Informed Consent Statement

Study Title: Human Alcohol Seeking Despite Aversion

NCT number: NCT03648840

07/14/2020

INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR

Human Alcohol Seeking Despite Aversion

You are invited to participate in a research study of the relationship between the response to visual (images) and/or auditory (sound) stimuli and alcohol related behavior. You were selected as a possible subject because you called our study line or participated in previous studies and expressed interest. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

The study is being conducted by Drs. Martin Plawecki of the Department of Psychiatry, Indiana University School of Medicine and Dr. Melissa Cyders of the Department of Psychology at IUPUI. It is funded by the National Institute on Alcohol Abuse and Alcoholism, Rockville, MD.

Important Information

This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

1. **Why is this study being done?**
   The purpose of this study is to determine whether images and sounds affect a person's drinking behavior. For more information, please see the *Study Purpose* section below.

2. **What will happen to me during the study?**
   Today we will collect information from you to determine if you are appropriate for the study. If you are enrolled in the study, you will attend two full day (7:30-7:00) sessions where we will infuse you with alcohol while we measure your brainwaves and you perform tasks and answer questions. For more information, please see the *Procedures for the Study* section below.

3. **How long will I participate?**
   If you are enrolled in the study, we will schedule the sessions as soon as possible, with the two sessions scheduled 1-2 weeks apart.

4. **Will I benefit from the study?**
   We don't expect you to receive any benefit from taking part in this study, but we hope to learn things which will help scientists in the future.

5. **Will taking part expose me to risks?**
   Taking part in this research may expose you to significant risks. It is very important that you understand the risks before you decide whether to participate. Some of the most common risks include: There is a risk that the images and sounds you see and hear could be disturbing. There is a risk of loss of confidentiality. When we draw blood or place a catheter in your arm, there is a risk of discomfort, and a risk that the catheter could dislodge causing fluid to flow into tissues around your vein. If you drink more than you normally do, there is a risk you could become nauseous or get sick. There are several risks associated with the fMRI scan that are listed in detail below, and there are other possible risks not listed here but described later in this consent. For more details, please see the *Risks of Taking Part in the Study* section below.

6. **Do I have other options besides taking part in this study?**
   You may choose not to take part or may leave the study at any time.

7. **Will I be paid to participate?**
   Payment for your time or travel is available if you decide to take part in this study. For more information, please see the *Payment* section below.

8. **Will it cost me anything to participate?**
   Taking part in this study may lead to additional costs to you or your insurance company. For more information, please see the *Costs* section below.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this study.

STUDY PURPOSE

The purpose of this study is to determine the relationship between the response to visual (images) and/or auditory (sound) stimuli and alcohol related behavior. In this study, you will perform work tasks in order to receive rewards of either alcohol or water delivered via your veins (infusions) to see if your choices are related to other factors, such as your family history of alcohol use, your subjective feelings about the alcohol exposure, and your recent drinking history and style. We will record electrical signals and may take pictures of your brain to help us determine what effects the stimuli have on your behavior, how your brain responds to those stimuli, and if your responses are related to how your brain works.

NUMBER OF PEOPLE TAKING PART IN THE STUDY

If you agree to participate, you will be one of 300 subjects who will agree to participate in this research.

PROCEDURES FOR THE STUDY

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

Screening Procedures:

Submit to a physical exam by an Indiana CTSI Clinical Research Center (CRC) nurse; provide approximately a teaspoon of blood drawn from a vein in your arm for testing liver function; provide a cup of urine for drug testing and, if female, pregnancy testing; complete various questionnaires and structured interviews regarding your alcohol use, your family's history of alcoholism, and past history of aversive/traumatic experiences. You will also be introduced to the machines that will be used for testing in this study in the setting where the study visits will be performed. Some or all of the interview measures, with the exception of those activities that require in-person screening such as the blood draw and urine sample testing, may be conducted on-line. After the interview measures are complete, you will be compensated with $25.00 in cash, electronic gift card, or mailed a check or gift card for $25 depending on how the interview was completed. If you complete the online portion of the interview, but are withdrawn from the study before completing the in-person portion, you will be compensated with $15 in electronic gift card, or mailed a check or gift card. If there is a significant delay between the online and in-person portion of the interview, you may request compensation of $15 in electronic gift card, or mailed a check or gift card. When you come in for the in-person portion of the interview, you will also receive a parking voucher to pay for your parking fees, or a bus pass if you rode the bus.

If you have already completed and been compensated for a related alcohol study interview or participation, and the information collected from that project was used to evaluate your eligibility to participate in this study, you will not have to complete the interview for this study and will not receive compensation for it. We may update a limited amount of the information you provided at that earlier interview.

Experimental Procedures:

After your interview:

You will attend two or three sessions during outpatient visits to the Neural Systems Lab (NSL) at University Hospital and the Neuroscience Research Center. You will agree on a schedule for testing with study staff. You may receive phone and/or email messages that increase in frequency as the dates for testing approach. You will go about your normal life, including usual drinking habits, but not eat anything nor drink alcohol from 10 pm on the evening before the testing sessions.

Procedures for the two infusion sessions:

Orientation to Laboratory: On the day of infusion testing, you will arrive at the NSL by 7:30 am, or other time agreed upon with study staff, and undergo a brief physical exam by Indiana (CTSI) Clinical Research Center (CRC) Nurses, testing of urine for substances and pregnancy, and documentation of zero breath alcohol concentration before a 550 calorie breakfast is served. We will record your recent drinking since the last time you were in the lab.

Preparation for Testing: A catheter (a small tube) will be put in a vein at the elbow of one arm. You will be instructed in the use of the alcohol breath meter and be familiarized with the constant attention work task, subjective response questions, and image rating system under NSL technician supervision.

Brainwave collection: You will be fitted with an elastic cap that places small electrodes near your scalp, and then have some gel squirted into each electrode so that a good contact is made with your scalp. You also may have one electrode pasted onto your chest or neck so we can record your heart beat while being fitted with the elastic cap with electrodes. We will record your brainwaves from the electrodes on your scalp, along with your heart beat from the electrode on your chest or neck.

Preparation for Infusion: You will be prompted for a bathroom break and the catheter will be connected to the infusion pumps. You will complete a set of baseline measures. At approximately 9:30am, the infusion will begin. You will be unaware of your breath alcohol level and the rate of the infusion at all times. You will be allowed to speak with the technician at any time.

Infusion rate profile computation: We administer alcohol via your veins, or an infusion, using a solution of ~6.0% (v/v) ethanol in half-normal saline, prepared by the IU Health's research pharmacy. An individualized model of your characteristics (age, height, weight, gender) will be used to calculate the alcohol infusion. The safety limit will be set to 0.180 g/dL, more than twice the legal limit for driving. At the beginning of the infusion, you will be given alcohol to produce a breath alcohol concentration of 0.060 g/dL. Breath alcohol concentration is a measurement of the amount of alcohol in your breath, which is related to how much alcohol is in your blood. (The legal limit for driving a car after alcohol is a breath alcohol concentration of 0.080 g/dL.) While at a breath alcohol concentration of 0.060g/dL, you will repeat the measures completed at baseline. Then, after a 20-minute testing period, you will perform the constant attention task in order to receive rewards of either alcohol or water after choosing which of the two rewards you prefer. The constant attention task is a work task in which you press a button within a specific amount of time in response to a cue presentation. Throughout the infusion session, you will occasionally be asked to answer several subjective questions describing how you feel.

The infusion will conclude approximately three hours after it begins, and you will be served a lunch from the CRC kitchen. For the first infusion session, after testing is complete, you will remain on the CRC until 7pm or your breath alcohol concentration reaches 0.035 g/dL and you show no signs of intoxication, whichever is later. For the second infusion session, after testing is complete, you will remain on the CRC until you may be safely released and either 1) until the time you were discharged for the first session, 2) 7pm, or 3) your breath alcohol concentration reaches 0.035 g/dL and you show no signs of intoxication, whichever is later. If for either session you are required to stay past 7pm, you will be compensated at the rate of $15/hour in 20 minute increments for the time past 7pm that you have to stay, but you will not be paid this additional compensation until the end of the study. After 6pm you will be offered dinner from the CRC kitchen.

Upon discharge from the CRC, you will be paid in cash $100 for the first session and $175 for the second session, plus any additional compensation as noted above. If you terminate participation prior to the completion of testing, you will be paid $15/hour for your time on the day of testing or the regular fee for that day of testing ($100 or

$175), whichever is less, and be allowed to leave as soon as your breath alcohol concentration falls below 0.035 g/dL and you show no signs of intoxication, or a ride has been arranged for you.

Some subjects will be selected to participate in an fMRI brain imaging session, and if you are selected and agree to complete the brain imaging portion, you will do the following procedures:

You will agree on a day and time to attend the fMRI session at the Neuroscience Center. On the day of testing, prior to entering the imaging room, you will be asked to empty your bladder since emptying the bladder will be more difficult once the session is under way. If female, you will be asked to provide a urine sample to screen for pregnancy. We will record your recent drinking since the last time you were in the lab. You may be required to wear a hospital gown during the study, but it is unlikely. A changing room will be provided, and your privacy will be respected at all times.

Once you enter the scanning room, you will have some pads placed around your head to help you refrain from moving during the session. Even the slightest movement (such as that associated with breathing) can affect this procedure.

You may be provided with viewing glasses or headphones while in the scanner. If no headphones are provided, you will be provided with earplugs to protect your ears against the loud noise of the scanner. Special sensors for painlessly measuring heart rate, breathing, and/or brain electrical activity may be attached to your body during the study.

A series of short (approximately 5 minute) scans will be made to obtain images of your brain's anatomy (appearance). A longer (approximately 15 minute) scan may be performed in order to image blood vessels in your brain. During these scans the scanner will make tapping sounds. A number of long research scans, varying from 5-20 minutes, will be performed. You may be asked to perform a variety of mental tasks requiring you to pay close attention to things that you see or hear, and to concentrate. During these scans, the researcher will instruct you in performing the tasks designed to activate regions of your brain.

The entire procedure will take about one and one half hours. Occasionally, some individuals experience feelings of claustrophobia during the study. Some people have reported tingling or tapping sensations, or muscle twitches in different parts of their body during the imaging procedure. These sensations are not hazardous. If, however, the feeling causes you discomfort, notify the researcher at any time, and the study will be stopped. Occasionally, people who have clasped their hands tightly together during the study have reported a feeling of electrical shock and/or tingling in their hands and arms. This is also not hazardous, but to prevent this occurrence you should not clasp your hands during the study.

RISKS OF TAKING PART IN THE STUDY:

While on the study, the risks are:

You may experience discomfort from viewing the images or hearing the tones, but you may discontinue at any time and will be compensated for your time spent participating in the study.

Drawing blood from your vein requires the insertion of a needle and can result in temporary soreness and bruising where the blood is drawn.

There is a risk of physical discomfort that goes with inserting a small tube into a vein on the inside of one of your elbows, along with a possibility of bruising or infection that goes with having that tube in place.

There is a possibility that the tube could be misplaced or slip out of your vein while the alcohol is being infused, leading to infusion of alcohol in the tissues surrounding that vein and short-term discomfort.

There is a possibility that the rapid infusion of alcohol in your vein could cause irritation to the inside of your vein and lead to a burning sensation for a few minutes each time you "order" more alcohol.

However much or little alcohol you choose to self-administer, you must stay at the Indiana CTSI Clinical Research Center (CRC) until at least 7 pm on the day of testing, but you may have to stay longer if your breath alcohol concentration has not gone down to 0.035 g/dL yet or you appear to be intoxicated.

If you are a smoker, you may experience nicotine withdrawal because smoking is not permitted at the CRC.

If you choose to administer a lot more alcohol than you typically enjoy, there is a possibility that you may become intoxicated or get a headache or become nauseated (sick to your stomach) or even vomit. In addition, any time you are exposed to alcohol, you will have the urge to urinate more often than usual for a few hours.

While on the study, there is a risk of loss of confidentiality of your data.

The risks of applying the electrode gel and adhesive tapes are that your skin might react to those substances by becoming red and itchy. There is a potential risk of exposure to electrical shock because the head is connected to an electronic system used to measure brainwaves. This equipment meets OSHA standards and the risk of shock is very small.

Due to the magnetic fields which are present in the MRI scanner, loose magnetic objects (pocket knives, key chains, necklaces, earrings, etc.) can fly into the magnet with great force, if brought into the environment of the MRI scanner. You will be asked to remove such objects from your clothes and body in order to prevent this. There are some individuals who should not participate in an MRI study. These include persons with some types of metal parts in their body, such as clips used to close arteries in the brain or some types of prostheses (fake body parts), or persons with electronic implants, such as cardiac pacemakers. The magnetic field in the scanner can cause displacement or malfunction of these devices. We know of no risks or adverse effects from the radio signals used in this study.

Women who are pregnant should not participate in this study. If you are a woman of child-bearing potential, you should be advised that risks of MRI to a fetus are possible, but as yet unidentified. Alcohol is also potentially dangerous to a fetus. Therefore, if you are female you will have brief (urine) test for pregnancy, which must indicate that you are not pregnant, in order for you to participate in the study.

There are no known health risks to doing the tasks inside and outside the MRI scanner. Some individuals may nevertheless feel anxiety or become frustrated when performing the tasks. The tests and/or the associated MRI scanning can be stopped at any time, if you desire.

Collision hazard. The magnetic field near the MR scanner is strong enough to attract objects containing iron with great force. Near the magnet this force can be strong enough to pull objects in and cause them to fly down into the magnet. Such objects can become very fast moving objects that can cause injury or death. We have established a security zone to prevent objects containing iron from coming close to the magnet.

Radio-wave Effects. If metal wires or electrodes, such as electrocardiograph (ECG) leads (wires), are attached to you while in the scanner, the energy created by the imaging coils of the MR scanner (the cage over your head) may make enough electrical current in the wires to cause burns where the electrodes or wires contact your skin. The scanner operator is well aware of this risk and knows the proper methods to use to avoid this problem.

Nerve stimulation. Some subjects undergoing the rapid scanning procedures which will be used in this study have experienced minor nerve stimulation effects, such as muscle twitches and tingling sensations. There are no known risks associated with these effects. The devices used in our research create varying magnetic fields that are within the limits specified by the Food and Drug Administration (FDA).

Claustrophobia. The confining conditions of the MR scanner can cause claustrophobia (feelings of being closed in) in some people. If you experience claustrophobia during the study, the study will be stopped.

Hearing. The MR scanner produces tapping sounds during operation which may reach objectionable levels. To minimize any discomfort, you will be provided with disposable earplugs or headphones. The volume of any auditory stimuli will be calibrated to your hearing.

THE FOLLOWING MEASURES WILL BE USED TO MINIMIZE THE RISKS LISTED ABOVE:

If the images and tones presented during the study cause too much discomfort or distress, you can discontinue your participation.

The tube will be inserted into your arm by skilled nurses who use techniques designed to minimize discomfort and the possibility of infection and the chances that the tube will slip out of your vein.

The concentration of alcohol in the liquid infused into your vein is kept at 6%, and the liquid is preheated before it is infused to reduce the possibility of an unpleasant sensation.

You will be offered nicotine gum or a nicotine patch if you experience nicotine withdrawal or at the beginning of a session if you request it.

During the infusion session, we will be measuring your breath alcohol concentration to make sure that the concentration does not get too high, and we will be asking you questions about intoxicating effects, and remind you that you should be seeking only pleasant effects of alcohol self-administration.

We will keep your records in a secure location and limit the access to those records to the people who are conducting and analyzing the results of this study, unless required by federal regulations to provide those records to other people for review or you give us written permission to share those records with others.

If a skin reaction to the gel or adhesive tapes appears at any time, we will stop the infusion and remove the gel and tape.

BENEFITS OF TAKING PART IN THE STUDY

You will not personally benefit by taking part in this study.

ALTERNATIVES TO TAKING PART IN THE STUDY

You are welcome to decline to take part in this study. You may choose not to take part or may leave the study at any time.

WILL I RECEIVE MY RESULTS?

We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, you can decide whether you want this information to be provided to you. For example, we will run some laboratory tests from the blood taken at interview. We will notify you of any clinically significant abnormal laboratory values that may preclude you from participating. If you decide that you want this information, you may need to meet with professionals with expertise to help you learn more about your research results. The study team/study will not cover the costs of any follow-up consultations or actions. Please initial one of the following options:

_____ Yes, I want to be provided with this information.
_____ No, I do NOT want to be provided with this information.

CONFIDENTIALITY

We will keep your personal information confidential. We cannot guarantee absolute confidentiality. Your identity will be held in confidence in reports in which the study may be published. We will keep your information for about seven years. Your identity and participation in this study will become part of databases maintained by the Indiana University School of Medicine and the Indiana CTSI Clinical Research Center.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the IU Institutional Review Board or its designees, the Indiana CTSI Clinical Research Center, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP) and the National Institutes of Health (NIH), who may need to access your medical and/or research records.

For the protection of your privacy, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use any information, documents, or specimens that could identify you in any civil, criminal, administrative, legislative, or other legal proceeding, unless you consent to it. Information, documents, or specimens protected by this Certificate may be disclosed to someone who is not connected with the research:

(1) If there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases);
(2) If you consent to the disclosure, including for your medical treatment;
(3) If it is used for other scientific research in a way that is allowed by the federal regulations that protect research subjects
(4) For the purpose of auditing or program evaluation by the government or funding agency

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?

Information or specimens collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

GENETIC INFORMATION

This research follows the Genetic Information Nondiscrimination Act (GINA), a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to request the genetic information we get from this research and to discriminate against you based on your genetic information.

Your signature on this consent form gives us permission to study your DNA (genetic information that we get from your blood) at any time in the future in order to look for relationships between your genes and other variables. If you do not qualify to participate in this study, we may still look for relationships between your genes, your family history, and your behavioral, personality, and health information collected during the screening visit. Your DNA may also be studied to help detect any genetic influences that increase the risk of alcohol dependence. We may use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

The genetic information that comes from your participation in this study will never be identified with your name or social security number. In most cases the samples collected will need to be identified so that it can be linked to your study information; however, your identity will not be released to anyone outside the study. The blood and genetic information will be stored in secure, locked cabinets in the Neural Systems Lab research office or in a locked laboratory at the Indiana Alcohol Research Center. To minimize the risk of loss of confidentiality, the sample will be registered and processed by an experienced technician. No personal information will be recorded on the sample itself. Rather, the assigned subject number will be placed on the envelope or tube containing the sample. The subject number will be linked to your personal information. Personal information linked to your sample will be maintained in protected files. These files will be secured by encryption using a secret code and by safety procedures that prevent unauthorized access to computers and files. The stored information will be

available only to scientists in this study, or to other researchers who gain institutional review board approval to use this information in similar research. The investigators in this study plan to keep your blood sample and DNA indefinitely, and then use them later in analyses for this project.

COSTS

Taking part in this study will not lead to added costs to you or your insurance company, except possible costs described in the section entitled 'Compensation for Injury', below.

PAYMENT

You will receive payment for taking part in this study. You will receive $25.00 for completing the screening interview, unless you already received compensation for an interview with another alcohol related study. If you complete the online portion of the interview and are withdrawn before completing the in-person portion of the interview, you will be compensated $15. If there is a significant delay between the online and in-person portion of the interview, you may request compensation with $15 in electronic gift card, or mailed a check or gift card. Upon discharge from the CRC, for the infusions you will receive $100.00 for completing the first session and $175.00 for completing the second session. If you are selected and choose to participate in the brain imaging session, you will receive $100.00 upon discharge. If you fail to complete a testing session or withdraw early, you will be paid $15/hour for the time spent participating on that day. You will be paid $15/hour for any time you have to stay past the 7pm discharge time in 20 minute increments.

COMPENSATION FOR INJURY

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

CONTACTS FOR QUESTIONS OR PROBLEMS

For questions about the study or a research-related injury, contact the researchers, Drs. Plawecki or Cyders at (317) 948-6550. After business hours, please page Dr. Plawecki at (317) 312-2506.

In the event of an emergency, you may contact Dr. Plawecki by calling (317)944-5000 and asking that he be paged.

For questions about your rights as a research participant or to discuss problems, complaints or concerns about a research study, or to obtain information, or offer input, contact the IU Human Subjects Office at contact the IU Human Subjects Office at 800-696-2949 or irb@iu.edu.

VOLUNTARY NATURE OF THIS STUDY

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your decision whether or not to participate in this study will not affect your current or future relations with the Indiana University School of Medicine and IU Health.

Your participation may be terminated by Drs. Plawecki or Cyders without regard to your consent in the following circumstances: you do not cooperate with the study rules, you miss the scheduled infusion session, you show up for a session with a non-zero breath alcohol concentration, testing of your urine sample is positive for any drug of abuse, or, for women, testing of your urine sample indicates that you are pregnant, or if in the clinical judgement of the investigator it would not be safe and/or prudent for you to continue participating.

SUBJECT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. My signature of consent may be electronic or physical, depending on the format of the interview I am participating in.

I will be given or emailed a copy of this informed consent document to keep for my records. I agree to take part in this study.

Subject's Printed Name:_____

Subject's Signature:_____**Date**:_____
(must be dated by the subject)

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____**Date**:_____