# Informed Consent

Version #6; 1/18/23

MUSC Specialized Center of Research Excellence (SCORE) on Sex Differences: Stress-Reactivity and Cannabis Use in Cannabis-Using Older Adults

Short Title:
Stress-Reactivity and Cannabis Use in Cannabis-Using Older Adults (PUMA)

NCT05072795
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**Medical University of South Carolina**
**CONSENT TO BE A RESEARCH SUBJECT**

**TITLE OF RESEARCH:** *MUSC Specialized Center of Research Excellence (SCORE) on Sex Differences:* Stress-Reactivity and Cannabis Use in Cannabis-Using Older Adults

*Concise Summary*

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. The purpose of this study is to learn more about how cannabis use affects memory and thinking, and stress response, in older adults.

If you agree to participate, you will undergo screening to confirm that this study is right for you. Once screening is complete, you will complete questionnaires, blood and saliva tests, memory and thinking skills tests, and brain Magnetic Resonance Image (MRI). Participants will then complete CREMA sessions (Cue Reactivity Ecologic Momentary Assessment) at home, three times a day for a week. CREMA sessions include looking at stressful and neutral pictures and rating stress and craving. During this week, female participants (only) will also collect and store additional saliva samples each morning for hormone testing. At the end of this week, you will return to the clinic and participate in a stress task. The total time you will be in this study is about two weeks.

There are risks to the study which are described in this document. Some of the risks include exposure to stress, bruising or discomfort from blood draws, and MRI risks. There is a risk of loss of confidentiality, but the researchers will code the samples and research information to protect privacy and minimize risk. There will be no direct benefit to you from participating in this study. However, it is hoped that the information gained from the study will help improve understanding of the effects of cannabis use on memory and thinking among older adults. This is not a treatment study. You do not have to participate in this study and you can stop participating in the study at any time.

If you are interested in learning more about this study, please continue to read below.

## A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study that is sponsored by the National Institute on Aging and the National Institute on Drug Abuse. Please read this consent form carefully and take your time making your decision. As study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand.

The purpose of the study is to evaluate how cannabis use affects memory and thinking skills and response to stress in older adults. The study will also relate cannabis use to Alzheimer's Disease

(AD) biomarkers (measurable substances in blood that indicate condition), and test whether sex and hormones play a role in these effects. You are being asked to participate because you are between the ages of 50 and 80 and have indicated that you use cannabis products on a regular basis. The investigator in charge of this study is Dr. Andreana Benitez. This study is being conducted at the Departments of Neurology and Psychiatry at the Medical University of South Carolina (MUSC) and will involve approximately 50 volunteers.

## B. PROCEDURES

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

Eligibility Assessment

You will be evaluated first to see if you meet the study requirements. Part of this visit may be done remotely. In that case, you will be asked to find a private location to have a video call with study staff using an online program called Doxy.me. Research personnel will ask you questions about your mental health, substance use, medical history, and personal history. You will be asked questions about your physical health and medications you are currently taking or have taken in the past. You will be asked about how often you have been using cannabis products over the past year and about cigarette smoking and other substance use. You will be asked to stop using marijuana and alcohol for at least 12 hours prior to visits on Study Day 0 and Study Day 8. You will be asked to stop all other drugs of abuse while you are on the study, until you complete study Day 8.

Day 0: Study Visit

If you are eligible to participate in the study, you will be scheduled to come to the clinic for Study Day 0. You will be asked to stop using alcohol and cannabis products for at least 12 hours before this visit and to fast for at least 8 hours before the visit. If you are a female of child bearing potential, you will undergo a urine pregnancy test when you arrive. This test must be negative for you to complete all other study procedures. When you arrive, a urine, saliva and breath sample will be collected to test for drugs of abuse and alcohol. After ensuring your eligibility to proceed, you will do the following:

*Vitals and fasting blood draw.* We will collect no more than 1 tablespoon of blood and measure your height, weight, blood pressure, and pulse. It is required that you not eat or drink anything other than water for at least 8 hours before this blood draw.

*Memory and thinking skills tests.* You will undergo these tests either in paper-and-pen or computerized formats. We will record your verbal responses on some parts of the tests.

*Brain MRI.* Magnetic resonance imaging (MRI) uses a magnet and radio waves to make images of your brain. You will be asked to lay on a narrow bed and then slid into a small tunnel approximately 6 feet in length and over 2 feet in diameter. You will hear a loud machine-like noise.

Days 1-7: Cue Reactivity Ecologic Momentary Assessment (CREMA)

On Days 1- 7 you will complete the CREMA at home using an iPhone. You will be trained on how to do this during the Study Visit (Day 0) and will be given written instructions for using the app at home. If you do not have an iPhone or do not wish to use your own, we will provide one to you for the duration of the study. CREMA is an app that allows you to complete study procedures on an iPhone and provides information about your response to different types of cues in a real-world setting. You will complete three CREMA sessions a day during the study for a total of 21 sessions. Each day, two CREMA sessions will show either stressful or neutral pictures and ask you to rate your current levels of stress, craving, and mood. For the third CREMA session, you will just be asked to rate your mood, craving, and recent drug use without being shown pictures. If you were given an iPhone to use, you will return it to study staff at the end of the study. *Female participants will also be asked to collect a saliva sample each morning, for a total of 7 collected samples. These samples will be brought back to the study team on Day 8.*

Day 8: Stress Reactivity Task

On Day 8, you will be scheduled to come to the clinic to participate in a stress reactivity task. You will be asked to arrive at 11 am and to avoid caffeinated beverages and use of cannabis products for at least 12 hours before this appointment. If you are a female of childbearing potential, you will undergo a urine pregnancy test. You will provide breath, urine, and saliva samples that will be tested for alcohol and drugs of abuse. Approximately thirty minutes after you arrive, a blood pressure cuff will be placed on your arm. Throughout the remainder of the procedures, you will provide saliva samples for hormone measurement, will rate your mood and level of cannabis craving, and your heart rate and blood pressure will be measured. During the actual task, you will give a brief speech and solve a math problem out loud in front of a group of strangers. If you are unable to attend the clinic on Study Day 8, you may be re-scheduled for the following day. However, after Day 9 the study procedure cannot be re-scheduled.

## C. DURATION

Your study participation will last approximately two weeks. The Eligibility Assessment will take about 1.5 hours. Study Visit (Day 0) will take about 3 hours. You will spend approximately 30 minutes a day completing study activities at home on Days 1-7. Day 8 will take about 3 hours.

## D. RISKS AND DISCOMFORTS

Blood Draw: Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely.

Questionnaires/tests: It is possible, though unlikely, that the questionnaires and/or tests that you will undergo could cause some stress and/or anxiety. If this happens to you, you will be able to stop and take breaks, and you can stop at any time. Stopping the questionnaires/tests will not affect your further participation in the study.

MRI: There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from participation in this research study. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner. Please inform the study staff if you have a history of claustrophobia (extreme anxiety in close spaces). This may also be a contraindication to participation in the study.

Incidental Findings: We are performing the MRI solely for the research purposes described above. It is not a clinical MRI intended for diagnostic or therapeutic purposes. If you want your MRI to be reviewed by a physician so that the physician can look for medical issues, you can request a copy of your scan. We will provide a CD copy of your MRI at no charge.

Stress Task: Participation in the speech and math task may cause some anxiety and feelings of stress. Some of the CREMA sessions may also cause anxiety but should be no more stressful than events encountered in everyday life.

Confidentiality: There is a risk of a loss of confidentiality as a result of participation in this study. Information about you, as well as your image, will be kept in password-protected databases and computers and will only be accessible by the principal investigators and research staff. To ensure confidentiality, all participant information (questionnaires and identifying information) will be identified only by your code number and kept in locked cabinets and in password-protected databases. You should also know that if you threaten to harm yourself or others or give information about child or elder abuse, this information will be reported to appropriate authorities as required by law.

Your urine will be screened for the presence of cannabis and other potentially abused or illegal drugs. These results will not be part of your medical record but will be kept in research records maintained by the investigator. Every effort will be made to protect the confidential nature of this information. However, there may be circumstances under which the investigator will be legally required to release this information.

The Investigator reserves the right to discontinue study participation for any individual who is determined to be a threat to self, staff, or other study participants, or who is unable to complete the study assessments or provide informed consent.

## E. MEDICAL RECORDS AND/OR CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except if you have consented to the

disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you are an MUSC patient you have an MUSC medical record. If you have never been an MUSC patient, a MUSC medical record will be created for the purposes of this study. All information within your medical record can be viewed by individuals authorized to access the record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law; however, there is the possibility that your research information will be disclosed.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self or others

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

## F. BENEFITS

There will be no direct benefit to you from participating in this study. However, it is hoped that the information gained from the study will help improve understanding of the effects of cannabis use on memory and thinking among older adults.

## G. COSTS

Since this study is not occurring in the context of clinical care, there will be no cost to participate in this study if you use a study cell phone. If you choose to use your own phone for CREMA, any cellular data and usage rates assessed by your carrier will apply. All study-related tests and procedures will be paid for by the Sponsor.

## H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will be compensated as follows:

| | |
|---|---|
| Eligibility Assessment: | $50 |
| Study Visit (Day 0): | $55 (for brain MRI) |
| | $40 (for vitals and provision of blood and saliva samples) |
| | $50 (for neurocognitive testing) |
| CREMA (Days 1-7): | $105 (maximum, for $5/completed CREMA session with 21 total sessions) |
| | *$70 (maximum, for $10/completed saliva sample with 7 total samples – female participants only)* |
| TSST (Day 8): | $50 |
| *Total:* | $350 per participant upon the completion of all procedures (males only) |
| | *$420 per participant upon the completion of all procedures (females only)* |

Payment for study visits will be made using a pre-paid debit card, called a ClinCard. You will receive payments after completion of each procedure as outlined above. In the event that the Screening & Eligibility Assessment is initiated via telehealth, the ClinCard will be mailed to you after completing the session. Clincard works like a bank debit card and you may use the card to purchase goods or services everywhere Debit MasterCard is accepted. You will be given a ClinCard at the beginning of the study. Each time you receive payment for participation in this study, the money will be added to the card, as outlined in the payment schedule above. Details of the debit card system are explained on an additional sheet.

Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

## I. ALTERNATIVES

This is a voluntary research study. You may choose not to participate. If you are interested in treatment for your cannabis use, referrals will be provided to you.

## J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

## K. DISCLOSURE OF RESULTS

Results of the research will not be shared with you. However, any clinically relevant information that is discovered will be discussed with you. If an incidental finding is identified on MRI, you will be contacted by telephone and will be given a CD copy of your MRI images (sent by mail or given in-person) to assist with your clinical follow-up.

## L. AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information MUSC may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and MUSC committees having authority over the study such as:
  - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study or, if you are participating in a study designed for the development of a drug or device, your authorization will remain in effect until the drug or device is approved by the FDA or until the company's application to study the drug/device is withdrawn. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact MUSC's Privacy Officer at (843) 792-8740.

## M. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

## N. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

## O. COLLECTION OF SPECIMENS

As part of this study, we would like to store blood, saliva, and urine specimens collected from you for future research on cannabis use or Alzheimer's Disease. This future research may be conducted by Dr. Andreana Benitez or by other researchers who obtain IRB approval for their research. This research will not involve genetic studies. There are several things you should know before allowing your blood, saliva, and urine to be studied or to be stored.

1. The specimens will be labeled with a code that only study personnel can link back to you. Researchers outside of this study will not be given a link between the code number and your name or any other identifying information. While we hope this will prevent any potential loss of privacy or confidentiality, we cannot make any guarantees.
2. In addition to your name, other information about you might be connected to your sample. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to investigators studying your specimen. Such information might be important for research or public health. It is possible that this information (including genetic information) might come to be associated with your racial or ethnic group.
3. The specimens obtained from you in this research may help in the development of a future commercial product. There are no plans to provide financial compensation to you should this occur.
4. In this study, investigators will not tell you what they find out about you, nor will they contact you if a test becomes available to diagnose a condition you might have or later develop.

You may request at any time that your research samples be removed from storage and not be used for future research. If you decide you want your samples removed, you may contact Dr. Andreana Benitez via written communication at the following address: 97 Jonathan Lucas Street, CSB 301, MSC 606, Charleston, SC 29425. Once the request is received, and if your samples have not already been used for other research, they will be destroyed. If you do not make such a request, your specimens will be stored indefinitely or until completely used.

## P. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below for paper consents, or scroll down to the bottom of the screen and select your choice electronically:

____Yes, I agree to be contacted
____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.
In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

## Volunteer's Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Andreana Benitez at (843) 792-8274. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, please sign below for paper consent or scroll to the bottom of the screen to provide an electronic signature.

_____ _____
Person Obtaining Consent Date

_____ _____
Signature of Participant Date