

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

TITLE OF RESEARCH: Sex differences in neurobehavioral response to acute THC in adults with cannabis use disorder

NCT07225777

Concise Summary

You are being asked to volunteer for a research study. Research studies are completely voluntary and include only those who wish to participate. The purpose of this study is to examine how men and women that use cannabis (marijuana) regularly respond to different kinds of rewards. We hope this information will help others develop treatments for people who are addicted to cannabis.

If you wish to participate, you will first attend a screening visit for eligibility. If you are eligible and still wish to participate, study participation will include 2 in-person laboratory visits that take place at least 2 days apart. Visits will last around 7 hours each. At one visit you will orally self-administer capsules containing delta-9-tetrahydrocannabinol (THC), the primary psychoactive chemical in cannabis, and at the other visit you will receive a placebo. A placebo is an inactive substance that looks just like the capsules containing THC. The order in which you receive each treatment will be randomized, like the flip of a coin. You will also complete a 1-hour brain scan and answer questions about how you are feeling (e.g. "Do you feel a drug effect right now?") at both visits. At the first laboratory visit, your blood will be drawn to assess certain genes related to how your body processes cannabis.

Potential benefits for participating in the study include detailed substance use assessments and treatment referrals, if needed. Study outcomes may be used to inform medication development for cannabis use disorder. Potential risks involved in study participation include loss of confidentiality, discomfort following a moderate-to-high dose of oral THC, discomfort during a blood draw, and psychological discomfort during an extended brain scan. Participants are free to end study participation at any time without risk of consequences. This is not a treatment study. You do not have to participate if you don't want to.

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

A. PURPOSE OF THE RESEARCH

This study is being conducted to understand how sex contributes to differences in how people that use cannabis regularly respond to rewards. This study will specifically examine differences in brain activity between men and women when exposed to different kinds of rewards (THC, money) using imaging. There is evidence to suggest that men and women respond differently to these rewards, but no research has been conducted looking at sex differences among people that use cannabis regularly. This study will also examine how different genes affect how people feel when they use cannabis. If there are sex or genetic differences, this study may guide person-specific treatment development for cannabis use disorder.

This study will include oral administration of synthetic delta-9-tetrahydrocannabinol (THC; MARINOL®) or a placebo (inactive substance). THC is the chemical component of cannabis that produces its hallmark effects (“high”, hunger, drowsiness). In this study, oral THC will be used to simulate the rewarding effects of recreational cannabis use; this study is not assessing THC as a potential treatment. Some potential risks related to use of THC include stomach pain, dizziness, nausea, paranoia, somnolence (sleepiness), abnormal thinking, and vomiting. MARINOL® is approved by the FDA for use in certain medical conditions, but its use is considered investigational for the purpose of this study.

Please read this consent form carefully and take your time making your decision. As the principal investigator or study staff discusses this consent form with you, please ask them to explain any words or information that you do not clearly understand. You are being asked to participate in this study because you are between the ages of 21 and 45 and have indicated that you use cannabis on a regular basis. The study is sponsored by the National Institute on Drug Abuse. The investigator in charge of this study at MUSC is Dr. Erin Martin, Ph.D.. The study is being done at the Addiction Sciences Division of MUSC. Approximately 40 people will take part in this study.

B. PROCEDURES

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

1. You will first be evaluated to make sure you are eligible to participate in the study. This process will take approximately 3 hours. Research personnel will ask you questions about your psychiatric, substance use, and medical history. You will be asked about your current health and if you are currently taking or have taken any medications. You will be asked about your cannabis use over the past year, about your menstrual history (if applicable), and about use of nicotine and caffeine. You will be asked to provide a urine sample that will be tested for recent drug use and pregnancy (if applicable). If you are of childbearing potential, you will be tested for pregnancy first. If the pregnancy test is positive, we will not test for drug use, and you will not be allowed to participate in the study.
2. If you are eligible for the study following evaluation, you will be asked to return to MUSC for your Day 1 study visit. If you are female, you will be asked to track your menstrual cycle and contact study staff when your menses begins. Day 1 will take place within 3 days of the start of menses.
3. You will be reminded by the investigator to not use cannabis starting at 7:00pm the day before your Day 1 visit. You will also be asked to fast overnight starting at 7:00pm the night before your visit, and to not eat breakfast the day of the visit.
4. You will be asked to arrive at MUSC by 9:00am for your Day 1 study visit. You will be provided with transportation to and from the visit. The visit will take place in the laboratory and last about 7 hours (9:00am-4:00pm). Urine, breath, and saliva samples will be collected at the start of the visit to assess recent drug and alcohol use. The urine sample will be tested for pregnancy (if applicable). If the urine sample is positive for pregnancy, the sample will not be tested for drug use, and your study participation will end at that time. If the urine samples is positive for any

drugs other than cannabis, your study participation will end at that time. If the saliva drug test is positive for any drugs, including cannabis, your study participation will end at that time. You are asked to not smoke cigarettes or use a nicotine vaporizer during laboratory visits; if you are nicotine dependent, you will be provided with a nicotine patch.

5. After urine, breath, and saliva samples have been collected, you will complete questionnaires regarding your recent substance use and how you are feeling. The latter questions will be asked 6 more times over the course of your visit at regular intervals and will take around 5 minutes to complete. You will also be provided with a light breakfast (toast with jam).
6. After breakfast, you will have your blood drawn (10mL or approximately 2 teaspoons). Blood samples will be used to examine genetic differences that could contribute to the results seen in the study. Genetic research is research to identify genes that cause or contribute to a disease or trait is an increasingly important way to try to understand the role of genes in human disease. Important terms in genetic research are:
 - i. DNA: Your genes are made up of DNA. DNA is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child.
 - ii. RNA: RNA is short for ribonucleic acid. RNA is a genetic material that has a major role in making proteins.
 - iii. Proteins: Proteins are the building blocks of your body, cells, and organs.
7. At approximately 9:40am, you will be given capsules containing either 40 mg THC or a placebo. You will receive one or the other at each visit, and the order in which you receive the capsules will be randomly determined (like the flip of a coin). If you attend both study visits, you will receive both substances. The capsules will be taken with water.
8. At approximately 11:40am, you will be escorted to the Center for Brain Imaging where you will complete a 1-hour magnetic resonance imaging scan. Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise. You will complete one task in the scanner where you will press buttons to either gain or lose monetary rewards, but most of the scan will be spent quietly lying still.
9. Once the scan has been completed, you will be provided with lunch. You will be discharged from the Research Nexus at approximately 4:00pm and provided with transportation home.
10. At the end of the Day 1 visit, your Day 2 visit will be scheduled. The Day 2 visit will follow the same procedures as Day 1, except the blood draw will not be repeated. Your study participation will end following completion of the Day 2 visit.

C. DURATION

Participation in this study will consist of 3 in-person visits. The first visit (screening) will last up to 3 hours, and the other two visits will last 7 hours each. Visit scheduling will be dependent on availability of the participant, research staff, and MRI scanner. The minimum time to complete the study is 5 days.

D. RISKS AND DISCOMFORTS

The interviews that you will receive during the course of the study involve limited risks or discomforts beyond those of a standard clinical interview situation, such as feeling upset at the review of your psychiatric status, boredom, or fatigue. If a question makes you uncomfortable, you may refuse to answer it. There is a chance that some of the questions may increase your desire to use cannabis. Research staff will be available to discuss this with you and provide you with treatment resources if you would like them.

There is a risk of a loss of confidentiality of your personal information as a result of participation in this study. Information about you will be kept in password-protected databases and computers and will only be accessible by research personnel. In order to ensure confidentiality, all of your information (questionnaires and identifying information) will be identified only with a code number and kept under lock and key 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 the appropriate authorities as required by law.

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

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. If you are pregnant or become pregnant and test positive for illegal drugs, South Carolina law requires that the SC Department of Social Services (DSS) be notified. You will be at risk of going to jail or losing custody of your children. To prevent pregnancy, you are encouraged to use non-hormonal birth control methods if you are of childbearing potential. Examples of non-hormonal birth control include condoms, the copper intrauterine device (IUD), and abstinence.

There have been no ill effects reported from exposure to the magnetism or radio waves used in the MRI. 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. Lying in the scanner for up to 1.5 hours may be uncomfortable for you.

Oral THC may have side effects such as stomach pain, dizziness, nausea, paranoia, somnolence

(sleepiness), abnormal thinking, and vomiting. You were recruited for this study because you reported using cannabis regularly in the past month, meaning you likely have a tolerance to the effects of THC. This makes it less likely for you to experience these side effects. Trained nursing and psychiatric staff will be available if needed to ensure your safety and you will be provided with transportation to and from dosing sessions to avoid risks related to driving will impaired. All side effects associated with taking oral THC are expected to be mild and temporary.

Oral THC can also cause changes in blood pressure or heart rate that could be dangerous for people with heart disorders, and might increase the risk of seizures in people with seizure disorders. People with a history of heart or seizure disorders will not be included in this study to reduce potential risk.

The oral THC used in this study is formulated using sesame oil. People with a sesame oil allergy might therefore have an allergic reaction to the study drug, which could include lip swelling, hives, rash, oral lesions, skin burning, flushing, and throat tightness. People with a known sesame oil allergy will not be included in this study to reduce risk.

Blood samples obtained in this study will be used for genetic research. Genetic research studies may present unique risks to human subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of confidentiality (private information), loss of insurability and employability, paternity, and social stigmas. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members. Genetic research raises difficult questions about informing you and other subjects of any results, or of future results. Some people feel anxious about the possibility of having a defective gene that would place them or their children at risk. Some people want to know what is found out about them; others do not. The risks of knowing include anxiety and other psychological distress. The risks of not knowing what is found include not being aware if there is treatment for the problem being studied. But these risks can change depending on whether there is a treatment or cure for a particular disease and on how clear the results are. If there is a medical reason to seek specific information from you, your doctor will tell you this. A process called "genetic counseling" is often appropriate in such cases; you should ask your doctor or nurse about this if you have any questions.

South Carolina law, mandates that your genetic information obtained from any test or from this research, be kept confidential. Our state law prohibits an insurer using this information in a discriminatory manner against you or any of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then we must take all steps to protect your identity. You will still be responsible for paying for health care, however. The Medical University of South Carolina will not be responsible for such costs, even if care is needed for a condition revealed during research or clinical testing.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

The experimental procedures may have unknown side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

The investigator reserves the right to discontinue your study participation if you are determined to be a threat to self, staff, or other study participants, or if you are unable to complete the study assessments.

E. 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 unless you have consented to the disclosure. More specifically, identifiable information or biospecimens will not be shared with your medical providers who are not involved in this research unless you authorize the study to disclose information to them, or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Information about your study participation will not be in your MUSC medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record. A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must authorize the researchers to release it.

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 and others, but there could be 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

Direct benefits to you from participating in this study include detailed assessments of your substance use and referral to treatment if needed. It is hoped that the information gained from the study will help inform treatment development for cannabis use disorder.

G. COSTS

There is no cost to you for participating in this study.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will be paid up to \$538.00 for participation in this study. A breakdown of payment information is below:

Item	Payment
Screening Visit	\$30
Study Visit 1	\$150 for visit completion Up to \$104 based on study task performance (average amount earned = \$21)
Study Visit 2	\$150 for visit completion Up to \$104 based on study task performance (average amount earned = \$21)
Total Possible Compensation	\$538

Payment for study visits will be made using a pre-paid debit card, called a ClinCard. It 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. You will receive payment at the end of each in-person visit.

ClinCard is administered by an outside company called Greenphire. Greenphire will be given your name, address, SSN and date of birth. They will use this information only as part of the payment system, and it will not be given or sold to any other company. Greenphire will not receive any information about your health status or the study that you are participating in. Bankcards can only be issued to an adult. If you are younger than 18 years, payments to you may be issued to your parent, in trust for you.

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 not a treatment study. Resources for addiction treatment may be provided upon request.

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

The MRI scan will be used to answer research questions, not to examine your brain medically. This MRI scan is not a substitute for one a doctor would order. It may not show problems that would be picked up by a medical MRI scan. Nevertheless, if research staff or a study doctor reviewing your MRI scan believes there may be a medical issue in the scan, we will ask your permission to contact your primary care physician. If you do not have a primary care physician, we will assist you in finding a doctor to follow up on any finding that may not be normal.

After the study has been completed, you may access your own study results by personal request. To receive your results, please contact the Principal Investigator (see contact information below) in writing.

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. CLINICAL TRIALS.GOV

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.

N. COLLECTION OF SPECIMENS

IRB Number: «ID»
Date Approved «ApprovalDate»

As part of this study, urine, blood, and saliva samples will be collected from you. Saliva samples will be used to assess recent substance use at study visits only and will be destroyed as soon as drug test results are read. Urine samples will be tested upon collection for recent substance use and stored at MUSC until quantitative analysis of cannabinoid metabolites can be conducted. These samples will not have any information that could identify you and will only be labeled with your study ID number and the time of collection. Once analysis has been completed, urine samples will be destroyed. Blood samples we collect will be sent to Eremid Genomic Services for analysis of your genetic data. These samples will not have any information that could identify you and will only be labeled with your study ID number. Research will not include whole genome sequencing. Study personnel at Eremid will not have access to any of your identifying information. After the study has been completed, all samples shipped to the Eremid will be destroyed. You may also request to have your samples be destroyed by contacting the Principal Investigator in writing (see contact details below).

O. 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:

____ 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. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records. 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.

Volunteers 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. Erin Martin at (843) 876-3528 or marterin@musc.edu. 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.

_____ Signature of Participant	_____ Date	_____ Name of Participant
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_____ Signature of Person Obtaining Consent	_____ Date
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