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Participant Information Sheet- Opiate dependent

Title: Characterising the neurobiology of detoxification and early abstinence in opiate addiction: is there a role for NK1 antagonism to improve outcomes? (NCORE)

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You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

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

What is the purpose of this study?

The main purpose of the study is to improve treatment for detoxification and relapse prevention in opiate addiction. In particular we want to find out if a medication that treats chemotherapy-induced nausea and vomiting, aprepitant, may be helpful. We will do this by investigating the effects of aprepitant on brain function in opiate dependent individuals during methadone treatment, and again, after achieving abstinence from methadone.

Our research uses brain-imaging techniques to detect subtle changes in brain function while performing certain psychological tasks. The tasks measure brain processes that are important in opioid dependence. We believe that aprepitant could be a useful treatment for relapse prevention or to assist with opiate detoxification by improving these brain processes. We will therefore study how aprepitant affects brain responses to the tasks and compare the results with those from a control group who do not have opiate dependence.

Why have I been chosen?

You have been chosen to participate because you have a history of opioid dependence, because you are currently taking methadone and because you are planning to reduce your methadone dose with a view to achieving abstinence and/or have achieved a low dose. We need up to 35 individuals like yourself to complete the study.

Do I have to take part?

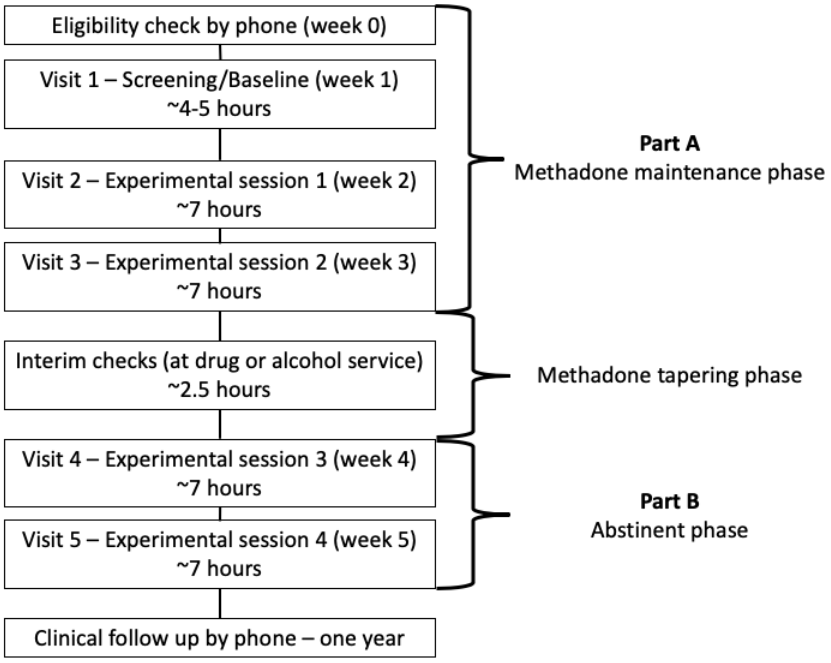
No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You will be free to withdraw at any time and this will not affect your care.

What will happen to me if I take part?

If you decide to take part you will be asked to attend 5 visits in total at the Imperial Clinical Research Facility (ICRF) in the Hammersmith Hospital. Brain scanning (visits 2 to 5) will take place in the Imperial College Clinical Imaging Facility (CIF), which is at the same location. We will arrange taxi transport for all visits.

- Visit 1: Consent and screening visit (4-5 hours).
- Visits 2 and 3: Study days (~7 hours each, 1 week apart) when you are still taking your usual methadone dose.
- Interim session: To be completed at your usual drug & alcohol service (~2.5 hours).
- Visits 4 and 5: Study days are identical to visits 2 & 3 (~7 hours each, 1 week apart) but will only be completed once you have stopped taking your methadone.

The following schematic outlines the study session days and where these will take place.



Screening Visit 1

We will discuss the study in detail with you. If you agree to take part, a doctor will take a detailed history of your previous health and perform a physical examination to check your current health. You will be asked questions about your drug and alcohol use and psychiatric history. You will need to complete a urine test for drugs of abuse and pregnancy (if applicable), and a metal-check questionnaire to check you are safe to have an MRI scan. We will not share the results of any of these tests with your clinical team or GP without your permission. We may request additional medical information from them concerning your suitability to participate.

After confirming your eligibility, you will complete some questionnaires about your drug history, personality traits and mood. The questionnaires will take approximately 1 hour to complete. You will also complete some psychological tasks (computer games) which are designed to test different types of brain function such as attention, memory and impulsivity. The tasks will take approximately 2 hours to complete. You will be able to complete some of the questionnaires and tasks at your usual drug and alcohol service if this is more convenient.

The visit will take approximately 4-5 hours at a relaxed pace and refreshments will be provided. You will be able to take smoking breaks if required.

Study Visits 2 to 5

If you are suitable for the study, you will be required to attend 4 further visits lasting approximately 7 hours, at least a week apart. A taxi will transport you to the research centre in the morning of each study day. Timings may change slightly, but we will normally ask you to arrive at around 9am and stay until approximately 4pm. We will provide you with breakfast. You will not be eligible if you feel unwell, or have taken alcohol or drugs of abuse in the previous 24 hours.

IMPORTANT: For visits 2 and 3, you will be required to bring your usual dose of methadone with you to the study centre where we will observe you taking it. This is important because we need to time the dose of the study medication, aprepitant, to occur as soon after your methadone dose as possible. We will help with any arrangements required for you to bring your methadone with you.

The following information will be recorded:

- Urine test for recreational drugs
- Breath test for alcohol
- Medications since your last visit

Once we have confirmed eligibility, study procedures will be conducted as follows:

- Taking your usual methadone dose
- Administering the study medication
- Vital signs; blood pressure, pulse, oxygen saturation, breathing rate.
- Questionnaires and rating scales with pencil and paper or on a computer
- Computerised games to test emotion, reward sensitivity and memory
- Brain scanning

We will repeat the questionnaires and vital signs measurements at regular intervals during the day. You will be given a sandwich lunch. At about 6 hours after dosing we will check your health and if this is satisfactory you will be allowed home by taxi. If you are still feeling the effects of the drug, we will ask you to stay until we are happy for you to leave.

Brain scan

Approximately 4 hours after dosing you will have a brain scan at the imaging facility (approx. 5 minute walk away). A researcher will accompany you and stay with you during the scan. This will take approximately 90mins 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. These tasks are essentially short games. During one task you will be able to win a small amount of money (approx £10).

During the other two tasks you will view images of neutral, distressing and opioid addiction related images (cues) which are designed to evoke a stress and craving response. In the event of a failed scan, this will be repeated at the same visit where possible. However, it may be necessary for you to return at another date for a repeat scan, entailing an additional visit.

Interim session

During the study, we will monitor your progress with methadone reduction. This will take place at your own convenience either by telephone or at your usual clinical appointments. Following successful abstinence from methadone, you will be asked to repeat some of the psychological tasks (computer games) which are designed to test brain function such as attention, memory and impulsivity. Again, this will take place at your usual drug and alcohol service for convenience.

Follow-up

We will telephone you after each visit to check on your health and arrange payment. After study completion, we will telephone you at regular intervals (once every 3 months) for up to a year, to monitor your progress.

Blood tests

Genetic make-up (genes that we inherit from our parents) may help to explain differences in the way that opioid dependence affects people. You will be asked to sign a specific consent form to provide a small blood sample (15ml, ~3 teaspoons) to identify these genes. This is optional and you may decline if you wish. This will not affect your eligibility to participate in the study. The sample will be stored anonymously, and sent to a research laboratory where it will be used to obtain your DNA for 'genotyping' at the end of the study. Samples will be stored until analysis is complete, or according to your wishes in the consent form. Your results will be coded and will not identify you by name. Only the research team will be able to link your name with the sample. You will not be told the results of any genetic test.

Compensation

For completing the whole study you will receive £330 in recognition of the time and inconvenience of taking part. You can receive this directly into your bank account, or as vouchers if you prefer. This includes payment of £50 for the screening visit and £70 for each study visit. Travel expenses will be paid and you will also receive any winnings made while in the scanner. If you fail to complete a study day, you will receive payment on a pro-rata basis, at the discretion of the research team.

What drug is being tested?

On each of the four study days you will be given a capsule to take orally with water. It will be either be a drug called aprepitant (320mg), or a placebo dummy pill. Aprepitant is used clinically and has been licensed for many years for treating nausea in people receiving chemotherapy for cancer. It has also been tested as a possible treatment for people with depression, anxiety and alcoholism. Aprepitant is safe and well tolerated. The dose used in this study (320mg) is higher than the usual dose prescribed for nausea (125mg), but is still safe and well-tolerated. This dose has been chosen to ensure that there is enough drug to elicit a response. This is because there is evidence that doses of 300mg and above are required to produce effects on brain function such as antidepressant and anxiolytic effects.

The dosing will be randomised, double-blind and crossed-over. This means that you will receive both medications, one at each visit in a random order, but you and the researchers will not know which one is which. This is so that any changes in the measurements we take are not biased by expectation.

From our experience with aprepitant, we do not anticipate any issues from this dose. The medication will only be taken once at each visit, rather than daily. In studies of single doses, few side effects have occurred at doses of 320mg. The most common side effects that have occurred in patients taking the drug regularly are mild and should resolve whilst you are with us and include hiccups, upset stomach or indigestion, constipation, diarrhoea, headache, fatigue, headache and dizziness.

What do I have to do?

- Attend the study days, or let us know in plenty of time if you cannot be there.
- Report any changes in your health or medications to one of the study team.
- Not take any alcohol for 24 hours before each study day.
- Not consume cannabis or other illicit substances (including heroin) for at least 1 week before each study visit
- Take the same dose of methadone for study visits 2 and 3 which will take place approximately 1 week apart.
- Bring your usual dose of methadone with you to study visits 2 and 3.
- Remain engaged with addiction services to reduce your methadone dose towards abstinence

What are the risks of taking part?

MRI scanning is a routine procedure in medical practice and has not been found to be harmful. There is a very small risk of nerve stimulation, which would be noticed as a 'pins and needles' sensation, probably in the tip of the nose, back of the neck or shoulders during the scan. The MRI scanner consists of a powerful magnet. Therefore, you must not have a scan if you have a heart pacemaker, metal injuries to the eye, a shotgun injury or metallic objects (e.g. pins, clips) inside your body near to your head. Any metal objects on your person, including piercings will need to be removed before the scan. The scanner may damage credit cards and some watches so we will provide you with a secure place to leave these valuables. The radiographer will check possible risks with you before you go into the scanner. MRI scans do not involve any radiation. The MRI scanner is very noisy. This is normal and the scanner cannot hurt you in any way. You will be provided with ear plugs and head phones to minimise any discomfort. There is a microphone inside the MRI scanner so that you can talk to us at any time. It is quite 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.

One of the MRI scanner tasks, the cue-reactivity task, is designed to cause drug craving. This is part of what we are measuring in this study as it is an important reason why individuals struggle to stay clean. You may therefore find some of the images challenging. The study team are experienced and well placed to offer appropriate support afterwards to reduce any remaining cravings before you leave.

There is no indication of a drug interaction between aprepitant and methadone, but aprepitant medication may change the way in which you perceive the effect of your methadone. We are interested in measuring this change, and it will be assessed as part of the study. Aprepitant will not induce any opiate withdrawal.

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

There is no risk from any of the other measurements, except for a small risk of bruising from providing the blood sample.

What are the possible benefits of taking part?

You will not benefit from taking part but the information we get might help improve the treatment of people with opiate dependence in future.

What will we do if we notice something is wrong?

Although unlikely, it is possible that whilst performing normal medical checks and MRI scanning we may identify an illness or abnormality that you did not realise you had. In the event that a major abnormality is found, you will be informed and your GP contacted with your permission.

How will we use the results of this research?

Our research into brain mechanisms of addiction includes the study of targets ('receptors') in the brain which aprepitant affects. We have already done a similar study in alcohol and poly-substance dependent individuals, so we will compare their results with opiate dependent individuals and investigate the effect of methadone treatment. We will publish the results of this study in a scientific journal, and present the findings at meetings and conference, including those which Users attend. Some of the results of this study will be used toward a PhD qualification.

What if something goes wrong?

There are doctors at the research centre at all times who will provide emergency medical cover if required. If for any reason you cannot return home at the end of a study day due to drug effects, a bed can be arranged at the Hammersmith site overnight.

You will be given a contact card (similar to a credit card) with details of the study, and emergency contact details to carry with you.

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring 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. 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, Joint Research Compliance Office.

If you wish to complain, or have any concerns then you should contact the Principal Investigator (Professor Anne Lingford-Hughes, contact details on page 1).

Confidentiality

All information collected about you will be kept strictly confidential and stored and processed according to the Data Protection Act. We will not share any confidential information, or the result of any tests e.g. urine drug screen, with your GP or clinical team without your permission. However, should there be any concerns about risks of harm to you or anyone else, a clinical decision will be made with regard to disclosure of information and appropriate support will be discussed with you. The research data we collect from you are anonymised, so they can only be identified by a subject number. With permission, you may be contacted for follow-up studies related to this project in the future.

Who is responsible for my data?

Imperial College London is the sponsor for this UK based study. We will use information from you and your medical records in order to undertake this study and will act as the data controller. We are responsible for looking after your information and using it properly. Imperial College London will keep identifiable information about you for 10 years after the study has finished in relation to data subject consent forms and in relation to primary research data or according to your wishes on the consent form.

Further information on Imperial College London's retention periods may be found at https://www.imperial.ac.uk/media/imperial-college/administration-and-support-services/records-and-archives/public/RetentionSchedule.pdf.

Your rights

Your usual statutory rights to access, change or move your information are limited, as we need to manage your information in specific, lawful 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.

Legal Basis

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.
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.

International Transfers

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (EC) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient

organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

Who will have access to my data?

Personal data: Imperial College Healthcare NHS Trust (Hammersmith Hospital) and Imperial College London will collect personal information from you for this research study in accordance with our instructions.

Individuals from regulatory organisations may look at your medical and research records to check the accuracy of the research study.

Imperial College Healthcare NHS Trust and Imperial College London will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Imperial College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Imperial College Healthcare NHS Trust will pass these details to Imperial College London along with the information collected from you and your medical records. The only people in Imperial College London who will have access to information that identifies you will be people who need to contact you about the research study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, or contact details.

If you wish to raise a complaint on how we have handled your personal data or if you want to find out more about how we use your information, please contact Imperial College London's Data Protection Officer Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ, 020 7594 3502, dpo@imperial.ac.uk. If you are not satisfied 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). The ICO recommends that you seek to resolve matters with the data controller (us) first before involving the regulator.

Research data: When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/).

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Other information

This study has been approved by the West London & GTAC Research Ethics Committee. It has been reviewed and funded by the Medical Research Council (MRC). The study will follow the ethical principles laid down in the Declaration of Helsinki.

Contact Details

If you have any questions, please do not hesitate to contact the research team at the address provided on page 1. Dr Katherine Herlinger, is the study doctor, and can be contacted on **07745 300 960** during working hours (09:00-17:00) or at katherine.herlinger@nhs.net.

You can also contact the Patient Advice and Liaison Service (PALs) which offers independent advice for your concerns, suggestions and queries. They are available Monday to Friday 9am-5pm on the following number; 02033133322 or at **IMPERIAL.PALS@NHS.**