Informed Consent

Ovarian Hormones, Reward Response, and Binge Eating in Bulimia Nervosa: An Experimental Design

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: July 13, 2021
IRB Study # 19-2343
Title of Study: Neurobiology of Bulimia Nervosa
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Funding Source: National Institutes of Health (NIH)

CONCISE SUMMARY

The purpose of this study is to examine the role of the ovarian hormones' estrogen and progesterone in eating behaviors and the response to reward in women with an eating disorder. The information we learn from this study may help us better understand the role ovarian hormones may have in the development of an eating disorder. After a one-month screening period, study participants will take study medications for 3-months. The study medications will change estrogen and progesterone levels. While taking the study medications, participants will complete self-report questionnaires and behavioral tasks. The study medications are not being used to treat your eating disorder. They will help us understand how changing your hormone levels changes your eating behaviors.

Study appointments will occur every 2-weeks while taking the study medications. There will be 8 study visits and one follow-up survey. Some study visits will last approximately 45 minutes and some visits will last up to 3 hours. You will also be asked to complete an online survey 8-weeks after you stop taking the study medications. After study completion, interested participants can meet with the study Principal Investigator, Dr. Baker, to obtain a comprehensive report on how their eating behaviors changed when taking the study medications.

There are risks associated with taking the study medications as described in detail below. Some risks include: dizziness, breast tenderness, nausea, vaginal bleeding, headache, fatigue, and changes in mood.

Participation in this research study is voluntary. If you are interested in learning more about the study, please continue reading below.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.
You may refuse to join, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to determine the role of ovarian hormones (estrogen and progesterone) in eating behaviors and the response to reward in women with the eating disorder bulimia nervosa. We will investigate the role of these hormones on eating behaviors by using a hormone "challenge." The hormone challenge involves two phases. During phase one, you will receive Lupron, a medicine that will temporarily turn off your ovaries during the study. Lupron reduces the levels of estrogen and progesterone in your blood. During phase two, you will continue to receive Lupron and you will take pills that contain estrogen or progesterone or placebo. A placebo is a medication without any active ingredients. You will take the pills daily for 8-weeks and will not know whether the pills contain estrogen, progesterone, or placebo. You will begin taking these pills one month after your first dose of Lupron. After the hormone challenge, you will stop taking all study medications and your hormone levels will return to normal.

You will complete self-report questionnaires throughout the hormone challenge. At randomly scheduled times during the hormone challenge, you will also complete behavioral tasks related to reward. This will help us understanding how changing your hormone levels impacts your eating behaviors and how you respond to rewards.

Previous studies have shown that estrogen and progesterone play a role in food intake and overeating. It remains unclear why changes in estrogen and progesterone cause changes in food intake and overeating in some women and not others. You are being asked to participate because you are a woman between the ages of 18 and 42 with bulimia nervosa and have monthly periods.

Are there any reasons you should not be in this study?

You should not be in this study if any of the following apply to you:

- peanut allergy
- endometriosis (an illness related to abnormal tissue growth around the uterus)
- enlargement of the ovaries
- liver disease
- breast cancer (self or family history)

- a personal or family history of blood clots
- undiagnosed/abnormal vaginal bleeding
- porphyria (a rare genetic blood disorder)
- diabetes mellitus
- osteoporosis or osteopenia
- malignant melanoma (a type of skin cancer)
- gallbladder or pancreatic disease
- heart or kidney disease
- cerebrovascular disease (stroke)
- currently smoking >10 cigarettes daily
- epilepsy or history of seizures
- a history of suicide attempts or bipolar disorder/psychotic episodes
- current substance misuse
- frequently use diuretics or laxatives
- recurrent migraine headaches with aura
- history of pregnancy-related deep vein thrombosis
- irregular menstrual cycle
- body mass index (BMI) greater than 35
- currently pregnant, planning to become pregnant, or lactating
- taking any medication or have any other medical history that is contraindicated for the medications used in this study
- unwilling to use barrier contraceptive during the study

In addition, you will not be permitted to participate if you have a first degree relative (immediate family) with breast cancer that occurred before menopause, or breast cancer presenting in both breasts, or if you have multiple family members (greater than three relatives) with breast cancer.

If you are using birth control you can join the study, but you must enter a washout period (i.e. stop taking the birth control and instead use a barrier contraceptive) and have 3 regular periods before you can begin the study procedures.

We also ask that you do not change any mental health treatment you may be receiving throughout the duration of the study (e.g., start or stop psychotherapy).

How many people will take part in this study?

There will be approximately 15 people in this research study.

How long will your part in this study last?

This study will include 8 visits over the course of 5 months. You will have study visits every 2-weeks. Study visits will range from approximately 45 minutes to 3 hours. Most study visits may be able to take place at your home provided that you live within 45 miles of UNC Hospitals. The hormone challenge will last 3-months. Prior to beginning the hormone challenge, we will track your eating behaviors for one menstrual cycle. Eight-weeks after the completion of the hormone challenge, we will ask you to complete questionnaires regarding your eating behaviors, mood, and experiences in the study. During specific time points during the protocol (described below), we will also collect blood and/or saliva samples from you. A portion of these samples will be stored for future use. We will store these samples indefinitely.

What will happen if you take part in the study?

1. Clinical and Health Screening:

You will undergo a screening process to determine if you are eligible for the study. In order to protect you from adverse medication effects and ensure you are healthy enough to participate in the study, you will be screened with a medical and psychiatric history and have laboratory tests completed. During the initial screening you will be asked questions about your physical and mental health as well as questions about any symptoms you may be experiencing now. You will also be asked to complete questionnaires about your eating behaviors, personality, mood symptoms, and trauma history. You may choose not to answer any or all of the questions for any reason. As part of the Clinical Health and Screening, approximately 2 tablespoons (about 30 mls) of blood will be drawn to test your liver and kidney function and electrolytes. If you are eligible for the study, the results of your laboratory tests will appear in your UNC Health Care medical record.

You will receive a pregnancy test prior to enrolling in the study. You may not participate in this study if you are pregnant because the study drugs (Lupron, estrogen, and progesterone) may be associated with birth defects. The study will cover the cost of the pregnancy test. However, a negative pregnancy test does not rule out the presence of a very early pregnancy. If you enroll in the study, you will need to use barrier contraceptive methods (diaphragm or condom or both) for the entire time you are in this study. To prevent pregnancy, we strongly recommend that you also continue barrier contraception until you have three regular menstrual cycles after the study has ended.

We also require that you have had a gynecological exam within the last year and PAP smear within the past 3 years. If you have not, this can be completed with the study gynecologist or you can have this exam with your own doctor, provided you are willing to release these medical records to the study investigators for review. If you choose to have the exam conducted by your own provider, there may be a cost associated with the exam. The research study will not cover the costs of this exam. If you have had a gynecological exam within the past year and PAP smear in the past 3 years, you can forgo the gynecological exam if you are willing to provide study investigators with the medical records for review. If you have the exam with the research study gynecologist, the appointment and results will become part of your UNC Health Care medical record.

During this initial period, you will also complete a screening period during which we will track your eating behaviors for one menstrual cycle. To do this, you will be asked to complete a short questionnaire each morning. Completing this questionnaire should take less than 5 minutes.

2. Hormone Procedures:

For this study we will use a hormone "challenge." The hormone challenge involves two phases. During phase one, you will receive Lupron, a medicine that will temporarily turn off your ovaries during the study. Lupron reduces the levels of estrogen and progesterone in your blood.

During phase two, you will continue to receive Lupron and you will take pills that contain estrogen or progesterone or placebo. A placebo is a medication without any active ingredients. You will take the pills daily for 8-weeks and will not know whether the pills contain estrogen, progesterone, or placebo. You will begin taking these pills one month after your first dose of Lupron. After the hormone challenge, you will stop taking all study medications and your hormone levels will return to normal. You will complete self-report questionnaires throughout the hormone challenge. At randomly scheduled times during the hormone challenge, you will also complete behavioral tasks related to reward. This will help us understanding how changing your hormone levels impacts your eating behaviors and how you respond to rewards.

Once you are determined eligible for the study and finish the screening period, we will ask you to have an injection of 3.75mg Lupron into a muscle, once a month for three months. Prior to your first Lupron injection, you will attend a "long study visit" which will last up to 3-hours. At this visit you will complete study questionnaires and behavioral tasks related to your response to reward. After you finish the study procedures, you will receive your first injection of Lupron. You will then have study appointments every two weeks after the first Lupron injection. During the first month of Lupron, you will have two clinic visits that will last approximately 45 minutes.

Four weeks after the first Lupron injection, we will ask you to begin taking two pills daily that contain estrogen or progesterone or placebo (i.e., capsules with no active ingredients). You will take the pills daily for 8-weeks. You will not be aware of the real nature (hormones versus placebo) of the pills you are taking, but you will know that during the 8-week period you will receive a total of 4-weeks of active medication, which will be either estrogen or progesterone (you will never receive both estrogen and progesterone at the same time). During the active medication period, you will receive 4 mg of estrogen (17-beta estradiol) or 400 mg of progesterone. You will not be aware of the exact time the capsules are switched from placebo to active medication or vice versa.

During medication administration you will continue to have study appointments every 2-weeks, for a total of four visits. Three of these visits will be long study visits and one visit will be a clinic visit. The long study visits will be randomly assigned across the 8-week medication period. You will receive your study visit schedule (i.e., when your long study visits will take place) for the 8-week medication period once you begin taking study medications.

The medications being used in this study (Lupron, Estrogen capsules, Progesterone capsules) are approved by the FDA and are being used within that approval for this study.

3. Blood and Saliva Samples:

Blood and saliva samples will be taken at specific times during the course of the study. All blood samples will be drawn in the following way: you will be asked to sit down and a small plastic tube (catheter) will be placed in an arm vein, the blood sample will be drawn, and the catheter removed. During the clinical health screening visit approximately 30 ml (2 tablespoons) of your blood will be drawn. At specific times during the course of the study you will also provide saliva samples (2mL) by drooling into a cup. Estrogen and progesterone levels will be assessed from

the saliva samples. A portion of the saliva samples will be saved for the future assay of appetite hormones.

After completing the hormone challenge, we will ask you to complete an online follow-up survey 8-weeks after your last study visit. At the end of the study, we will discuss the study results and their meaning with you.

Is this study providing treatment for an eating disorder?
No, this research study is not providing you with treatment. The purpose of this research study is to determine the role of estrogen and progesterone on eating behaviors and the response to reward in women with bulimia nervosa.

Even though you will be taking medications, we are not examining the potential for the study medications as treatment for an eating disorder. Participating in this study does not serve as a replacement for eating disorder treatment or continued medical monitoring. The study investigators will not be your treatment providers but are conducting a research study and monitoring your safety while you are enrolled in the study. Because an eating disorder can be associated with negative medical side effects, it is important that you have a physician who is regularly monitoring your risk for these side effects. If you do not have a primary care physician, we can provide you with referrals. If you are in need of any medical care or treatment during the course of the research study, you will be referred to your own treatment provider. The research study will not cover the costs of any treatment that you need during the course of the study. Although there are some exceptions (e.g., certain medications), you can be in this study while you are receiving treatment (e.g., therapy) for an eating disorder. However, we ask that during the course of the research study you do not start, stop, or change your treatment. If your treatment does change, we ask that you notify the investigators immediately.

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. There is little chance you will benefit from being in this research study. However, you may learn about your sensitivity to changes in estrogen and progesterone levels and how your eating behaviors change in response to estrogen and progesterone, which may be useful for you.

What are the possible risks or discomforts involved from being in this study?
1). Lupron (leuprolide acetate 3.75mg) causes the ovaries to stop working while it is being administered. Lupron may cause the same side effects that are seen when the ovaries stop functioning permanently (menopause). The most common side effect of Lupron is hot flushes (flashes), occurring in 4% to 89% of women taking the medication. However, episodes of flushing often decrease with continued use of the medication. Skin irritation may also occur at the site of injection. The most common side effects of Lupron are headaches (10% of patients) and breast tenderness (6% of patients). A majority of the side effects reported by patients were of minimal, mild, or moderate severity. Your menstrual periods may be irregular for 2-6 months after the last Lupron injection. Side effects are reversible after the Lupron treatment is stopped. You should not conceive a pregnancy until 3-months after the last Lupron injection.

Other more common side effects associated with Lupron include:

- Vaginal inflammation (19% of patients)
- Changes in mood (16% of patients)
- Muscle aches (13% of patients)
- Trouble sleeping (10% of patients)
- Decreased libido (6% of patients)
- Dizziness (6% of patients)

Less frequent side effects include:
- Blurred vision
- Memory problems
- Diarrhea/Constipation
- Nausea
- Hair loss
- Facial swelling and/or itching

More rare but serious risks: Thrombophlebitis, pulmonary embolus, and congestive heart failure have occurred rarely in patients receiving Lupron, but a causal relationship to the drug has not been established. You may also experience a slight decrease in bone density (thinning of the bones). The decrease in bone density is usually reversible and should not be related to an increased risk of bone fracture because of the short time you will receive Lupron treatment. You should not be in this study if you have osteoporosis.

Given the dose and length of time you will be given Lupron, the risk of developing severe side effects is small. Nevertheless, you will be monitored closely to see if side effects develop, and the medication will be stopped if side effects become intolerable.

2) Estrogen capsules (Estrace, Micronized 17-beta-estradiol) – The risk of developing side effects is small because of the dosage and short period of time that you will receive estrogen treatment.

The more common side effects associated with estrogen are:
- Breast tenderness or enlargement (29% of patients)
- Headache (18% of patients)
- Abdominal cramps (16% of patients)
- Fluid retention (swelling/bloating) (10% of patients)

Less frequent side effects include:
- Increased blood pressure
- Dizziness
- Vomiting
- Vaginal bleeding
- Depression
- Nausea
- Darkening of the skin - in the rare event that you experience spotty skin darkening, it may not disappear completely

There is a significantly increased risk of stroke following estrogen therapy in individuals with migraine with aura, as compared to individuals without aura, and as such, women with a history of recurrent migraine with aura will not be allowed to participate in this study.

3) Progesterone capsules (Micronized progesterone) - Progesterone is commonly used to treat a variety of gynecological disorders. Side effects are not common and are usually mild.

The more common side effects associated with progesterone are:

- Vaginal bleeding consistent with a heavy period (20 to 30% of patients)
- Dizziness (24% of patients)
- Abdominal cramps (20% of patients)
- Headache (16% of patients)
- Breast tenderness (16% of patients)
- Viral infection (12% of patients)
- Joint pain (12% of patients)
- Changes in mood (11% of patients)
- Fluid retention (swelling/bloating) (10% of patients)
- Drowsiness/fatigue (10% of patients)

Less frequent side effects include:

- Vaginal discharge
- Jaundice
- Chest pain
- Weight change
- Depression
- Decreased sexual desire
- Skin color changes
- Diarrhea or flatulence

More rare but serious risks: Estrogen use increases the risk of certain medical problems including gallbladder problems, blood clots, and it may increase the risk of certain types of cancer and a stroke. However, this risk is minimized because of the dose and the short period of time estrogen is used in this study. This risk is also influenced by age with women over 50 years of age being at risk.

Lupron, estrogen, and progesterone may also cause an increase in birth defects if they are taken during pregnancy. Therefore, you should not become pregnant during this study. A pregnancy test will be given prior to enrollment, and you will not be allowed to participate if you are pregnant. The study will cover the cost of the pregnancy test. However, a negative pregnancy test does not rule out the presence of a very early pregnancy.

If you experience symptoms such as severe mood symptoms, nausea, vomiting, or extreme fluid retention (bloating or swelling) from any of the study medications, you will have the dose adjusted until you feel relief. If you do not feel relief, then drug treatment will be discontinued. If significant vaginal bleeding or any other gynecological problem occurs, we will arrange for a

visit with a UNC gynecologist, which may include using an ultrasound that is inserted vaginally. If you experience marked discomfort during the insertion of the ultrasound probe, then the procedure will be discontinued. Otherwise, there are no additional associated risks or discomforts with the ultrasound probe. If the gynecologist finds any abnormality during the ultrasound, further testing may occur. The research study will not cover the costs of treatment or medical exams; you will need to cover these costs. You will not be reimbursed for any expenses your insurance does not cover. If you do not have insurance, you may be asked to cover the costs of these expenses yourself. If breakthrough bleeding occurs and is intolerable, you will be withdrawn from hormone replacement (which should precipitate a period).

You will be followed closely to see if side effects develop from the medications. If you experience medication side effects during the study, the dose will be changed, but you must not change your medication dose without consulting the investigator. If adequate relief cannot be achieved by changing the dose, the drug will be stopped. Dropping out of the study will not interfere with any medical treatment you were receiving at UNC Hospitals.

5) Eating behavior changes –Given your own estrogen and progesterone levels fluctuate during your menstrual cycle, we expect that any changes in eating behaviors that may occur with the study medications would mimic changes that you may or may not observe during your menstrual cycle. However, there is still a risk and it is possible your eating behaviors will worsen during the course of the study. If you experience a significant worsening in your eating disorder (e.g., overeating, binge eating, purging), we ask that you inform us immediately. We will also assess your eating behaviors each day during the study and at your bi-weekly visits. If you experience severe and distressing changes in your eating behavior that interfere with your safety in the study, then you will not be allowed to continue in the study. We will provide you with treatment referrals, including referrals to the UNC Center of Excellence for Eating Disorders or providers within the community. The research study will not cover any costs associated with this treatment.

6) Mood changes – If you have a history of depression, you may be at higher risk for developing mood symptoms during the study. If you have never experienced an episode of depression in the past, then your risk of developing mood symptoms during this study are very low, but this risk still exists. If you experience any depression symptoms, <u>including thoughts about death or suicide</u>, we ask that you inform us immediately. We will assess your mood each day during the study and at your bi-weekly visits. The majority of participants complete the daily mood rating every day, and if you miss a day, we will contact you to do a safety assessment over the phone. If you experience severe mood symptoms or suicidal thoughts, then you not be allowed to continue in the study. We will provide you with treatment referrals, including referrals to UNC providers or providers within the community. If a treatment provider cannot see you in a timely fashion, Dr. Baker will provide short-term care (up to 3 sessions) at no cost to you. Otherwise, the research study will not cover any costs associated with treatment.

Given the relatively brief nature and moderate severity of any mood symptoms that you may experience during this study, we do not anticipate that your mood symptoms will adversely impact you. Nonetheless, we cannot guarantee the absence of effect, nor can we anticipate every risk that may result from your participation in this study.

7) Clinical interviews and self-report questionnaires contain questions regarding sensitive personal information. It's possible you may become upset or embarrassed when discussing current or past distressing life events. You have the right to not answer any question you are not comfortable answering.

8) Blood drawing - You may experience some discomfort or temporary pain at the site of the needle entry. There is a small risk of fainting and local infection.

9) There may be uncommon or previously unknown risks. If you have any symptoms or unexpected side effects during this protocol, please call the study investigators right away.

Addendum for Patients with a History of Episodic Headaches: Lupron and estrogen treatment have been reported to aggravate migraine headaches. If you have a history of recurrent migraine headaches with aura you may not participate in this study. Once Lupron is injected into your body its effects last for about four weeks and you may experience an increase in headache frequency while under its influence. If this does happen, we will do our best to manage the pain. If your headaches become severe enough to require repeated medication, we may decide with you to discontinue your participation in this study.

Addendum for Patients with a History of Epilepsy: There is some evidence that estrogen may increase the potential for seizures in some people. If you have a history of seizures, you may not participate in the study. Progesterone has been shown to have the opposite effect. The likelihood of inducing seizures in someone who has been seizure-free should be very low. However, this possibility exists. If you develop a seizure, your participation in the study will be stopped, and after assuring that you are medically stable, we will return you to the care of your primary physician for any follow up that will be required.

Addendum for COVID-19: You may experience the potential risk to COVID-19 exposure during in-person study visits where Lupron injections or blood draws occur when study staff will need to maintain less than 6ft distance. Our study team and UNC will be taking every precaution possible to protect you and the study team from COVID-19, including virtual video or telephone visits when possible, with limited in-person contact to every degree possible. During the in-person visits we will require masks at all times which will be provided to you by the study team, maintaining 6ft distance when possible, COVID-19 prescreening for yourself and staff at various timepoints including the day of the study visit, frequent cleaning with 90% alcohol or 1:10 Bleach solution, cleaning between each subject, handwashing requirements every hour for you and all staff, and before and after any contact with any subject. While the study team will be taking every pre-caution possible to protect yourself and the study staff there may still be a risk of COVID-19 exposure due to the possibility of the COVID-19 virus lingering in spaces from asymptomatic carriers.

If you have direct or even secondary contact with any suspected or confirmed cases of COVID-19 or experience any known symptoms of COVID-19, the study team will reschedule your study visit until the case is confirmed negative or until you've quarantined for at least 14 days from the

first symptom. This may affect your ability to continue to participate in the study. If you experience any symptoms of COVID-19 including but not limited to: cough, fever, sore throat, shortness of breath, loss of smell or taste, vomiting, diarrhea, shaking with chills, etc. you will be asked to notify the study team immediately and contact your Primary Care Provider and your local COVID-19 hotline to get tested for COVID-19. We will not cover the cost of the COVID-19 test. The study team and UNC are not responsible for any care or treatment of COVID-19.

What are the risks to a pregnancy or to a nursing child?

You may not take part in this study if you are pregnant, nursing, or planning to get pregnant. You will take a pregnancy test to make sure that you are not pregnant before starting the study. You will also take a urine pregnancy test prior to each Lupron injection, which will be paid for by the research study. A negative pregnancy test does not rule out the presence of a very early pregnancy. Pregnant women cannot participate because the study medications may have adverse effects on an unborn child. You will need to use barrier contraceptive methods (diaphragm or condom or both) while you are in this study. We strongly recommend that you continue barrier contraception until you have had at least three regular and consecutive menstrual periods after the study has ended. If you become pregnant during the study, you should notify the researcher right away.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

You will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of our records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of your personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety. Your identity will be protected by assigning you an ID number and omitting your name and other identifying information from scientific reports of the study. We may use de-identified data and/or specimens from this study in future research without additional consent. Information you provide as part of this study, including saliva samples, survey results, and clinical interview responses, may also be included in a database for future research or scientific reports or shared with scientists not affiliated with this study or UNC. No personal identifying information will be shared with these scientists and your individual identity will not be revealed. Researchers using these databases or information cannot learn your identity.

Because this study is funded by the National Institute of Mental Health (NIMH), researchers will share your de-identified information so that it can be used by other scientists for future studies. Your coded information will be submitted to the NIMH Data Archive (NDA) at the National Institutes of Health (NIH). NDA is a large database where de-identified study data from many NIMH studies is stored and managed. De-identified study data means that all personal

information about you (such as name, address, birthdate, and phone number) is removed and replaced with a code number. All data placed into the NDA will be coded and de-identified by the researchers at UNC and NDA will never receive the code or any other information that would enable the identification of the individuals who are the source of the data. Sharing your de-identified study data helps researchers learn new and important things about mental health and substance use more quickly than before.

During and after the study, the study researchers will send de-identified study data about your health and behavior obtained from this study to the NDA. Other researchers across the world can then request your de-identified study data for other research. Every researcher (and institutions to which they belong) who requests your de-identified study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about mental health and how to help others who have problems with mental health and substance use.
NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA. You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA. If you know now that you do not want your data in the NDA, please tell the study researcher today. If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff who conducted this study, and they will tell NDA to stop sharing your study data. Once your data is part of the NDA, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about NDA, this is available on-line at http://nda.nih.gov.

Identifiable data collected about you as part of this study and the file that links your ID number with your data will be accessible only to those working on this study at UNC, including research assistants and the Principal Investigator, Dr. Baker. All computer files are kept on secure computers on a secure network. If the researchers learn that you or someone else is in serious danger of harm (such as in cases of child abuse), they may make disclosures to protect you and/or the other persons.

Audio recordings of your clinical interviews will be identified by your study ID number only and stored on a secure computer accessible only to members of our research team. The recordings will be destroyed at the end of the study. Only your research ID number will be tape recorded along with your interview. You may request to have the audio recording turned off if you are uncomfortable with recording your interview.

Check the line that best matches your choice:
_____ OK to audio record me during the study

_____ Not OK to audio record me during the study

A copy of this consent form will be given to you.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

By signing this informed consent document, you agree that some of the information generated by participating in this study may be included in your medical record (e.g., results of lab tests and the gynecological exam) and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

Under North Carolina law, researchers are required to report information about the abuse or neglect of a child or disabled adult to local or state authorities.

Will you receive results from research involving your specimens?

Most research with your blood or saliva specimens is not expected to yield new information that would be meaningful to share with you personally. There are no plans to re-contact you or other subjects with information about research results. The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

What will happen if you are injured by this research?
All research involves a change that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses, or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?
You may receive up to $900 for your participation in this study. Only those participants who complete all aspects of the study as outlined below will receive the full $900. If you are withdrawn from the study by study staff, you will receive compensation for those study activities you completed. With the exception of the Clinical Health Screening Visit, you will receive a majority of the study compensation upon study completion according to the schedule below. However, you will receive a portion of the 'long study visit' compensation at that study visit. The exact amount that you receive during this visit will be determined based upon your responses to one of the behavioral tasks. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

If you are required to travel at least 10 miles to attend the study visits for the 3 Lupron injections at UNC, you will be provided travel/mileage reimbursement at 0.56cents per mile, for a maximum of 100 miles. For any study visits you attend at UNC, you will also receive vouchers to park in the Dogwood Deck at UNC Hospitals as instructed by the research team. This should cover the cost of your parking. If you choose to have the gynecological visit with the research study gynecologist this will occur at the UNC Hillsborough Hospital campus. If you are required to travel at least 10 miles to attend the gynecological appointment, you will also be provided travel/mileage reimbursement at 0.56cents per mile, for a maximum of 100 miles.

At the end of the study, you can choose to receive feedback regarding your individual response to the hormone challenge from the study Principal Investigator.

Long Study Visits	

Clinical Health Screening Visit	$20
Long Visit 1 (before medication administration)	$50
Long Visit 2 (during medication administration)	$75
Long Visit 3 (during medication administration)	$75
Long Visit 4 (during medication administration)	$75
Other Study Activities	
GYN exam	$30
Screening phase (1 menstrual cycle)	$30
Short Clinic Visits (3 visits, $20/each)	$60
Lupron Injection (3 injections, $5/each)	$15
Completion of daily survey and medication adherence during hormone challenge ($5.41/day 84 days)	$455
Follow-up survey	$15

In addition, for each daily survey you complete, you will be entered into a drawing to receive one of three $20 gift cards. Each participant in this study has approximately a 20% chance to win a gift card, and the more daily surveys you complete, the more chances you have to receive the additional gift card.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted

above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?
If you enroll in this study, you may have costs, including transportation to the appointments at UNC as well as any incidental expenses, such as childcare costs, if you have children. There will be no other costs to you for participating.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?
This research is funded by the National Institute of Mental Health (NIMH). This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

ClinicalTrials.gov Registration
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____

Signature of Research Participant Date

_____

Printed Name of Research Participant

_____ _____

Signature of Research Team Member Obtaining Consent Date

_____

Printed Name of Research Team Member Obtaining Consent

Required information for NIMH NDA data deposit:

Participant's Full Legal Name as it appears on Birth Certificate**:**

_____ _____

Participant's Location of Birth as Identified on Birth Certificate**:**

_____ _____