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Centre Name: Centre for Psychedelic Research

Study Protocol number: Edge 182996

REC Reference:

Full Title of Project: PsiloGambling: Multimodal brain and physiological biomarkers of action of a 5-HT2a receptor agonist in Gambling Disorder

Contents

Participant Information Sheet

You are being invited to take part in a research study. Before you decide whether to participate, it is important to understand why the research is being done and what it will involve. Please read this information carefully, and feel free to talk it over with others. If you have any questions, you can ask us at any time. Take time to decide whether or not you wish to take part.

This information sheet is split into the following:

- *Summary information of the Participant Information Sheet*
- *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.*

Study Summary Information

What is the purpose of the study?
This study is investigating whether a 5HT2a agonist (psilocybin, a psychedelic substance found in 'magic mushrooms'), changes brain function and biomarkers of Gambling disorder as observed using neuroimaging tools including functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). We want to use the brain scans to help characterise psilocybin on addiction-related brain and peripheral biomarker function in Gambling disorder.

Who are we looking for?
We are looking for people who:
- have a DSM-5 diagnosis of Gambling disorder
- are registered for treatment with the National Gambling Clinic (NGC)
- are over 18 years of age
- are able to read, comprehend and record information written in English

We believe that you meet these criteria and may be eligible to take part in the study.
You would be one of up to 35 participants taking part.

Do I have to take part?

No, taking part is voluntary. You can choose to leave the study at any time by telling the study team that this is what you want to do, without giving a reason. Your decision will not affect your current or future care in any way.

What will happen to me if I take part?

See Figure 1 on page 5 for an overview diagram of the study. We will start with a screening process to check your health and ensure it's safe for you to take part in the study. If you are eligible and decide you would like to take part, you'll visit Hammersmith Hospital at least 8 times (including the screening visit).

The total duration for participating in the study, from the screening visit to the final visit, will be approximately 4.5 months.

Following screening, completion of the informed consent form and enrolment into the study you will begin study procedures. This will be done in a dyad consisting of 2 study team members who are clinically qualified to deliver psilocybin. Their role is to help you feel safe and supported throughout. They have been trained by clinical members of our team who have an extensive experience of working with psilocybin. These staff may include qualified clinical psychologists, psychiatrists, psychotherapists, or appropriately trained members of the clinical research team. All guides will receive study specific training and will work under clinical supervision.

The study has the following parts:

Preparation

During the weeks before the psilocybin session, you will meet with two guides from Imperial in two sessions. The preparation visit one will last 7-8 hours, and preparation visit 2 will last 4 hours. These visits will take place at the Imperial Clinical Research Facility (ICRF, Imperial College Healthcare Trust (ICHT) at Hammersmith Hospital, and at Perceptive Inc Imaging Centre in Burlington Danes Building, located next to the Hammersmith Hospital site (please refer to the map at the end of this document). The guides will be with you throughout the process, starting with these 'preparation' sessions. These visits will occur 9 days and one day before you receive psilocybin, you will come to our clinic where you will have the preparation session along with brain imaging (magnetic resonance imaging, MRI and electroencephalogram, EEG), complete some tasks and fill out some questionnaires. During these 'preparation' visits, you'll meet your guides in person. They will support you in getting ready for the psilocybin experience, helping you feel comfortable and prepared for the dosing session.

Dosing day

This visit will take place at the ICRF at Hammersmith Hospital. On this day, which will last approximately 8 to 9 hours in total, you will be with Imperial researchers and the guide team to ensure that you are ready for the psilocybin experience. You will be given one dose of psilocybin in

the form of capsules, and your guides will stay with you throughout the session, which lasts up to 6 hours. You will be provided with an eye mask and there will be music playing through the headphones, alongside speakers in the room. You will also receive an EEG scan at points throughout the experience. A doctor, one of the study medics, will always be nearby.

After dosing

The next day, you will come back to the ICRF for a two-hour integration session, followed by two hours of questionnaires. A week later, you'll return to the ICRF and Perceptive Inc Imaging Centre for another 'integration' session and a brain scan where you'll again complete some tasks. There will be another integration session three weeks later (one month after dosing), which will also be done in person at the ICRF. All integration sessions provide psychological support and an opportunity to talk through your psilocybin experience with the study guides. At the end of this period, 12 weeks after dosing, you will visit the ICRF and Perceptive Inc Imaging Centre for a final follow-up where the study team will do a final fMRI and EEG scan and ask you about how things have been during the follow up study period. You will be asked to fill out some final questionnaires and will have some interviews with the study team.

Other information

While you may experience improvements to your Gambling disorder symptoms if you take part, it's important to understand that the purpose of this study is not to provide treatment, The purpose of this study is to observe and characterise the effects of psilocybin in your brain and peripheral biomarkers. If at any time you feel triggered to return to gambling during the study, we will work with you to try to support you. We will continue to work collaboratively with you and the team at the National Gambling clinic. The study team would encourage you to lean on your support network as much as you need to if you have any challenging experiences during the study.

If you wish to take part in the study, we require a commitment that you will attend all follow up visits, complete all required tasks and questionnaires and will remain contactable for follow up. It's important to be aware that at some visits there are multiple questionnaires to complete, which may take some time, but we will ensure you have breaks if you find this too much. For questionnaires to be completed online, via our online system called REDCap, you will receive automated SMS notifications to your phone and emails to remind you to complete them at the required timepoints.

This study is open to both smokers and non-smokers. If you do smoke, you should be able to go for several hours without a cigarette, but you can use nicotine replacement. You should not be dependent on any other drugs or alcohol. If you have questions regarding this, please do speak to the study team.

There are certain medications which you cannot take as part of this study. This will be discussed with you at screening if you decide to take part. You should continue to take your usual medication

as prescribed and should not make any changes to your medication without the guidance of the prescriber or your GP.

What if there is a problem?

In the unlikely event that something goes wrong with your physical health after being given Psilocybin, you will be looked after by a medical doctor who will be present during the dosing sessions. If something was to happen which requires emergency care, we have emergency facilities in the research unit and also in the hospital next to it. If during the study you were to lose the capacity to consent, you would be withdrawn from the trial and any data already collected could be retained There are certain circumstances, at the study medic's discretion, where you may be withdrawn from the study. These include if you withdraw your consent to participate, or if you no longer have capacity to consent to participate. It also includes if your mental or physical health deteriorates and it's deemed by the study medic unsafe for you to continue. Further reasons include if ongoing participation will negatively impact your clinical care, or if there is persistent non-compliance with the protocol.

If you were to be withdrawn identifiable data or tissue already collected with consent would be retained and used in the study, but no further data or tissue would be collected or any other research procedures carried out.

You should not be enrolled in any other studies of new medications at the same time as this study.

For any emergent behaviours that the study team deem to be clinically relevant, a risk management plan will be formulated by team clinicians that might include, but would not be limited to, facilitating access to appropriate acute mental health services. In addition, NGC clinicians will be updated of any significant change to participants' risk.

Second point of contact

We will ask you to share a second point of contact during the study where possible. This could be a friend, family member or sponsor. If we cannot get in touch with you during the follow up period, we may contact them to ask for updated contact details. We ask that you tell the contact about the study and explain that you have given their contact details to the study team for this purpose. We will not share any information about your participation with this individual.

Will I be paid for taking part in the study?

You will be compensated for your time completing study visits with payments made within 3 months of you finishing the study. The details of payments for each visit are provided in section 2. All travel will be reimbursed.

Study Summary Information Sheet Data Protection

Research Study Title:	Psilogambling: Multimodal brain and physiological biomarkers of action of 5-HT2a receptor in Gambling Disorder
IRAS ID:	356419

In this research study we will use information from you, your medical records, your usual treating team at the NGC and your GP. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. These will include Imperial research team members and support staff.

Everyone in the study team will keep the data collated as part of this study, including your personal data, safe and secure. We will also follow all privacy laws and legislation that are relevant to the specifics of the study.

At the end of the study, we will save some of the data in case we need to check it and/or for future research.

We will make sure no-one can work out who you are from the reports we write.
The information pack tells you more about this.

Further questions
If you have any further questions or would like more information about the study, please contact the study team using the following details

Email: r.zafar19@imperial.ac.uk or frederick.page@imperial.ac.uk
Telephone: +447565542074 or +447807779024

Thank you for considering taking part in this study.

Part 1: Detailed information on the conduct of the study

What is the purpose of the study?

The purpose of this study is to observe changes in brain activity as measured using fMRI and EEG under the drug psilocybin in a group of people with Gambling disorder. We will also be looking how these brain changes in activity relate to reward processing, cognitive function and behaviour as measured using questionnaires. All participants within this study will receive this drug. The findings of the study will contribute to neuroscience and may help inform future research into psychedelics and addiction disorders.

What drug is being used in the study?

We are investigating the compound psilocybin. It is 5HT2a agonist, a psychedelic substance and the main active ingredient in “magic mushrooms”. Recent studies have shown that psilocybin may interact with the brain’s mesocorticolimbic reward system, which is linked to several important functions in our body, including addiction-related processes.

The team at Imperial College is one of the most experienced groups in the world at delivering psilocybin brain imaging studies and has used this compound in previous and ongoing studies in participants with multiple conditions and healthy volunteers.

What are the effects of psilocybin?

Most people find the effects of psilocybin quite pleasant; others can get anxious or have difficult experiences, so we will prepare you for this. Psilocybin can have many different effects, which can be different for each person. Some of the common effects include:

-a feeling of euphoria, energy or excitement.
-changes to how things look - for example sizes or shapes of things can change.
-some people may see shapes and colours, or the room may appear to get bigger or brighter.

The effects of psilocybin can last about 6 hours. You will be encouraged to close your eyes during the experience. Some people report that they see shapes or colours, and sometimes liken it to dreaming. Such dream-like experiences can sometimes feel more real than a normal dream. Time may appear to pass slower than usual, and as a result some people find it may be hard to judge how much time has passed. People sometimes report a difference in perception, feel their emotions are magnified or changes to how they think.

It is not uncommon for people to have visions of their pasts; for example, they might feel as if they are remembering or even reliving events from their childhood. However, these could equally be more ‘symbolic’ in nature, similar to dreaming rather than recollections of true events that happened in the past. Sometimes it’s difficult to know either way. The study guides will support you if this were to happen.

Some people may have difficulty putting their experience into words (ineffable). Whatever experience you have, you will be invited and supported by the study guides to approach it with a mindset of curiosity and openness.

Will I be able to take psilocybin again after the study has ended?

No. Psilocybin is a Schedule 1 Controlled Drug in the UK. This means that it cannot be prescribed outside the study.

Will I be paid for taking part in the study?

The cost of travel expenses will be covered. You will be paid for completing key visits by voucher. You will receive the voucher within 3 months of completing your final visit. If you take part in all study visits, complete all MRI and EEG scans you would be eligible for a payment of up to £612.50. If you choose to withdraw, or are found to no longer be eligible to continue in the study, you will receive the equivalent payments as shown in figure 2 corresponding to the visits you completed. Please be aware, if you choose to not opt into wearing the fitness tracker for this study, this will not affect the payments you receive.

What will be expected of me if I take part in the study?

- Turn up for all visits on time.
- Plan the dates and times of your visits in advance.
- Do not use alcohol within 24 hours of each study visit.
- Do not drive after the dosing visit for the rest of the day.
- Do not operate machinery 24 hours post the dosing session.
- Inform the study coordinator if any events happen that may affect your participation in the study. These will be assigned to you at the start of your onboarding and will be either; Dr Rayyan Zafar, Freddie Page, Patrick Kleine and Sofia Venturini. Their contact details will be provided to you at screening.
- Complete questionnaires when asked to do so.
- Complete four brain (MRI) scans, including tasks, lasting up to 75 minutes each.
- Complete four EEG scans, 3 lasting up to 90 minutes each and one whilst under psilocybin
- Use an adequate form of contraception from enrolment and for 28 days after receiving psilocybin.

You are able to exercise as normal, continue your usual diet, donate blood if you wish to but there are considerations regarding medication, alcohol, other substances and contraception/pregnancy – please see below.

What sort of people are we looking for?

We are looking for people over the age of 18, who have a diagnosis of moderate to severe Gambling disorder as per the DSM-5 criteria and who are seeking treatment from the National Gambling Clinic.

You will need to undergo a screening with a study medic (doctor) to see if you can take part. We will also need to contact your GP, mental health team or keyworker to tell them you are taking part in the study. We may also need to ask them to provide information about your medical history.

What if I am on other medication?

There are some medications that you cannot take whilst you are taking part in the study. This is because they affect how the study drug works, which may not be safe. The study medic will talk to you about your medications as part of the screening process.

For example, regular use of the following medications would mean you could not take part in the study:

-Some antidepressants (e.g. mirtazapine, trazadone)
-Some painkillers (e.g. tramadol, tapentadol)
-Some mood stabilisers or antiepileptics (e.g. lithium, carbamazepine)
-Monoamine oxidase inhibitors (e.g. selegiline, moclobemide or phenelzine)
-Some antipsychotics (e.g. risperidone, olanzapine, quetiapine)
-Alcohol dehydrogenase inhibitors, aldehyde dehydrogenase inhibitors and UDG modulators eg. Fomepizole

Please note this is **not** a complete list – please contact the study team if you have any questions or would like to discuss your medication with them.

Alcohol and other drug use

It is recommended that in early recovery you do not use any mind-altering substances including alcohol or other drugs.

We will ask you to tell us how much alcohol and/or illicit substances you consume each week. It is important that you are open and honest about this. This is because alcohol and other drugs can affect the results of the study, and we need to make sure that it is safe for you to take part as some drugs may affect the way that psilocybin works.

When enrolled in the study, you will be required to limit alcohol consumption to no more than 14 units of alcohol per week. You should not drink any alcohol 24 hours before each study visit. An alcohol breathalyser test will be done at at screening and at Visit 4 (dosing session).

In addition, you will be asked to abstain from using cannabis and all other recreational drugs (e.g., cocaine, ketamine, ecstasy/MDMA, other psychedelics) for the period you are involved in the study, from screening to your final visit. To ensure your safety, the study team will perform a urine drug screen at Visit 1 (screening visit) Visit 3 (preparation session) and Visit 4 (dosing session) to check for any drugs in your body. If you have a positive urine drug screen, then we will share the results with you, and discuss if you are able to take part in the study. We may have to exclude you from that study visit.

Contraception

Due to possible risks to an unborn child during pregnancy, all people of childbearing potential must agree to use adequate contraception from the point of enrolment until 28 days after the day you receive psilocybin. For participants assigned female at birth, this includes hormonal contraceptives (such as the combined pill, patch, or implant), intrauterine devices (IUDs), permanent contraceptive procedures and sexual abstinence. For participants assigned male at birth, this includes condoms or sexual abstinence. You will need to discuss and confirm your chosen method of contraception with the study team before you can take part in the study. If contraception fails, additional precautions may need to be taken.

Pregnancy

If you are pregnant at the time of pre-screening or screening, for safety reasons you will not be able to participate in the study. Participation requires that women of child-bearing age undergo a pregnancy test at the screening visit and the dosing visit, as well as before all MRI scans.

If you are enrolled in the study and become pregnant during the study, or if you have a partner who became pregnant during this time, this must be reported to the study team. Any pregnancy that occurs prior to dosing will result in withdrawal from the study.

In the event of pregnancy during the study, a study medic will ask for consent from the pregnant individual to follow the pregnancy until the end of the pregnancy (including premature termination) to determine the outcome and status of the mother and child. This is because the study medics would need to assess for any adverse outcomes of the pregnancy that could be related to the study drug.

If you were to become pregnant during the study, you would be advised to seek pregnancy care through usual routes in primary care.

Menstruation

There is increasing awareness and evidence that hormonal fluctuations related to the menstrual cycle affect psychedelic experiences. If you are someone who has periods, we will therefore ask you at screening and dosing to let us know the start date and length of your last period, and if you are experiencing any symptoms related to your period (such as premenstrual syndrome, or PMS).

Gut Microbiome Sampling

As part of this study, we are also investigating how psilocybin may affect the gut microbiome – the diverse community of microorganisms (including bacteria, viruses, and fungi) that live in your digestive system. We will ask you to collect two stool samples at three points during the study and complete a short online diet questionnaire after each one. You will receive home collection kits with detailed instructions. Each kit contains two collection devices, and you will be asked to collect two stool samples (one for each device) from a single bowel movement. Each collection device has a stabilising solution that preserves the sample at room temperature, so you do not need to refrigerate

or freeze them. Each kit will also include a prepaid Royal Mail return package with which you will post samples from any Royal Mail post office.

The samples will be sent via post to the University of Exeter for storage and analysis sent back to Imperial College London for further analysis and destroyed within one year of the study ending, unless the participant has consented to long-term storage of samples whereby they will be stored under a Human Tissue Bank. Data acquired from analysis of these samples will be stored up for a minimum of 10 years after completion of the study.

Where will the study take place?

All in-person study visits will take place at the National Institute for Health Research/Welcome Trust Clinical Research Facility (ICRF) at the Hammersmith Hospital on Du Cane Road, West London.

All imaging visits will be conducted by Perceptive Imaging Inc, located next to the Hammersmith Hospital site. On these days, some study activities may be conducted at the ICRF also. A map has been included at the bottom of this document, on the last page.

What are the disadvantages of taking part in the study?

Taking part in this study could have some disadvantages, including:

-Multiple visits to the study centre.
-Large number of questionnaires to complete, which may be burdensome at times.
-Short term anxiety around taking the psilocybin (the study drug).
-Revisiting challenging or upsetting themes or experiences during the study.
-Potential triggering questions, images/videos related to gambling.

The clinical interview will focus on your upbringing, family life and experience of life as well as your gambling history and recovery plans. This may bring up sensitive issues – but they are relevant to any study of Gambling disorder. We will be able to provide support and guidance, which will help reduce any worries you may experience.

As part of the study, you will take part in four brain scans (fMRI). These scans are safe, non-invasive, and commonly used in research. Each scan lasts around 75 minutes and involves lying still in the scanner while your brain activity is measured during a series of simple tasks. A trained researcher will accompany and support you throughout.

The purpose of these scans is to help us understand how psilocybin may affect brain processes related to gambling addiction and recovery.

One of the tasks involves viewing short video clips designed to explore how the brain responds to emotional and motivational cues. These include everyday scenes such as household chores,

playing music, social interactions, and nature. Some clips will also contain gambling-related content, such as people using roulette wheels.

It is important that we complete this task because it will help us understand how taking psilocybin affects how people respond to seeing images which might be triggering or remind them of gambling. The study team discussed the plans of using such cues in the scanner with a group of people who had previously been enrolled for treatment at the National Gambling Clinic and there were no cue-reactivity related adverse responses recorded by participants.

Because some of the content may bring up difficult emotions or cravings, you will be supported with preparation beforehand and appropriate psychological care afterwards. Your wellbeing is central to the study, and we are committed to ensuring you feel safe and cared for throughout. You will be given the telephone number for the study medical team, who you can call if you are feeling cravings in the day after the cue reactivity tasks. You will also have access to support after and can contact the study medics at any point during the study, as well as your usual team at the National Gambling Clinic and any other community support you normally have.

If you currently have private medical insurance, please check with your provider before agreeing to take part in the study, to confirm that it does not affect your current medical insurance. We do not expect to uncover any medical condition you may be unaware of, but if we do, you will be informed immediately, and the next steps will be discussed with you. Any unexpected findings could increase future insurance premiums or make it more difficult to obtain insurance.

What are the advantages of taking part in the study?

Taking part in this study has some advantages, including:

-Opportunity to take part in the world's first investigation of psilocybin in Gambling disorder.
-You will help advance our understanding of how psychedelic drugs work in the brain.
-You will receive treatment as usual from the NGC as part of this that may be helpful for you.

We cannot promise that the study will help your gambling, but the information that we get may inform future research into psychedelics and addiction disorders.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the drug that is being studied. If this happens, the study medic will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, the study medic will make arrangements for your care to continue. If you decide to continue in the study, you will be asked to sign an updated consent form.

Also, on receiving new information, the study medical team might consider it to be in your best interests to withdraw you from the study. They will explain the reasons and arrange for your care to continue.

What will the study involve?

If you take part in the study, you will have **8 visits** in total. These visits will be a combination of in person (at the clinic) and remote (either via phone or video call).

As part of these visits, you will have four MRI brain scans, four EEG brain scans and undertake multiple questionnaires, behavioural and psychological assessments.

> *"I'd love to see my brain scan. I really would because it kind of gives tangible evidence that it's not just you that your willpower is just not failing. It's evidence that actually you've got something wrong in your brain"*
>
> **Person with gambling disorder for 10 years**

Pre-screening – what will it involve?

If you are interested in participating, an approximately 60 minute pre-screening appointment with a member of the study team will take place via telephone or online video call (Microsoft teams) at a mutually convenient time. This will explore your interest in taking part in the study. It will also check you are eligible to take part. You will be asked some questions about your health, gambling and substance use and to see if it is safe for you to take part, and to have MRI and EEG (brain) scans.

The study team will ask for your consent to request a copy of your summary care record (SCR) or medical records from your GP.

Visit 1: Screening visit – What will it involve?

This visit will take place at the Imperial Clinical Research Facility (ICRF), Imperial College Healthcare Trust (ICHT) at Hammersmith Hospital (please refer to the map at the end of this document). The visit should take no longer than 5 hours. You will meet with members of the research team for the first time face to face. We will discuss the study with you to ensure you understanding. This is a good time to ask questions about the study. If you would like to proceed, and the study team are in agreement, you will be asked to sign a consent form.

You are free to withdraw consent and discontinue the study at any point post-signature. We will provide you with a copy of the signed consent form. To initiate this procedure, please inform any of the study team members you have been in contact with. They will contact you to discuss the steps for withdrawing from the study and will notify the clinical team at the National Gambling Clinic. This will not affect your care in any way now or in the future.

Optional: If you are wishing to participate in the optional procedure of wearing an Oura ring for the study, we will provide you with privacy wording from the company related to data management and storage prior to consenting to this optional clause in the consent form. Imperial College will not be the data controller for the data collected by Oura. Oura's privacy policy will apply for the data collected as part of this optional component. In order for us to use this data as part of the study, you will have to give Oura your consent to share that data with us.

We usually start with the most important assessments first to ensure your eligibility and do not waste your time. We know that this can be disappointing for people. However, it is important that you do not withhold information as this may put yourself at risk of harm. We will inform you of ineligibility to participate in a considerate way.

At the screening visit, a study medic will review your medical record, to confirm that there is nothing which would rule you out of taking part in the study. They will also perform a physical examination including height, weight and vital signs and routine physical examination tests. This will include an ECG (electrocardiogram, a measure of the heart's electrical activity), a menstrual cycle check (if relevant), a urine drug screen and a pregnancy test. We will also check your blood pressure and heart rate (as well as oxygen saturation if necessary, and a urine drug screen, alcohol breathalyser and pregnancy test if applicable. They will take a routine blood test to check liver and kidney function, and electrolyte levels (as well as other things concerning your general health). The blood sample will be labelled with your name as this is necessary for processing and testing at Imperial College Healthcare NHS Trust (ICHT). It will be analysed immediately upon collection within the ICHT lab and destroyed upon completion of analysis. Members of the study team will check the blood results to add them to your study file, but any directly identifiable information to you will be removed. These results will be added to your NHS medical records as per routine procedure. If the results of your blood tests or your ECG are not normal, you may not be able to take part in the study.

DSM-5 Gambling Disorder will be confirmed by a qualified member of the research team and questionnaires will be used for assessment of psychiatric and gambling history and other relevant demographic details will be collected.

We will administer a variety of questionnaires at this visit. For example, these questionnaires will assess current levels of depression anxiety, stress and wellbeing or your safety to undergo an MRI scan. If you feel particularly triggered by any of the content of these questionnaires or tired, please ensure you inform the study team. We can take regular breaks if necessary or follow-up triggering questionnaire content with an appropriate healthcare team.

Two computer-based tasks will be completed at this visit. These tasks will take approximately 25 minutes to complete. These tasks will explore decision making and how your mood interacts with your interpretation of facial recognition.

You're allowed to bring personal devices (e.g. mobile phone) with you to all visits. However, we ask participants to refrain from using their mobile phones during the dosing session.

If I am considered eligible for the study, what happens next?

Visit 2: Preparatory Session & Baseline Assessments – *in-person*

This visit will take place at both the Imperial Clinical Research Facility (ICRF), Imperial College Healthcare Trust (ICHT) at Hammersmith Hospital, and at Perceptive Inc Imaging Centre in Burlington Danes Building, Hammersmith Hospital (please refer to the map at the end of this document). The visit will take around 7-8 hours and will take place around 9 days before dosing visit (Visit 4), and within 1 month of the screening visit (Visit 2). This will give you the chance to meet the study team again. We will show you where you will have your dosing session and explain more about it. You will get to spend more time with the two guides who will be with you during your dosing session who will prepare you for the dosing. The guides will discuss means of supporting you during the dosing, including the possibility of supportive touch, such as a hand hold, if that is something you potentially wish to request from them if the experience becomes challenging. They will discuss in detail what this could be like and set boundaries with you up to your discretion.

This will take about **2 hours** with breaks. You will have an MRI and EEG brain scan. The scanning procedures will take approximately 2 hours, including getting ready for the scan, familiarisation with the process and getting into the scanner and will take place in the morning. The actual MRI scan itself will take about 75 minutes and 40-70 minutes for the EEG, depending on the day. You will be asked to complete a series of tasks during the scans. We will assess the time between each of your heartbeats (HRV), electrical signals of the contraction of your stomach muscles (EGG), and vital signs (HR, BP, SpO2). We will also ask you to complete further questionnaires and conduct a structured interview.

At this visit, you will have a blood test to take two blood samples (max 16mls) testing for measurement of markers in the blood that are of relevance to the research (including sBDNF levels and other immune and genetic markers). These blood samples will be initially stored in the Commonwealth Building at Hammersmith Hospital and then sent to two accredited laboratories for analysis. These samples will be labelled with your participant ID.
We will keep any remaining samples up to one year post the study closure. However, if you consent to on the consent form, we will retain your samples for an extended period of time that may help to contribute to future and further research. This is optional, and if you do not wish for your samples to

retain post 1 year of the study ended, let the study team know and select no to this optional consent clause.
You will also have a pregnancy test if applicable.

All brain imaging sessions will happen in the morning and the preparatory sessions will happen in the afternoon.

Optional: You will be given a fitness tracker ring, if you agree to wear it, for measurement of heart rate variability, body temperature and sleep quality data (please see page 19 for more information on this). Additionally, you will receive your first home collection kit. Using this kit at home, you will be asked to collect two stool samples from a single bowel movement a maximum of three days before your psilocybin session. Following collection, you will post your samples using the prepaid Royal Mail package provided and complete an online diet questionnaire, where you will be asked to recall your dietary intake within 24 hours of stool sample collection.

You can continue to contact the emergency phone contract details of the on-site study medic, as this visit falls within the 48 hours after the dosing visit if you have any urgent concerns.

Visit 3: Preparatory Session – *in-person*

This visit will take up to 4 hours and will take place in person one day before dosing (where you are given psilocybin). It will take place at both the ICRF and Perceptive Inc Imaging Centre at Hammersmith Hospital. This will be with one or more members of the study team who will be with you during your dosing session, giving you the opportunity to get to know your guides better and to prepare for the dosing. Please ask any questions or tell us if you are worried about anything. The guides will discuss means of supporting you during the dosing, including the possibility of supportive touch, such as a hand hold, as discussed previously.

You will also have a second MRI scan at this visit that will reflect the same tasks as you did in the first scan. This will take about 75 minutes. There will also be further questionnaires to complete.

At this visit, you will have a urine drug screen; if the test comes back positive for drugs of abuse, the reason for this will be explored and the session rescheduled if needed. You will also have a pregnancy test if applicable. We will also check your blood pressure and heart rate (as well as oxygen saturation if necessary).

You can continue to contact the emergency phone contract details of the on-site study medic, as this visit falls within the 48 hours after the dosing visit if you have any urgent concerns.

All brain imaging sessions will happen in the morning and the preparatory sessions will happen in the afternoon.

Visit 4: Dosing Session – *in-person*

This visit will last between 8 – 9 hours. We will ask you to arrive at the ICRF at Hammersmith Hospital in the morning. On dosing day, you will be asked to provide a urine sample for a urine drug screen and to take an alcohol breathalyser test to make sure that it is safe for you to take psilocybin in the study. We will also check your blood pressure and heart rate (as well as oxygen saturation if necessary). We will also ask if there has been any recent adversity (medical, psychological or social) prior to the dosing. Women of child-bearing potential will be required to complete a pregnancy test and asked questions related to the timing and duration of their last period.

Members of the study team, which include the researchers, study medic and the two study guides will spend some time talking to you to prepare you for having a dose of psilocybin. The guides will talk more to you about how best to manage the effects of the drug and relaxation techniques, as well as how they will support you during the dosing.

We will help prepare you for the experience by asking you to lie down. We will dim the lights and play relaxing music. We will use guided imagery to help you to relax. Once you are relaxed, we will provide you with an eye mask and we will give you the dose of psilocybin to take.

After you have taken the psilocybin, it will only be the guides present with you in the room, who will sit either side of you or nearby. The other researchers and study medic will always be in a nearby room to help if needed. We will not speak to you for a bit, and we would encourage you not to speak to us. But if you do want to speak to us, then that is fine too. We will “check-in” with you regularly. In other words, we will ask you how you are feeling regularly.

The effects of psilocybin usually start about 45 minutes after you have taken it. It typically is most intense in the first 2-3 hours. The experience can last about 5-6 hours, and your guides will be present throughout to support you. You can eat a light lunch and fruit if you would like. About 5 hours later, we will talk to you about your experience. We will ask you to do some more questionnaires to rate your experience.

Sometimes people can find difficult feelings come up during the dosing session. In other studies, we have done, we have found that going through difficulty can help you overall. For example, if a memory of a bad experience comes up during the session, the person can feel less bothered by it and more “at peace” with the experience. Sometimes, on rare occasions people can feel very anxious. If this happens, you can talk to the study guides to help you with relaxation techniques to reduce the anxiety. If this doesn’t help, or the study medic is concerned for your safety, a single dose of a fast-acting anti-anxiety medication (called a benzodiazepine) can be prescribed by the

medic and administered, which will help alleviate any anxiety or emotional distress. It is very rare for a medication to be used – relaxation techniques are usually sufficient.

Psilocybin is a safe drug for your body. So even if you feel strange, your body won't be in danger. We will have gone through your medical and psychiatric history to make sure it is safe for you. Several hundred people have had similar doses of psilocybin in studies over the last 10 years.

The study team will be with you for the entire duration of your experience. As the day draws to a close, you will be assessed by the medic to make sure you are ready to leave the centre. Before you leave, you will be asked to complete some questionnaires about your experience. Details of menstrual cycle will also be taken for women of child-bearing potential. We ask that you remain for the duration of the day in the research facility, until around 4:30-5:30 pm, when the medic will check you are comfortable and safe to leave. For safety reasons you should not drive for the rest of the day or operate machinery, and should leave the centre with a trusted contact, such as a relative or friend. If this is not possible, a taxi will be ordered and a trusted contact should meet you at home. We ask that you make contact with us once you return home. You will be provided with details of who to contact in the study team in case of any emergencies. During dosing you will also receive an EEG scan that will passively measure your brain activity at various timepoints throughout the experience, and passive monitoring of HRV.

You will be given your second home collection kit after the acute effects of psilocybin have worn off. You will be asked to collect two stool samples from your first bowel movement after the dosing session. As before, you will post the samples and complete the 24-hour dietary recall questionnaire.

After the dosing, you will also have a blood test to take two blood samples (max 16mls) for measurement of the same markers as the samples taken during the Visit 2. This samples will be stored and sent for analysis as per Visit 2.

You will be provided with emergency phone contact details of the on-call study medic, which can be contacted anytime until 48 hours after the dosing visit if you have any urgent concerns.

Visit 5: Integration Session 1 – (Day +1) – *in-person*

The day after your dosing session, you will come back to the ICRF at Hammersmith Hospital. This visit will take about 4 hours in total, and there will be opportunities for breaks, as well as refreshments (drinks and snacks). We will ask you to complete follow up questionnaires and take part in an interview and integration session with your study guides. We will ask about your interpretation of your experiences from the previous day, how you slept and how you feel now. This session will help you to understand how best to make use of the session.

You can continue to contact the emergency phone contract details of the on-site study medic, as this visit falls within the 48 hours after the dosing visit if you have any urgent concerns.

Visit 6: Integration Session 2 – (Day +7) – *in-person*

This visit is very similar to visit 5 (integration 1) and happens 7 days after your dosing session, in the ICRF and Perceptive Inc Imaging Centre at Hammersmith Hospital. It will last approximately 7-8 hours. you will have another MRI brain scan which will be the same as the one you had at your first and second visit as well as an EEG scan similar to your first visit. This scan itself will take about 75 minutes for the MRI and 60 minutes for the EEG. We will also record HRV, EGG, and vital signs (HR, BP, SpO2), administer a pregnancy test (if applicable) and review of your drug, alcohol and gambling history since this measure was last taken. You will take also part in an interview and integration session with your study guides and we will ask you to complete some questionnaires and the two computer-based tasks completed in visit 2 in the afternoon.

At this visit, you will also have a blood test to take two blood samples (max 16mls) for measurement of the same markers as the samples taken during the Visit 2. This samples will be stored and sent for analysis as per Visit 2.

You can continue to contact the emergency phone contract details of the on-site study medic, as this visit falls within the 48 hours after the dosing visit if you have any urgent concerns.

Visit 7: Integration 3 – 1 month (Day +28) – *in-person*

This session will last 3 hours at the ICRF, Hammersmith Hospital. First, there will be an integration session, lasting up to 1 hour. This will then be followed by 2 hours for questionnaires and review your drug, alcohol and gambling history from your last visit. You will be asked to return the wearable device.

Visit 8: Integration 4 & 3 Month Follow Up – *in-person*

Your final visit will be an in-person visit at 3 months at the ICRF and Perceptive Inc Imaging Centre at Hammersmith Hospital and will take 7-8 hours. During this visit, you will meet with your study guides to take part in an interview and integration session, complete some questionnaires and review your drug, alcohol and gambling history since your last visit, integration will happen in the afternoon and the brain imaging visits in the morning. A pregnancy test will be administered if applicable. We will also conduct the final MRI scan and a shorter 50 minute EEG scan on this visit which will be similar to the ones done in visit 2, 3 and 6. We will also record HRV, EGG, and vital signs (HR, BP, SpO2). You will also be required to complete the two computer-based tasks as in visit 2 and visit 6.

You will receive your final stool collection kit at this visit, and follow the same collection process as before. You will also have a blood test to take two blood samples (max 16mls) for measurement of the same markers as the samples taken during the Visit 2. This samples will be stored and sent for analysis as per Visit 2.

If at any point during or after the study you feel like your wellbeing has worsened, you can get in touch with us to talk about this. You will be able to contact the study guides at any time outside of the arranged follow up appointments. If you do not feel well enough to contact us yourself, then you could ask a friend or family member to get in touch with us instead.

You can continue to contact the emergency phone contract details of the on-site study medic, as this visit falls within the 48 hours after the dosing visit if you have any urgent concerns.

Wearable Device

You will be optionally asked to wear a wearable fitness tracking device, an Oura ring, from Visit 2 (preparatory session and baseline) to Visit 7 (1 month follow-up), when it will be returned to the study team. This is an optional component of the study, which you do not have to consent to, and there will be no extra payment for choosing to take part. If you decide to opt out at any point following consent you are allowed to do this for this component of the study and we will help you to delete your account as indicated. If you agree to wear this, this wearable device will collect information such as temperature, heart rate, blood oxygen saturation and sleep duration. Data is recorded directly onto the device and transmitted to a paired smartphone via encrypted Bluetooth connection. You will wear the ring on the finger of the finger of your non-dominant hand continuously, including overnight with exceptions only for activities in which wearing it poses a safety risk (e.g. contact sports, heavy lifting, operating machinery) or may damage the ring (e.g. prolonged water exposure).

Wearing the device poses extremely low risks. For the purpose of this study, it is important to outline these to all participants. You may experience minor skin irritation, pressure, discomfort or an allergic reaction whilst wearing the ring. An extremely rare risk is swelling or constriction if worn when changes of finger size (for example in heat). The team will conduct a fitting with you to minimise these rare risks to ensure you are safe to proceed with this procedure. Some participants may also begin to over monitor their health, misinterpret, or experience sleep anxiety. If you begin to experience this, let the study research team know. If these experiences become overwhelming, it is important to remember you can stop this optional procedure of the study at any point without it affecting your participation in the rest of the study.

You will receive detailed verbal and written guidance on appropriate wear, upkeep and when to temporarily remove the device, as well as SMS reminders every 5 days prompting you to charge and sync it with the Oura app on your smartphone to promote adherence. You will also receive guidance about installing and removing the app on your smartphone.

Physiological data collected using Oura rings (e.g., HRV, sleep parameters) will be passively recorded in a continuous manner throughout the dosing period. Per Oura's privacy policy (https://cloud.ouraring.com/legal/teams/privacy-policy), participant data will be stored on the Oura Cloud via the Oura mobile app that each participant will be invited to download onto their phone. The Oura Cloud uses encryption, pseudonymization and access right systems to ensure the privacy of participant data. The study team will access the Oura Cloud to download the data to the Centre for Psychedelic Research, Imperial College London. Once data collection is complete, the study team can assist you in making a request to delete your data from Oura Cloud.

It is important to note, this optional study procedure is not diagnostic tool and not used for medical decision-making. If you have any questions or concerns related to this optional study procedure, at any point, please contact the study team.

All devices must be returned to the study team members upon visit 7 of the study.

What happens when the research study stops?

At the end of the study, we will provide information of groups for people who have also taken place in psychedelic studies, which you may be interested in joining. This is optional.

After the end of the study, a summary of findings from the study will be prepared and published usually within 1 year. This will include no personally identifiable information. We will also ask you whether you would like the findings shared with you directly.

Video and audio recording

For the safeguarding of yourself and the research team, and for research purposes, we will have audio recording of the preparation, dosing and integration sessions as part of this study. For added detail, we can also use video recording; however, some people might find this too invasive, so this is optional. A record of you talking about your expectations, response to the study drug and surrounding experience in the study may be useful in understanding how your experience progressed and whether anything you do or say can be used to explain your psilocybin administration. There might also be opportunities to take part in filming for future public awareness documentaries on the study.

Any audio recorded material will be transcribed by a member of the study team for research purposes. It will be securely stored on a storage drive only accessible to members of the study team. If we wished to present a recording of you in a scientific presentation or for public engagement, for example, we would ask your permission for this and you would have the right to refuse this. If we were to use a quote from you in a scientific presentation or publication, this would be anonymised

and we would seek your consent. The recorded material will be stored for 10 years but can be destroyed (via deletion of digital files) at any time upon your request.

What happens if something goes wrong?

There are doctors at the research clinic at all times who will provide emergency medical cover if required. You will be provided with details of who to contact in case of any problems or a medical emergency once you've left the clinic. You will be provided with a participant ID card that will contain the 24-hour contact number should you feel the need to use this. You will have access to this:

- 24 hours after all MRI imaging visits
- 48 hours after the dosing session

If, for any reason, you are unable to get hold of the team during this time, please seek medical advise called 111/999.

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 Investigator (Insert name and contact details). The normal National Health Service 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.

All neuroimaging and clinical assessments will be reviewed by appropriately qualified clinicians (e.g., a consultant neuroradiologist for MRI data). Any incidental findings of potential clinical significance will be documented and referred for further review by the study's medical lead. If the finding is confirmed to warrant clinical follow-up, you will be informed as soon as possible by a qualified clinician, who will explain the nature of the finding and discuss next steps. With your consent, a written report will be forwarded to your GP and/or relevant clinical care team to ensure appropriate follow-up. Findings judged to be clearly non-clinically significant will not be routinely reported.

Who has reviewed the study?

This study has been reviewed and given a favourable opinion by London Bridge REC, a research ethics committee. The study will follow the principles of Good Clinical Practice.

Who is organising and funding the research?

This research will be conducted by the Centre for Psychedelic Research at Imperial College London and National Institute for Health and Care Research (NIHR). The sponsor is Imperial College London

and funding has been received from the Wellcome Trust, a philanthropic donation to the Centre for Psychedelic Research and the UKRI.

What will happen next?

If you choose to take part, we will contact you after you have received and read this information sheet and a time will be arranged for a screening visit. We would also like to contact your GP or mental health practitioners involved in your care to establish your background history and confirm whether you are appropriate to enter the study. If you could provide their details, then we can contact them straight away and delays to your entry in the study will be minimised. We will give you directions to the study centres where screening and scanning sessions will take place. More time can be given if you have not yet had a chance to read through the information sheet.

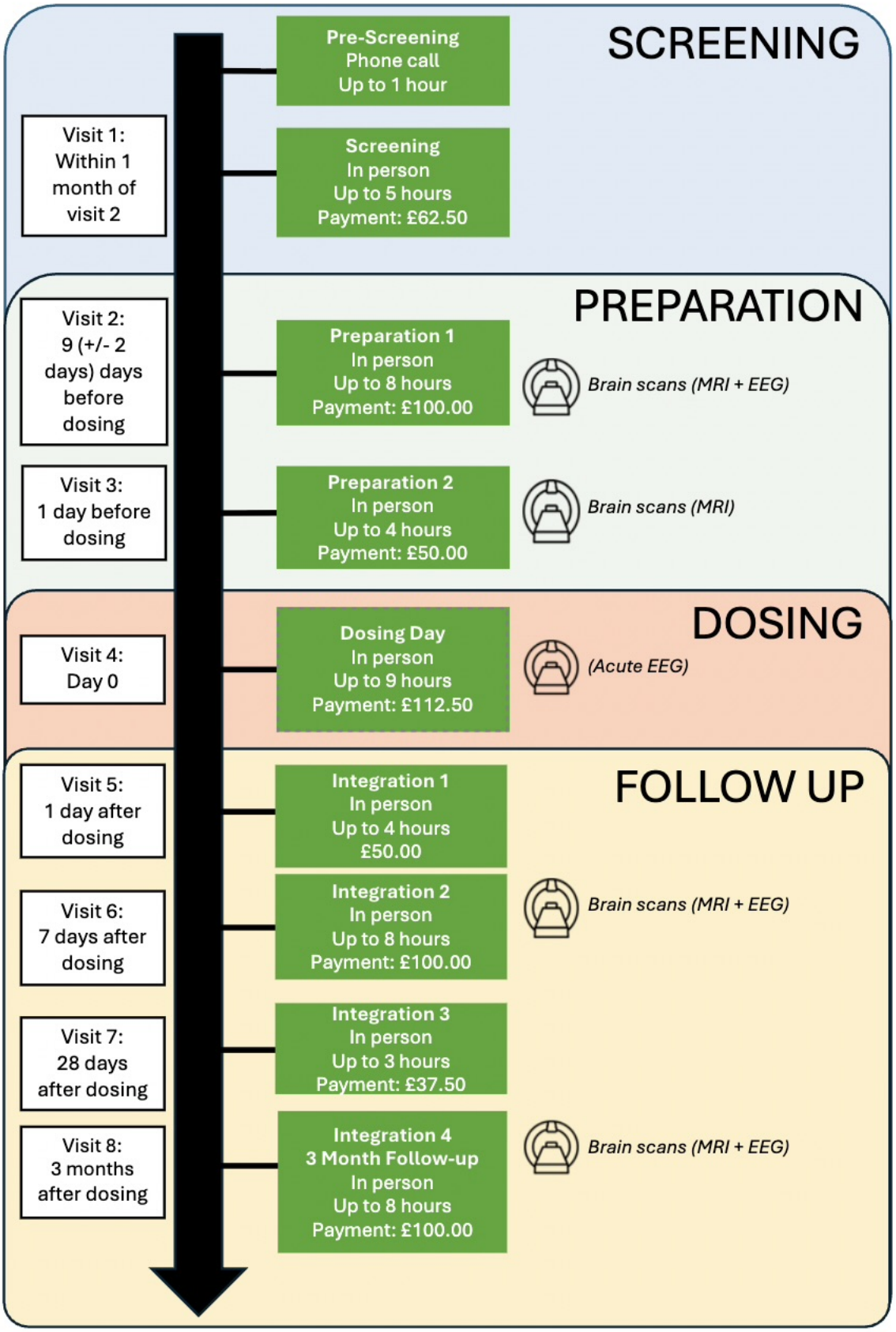
Contact for further information

If you have any further questions or would like more information about the study, please contact the study team using the following details

Email: r.zafar19@imperial.ac.uk
Telephone: ++447565542074

Figure 2. Study overview diagram

The diagram below outlines the study visits, durations and the amount you could be paid if you complete the visit.


SCREENING
Visit 1: Within 1 month of visit 2
Pre-Screening
Phone call
Up to 1 hour
Screening
In person
Up to 5 hours
Payment: £62.50
PREPARATION
Visit 2: 9 (+/- 2 days) days before dosing
Preparation 1
In person
Up to 8 hours
Payment: £100.00
Brain scans (MRI + EEG)
Visit 3: 1 day before dosing
Preparation 2
In person
Up to 4 hours
Payment: £50.00
Brain scans (MRI)
DOSING
Visit 4: Day 0
Dosing Day
In person
Up to 9 hours
Payment: £112.50
(Acute EEG)
FOLLOW UP
Visit 5: 1 day after dosing
Integration 1
In person
Up to 4 hours
£50.00
Visit 6: 7 days after dosing
Integration 2
In person
Up to 8 hours
Payment: £100.00
Brain scans (MRI + EEG)
Visit 7: 28 days after dosing
Integration 3
In person
Up to 3 hours
Payment: £37.50
Visit 8: 3 months after dosing
Integration 4
3 Month Follow-up
In person
Up to 8 hours
Payment: £100.00
Brain scans (MRI + EEG)

Further Information: MRI Scanning

What is an MRI scan?

A scientist in a lab coat places a person's head in an MRI scanner.

An MRI (Magnetic Resonance Imaging) scan is a routine procedure in medical practice and has not been found to be harmful. It involves lying in a "tunnel" and staying still for the duration of the scan. During two of the study visits you will have an MRI brain scan at the imaging facility (approx. 5 minute walk away from the clinic). A researcher will accompany you and stay with you during the scan. The scan will take about 75 mins, and we will ask you to complete some tasks while you are in the scanner. The MRI scanner will take structural pictures of your brain, and images of your brain while you are performing certain tasks.

The MRI scanner uses powerful magnets. This means that it is not safe for everyone. You must not have a scan if you have a heart pacemaker, metal injuries to the eye, implant, shrapnel, a shotgun injury or metallic objects (e.g. pins, clips) inside your body near to your head. You will be asked to change into a hospital scrubs and remove any metal objects from your body such as keys or coins.

The MRI uses radiofrequency waves to do the scan. This can cause your head and body to warm up slightly. Most people do not notice this. We keep the scanner room cool so you will be comfortable and provide blankets for warmth if needed. If you feel uncomfortable during your scan, you can tell us immediately and we will stop the scan. The scanner may damage credit cards and some watches so we will provide you with a secure place to leave valuables. The MRI operator will check possible risks with you before you go into the scanner.

The MRI scanner is noisy. This is normal and the scanner cannot hurt you in any way. You will be provided with ear plugs and headphones to minimise any discomfort. There is a microphone inside the MRI scanner so that you can talk to us at any time. It is common to feel slightly anxious when you are first placed in the MRI scanner, but this normally passes. You will be free to leave the MRI scanner at any time should you wish to stop the scan. You may not be able to take part in this study

if you are claustrophobic (nervous in small spaces). Please make sure you discuss this with the study team before deciding if you would like to take part.

Are there any risks from having an MRI scan?
MRI scans involve minimal risk. There are no serious side effects of being in an MRI scanner - millions of scans are carried out across the world each year. Some people have reported minor side effects. These have included feeling dizzy, feeling claustrophobic or nauseous. These effects disappear after leaving the scanner.

What happens if you find something unusual on my MRI scan?
Sometimes we find unexpected things on your MRI scan. If this happens, we will tell you. After looking at your scan, if the MRI operator or study team thinks that it is appropriate, we can forward your scan to a radiologist (a doctor who specialises in scans) or your GP for further investigation or referral if this is appropriate. Early detection of problems may have the benefit of earlier treatment for any abnormality. In a small number of cases, it can have implications, so it may affect future employment or insurance.

Further Information: Electroencephalography (EEG)

A person wearing a wet EEG cap representing a cap that would be used in the study.

During the study at several time points we will be using a brain imaging tool called EEG. This will involve placing a cap of electrodes on your head to record your brain's electrical activity. We will check if you are comfortable wearing this, and we ask that you inform us immediately if it is not. There are no known risks associated with EEG. The electrodes and the device used to record your brain waves are electrically isolated so there is no possibility of shock, even in the unlikely even of an electrical fault in the equipment. Brain scanning via EEG is a major part of this study, and you must be able to tolerate wearing an EEG headset to participate. You will not be able to have an EEG recording if you have a history of epilepsy or migraines. The headset is designed to be comfortable and are often worn by people when asleep in sleep research. This is often compared to what it feels like to wear a swimming cap or 'beanie' hat.

During the EEG, we will also need to place electrodes on your chest and abdomen to collect cardiac (ECG) and gastric stomach (EGG) signals. To collect a reliable signal, we may need to shave and clean a small (~3x3cm) patch of skin underneath each electrode

Further Information: Psilocybin

There is great variability in the effects people can experience, eg. in our first depression study, 3 out of 20 patients did not experience any subjective effects from a high dose of psilocybin (25mg), and we could not always be sure why this was the case. Some people have reported experiencing psychological insights on psilocybin that provide a useful new perspective on the potential causes of their illness. Research suggests that psilocybin may be effective as an aid to psychotherapy or 'talking' therapies.

Psilocybin may increase how suggestible people are. This can increase both the inherent power difference between guides and participants, and the meaning given to their psychedelic experience. Establishing and nurturing a trusting relationship with your guides is an important part of the process, to create a safe space for you to discuss with them whatever comes up, without fear of judgement. The guides themselves will also be noticing what comes up for them during their process of guiding for you, and they will be exploring it in supervision with other members of the therapy team to consider how best to support you. Your guides will be there to support you in making sense of your experience.

Are there any risks associated with taking psilocybin?
There are risks when putting any drug in your body. However, psilocybin is a relatively safe compound, and it has limited risks when used in human studies. In the 1950s and 1960s, thousands of patients were treated with it. Hundreds of people have taken psilocybin in modern scientific studies – with over 250 people having taken it as part of studies run by our group. This means we have some of the best experience and data to help us to understand the effects and side effects of using psilocybin.

Anxiety that can be associated with psilocybin is normally short lived and helped by support and guidance from the guides. We know that developing a trusting relationship with your guides and research team is important in decreasing the chance of you developing anxiety or paranoia. We will try and make you feel as comfortable and relaxed as possible for your psilocybin experience. If you do feel anxious, we will always be there for you, and you can always talk it through with us.

Psilocybin can in some people result in longer-lasting changes of their 'worldview', or their understanding of reality and their place in it. While this can be positive and meaningful, for some this can be challenging, confusing and possibly frightening. If this were to happen, you would be supported by the guides in working through these difficult feelings or experiences, to make sense of them and potentially learn from them in a positive way that benefits your mental wellbeing.

You should not feel bad if you do feel anxious or afraid. It is better not to fight the anxiety or the bad feelings, rather approaching them with curiosity. We will talk to you about trying to accept it, let it go and allow the feelings to unfold naturally. There is some evidence that "facing up" to your fears and anxieties when you have taken psilocybin can have positive future effects.

In our previous study where we used psilocybin in patients with depression, the main side effects reported by patients who took two doses of psilocybin (10mg and then 25mg of psilocybin one week later) were anxiety surrounding the experience of taking psilocybin itself (over 50% of people) and headaches that lasted up to 1-2 days after the experience (40% of people). 25% of people reported some nausea. Further details on side effects are provided below.

For exceptional cases of severe panic that were unresponsive to psychological intervention, or where the participant's behaviour was putting themselves and/or staff in danger, a 'rescue medication' such as Lorazepam or Midazolam oromucal formulation, will be available. Consent for such medication will be sought from you ahead of study participation, these discussions will be led by the study medics.

You will be signposted to psychedelic clinical study support groups for further queries out of study including the organisation PsyPan, which are a psychedelic participant advisory network. We also have capacity to arrange additional ad-hoc integration sessions with your guides if required.

Summary of the side-effects of psilocybin:

Common (over 50%)

1. Nausea
2. Visual hallucinations, feeling of unreality and changed sense of time
3. Increased short term anxiety after taking the drug, which usually reduces over several hours
4. Increased heart rate and/or blood pressure

Less common (about 10-40%):

1. Dizziness, blurred vision, drowsiness and sleepiness
2. Headache
3. Vomiting
4. A 'bad trip' i.e. negative thoughts and mood during the short-term drug effects. In other psilocybin studies, good preparation, support during the experience and integration helped mitigate negative impacts of this. With support, challenging content can be worked through and contribute to a psychological 'breakthrough' on the part of the patient. Recent evidence indicates that challenging psychological experiences in supportive environments can produce therapeutic benefits, improving psychological well-being in the long-term.
5. Temporary suspiciousness, which is usually short-lived.

Rare:

1. Estimated <1% of psychedelic users overall: Flashbacks or persisting visual changes lasting beyond the acute drug effects, which are considered distressing. It may be more common to experience some visual changes that last after the acute drug effects, such as intensified colours and lingering visual images, but very rarely are these considered distressing, and there are no known cases reported in participants of previous psychedelic clinical trials.
2. Worsening of your mental state after the drug experience. This is rare, but there is growing research as to what can support people to feel better again if there are enduring difficulties after a psychedelic experience. If you would like to know more about the published scientific literature on psilocybin, then please ask a member of the research team.

End of the Research and Results of the Study

You will be informed of the study results following the end of study period once data has been analysed and published. Participants will be sent a plain language summary and the scientific paper within a week of publication and the study team will organise appropriate public facing communications to disseminate the research of which the participants will be informed. After the end of the study, a summary of findings from the study will be prepared and published usually within 1 year. This will include no personally identifiable information. We will also ask you whether you would like the findings shared with you directly.

Part 2: Data Protection

HOW WILL WE USE INFORMATION ABOUT YOU?

Research Study Title:	Psilogambling: Multimodal brain and physiological biomarkers of action of 5-HT2a receptor in Gambling Disorder
IRAS ID:	356419

Imperial College London is the sponsor for this study and will act as the Data Controller for this study. Being a Data Controller means that we are responsible for looking after your information and using it appropriately plus are responsible for explaining this to you. Imperial College London will keep your personal data for:

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

The study data will then be fully anonymised and securely archived or destroyed.

The study is expected to finish in July / 2027

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 and from your medical records, your usual treating team at the National Gambling Clinic and your GP for this research project.
This information will include your:

- Name
- Initials
- Date of birth
- NHS number
- Contact details
- Video and voice recordings of participant study visits
- Physical (including genetic and immunity data and psychological information

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.
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.
Imperial College London is the sponsor of this research, and is responsible for looking after your information. We will keep all information about you safe and secure by:

- Data management plans have been created and reviewed in line with Imperial's Information Governance Policy Framework. This covers the collection, movement, processing and storage of the data.
- Data to be stored in a dedicated secure environment which underpins security measures.
- Robust pseudonymisation has been implemented to prevent identification
- Access controls have been implemented to ensure only key personnel can access the data.

Some of your information will be sent to other research partners in the UK, Europe and the United States of America. They must follow our rules about keeping your information safe.
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 i.e. finger prints or facial recognition and genetic data, racial and ethnic data etc.), Imperial College London rely on "scientific or historical research purposes or statistical purposes

INTERNATIONAL TRANSFERS

We may share data about you outside the UK for research related purposes to:

- To provide access to a data processor / service provider who will utilise your personal data as instructed by us.
- To share with a third party organisation / collaborator who are also involved in the study.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain

circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- University of Oslo, Norway
- The University of Colombia, New York (USA)
- Ambra Health (USA)
- Optional consent: Oura Health LTD

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following

- (some of) the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- we use specific contracts which stipulates that personal data must maintain the same level of protection when outside the UK as it has within the UK. For further details visit the Information Commissioner's Office (ICO) website - www.ico.org.uk
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- we have procedures in place to deal with any suspected personal data breach. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website - Personal data breaches: a guide | ICO

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.

- the following Research Collaborators / Partners in the study
  - The University of Oslo and the University of Colombia – as part of this study, we will take blood samples for immunity and genetic analysis. These samples will potentially enable the study team to understand addiction further. The University of Oslo is based in Norway and The University of Colombia is in New York. Both Universities will contractually have to abide by the Data Protection laws in the UK. Your data will be coded by the unique participant identification number. Any blood samples remaining within Imperial College London will be registered with a Human Tissue Authority licensed establishment in accordance with the UK Health Research Authority regulations for long term storage.
  - The University of Exeter if you consent to give stool samples, these samples will be sent to the University of Exeter to analyse the link between the gut-biome and addiction. Your samples will be coded by your unique participant identifier.
  - Perceptive Imaging Inc– Perceptive will host the brain imaging for this study. To ensure your safety, the company will need to read your most up to date care record and know your identifiable information. Your scans will be coded by your unique participant identification number. This data will be kept for 25 years by Perceptive inc as per their data storage policy. Perceptive uses a sub-processor to support their delivery of brain imaging reviews called Ambra Health. Perceptive and Ambra Health have an agreement in place that applies EU Standard Contractual Clauses and the UK Addendum, alongside technical and organisational measures to keep your data safe. All such imaging transferred will be pseudonymised, labelled with an identification number. No other personal data will be transferred between Perceptive Imaging Inc and Ambra Health.
  - Oura Health LTD is a company responsible for the fitness tracker (Oura Ring) used within this study. The company is not allowed to send data to any third party without your consent as per our signed contract. You will be requested to read the following online information regarding Oura's privacy policy before agreeing to this optional clause of the study: https://ouraring.com/privacy-policy
  - Data related to OURA rings and microbiome data will be shared with the university of Exeter. Bloods will be analysed and data will be shared between both Colombia University and Oslo University with listed collaborators.

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.

COMMERCIALISATION

Samples and data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

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.
- you have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

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

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK.

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to r.zafar19@imperial.ac.uk or frederick.page@imperial.ac.uk, or
- by ringing us on +447565542074.

COMPLAINT

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to [**email**], or by ringing us on [**phone number**].

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk / via telephone on 020 7594 3502 /or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

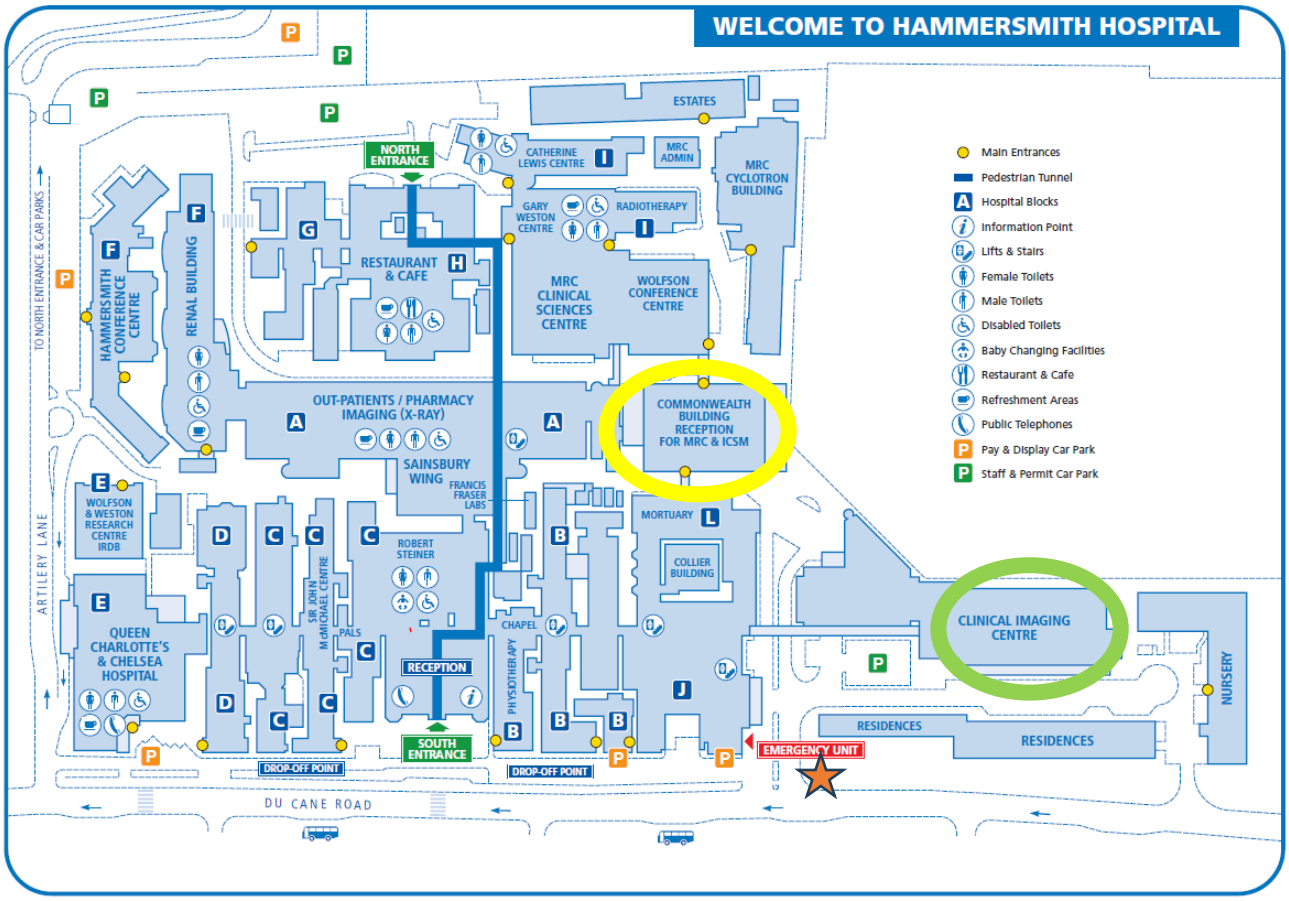
Thank you for reading this sheet, and your interest in taking part in our study.

Appendix: How to find us

How to find us

Nearest underground stations White City (Central Line), East Acton (Central Line) or Wood Lane (Hammersmith and City, Circle Line). The Hammersmith campus is well connected with buses including the 7, 70, 72, 272 and 283. Please check Transport for London for up-to-date travel information.

From White City underground station, it takes about 15 minutes to walk to us. Turn right on exiting the station; this road is called 'Wood Lane'. Walk along Wood Lane, past the BBC buildings, under the Westway flyover and turn left at Du Cane Rd. Walk past the playing fields and turn right at Costcutter. The CRF is a large silver and black building with some yellow framing. The entrance to the CRF is a revolving door with a large yellow frame around it. The Burlington Danes Building (a large silver building with a glass front) contains the scan centre called 'Perceptive'.



See the **CRF** circled in **yellow** – where screening will take place. On Du Cane Rd, turn right at Costcutter shown as an orange star on the map. The CRF is a large black, yellow and silver building ahead and to the left (see the photo below, the CRF is on the ground floor of this building).

The **Burlington Danes** building (which contains the scanning centre 'Perceptive') is to the right of the CRF (we'll show you this when you come in for your screening), connected by a bridge or walkway (see photo below).

The CRF is on the ground floor of this building. Go through the yellow-framed revolving door. This is where you will come for your first visit.

This is the Burlington Danes Building. The entrance is the large glass-fronted area.

Screening & Study Location
NIHR/Wellcome Trust Imperial CRF,
Hammersmith Hospital
160 Du Cane Rd,
London,
W12 0NN
020 3313 8070

Scanning Location
Perceptive
Burlington Danes Building,
160 Du Cane Rd,
London
W12 0NN
0208 008 6218.