Cannabidiol as an Adjunctive to Prolonged Exposure for the Treatment of PTSD

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Title of Study: Cannabidiol as an Adjunctive to Prolonged Exposure for the Treatment of PTSD	
Principal Investigators: Catherine Ayers, PhD	**VAMC:** VA San Diego Healthcare System
Subject Name:	**Date:**

1) Purpose of this research study

Principal Investigators, Catherine Ayers, PhD, and colleagues are conducting a research study to find out more about how to improve treatments for posttraumatic stress disorder (PTSD). This study will compare Cannabidiol (CBD) vs. placebo (inactive pill) among Veterans who will also concurrently receive prolonged exposure therapy (PE), an evidence based psychotherapy for PTSD. CBD is naturally found in the cannabis plant, and is therefore a schedule 1 controlled substance. The federal government defines Schedule 1 substances as drugs with no currently accepted medical use and a high potential for abuse. CBD is not currently approved for the treatment of PTSD. The purpose of the study is to determine whether 300mg of twice daily oral CBD can improve patients' response to psychotherapy for PTSD.

You have been asked to participate because you may have PTSD, you are currently reporting problems, and/or your healthcare provider believes you may qualify for this study. There will be approximately 200 participants at this VA site. The entire study will take about 5 years.

2) How long the study will take

Your participation will take approximately 1-2 hours each time you have a scheduled appointment, and you will have 19 appointments scheduled over a 10-month period.

3) What will happen to you in this study

If you agree to be in the study, the following will happen to you:

a. You will be interviewed to see if you are eligible for the study. This takes 90 minutes. If you are eligible, you will also fill out some questionnaires that take about 1 hour to complete. This first appointment will take approximately 2-3.5 hours and be conducted via telehealth.
b. You will complete laboratory tests to determine whether you are eligible to participate in the research study. These tests will include a blood draw (approx. 2 tablespoons) to test blood count and liver functioning, and urine samples to test for use of illicit substances and pregnancy (only in women of childbearing potential). Participants who do not have a documented physical examination in their medical chart within the past 6 months will receive a brief screening physical examination performed by a study physician. This examination is for determining study qualification only, and is not intended to be used for diagnostic purposes.
c. Prior to randomization, your assigned therapist will meet with you for one hour to review personal pros and cons of participation. During this meeting any barriers to participation will also be discussed. You will also be given the opportunity to discuss questions or concerns you may have about participating in the study
d. You will then be randomly assigned (as if by the toss of a coin) to one of two groups. Group

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I will receive 12 sessions of Exposure therapy (PE) delivered via telehealth and 16 weeks of Cannabidiol (CBD). Group 2 will receive 12 sessions of PE and 16 weeks of Placebo (PL). You will have up to four months to complete the therapy.

e. During your 12 sessions of psychotherapy, you will complete a short set of questionnaires with your provider before every session. These take about 5-10 minutes to complete.
f. All participants will meet with a physician or nurse via telehealth to go over their medical history, have a physical health screening, and review laboratory tests to ensure they are generally in good health and able to take the study medication. The nurse or physician may request that you recomplete laboratory tests throughout the study if clinically indicated.
g. Treatment sessions and portions of assessments will be audio-recorded so that they may be reviewed by supervisors to make sure that the therapy and assessments are being administered properly.
h. You will complete the 1st post treatment interview and questionnaires at the end of the 16 weeks of medication treatment, which will take about 2 hours, and you will be compensated $25.
i. You will be asked to complete the 2nd post-treatment assessment and questionnaires 1 month after your 1st post-treatment appointment, and you will be compensated $25.
j. You will be asked to complete the 3rd and last post treatment assessment 3 months after completing your 1st post-treatment assessment, and you will be compensated $25.
k. Information from the medical record will be utilized as noted in the HIPAA Authorization.

4) Which procedure(s) or treatment(s) are done for research only

The techniques employed in this study are Prolonged Exposure therapy (PE), which has been shown to be effective in the treatment of trauma-related disorders and is not experimental. Cannabidiol (CBD) is a schedule-I controlled substance that is being tested in this study as an investigational new drug. If you qualify for the research study, you will take part in one of two treatments, PE+CBD or PE+ placebo. This is the first study to test the combination of PE and CBD. Thus, the experimental portion of this study is to test if CBD will improve the existing psychotherapy PE in helping individuals cope with the negative consequences of having experienced a traumatic event.

5) RISKS <u>reasonably</u> to be expected

Participation in this study may involve some added discomforts. The procedures used are likely to cause:

a. The interview questions and or questionnaires may produce discomfort or anxiety from discussion of personal, emotional, or anxiety-producing topics.
b. During treatment, you will be encouraged to talk about your problems and to engage in activities that you may be avoiding, so some increased discomfort may occur. Study staff is trained to handle any distress that arises. Additionally, you will be given a 24-hour contact phone number to call in the event of increased symptoms.

c. Participants will be informed of the risks associated with the use of cannabidiol, including all clinically significant warnings registered with the FDA. If the study staff learns of any new possible risk or side effects of this drug, participants will be notified immediately. Common side effects may include but are not limited to: headaches, nausea, dry mouth, drowsiness, sleepiness psychomotor slowing, lightheadedness, weight loss, and or/insomnia. If you experience significant side effects of drowsiness, sleepiness or psychomotor slowing that would impair your ability to drive you will be required to arrange alternative transportation to and from study visits. Tell your doctor if you have unlikely but serious side effects of cannabidiol.
d. Your confidentiality will be protected to the extent permitted by law; however, there is always a risk of breach of confidentiality. Loss of participant confidentiality is possible, including data collected regarding your participation in a schedule-I controlled drug study. (see Section 12 below).
e. Your confidentiality will be protected to the extent permitted by law; however, there is always a risk of breach of confidentiality. Loss of participant confidentiality is possible, including data collected regarding symptoms.

Other potential risks of this study include:
There is risk with using the investigational drug, cannabidiol, during pregnancy. Participants who are pregnant or breastfeeding will not be eligible to participate in the study. All female participants of childbearing potential will be screened for pregnancy at the start of the study and asked to use an effective means of birth control throughout the study if they choose to participate. Female participants of childbearing potential who choose to participate will also be asked to complete urine pregnancy screens at weeks 4, 8, 12, and 16.

There are also risks associated with completing a blood draw, such as bruising, pain, infection, etc. As with any investigational new drug, cannabidiol administration may involve other risks that are not known at the present time. If the study staff learns of any new possible risk or side effects of this drug, participants will be notified immediately.

Finally, there may be job-related risks to you if your employer prohibits the use of schedule 1 substances.

Unforeseeable RISKS
Because this is an investigational study there may be some unknown risks that are currently unforeseeable, including possible undiscovered drug toxicity. You will be informed if the researchers learn of any change in the amount of risk to you.

6) BENEFITS <u>reasonably</u> to be expected.
There may not be any direct benefit to you from these procedures. You may or may not

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experience reduction in your trauma-related symptoms. Additionally, the study investigator may learn more about how to effectively treat PTSD, which could benefit the institution, other veterans, and/or society at large.

7) Voluntary nature of participation and right to withdraw without penalty.
Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without jeopardy to the medical care you will receive at this institution or loss of benefits to which you are entitled.

8) Alternatives to the research procedure or treatment
If you choose not to take part in this study, you can seek care through the VA or through community providers. Your decision about whether or not to participate in this study will not affect your relationship with VA or your ability to receive care and benefits.

9) Procedure for the orderly termination of a volunteer's participation
If you decide that you no longer wish to participate in this study, please call Dr. Ayers at XXX-XXX-XXXX or the main study phone at XXX-XXX-XXXX . You will be asked to come in for a final meeting with your therapist so that the investigator can determine how to best meet your future treatment needs.

Your participation in this study may be stopped if the investigator decides that stopping is in your best interest. Patients who are discontinued from the study for any reason will be given a referral for further treatment if necessary. If you do not participate in study procedures (for example, not completing questionnaires/interviews, not attending therapy sessions) or if the study is stopped, your participation will be terminated.

10) Information learned from the study will be shared with you
While you are a participant in this study you will be told if any important new information is found that may affect your wanting to continue.

If the results of this research might influence your medical care after you have completed your participation, the investigators will contact you to let you know these results.

11) Care provided if you are injured as a result of this study
The VA will provide necessary medical treatment should you be injured as a result of participating in this study and following study procedures. You will be treated for the injury by the VA at no cost to you or your insurance but no additional compensation is available.

12) Privacy and confidentiality

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Participation in this study may involve a loss of privacy, but information about you will be handled as confidentially as possible. If you are not already a VA patient, a medical record including your name and Social Security number will be entered in the VA Computerized Patient Record System (CPRS). Additionally, we will collect your Social Security number for CPRS review, electronic payment and tracking purposes.

Your research records will be labeled with a code number. The list that matches your name with the code number will be kept in a locked file in the research team's office. Any research records that identify you will be kept only as paper records in a secure VASDHS location, or as files behind the secure VASDHS computer firewall.

Your data will be retained after the study is complete (i.e., research records labeled only with your study number; does not use your name or any other information that could identify you). Dr. Ayers, Principal Investigator, and her research collaborators on this study will maintain these databases and samples.

In addition, audio recordings of your treatment sessions may be reviewed by study investigators. These recordings will be stored as digital files behind the secure VASDHS firewall and may be reviewed here to ensure that treatment is being delivered as planned. No personal health information (PHI) will be used to label the audio recordings, only a code will be used, and the key to the code is only accessible to the research staff at the San Diego VA. For fidelity monitoring purposes, we will randomly select sessions (your recorded audio therapy session may or may not be selected) for potential review by supervisors. These recordings will be destroyed in accordance with VHA Record Control Schedule (RCS-10) and under the direction of the VA Records Control Manager. We will keep confidential all research and medical records that identify you to the extent allowed by law. Any presentations or publications from this information will not identify you.

However, you should know that there are some circumstances in which we may have to show your information to other people. For example, the Federal Office of Human Research Protections, the General Accounting Office, the VASDHS R&D Committee, the VASDHS Institutional Review Board, the Research Advisory Panel of California, and/or federal compliance officers may look at or copy portions of records that identify you.

13) Payment

Costs to you or your insurance

There will be no costs to you or your insurance for any procedures or testing done as part of this research study. If you receive a bill for services that you think could be related to your participation in this study, you should contact the study team at XXX-XXX-XXXX.

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Medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services. The study drug Cannabidiol or Placebo and medical exams will be provided to you at no cost.

Payment for participating
You will be compensated $25 for the 1st post-treatment assessment (at the end of treatment), $25 for your 2nd post-treatment assessment (1 month after your 1st post-treatment assessment) and $25 for your 3rd post-treatment assessment (3 months after your 2nd post-treatment assessment). Therefore, you will be compensated up to $75 for your time and effort in completing the follow-up assessments after treatment has concluded. These payments will be made directly to your bank account using electronic funds transfer. If you currently have a debt to the Federal Government, your debt may be subtracted from your funds transfer payment for study participation.

14) Additional Information
The VA San Diego Healthcare System provides oversight and resources for this study. Financial support for this study is provided by Clinical Science Research and Development

Information collected from this research study will be analyzed and published. These results will be based on outcomes for the entire group of participants and will not identify you as an individual. The data collected in this study includes: information that you provide about psychiatric symptoms, exposure to traumatic events, and treatment you have received. The data collected in this study will be used for the purpose described in this consent form. By signing this form, you are allowing the research team to access your medical records. The study team includes the researchers listed in this consent form and other personnel involved in this study at the VA San Diego Healthcare System. If you decide to withdraw from this study, you may revoke your approval for future use of your medical information. To do this, you must notify Dr. Ayers in writing. Data that has already been collected will remain with the research records.

Additionally, if you agree, data from this study may be submitted to the VA Center of Excellence for Stress and Mental Health (CESAMH) Biorepository. The CESAMH Biorepository is a research project at the VA San Diego Healthcare System (VASDHS) that allows researchers to collect and share information with each other using a data and biological sample bank. With the CESAMH Biorepository, researchers studying trauma, traumatic brain injury and posttraumatic stress disorder will be able to combine information collected from multiple research efforts into large collections for future research. CESAMH Biorepository researchers hope to use this data bank to learn new and important things about the biological mechanisms to trauma response. The ultimate aim of the CESAMH Biorepository is to better understand a person's response to trauma and in doing so, be able to create new avenues for treating trauma-related disorders.

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With your permission, the researchers of this study will provide your research information including demographics, responses to symptom assessments, and treatment adherence to the CESAMH Biorepository. Auditory recordings will NOT be provided to the repository. Your research information within the Biorepository will be labeled with a study code so that no identifiable information will be kept with research data. The list that matches your name with the code number will be kept in a locked file in the Biorepository team's office. Any research records that identify you will be kept only as paper records in a secure VASDHS location, or as files behind the secure VASDHS computer firewall. After research data are provided to the CESAMH Biorepository other researchers will be able to submit an application to access information within the CESAMH Biorepository for specific research projects. Experts whose responsibility is to protect health and science information will review every request carefully to minimize any risks to privacy.

Please indicate below if you agree to have your research information, including responses given to various health, behavior, and quality of life measures, provided to the CESAMH Biorespository for use in future research:

_____No _____Yes Initials: _____

The CESAMH Biorepository researchers are also interested in having you provide additional research information directly to health and well-being information. This process would require a separate enrollment into the CESAMH Biorepository and providing information for future research. In this case, the Biorepository will be given your contact information and they will contact you to determine if you would like to participate in that study.

Please indicate below if you also agree to be contacted by the CESAMH Biorepository to learn more about the project and how to participate.

_____No _____Yes Initials: _____

Clinical Trial: 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 results. You can search this Web site at any time.

Emergency Procedures
In the event that there is a public health emergency that requires limiting participant visits to the VASDHCS, your face-to-face assessment, psychotherapy, and medication management visits

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will be replaced with video teleconferencing and phone visits. Laboratory blood and urine tests will only be conducted at screening to ensure that you are eligible to take the study medication and as clinically indicated by your study physician.

Re-contact.
You may be eligible to participate in other research studies. Please check and initial one of the options below. If you choose to be contacted, research study staff will contact you by phone to give you more information:

☐ I **consent** to be contacted by telephone or letter about other research._____**(initials)**

☐ I **do not consent** to be contacted by telephone or letter about other research **(initials)**

15) **RESEARCH SUBJECTS' RIGHTS:** You have read or have had read to you all of the above. **You have been informed that you do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits to which you are entitled.**

In the event of illness or injury that you believe to be related to the study, or have questions about this research, you can call Dr. Catherine Ayers (XXX) XXX-XXXX during the day or Dr. Brian Martis (XXX) XXX-XXXX after hours (available 24 hours a day). If you have any questions or concerns about your rights as a research subject, the validity of a research study, or research personnel you can contact the Research Compliance Officer at 858-642-3817, VA Research Service at 858-642-3657, VA Regional Counsel at 858-642-1540, or the VASDHS Human Research Protection Program at 858-642-6320.

_____has explained the study to you and answered all your questions. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You will receive a copy of this consent form and a copy of the Health Insurance Portability and Accountability Act (HIPAA) Authorization that you signed. You will also receive a copy of the California Experimental Subject's Bill of Rights.

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By signing this form, you indicate that you have been informed of your rights as a research subject, and that you voluntarily consent to participate in this study. You have read this information, which is printed in English. This is a language that you read and understand. You have been informed what the study is about and how and why it is being done.

_____ _____
Subject's Signature Date

_____ _____ _____
Signature of Researcher obtaining consent Name (print) Date