Neuroscience-Informed Treatment Development for Adolescent Alcohol Use

NCT03238300

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

**TITLE OF RESEARCH:**
**Neuroscience-Informed Treatment Development for Adolescent Alcohol Use**

*If participants include those under 18 years of age: 1) The subject's parent or legal guardian 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.*

## A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or 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 this study is to evaluate how an active medication [an over-the-counter supplement N-acetylcysteine (NAC)] versus an inactive medication (e.g., sugar pill) affects the brain functions in adolescents who may or may not use alcohol. NAC 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.

The study is sponsored by the National Institute on Alcohol Abuse and Alcoholism. The investigator in charge of this study is Dr. Lindsay M. Squeglia. The study is being done at the Medical University of South Carolina and approximately 55 people will take part.

## B. PROCEDURES

*Overview:* For this study, you will first complete a screening visit to determine your eligibility for the study. If eligible, you will take NAC and an inactive medication given in the same form as the active drug for 10 days each, separated by 11 days, and you will attend a total five visits. You will not know when you will be receiving the NAC or the inactive medication. We will collect a saliva sample and a blood sample at Visit 1, Visit 2, and Visit 4. You also will be given breath and urine screenings at each visit. You will also receive a 1-hour MRI scan at Visit 1, Visit 2, and Visit 4. 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. Finally, you will be sent text reminders twice a day and/or e-mail reminders while you are in the study.

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

***Screening*** *(~2 hours):* You will come in for a screening visit to see if you qualify for the study. Parents/guardians of participants under 18 years old will participate in the screening, evaluation, and informed consent/assent procedure. The Informed Consent process may take place electronically and you may sign electronically. You will be given a paper or electronic copy of this form to keep. This visit will include a brief medical history, review of medications, and physical exam. Parents will **not** be informed about their child's substance use and youth self-report and lab data are confidential with the exception of any acute safety issues (e.g., suicidality, abuse). A urine sample will be collected for a urine drug test and pregnancy test (females only). The pregnancy test will be completed prior to the drug testing. Females testing positive or those who plan to become pregnant during the study period cannot participate in the study and no further study procedures will be completed. If you have recently completed the Youth Collaborative (YC) Intake study (Pro00094743) in the past 30 days, portions of this screening will have been completed. Data collected during that visit will be carried over and included in order to avoid repeating any data collection. Examples of such data include answers to completed surveys and questionnaires about your substance use. 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. If you complete the full screening visit, it could take up to 3 hours.

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 home and work addresses, and contact information of family and friends who may know how best to reach you.

***Visit 1****- Randomization 1 & Scan (2 hours):* You will be asked to complete questionnaires, urine drug tests, provide saliva and blood samples. You will then have a 1-hour MRI scan. After, you will receive your first 10-day supply of study medication with instructions.

You will be given both NAC and the inactive medication throughout the course of the study, but the study medication you receive first will be determined by chance. You will have a 50:50 chance (like the flip of a coin) of receiving either NAC or the inactive medication during the first 10 days of the trial. Neither you nor your study team will know which study medication you are receiving; however, the researchers can find out what you are taking if there is a need to do so. You will take 2 capsules of study medication twice a day (2 capsules in the morning and 2 capsules in the evening).

During the 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. After we remove metal from your clothing, you will be placed in the actual MRI scanner. You will be lying down and your head and shoulders will be inside the opening during the procedure. 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. 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-*** *Scan (1.5 hours):* 10 days after **Visit 1**, you will be asked to complete questionnaires, urine drug tests, provide saliva and blood samples again. You will then have your second 1-hour MRI scan (same procedure as the first scan). Afterwards, you will stop taking your study medication for 11 days.

***Visit 3-*** *Randomization 2 (30 minutes):* Eleven days after **Visit 2**, you will be asked to complete questionnaires and urine drug tests. After, you will receive your second 10-day supply of study medication with instructions.

The study medication you receive will be determined by which medication you have already received. If you already received NAC, you will then take the inactive medication and vice versa. However, neither you nor your study team will know which study medication you are receiving; however, the researchers can find out what you are taking if there is a need to do so. You will again take 2 capsules of study medication twice a day (2 capsules in the morning and 2 capsules in the evening).

***Visit 4-*** *Scan (1.5 hour):* On the following Monday (10 days after **Visit 3**) you will be asked to complete questionnaires, urine drug tests, provide saliva and blood samples again. You will then

have your third 1-hour MRI scan (same procedure as the previous scans). Afterwards, you will stop taking your study medication and your participation will be complete.

*Daily Reminders:* The day after you receive your first medication dose, you will be sent daily text and/or e-mails reminders to help you remember to take your medication. You may also be asked questions in these texts/emails. These reminders will be sent every day you are in the study.

*Medication Videos:* You will be trained on how to record and upload videos of yourself taking your morning and evening medication doses. Study staff will look at what time you took these videos to confirm that you are taking your study medication within the correct time frames.

*Pill Tracking:* In order to monitor that you are taking your study medication, we will use special pill bottle caps, that will send us information about when you take your medication.

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. DURATION

Participation in the study will include a screening visit and 4 subsequent visits over a period of approximately 31 days.

## D. RISKS AND DISCOMFORTS

There are risks involved with participating in this study, including risks associated with N-acetylcysteine (NAC), the MRI scan, study procedures, and loss of confidentiality.

All medications may cause side effects and there are several known risks and discomforts associated with NAC. Your condition 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 N-acetylcysteine (NAC)
   In this study, you will be taking NAC orally (by mouth). The most common side effects seen when NAC is taken by mouth include diarrhea, nausea, vomiting, and headache.

These side effects are usually mild and go away even with continued use of NAC. There is also a risk of a skin reaction, such as flushing, itching, or rash. The dose of NAC (2400 mg daily) used in this study is much less than the dose patients receive for acetaminophen overdose. In addition, NAC has been used up to 3500 mg in adult subjects orally in the treatment of Alzheimer's disease. Although we have observed mostly mild side effects of 2400 mg NAC in our studies involving adolescents and adults, and no significant differences in side effects between NAC and the inactive medication, it does not rule out the possibility that more serious side effects may occur. Some patients who have taken intravenous NAC (liquid NAC in a vein) for the treatment of acetaminophen overdose have had more serious reactions. Allergic reactions have occurred in about 5% of patients taking intravenous NAC. These reactions may be mild, consisting of flushing, rash, and itching. Less common side effects include trouble breathing, low or high blood pressure, fever, and hives. If untreated, such a reaction could lead to death. Even more rare serious side effects of intravenous NAC are irritability, confusion, and seizures. These reactions (severe allergic reaction or seizures) have never been reported when NAC is taken orally (by mouth), as it will be in this study.

It is highly unlikely (probably less than one chance in several thousand) that you will have a severe allergic reaction to NAC. In the event that you begin to experience mild itching or localized rash, we will advise you to take an antihistamine medicine, like Benadryl (diphenhydramine). If you have trouble breathing, the emergency medical system (EMS – call 911) should be called, and you should be transported to the nearest emergency room for immediate treatment. The likelihood of a seizure is probably even less than the likelihood of a serious allergic reaction.

Because NAC 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 treatment phase. 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 "street" drugs.

It is unknown how the drugs in this research study will affect an unborn baby. If you are a female able to have children, you should not become pregnant or nurse a baby while in this research study. If you become pregnant during the study, you must notify the research staff immediately. The research staff will wish to follow the outcome of any pregnancy and condition of any newborn and report this to the study sponsor. In addition, if you are a female able to have children, you must agree to use at least one of the following methods of birth control:

- oral contraceptives (birth control)
- contraceptive patch
- barrier (diaphragm or condom)

- intrauterine contraceptive system
- levonorgestrel implant
- medroxyprogesterone acetate contraceptive injection
- complete abstinence from sexual intercourse
- hormonal vaginal contraceptive ring

2) Risks associated with MRI

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. You also may skip questions and/or stop the questions or tasks at any time if you feel uncomfortable. During the MRI scan, there are potential risk 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.
- The MRI scanner is noisy and there is a risk of hearing damage if participants do not wear earplugs. To eliminate this risk, earplugs will be given to wear during each scan.
- 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.
- If pregnant, participants will not be eligible to continue in the study.
- Unknown Risks: The experimental procedures may have unknown side effects. The researchers will let you know if they learn any new information regarding side effects.

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) Phlebotomy

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 locked secure location 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. Likewise, we do not share with you any information they provide us. 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 treatments 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.

## E. BENEFITS

You may benefit from participation in this study. However, 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 NAC affects the brain.

While the MRI scan is a research scan and these images do not have the same quality or specifications as a clinical scan, you may benefit from knowing that one of the medical staff on this study will briefly review the structural MRI scan to determine if there are any obvious structural abnormalities of your brain. You will be contacted by the PI and/or the neuroradiologist if there are obvious abnormalities. If by chance something abnormal is observed, one of the Investigators on this protocol will contact you and counsel you as to what clinical referral would be appropriate. If the possibility of such a situation is too stressful for you, your child should not participate in our study. It is important to understand that this research MRI scan is not the same as a clinical MRI scan, and should not be thought of as one. It is not a full clinical study and will not be read by a radiologist.

## F. COSTS

There will be no cost to you as a result of participation in this study. You will be receiving text reminders twice a day, which could result in charges on your phone service plan. If problems arise with this, we can send the reminder via e-mail instead.

## G. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will receive $460 for completing all 5 visits. Also, you can earn up to a $40 bonus ($2 per day that you are receiving medication) if you take each dose of medication, or provide staff with an explanation for why the medication was not taken, within a 4 hour requested time window. If you do not take the medication due to adverse side effects, you will need to discuss these side effects with research staff. Participants experiencing adverse side effects interfering with their ability to participate may be taken off the medication. If you are unable to finish the study, you will be prorated for number of completed visits. You are also eligible for a $50 referral bonus for each individual you refer who successfully randomizes into this study. Mileage reimbursement may be available.

If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a tax form (Form 1099).

## H. ALTERNATIVES

Participants who wish to receive additional information on 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.

## I. 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 in order 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.

## J. SIGNIFICANT NEW FINDINGS

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

## K. 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.

## L. 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.

## 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. 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, 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. 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 contact the Medical University of SC Hospital Medical Director (843) 792-9537 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, you should sign below or if consenting electronically scroll to the bottom of the screen and sign.*

| | | | |
|---|---|---|---|
| Signature of Parent/Legal Guardian *(if under age 18 only)* | Date | Signature of Person Obtaining Consent | Date |
| Printed Name of Parent/Legal Guardian | | Printed Name of Person Obtaining Consent | |

Signature of Adult Participant or Printed Name of Minor Participant _____ Date _____

Printed Name of Adult Participant

***15-17 years of age:**
**"My participation has been explained to me, and all of my questions have been answered. I am willing to participate."**

Signature: _____

Age: _____ Date of Birth:_____