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:
Physiological Studies to Investigate the Effects of Kisspeptin on Human Brain Processing.

You are being invited to take part in a 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. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

If you do decide to take part, please let us know beforehand if you have been involved in any other study during the last year. **You are free to withdraw at any time without explanation.**

What is the purpose of the study?

Kisspeptin is a naturally occurring substance found in the blood of healthy people. Kisspeptin is important for the regulation of reproductive hormones in humans and it may also affect emotions and behaviours through other actions in the brain.

This study aims to see whether kisspeptin can bring about changes in emotions, mood or memory in humans. We will use a type of brain scan called functional magnetic resonance imaging (fMRI) to look for changes in brain activity when kisspeptin is given compared to placebo.

Primary Aim: To determine if there is any difference in brain activity on fMRI when kisspeptin is given compared to placebo.

Secondary Aims: To determine if changes in brain activity with kisspeptin are related to:-
- Other blood hormone changes
- Changes in your mood, emotions and memory

Why have I been invited?

We are interested in how the hormone Kisspeptin affects brain processing in different people and different settings.

You should **not** take part in this study if:

1) you take any medications or have any allergies which we feel will interfere with the study or will cause you harm;
2) you have any past or present illnesses which we feel will interfere with the study or will cause you harm (these may include significant kidney, liver, heart, and thyroid disease or a history of any cancer);
3) 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;
4) you have been part of a clinical trial within the last **3 months;**
5) you are pregnant or breastfeeding;

6) you have any implanted metal in the body that would make it unsafe for you to have an MRI scan (although you may be eligible for the non-fMRI part of this study: detailed below)

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. We will ask your permission to do this when you sign the consent form.

What will happen to me if I take part?

If you agree to take part in this study, we will invite you to the NIHR Wellcome Trust Clinical Research Facility at Hammersmith Hospital or the Clinical Research Facility at St Mary's Hospital for a screening visit lasting around 1 hour. During this visit, if you are female and of child bearing age, we will ask you to provide a urine sample for a pregnancy test. 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 also ask you some questions and ask you to complete questionnaires regarding your general health, psychological and emotional 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 this 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.

Following your screening, if you are eligible to take part, you will be either asked to attend the Invicro Centre for Imaging Sciences at Hammersmith Hospital (for the fMRI study) or the Clinical Research Facility at Charing Cross Hospital (for the non-fMRI study); the differences between these studies will be explained below. Both studies involve two study visits which will both have the same format. Each study visit will start in the morning and last up to four hours. There will be a break of at least one week between each study visit. If you volunteer to take part in both the two fMRI and two non-fMRI study visits, there will be a six-week period between the study phases. Please note that depending on your preference, you may volunteer for the two fMRI, the two non-fMRI or all four study visits.

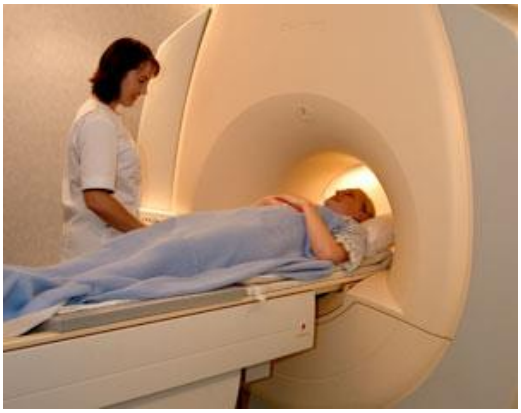
For both the fMRI and non-fMRI studies, at one study visit you will receive the naturally occurring hormone kisspeptin, and during the other study visit you will receive a placebo. The order of study visits will be decided at random and you will not be informed whether you received kisspeptin or placebo during your study visits so that this does not influence your responses.

fMRI Study: During each study visit you will have an fMRI brain scan for up to 75 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. The machine can be noisy and feels like a narrow tunnel so you should not take part if you are claustrophobic. You can communicate with the scanning staff at any time during the scan using a microphone. As part of the standard procedure for fMRI scanning, you will be asked to do some tasks. These may include looking at images, some of which may be arousing, smelling an odour and being asked to rate how it makes you feel, or completing puzzles designed to test different parts of your brain. At the beginning and end of the study you will also be asked to complete some questionnaires so we can assess your mood and emotions before and after receiving kisspeptin or placebo.

One of the normal functions of kisspeptin is to control sexual behaviour (including arousal). If you are a man one of the fMRI tasks may involve watching erotic videos whilst in the scanner, which may result in erections. To assess this (termed 'penile tumescence'), a small and painless cuff (similar to that used to measure your blood pressure) may be placed on your penis using a condom, before the fMRI begins. This will be left on throughout the fMRI scan and removed before going home. You will be shown this device before your first study visit so that you are acquainted and comfortable with the set-up.

Throughout each visit, we will monitor your heart rate and blood pressure. A 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 stress hormone levels. 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 screening and both study days will be no more than 290mls, which is significantly less than that taken during a blood donation session (470ml).

Picture of an fMRI Scanner



At the end of each study visit, the cannula(s) will be removed from your arm and you will be allowed to leave after a brief period of observation.

We ask a specialist consultant doctor (a radiologist) to look at your fMRI 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 fMRI 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.

Non-fMRI Study: This part of the study happens at the Clinical Research Facility at Charing Cross Hospital and also involves two study visits as above, but without an fMRI scan. As in the fMRI visits, two cannulas will be inserted into your arms – one to receive an infusion of kisspeptin or placebo and a second to collect blood samples (same volumes as in the fMRI study). This infusion will last around 75-minutes, during which you will complete tasks (see fMRI study). Throughout each visit, we will monitor your heart rate and blood pressure.

Route of Administration: For both the fMRI and non-fMRI study, kisspeptin will be administered intravenously (into the vein) via a cannula. For some of the studies, kisspeptin may be administered via a nasal spray, which is similar in appearance to the nasal sprays commonly used to treat a blocked and runny nose.

What do I have to do?

The only restrictions on your lifestyle are that you are asked to refrain from taking strenuous exercise, alcohol, caffeine and sexual activity from midnight before each study visit.

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 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.

fMRI scanning is painless, involves no 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 75 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.

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 will be the minor discomfort of cannulae insertion which can cause minor temporary bruising.

What are the possible benefits of taking part?

The information that we get from this study will help us to better understand the role of kisspeptin in human brain processing.

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.

What happens when the research study stops?

Once the study has finished, the results can be made available to you and/or your GP should you wish. If you have any problems immediately following the study, then you should contact one of the research doctors on the numbers provided below.

The blood samples that are taken from you during the study may be kept in secure storage at Imperial College London for further analysis 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 fully anonymised at all times 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 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 or Dr Lisa Yang/Dr Edouard Mills (020 7594 2489). 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 AHSC Joint Research Compliance Office or the Patient Advice and Liaison Service (PALS) at Imperial College Healthcare NHS Trust.

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. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

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 research notes and personal data will be held on password-protected computers and may be accessed by responsible individuals at Imperial College London, Imperial College Healthcare Team, Invicro Centre for Imaging Sciences and regulatory authorities, for study and audit purposes. Only personal information that is deemed essential to the study will be held by the research team and all such records will be destroyed after 10 years.

What will happen to the results of the research study?

The results are likely to be published in the six months following the study. Your confidentiality will be ensured at all times and you will not be identified in any publication. At the end of the study, the results of the study can be made available to you and/or your GP should you wish.

Who is organising and funding the research?

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

Expenses

You will receive a payment of £100 per study visit to cover all expenses including inconvenience and travel.

Who has reviewed the study?

This study has been reviewed by the London Riverside Research Ethics Committee.

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 Lisa Yang, Dr Edouard Mills, Dr Alexander Comninos or Professor Waljit Dhillo will be available by telephone at any time and can be contacted through Professor Dhillo's PA (020 7594 2489) or the hospital switchboard (020 8383 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.