Informed Consent Form

TITLE: Neuroendocrine Risk Mechanisms for Post-traumatic Stress Disorder in Women

NCT NUMBER: NCT03973229

IRB APPROVAL DATE: May 28, 2024

You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 300 people who are being studied, at Emory.

Why is this study being done?

This study is being done to answer the question: What is the relationship between trauma, brain activity and hormone levels? You are being asked to be in this research study because your participation will help us to better understand how women's changing hormone levels effects their mental health and brain activity.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?

If you are eligible and want to be part of the study, you will participate for 4 months (5 study visits). The researchers will ask you to do the following: Track your menstrual cycle on a smartphone app, share mental health symptoms, complete 2 MRI scans, and wear a skin patch that contains estrogen and one that does not. ALL of these procedures will be paid for by the study.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?

The study will take time. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include the risk of being upset by talking about your traumas, becoming uncomfortable or bored in the MRI scanne, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the "What are the possible risks and discomforts?" section of this document.

Alternatives to Joining This Study

Since this is not a treatment study, the alternative is not to participate.

Costs
You WILL NOT have to pay for any of the study procedures.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you. Take time to consider this, and talk about it with your family and friends.

Emory University and Grady Health System
Consent to be a Research Subject / HIPAA Authorization

Title: Neuroendocrine Risk Mechanisms for Post-traumatic Stress Disorder in Women

Principal Investigator: Jennifer Stevens, PhD

Study-Supporter: National Institute of Mental Health, National Institute on Alcohol Abuse and Alcoholism, Emory University School of Medicine and the Georgia Clinical Translational Science Alliance

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?
The purpose of this study is to look at the relationship between trauma, brain activity, and hormone levels. You are being asked to be in the study because you have been enrolled in our Grady Trauma Project study and meet all eligibility criteria. The information gathered in this study will be used to help improve the care of people recovering from a traumatic event in the future.

As part of this research, we are asking some female participants that have been recruited through Grady Trauma Project to record their menstrual cycle using the smartphone application “Clue”, collect saliva and blood samples, urine ovulation tests, answer a few questions about your current mood and complete an MRI scan. Prior to the MRI scan, you may be assigned to wear a hormone patch for 1 to 2 days, or a placebo patch that will not release hormones.

This is not a treatment study. Although this is not a treatment study, we will provide you with referral material to help you cope with your traumatic experience and to find appropriate treatment as needed to help you during this process.

How many people will take part in this study?

A total of approximately 300 people that have already been enrolled in the GTP study at Grady Memorial Hospital will take part in the study.

What will happen if you take part in the study?
A researcher will briefly teach you about your menstrual cycle. They will then help you to download a menstrual cycle-tracking application, "Clue" on your phone. The personal email address that you provide the study staff will be used to access the data that you enter into the Clue app during your two months of tracking. You will be given ovulation tests to take home with you. You will use the app at home to record the timing of your menstrual period and results of the ovulation tests for two full, complete cycles (about two months).

During one of these months of tracking we will ask you a few (10-12) questions each evening about your day and your current mental health and alcohol use. We will teach you the process of how these questions work at your first visit.

After two months of tracking your cycle on the App you will be invited back to complete an MRI scan. Before the MRI scan you will give a saliva sample and a blood sample. A trained researcher will collect the blood sample while you sit in a comfortable chair. **You will complete two brief questionnaires about how you feel that day before the start of the MRI scan. During one of the questionnaires when you are talking about a stressful event in your life you will wear small sensors on your fingers to record the amount of sweat on your hands. At this point you will complete 2 MRI scans; one per month. You will be asked to wear a patch for 1-2 days before and during each MRI scan. The first month, you'll be randomly selected to wear a patch that contains an estrogen supplement, or a placebo patch. The second month you'll switch over to the other version of the patch (either estrogen or placebo).** During the MRI, you will be asked to lie still and for part of the time you will be asked to complete short computer tasks. Each task will be explained to you before the scans. The MRI will take about 1 hour.

Who owns my study information and samples?
If you join this study, you will be giving your samples and information. You will not receive any payment if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study. You may request that we remove your data from the study if you do choose to withdraw.

What are the possible risks and discomforts involved from being in this study?
Psychological tests and interviews sometimes can bring up painful emotions. These emotions may include sadness, worry, or increased anxiety. If you have trauma-related stress symptoms, you may have an increase in nightmares or flashbacks related to your traumatic experiences. You are free not to answer any questions you wish. You may stop participating in the study at any time. This will not in any way affect your future care.

There is no risk or discomfort expected in the collection of the spit sample. When blood samples are taken, you could feel lightheaded. Bruising or bleeding and slight pain can occur at the site of the needle insertion. This usually is a temporary discomfort. Rarely, infection may also occur around the area of needle insertion.

During the MRI, you may become tired from lying in the scanner, or may become uncomfortable from lying in one position for a long period of time. If you become too hot or too cold you may ask us to adjust the room temperature or give you a blanket. Some individuals experience mild anxiety or claustrophobia (fear of small spaces) while lying in the scanner. If this happens, you may ask to leave the scanner at any time. The MRI machine makes loud metallic popping sounds that you may find irritating while it is taking pictures. You can ask to stop the MRI scan any time you want. There are no risks of physical injury. Magnetic resonance imaging uses magnetism and radio waves (not x-rays) to make pictures. It has been in use for more than 20 years and millions of people have had MRI scans without injury. Therefore, MRI is thought to be safe, although no one can guarantee that there are no long-term negative health

effects to individuals undergoing scans or to fetuses in pregnant women undergoing scans. The only known risks are to individuals with cardiac pacemakers and certain types of metallic implants. If you have either of these, you cannot participate in this study because of effects the magnetic field could have on the pacemaker or metallic implant. Be sure to tell us if you know or think that you have a pacemaker or metallic implant such as an aneurysm clip. All the equipment and MRI methods used in this study are standard and have been approved by the U.S. Food and Drug Administration.

If you participate in the component of the study involving an estrogen patch, your estrogen levels will increase during the time that you are wearing the patch. Because we are administering only one dose (100 µg patch), and this dose will increase your estrogen to a level that is in the normal range for a woman of your age, we do not expect any significant side effects. We do not anticipate any medical complications from administration of this dose and frequency.

You will be getting a scan for research purposes only. The research does not require health professionals to read the scan. The researchers are not qualified to interpret the images for healthcare purposes. Do not rely on the scan for clinical or diagnostic purposes. However, if the researchers have a question about something they see on the scan they will tell you, and ask you if you want the scan sent to a qualified health professional for review and any further medical treatment. You or your insurance company may have to pay for the review and any such treatment.

The biggest risk to you is the release of your health record information. Study staff has worked to lower this risk to your confidentiality. The chance that any study info would be given to someone else is very small. All of your information in the study will be associated with a subject identification number instead of your name. Reports about any research done in the future with your info will not be given to you or to your doctor, will not be put in your health records, and will not affect your future health care.

Withdrawal from the study will not affect your future care. There also may be unknown risks, discomforts or side effects.

Will I benefit directly from the study?

There may be no benefit to you from being in this study. This research may help us understand why some people develop long-lasting Posttraumatic Stress Disorder and Depression following trauma, and to use this information to eventually develop better treatments and interventions to prevent these problems and to better help people to cope after a trauma.

Will I be compensated for my time and effort?

You will be compensated for your time and travel in the amount of $50.00 for the initial study visit and survey completion, $50 per month for the completion of daily mobile menstrual cycle reporting, and $125.00 for the MRI visit including blood and saliva collection. You will also receive $1 for each day that you answer all of the short questions (or $0.25 per survey answered) and an up to an extra $50 if you answer at least 70% of the days (20 days) - $10 each in weeks 1, 2, and 3 and $20 in week 4.

What are my other options?

Since this study is not a treatment study your option is to not participate.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.
- Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), including your de-identified genetic information, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data [and specimens] from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

We will use your sample and data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Controlled access databases

Your individual genomic data and health information will be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database will agree not to attempt to identify you.

How is my Genetic Information Protected? What are the Risks?

The Genetic Information Nondiscrimination Act (GINA) is a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege

In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

Medical Record

If you have been an Emory and Grady Health System patient before, then you already have an Emory and Grady Health System medical record. If you have never been an Emory and Grady Health System patient, you do not have one.

We will take reasonable steps to keep copies of this form out of Emory and Grady Health System's medical records system. If we aren't successful in keeping these forms out, despite our efforts, we will take steps to remove them. If they cannot be removed, we will take steps to limit access to them.

We will keep a separate research record of all study tests and procedures that we will use for research purposes. This research record will not be a part of your medical record.

In Case of Injury

If you get ill or injured from being in the study, Emory and Grady Health System would help you to get medical treatment. Emory, Grady Health System, and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory, Grady Health System, or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Stevens at 404-778-1698. You should also let any health care provider who treats you know that you are in a research study.

Withdrawal from the Study
You have the right to leave a study at any time without penalty.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Costs
There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your menstrual cycle history that you tell us.
- Information about your eligibility for the study from the parent Grady Trauma Project study (IRB 00078593)

Purposes for Which Your PHI will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study.

- Emory and Grady Health System may use and disclose your PHI to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory and Grady Health System offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Grady Research Oversight Committee, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Office for Human Research Protections.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: Dr. Jennifer Stevens, [redacted]

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Stevens at [redacted]

- If you have any questions about this study or your part in it,
- If you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- If you have questions about your rights as a research participant.
- If you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75

If you are a patient receiving care from the Grady Health System and have a question about your rights, you may contact the Office of Research Administration at research@gmh.edu

Contact for Future Studies

The Researchers may wish to contact you for participation in future studies. Please indicate by checking a box below whether you would be interested in being contacted for future research studies.

☐ I give my permission to be contacted for future research studies.

☐ I do NOT give my permission to be contacted for future research studies.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the form to keep.

_____

Name of Subject

_____ _____

Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____

Signature of Person Conducting Informed Consent Discussion **Date** **Time**