HIC#: 2000023100
NCT03980184

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 4 (2016-2)

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Guanfacine to Improve Substance Use Outcomes in Women

Principal Investigator: Rajita Sinha, 2 Church Street South, Suite 209 New Haven CT

Funding Source: National Institute on Drug Abuse/NIH/DHHS

Invitation to Participate and Description of Project

You are invited to take part in a research study designed to look at the effects of a study medication on your craving, thinking and substance use. You have been asked to take part because it is our understanding that you are seeking treatment for your substance use. Approximately 100 people will be recruited for this study.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, and possible benefits. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Purpose

The purpose of this research study is to see if the study medication called Guanfacine reduces the desire to use substances (including alcohol), and also reduces substance use in individuals who are dependent on substances, such as cocaine, alcohol, marijuana and nicotine. You may only be using some of these substances. You may or may not experience craving for substances when you are in stressful, neutral or substance-related situations. We will check your craving and mood to see the effect that these situations may have on your substance craving. Guanfacine is an FDA approved medication that has been used to treat Attention Deficit and Hyperactivity Disorder (ADHD) and tic disorders in children. It has been also used for other indications for which it is not FDA approved. One of these is post traumatic stress disorder (PTSD). We are trying to see if it will prevent or reduce substance use relapse related to stress. These findings may also help us understand the physical and mental effects of stress, so as to better understand the factors that lead to substance use and relapse.

In addition, the purpose of this study is to determine if Guanfacine can be used in combination with standard substance abuse treatment to prevent relapse, and increase compliance with treatment.

APPROVED BY THE YALE UNIVERSITY IRB 5/10/2018 VALID THROUGH 5/1/2019

Description of Procedures

If you agree to take part in this study, and after the intake, you will be seen two times a week at the Yale Stress Center (YSC) at 2 Church Street South for 10 weeks. While being seen at the YSC, you will be offered outpatient substance abuse treatment, as well as urine screens and breathalyzers.

Intake procedures

If you agree to take part in this study, you will be asked to complete 2-3 intake appointments. Intake appointments take approximately 1.5 hours to complete. During these appointments we will ask questions about your substance use, demographics and health history. You will also complete a physical examination and blood work to ensure that all inclusion and exclusion criteria for the study are met.

As this study encourages abstinence from substances including alcohol, during the intake and throughout the study, we will assess for alcohol and substance withdrawal symptoms. The risks associated with stopping drinking and other substances may include: anxiety, shakiness, confusion, rapid heart rate, fever, and in rare cases, life-threatening seizures. These risks and the treatment required for these possible risks will be thoroughly reviewed with you during the intake process by both the clinical research staff. If you show clinical signs of alcohol withdrawal, you will be evaluated by the study doctor who will refer you for treatment for alcohol withdrawal. Depending on the severity of your alcohol withdrawal symptoms, she may send you for medical detoxification assessment and treatment to the Yale New Haven Hospital – Emergency Room (YNHH –ER) or to a medical detoxification facility such as Southern Connecticut Rehabilitation Center (SCRC). The detoxification treatment and referral is not part of this research study and your decision to take part in the research study will not be affected by your clinical treatment for alcohol withdrawal.

Outpatient treatment

You will be seen at the YSC two times a week with 1x per week individual substance use counseling with a psychologist or qualified counselor. You will be asked about your substance use and other psychological and physical problems that you may be experiencing. You will do questionnaires, which include questions about any side effects you may be experiencing.

Each time that you visit the clinic, we will obtain a urine sample for drugs and take a sample of your breath by asking you to blow into a breathalyzer to see if you have recently consumed alcohol. These procedures are for research purposes only. We also ask encourage you to reduce and abstain from substance use. In the event that your substance use increases or gets worse, you will be offered inpatient treatment or referred to a higher level of care at another facility. Your progress will be reviewed with you at each appointment.

After you are admitted to outpatient treatment, you will be started on either a placebo or the study medication, Guanfacine. A placebo is a dummy pill that does not contain any medication and is used for the comparison purposes of this study. You will be randomly assigned to one of these conditions: the first condition involves slowly increasing the dose of Guanfacine over the course of 2 weeks and then maintaining you at 3 mg per day or your “best” dose of Guanfacine until week

9, at which point your dose will be slowly deceased. For the second condition you will receive placebo medication throughout the study from week 1 to week 10.

The assignment to the first or second condition will be done by random selection, which means that it will be decided by the luck of the draw, and not selected deliberately because of any special characteristics or problems you have. After taking the first dose of study medication, we will ask you to stay while we check your pulse, blood pressure and other withdrawal symptoms. If you have any side effects from taking Guanfacine, you will meet with the research nurse or doctor who will check your symptoms and may adjust your dose if required.

The study drug is to be taken two times daily. Your study drug dose will be slowly increased up to your "best" dose up to 3 mg daily over the first 2 weeks. You will not know whether you are taking placebo or Guanfacine. We will prompt you on a smartphone using an application called MetricWire to remind you to take your study medication, and make ratings on your mood, craving, and tell us about your substance consumption. To check that you are taking your study medication, we will be collecting urines, and doing a blood draw at weeks 3, 6, and 9.

In week 9, your study medication will be reduced slowly down to zero over the course of 5 days. We will continue to check your pulse, blood pressure and withdrawal symptoms at each appointment. You will be asked to stay for up to one hour each time you come to the clinic during this week for monitoring.

If at any point during the 10-weeks you have any side effects from taking the medication, you should tell the investigators by calling the cell phone number 203-859-2840. If you would like to stop taking the medication, you may stop taking the next dose and we will schedule you for an appointment at the clinic within the next day so that we can slowly reduce your study drug dose.

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.

Laboratory sessions

To help us understand stress and addiction, you will complete two laboratory sessions: one in the first week before you start taking the study drug, and again in Week 9. We need you to abstain from any drug use for at least 48 hours prior to these laboratory sessions. To prepare for these sessions, we will interview you to tell us about specific events from your personal life, events that were stressful for you, and those that are associated with using alcohol and drugs. Stories about these situations will be put together with you. These stories will be later played back to you during the laboratory sessions and you will be asked to briefly imagine these situations. In addition to these stories we will ask you to select some situations that are neutral and relaxing from your own experiences. The neutral relaxing events that you select will also be described to you in a laboratory session and you will be asked briefly imagine that situation as well.

After completing the interview sessions, you will have a training session. The research assistant will meet with you and train you on how to generate and hold an image in your mind's eye. We

will guide you through imagining some common scenes such as reading a popular magazine and doing sit-ups in gym class, and train you on how to focus and keep the image in your mind.

We will also train you on how to get your body to relax by using relaxation procedures. The purpose of this training will be so you can clearly imagine the scenes that we describe to you in the laboratory sessions and so you can get yourself to become completely relaxed after imagining the scenes. In this session, we will once again describe the laboratory procedures to you and show you around the testing room. In addition, we will provide you with clear instructions on how to fill out questionnaires on your feelings and craving.

After the training session, you will take part in the laboratory sessions. During the laboratory sessions we will place headphones on your ears. After a brief relaxation period, you will be given instructions on the imagery task and you will then hear a story over the headphones. Your task will be to imagine yourself in the situation being described and relive it 'as if' it were happening to you at that moment. At various times during the session we will place a small cotton ball in your mouth for you to hold on the side against your cheek for 2-3 minutes. This cotton ball will soak up saliva. We will collect the cotton ball in 3 minutes and place another one in your mouth every 10-15 minutes. Your saliva will then be analyzed for naturally occurring chemicals that your body produces regularly.

The story you will hear will be a description of one of your personal situations that you described to us during the intake or a description of the neutral situation that you selected. The order of the stories will be selected randomly; you will not be told of the order of the stories presentation. After the imagery period, you will remain seated. From time to time, the research assistant will enter to collect saliva and you will also be asked to make some ratings of your feelings and alcohol and drug craving. You will also be asked to complete some brief mental tests.

During the course of the imagery session you may have some alcohol craving and changes in feelings due to your recall of personal events that were stressful or alcohol related. At the end of the laboratory session, we will give you relaxation instructions to help you reduce your craving and bring yourself into a relaxed mood. Once you are returned to your original mood state, the session will be over.

Each laboratory imagery session will last for about two hours. You will be given brief rest periods if you so desire. Should you feel anxious or unduly uncomfortable at any time during the session, you may ask that the session be stopped.

Risks and Inconveniences

The main risks that might occur if you decide to participate in this study have to do with taking the study medication Guanfacine, possibility of alcohol withdrawal if you are using alcohol heavily, blood draws and imaging you own stressful and drug-related situations briefly in the laboratory sessions. These are explained below:

i. Guanfacine: There are some risks associated with taking Guanfacine. Possible side effects commonly associated with Guanfacine include: low blood pressure, drowsiness, dry mouth, impotence, constipation, and dizziness. Usually all symptoms will disappear over time. If you regularly take barbiturates, sedatives, or drink alcohol, you should not take Guanfacine. We will make a full assessment of your intake of these substances when you start the study and will continue to monitor your breath and urine samples for recent alcohol consumption and use of other drugs. Guanfacine is used to treat hypertension. It has also been used to treat ADHD in children. We are currently studying its effects on alcohol relapse prevention for a period longer than the typical 7-10 days. While taking Guanfacine, you must exercise caution when operating dangerous machinery or driving motor vehicles until it is determined that you are not drowsy or dizzy from the study drug. The long-term use of Guanfacine for alcohol addiction is experimental, knowledge of its side effects may be incomplete and its use may involve risks that are currently unknown and unforeseeable.

ii. Alcohol Withdrawal and Abstinence: Abstinence from alcohol poses a risk of alcohol withdrawal symptoms. The risks associated with stopping drinking may include: anxiety, shakiness, confusion, rapid heart rate, fever and in rare cases, life-threatening seizures. These risks and the treatment required for these possible risks will be thoroughly reviewed with you during the intake process by both the clinical research staff. If you show clinical signs of alcohol withdrawal, you will be evaluated by the study doctor who will refer you for treatment for alcohol withdrawal. Depending on the severity of your alcohol withdrawal symptoms, she may send you for medical detoxification assessment and treatment to the Yale New Haven Hospital – Emergency Room (YNHH –ER) or to a medical detoxification facility such as Southern Connecticut Rehabilitation Center (SCRC). The detoxification treatment and referral is not part of this research study and your decision to take part in the research study will not be affected by your clinical treatment for alcohol withdrawal. As the treatment may lead to alcohol abstinence, we will assess alcohol withdrawal symptoms throughout the study period. If you show moderate to severe clinical signs of alcohol withdrawal, we will refer you to alcohol detoxification treatment as described above.

iii. Drawing of Blood: Blood will be drawn at your intake physical, and at 3, 6 and 9 weeks to check that you are taking your medication, to check your liver function, and if you are female, to see if you are pregnant. The total amount of blood drawn during the study is less than a can of soda and less than a regular blood donation. People who are in good health are not usually affected by this kind of blood loss. However, to be safe, you should not donate blood for at least 8 weeks after the three laboratory sessions.

iv. Imagining stressful and drug cue situations in the Laboratory Sessions: You will imagine your own reported stressful and drug related situations along with a neutral relaxing situation briefly during the laboratory sessions. This may lead to some passing feelings of anxiety, distress or drug craving. We find that these feelings are temporary and tend to go away after the session. To help with making them go away, we will help you do progressive muscle relaxation so you can make these feelings go away quickly. We will also offer a brief counseling session if you need to speak with someone about how you are feeling.

Benefits

There are no known benefits to you at this time. There are benefits to society, which would result from increased knowledge about treatments for substance abuse.

Economic Considerations

You will earn chances to win a prize ranging from 0 to $100 for each scheduled appointment that you keep. You will earn a chance to draw a prize, regardless of whether the urine sample you provide is clean or not. For every two biweekly appointments you attend, the chance to draw a prize from a fish bowl increases by one. The fish bowl prizes are valued at $0, $1, $25, or $100. If you miss your scheduled appointment, or do not take your study medication as directed, the number of draws will be reset to one.
In addition, you will receive $25 for completing the intake appointment phase, a $25 bonus at weeks 4, 8 and 10, and $5 for returning your medication packet each week. You will be compensated $2 per day for completing the daily smartphone app surveys, and a $6 bonus for completing all 7 surveys for the week. If you complete all aspects of the study, the most you can make is $350 plus the various amounts you will win for keeping your appointments and taking your study medication.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.

Alternatives

You may be able to enroll in behavioral treatment recovery groups and twelve step based self-help groups such as Narcotics Anonymous outside of this study. If you wish to enroll in one of these alternative treatments, research staff will help you arrange this treatment. However, you are not allowed to initiate any medication treatment for tobacco dependence and alcohol dependence during the course of this study. There are no FDA approved medications for the treatment of cocaine or cannabis dependence. We will help you in making referrals to outpatient treatment for behavioral and medications if you choose after the completion of the study.

Confidentiality and Privacy

If you decide to take part in this research study, you will be required to give us information about your substance use, criminal behavior, and HIV status. We will receive a Certificate of Confidentiality (CoC) issued by DHHS/NIDA. 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 protection offered by the CoC does not stop us from voluntarily reporting information about suspected or known sexual, physical, or other abuse of a child or older person, or a participant's threats of violence to self or others. If any member of the research team is given such information, he or she will make a report to the appropriate authorities. When the CoC is obtained, we will inform all active study participants.

Because this research is sponsored by the Department of Health and Human Services through NIDA, staff from that and other DHHS agencies may review records that identify you only for audit or program evaluation. They cannot report anything that would harm you or other research subjects.

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. All information collected on you will be kept in a locked cabinet or password protected on a computer. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and date of birth. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for five years, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely until it is destroyed.

The information about your health that will be collected in this study includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this study.
- Records about phone calls made as part of this research
- Records about your study visits

Information obtained during this research regarding

- HIV / AIDS
- Hepatitis infection
- Sexually transmitted diseases
- Other reportable infectious diseases
- Physical exams
- Laboratory, x-ray, and other test results
- Questionnaires

- The diagnosis and treatment of a mental health condition
- Use of illegal drugs or the study of illegal behavior
- Records about any study drug you received

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator at Yale University (Dr. Rajita Sinha) and the Co-Investigator at Stonybrook University (Dr. Helen Fox)
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about the drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the study

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, by deciding to take part in a double blinded treatment study and sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

In Case of Injury

If you are injured while in the study, seek treatment and contact the Principal Investigator, Dr. Rajita Sinha at 203-737-5805 as soon as you are able.

The Yale School of Medicine do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing from the Study

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments. The researchers may withdraw you from participating in the research if you repeatedly do not show up for appointments, do not take your study medication, or are found ineligible for the study.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to Rajita Sinha PhD at the Yale Stress Center, 2 Church Street South, Suite 209, New Haven CT 06519.

If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use (and give out) information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

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

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Rajita Sinha 203-737-5805. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.