Information Sheet for Research Participants

You will be given a copy of this Information Sheet and a signed copy of your consent form to keep, should you decide to participate in the study.

Study title:
Effects of Kisspeptin in Postmenopausal Women with Hypoactive Sexual Desire Disorder (HSDD).

We'd like to invite you to take part in our research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives, and your GP if you wish, before deciding if you would like to take part. Please do ask us if there is anything that is not clear or if you would like more information. **You are free to withdraw at any time without explanation.**

Summary

We wish to study brain activation whilst viewing erotic material when the naturally occurring hormone kisspeptin is given to patients with HSDD. This will help us understand more about this condition which may help us develop new treatment options in the future.

What is the purpose of the study?

Hypoactive Sexual Desire Disorder (HSDD) is characterised by a lack of sexual desire, fantasies, or thoughts, that is troublesome for an individual. It is a relatively common condition in postmenopausal women, affecting between 9 in 100 women with a natural menopause and 26 in 100 women with a surgical menopause. It can have a significant impact on a woman's quality of life and can lead to stress, anxiety, sadness, and problems with relationships. Unlike in premenopausal women with HSDD, there are currently very limited treatment options available for postmenopausal women with this condition. Therefore, we need to develop a better understanding of how and why this condition occurs, to develop better and safer treatments.

Kisspeptin is a naturally occurring hormone found in the blood of healthy people, which is important for the regulation of reproductive hormones. Kisspeptin also has important roles in controlling behaviour and emotions in humans through its actions in the brain.

We will perform a type of brain scan called functional magnetic resonance imaging (fMRI) whilst women with HSDD are watching erotic videos. We will look for changes in brain activity when kisspeptin is given, compared to placebo. This will help us understand whether this hormone is involved in postmenopausal women with HSDD and help us develop improved treatments. We aim to perform this study in approximately 38 women.

Primary Aim: To determine if there is any difference in brain activity if kisspeptin is given compared to placebo, when women with HSDD are viewing erotic material.

Secondary Aims: To determine if changes in brain activity with kisspeptin are related to: -

- Other blood hormone changes
- Changes in behaviour
- Changes in body temperature

Who should take part?

We are looking for up to 38 women who have been concerned by their low sexual desire for at least 6 months who are:

- Women ≥ 40 years old
- Postmenopausal (i.e., no period for > 1 year) and caused by natural menopause.
- Heterosexual.
- Right-handed.
- In a relationship for at least 6 months.
- Body mass index (BMI) of 18-30 kg/m2.
- Be receiving Hormone Replacement Therapy (HRT) for at least 6 months.

You should not take part in the study if:

- You have any other medical or psychological conditions or are taking any medications (other than HRT), which we feel will interfere with the study or cause you harm.
- You have been part of a research study within the last two months.
- You have a history of unresolved sexual trauma/abuse.
- You have another sexual disorder.
- You are receiving any treatment for HSDD (other than HRT) at the time of screening.
- You have any problems with your vision which would impair your ability to view erotic material.
- You have any reason which means that you would not be able to have an MRI scan, such as metal in the body (such as a cardiac pacemaker, neurostimulators, brain aneurysm clips and metal in your eyes), you are unable to lie flat or if you are claustrophobic.
- You have donated blood in the last 3 months or intend to donate blood in the three months after you take part in this study.

A full list of inclusion and exclusion criteria will be reviewed at a screening visit.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. If you need to withdraw from the study for whatever reason, we may still use any information or samples that we have collected from you up to that point.

What will happen to me if I take part?

If you agree to take part in this study, you will expect to be involved with the research study for approximately three months. Firstly, we will ask you to fill in a questionnaire which you should have received with this leaflet, to check if you are broadly suitable for this study. If so, we will schedule a telephone call with one of the research team who will discuss more details about your medical and sexual history to help determine if you are eligible to take part. We will then invite you for a screening visit lasting no more than 2 hours. This will take place at either the NIHR Imperial Clinical Research Facility at Hammersmith Hospital (White City) or the Endocrine Clinical Research Unit at Charing Cross Hospital (Hammersmith). These locations are all part of Imperial College Healthcare NHS Trust. During this visit, we will ask you questions about your medical and sexual history and ask you to fill in questionnaires to determine if you are suitable for the study. To ensure you are fit and healthy to take part in the study, a general physical examination will also be performed, blood will be taken from your arm for standard blood tests and a recording of your heart (ECG) will be taken.

One of our study doctors will ask you some questions regarding your general health and psychological wellbeing. Some of these questions may relate to your mood, how you feel about sex, or any problems you may have with sexual function. Our study doctors are trained and experienced in discussing these issues, and you are not obliged to answer any questions that you do not feel comfortable with. If any new conditions are diagnosed that you may not be aware of previously, you will have the opportunity to discuss these with the study doctor, and, if you consent, we will contact your GP to arrange further management. In this situation, after taking time to

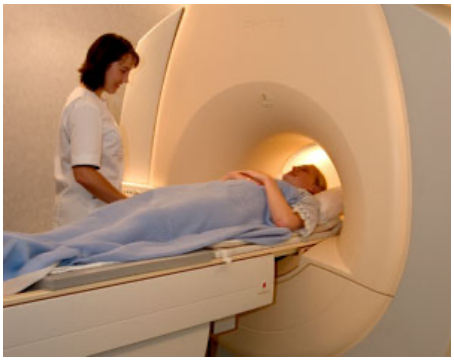
consider, if you still wish to take part and you meet all other eligibility criteria, then we will be happy to include you in the study. If during your screening visit, severe features of any mental health disorder (for example severe depression) are identified, this will be discussed urgently if appropriate with your GP or the Imperial College Healthcare NHS Trust Psychiatry Liaison Team.

Following your screening, if you are eligible to take part, you will be asked to attend the Invicro Imaging Centre on the Hammersmith Hospital campus (White City). You will be asked to attend for two study visits (separated by a minimum of 1 month) which will both have the same format. Each study visit will start in the morning and last no more than four hours. If you are receiving cyclical HRT (also called sequential HRT; where you take oestrogen every day and add progestogen for 10 to 14 days in a month), we will ask you to attend your study visits on days 7-14 following your last progestogen dose.

During one study visit you will receive kisspeptin and during the other study visit you will receive a placebo. Both kisspeptin and the placebo are administered via an injection under the skin of your tummy. The order of study visits will be decided at random. Neither you nor the study doctor will know whether you received kisspeptin or placebo as the injections will look identical. This is so that this does not influence the study in any way e.g., your responses to questions.

During each study visit you will be asked to change into medical scrubs, and you will have an fMRI brain scan for approximately 45 minutes. fMRI is safe and widely used in clinical practice. During the scan, you will be asked to lay flat and still inside the scanning machine, which is a large doughnut-shaped machine, open at each end (shown in **Figure 1**). The machine is noisy when it is scanning, but you will be provided with ear plugs and headphones to make it more comfortable. You can communicate with the scanning staff at any time during the scan using a microphone and call bell. You will lay your head on a headrest which acts as an aerial to pick up the image information. This will have a mirror on it so you can see a screen and during the scan, you will be asked to view some videos. Some of these videos will be of a sexually explicit nature (for example a man and a woman having sexual intercourse) and have been taken from commercial adult films (by a female erotic film director and producer). The videos that you will be shown have been selected by an independent focus group of postmenopausal women as suitable and arousing.

Picture of an fMRI Scanner



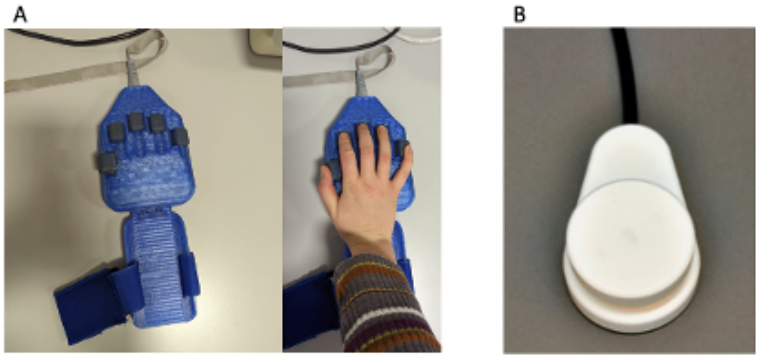
During the fMRI brain scan, you will complete two fMRI tasks:

1. Short videos task: during this task you will be shown 20 second segments of sexually explicit videos (described above), alternating with non-sexual videos (for example a man and a woman exercising together). This task will approximately 12 minutes,
2. Long video task: during this task you will watch a continuous erotic video (described above). This task will approximately 12 minutes,

Alongside these scans we will ask you to indicate how sexually aroused you are feeling, using a hand-held device. For the short videos task, you will be asked to rate your level of arousal for each video on a scale of 1 to 20 (1 = very sexually unarousing and 20 = very arousing) by using your index and middle fingers to move up and down a scale which you will see on the screen (shown in **Figure 2A**). For the long video task, you will be asked

to rate your level of arousal (on a continuous scale from “Not at all sexually aroused” to “Very sexually aroused”) in real time using a scroll wheel (shown in **Figure 2B**). Before each visit, you will receive an education session and be familiarised with the devices. During the fMRI scan, we will also be monitoring your body temperature (called thermography; also known as thermal imaging). This is done via a special camera to measure the temperature of your skin between your hips and upper legs whilst clothed.

Figure 2: Picture of fMRI response devices



Throughout each visit, we will monitor your heart rate and blood pressure. A small plastic tube called a cannula will be inserted into your arm to collect blood samples at regular intervals during the study. These samples will be sent for analysis of sex hormones and other substances. You may feel a little discomfort when the cannula is inserted. The amount taken in the blood samples is approximately equivalent to two teaspoonfuls on each occasion. The total amount taken during both study days will be less than 300mls, which is approximately the same volume as a can of Coke and significantly less than the amount taken during a blood donation session (470ml).

At the end of each study visit, the cannula will be removed from your arm, and you will be allowed to leave after a brief period of observation. A follow up questionnaire will be emailed (from Imperial.FemaleHSDD@nhs.net) to you by the study team 48 hours after each study visit asking about sexual desire and arousal and menopause symptoms in the 48 hours since your study visit. We will ask you to return your completed questionnaire to us by email.

We ask a specialist doctor (a radiologist) to look at your MRI brain scans, and very rarely, we may detect an abnormality that needs further investigation. If this happens, we will provide your GP with the findings of the MRI scan, who will arrange the appropriate specialist referral. Unfortunately, if we do find a significant abnormality, you will not be able to participate further in the study.

What do I have to do?

The only restrictions on your lifestyle are that you are asked to refrain from taking strenuous exercise, alcohol, and caffeine from midnight before each study visit. We will also ask you to refrain from all sexual activities (including watching erotica/pornography) for 24 hours before each study visit.

What are the possible benefits of taking part?

Although the study may not immediately benefit you, by taking part in this study, you will help us better understand the role of kisspeptin in HSDD. By contributing to our knowledge of this condition, this could help to develop new treatments, which could benefit you and other sufferers in the future. Sometimes the questionnaires we perform may reveal additional information about your health which can be helpful for your GP to know about. We will ask your permission before sharing this information. If we are concerned about your mental health at any point during the study, we will discuss this urgently with your GP or the Imperial College Healthcare NHS Trust Psychiatry Liaison team.

What are the possible disadvantages and risks of taking part?

Kisspeptin is a naturally occurring hormone that has been given to hundreds of human participants by our study group and others with no known side effects. The dose of kisspeptin we give you does not exceed the maximum safe dose given to other human volunteers; therefore, we do not anticipate any problems with giving kisspeptin to you. There may be the minor discomfort of cannulae insertion which can cause minor temporary bruising.

fMRI scanning is painless, involves no ionising radiation, and has no known health risks. However, you will be asked to lay still inside a confined space within the scanner for up to 60 minutes. You should therefore not take part in the study if you suffer from claustrophobia (fear of closed spaces) or do not think you would be able to lie still for this length of time. The fMRI scanner contains a very strong magnetic field. Participants with any type of metal implanted in their body which could move in this field will not be able to take part in this study for safety reasons. This will be carefully screened for at the time of the initial health check.

During the MRI part of the scan, some of the MRI sequences used may be classified as research sequences and we may use an ariel (radiofrequency coil) to collect the data that is not provided by the manufacturer. This means that the MRI scanner will be used in a different way to what is standard by the manufacture (we call it “off-label”). Using the scanner in this way could help to reduce the scan time and provide better quality or more useful image data for the research study.

What are the side effects of taking part?

From our previous studies we do not expect any side effects, but the unexpected can occur. During each study visit, at least one experienced doctor will monitor you closely. If you suffer from any ill effects during the visit, you should report them to the doctors monitoring you immediately. If you suffer from any ill effects afterwards you should report them to one of the research doctors on the contact number below, by email (Imperial.FemaleHSDD@nhs.net) or when you next see them. All adverse effects will be recorded in an adverse event form and placed in your personal research file. You may ask for the study to stop at any time without prejudice and if there are any significant side effects, the study will be stopped.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study, you will be asked to sign an updated consent form. Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study.
If you lose capacity during the study, you will be withdrawn from the study. However, any data (such as your questionnaires) and samples that we had already collected when you were able to give consent may be used in the study. We will seek your informed consent for this at the screening visit. If you do not consent to this and you lose capacity during the study, your blood samples would be disposed of in accordance with the Human Tissue Authority’s Code of Practice following completion of the study and not kept for use in future ethically approved research, and your questionnaires will be securely disposed of.

What happens when the research study stops?

Once the study has finished, the results are likely to be published in the 12 months following the study. Your confidentiality will be ensured at all times, and you will not be identified in any publication. Participants will be provided with a copy of the published manuscript if they wish. Participants will also be given a lay summary of the results of the study if they wish. They will be asked to contact the research team 6 months after the completion of the study if they would like to receive the lay summary of the results.

Kisspeptin will not be available to you after the end of the trial. There are additional stages of development and approval required before it becomes readily available.

With your consent, the blood samples that are taken from you during the study may be kept for up to 10 years in secure storage after initial analysis at Imperial College London for analysis in future research, after the study finishes. If this is not required, we will dispose of your samples safely and securely in keeping with NHS clinical

codes of practice. Your samples will be always pseudonymised and only accessed by authorised study researchers. We will ask for your written consent to keep your samples at the initial screening visit. However, if you decide not to give permission for this, you can still take part in the study.

What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigators: Professor Waljit Dhillo, Professor Alexander Comninos, Dr Edouard Mills or Dr Jovanna Tsoutsouki (020 7594 3487). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential.

It is a requirement that your GP is informed, with your consent, of your participation in this study. At your first screening visit, you will be registered with Imperial College Healthcare NHS Trust where your blood samples will be analysed. All information held on NHS computer systems will be strictly confidential and treated in a similar manner to that of other NHS patients and will only be used by members of the research team to request and review the results of your blood tests.

Your imaging data will be stored on Invicro's radiology information system indefinitely, in a pseudoanonymised form. Invicro will also hold your study file and consent forms, which will be archived in a secure off-site document storage facility. As per regulatory requirement, data will be archived for 30 years.

Who is organising and funding the research?

This study is being organised by the Section of Endocrinology and Investigative Medicine at Imperial College London. The study will be funded by the National Institute for Health Research (NIHR).

Expenses

You will receive £200 (i.e., £100 per study visit) on completion of the study to cover expenses including travel costs, time off work and lost earnings. Unfortunately, we cannot offer expenses for the initial screening visit.

Who has reviewed the study?

This study has been reviewed by the London – Westminster Research Ethics Committee. This study was given a favourable ethical opinion for conduct in the NHS by London – Westminster REC.

Contact for Further Information

If you experience any problems during the study, you may withdraw at any stage. The main doctors involved in the study, Dr Edouard Mills, Dr Jovanna Tsoutsouki, Professor Alexander Comninos or Professor Waljit Dhillo will be available by email (imperial.femaleHSDD@nhs.net) or telephone at any time and can be contacted through Professor Dhillo's PA (020 7594 3487) or the hospital switchboard (020 3313 1000) which has home and mobile phone numbers for all the doctors involved in the study and can contact them at any time outside normal working hours.

Thank you for reading and for your interest in our study.

GDPR

HOW WILL WE USE INFORMATION ABOUT YOU?
Imperial College London is the sponsor for this study and will act as the Data Controller for this study. This means that we are responsible for looking after your information and using it appropriately. Imperial College London will keep your personal data for:

- 10 after the study has finished in relation to data subject consent forms.
- 10 after the study has completed in relation to primary research data.

The study is expected to finish in August 2026

For more information / confirmation regarding the end date please contact the study team, see '**WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED'** for contact information.

We will need to use information from you for this research project. This information will include your NHS number, name and contact details.

People within the College and study team (see section sharing your information with others) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate**.** We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

• Imperial College London - "performance of a task carried out in the public interest"); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on "scientific or historical research purposes or statistical purposes.

INTERNATIONAL TRANSFERS
There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS
We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

- Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring

accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

POTENTIAL USE OF STUDY DATA FOR FUTURE RESEARCH

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have because some research using your data may have already taken place and this cannot be undone.

- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you if this could affect the wider study or the accuracy of data collected.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to imperial.femaleHSDD@nhs.net, or