciousness or any other event that could be related to seizure.

WITHDRAWAL FROM STUDY

If you first agree to participate in the research study and then you change your mind, you are free to withdraw your consent and stop your participation at any time. If you decide to withdraw from the study, you will not lose any benefits to which you would otherwise be entitled and your decision will not affect your ability to receive medical care for any condition.

If you want to stop being in the study you should tell the investigators or study staff. You can do this by phone by calling Dr. Cheng at (650) 493-5000 ext. 63617.

The investigators may also withdraw you from the study without your consent for one or more of the following reasons: Failure to follow the instructions of the Protocol Director and/or study staff; if the Protocol Director decides that continuing your participation could be harmful to you; pregnancy; if you need treatment not allowed in the study; if you start using drugs and/or alcohol outside of the study requirements; if the study is cancelled; for other administrative reasons; or for other unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences when you join any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions. This study involves the following risks, discomforts, and possible inconveniences:

rTMS Risks

A few patients receiving rTMS have had a seizure. All of the reported seizures resolved promptly on their own and none had any lasting effects or adverse impact on the patients. There is little evidence of risk of seizures using rTMS the way it will be used in this study.

In the unlikely event that a seizure does occur, you will be closely monitored and treated for any medical or psychological consequences. Lab tests will be drawn and you will be seen by a neurologist as soon as possible. The facility where the rTMS studies are performed is fully equipped to safely handle a seizure. You will be given a letter regarding the seizure to share with your primary health care provider. The letter will indicate that the seizure during rTMS does not increase your risk for future seizures.

It should be noted that one study participant had new onset of seizure six months after the last active rTMS treatment. To assess the risk of seizure associated with rTMS, this study is changing the follow up monitoring period from 4 months to one full year. During that one year, we would like you to contact us if you experience any seizure, lapse of consciousness or any other event that could be related to seizure. If seizure occurs during the follow-up period, we will connect you with the appropriate health care team for a thorough evaluation and proper treatment. At the completion of this follow-up period, we would like to contact you by phone to inquire about your health condition potentially related to seizure.

rTMS treatment can result in mild to moderate headaches in as many as 30 out of 100 of patients. Some people also report discomfort at the site of rTMS stimulation. This occurs in around 15 out of 100 of patients. Headaches and site discomfort readily responds to acetaminophen or ibuprofen. Discomfort may improve over time or goes away.

There is a small risk of dental pain with rTMS, during or immediately after the treatment. If this occurs, let your study doctors and nurses know and they may be able to move the rTMS coil position or provide you with a bite block to reduce this pain or make it not happen.

rTMS treatment may produce movement or tingling of the arm, leg, face or scalp. You may also experience a temporary feeling of numbness in the face.

There is a possible risk of hearing loss due to the light clicking sounds made by the device. You will wear ear protection during your rTMS sessions. This should greatly reduce the possibility of hearing loss.

The rTMS operator will monitor you for ear protection, coil placement, and seizure activity during all sessions.

In some people, daily rTMS can cause them to have increased energy, no need for sleep, and rapid racing thoughts. This is called mania. If you notice these changes let your primary physician and the study team know.

Your study investigator will be monitoring you during your participation to see if you are experiencing any side effects. It is important that you report promptly any side effect to study staff. If you feel, or your study investigator feels, that the side effects are not well tolerated, treatment may be stopped altogether and you may be withdrawn from the study.

The possibility of long-term risks is unknown. In previous studies, animal and human brains have shown no evidence of any kind of damage from rTMS. As with any experimental treatment, there may be unforeseen risks associated with this device. You will be informed of any new information that is developed during the study that might affect your willingness to continue your participation.

There is a chance that laboratory results, or other tests done as part of the research study will show an abnormality that you did not know about. You will be referred to your usual health care provider to follow-up on any unexpected findings. Your consent to this study serves as consent to contact your personal (Non-VA) physician. You and your physician can arrange the necessary work-up and treatment and you would be responsible for any costs associated with this healthcare.

Other Risks
If you are taking any drugs that may increase the risk of having a seizure, you will need to be taken off those drugs before you can participate. You and your physician will need to discuss the feasibility of your discontinuing any such medication. Withdrawal from such drugs may cause discomfort or illness.

Risks of the usual care you receive are not risks of the research. They are not included in this consent form. You should talk with your health care providers about risks of usual care.

There are virtually no risks involved in the cognitive testing and psychosocial measurements other than the anxiety that can be associated with any test. It is possible that you might become tired or frustrated by some of our testing. You may find answering the questionnaires annoying, boring, or repetitive. If this happens, please tell us and we will take a break or continue the questions another day.

Drawing blood is a routine procedure involving the possibility of slight bruising and/or infection at the needle puncture site. There may be some discomfort during insertion of the tube for withdrawing blood. On rare occasions some patients have fainted while having their blood drawn. A clot could also form in the vein, resulting in temporary pain or tenderness in the area where the tube was placed. Infection is rare. To minimize these risks, experienced medical personnel will handle all the blood drawing procedures. There is also a risk of scarring at the site of needle insertion with individuals having more pigmented skin having a greater risk of this occurring.

If, in an interview, you disclose that (a) you intend to harm yourself or someone else, (b) that a child had been abused or neglected, or (c) that an elder or dependent had been abused, we are required by California law to notify the appropriate authorities.

POTENTIAL BENEFITS

We can't promise that you will get any benefits from taking part in this research study. However, possible benefits may include improvement in cognitive function or quality of life. The information that is obtained during this study may be scientifically useful and may lead to greater knowledge about the treatment of cognitive impairment.

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY DIRECT BENEFITS FROM THIS STUDY.

ALTERNATIVES

You may choose not to participate in this study. If this is your decision, there are other choices including the standard treatments provided by a local clinic. Alternative treatments include behavioral medicine and cognitive rehabilitation.

PARTICIPANT'S RIGHTS

Your participation is voluntary. You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. You have the right to refuse to answer particular questions.

If you decide not to participate, tell the Protocol Director. You will still receive care for any disease and will not lose any benefits to which you would otherwise be entitled.

You will be told of any important new information that is learned during the course of this research study, which might affect your decision or your willingness to continue participation in this study.

We will send information about cognitive assessments and clinical results to your personal physician if you request this in writing.

ClinicalTrials.gov

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 study and study results. You can search this Web site at any time.

CONFIDENTIALITY

We will keep your name and all the information you tell us in this study as confidential as possible. Your laboratory results, including your urine drug screen results, will be accessible in your VA medical record (CPRS). The responses to questions concerning illegal drug use could be self-incriminating and harmful to you if they became known outside the study. As mentioned earlier, your urine screen results for drug use may be disclosed to your primary physician if we think that you are using drugs in a risky manner.

We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

Because this study involves an investigational device, the Food and Drug Administration may also have access to information about you collected in this study.

FINANCIAL CONSIDERATIONS

Payments
You will be compensated for your time and inconvenience. You will be responsible for arranging transportation to and from all visits. You may be reimbursed for your travel, to and from study visits. Travel by car will be calculated based on google maps to and from home address to the VA Palo Alto, using the shortest calculated distance per mile, and paid at the standard VA rate. If you elect to travel on public transit, we will reimburse the actual cost of transportation up to $45.00 round trip.

Study payments include:

- Screening/Baseline Phase: $40
- Intervention Phase: $200
- Follow-up Phase: $60

If you withdraw or stop early in any of the three phases you will be paid according to what phase you are in. For example, if you withdraw at any time in the intervention phase you will receive payment for $30 for screening phase and $200 for the intervention phase but not $60 for the follow-up phase. If you complete all three phases you would receive a total of $300. If you received sham treatments and return for the active TMS treatments at the end of the study you will repeat the treatment phase. The follow-up phase will only be repeated if administering personnel is available. You will receive additional study payments for the repeat of these study phases ($200 for treatment and $60 for follow-up).

At the end of each study phase, a voucher will be given to you by the research staff. This voucher may be taken to the agent cashier at the VA Palo Alto to be redeemed for cash.

If you live more than 50 miles from the VA Palo Alto, or have late night study activities followed by early morning study activities, we may be able to arrange for accommodation at the VA Defenders Lodge.

Costs
You will not have to pay anything to be in this study.

Sponsor
The Department of Veterans Affairs is providing financial support and material for this study.

CONTACT INFORMATION

Questions, Concerns, or Complaints
If you have any questions, concerns or complaints about this research study you should ask the Principal Investigator, Dr. Jauhtai Cheng. You can call him at (650) 493-5000 ext. 63617. You should also contact him at any time if you feel you have been hurt by being a part of this study.

Appointment Contact

If you need to change your appointment, please contact study staff at (650) 496-2578.

Independent Contact
If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, and would like to speak with a person who is independent of the research, call the Stanford Institutional Review Board (IRB) at (650) 723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 3000 El Camino Real, Five Palo Alto Square, 4th Floor, Palo Alto, CA 94306.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for Veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on a number of factors. In most circumstances, the treatment must be provided in a VA medical facility. No other form of compensation for injuries is available. However, by signing this form you have not released the VA from liability for negligence. For further information, you may call the Human Protections Administrator at (650) 493-5000, ext. 67593 or the V.A. Regional Counsel at (415) 750-2288.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a human subject you have the following rights. These rights include but are not limited to the subject's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you (by phone or letter) about related studies that may be of interest to you?

Title of Study: Repetitive Transcranial Magnetic Stimulation for Dementia	
Principal Investigator: Jauhtai Joseph Cheng, MD	VAMC: VA Palo Alto HCS

_____ Yes. I would like to be contacted for future research opportunities.

_____ No. Do not contact me about future research opportunities.

Signing your name means you agree to be in this study and that you were given a copy of this consent form.

Signature of Participant Date

Print Name of Participant

Signature of Legally Authorized Representative Date

Print name of Legally Authorized Representative

Representative's Authority to Act for Subject

Person Obtaining Consent:

Signature of Person Obtaining Consent Date

Print Name of Person Obtaining Consent

Title of Study: Repetitive Transcranial Magnetic Stimulation for Dementia	
Principal Investigator: Jauhtai Joseph Cheng, MD	VAMC: VA Palo Alto HCS

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

☐ Confirm the participant signed the VA HIPAA Authorization (VA 10-0493)

Signature of Person Obtaining HIPAA Authorization confirmation Date

Print name of Person Obtaining HIPAA Authorization