Meets 2018 Common Rule Requirements

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES (USU)/ WALTER REED NATIONAL MILITARY MEDICAL CENTER (WRNMMC) CONSENT TO PARTICIPATE IN RESEARCH

Title"**C**AREN versus **A**ugmented **R**eality: **E**xpanding 3MDR Therapy for **PTSD**: A Randomized Controlled Trial (CARE4PTSD 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 carefully review this information. 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 potential participation in this research study. You do not have to take part in this study. Participation is voluntary. . You may also leave the research study at any time without penalization.

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

Your decision will not affect your future care at Walter Reed National Military Medical Center (WRNMMC) or in the Department of Defense.

1. KEY INFORMATION:

This study is designed to try to see if a new approach to posttraumatic stress disorder (PTSD) works equally well whether delivered in a complex virtual reality environment that is only available in a few places in the world, or with a common treadmill and special goggles that allow you to see what is around you and at the same time see things in virtual reality, since the treadmill and goggles could easily be made much more widely available.

Taking part in this research study is voluntary, and you can change your mind at any time. If you choose to take part, you would first do an assessment to see if you are eligible. If you are eligible, you would then be randomized to either use the goggles or the complex environment. In either case, you work with a therapist and receive the same approach for a total of 10-14 sessions about once each week. In the first two sessions, you would get to know the therapist and choose some music and pictures that will be used in the virtual reality sessions. In the third session, you would try out the virtual reality to see how it works. Then you would do between 6 and 10 sessions with the virtual reality, either through the goggles or in the complex environment. Each of these sessions would take 60-90 minutes, and you will be walking on a treadmill at a comfortable pace for about an hour, listening to music and looking at and talking about pictures that you have chosen. You would then do one wrap-up session to review and discuss how your symptoms have changed during the study. You would also do follow up assessments 3 and 6 months later to see how your symptoms are. This means your total time in the study will be about 9 months.

Everyone in the study will receive the same approach, which previous work by both us and other researchers shows has a good chance to improve PTSD symptoms. There is a possible risk of

(USUHS) IRB 1
IRB NUMBER: USUHS.2021-076
IRB APPROVAL DATE: 04/22/2021

"cyber sickness", which could include dizziness or nausea, as well as fatigue or sweating from walking on the treadmill. There are other treatments for PTSD, involving talking to a therapist or taking medications, that you might be able to get from a behavioral health specialist.

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. This study is for those with PTSD who are eligible for care in the Department of Defense (DoD) healthcare system. The purpose of this research study is to compare how much PTSD symptoms change with an intervention delivered in two different ways: either 1) walking on a regular treadmill while wearing goggles (known as augmented reality head-mounted display, or AR HMD) that allow you to see the treadmill and things around you in the real world, while also seeing pictures in a virtual world, or 2) walking inside a cave-like fully immersive virtual reality environment known as the Computer Assisted Rehabilitation Environment (CAREN).

There will be 60 people taking part in this study at USU/WRNMMC over a period of about 2 years.

The total time that you may take part in this study is about 9 months, which includes an initial assessment of about an hour, 10 to 14 intervention sessions about once a week that will each last about 60-90 minutes, a follow up assessment immediately after finishing your last session that will take about an hour, and follow ups 3 and 6 months later that will each take about 10 minutes.

This study is looking at an approach called Motion-assisted, Multi-modular Memory Desensitization and Reconsolidation (3MDR), which has not been well-studied. This means that 3MDR is considered experimental for the treatment of PTSD. Studies in The Netherlands and the United Kingdom have reported successful results with 3MDR in military service members with treatment-resistant PTSD, and we have also found significant improvement in symptoms here in a small pilot study of service members and their family members.

The 3MDR approach includes uses some parts of virtual reality exposure therapy, which we and others have found to be effective for PTSD. In this case, you are able to choose pictures and music that are blended into the virtual environment while you walk on a treadmill. Delivering the 3MDR approach with goggles is experimental and has not been tried before. It is being tested here because the CAREN is a very complex and expensive system that is only available in a handful of places around the world, and if we are able to show that the approach works equally well with goggles, it could be made much more widely available.

At the end of this research study, we will share and discuss your individual results, or PTSD scores, with you. This will be during the last intervention session, and will include a discussion of whether you might benefit from any further therapy for your symptoms, and how and where you might get it.

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 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 and depression 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. This is usually not necessary, but on occasion it may be helpful to do so, either to ensure that the study complements and does not interfere with any treatment you are receiving, or to help you get follow up care that may be helpful to you when you are finishing the study.
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 use the CAREN, and the other group will use the goggles. Both groups will otherwise engage in the same active approach to their PTSD symptoms, no one will receive a "placebo" or be put on a waitlist.
4. Take part in 10 to 14 study sessions, each lasting up to 90 minutes, over a period of 10 weeks. After 10 sessions, we will check how your symptoms are, and your therapist will talk with you to be able to make a joint decision about whether to do more sessions. If you continue to do more, the same discussion will happen again after your 12th session.
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. If you are randomized to the CAREN group, you will wear a full-body safety harness and walk continuously on a treadmill in the CAREN briefly in session 3 to have a chance to get used to it, and then for 60-90 minutes starting in session 4, and continuing up through at least session 10, and as long as session 14. In session 3, you will also be given an explanation of how the CAREN will be used for the study and briefed on the system's safety features. In sessions 4-14, 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. After your final session, the principal investigator (PI) and your 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. If you are randomized to the goggles group, you will not need to wear a harness, but there will be a cord that you can pull to stop the treadmill if you start to lose your balance or have other difficulties during study sessions; the same approach described above will be taken, in which you will first get used to walking on the treadmill

with the augmented reality goggles in session 3, and then experience the music and pictures of your choice during sessions 4-14.

8. Whether in the CAREN or goggles group, you will review with the study therapist at the end of each session how you felt about being on the treadmill, listening to the music and looking at the pictures.
9. Complete questionnaires at the beginning (taking ~60 minutes), after your 6th intervention sessions (~2 minutes), again after your 8th intervention session if you do that many, and end of the study intervention period (~60 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.
11. If you have an injury while you are taking part in the study that results in your not being able to walk on a treadmill for an hour at a time, you can pause the study and re-start when you are able to walk again. If you pause the study for this or any other reason for more than 30 days, we will ask you to repeat the last completed study session to bring you up to speed when you resume.
12. If there is concern about disease transmission from a global pandemic, or other potential health hazards, completion of this consent, all questionnaires and assessments, and the first two preparatory sessions, as well as the post-intervention and 3- and 6-month follow up assessments, can all be completed on-line and/or by video teleconference (VTC), instead of in person. In addition, you may be asked to wear personal protective equipment (PPE) such as a facemask, gown, and gloves, and the study staff may as well, to protect you and other study participants.

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, such as illicit drug use, 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. For the group wearing goggles, there is no well around the treadmill, but injury may still be possible if you were to fall while walking on the treadmill, though you will be walking at a comfortable pace, not running, and there is a cord you can pull to stop the treadmill, so significant injury is unlikely.
- 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 treadmill. This is more likely in those who do not regularly exercise.
- Due to the immersive nature of the CAREN and the augmented reality goggles, the virtual environment may cause nausea, dizziness, and /or headache. The goggles may also cause some discomfort to your head or chafing of the skin, as it is strapped to your head throughout the session.
- If significant suicidal or homicidal ideation is expressed either upon initial assessment, which would render the individual ineligible for the study, or during the course of the study participation, the PI will determine the most appropriate actions to take in order to protect the participant and others in the community. For active duty military personnel, this may require notification of their commanding officer and could therefore impact one's duty status.

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 PI. 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 during the course of the research, they will help you work through it to try to improve these symptoms, but will also consider and discuss with you possible referral 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 or augmented reality goggles 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 an hour or more, even at a comfortable pace, could result in earlier onset of labor. You may still take part in the study if you are pregnant or become pregnant, but should be aware of this possible risk, and we will be happy to discuss further with you whether you want to take part in or continue with the study while pregnant, or if you would rather wait until after your baby is born.

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. You are also likely to get more exercise, by walking on a treadmill. 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 and others with PTSD.

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. For the first assessment, if you it is found that you are not eligible for the study after the first brief questionnaires, you will not be eligible for compensation, but if you complete the more detailed assessment that takes about an hour and are then found not eligible, you will be compensated $75. 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 at the time you complete the baseline assessment, and $75 will be added to the card at the time you finish each assessment.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

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

10. 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
Deputy Director, Center for Neuroscience and Regenerative Medicine and Traumatic Brain Injury Research Center
Uniformed Services University
Staff, Internal Medicine, Walter Reed National Military Medical Center
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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. As sponsors of this research, these centers may have access to your research data in accordance with DoDI 3216.02.

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. LOCATION OF THE RESEARCH:

Depending on which arm of the study you are randomized to, procedures will take place at either:
National Intrepid Center of Excellence
Walter Reed National Military Medical Center
Palmer Rd S.
Bethesda, MD 20814

Clinical Research Unit
Second Floor, Building 17
Department of Medicine
Uniformed Services University
4301 Jones Bridge Rd
Bethesda, MD 20814

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

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

15. 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:
https://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf

The research team will keep your research records. These records may be looked at by staff from the Center for Neuroscience and Regenerative Medicine (CNRM) or Center for Rehabilitation Sciences Research (CRSR), or the Institutional Review Board (IRB) at USU or WRNMMC as

part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

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.

Those who have access to your records as identified above 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.

Information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified.

16. LONG TERM USE OF DATA

The investigator has requested to save selected data collected from your participation in this research study for possible use in future research. You have the option either to not allow any further use of your data, or to allow the use of de-identified data to be used in future studies. This means that any data, such as your responses on questionnaires, would be used, but it would not include your name, date of birth, or anything that might allow you to be identified personally. This future research may be in the same area as the original study or it may be for a different kind of study. You will be provided with a choice at the end of this consent form to allow or deny use in future research studies.

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.

17. USE OF INFORMATION

During this research study, you could be asked to provide the following types of information: responses to questions about symptoms of things like PTSD, depression and sleep.

The information that we obtain from you for this study might be used for future studies, if you agree to that use below. We would first remove anything that might identify you from the information and specimens. If we do so, that information may then be used for future research studies or given to another investigator without getting additional permission from you.

18. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part which means 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 or loss of benefits to which you are otherwise entitled.

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.

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.

Should you choose to withdraw, you must notify the Principal Investigator or your therapist, either verbally (in person or by phone) or in writing (letter or email). If you withdraw before finishing the study, your symptoms may not improve as much as they would have with completing the study.

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

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

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.

If you withdraw, your questionnaire responses (data) that have been collected up to that point will remain in the study database.

20. 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 using the contact information in the section below.

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.

21. 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.

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Staff, Internal Medicine, Walter Reed National Military Medical Center

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Professor of Medicine
Deputy Director, Center for Neuroscience and Regenerative Medicine and TBI Research Center
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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 Should any further questions arise concerning my rights or study related injury, please contact the **Human Protections Administrator (HPA), Petrice B. Longenecker, PhD, MA, CIP at 301-295-0819.**

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:

With regard to storage of de-identified data:

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

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

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

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been

explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research 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

(If your research involves children and requires parental consent, then include this section and signature lines as appropriate.)