WALTER REED NATIONAL MILITARY MEDICAL CENTER
CONSENT TO PARTICIPATE IN RESEARCH

1. **PROTOCOL TITLE:** "Clinical Trial of 3MDR to Treat PTSD with Mild TBI, with and without Eye Movement (3MDR Study)"

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your participation in this study. If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about, including the risks and possible benefits to you.

Please tell these researchers if you are taking part in another research study.

You do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty.

Your decision will not affect your future care at Walter Reed National Military Medical Center (WRNMMC).

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you have a diagnosis of posttraumatic stress disorder (PTSD), or think you may have PTSD, as well as a history of at least one mild traumatic brain injury (mTBI). This study is for active or retired service members who have both PTSD and at least one mTBI (concussion). The purpose of this research study is to learn about the symptoms of all individuals in an immersive virtual reality environment and determine how symptoms compare between individuals who perform a dual-task to those that do not. Dual-tasking means that you will be asked to perform two tasks at the same time. In this case, the second task will involve moving your eyes back and forth while you are walking. The total time that you may take part in this study is up to 8 months, which includes an initial assessment of up to 30 minutes, 10 sessions every 1-2 weeks that will each last about 60-90 minutes, and follow up assessments, and at 3 and 6 months, that will each take about 10 minutes.

There will be 20 people taking part in this study at WRNMMC over a period of 12-18 months.

Motion-assisted, Multi-modular Memory Desensitization and Reconsolidation (3MDR) is considered an experimental approach for individuals with both PTSD and mTBI. A few studies have successfully used 3MDR for PTSD in military service members in other countries, but it has not been studied before in those with both PTSD and mTBI, and there is also very little experience with its use in women. This study combines 3MDR with aspects of virtual reality exposure therapy (VRET) and Eye Movement Desensitization and Reprocessing (EMDR), within the Computer Assisted Rehabilitation Environment (CAREN). It is important to determine how effective it may be in both male and female U.S. military service members, as well as whether eye movements are an important part of this approach.

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you will need to have some tests and provide some information so that the Investigator can confirm that you qualify for the study. This is called the "Screening Process". You will be asked questions about your medical and mTBI history, symptoms, and medications to confirm that you are eligible.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will be asked to do the following research activities:

1. Answer some questions about your military and health history. This will include your age, branch of service, rank, years in service, number of deployments, history of traumatic brain injury, PTSD symptoms, and current medications. This information will be used to describe the overall population of service members who choose to participate in this study.
2. Allow the study team to contact your health care provider(s) to explain the study to them.
3. Be randomly assigned to one of two groups. Randomization is a process like flipping a coin and means you will have a chance of being assigned to either of the groups. One group will receive the dual-task, and the other group will not. Both groups will receive an active approach to their PTSD symptoms, no one will receive a "placebo" or be put on a waitlist.
4. Take part in 10 study sessions, each lasting up to 90 minutes, over a period of 10 weeks.
5. Choose 2 songs, one to remind you of the time when your trauma occurred, and another to bring you back to the present time. The therapist can help you with your choices if needed.
6. Choose 14 pictures which will be used during the study sessions, as reminders of impactful moments in your past. The therapist can help you with choosing pictures if needed.
7. Wear a full-body safety harness and walk continuously on a treadmill in the Computer Assisted Rehabilitation Environment (CAREN) for approximately 30-60 minutes during sessions 3-9. In session 3, you will be given an explanation of how the CAREN will be used for the study and briefed on the system's safety features. In sessions 4-9, a virtual environment will be utilized and your pre-selected pictures will be displayed. You will be asked to describe the feelings and emotions associated with your traumatic experience as presented in those pictures. The music you choose will also be played while you are walking, before and after the pictures are shown. In the 10th session, the therapist will discuss how your symptoms have changed during the course of your study participation, and what would be best for you to do going forward from that point.

8. Review with the study therapist at the end of each session in the CAREN how you felt about being on the treadmill, listening to the music and looking at the pictures.
9. Complete questionnaires at the beginning (taking ~30 minutes), middle (~2 minutes), and end of the 10-week study session period (~10 minutes).
10. Complete two follow-up assessments, conducted either by telephone or in person, 3 and 6 months after concluding the 10 sessions, with each assessment lasting about 10 minutes.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there is a risk of:

- Emotional distress related to discussing feelings about your traumatic experiences, but the study therapist is trained to help you with this.
- Adverse impact on your career if you are an active duty service member and we learn of something that puts your well-being or that of members of your unit at risk, or of illegal activities, that require us to inform your command.
- Breach of confidentiality. We do not put any record of your participation in this study in your medical records, and efforts are made to protect your research study records, such as using codes rather than personal identifiers, but there is still a risk that someone could get access to personal information in your records or other information researchers have stored about you.
- Injury. The CAREN has a treadmill on a platform that is seated inside a well which is several feet deep; falling in this well could result in injury. There is a railing around the well to protect you, and while you are on the CAREN, you will be placed in a harness and the therapist will also be in a harness on the platform with you. You will both be supervised by the CAREN engineer, who has many years of experience in its operation. In addition, emergency stop buttons, trip sensors, and software filters are incorporated to ensure safety.
- Skin chafing or irritation from the safety harness while walking on the treadmill, though the harness can be adjusted to your liking.
- Sweating, fatigue, or short of breath, depending on your level of conditioning. The treadmill speed can be adjusted to ensure you are comfortable with the pace, so be sure to let the therapist or engineer know if you are uncomfortable in any way.
- Muscle strain or soreness that may bother you when walking or performing daily activities. Soreness may last for up to 48 hours after being on the CAREN. This is more likely to occur in individuals who do not regularly exercise.
- Due to the immersive nature of the CAREN, the virtual environment may cause nausea, dizziness, and /or headache.

If you have any of the above concerns during the study, or other concerning symptoms develop, please alert one of the research staff or the Principal Investigator. While all the risks that we know about have been listed above, there may be other risks that we do not know about at this point in time. If we find that there was a risk to you that was not known at the time of your participation in this study, and the risk might have some effect on your health, you will be informed.

If something in this research makes you uncomfortable or upset, you may choose to stop taking part in this research at any time without loss of benefits; you may request that the research team discuss whether other approaches might be helpful to you at that time. If the research team notes any distress, anxiety, or increased symptoms associated with the research, they may refer to your primary care physician or to another medical care provider to help with such symptoms.

If you are a FEMALE ABLE TO BECOME PREGNANT and you want to take part in this study, you should know that there is no evidence that the CAREN might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. However, pregnancy can make it more difficult for you to maintain your balance, which could put you at greater risk for a fall, which could adversely impact you or your unborn child, and walking on a treadmill for up to an hour, even at a comfortable pace, could result in earlier onset of labor. Therefore, while you will not be required to take a pregnancy test before you can participate in this study, we will ask about the date of your last menstrual period. You are asked not get pregnant while in the study session phase of this study. The only completely reliable methods of birth control are not having sex or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy.

If you become pregnant or feel you might be pregnant, contact your personal physician and the principal investigator of this study listed in the Contact Information section at the end of this document.

There may also be other risks of taking part in this study that we do not yet know about.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?:

The possible benefits to you as a research participant in this research study are that your symptoms may improve. However, there is no guarantee that you will benefit from being in this research. The study results may also help us to learn more how best to help future service members who have both PTSD and mTBI.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

There may be other options for addressing your symptoms. Alternative approaches that may be available to you may include medications and/or other various types of psychotherapy or “talk” therapy. You should talk with your personal physician (if applicable) about these options. Choosing not to take part in this research study is also an option. There may be other research studies involving experimental approaches that could be helpful to your condition.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

Yes. If you are not a federal government employee (e.g. you are a military retiree, a reservist not in active duty status, or a military dependent), you will receive $75 for the completion of each study assessment session: baseline, post-session 10, and at 3 and 6 months after completing study sessions, for a total of $300 if you complete all four study assessments. There is no payment for the study sessions. Payment will help compensate for your travel expenses as well as other costs

incurred by participation in the study. If, by your report, you are an active-duty service member, a reservist in active duty status, or a civilian federal employee, and are determined to be in a non-duty status at the time that the assessment is conducted, you will be also eligible for this compensation. However, if you are in a duty status at the time, you will not be eligible for compensation. You will receive a debit card for any compensation to which you are entitled.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

10. WHO IS CONDUCTING THIS RESEARCH?

This research is being conducted by a team of clinical researchers, who are based at Walter Reed National Military Medical Center and Uniformed Services University. The study is led by Dr. Michael J. Roy, MD, MPH, whose positions and contact information are provided in section 13 below.

11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

This is an investigator-initiated research study that is sponsored by the Center for Rehabilitation Sciences Research (CRSR). This study will also be conducted in collaboration with the Center for Neuroscience and Regenerative Medicine (CNRM). CNRM will provide some of the resources, such assistance with recruitment and analyzing study information.

12. SOURCE OF FUNDING:

Funding for this study has been provided by the Center for Rehabilitation Sciences Research at Uniformed Services University, Bethesda, MD.

13. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

Michael J. Roy, MD MPH, Fellow of the American College of Physicians
Director, Division of Military Internal Medicine
Professor of Medicine
Principal Investigator, Recruitment Core, Center for Neuroscience and Regenerative Medicine
Uniformed Services University
Staff, Internal Medicine, Walter Reed National Military Medical Center
Bethesda, MD
Phone: (301) 295-9601
e-mail: michael.roy@usuhs.edu

14. LOCATION OF THE RESEARCH:

All study procedures will take place at:

Walter Reed National Military Medical Center
8901 Wisconsin Ave,
Bethesda, MD 20889

Data Analysis will be conducted at:
Department of Medicine
Uniformed Services University
4301 Jones Bridge Rd
Bethesda, MD 20814

15. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

There are no financial interests or other personal arrangements that WRNMMC, the research team members, or their immediate family members, might have in this study.

16. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at: http://www.dtic.mil/whs/directives/infomgt/forms/eforms/dd2005.pdf.

Procedures to protect the confidentiality of the data in this study include but are not limited to: Your research records will not be disclosed outside of WRNMMC or USU. Data will be stored in a secure database which is maintained by the Center for Neuroscience and Regenerative Medicine (CNRM) behind the firewalls at the National Institutes of Health but your data will only be identified only by a unique code number, not your name, social security number or any other personal identifier that could be associated with you. A link between the code will be kept in a protected file in a secure location, with access strictly limited to authorized research study personnel. Data collected during this study will be shared with CNRM and organizations associated with CNRM including CRSR, the Uniformed Services University, US Department of Defense and Henry M Jackson Foundation. Your name and personally identifying information will be removed before the data is shared so that the shared data will not contain any information that could identify you. By signing this consent document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data. Your name or other ways to identify you personally will not appear in any published paper or presentation related to this study. Your research records may be shared with research collaborators at other sites, but in this case will only be identified by a unique code number, not with any personal identifying information.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

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

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

Michael J. Roy, MD MPH
Paula Bellini, MA
Matthew Richter, MD
Charline Simon, MA
Hannah O'Malley, BA
Kerri Dunbar, MA

Those listed above will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

17. LONG TERM USE OF DATA

The investigator has requested to save select coded data collected from your participation in this research study for possible use in future research. This select coded data will be shared with CNRM, but your name and personally identifying information will be removed before the data is shared so that the shared data will not contain any information that could identify you. You have a number of options with regard to this request. If the stored data has a code, or an identifying link, you can request to be contacted and sign a separate consent form to allow the use or available of this data in another study. You may also choose either to not allow any further use of your data or give consent now for the use your data to be used in future studies. This future research may be in the same area as the original study or it may be for a different kind of study.

Any future research using your retained data will require a research protocol for the proposed study approved by an Institutional Review Board (IRB) (a committee responsible for protecting research participants) or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

18. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately at (301) 295-9601.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

19. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

You may withdraw your consent at any time and stop participating in this research study without affecting your eligibility for care or any other benefits to which you are entitled.

If you are receiving attention as part of this research study, you will no longer be eligible for such research-related attention. Contact your personal physician to discuss medical treatment for your condition.

Your taking part in this study may also be stopped without your consent if the military mission requires it, or if you lose your right to receive medical care at a military hospital. The principal investigator of this research study may terminate your participation in this research study at any time if he determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

20. VOLUNTARY PARTICIPATION:

The decision to take part in this research study is completely voluntary on your part. You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

21. INCIDENTAL FINDINGS

There is a possibility that during your participation we may identify an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away.

You do not have an option to decline receiving information about an incidental finding. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding.

We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

22. CONTACT INFORMATION:

Principal Investigator (PI)
The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Michael J. Roy, MD MPH, Fellow of the American College of Physicians
Staff, Internal Medicine, Walter Reed National Military Medical Center
Director, Division of Military Internal Medicine
Professor of Medicine
Principal Investigator, Recruitment Core, Center for Neuroscience and Regenerative Medicine
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Phone: (301) 295-9601
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Institutional Review Board (IRB) Office
If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at: (301-295-8273) or 8901 Wisconsin Ave, Bethesda, MD 20889

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

Please initial the sentences that reflect your choices, and then sign below:

_____ I do not authorize the storage of data collected as a part of this study for future use in research studies.

_____ I authorize the storage of data collected as a part of this study for future use in research studies.

With regard to future research studies done on stored data that has a link to my personal identity:

_____ I do not wish to be notified by investigators in the event of research findings of potential impact to my family members or myself.

_____ I wish to be notified by investigators in the event of research findings of potential impact to my family members or myself. I agree that my current principal investigator may use any appropriate identifier to locate me in the future.

With regard to sharing my contact information with other investigators:
_____ I do not authorize sharing of my contact information with other researchers in the future, even if I might be eligible for other research studies.

_____ I authorize the sharing of my contact information with other researchers conducting future studies, if I might be eligible for them.

SIGNATURE OF PARTICIPANT

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT
(Can only be signed by an investigator or staff approved to administer consent)

_____

Printed Name of Administering Individual

_____ _____

Signature of Administering Individual Date