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INFORMATION SHEET FOR STUDY VOLUNTEERS

Study title: Synaptic imaging and network activity in treatment resistant depression (SIGNATURE)

Principal Investigator: Prof. Mitul Mehta
Version 2 Dated 21 July 2021

Research Ethics Committee number: 21/LO/0493 **IRAS ID**:297200

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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 brain scans of people with Bipolar Disorder or Major Depressive Disorder after a period of treatment with ketamine and a placebo treatment.

Before you decide if you'd like to take part, it is important to understand why the 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 you would like to take part in this study or not.

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.

Please 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 2 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.

Part 1

What is the purpose of this study?

Depression is one of the most common health conditions worldwide and can have a severe impact on an individual's ability to function and their quality of life. People with Major Depressive Disorder (MDD) have a persistent low mood, loss of motivation, and experience reduced pleasure from previously enjoyable activities. Depressive symptoms are also a key feature of Bipolar I and Bipolar II disorder, in which periods of depression alternate with periods of abnormally elevated mood.

While drug treatments and psychological therapies exist for depression, around 30% of patients fail to successfully respond to any of these treatments. When patients fail to respond to two or more treatments, this is often called treatment resistant depression, or TRD. However, recent research has suggested that some medications which are usually prescribed for other purposes may also have benefits for treating the symptoms of depression. Ketamine, a widely used anaesthetic, has recently emerged as an effective, rapid acting antidepressant with promising effects in treatment resistant depression.

The aim of this study is to understand more about why ketamine could be effective at treating depression. To do this we will use state-of-the-art brain imaging techniques to see how brain activation patterns change when people have taken the treatment, and how this relates to any changes in their symptoms. This will help us understand more about the illness itself and how we might be able to treat it better.

Why have I been invited to take part?

We are inviting people with major depressive disorder or bipolar disorder who are currently experiencing a depressed episode, and who have been previously prescribed at least two treatments for their symptoms but did not respond to these treatments. Up to 50 people will take part in this study at one site in the UK.

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 will taking part involve?

Taking part in the study involves 11 visits to the Centre for Neuroimaging Sciences, Kings College London at Denmark Hill. The visits will be spread over a period of a minimum of approximately 6 weeks and a maximum of 13 weeks.

- Visit 1: A screening visit to assess whether you are suitable for the study.
- Visit 2: An imaging visit where you will have an MRI scan and an EEG scan to assess your brain function. We will also assess your memory, concentration and mood using tasks and questionnaires.
- Visits 3-5: Three shorter visits where you will receive the study medication or placebo. We will explain more about the placebo later in this information sheet.
- Visit 6: A second imaging visit where you will have another MRI and EEG scan, and complete similar tasks and questionnaires as visit 2.
- Visits 7-9: Three shorter visits where you will receive the opposite to what you received in visits 3-5 - either the study medication or placebo.
- Visit 10: A third imaging visit where you will have another MRI and EEG scan, and complete similar tasks and questionnaires as visits 2 and 6.
- Visit 11: A final visit with some short questionnaires and health checks.

We will also ask you to practice some tasks on your smartphone or home computer for 8 days between visits 6 and 7 and for another 8 days between visits 10 and 11.

We understand this may seem like a lot of visits, but we will provide transport to and from the testing centre for visits 2 – 11 and provide support and information throughout the study. We will provide appropriate meals and refreshments for both you and your carer/relative if you chose to be accompanied by one.

The following paragraphs explain what will happen at each visit in more detail. There is quite a lot of information here and we will also talk you through it at your screening visit. You do not have to memorise this - it is just for your information, and you will be advised what to do throughout the study.

Visit 1: Screening Visit

You will be asked to attend a screening session lasting approximately 2 hours to ensure that you are suitable to take part in the study. It can be scheduled on a day that is convenient for you. You will have an opportunity to discuss the study with one of the investigators and ask any questions you may have. If you are happy to proceed you will be asked to sign a consent form. The following assessments will then be performed:

- A check of your current health status, medical history and any previous and current medications you are taking. We will also ask some questions about any caffeine, nicotine, alcohol and/or recreational drug use.
- A physical examination including a measurement of weight and height, blood pressure (BP) and heart rate, temperature and breathing (respiratory) rate, and alcohol breath test.
- ECG (Electrocardiogram). This is a common procedure which records your heart's activity.

- Psychiatric examination, during which the study doctor will ask you questions about your mental health history, any symptoms you are currently experiencing, your general mood and any suicidal thoughts you may have now or in the past.
- We will ask you to complete some self-report questionnaires that will ask you about your depressive symptoms.
- Some short cognitive assessments, which are tests of things like your memory and verbal ability.
- Blood and urine samples will be taken to check on your general health and how well your liver, kidneys and other organs are functioning. A sample of your urine will be taken to check for recreational drugs and, if you are female who is able to get pregnant, a urine pregnancy test.
- A radiographer will ask you some questions to determine if you are suitable to have an MRI scan. We will also simulate the experience of having an MRI scan in a mock scanner to ensure you are comfortable with the environment, and you will be able to practice some of the tasks will we ask you to perform during the real scan.

We will look at the results of some of these assessments to understand if you are suitable to take part in the study. If you are suitable and still happy to take part, we will invite you back for the visit described below. At this point you will be randomly assigned into one of the treatment arms which will determine which medication you will receive at the treatment visits. Randomisation means that you are put into a group by chance, like flipping a coin. You will be assigned to one of two groups – one where you will receive the placebo during the first part of the study and ketamine during the second part; or the other group where you will receive ketamine first and placebo second. There are more details about these medications on page 10 of this information sheet.

Visit 2: Imaging Visit One

This visit will take place within 4 weeks of your screening visit and will last approximately 7 hours. During the visit you will be able to take breaks between the tasks and assessments. We will ask you not to eat or drink anything other than water when you wake on this day. We will give you a light breakfast soon after you arrive (you will be able to pick from a few different options). All other meals and snacks will be provided as appropriate.

When you arrive at the centre you will be asked about any medication you have taken since your screening visit. We will ask you some questions about your symptoms and ask you to complete some short questionnaires. We will administer an alcohol breath test and do some blood tests. These tests are to check for certain proteins and hormones in your blood that could help us understand the results we see on your brain scans.

During this visit we may also ask to take an additional small one-off sample of blood for pharmacogenomic testing, which involves studying how genes affect a person's response to medicines. This part of the study is optional, and you do not have to agree to give this extra blood sample if you do not want to. There are more details on this in the pharmacogenomic testing section below.

You will be asked to have an MRI scan which will last about 1½ 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. The scanner consists of a powerful magnet, but you will not feel any force or special sensation inside of the magnetic field because your body is insensitive to it. **An MRI is different to an x-ray because MRI scanning does not involve any ionising radiation.**

Because of the powerful magnetic field, 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
- Have received a gun-shot injury
- Have a heart pacemaker

The radiographer will go through a list of possible risks with you before you go 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 space. There is a microphone inside the scanner so that you can talk to the study team at any time if you want to. If you do feel uncomfortable you can let the scanner operator know and the session will end. You will also have an alarm buzzer that you can press if at any time you feel that you need to come out of the scanner, and the scan will immediately stop. At the screening visit we will ask you to lie down inside a mock scanner to give you an idea of what the actual scan will be like and to check you are comfortable with the environment.

During the MRI scan you may feel mild vibrations throughout your body. The machine will make a loud knocking noise. This is normal. You will be given earplugs to protect your ears.
For more information about what it is like to have an MRI scan, please visit: https://www.youtube.com/watch?v=6vtKS-MA5n4

Whilst lying inside the MRI scanner you will be asked to complete some 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. You will be given the opportunity to win a small amount of extra money whilst carrying out some of these tasks, which will be paid at the end of the

visit. This does not affect your compensation for taking part in the study, which will always be paid if you complete the visits.

EEG

After the MRI scan we will perform another brain imaging method called electroencephalography (EEG). EEG involves wearing a special cap on your head which measures small signals of electrical activity on your scalp. This is a common and safe test and does not produce any electric stimulation. When the cap has been fitted, a gel will be applied to ensure a good contact with the skin. While you are wearing the cap we will ask you to complete some short computer tasks. The entire procedure will take around one hour. After the EEG test the gel will need to be washed out of your hair. There are facilities to wash your hair during your visit unless you would prefer to wash it at home.

After the EEG we will ask you to complete some computer based cognitive tests. These are short tasks designed to test things like your memory and attention. It may be possible to complete these the next day at home, using an app on your smart phone or on a computer.

Visits 3-5: First Infusion visits

The next visit will take place within seven days of your last visit, and is followed by another two similar visits, each 3-5 days apart. Each visit will last about 2 hours, although the last visit may last up to 3.5 hours. We will ask you not to eat or drink anything other than water when you wake on the morning of the third infusion visit. We will give you a light breakfast (the same as the one we gave you at the imaging visit) soon after you arrive

At the start of each of these visits we will ask you some questions about your recent health, and any medication you may have taken since your last visit. We will conduct an alcohol breath test and take a urine sample to check for recreational drugs at each visit. At the first of these three visits we will also perform a urine pregnancy test (if you are female who is able to get pregnant). We will ask you some questions about your symptoms and ask you to fill in some questionnaires about your mood.

At each visit you will receive an infusion of the study medication. An infusion involves administering the medication in liquid form over a period of 40 minutes via a cannula (a small plastic tube which allows the medication to be administered directly into a vein into your arm). This study is double-blind, which means you will not know which treatment you have received, and neither will the study team. However, it is possible for the study team to quickly find out which medication you have received if required. You will receive the same infusion at each of these 3 visits. We will ask you to fill out some questionnaires during and following the completion of the infusion.

During the third infusion visit we will take three separate blood samples over the course of about 3 hours from the start of the infusion to check for the levels of the medication in your blood.

Visit 6: Imaging Visit Two

This will take place on the day following the third infusion visit (visit 5). This visit is identical to the first imaging visit and will involve an MRI and EEG scan along with the other blood tests, assessments and questionnaires described above. The EEG scan may last 30 minutes longer during

this visit. At the start of the visit we will conduct an alcohol breath test and ask you to provide a urine sample to check for recreational drugs.

At the end of this visit we will show you two computerised tasks that you will need to practice every day for a week before your next visit. You will be able to perform these tasks on your smartphone or on a computer at home. If you do not have access to this equipment we may be able to provide you with a device for the duration of the study.

Visits 7-9: Second Infusion visits

After a minimum of 8 days you will return for the second set of infusions. These will again be given over 3 visits, each 3-5 days apart. We will ask you not to eat or drink anything other than water when you wake on the day of your third infusion. We will give you a light breakfast soon after you arrive.

The infusions will be of either ketamine or placebo, whichever you didn't receive in the first set of visits. The three visits will be the same as the first infusion visits (see visits 3-5 above), but on the first of these visits we will also test you on the tasks you have been practising at home. At the start of each of these visits we will conduct an alcohol breath test and ask you to provide a urine sample to check for recreational drugs.

Visit 10: Imaging Visit Three

This will take place the day after your last infusion visit (visit 9). This visit will be identical to visit six and will involve an MRI and EEG scan along with the other blood tests, assessments and questionnaires described above. At the start of each of these visits we will conduct an alcohol breath test and ask you to provide a urine sample to check for recreational drugs. You will be asked to practise some new computerised tasks at home for the week leading up to your next visit.

Visit 11: Follow up

This visit will take place a minimum of 8 days following your last imaging visit (visit 10) and will take about 2 hours. We will ask you about your general health and any medication you have taken since your last visit. We will take a urine sample to check for recreational drugs and, if you are female who is able to get pregnant, a urine pregnancy test. We will ask you some questions about your symptoms and ask you to complete some short questionnaires, and a blood sample will be taken for hormone and protein analysis.

We will also test you on the tasks you have been practising at home.

Early end of study

If you leave the study before the scheduled end, you will be requested to attend a final visit which will last about an hour. We will ask you about your general health and any medication you have taken since your last visit. We will take a urine sample to check for recreational drugs and, if you are female who is able to get pregnant, a urine pregnancy test. We will ask you some questions about your symptoms and ask you to complete some short questionnaires, and we will ask to take a blood sample for protein and hormone analysis.

The table below indicates what happens at each study visit:

Activities to be performed	Screening period, visit 1	Imaging Days			Infusion Days			Follow-up, visit 11
					1	2	3	
		Visit 2	Visit 6	Visit 10	Visits 3 & 7	Visits 4 & 8	Visits 5 & 9	
Signing informed consent	X							
Current health status/wellbeing	X	X	X	X	X	X	X	X
Medical history	X							
Medication use	X	X	X	X	X	X	X	X
Physical and psychiatric examination	X							
Blood pressure, heart and breathing rate, temperature and ECG	X							
Alcohol breath test	X	X	X	X	X	X	X	X
Study medication is administered					X	X	X	
MRI		X	X	X				
EEG		X	X	X				
Computer based tasks		X	X	X				
Learning tasks*					X			X
Verbal and memory tests	X							
Questions about depression symptoms, mood, depression or suicidal thoughts	X	X	X	X	X	X	X	X
Urine sample – recreational drugs	X	X	X	X	X	X	X	X
Urine sample – pregnancy	X				X			X
Urine sample – general health	X							
Blood samples - general health	X							
Blood sample - study medication			X	X			X	
Blood samples for protein and hormone biomarkers		X	X	X				X
Blood samples for pharmacogenetics		X						

*To be practiced at home for 8 days prior to visit

What restrictions do I need to follow during the study?

- You'll be asked to not drink alcohol for 12 hours before each study visit.
- You'll be asked to not eat or drink anything other than water from waking until we give you breakfast at visits 2 (imaging visit one) and visits 5 and 9 (the third infusion visit).
- You will have to abstain from caffeine (coffee, tea, cola etc) and smoking (tobacco, vape) from waking on the morning of each visit until you have completed the study visit. Whilst you are in the clinic, any tea or coffee provided will be decaffeinated.
- You cannot consume grapefruit juice or Seville oranges, or products containing these for 24 hours prior to a visit.
- You will have to abstain from strenuous exercise (e.g., heavy lifting, weight training and aerobics) for 24 hours prior to admission for each study day and you will be warned not to drive or operate machinery from the time of dosing until 24hrs post dose at each study session involving an infusion.
- If you need to take any medication other than what you were taking at the time of your screening visit, you must inform the study team.
- You must continue to take all of your normal medications throughout the study.

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 (including high blood pressure or heart problems), or severe head injury.
- If you have a history of major psychiatric disorder other than bipolar disorder or major depressive disorder, or if you have one or more immediate family members with a current or previously diagnosed psychotic disorder. We can discuss this with you before or at the screening visit.
- If you are regularly taking medication other than that used to treat your depression or bipolar disorder. There are some exceptions to this which 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 or have a history of significant substance abuse problems.
- If you consume alcohol in excess of 28 units per week, or consume more than 6 caffeinated drinks per day, or smoke more than 5 cigarettes a day
- If you have recently (in the last week) had a flu vaccination.
- If you cannot speak English
- If you already have a good knowledge of the Cantonese or Mandarin language (this is due to one of the learning tasks we will ask you to do).
- 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
    - Have received a gun-shot injury
    - Have a heart pacemaker

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

What are the possible benefits from 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?

STUDY MEDICATION

Ketamine: Ketamine is commonly used as an anaesthetic. You should be aware that it is sometimes used recreationally and some recreational users become dependent after regular use. Ketamine can affect your blood pressure so you will not be included in the study if you have a history of high blood pressure or other heart problems. When you receive ketamine you may feel your heart beating faster. At high doses, ketamine can also cause strange experiences (such as feeling disconnected from your body or other distortions of sense). Importantly, the doses to be used in this study have been used previously and are well-tolerated in healthy volunteers and people suffering from depression. They are well below doses used in anaesthesia. The strange experiences typically occur at higher doses but have been reported at the dose to be used in this study. If they should occur you may find them unpleasant and frightening. If this happens the infusion will be stopped immediately, and any strange experiences should rapidly fade. You may also feel nauseous when we stop the infusion and some people feel slightly clumsy or drunk for about one hour afterwards. You will be monitored during and after the infusion and a qualified clinician will always be present during the study periods.

Placebo (Midazolam): When testing the effectiveness of medications, it is standard practice to compare the effect of the medication being tested against the effect of taking an inactive placebo. A placebo is something that may look like the medication but it does not have any of the active ingredients in it, for example a sugar pill or saline (salt water) infusion. This is to protect the results from the placebo effect, which is a phenomenon where people report positive effects after taking a medication regardless of whether the drug treated the condition or not. Normally in a placebo-controlled study, both the participant and the research team do not know when the treatment or the placebo are being given. This is called a double-blind study.

Because ketamine can sometimes produce the experiences described above, we cannot use a simple sugar pill as a placebo in this study as it will be obvious to both the participant and the

research team when the ketamine treatment has been given. Therefore, in this study we are using midazolam as an active placebo, as this medication can produce similar effects to those described above without producing the antidepressant effect of ketamine and so we would not expect midazolam to have any effect on your depression. Midazolam is a short-acting medication that belongs to class of drugs called benzodiazepines. It is commonly used as a sedative for medical procedures.

Some reported side effects of midazolam include reduced alertness and drowsiness, headache, hypotension, dizziness, dry mouth and nausea. In this study, a very small dose of midazolam will be given. You will be monitored during and after the infusion and a qualified clinician will always be present during the study periods.

STUDY PROCEUDRES

Blood tests: Blood will be taken for laboratory testing to check your health, and to measure level of proteins, hormones and the amount of study medication in your blood. The maximum volume of blood taken at any single visit is approximately 26 mL (approximately 5 teaspoons). The total amount of blood that will be taken over the course of the study is approximately 102 mL (approximately 17 teaspoons). Risks associated with drawing blood from your arm and/or inserting a cannula in your arm include 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 one of the study team if you have any of these, since you may not be able to have an MRI if you do. A radiographer will carefully check that you are safe to have an MRI scan at your screening visit.

Risks associated with electrocardiograms: An electrocardiogram (ECG) is a test that indicates how the heart is working. You will have small, soft pads, placed temporarily on different parts of your body. There is no pain or discomfort during an ECG; however the patches may cause a skin reaction such as redness or itching. Taking the pads off may cause localised irritation to the skin and/or hair loss, similar to having a plaster taken off.

Risks associated with EEG: If you have extremely sensitive skin you may experience a skin reaction to the cleansing lotion or gel used. Occasionally people develop a temporary headache from wearing the EEG cap.

Unexpected tests 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 this study.

What is involved in the optional pharmacogenomic testing?

There is growing evidence that differences in people's genes known as DNA (genetic material) may lead to certain diseases and cause differences in the way they respond to medicine. The study team want to look at the genes in the blood samples collected from you to learn if genes affect people's response to the study medication. This will involve taking a single additional blood sample during the second study visit. Participation in this part of the study is optional. Refusal to participate will involve no penalty or loss of benefits to which you would otherwise be entitled.

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 £500 to compensate you for your time if you complete the study. 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). Payment may be made in instalments at the end of each block of visits. You will also have the opportunity to win up to £20 in the tasks completed at each of your imaging visits.
For attending a full screening visit you will be paid £25. You will receive this compensation regardless of whether you are suitable to take part or not.
We will arrange a taxi to pick you up and take you home for study visits 2-11 and will reimburse any reasonable travel expenses for you and your carer/relative if they are accompanying you, on production of receipts for the screening visit (visit 1).

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 will happen if I don't want to carry on with the study?

Your participation in this study is strictly voluntary; it is your own personal decision whether to participate in this study or not. If you decide to participate, you may choose to withdraw at any point during the study without providing reasons. If you withdraw your present and/or future medical care will not be affected and you will incur no penalty or loss of benefits to which you may otherwise be entitled.

Your study participation could be discontinued by the study doctor, without your consent, for any of the following reasons:

- The Sponsor, regulatory authority or ethics committee cancels the study;
- The study doctor thinks that removing you from the study is in your best interests;
- You need extra medication that would interfere with the study;
- This is necessary to meet the requirements of the study;
- You are not co-operating or you have not followed the directions given by the study doctor.

Should you decide to withdraw from participation in the study you must notify the research team. We will ask you to undergo a final examination.

If your participation in the study is terminated for any reason, information related to your participation in the study that was collected prior to termination of your participation may continue to be used and disclosed by the study team for the purposes described in this consent form. If you withdraw your consent to participate in the study, you have the right to request that all previously retained identifiable blood samples are destroyed to prevent further analyses. The study doctor and Sponsor may continue to use and distribute any information and test results gathered in connection with you taking part in this study prior to your request to stop testing.

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.

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 National Health 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.

Part 2

Who is organising and funding the research?

Kings 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. The study is funded by two pharmaceutical companies: H. Lundbeck A/S and Sosei Heptares.

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 – City and East Research Ethics Committee. This participant information sheet has been reviewed by the FAST-R reviewers, a team of people with experience of mental health problems and their carers, who have been specially trained to advise on research proposals and documentation

Will my 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. Your data will be processed in accordance with the standards set by the General Data Protection Regulation 2016 (GDPR).

How will you use information about me?

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.

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 H. Lundbeck S/A and Heptares Therapeutics Limited, the pharmaceutical companies that have funded the study. They must follow our rules about keeping your information safe.

What about the online tasks data?

We will use two cloud-based servers to collect some of the data for our study. These are cloud software platforms specifically developed for collecting research data like this. Online cognitive task data will be hosted on Amazon EC2 (Europe) server, and the online depression questionnaire data is hosted on U.S.-located, hardened servers. All data going to and from and stored on these servers is encrypted and will be identified using codes, not your name. The KCL research team owns and has complete control over the data. The data from one of the web-based learning tasks will be encrypted and stored on secure servers owned and operated by The University of Melbourne (the university that developed the task) which can only be accessed by authorised personnel. This data is also only identified using codes, not your name, and will be securely returned to the KCL research team at the end of the study for analysis.

What will happen to any samples I give?

Only the research team and relevant laboratory staff 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. After the results have been analysed, the samples will be disposed of in accordance with the Human Tissue Authority's Code of Practice.

Viapath Analytics LLP (Francis House, 9 King's Head Yard, London SE1 1NA) will analyse the blood samples we take at screening to check your physical health. They will also analyse the blood samples we take during the study to check for the levels of different proteins and hormones in your blood.

Analytical Services International Ltd (6 Baldwin Crescent, London, SE5 9LQ) will analyse the blood samples we take during and after the infusions, to check for the levels of the study medication in your blood.

BRC BioResource Centre Maudsley, Genomics & Biomarker Core Facility (SGDP Centre, IoPPN, De Crespigny Park, London SE5 8AF) will analyse the blood samples we take for the optional pharmacogenomic testing, if you have consented to take part in that portion of the study.

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

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.

The data from the analysis of your samples and the other procedures you will undertake in this study (MRI, EEG, questionnaires and other assessments) will be made available to other researchers after the end of the study. Such sharing of data is increasingly common. Your data will remain anonymised and you will not be identifiable in any of the shared information.

What are my choices about how my 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.

Where can I find out more about how my information is used?

- Online: www.hra.nhs.uk/information-about-patients/
- By asking someone in the research team (see details at the end of the information sheet)
- Contacting the Chief Investigator (Prof Mitul Mehta, Mitul.mehta@kcl.ac.uk)
- Visiting the KCL website: https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research.aspx
- By contacting King's College London's Data Protection Officer, Mr Albert Chan at info-compliance@kcl.ac.uk

What will happen to the results of the study?

The results of the study may be published in scientific or medical journals, presented at conferences. You will not be identified in any report or publication. In addition, the information collected during this study, including your MRI scans, may be added to research databases and used in the future by the Sponsor and its affiliated companies to:

- study better measures of safety and effectiveness
- study other therapies for participants
- develop a better understanding of disease(s) included in the study
- improve the efficiency, design and study methods of future clinical studies.

Information about the design, progress, and results of this study may also be posted on other publicly accessible websites, but you will not be personally identified on any of these websites.

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: Dr. Peter Hawkins
Address: Centre for Neuroimaging Sciences,
King's College London, De Crespigny Park, London SE5 8AF

Contact telephone number: 02032283058
Email: peter.hawkins@kcl.ac.uk

Thank you for reading this information sheet and for considering taking part in this research

This completes Part 2 of the Information Sheet.