The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION BY SUBJECT FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: 16-0087 Name of Subject: _____

STUDY TITLE: Spatiotemporal Dynamics of Flibanserin in the Female Brain

Doctors Directing Research: Dr. Stephanie Cacioppo, Dr. Jon Grant, & Dr. Royce Lee
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You are being asked to participate in a research study. A member of the research team will explain what is involved in this study and how it will affect you. This consent form describes the study procedures, the risks and benefits of participation, as well as how your confidentiality will be maintained. Please take your time to ask questions and feel comfortable making a decision whether to participate or not. This process is called informed consent. If you decide to participate in this study, you will be asked to sign this form.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate how your brain waves and your subjective desire or sexual activity change after an 8-week intake of Addyi (Flibanserin; 100mg at bedtime)- an FDA approved drug for the treatment of hypoactive sexual desire disorder (HSDD) in premenopausal women or after an 8-week intake of a placebo (sugar pill). Flibanserin is not FDA approved for hypoactive sexual desire disorder in post-menopausal women.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 120 people with HSDD will take part in this study at the University of Chicago.

WHAT IS INVOLVED IN THE STUDY?

The study lasts 8 weeks and includes three office visits. During the first visit, you will be randomly assigned to the treatment group (group who takes the Flibanserin) or the control group (group who takes the placebo). Neither the study personnel nor you will know whether you are taking the study drug or the placebo. This is what is meant by "blinding." Whether you receive the study drug or the placebo is based on a 50/50 chance, like flipping a coin. In all, 60 subjects will receive the Flibanserin and 60 subjects will receive the placebo.

Before, during, and after the 8-week regimen, you will be asked to fill out a series of questionnaires (e.g., demographics, questions about body image and sexual desire) and do a behavioral visual task on a computer while your brain activity (brain waves) are recorded using a

non-invasive high-density electroencephalogram (EEG) system.

During your first visit (**Visit 1**), the following will occur:

- The study will be discussed with you and you will be asked to sign this consent form.
- You will be asked to take a urine pregnancy test to ensure that you are not pregnant at the time of the study. The pregnancy test must be negative for you to participate in the study.
- A review of your medical history and your medications will be completed.
- Your vital signs will be taken. This includes height, weight, blood pressure, pulse, respiratory rate, and temperature. As part of taking your blood pressure and pulse, you will be asked to first lie down for 5 minutes, and then your blood pressure and pulse will be taken the first time. You will then be asked to stand for one minute, after which we will take your blood pressure and pulse again. After standing for 2 more minutes, we will measure your blood pressure and pulse one more time.
- A review of your family history, a review of family medical issues and psychiatric issues will be discussed with you.
- You will complete several questionnaires, including questions about your body image and your sexual desire.
- You will do a behavioral visual task on a computer while your brain activity (brain waves) is (are) recorded using a non-invasive, high-density electroencephalogram (EEG) system.
- Your eye-movements will also be recorded using a non-invasive eye-tracking system.
- Study drug (Flibanserin or placebo) will be given to you. You will take the study drug or placebo, whichever you are given, each night at bedtime. **Do not drive, operate machinery, or do other things that require clear thinking until at least 6 hours after taking flibanserin** and until you know how flibanserin affects you. If you have any questions about this, please ask a member of the study staff.
- You will be given a parking voucher or $5 for public transportation and a $20 monetary compensation for participating in the study thus far.

- **Estimated Duration of Visit 1: 2 hours**

One week after your first visit, we will call you on the phone to see how you are doing and ask if you have been experiencing any side effects.

- **Estimated Duration of Phone Call 1: 15 minutes**

Two weeks after your first visit, you will call you again and ask you a few questions. These questions will be about your mood, your weight, your sexual desire, and any side effects you may be experiencing.

- You will be asked to complete some of the questionnaires that you completed at your first visit.
- You will continue to take the study drug or placebo each night at bedtime.

- **Estimated Duration of Phone Call 2: 30 minutes**

Four weeks after your first visit, you will return for your second visit (**Visit 2**), in which the following will occur:

- You will complete the questionnaires again.
- Your vital signs will be taken again.
- You will do the behavioral visual task on a computer while your brain activity (brain waves) is (are) recorded using a non-invasive, high-intensity EEG system.
- Your eye-movements will also be recorded using a non-invasive eye-tracking system.
- You will continue to take the study drug or placebo each night at bedtime.
- You will be given a parking voucher or $5 for public transportation and a $20 monetary compensation for participating in the study thus far.

- **Estimated Duration of Visit 2: 1 hour**

Eight weeks after your first visit, you will return for your third and final visit (**Visit 3**), in which the following will occur:

- You will complete the questionnaires again.
- Your vital signs will be taken again.
- You will do the behavioral visual task on a computer while your brain activity (brain waves) is (are) recorded using a non-invasive, high-intensity EEG system.
- Your eye-movements will also be recorded using a non-invasive eye-tracking system.
- You will stop taking the study drug or placebo after this visit.
- You will be given a parking voucher or $5 for public transportation and a $20 monetary compensation for participating in the study thus far.
- In addition, you will receive a $50 for your completion of the entire study.

- **Estimated Duration of Visit 3: 1 hour**

Behavioral visual task: You will be shown some desirable or neutral images and/or words on a computer. No pictures involving nudity will be presented. However, some of these images may be stressful, but should not be overwhelming. If you feel uncomfortable at any time, please alert the study staff immediately.

During the behavioral visual task, an EEG cap will be placed gently on the surface of your scalp. The cap contains 128 sponge-electrodes, which rest on the scalp and record brain electrical activity by calculating potential differences between each electrode and a reference electrode. Electro-conductive solution including water, potassium chloride and shampoo will be applied to the recording electrodes. No paste or gel will be applied between the electrodes and your scalp. This is a great advantage of this non-invasive EEG method, which allows setting up the cap in under 15 minutes of each testing session. During recording of your brain waves, you sit comfortably in a chair, while you will be required to fixate on a cross in the middle of the screen and hit buttons on a keyboard when presented with perceptual target stimuli. Standard EEG recording equipment protects the volunteer from any hazard of electrical shock using isolated grounding procedures.

An eye-tracking system will also be in the room to record your eye-movements during the task. Both EEG and eye-tracking recordings are non-invasive approaches, which means that EEG and eye-tracking recordings can be performed without harm.

During this study, Dr. Stephanie Cacioppo and her research team will collect information about you for the purposes of this research. This information includes name, date of birth, demographic

information, phone numbers, e-mail addresses, and the results of your study-related tests. Your behavioral data and EEG scan will be performed with a code number in the data field where a name would ordinarily go. Data from this study may be used in research publications or presentations or a registry shared between University of Chicago investigators. Your name and other identifying information will NOT be part of this data set.

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for 8 weeks where you will take the study drug or placebo each day. There is no long-term follow-up after you stop the study.

Dr. Cacioppo may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study;
- You drink alcohol during the 8 weeks;
- Your medical condition changes;
- The study drug is no longer available;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

Addyi (Flibanserin) has a black box warning: the use of the study drug and alcohol increases the risk of hypotension (low blood pressure) and syncope (fainting). A black box warning means that the Food and Drug Administration (FDA) labels alcohol as having serious risks if combined with Flibanserin.

Addyi (Flibanserin) may interact with alcohol. By agreeing to participate in the present study and by signing this consent form, you also agree NOT to drink alcohol or beverages including alcohol while taking Addyi (Flibanserin) for a period of 8 weeks.

The most serious side effects observed in people taking Flibanserin are hypotension (low blood pressure) and central nervous system (CNS) depression. CNS depression refers to physical symptoms such as decreased rate of breathing, decreased heart rate, or loss of consciousness because of inhibited brain activity. If you experience any of these side effects, please notify the study doctor immediately. Appendicitis is also a risk associated with the study drug.

The most common side effects observed in people taking the study drug Addyi (Flibanserin) include:

- Dizziness
- Sleepiness
- Nausea
- Fatigue
- Insomnia
- Dry mouth

Other side effects include: anxiety, constipation, abdominal pain, menstrual spotting, rash,

sedation, fainting (syncope), spinning sensation (vertigo), and distressing dreams.

Oral contraceptives increase the likelihood of side effects occurring.

Flibanserin may interact with certain medications including central nervous system (CNS) depressants (such as diphenhydramine, opioids, hypnotics, benzodiazepines), antifungals (ketoconazole, itraconazole, posaconazole, fluconazole), antiviral drugs (telaprevir), antiretroviral drugs (ritonavir, saquinavir, nelfinavir, indinavir, amprenavir, atazanavir, fosamprenavir), antibiotics (clarithromycin, telithromycin, ciprofloxacin, erythromycin, rifabutin, rifampin, rifapetine), antihistamines (cimetidine, ranitidine), antidepressants and selective serotonin reuptake inhibitors (SSRIs) (nefazodone, fluoxetine, paroxetine), plants and plant-based medications (ginko, grapefruit juice, St. John's wort, digoxin), protein pump inhibitors, protease inhibitors (boceprevir), barbiturates (phenobarbital), selective immunosupressants (sirolimus), seizure medication (carbamazepine, phenytoin), hyponatremia medication (conivaptan), hypertension medication (diltiazem, verapamil), and some medications used to treat high blood pressure, chest pain (angina), or other heart problems. Please tell us all medications and supplements you use. Please also inform the study doctor in the event that you begin taking any new antibiotics.

If you are pregnant or plan to become pregnant, you must let us know immediately as you are not eligible to participate in this study. It is unknown if Flibanserin will harm a fetus. Because of the potential for serious adverse reactions including sedation in a breastfed infant, breastfeeding is not recommended during treatment with Flibanserin.

You may be diagnosed with hypoactive sexual desire disorder. This may cause you feelings of distress. If you would like any treatment resources when the study is completed, we can provide you with that information.

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could influence your willingness to continue, this new information will be discussed with you.

The study team will also ask you questions about your mood and behaviors. These questions may make you feel uncomfortable. If at any time you would like to stop the interview, please let a member of the study staff know.

Again, do not drive, operate machinery, or do other things that require clear thinking until at least 6 hours after taking flibanserin and until you know how flibanserin affects you. If you have any questions about this, please ask a member of the study staff.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other individuals with hypoactive

sexual desire disorder in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:
Addyi (Flibanserin) is FDA approved for the treatment of hypoactive sexual desire disorder in premenopausal women. An alternative option may be choosing to take Flibanserin without participating in the study for premenopausal women. Psychotherapy is an alternative option for both premenopausal and postmenopausal women with hypoactive sexual desire disorder. The decision whether or not you wish to participate in this study will not affect your care at the University of Chicago Medical Center**.**

WHAT ARE THE COSTS?

Clinical services provided during a clinical trial are either research-related or related to usual medical care. Research-related services are done to complete the research and the costs are not the responsibility of you or your insurance.

The costs that are considered research-related for this study may include any additional laboratory tests, physician visits, imaging, procedures or other clinical services that are dictated by the research protocol and only required because you are part of this study.

Usual medical care costs include any and all services that are considered medically necessary for your disease and would be done even if you were not part of this research study. This may include laboratory tests, physician visits, imaging, procedures, and other clinical services that your physician orders for your routine care. The cost of this usual, ongoing medical care will be the responsibility of you or your insurance, and may include deductibles and co-payments. Similarly, this care will be subject to all the same requirements and restrictions of your insurance.

If you have questions about whether specific clinical services are research related or usual medical care, please speak to your physician or research contact person.

If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. You must notify Dr. Cacioppo or Dr. Grant as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Cacioppo or Dr. Grant know right away.

WILL I BE PAID FOR MY PARTICIPATION?

You will receive up to $125 monetary compensation for your participation in the study. You will receive the first payment of $20 at the end of visit 1, another $20 at the end of visit 2, another $20 at the end of visit 3. If you complete the entire study, you will also receive a $50 bonus at the end of visit 3. Also, after each visit, you will receive a parking voucher or $5 for public transportation.

WHAT ABOUT CONFIDENTIALITY?

Study records that identify you will be kept confidential. All of the data will be kept in a secure computer server and in locked filing cabinets only accessible to the research team. The data collected in this study will be used for the purpose described in the form. By signing this form, you are allowing the research team access to your medical records, which include Protected Health Information. Protected Health Information (PHI) consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. However, our study records will not include any identifiers. Your data will be thus de-identified using a coding system. Your behavioral data and EEG scan will be performed with a code number in the data field where a name would ordinarily go. Data from this study may be used in research publications or presentations or a registry shared between University of Chicago investigators. Your name and other identifying information will NOT be part of this data set.

As part of the study, Dr. Cacioppo and her research team will report the results of your study-related procedures and tests explained above to Valeant Pharmaceuticals. These include research de-identified test results. This information is being sent because that might help Valeant Pharmaceuticals understand the effect of Flibanserin on the female brain. The study sponsor or their representatives, including monitoring agencies, may also review your de-identified medical record. Please note that these individuals may share your health information with someone else. However, our study records and medical records will not include any identifiers. Your data will thus be coded.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board, a committee that oversees the research at the University of Chicago, may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

If health information is shared outside the University of Chicago, the same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Cacioppo is not required to release to you research information that is not part of your medical record.

This consent form will be kept by the research team for at least six years. The study results will be kept in your research record and be used by the research team indefinitely. At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results. Any research information in your medical record will be kept indefinitely.

Data from this study may be used in medical publications or presentations. Your name and other

identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

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 ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. If you choose not to participate in this study, your care at the University of Chicago/University of Chicago Medical Center will not be affected. You may choose not to participate at any time during the study. Leaving the study will not affect your care at the University of Chicago/University of Chicago Medical Center.

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Cacioppo in writing at the address on the first page. Dr. Cacioppo may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed copy of this document. This consent form document does not have an expiration date.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

You have talked to a member of the study team about this study and you had the opportunity to ask questions concerning any and all aspects of the research. If you have further questions about the study, you may call Dr. Cacioppo at (773) 702-6983.

If you have a research related injury, you should immediately contact Dr. Cacioppo at (773) 702-6983 or Dr. Grant at (773) 834-1325.

If you have any questions concerning your rights in this research study you may contact the Institutional Review Board, which is concerned with the protection of subjects in research projects. You may reach the Committee office between 8:30 am and 5:00 pm, Monday through Friday, by calling (773) 702-6505 or by writing: Institutional Review Board, University of Chicago, 5841 S. Maryland Ave. MC-7132, I-625, Chicago, Illinois 60637.

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT
I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of Person Obtaining Consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:
Signature of Investigator/Physician _____
Date: _____ Time: _____ AM/PM (Circle)