Example Approved Study Consent Form

Date of Approval: April 02, 2019

Clinical Trial Name:
Remediation of Impaired Self-Regulation in Patients with Mild TBI

NCT #02260570

Date of Document Upload: May 12, 2022

Department of Veterans Affairs

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

Subject Name: **Date:**
Title of Study: Remediation of Impaired Self-Regulation in Patients with Mild TBI
Principal Investigator: Andrew Kayser **VAMC:** VANCHCS

The rights below are the rights of every person who is asked to be in a medical research study. As an experimental subject, you have the following rights:

1. To be told what the study is trying to determine.
2. To be told what will happen to you and whether any of the procedures, drugs, or devices is different from what would be used in standard practice.
3. To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to you for research purposes.
4. To be told if you can expect any benefit from participating and, if so, what the benefit might be.
5. To be told the other choices you have and how they may be better or worse than being in the study.
6. To be allowed to ask any questions concerning the study, both before agreeing to be involved and during the course of the study.
7. To be told what sort of medical treatment is available if any complications arise.
8. To refuse to participate or to change your mind about participating after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated consent form.
10. To be free of pressure when considering whether you wish to agree to be in the study.

If you have other questions, please ask the researcher or research assistant.
You may also ask the VA Northern California Health Care System (VANCHCS) Human Research Protection Program (HRPP). The HRPP protects volunteers in research projects. You may call the HRPP at (916) 366-5359 from 8:00 a.m. to 4:30 p.m. Monday through Friday. You may also write to the HRPP. The address is: VANCHCS HRPP (151), 10535 Hospital Way, Mather, CA 95655. You may also call VA Chief Counsel at (415) 750-2288.

_____ _____
Signature of Participant Date

Version date: 005/11/2017
SUBJECT'S IDENTIFICATION (I.D. give name - last, first, middle; social security number; address and phone number)

VA File 14-06-00720-MTZ
IRB Approval Date: 04/02/2019
Expiration Date: 05/01/2020

VA Northern California HEALTH CARE SYSTEM

Subject's Initials _____

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Principal Investigator: Andrew Kayser **VAMC:** VANCHCS

Purpose of the Study

This is a research study. Research studies only include subjects who choose to take part. You do not have to be in this research study. You should read the information that follows. Please ask questions about anything you do not understand before deciding if you want to be in this research study. Please take your time to make your decision.

You qualify to take part in this project because you are between the ages of 18-50 years old and have a history of mild traumatic brain injury (mTBI, also known as a concussion), or you are a control subject (meaning you have not had a mTBI). We hope to learn more about the possible effects of mTBI on decision making.

The purpose of this study is to test whether a one-time dose of tolcapone, a medication that affects a brain chemical called dopamine, can improve decision making in people who have a history of mTBI. We will ask you to make decisions while you are in the MRI scanner so that we can measure the function of the brain at the same time.

Researchers are studying this issue because some people with a history of mTBI feel that their decision making has been affected.

Study Length

You will be in this study for a total of 3 visits. The first visit will be a screening visit to make sure that the medication and MRI scanning are safe for you. We will also ask you to complete some paperwork. This visit will take place either at the VA or at the UCSF Gallo Clinic located at U.C. Berkeley, whichever is more convenient for you. The second and third visits will take place at the MRI scanner facility on the U.C. Berkeley campus. These visits will be set up at a time that is convenient for you, approximately one week apart.

Researchers will conduct this study for 5 years, but you will only be in the study for the 3 visits described in the previous paragraph.

1. Researcher's Financial Disclosure

The study investigator and staff are conducting this study entirely for research. They have no personal and no financial interest in this study. This research is funded by the VA Rehabilitation and Research Development Service (VA RR&D).

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2. Study Procedures

There will be about 80 subjects taking part in this study at VANCHCS.

Researchers will ask you to do the following things:
You will come to the research clinic at the VA NCHCS facility in Martinez or the UCSF Gallo Clinic located at UC Berkeley for the screening visit, and then, if you qualify, to the MRI scanner at UC Berkeley for 2 more visits. These visits will be scheduled when it is convenient for you. Visits will usually be completed within 6 weeks, but it could take longer depending on your schedule or the MRI scanner schedule. The screening visit will be about 2 hours long, but could be longer depending on your health. The MRI sessions will each be about 5 hours long.

Tests at the screening visit:
Procedures that are part of the screening process:

- Physical exam:
  At your first visit, you will have a physical exam.
- Medical History:
  Researchers will ask you about your medical history and review your medical chart.
- Questionnaires:
  Researchers will ask you to complete paper and computer questionnaires that evaluate different factors that could affect decision making.

Your screening visit will take place either at the VA NCHCS facility in Martinez or at the UCSF Gallo Clinic located at UC Berkeley, whichever is more convenient for you.

Standard procedures being done because you are in this study:

- Blood test:
  Researchers will draw a blood sample at your screening visit, either at the VA NCHCS facility in Martinez or at the UCSF Gallo Clinic located at UC Berkeley, whichever is more convenient for you. Researchers will draw about 2 teaspoons of blood by inserting a needle into a vein in your arm. If researchers are unable to obtain your blood sample, you may be referred to the Quest Diagnostics blood drawing facility that is most convenient for you. The facility closest to UC Berkeley is located at 2999 Regents Street in Berkeley, CA. Researchers will test your blood for liver function. Your blood sample will be analyzed at either the VA laboratory, if it is obtained at the VA, or at a Quest Diagnostics laboratory facility, if it is obtained at the UCSF Gallo Clinic located at UC Berkeley. If you have had your liver function tested within the past 6 months, you may

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sign a form to allow the researchers to get these test results instead of having a blood draw.

- Urine test:
  Researchers will ask you to provide a urine sample. Researchers will test you urine for drugs of abuse. These results will not be recorded. However, if you test positive for drugs of abuse other than marijuana, you cannot be in the study.
- Breathalyzer test:
  Researchers will ask you to blow into a tube attached to a small device that will test for alcohol. If you have alcohol in your system when are being screened, you may not participate in this study
- Pregnancy test:
  Because the drug in this study may affect a fetus, pregnant women may not take part in this study. If you have had your first menstrual period, researchers will test your urine to make sure you are not pregnant.
- Saliva test:
  Researchers will ask you to provide a saliva sample. This sample will be used to look at the gene for catechol-O-methyltransferase (COMT). The study medication, tolcapone, may affect your decisions differently depending on which version of this gene you have. The tests for this gene will take place at the University of California at San Francisco.
- Current medicine use:
  Researchers will also ask you about the medicine you take. The researcher will review drugs that would prevent you from being in this study.

Study tests at the MRI visits
You will continue in the study if the screening exams, tests or procedures show that you can. These visits will take place on the University of California at Berkeley campus, in the Brain Imaging Center facility.

Standard procedures being done because you are in this study:

- Researchers will ask you about medical problems and medicines. Researchers will use this information to decide if it is all right for you to take part in the study or stay in the study.
- Researchers will repeat the urine test for drugs of abuse and the breathalyzer test before each MRI session.
- Researchers will also measure your blood pressure and pulse.

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- At each visit, you will provide a urine sample to test for drugs of abuse. If you have a positive test for a substance other than marijuana, this information will not be written down in your research record.
- At each visit, you will do a Breathalyzer test to test for alcohol.
- Researchers will complete a physical exam at the screening visit.
- At each visit, women will have a urine pregnancy test.

Procedures that are being tested in this study:

- You will receive a study medication at both MRI visits. This is a cross-over Trial. In a cross-over trial, subjects get each of the study pills in turn. On one visit, the pill will be the active drug, tolcapone, and on the other visit, the pill will be a placebo (a sugar pill with no active drug). Neither you nor the researchers will know which pill you get on each visit. However, if there is an emergency, the researchers can find out which pill you received.
- At both MRI visits, you will do behavioral testing. These tests will evaluate how you make decisions. You will be asked to make decisions about how to allocate money and in response to visual stimuli (pictures).

This study includes experimental items. The study medication, tolcapone, has been approved for use in people by the Federal Drug Administration (FDA). However, it has not been approved for the treatment of changes in decision making. This research study is attempting to find out if tolcapone could be helpful for changes in decision making.

Tolcapone affects the level of a brain chemical called dopamine. We will ask you not to participate in this study if you have recently used medications that also affect dopamine levels (such as tolcapone itself or any of the following: levodopa/carbidopa, entacapone, amantadine, pergolide, pramipexole, ropinirole, selegeline, isocarboxazid, phenelzine, tranylcypromine, clozapine, olanzapine, quetiapine, risperidone, ziprasidone, aripiprazole, fluphenazine, haloperidol, perphenazine, pimozide, thiothixene, trifluoperazine, loxapine, molindone, chlorpromazine, mesoridazine, thioridazine, dextroamphetamine, dexmethylphenidate, dextroamphetamine, methylphenidate, cocaine, or methamphetamine).

This study will also use the following procedures:

- MRI Scan:
  In two sessions separated by at least one week, you will have a MRI. For the MRI exam, you will lie down on a narrow bed. You will then move into a tunnel that is approximately

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6 feet long by 3 feet wide and open at each end. You will need to lie there quietly for about one and a half hours, during which time there will be a loud banging noise. You may feel warm during this procedure.

The MRI scan of your brain is for research. The MRI pictures for this study are not meant to evaluate your health.

In non-research, MRI pictures can be part your care. Specially trained physicians (radiologists) read MRI scans. Your MRI pictures will not receive any routine clinical review. This means that researchers may not notice all abnormal findings.

However, researchers may find a problem when they review your MRI pictures. If this happens, they will notify the researcher in charge of this study, Andrew Kayser. Andrew Kayser MD and another study researcher, Mark D'Esposito MD, are physicians who specialize in neurology. They routinely look at MRI pictures. If necessary, they may ask another specially trained physician (a radiologist) to help you obtain a more complete review of your MRI scan. The researcher in charge of this study will discuss these possible problems with you. Researchers will cover your name when the physician checks your MRI pictures. This physician can find out if any clinical health condition is present. If the physician thinks a health problem is present, we will give you a copy of the MRI picture. You can take the MRI picture to take to the physician of your choosing, at your expense. If you prefer, we can send the pictures electronically; there is a small risk that someone else could view electronically sent files.

3. Potential Risks and Discomforts

You may have adverse events or discomforts while on this study. These may occur at the time of the research or later. You should discuss these with the researcher and/or your regular physician. Risks and side effects related to the tolcapone we are studying include:

Physical Risks: Tolcapone

Likely

- a slight drop in blood pressure

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Less Likely

- nausea
- headache
- dizziness
- lightheadedness

Rare But Serious

- liver injury

In the greater than 40,000 patient years of tolcapone use, 3 patients with Parkinson's disease died because of liver failure associated with tolcapone. There were no cases reported in a healthy person after only a single dose of this medication. However, if you have a history of liver problems, you cannot be in this study.

Blood Draw Risks:

Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.

MRI risks:

The MRI machine acts like a large magnet. It could move iron-containing objects in the MRI room during your exam, which could in the process possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. Researchers will not allow you into the MRI room and have an MRI if you have a piece of metal in your body. Examples would be a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why researchers will ask you to wear earplugs. At times during the test, researchers may ask you to not swallow for a while, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women cannot take part in this study.

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Psychological Risks:
The behavioral procedures have been used extensively in previous research. The pictures and words are presented at a comfortable lighting level; the sounds are transmitted at a pleasant volume; and the button press responses require a very little effort. It is possible that you may become bored, anxious, or frustrated when completing these tasks.

Privacy Risks:

- Legal Risks:
  There is a real, but small risk of breach of confidentiality regarding medical and personal information. This risk will be minimized by following VA data protection procedures, including but not limited to, coding your data, storing electronic data on a secure network, and storing physical data in a locked cabinet, accessible only by authorized personnel.
- Employment or Economic Risks:
  There are no employment or economic risks that could result from your participation in this study. If you decide to no longer take part, that decision will not affect your care at the VA. We will do a genetic test only on your COMT gene. This test will be performed at the Genetics Core facility at the University of California at San Francisco. Different types of this gene are common in the general population. This gene is not used to diagnose any disease. It is unknown whether future information about this gene may affect employment or insurance. We will keep this information confidential unless required to provide it by law.
- Social Risks:
  There are no known social risks or stigma associated with participating in this research study.

Reproductive risks:
Because we do not know whether the drugs in this study may affect an unborn baby, you should not become pregnant or father a baby while in this study. You should not nurse your baby while on this study. If you are sexually active, you must use birth control. Ask about counseling and more information about preventing pregnancy.

For more information about risks and side effects, ask the researcher.

Unforeseeable Risk:
The researcher does not know all the side effects that may happen. You may experience a side effect or new risk that the researchers do not know about at this time.

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New Information:
The research team will contact you with any significant new knowledge or findings about tolcapone that would affect your willingness to continue in the research.

4. Expected Benefits to Subjects
You may not benefit from taking part in this research.

5. Expected Benefits to Others
We hope to learn more about decision making and the study medication, tolcapone, from your taking part in this study. The information we get from this study may help us to treat future patients with mTBI better.

6. Other Options to Taking Part in this Study
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. Your alternative is not to take part.

Please talk to your doctor about your choices before deciding if you will take part in this study.

7. Right to Withdrawal from the Study
Your taking part in this research is voluntary. You can stop taking part at any time.

If you choose not to take part in this study, you will not be penalized or lose any benefits to which you are entitled. Your decision will not affect your relationship with the researcher.

Tell the researcher if you are thinking about stopping or decide to stop. It is important to tell the study researcher if you are thinking about stopping.

It is also possible that the researchers will ask you to stop being in the study. For example, if you do not follow study instructions, develop a condition that would make the study unsafe for you, or experience a bad side effect, you will not continue in the study.

8. Confidentiality
We will do our best to keep your medical records and personal information private. However, we cannot guarantee absolute confidentiality. We will disclose your personal information if required by law.

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We will disclose your information to protect your rights or welfare. We will disclose your information if the researcher becomes aware that you may be a danger to yourself or to others. We will disclose your information if the researcher becomes aware that acts of child, elder, or dependent adult abuse or neglect may have occurred.

Researchers may publish or present the results of this study. They will not reveal your name or identity.

We will code your research data without using your name. The researcher holds the key to the code. We will add your information to a database. We protect these data on the computer with passwords. We store your information, research data, and related records in locked offices. We also use computer codes to access your secure medical records. This prevents access by unauthorized staff. We follow current VA policy that requires that identifiers and/or research records be destroyed in accordance with the VA record retention Schedule.

As the funding source for this study, VA RR&D may look at your research files and medical record. As collaborating study sites, UC Berkeley, and UC San Francisco may also look at your research files and medical record. This study involves a medication, tolcapone, that is regulated by the FDA (Food and Drug Administration). The FDA may choose to inspect research identifying you as a subject of this research.

Organizations may inspect and/or copy your research records for quality assurance and data analysis. One of these is the Institutional Review Board (otherwise known as the Human Subjects Subcommittee) at VANCHCS. The Institutional Review Board is a committee whose purpose is to review and monitor research studies that involve human subjects.

VA policy requires that a note be placed in your medical record that identifies you as taking part in this research.

A description of the 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.

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9. Research Related Injury

Diagnosis and treatment may be for routine care or for research. Some forms of diagnosis and treatment involve some risk of injury.

If you are injured as a result of being in this study, treatment will be available. If you are eligible for veteran's benefits, the costs of such treatment will be covered by the Department of Veterans Affairs. If not, the costs of such treatment may be covered by the Department of Veterans Affairs, or the study sponsor (VA Rehabilitation Research & Development office) depending on a number of factors. The Department of Veterans Affairs does not normally provide any other form of compensation for injury. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form. For further information about this, you may call the VA Chief Counsel at (415) 750-2288

10. Costs to Study Subjects

As a research subject, you are not required to pay for treatment received as a subject in a VA research program.

As a veteran-subject, you are not required to pay for care received as a subject in a VA research project. However, there is an exception. Some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payments will continue to apply to medical care and services provided by VA that are not part of this study.

This study will provide payments to defray the costs of transportation. However, study subjects will bear any costs related to time away from work.

11. Payment for Taking Part in the Study

In return for your time, effort and travel expenses, you will be paid for taking part in this study. You will receive $12 per hour for your time outside the MRI scanner, and $20 per hour for your time inside the MRI scanner. You may complete tasks that include monetary bonuses up to a total of $40. If you complete all 3 study sessions, you will receive an additional $100 completion bonus. Subjects who complete all 3 sessions can expect to earn approximately $325. A check will be mailed to you about 6 weeks after you have finished the study. If you do not complete the study, you will receive payment only for those parts of the study that you finished.

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12. Investigational Drugs
After you complete your part in the study, the VA is not obligated to provide the study medicine.

13. Future Use of Specimens
All samples, including your saliva sample for COMT gene testing, will be destroyed after the research team gets the information.

14. Future Use of Data
Data from this study (for example, MRI data) could be re-examined as part of future research. These data will be stored on study researcher Kayser's computer server without your personal identifying information. Only study researcher Kayser and his research team will have access to the data.

15. Re-Contact
You may be re-contacted to see if you are interested in participating in other research studies. You are under no obligation to take part in other research studies if you do not want to do so.

16. Questions About this Study
If you have any questions, concerns or complaints about this study, contact one of the researchers on this study: Andrew Kayser, MD, who specializes in neurology, at 925-372-2258.

17. Questions About Research Subject Rights
You may have questions about your research subject rights, or you may want to obtain information or offer input. You may also have questions that you feel cannot be discussed with the researcher. You may call the VANCHCS Human Research Protection Program. The phone number is (916) 366-5359. You may also call the VA Chief Counsel. The phone number is (415) 750-2288.

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RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Study researcher Kayser or a member of his research team has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

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

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call study researcher Kayser at 925-372-2258 during the day and the VA research line at 916-843-7000 extension 6051 after hours. If any medical problems occur in connection with this study, the VA will provide emergency care.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

_____	_____	_____
Participant's Name	Participant's Signature	Date
_____	_____	_____
Name of person obtaining consent	Signature of person obtaining consent	Date