Neurobehavioral Effects of Cannabidiol in Youth Alcohol Use Disorder

NCT05317546

08/08/2023

Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH:
Neurobehavioral Effects of Cannabidiol in Youth Alcohol Use Disorder

If participants include those under 18 years of age: 1) The subject's parent(s) or legal guardian(s) will be present when the informed consent form is provided. 2) The subject will be able to participate only if the parent or legal guardian provides permission and the adolescent provides his/her assent. 3) In statements below, the word "you" refers to your child or adolescent who is being asked to participate in the study.

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 the study includes evaluation of both the safety and the effectiveness of the study medication, which is called cannabidiol (or CBD).

Specifically, we are evaluating how CBD versus an inactive substance (i.e., flavored sesame oil) affects the brain in adolescents who may use alcohol. CBD has been approved by the Food and Drug Administration (FDA) for use in adults and children for other uses, but little is known about its effect on brain function in youth or on youth who may use alcohol. After eating a snack, participants will receive one dose of CBD (600mg) or inactive flavored sesame oil before two different magnetic resonance imaging (MRI) brain scans separated by approximately 2.5 weeks. We will collect saliva samples; blood, breath, and urine samples; you will be asked to smell alcoholic beverages while being monitored, and you will fill out several questionnaires at each in-person visit. You will be sent daily texts questionnaires while you are in the study. The full study will last approximately 1.5 months.

There are risks to the study drug that are described in this document. Some of the risks include dry mouth, diarrhea, reduced appetite, drowsiness, and fatigue. There is a risk of loss of confidentiality, but the researchers will code the samples and research information to protect privacy. There are no direct benefits to the participant, but we hope the information will help us develop treatments for youth who use alcohol. This is not a treatment study; however, all participants will have access to a trained clinician throughout the study.

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

A. PURPOSE OF THE RESEARCH

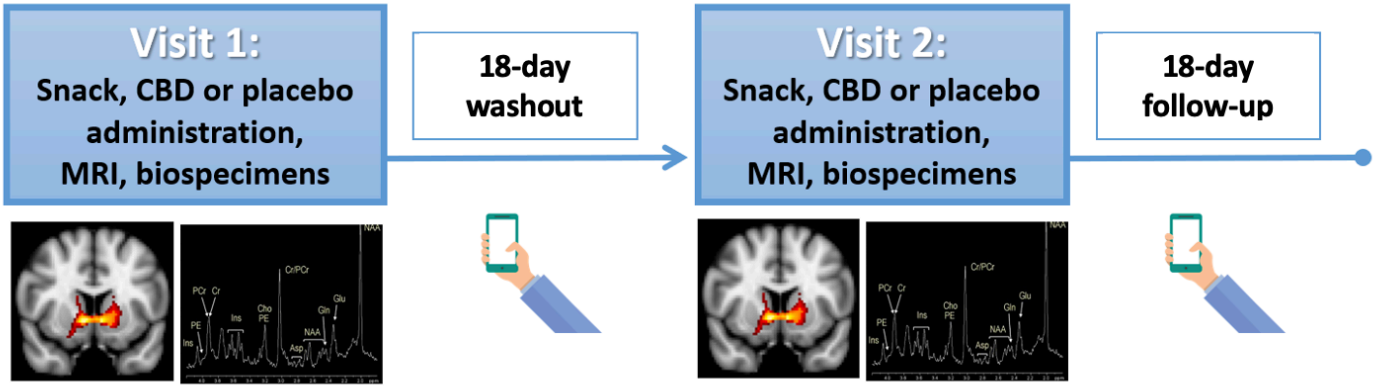
The purpose of this study is to understand if CBD may be an effective medication for youth who have problems with their alcohol use. You are being asked to participate in this study because you are between 16-22 years old and have used alcohol. A grant from the National Institutes of Health (NIH) will sponsor this study. Portions of Dr. Squeglia and her research team’s salaries will be paid by this grant. This study is being conducted at one site, the Medical University of South Carolina, and will involve 35 volunteers.

B. PROCEDURES

Overview: For this study, you will complete two magnetic resonance imaging (MRI) scans over the course of one month. Before each scan, you will take CBD or an inactive substance (flavored sesame oil; also referred to as "placebo"). You will not know when you will be receiving the CBD or the inactive substance. We will collect saliva samples, blood, breath, and urine samples and you will fill out several questionnaires at each in-person visit. You will be sent daily text questionnaires for approximately a month of the study. If you are unable to attend or complete a visit due to unexpected conflict (e.g., transportation issues, travel, University closings), arrangements may be made to remotely complete as much of the visit procedures as possible.

Parents will **not** be informed about their child's substance use and youth self-report and lab data are confidential except for any acute safety issues (e.g., suicidality, abuse).

Here is a visual overview of the study:



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

Screening (1 hour): If you have completed the Entryway Intake study in the past 30 days, portions of this screening will have been completed. Data collected during the Entryway Intake will be carried over and included to avoid repeating any data collection. Examples of such data include answers to completed surveys and questionnaires about your substance use.

Additional screening for this study will include a brief medical history and a review of medications by a trained clinician. A urine sample will be collected for a urine drug test and pregnancy test (only participants assigned female at birth). The pregnancy test will be completed prior to the drug testing. Individuals testing positive on the pregnancy test or those who plan to become pregnant during the study period cannot participate in the study and no further study procedures will be completed. Participants will need to take steps to avoid becoming pregnant during the study. We will also check

your pulse, blood pressure, temperature, and weight (vitals). You will be asked questions about your general substance use, mood, and alcohol use and craving.

The research team will use several methods of contact to keep in touch with you. We will ask you to provide us with phone numbers, e-mail addresses, current addresses, and contact information of family and friends who may know how best to reach you.

Visit 1 *(5 hours):* When you come in for your visit, you will be given Epidiolex (i.e., CBD) or the inactive substance (i.e., flavored sesame oil) to be taken with a snack which you will choose. You will receive both Epidiolex and the inactive substance, but the order you receive them will be determined by chance. You will have a 50:50 chance (like the flip of a coin) of receiving either CBD or the inactive substance during the first visit. For the second visit, you will receive whichever substance you did not receive the first time. Neither you nor your study team will know the order of the substances you are receiving; however, the researchers can find out what you are taking if there is a need to do so.

Before the scan, you will be asked to complete questionnaires, provide saliva (to measure the microorganisms in your body, such as fungi, bacteria, and viruses), and provide urine, breath, and approximately one tablespoon of blood to measure alcohol and other substance use. You will complete a task where you smell an alcohol of your choice and rate how you feel. You will then have a 1-hour MRI scan. A second saliva sample will be collected after the scan.

During the MRI scan the following will happen:

1. If you would like, you may first be introduced to the mock (fake) MRI scanner. This is a model of a scanner that is not magnetically active. It is used to introduce people (that may or may not have ever been in an MRI scanner) to the size, shape, and sounds associated with the scanning procedure. During the introduction to the mock scanner, you will be asked to lay down on the scanner bed. This bed will then be slowly pushed back into the tube of the scanner and we make sure you are comfortable enough to participant in the actual scan.
2. Before you go in the scan room, we will make sure you have no metal on your clothes or body. You will then lay down on the MRI scanner bed and your head and shoulders will be inside the MRI tube during the scan. You will be given earplugs to wear while you are in the scanner. You will be able to speak to and hear the research staff during the scan. While you are in the MRI scanner, we will take pictures of your brain during several scanning sessions. You will be asked to lay still in the MRI scanner during this time. In between each scanning session we will talk to you through the speakers in the MRI scanner to see how you are feeling. You will be given a pressure-sensitive ball which you can squeeze at any time to end the MRI scan if you feel uncomfortable. Furthermore, we will be able to hear you and will be talking with you over a speaker periodically to make sure that you are feeling well.
3. Several tasks will be completed during the 1-hour MRI scan. These tasks involve looking at different images on a screen and occasionally providing responses with a hand pad.

These procedures are completely non-invasive and painless. There is no radiation with MRIs.

Visit 2 *(5 hours):* About 18 days after **Visit 1**, you will go through the same procedures as the first visit. The study substance you receive the second time will be determined by which substance you have already received. If you already received CBD, you will take the inactive substance and vice versa.

Daily Texts: Beginning the day after your first MRI visit, you will be sent daily text questionnaires. These will continue until approximately 18 days after your second scan when your final remote visit is completed.

Final remote visit *(30 minutes):* About 18 days after Visit 2, you will have a phone or video visit. This will be a short visit consisting of some follow-up questions.

At any point in the study, you will have the opportunity to meet with a clinician if you would like to change your alcohol or other substance use. You can request this at any point. You will also be asked if you would like to meet with a clinician at the end of the study. Meeting with the clinician is optional.

At each MRI visit, you will be closely monitored for excessive drowsiness and fatigue prior to leaving the research facility.

You may be withdrawn from this study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

You may withdraw from the study at any time. If you decide to stop participating in the study, you are encouraged to talk to study staff first so that stopping can be done safely. Another reason to tell study staff that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful to you.

C. COLLECTION OF SPECIMENS

As part of this study, we would like to store blood and saliva specimens collected from you for future research on youth alcohol use. This future research may be conducted by Dr. Lindsay Squeglia or by other researchers who obtain IRB approval for their research. This research may involve genome sequencing studies. There are several things you should know before allowing your blood and saliva 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. Research results from any additional research will not be placed in your medical record.

4. Loss of privacy or confidentially is a risk of collection of specimens; however, we have procedures in place to minimize this risk (see C.1 above, Section E.5 below). There are no direct benefits to you for the collection, storage, and subsequent research use of specimens.

In this study, investigators will not tell you what they find out about you, nor will they contact you for additional consent nor 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. Lindsay Squeglia at the following email address: squegli@musc.edu. 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.

D. DURATION

Participation in the study will include a brief screening visit (less than one hour), 2 MRI visits (4-5 hours each), a remote follow-up visit, and daily text questionnaires (less than 3 minutes per survey) over a period of approximately 1.5 months. No more than 60 total daily text questionnaires will be sent if there are scheduling delays.

E. RISKS AND DISCOMFORTS

There are risks involved with participating in this study, including risks associated with CBD, the MRI scan, study procedures, emotional distress from answering personal questions, and loss of confidentiality.

In this study, you will be taking Epidiolex (CBD) orally (by mouth) one time. All medications may cause side effects and there are some risks and discomforts associated with CBD. You will be monitored closely by the medical clinician associated with the study. If the medical clinician or you decide to stop your participation in the study due to unwanted experiences or side effects, you will receive appropriate follow-up care as determined by the medical clinician.

1) Adverse Effects of Epidiolex (CBD)
   Though Epidiolex (CBD) is often well-tolerated, it can cause side effects, such as dry mouth, diarrhea, reduced appetite, drowsiness, and fatigue. CBD can also interact with other medications that some people take, such as blood thinners. These side effects are usually mild and go away even with continued use of CBD. Current medications will be reviewed by the clinician to assess for any potential interactions with CBD.

   Because CBD has not been evaluated in combination with many other medications, it will be important for you to report to the research staff any medications you may be taking before, during, or after the study. Medications include prescription medications from a doctor, over-the-counter medications that you may buy in a drug store, herbal medications that you may buy in a health food store, or any other drugs you are using.

"Increased risk of suicidal thoughts or behavior" is listed as a potential risk in the package insert of CBD, though a recent published review of multiple CBD clinical trials found no increased suicidality even at higher doses or with repeated dosing. Regardless, our team includes experienced clinicians who will carefully assess for suicidality and will manage any safety concerns.

2) Risks associated with MRI

We are performing imaging solely for the research purposes described above. It is not a clinical scan intended for diagnostic or therapeutic purposes. If you want your scan 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 an electronic copy at no charge.

The risks associated with MRI are minimal for individuals who do not have metal and are not claustrophobic. Some discomfort may result from lying in the scanner for up to 60 minutes. You will be welcome to take short breaks between the various tasks. During the MRI scan, there are potential risks that are detailed below.

Potential Risks of MRI:

- Although the risks from magnetic resonance imaging (MRI) are low, it is critical that participants do not have metal in the skull, metal implants, a cardiac or brain pacemaker, or old metal fragments in the eye or retina. If participants have a question about metal their body, they should inform the researchers and they will determine whether it is safe in an MRI scan.
- Some discomfort may occur from having to remain still while in the MRI scanner. During the scanning, an emergency ball will be given to squeeze if there are any feelings of discomfort or desire to be pulled out of the scanner.
- Although the MRI scanner is open on both ends, some people become anxious or claustrophobic (fear of small spaces) when entering the MRI scanner due to the feeling of being enclosed. If participants have a history of experiencing this, they should inform the study personnel.
- There is a chance that the technologist doing the scan could see something that does not look normal, in which case they would ask a radiologist to review the scan. If the radiologist recommends further action, we will contact you regarding their suggestion. This may cause you anxiety while you wait for further information or follow-up.

3) Interviews/Rating Scales (Questionnaires)

The questions that will be asked may be sensitive in nature and make you feel uncomfortable. You may be asked personal questions that you find distressing. You may refuse to answer any question(s) that you do not wish to answer.

4) 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.

5) Risk of Loss of Confidentiality
All study records will be placed in a locked, secure, limited access location. Your participation in the study and the information you provide will be treated as confidential. The information we collect will contain a code and not your name to protect your confidentiality. Codes linking numbers and names will be kept in a password-protected secure database and will not be accessible to anyone outside the research team.

The information you share with us is confidential. That means we do not share information you tell us with anyone outside our research team. This helps us maintain privacy so we are able to get honest answers. However, you should also know that if you threaten to harm yourself or others or give information about child or elder abuse or neglect, this information will be reported to appropriate clinical staff and other persons outside the research program as necessary to protect yourself and others as mandated by law.

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

F. BENEFITS

As part of the study, you can meet with a licensed clinician, which you may find to be beneficial. Given the investigational nature of this study, benefit cannot be guaranteed or promised. Information gained from this study may help other investigators have a better understand how CBD affects the brain.

G. COSTS

You will be receiving daily texts with a link to an online survey, which could result in charges on your phone service plan. We can also send the link via email if preferred. Otherwise, there will be no cost to you because of participation in this study.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will receive $300 for completing the two MRI visits ($150 V1 and $150 V2) and $25 for the screening. Also, you can earn a bonus of $1 per day for completing the remote text questionnaires (up to a maximum of $60). Mileage reimbursement may be available for participants who live who live more than 25 miles away. You will be reimbursed based on the state's most updated reimbursement mileage rate.

You have the choice between being paid in cash or through a pre-paid debit card, called ClinCard. ClinCard works like a bank debit card and you may use the card to purchase goods or services everywhere Debit MasterCard is accepted. If you choose to be paid via ClinCard, 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.

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. 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.

J. ALTERNATIVES

Participants who wish to receive information on mental health and/or substance use treatments will be referred clinically. Participation in this study is voluntary, and you may refuse to participate or discontinue participation at any time. If you choose not to participate, it will not affect your relationship with any current treatment provider or your right to health care or other services to which you are otherwise entitled.

K. CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed to meet the requirements of the study sponsor and related agents participating in the study.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of child abuse and neglect, or harm to self or others.

L. NIAAA DATA ARCHIVE ($NIAAA_{DA}$)

Data from this study will be submitted to the National Institute on Alcohol Abuse and Alcoholism Database ($NIAAA_{DA}$) at the National Institutes of Health (NIH). $NIAAA_{DA}$ is a large database where deidentified study data from many NIAAA studies is stored and managed. Deidentified study data means that all personal information about you (such as name, address, birthdate, and phone number) is removed and replaced with a code number. The date of your visits though, will be linked with your code number to support appropriate secondary use of the data. Sharing your deidentified study data helps researchers learn new and important things about alcohol problems more quickly than before.

During and after the study, the study researchers will send deidentified study data about your health and behavior to the $NIAAA_{DA}$. Other researchers across the world can then request your deidentified study data for other research. Every researcher (and institutions to which they belong) who requests your deidentified study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with $NIAAA_{DA}$. The study data provided to $NIAAA_{DA}$ may help researchers around the world learn more about alcohol problems and how to help others who have problems with alcohol. NIAAA will also report to Congress and on its website about the different studies using $NIAAA_{DA}$ data. You will not be contacted directly about the study data you contributed to $NIAAA_{DA}$.

You may decide now or later that you do not want your study data to be added to the $NIAAA_{DA}$. You can still participate in this research study even if you decide that you do not want your data to be added to the $NIAAA_{DA}$. If you know now that you do not want your data in the $NIAAA_{DA}$, please tell the study researcher before leaving the clinic today. If you decide any time after today that you do not want your data to be added to the $NIAAA_{DA}$, call or email the study staff who conducted this study, and they will tell $NIAAA_{DA}$ to stop sharing your study data. Once your data is part of the $NIAAA_{DA}$, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about $NIAAA_{DA}$, this is available on-line at https://nda.nih.gov/niaaa.

M. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the study, you will be notified.

N. 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.

O. 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.

P. CLINICAL TRIALS.GOV

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website 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.

Q. 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 or if consenting electronically, scroll down to the bottom of the screen and select your choice:

_____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 sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, employees of the sponsor, the FDA, 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. Lindsay M. Squeglia at (843) 792-5451. I may also 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 about my rights as a research subject in this study, 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.

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

Signature of Person Obtaining Consent	Date

If you wish to participate, you should sign below for paper consents, or scroll down to the bottom of the screen and sign electronically:

Signature of Adult Participant (18 years or older)	Date

If minors (ages 16-17) are research participants, both parents must sign this consent form, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal custody of a child.

Name of Authorized Representative #1	Relationship to minor participant: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #1	Date

Name of Authorized Representative #2	Relationship to minor participant: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #2	Date

For Minors 12-17 years of age: “My participation has been explained to me, and all my questions have been answered. I am willing to participate.”

Signature