

Official title of study: Nicotinic Cholinergic Modulation as a Novel Treatment Strategy for Aggression Associated With Autism

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**CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 1 (2014-4)**

**YALE UNIVERSITY SCHOOL OF MEDICINE – CHILD STUDY CENTER,
CONNECTICUT MENTAL HEALTH CENTER (CMHC)**

Study Title: Nicotinic cholinergic modulation as a novel treatment strategy for aggression associated with autism

Principal Investigator: Alan S. Lewis, MD, PhD

Funding Source: Autism Speaks Grant #9699 and Yale University Departments of Psychiatry (Marina Picciotto, PhD) and Child Study Center, (Fred Volkmar, MD)

Invitation to Participate and Description of Project

You are invited to participate in a research study designed to look at the value of transdermal nicotine in the treatment of aggression, irritability and agitation in young adults with Autism Spectrum Disorder. You have been asked to participate because you are an adult currently participating in a group or program developed for individuals with Autism Spectrum Disorders and have a primary caregiver with whom you have frequent contact.

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 research 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, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

Study in a nutshell

Participation in the study will involve taking a medication (7 mg nicotine patch) in the form of a skin patch for a total of three weeks. Some of these weeks you will receive a patch containing nicotine, and some of these weeks you will receive an identical appearing patch without nicotine (called a “placebo patch”). Wearing the placebo patch helps identify whether or not nicotine medication is beneficial. Neither you nor the study administrators will be told which patch you are wearing during the week prior to the rating visits. You will be assigned at random to a group which receives the nicotine patch first or a group that receives the placebo patch first. No matter which group you are in, the study is designed so that you will receive both the placebo and the nicotine patch by the time the study is completed. You have a 50% change of being assigned to either group. We are testing to determine whether there is a difference in irritability and other behaviors with nicotine versus without nicotine. We aim to enroll 16 subjects in our study.

What do I have to do if I participate?

The study involves three visits to the Yale Child Study Center or Connecticut Mental Health Center (CMHC). The first visit is the one during which this form will be reviewed and you will be able to decide whether or not you wish to participate in the study and a new outpatient chart may be created for you. Also, the study team will at this point determine whether you are a candidate for the study. If you decide to be in this study, and you will be visiting the CMHC as part of your study procedures, some information about your participation in this research study may become part of your CMHC medical record that identifies you. If you do not already have a medical record at CMHC, one may be made for your visit. The information that will be entered into your

medical record will include the following: name, date of birth, gender, date of visit(s), phone number, and address. If you are in fact a candidate and would like to participate, we will complete standardized rating scales by asking you and your primary caregiver questions to help us assess levels of anxiety, irritability, and aggression, as well as repetitive behaviors and ability to socialize with others. The specific rating scales are called the Aberrant Behavior Checklist, the State/Trait Anxiety Inventory, and the Social Responsiveness Scale-Adults. The purpose of the scales is to see if they are changed by our study treatment. We will also take your vital signs, which includes temperature, pulse and breathing rate, and blood pressure. The entire first visit should take about 90 minutes.

You will then go home with a set of patches to take in a specified order for the next three weeks. Each morning, you will wake up and place the patch on a clean, dry, and relatively hairless part of your skin. Appropriate sites include the upper arms, upper part of the chest, back, or abdomen. Patch placement will be varied each day to limit irritation. You will remove the patch at nighttime before sleep. The second visit will occur at the end of the first week. At this visit we will again repeat the scales as above with you and your primary caregiver, check your vital signs, and ask you about any side effects you may have encountered. This visit should take about 60 minutes. We will contact you by phone at the end of the second week to check in. The third and final visit will occur at the end of the third week. At this visit we will again repeat the scales as above with you and your primary caregiver, check your vital signs, and ask you about any side effects you may have encountered. This visit should also take about 60 minutes. You can also contact us at any time with questions.

Participation in this study requires that there be no non-study medication changes during the 3 weeks of participation. If a change to your medications becomes necessary, please contact the study physician.

We will not be accessing your medical record for this study, however we will collect your date of birth and full name. This is identifying information, which we will keep private. It is important for us to have this information to keep track of you throughout the study and for reporting purposes should you have any adverse experiences in the study.

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.

Risks and Inconveniences

The main burdens of this study are the use of a patch everyday for 3 weeks, and travel to the Yale Child Study Center or Connecticut Mental Health Center on three occasions. You will be compensated for these visits.

There are some risks associated with this study:

- Some people who use transdermal patches develop minor skin irritation. If this occurs, it will resolve following discontinuation of the patch. Varying the location of the patch from day to day reduces the likelihood of skin irritation. If irritation persists and is uncomfortable, please contact the study staff.
- Nicotine may result in side effects that are uncomfortable. Specifically, nicotine, like caffeine, can make some people feel stimulated. By this, you may notice that your heart is beating faster, or that you feel slightly anxious. You may feel mildly nauseous or lightheaded, which will eventually pass. If the symptoms do not improve within a few hours, please contact the study staff for further instructions. The study staff may instruct you to remove the patch, and the symptoms will resolve soon after patch removal.
- Nicotine may make it more difficult to sleep at night, a condition called insomnia. You will remove your patch prior to sleep at night. However, you may find it more difficult to sleep during the study period.

- Discontinuation of the nicotine patch after use for 7 days may result in symptoms of nicotine withdrawal, which include headache, stomach upset, nausea, anxiety, and irritability. Previous studies in adult non-smokers have shown this risk to be extremely rare, even after periods much longer than 7 days. However, nicotine patch has not been studied systematically in adult individuals with ASD. If you experience such symptoms, please contact the study staff.
- Nicotine is the addictive component in tobacco products such as cigarettes, and the addictive potential of nicotine is believed to be related to how quickly it is absorbed into the body. The nicotine patch delivers nicotine slowly into the body. Although unlikely, there is the potential you may become addicted to nicotine through use of the nicotine patch.

Benefits

Nicotine delivered through the skin may or may not improve symptoms of aggression, agitation or irritability you experience. Also, results from our study may contribute to generalizable knowledge about potential treatments for aggression and irritability in individuals with ASD.

Continuation of study drug after completion of the trial

The long-term use of the medication has not been studied in ASD, and there may be risks associated with continued use of which we are not aware. Therefore any discussion about continued use should be made in conjunction with your doctor.

Economic Considerations

You will be provided \$90 for completion of the first visit, and \$60 for each subsequent visit. If you leave the study between visits, you will not receive compensation for any uncompleted visits. If you present to a scheduled visit but have been unable to adhere to the study protocol, you will be paid for that visit but not for subsequent, uncompleted visits.

Treatment Alternatives/Alternatives

Treatment for aggression and irritability that occur in the context of ASD are available aside from the nicotine patch, and include behavioral therapies and drug therapies. An alternative to participating in this study would be to only continue on your existing medications, should you be taking any. Participation in this study does not require that you discontinue any existing medications.

Confidentiality

Your data will be de-identified 6 months after the study has concluded, and preserved in de-identified format for up to 5 years (at this point, any identifying information, including your name and date of birth, will be replaced by a study number which won't be traceable back to you).

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as required 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. Homicidal or suicidal intent must also be reported to appropriate authorities. We will make every effort to ensure your information is confidential. Information collected on hard documents will be stored in locked files to ensure confidentiality, and computerized files will be locked and password protected. Only individuals with security codes will have access to the computerized data. 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.

Representatives from the Yale Human Research Protection Program, the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.

In Case of Injury

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine, the Yale Child Study Center, and Connecticut Mental Health Center 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, and we will request that you return the study medication to us. The researchers may withdraw you from participating in the research if necessary. This may occur in circumstances where A) You were unable to adhere to the study protocol, B) Your vital signs became abnormal during participation and you no longer met inclusion and criteria, C) Your non-study physician feels it necessary to change your non-study medications during the 3 weeks of participation, D) Other unforeseen circumstances which will be at the discretion of the research team.

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, the Yale Child Study Center, or the Connecticut Mental Health Center.

When you withdraw from the study, 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.

HIC#: 1502015384

Authorization

I have read (or someone has read to me) this form and have decided to participate in the project described above or I have decided to allow my child or my ward to participate in the project described above. Its general purposes, the particulars of my or my child or ward's 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.

Name of Subject: _____

Signature of Subject: _____

Signature of legal authorized representative, if necessary: _____

Relationship: _____

Date: _____

Signature of Principal Investigator

Date

or

Signature of Person Obtaining Consent

Date

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Alan S. Lewis, MD, PhD at 518-441-8279.

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 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.