Patient Information Sheet

South London and Maudsley NHS Foundation Trust

King's College London

Study title
Identifying Neuroimaging Markers of Bipolar Depression

Principal investigators
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Introduction
You are being invited to take part in a clinical research study being conducted at King's College London to compare the differences and similarities in the brain scans of people with Bipolar Disorder during an episode of depression, people with Major Depressive Disorder during an episode of depression and people with no history of significant mental health problems.

Before you decide if you'd like to take part, it is important to understand why the clinical study is being carried out and what it will involve. Please take time to read the following information. This document explains the purpose of this study and what will happen if you take part. It is entirely up to you to decide whether or not you would like to take part in this clinical study.

You can change your mind and withdraw from the study at any time during your involvement, without giving a reason. Please feel free to ask the study doctor or researcher if there is anything that is not clear or if you would like more information on any of the points in this information sheet. Our contact details are at the end of the information sheet. Take time to decide whether you would or would not like to take part and discuss it with others, including your GP, if you wish.

If you wish to take part, you will be given this information sheet to keep and be asked to sign a consent form (you will be given a copy to keep and the original will be kept in a secure location at King's College London).

This information sheet is in two parts:

PART 1 tells you the purpose of this study and what will happen to you if you take part.

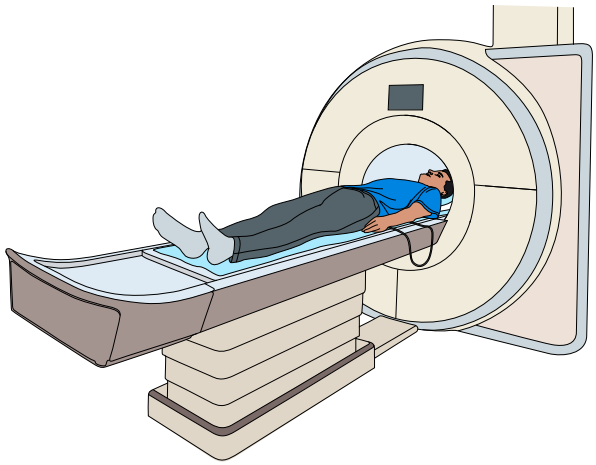
PART 2 gives you more detailed information about the conduct of the study.

What is the purpose of this study?

Bipolar disorder (BP) is a potentially lifelong and disabling condition. It is estimated that 1% of the adult population at some point in their life will experience bipolar I disorder (mania and depression), and 0.4% will experience bipolar II disorder (hypomania and depression). Mania is an extreme sense of wellbeing, energy and optimism. It can be so intense that it affects a person's thought and judgement. Individuals may believe strange things about themselves, make bad decisions and behave in embarrassing, harmful and occasionally dangerous ways. Like depression, it can make it difficult or impossible to deal with life in an effective way. A period of mania can affect both relationships and work. When it isn't so extreme, it is called 'hypomania'.

The processes in the brain which bring about depression are very poorly understood, and no reliable biomarkers exist. A biomarker is a biological feature that can be used to measure the presence or progress of disease or the effects of treatment. This study has been designed to try and identify brain scanning biomarkers which can be used in the future to help diagnose and treat patients and may be used to help in the development of new medications.

We will compare the differences in brain scans between people with Bipolar disorder (both bipolar I and II disorder) during an episode of depression, people with Major Depressive Disorder (MDD) during an episode of depression and people with no history of significant mental health problems. This will allow us to examine how brain function differs between these groups. We hope this study will help us to understand what patterns of activation in the brain are unique to bipolar depression.



Anhedonia (a loss of interest in activities you used to enjoy and a decreased ability to feel pleasure) is a core symptom of BP depression and MDD. This study will include tasks and assessments that assess these different components of anhedonia.

We will also look at the emotion processing areas in the brain which are known to be associated with mood disorders such as BP and MDD, so we will ask people taking part in the study to perform thinking and mood tasks whilst being scanned in an MRI scanner.

Why have I been invited to take part?

We are inviting people with bipolar disorder or major depressive disorder who are currently experiencing a depressed episode and people with no history of significant mental health problems to be involved in this study. Up to 90 people (30 in each group) will take part in this study at one site in the UK.

You have been invited to take part as you have bipolar disorder or major depressive disorder and are currently experiencing a depressed episode.

What will taking part involve? (1)

Taking part in the study involves two visits to the Centre for Neuroimaging Sciences, Kings College London at Denmark Hill:

- **Visit 1** - A **Screening Visit** (to assess whether you are suitable for the study).
- **Visit 2** - An **Imaging Visit** where we will assess your attention, memory, concentration and mood using tasks and questionnaires and you will have an MRI scan to assess your brain function.

The following paragraphs explain what will happen at each visit in more detail. There is quite a lot of information here and so we will be happy to talk you through it at your screening visit.

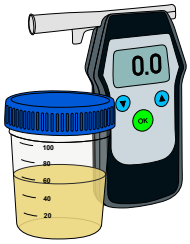
What will taking part involve? (2)

Visit 1 - Screening Visit

You will be asked to attend a screening session lasting approximately three and a half hours, to ensure that you are suitable to take part in the study.

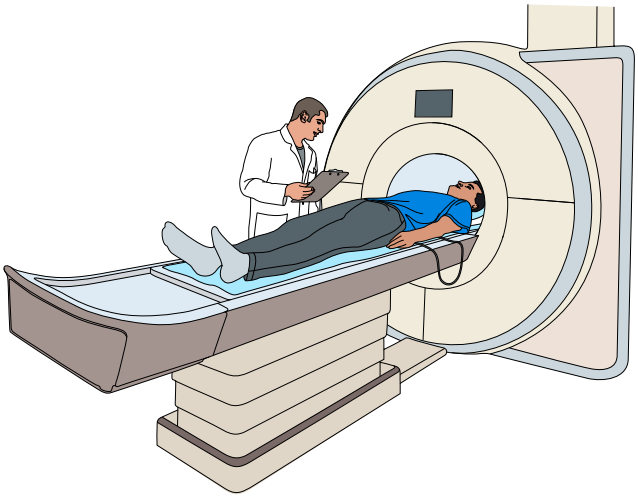
1. You will be asked to sign a consent form and we will ask you some questions about your past and current medical and mental health.

2. We will carry out a urine drug test and breath alcohol test and, if you are a woman who is able to get pregnant, a urine pregnancy test.

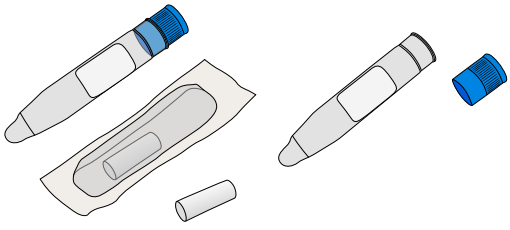


3. We will ask you to complete some questionnaires about your mood, memory performance and personality.

4. If you appear to be suitable for the study, you will be able to experience what it will be like in the MRI scanner as we have a “mock” scanner which looks just like a real scanner but does not have a magnet in it.



5. We will also show you the tasks that you will be asked to complete at your next visit and you will be given some saliva collection tubes to carry out a saliva collection to measure cortisol levels when you wake on the morning of your next visit - the procedure for doing this will be explained at your screening visit. Cortisol is a steroid hormone made by your adrenal glands. It helps your body to respond to stress, regulate blood sugar and fight infections.



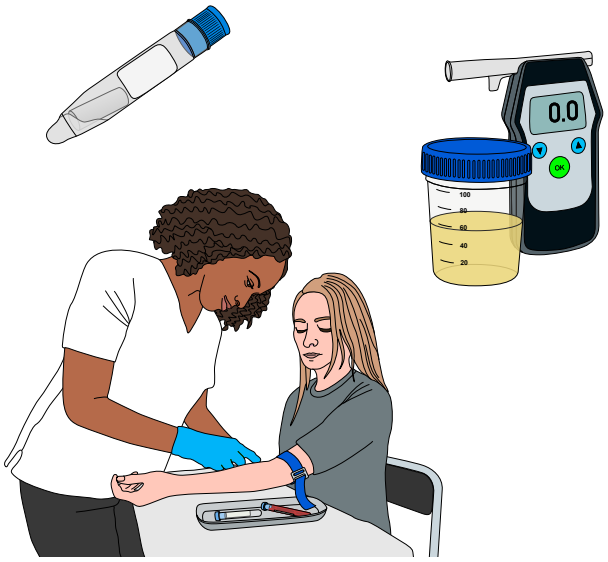
Saliva collection equipment

What will taking part involve? (3)

Visit 2 - Imaging Visit

This visit will last approximately 5 hours and will be scheduled on a day that is convenient for you. During the visit you will be able to take breaks between the tasks and assessments.

1. On the morning of your visit you will collect the saliva samples, as explained during your screening visit. You will need to bring these with you to the centre.

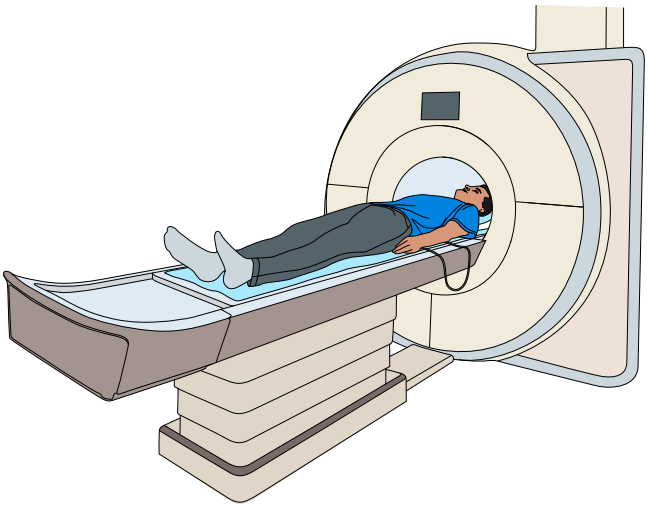


2. Once you arrive at the centre we will repeat the urine and breath alcohol tests and take a blood sample to measure inflammatory markers - these are proteins in the blood that increase in number when you get an infection, are stressed or damage any tissues in your body.

3. We will ask you to complete questionnaires which assess your mood and other aspects of your mental/emotional functioning. You will complete some detailed tests of your memory, attention and concentration with a researcher, and will complete some computer-based motivation tasks.

4. You will be asked to have an MRI scan which will last about one and a half hours. MRI scanning is commonly used to diagnose a number of diseases, but in this case it will be used to take pictures of the brain whilst at rest and whilst carrying out some tasks. In order for us to take pictures of your brain, you will have to lie as still as possible whilst you are in the MRI scanner.

5. Whilst lying inside the MRI scanner you will be asked to complete some more computer tasks which will appear on a screen which you can see in the mirrors positioned above your head. The exact nature of the tasks will be explained to you before the scan and, if necessary, you can practice performing the tasks outside of the scanner. You will be given the opportunity to win some money whilst carrying out some of these tasks.



What will taking part involve? (4)

Once all of the tasks, questionnaires and assessments are completed, your involvement in the study is complete.

The table below summarises what happens at each study visit.

What happens at each study visit	**Visit 1** screening visit	**Visit 2** imaging visit
Clinic visit	✓	✓
Medical and psychiatric history review	✓	
Current and previous medication check	✓	✓
Urine samples, pregnancy test (females able to have children only)	✓	✓
Breath alcohol test and urine drug screen	✓	✓
Mood, memory and personality questionnaires	✓	✓
Task practice	✓	
Saliva sampling collection at home when you wake up in the morning		✓
Review of your health status		✓
Blood sample		✓
Task completion		✓
Memory, attention and concentration assessments		✓
MRI scan		✓

MRI scans

MRI is a common procedure used in hospitals to monitor your health. MRI can also be used in research, to study the brain. Here at the Department of Neuroimaging, King's College London, we use MRI to try to find the causes of illnesses which affect the brain and to discover new treatments. When you volunteer for an MRI research study, you will be helping us to improve healthcare and people's quality of life. Your contribution can make a difference!

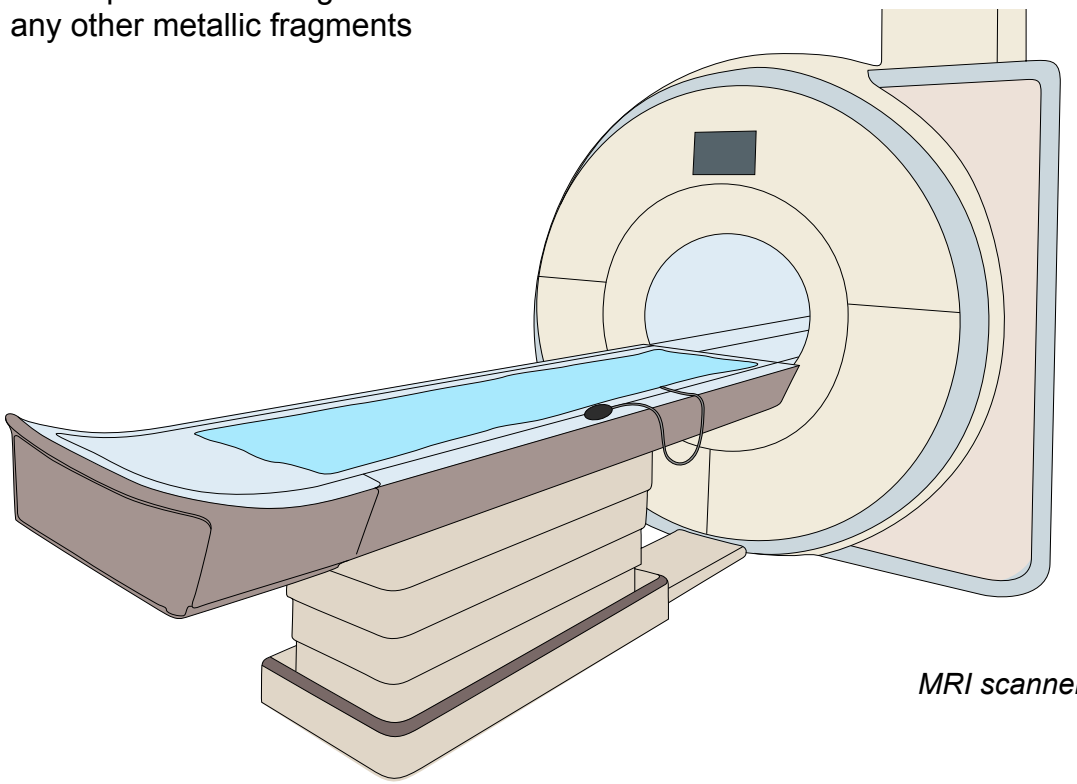
What is an MRI scan?

MRI stands for **Magnetic Resonance Imaging.** No X-rays are involved. Instead, it uses a strong magnetic field to produce images of organs and tissues, including the brain. The images can be used to diagnose illness and monitor the effect of treatment. They can also be used for research, to find out how the brain works when we are well, and to better understand illnesses and their treatments.

Can I have an MRI scan?

MRI is a technique that has a very low risk of harm. However, because of the strong magnetic field the MRI machine produces, having metals in your body (or in your pockets or clothes) can cause serious injuries. That's why before any MRI you will have a safety screening. You will answer some questions about things like any operations you may have had in the past. You might not be able to have an MRI scan if you have:

- a pacemaker or artificial heart valve
- artificial joints
- implanted devices (like an ear implant, drug pump, cardioverter-defibrilator, etc.)
- dental plates and bridges
- any other metallic fragments



MRI scanner

Having a brain MRI scan

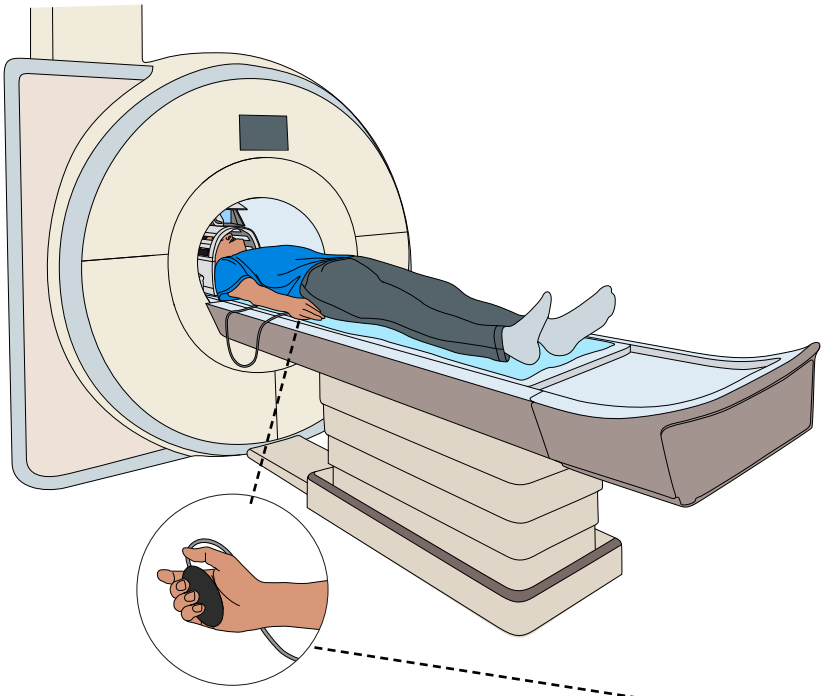
Before entering the MRI room, you will be asked to remove all metallic objects from your clothes and body. A radiographer will check that you are ready to enter the MRI room safely.

No metallic objects in pockets

You will be given some earplugs (and sometimes headphones) to reduce the scanner noise. You will then lie on a bed, which will move you into the scanner. Some people feel uncomfortable in the scanner, as space is limited. Therefore you should inform us beforehand if you are concerned about being placed in a rather confined tight space.

You will be asked to stay still while the scan takes place. Sometimes we will ask you to keep your eyes open and try to not fall asleep, but sometimes you can just close your eyes and rest. We might also ask you to do some computer-based tasks so that we can see how your brain responds while processing information.

Inside the MRI scanner



Buzzer to call the radiographer

The radiographer's desk

Radiographers will assist you throughout the procedure and you will be able to talk with them through an intercom at any time. If you feel uncomfortable, you can call them just by pressing a buzzer.

The scan can take from 15 to 90 minutes. This will depend on the reason for the MRI scan. Research sessions tend to be longer than standard clinical scans.

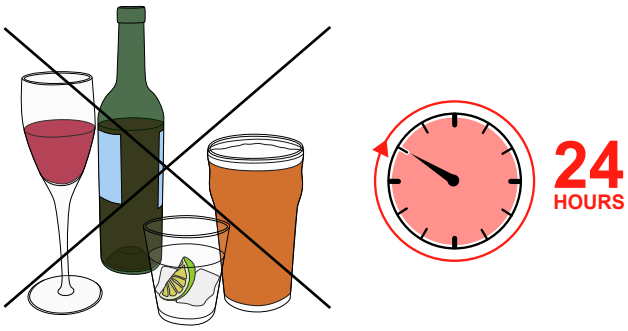
Do I have to take part?

No. Participation is entirely voluntary. It is up to you to decide whether you take part. You may refuse to take part or leave the study at any time without penalty or loss of benefits that you may otherwise be entitled to.

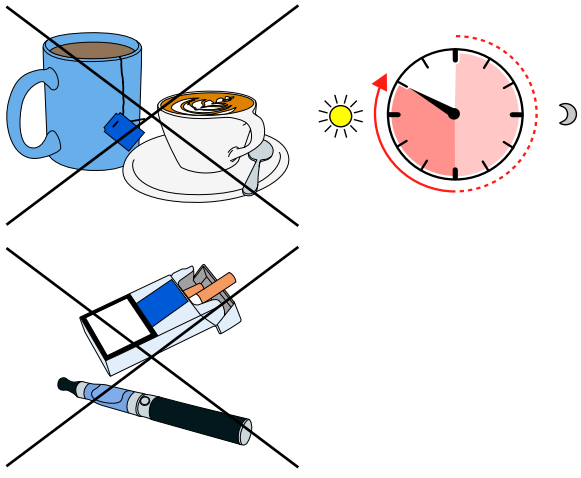
You should read this information sheet and if you have any questions you should ask the research team. You should not agree to take part in this research until you have had all your questions answered satisfactorily.

What restrictions do I need to follow during the study?

You will be asked to not drink alcohol for 24 hours before each study visit.



You will also have to abstain from caffeine and tobacco from waking on the morning of the MRI visit until you have completed the study visit.



Are there any reasons why I can't take part in the study?

The following reasons are likely to mean you can't take part in the study:

- If you have, or have had, any serious medical or neurological conditions, or severe head injury.
- If you have a history of major psychiatric disorder, (with the exception of bipolar disorder and major depressive disorder for participants with those conditions). We can discuss this with you before or at the screening visit.
- If you have taken part in a research study involving administration of an experimental drug within the last month or plan to do so in the next month.
- If you are currently regularly using recreational drugs such as cannabis or cocaine.
- If you have recently (in the last week) had a flu vaccination.
- For women: if you are currently pregnant, if you are trying to get pregnant, or if you are breast feeding.
- If you have a history of claustrophobia or are unable to lie still in an MRI scanner for a period of around 1½ hours.
- If you weigh more than 126kg (19 stone 12 pounds).

Because of the powerful magnetic field in the MRI scanner, you must not have a scan if you:

- Have had any metal injuries to your eyes.
- Have had metallic objects (including clips) inserted into your body during an operation.
- Have a tattoo on your head/neck, or if you
- have received a gun-shot injury, or
- have a heart pace-maker

We will go through a list of possible risks with you at your screening visit.

What are the possible benefits of taking part?

There is no specific direct benefit to you from taking part in the study.

However, the knowledge that we gain from this study could provide new information about bipolar depression and major depressive disorder which may benefit patients in the future.

What are the possible disadvantages and risks of taking part? (1)

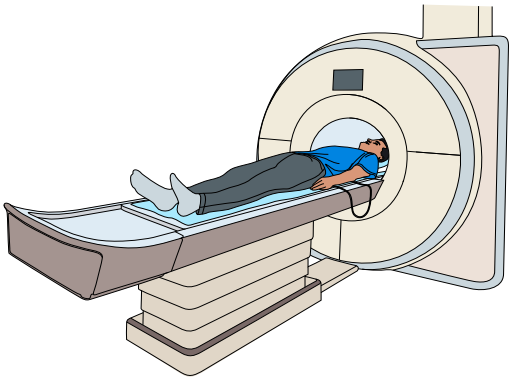
Blood tests

Taking blood samples bears the usual risks associated with blood sampling, e.g., possible bleeding from the puncture site, bruising, pain, blood clot formation, or local infection and swelling (inflammation) at or around the site where the puncture was made, all of which are rare occurrences.

In sensitive individuals, blood draws may sometimes cause them to become pale, nauseous, sweat, have a slower pulse or drop in blood pressure with dizziness or fainting in very rare cases.

MRI scanning

The magnetic field used in MRI scanning may harm people who have metal in their bodies, like certain clips, or staples from surgery. It also may cause problems with devices, such as pacemakers or neurostimulators. Please tell your study doctor if you have any of these, since you may not be able to have an MRI if you do.



What are the possible disadvantages and risks of taking part? (2)

Unexpected test results

You should be aware that there is a possibility that your participation in the study and the study tests may reveal an unexpected result that may have relevance for your physical or mental health. If this happens, we will discuss this with you and, if necessary, inform your GP who will arrange follow-up if necessary. In an emergency we will ensure that you are assessed either by our medical and psychiatric team or if more appropriate, in an Accident and Emergency department. If there are significant concerns about your or someone else's safety, the research team may deem it necessary to share information with your care team or the relevant authorities.

If you have a diagnosis of Bipolar Disorder or Major Depressive Disorder, some of the assessments made during the study may indicate that reassessment for your diagnosis may be appropriate. If this is the case, we will provide your GP with a copy of the assessments.

The information shared with your GP about unexpected tests results, or reassessment of your diagnosis may affect any insurance policies you may have.

If you do not wish for your GP to be informed of any significant findings or results, you should not take part in the study.

Will I be compensated for my travel expenses and time?

We sincerely appreciate the time you are giving up to take part in this study. You will receive £80 to compensate you for your time if you complete the study (£30 for the screening visit and £50 for the imaging visit). If you do not complete the study you will receive some of the payment, depending on how many visits you have attended (a pro-rata payment). You will also have the opportunity to win up to £20 in the tasks completed at your imaging visit.

We will reimburse any reasonable travel expenses on production of receipts and provide you with a light lunch during the imaging visit.

What if new information becomes available?

If unexpected information of potential clinical importance is found during the study we will discuss this with you and share the information with your GP or any other appropriate health care worker.

What if something goes wrong or I have problems while I am in the study?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see Contact Details below).

If you have any questions about your rights as a participant in the study, you may also contact the **Patient Advice and Liaison Service (PALS)** on the following number **SLaM PALS** contact details **freephone 0800 731 2864 (Option 2)** or by **email at pals@slam.nhs.uk**

If you remain unhappy and wish to complain formally, the contact point for any complaints before, during or after the study is **Gill Dale**, **Director of Research Quality at the Institute of Psychiatry, Psychology and Neuroscience**. **Email: Gill.dale@kcl.ac.uk**

If you have any questions or complaints regarding your rights as a research participant, you may contact the **NHS Complaints Advocacy** for assistance and support with your complaint. They can be contacted on **Helpline Number: 0300 330 5454**, **Textphone Number: 0786 002 2939**, or **e-mail: nhscomplaints@voiceability.org**

Every reasonable effort will be made to prevent any injury that could result from the study. If you believe you have an injury that is directly related to your participation in the study, you must inform your study doctor or his/her co-workers as soon as possible.

In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against King's College London and/or SLaM NHS Foundation Trust, but you may have to pay your legal costs. The normal NationalHealth Service complaints mechanisms will still be available to you (if appropriate). The University has insurance which provides no-fault compensation, i.e., for non-negligent harm, you may be entitled to make a claim for this.

This completes **PART 1** of the Information Sheet. Please continue to read the information in **PART 2** before you make your decision about taking part.

Who is organising and funding the research?

King's College London and **South London and Maudsley NHS Foundation Trust** are jointly sponsoring this study.

The study is being run by the **Centre for Neuroimaging Sciences** at the **Institute of Psychiatry, Psychology and Neuroscience, King's College London**.

Department of Neuroimaging & Department of Psychological Medicine

Institute of Psychology, Psychiatry & Neuroscience
Kings College London
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SE5 8AF

The study is funded by **H. Lundbeck A/S**, who are a pharmaceutical company.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a **Research Ethics Committee**, to protect your interests. This study has been reviewed and given favourable opinion by the **London Bridge Research Ethics Committee.**

This participant information sheet has been reviewed by the **FAST-R reviewers**, who are service users.

Information about you (1)

How will we use information about you?

We will need to use information from you and from your medical records for this research project. This information will include:

- Information that directly identifies you (such as your name, address, telephone number, health insurance number)
- Your age, sex, ethnic and racial background
- Information on your health and medical condition including your medical history
- Information about your biological samples and the results learned from analysing them

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead, this is called coded data. We will keep all information about you safe and secure.

Information about you (2)

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. We will also share a copy of your coded data with Lundbeck, the pharmaceutical company that has funded the study.

How your personal data will be used in compliance with General Data Protection Regulation (GDPR)

King's College London (KCL) is the lead sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake 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 properly.

KCL will keep identifiable information about you for 10 years after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

What are your choices about how your information is used?

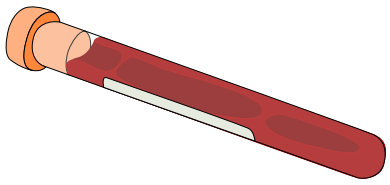
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

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.

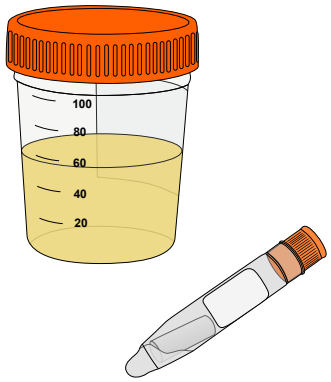
What will happen to any samples I give? (1)

Only the research team will have access to your samples (which will be only identifiable by a unique identification number).

Blood samples will be collected at the Centre for Neuroimaging Sciences at King's College London where they will be processed and stored securely until the end of the study. The inflammatory markers in the samples will be measured at the Stress, Psychiatry and Immunology Laboratory at King's College London. After the results have been analysed, the samples will be disposed of in accordance with the Human Tissue Authority's Code of Practice.



What will happen to any samples I give? (2)

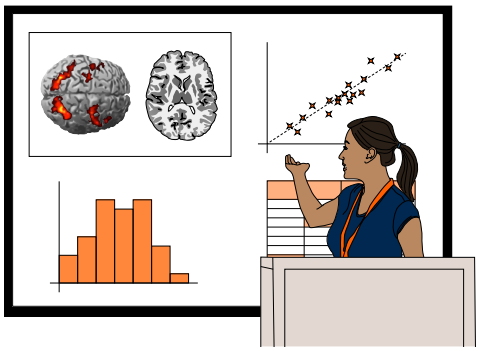


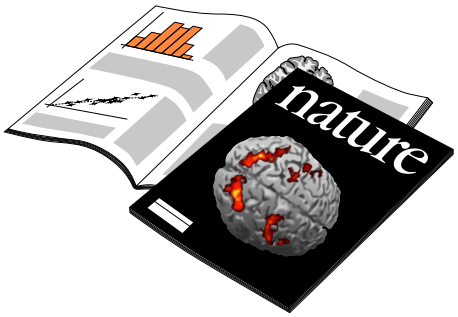
Urine samples will be destroyed on each study day as soon as the urine drug test and pregnancy test (if applicable) have been completed.

Saliva samples will be stored on site until the end of the study when they will be shipped to Biomarker Analysis Laboratory, Department of Psychology, Anglia Ruskin University, East Road, Cambridge for analysis. After the results have been analysed, the samples will be disposed of in accordance with the Human Tissue Authority's Code of Practice.

The tests performed with these samples are not intended to make determinations about your health or the likelihood you will develop any disease, so no test results will be provided to your doctor or put into your medical record. You will not have access to all your individual sample results from the study.

What will happen to the results of the study?





The results of the study may be published in scientific or medical journals or presented at conferences.

You will not be identified in any report or publication.

If you like, the researchers can share the results with you after the final participant completes the study and the data has been analysed.

Who do I contact for further information?

If you have questions about the study, please contact the study team members below. You are encouraged to ask as many questions as you would like so that you can decide if you wish to take part or not.

Contact details of researcher

Name:
Address: Centre for Neuroimaging Sciences
King's College London
De Crespigny Park
London SE5 8AF
Contact telephone number:
Email:

This completes **PART 2** of the information sheet.
Thank you for reading this information and for considering taking part in this research.