qMAP-PD UCL

Participant Information Sheet

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Study: Quantitative MRI for Anatomical Phenotyping in Parkinson's disease (qMAP-PD)
IRAS Number: 247033
Principle Investigator: Dr Christian Lambert
Contact: Dr Christian Lambert. **Tel:** 020 3448 4362 ext 84365
Email: ion.qmap@ucl.ac.uk

1. Introduction

We would like to invite you to participate in this research project. The aim of this work is to better understand the causes of variability between individuals. In this work we are focusing on a common disorder called Parkinson's disease and other conditions that may show similar symptoms in the early or pre-clinical stages. We are inviting people diagnosed with these conditions, and unaffected volunteers, to take part. Before you decide, it is important for you to understand why the research is being done and what it will involve.

2. What is Parkinson's disease?

Parkinson's disease is a common progressive disorder of the brain that becomes more likely with age. It is diagnosed by doctors based upon the clinical history together with a combination of muscle stiffness, tremor and slow movements on examination. Individuals begin to experience these symptoms once 70-80% of nerve cells within a brain region called the substantia nigra have already died.

There is evidence that Parkinson's disease begins in a different part of the brain up to 20 years before it is diagnosed. During this intervening period, called "*pre-clinical Parkinson's*", there are subtle problems such as loss of sense of smell or sleep disturbances, which are more likely to be experienced by individuals with the condition. However, these symptoms are also common in people who do not have the disease. It is not possible to identify who has pre-clinical Parkinson's, or how quickly the disease will progress once diagnosed.

Once diagnosed, disease progression is highly variable. Additionally, there are a number of conditions that can look like Parkinson's disease, particularly in the very early stages. It is mainly through repeated assessments over a longer period of time that these other conditions become apparent. Currently, there is no cure for Parkinson's and we don't yet know why people get the condition.

3. What is the aim of this study?

Currently there are no treatments that can slow or cure Parkinson's disease. One of the reasons for this is because the problems with movement only become apparent once 70-80% of the nerve cells have already been irreversibly lost. Also, once diagnosed, the way the disease progresses is highly variable among individuals, and it may be that different people require different types of treatment.

This work seeks to use detailed clinical assessments, non-invasive brain-scanning techniques (Magnetic Resonance Imaging, MRI) and inherited material (DNA, Genes) to understand why Parkinson's disease is so variable. With these, we aim to develop ways to predict how quickly the disease will progress based on an individual's brain structure, and diagnose the condition during the pre-clinical phase. By achieving these aims, strategies aimed at slowing the condition can be researched more accurately, and may help develop future treatments that are tailored to individual subjects and started before brain tissue is irreversibly lost.

4. Why have I been asked to participate?

You have been asked to participate because either you have one of the conditions that we are including in our study, or you are an unaffected individual. Your participation is entirely voluntary. Even if you decide to take part you are still free to withdraw at any time and without giving a reason.

5. Can you summarise what is involved?

On overview of the study is summarised below. Details for each are provided later in this information sheet.

A. Attending several assessment visits over the next four years, each lasting approximately 3.5-4h in total, where you will undergo a clinical assessment and examination and complete some simple computer assessments and/or questionnaires. Note certain groups will only be asked to attend a single assessment session, and you will be notified of this before you attend.

B. Complete some short (~20min) online questionnaires and assessments before each visit. These can be completed at the visits if you are unable to do this

C. Provide a small blood sample (approximately 50ml, or 3 tablespoons) at the start of the study, and again at the end of the study.

D. Undergo specialised MRI scanning lasting approximately 1 hour, repeated again after 3-4y for most participants.

E. Wear a wrist watch device to measure movements, on both wrists, for up to two weeks.

F. If applicable, agree to allow us to access the results and/or data from a previous dopamine transporter scan (DaTSCAN) and/or polysomnography sleep study (and if necessary contact the team who arranged/performed these for details) and/or the PREDICT-PD study.

G. Be re-contacted by qMAP-PD research team in the future (e.g. to answer follow-up questions and/or attend another assessment visit). This is optional and you could opt-out at any time.

H. Agreeing to have your samples and health-related information stored by qMAP-PD team and used in an anonymised form by researchers for many years. This is optional and you could opt-out at any time.

I. Agree to allow qMAP-PD team to check your health status over many years via NHS Digital. This is optional and you could opt-out at any time.

6. What are the benefits ?

There are no direct benefits to you as an individual. The information we learn through this study might help develop better ways to diagnose and to treat people with similar conditions in the future.

7. What are the risks ?

This study should not cause you any harm. We have chosen MRI scans and other measures that are safe, painless, relatively quick and comfortable. You may feel some minor discomfort when you have blood taken, and there are very small risks of bruising or a local infection, which can be treated. There is a risk of finding an unexpected abnormality on your tests ("*Incidental finding*") that may require further investigations via your GP, and could potentially have an impact on your future health.

8. What happens during the Magnetic Resonance Imaging?

As part of this study, you will undergo specialised MRI scanning to allow us to measure changes in your brain tissue. The MRI scanning will last approximately one hour in total. For the MRI, we will ask you wear some routine monitoring devices, including a chest strap to measure your breathing, some sensors on the skin of the chest to measure heart activity (electrocardiogram, ECG), and a finger sensor to measure your oxygen levels. Occasionally, we may ask to shave a small section of the chest hair to stick the ECG sensors on the skin. During the MRI, you will lie on a couch inside the scanner, with your head in a specially designed headrest, which is cushioned for comfort. Inside the scanner there are speakers, an intercom so that you can speak to us and a screen that will allow you to watch a film during the scanning. The scanner makes a loud clicking noise so we will give you earplugs to wear. You will have a hand-held buzzer so that you can stop the process at any time. Most participants will undergo the MRI scanning twice, with a 3-4y interval in-between.

9. Is MRI safe?

MRI is a painless and safe technique, which can obtain detailed pictures of the brain. As the name implies it uses magnetic fields to generate the pictures and unlike X-ray techniques there is no ionising radiation used. We are legally obliged to recheck your compatibility for MRI prior to any scanning session for safety purposes. Please inform us if any of the following apply to you:

- You have a cardiac pacemaker or an implanted medication pump
- If you have a history in the metal-working industry, or you might have been at risk of metal foreign bodies entering your eye area.
- You have a metal plate in the skull or metal objects inside the eye or skull
- You have had any form of previous neurosurgery, including the insertion of clips.
- You have any tattoos.

If you have a tattoo, we will need some more information about the location, colour and size of the tattoo before we can perform an MRI. In some circumstances we may not be able to recruit you into the study, because there is a risk that the inks used some types of tattoo may heat up during the scanning.

10. What happens if something suspicious is seen on my MRI?

The brain scans we do are not designed to diagnose disease, however abnormalities are occasionally detected during the scanning process. Most of these are no cause for concern. If an abnormality is noticed, it will be reviewed with a specialist doctor (radiologist) after your visit. If the radiologist agrees that it is potentially serious or requires further investigation (regardless of whether or not it might be treatable), we will inform your GP who will contact you. Your GP may refer you to specialists for further investigation and treatment. For this reason, you can only take part in the imaging study if you agree that we can tell both you and your GP if we notice a potentially serious abnormality on one of your scans.

It is important to understand that we will not notice all potentially serious abnormalities. If you do not receive any feedback from us about a potentially serious abnormality, you should not regard this as reassurance about your health, and it should not stop you from seeing your doctor about health concerns you might have.

13. Study schedule

The study is divided into five main stages. **Certain groups may not need to attend all of these,** and you will be notified by the investigator at or before the screening assessment (B). After consent and enrolment, at each assessment (B-E) we will always carry out a clinical assessment (taking details of your symptoms, carrying out an examination), and will ask if you are happy for a video to be made of part of your examination, so that this can be reviewed confidentially by another Neurologist who is working with the research team. There will also be some additional components depending on which visit you are attending, which are detailed below:

A. Pre-Screening Contact:

A member of the research team will contact you by telephone, and ask you some preliminary questions to check you meet the entry criteria and have received a copy of this information sheet. At the end of this, if you are eligible, you will be invited to attend a screening assessment session.

B. Screening Assessment:

Initially we will re-check your suitability for the study and MRI scanning, answer any questions you have and go through the study consent process. If you are happy to proceed, we will then take approximately 50ml (3 tablespoons) of blood from a vein in your arm. We will then assess your clinical history and examination, and ask you to complete a series of computer tests to measure certain aspects of your behaviour, decision-making, visual processing and personality. We have selected these measures as they have all previously been shown to either vary in the diseases we are studying, or impact some of the other measures we are collecting. During some of these computer tests, we will use sensors on the skin of the chest to measure heart activity. This session will last approximately 3-4h in total. At the end of this we will ask you to wear a special device on each of your wrists for the next 7-14 days. These devices looks like a digital wrist-watch, and will allow us to measure your movements over a 24h period; You would be free to take these off during this time if required, for example while washing/swimming. You will return these at the baseline assessment.

C. Baseline Assessment:

This will take place approximately 10-14 days after the screening assessment, and will last approximately 3h plus time for breaks. The baseline assessment is composed of MRI scanning (~1h), memory assessments (~1h), clinical examination (~30min), and some self assessments about the symptoms you are experiencing (~30min). We will invite you to complete some of these assessments online in the week before assessment. If you are taking medication for Parkinson's disease, we will ask you **not** to take your usual morning dose until just before the MRI scan. In this scenario, we will arrange for you to attend at the start of the day.

D. Follow-up 1 (+18 months):

This will take place approximately 18months after the baseline assessment, and will last approximately 3h plus time for breaks. Here we will repeat the memory assessments (~1h), clinical examination (~30min), some self assessments about the symptoms you are experiencing (~30min) and some of the screening behavioural testing (~30mins). We will invite you to complete some of these assessments online in the week before assessment. If you are taking medication for Parkinson's disease, we will ask you **not** to take your usual morning dose until we have performed the clinical assessment. In this scenario, we will arrange for you to attend at the start of the day. At the end of this, we will ask you to wear the wrist accelerometers over the next 10 days, and then return them using pre-paid parcels.

E. Follow-up 2 (+36-40 months):

This will take place approximately 36-40 months after the baseline assessment and is identical in structure to the baseline assessment, including a final blood test (~35ml, or 2 tablespoons of blood) if you agree. We will ask you to wear the wrist accelerometers over the next 10 days, and then return them using pre-paid parcels.

14. Future follow-up

Beyond follow-up 2 (i.e. after 4 years), we would not formally arrange to see you again. However, at some time in the future we may want to re-contact you to ask you some more questions to find out a bit more about your condition. Giving such additional help would be entirely optional, and you can opt out of this at any stage. Similarly, some participants might be asked in later years to attend another assessment visit (including questions, measurements including MRI and samples), although again attendance at such visits would be optional. With your consent, we will also share your name, postcode and date of birth with NHS Digital. The information we share will be used by NHS Digital and other central UK NHS bodies to provide us with information about your health status over the longer term without us having to contact you.

15. What will happen to my blood samples?

The inherited material (DNA, RNA, Genes) will be extracted from the blood at a local or national facility. The sample will be treated as a gift for research, stored and used in ongoing and future projects with the same study aims, by Dr Christian Lambert, his team or collaborating researchers. The chemical parts of the blood (plasma/serum) will also be stored if possible. Plasma/serum refers to the parts of the blood that do not contain red or white blood cells but contains chemicals that might be important for disease, for example sugar in diabetes and cholesterol in heart disease. Blood cells (red blood cells, white blood cells and platelets) may also be extracted and used to study markers of chemical and immune function which may be important in disease progression and in developing new treatments.

16. What if my blood test identifies a risk factor for another disease unrelated to the original research?

We will not carry out a comprehensive screen for variation related to all human diseases, but currently large-scale analysis means that a lot of genetic variation may be documented in your samples. The tests in this study are performed on a research basis and cannot be used for clinical care. However, if we come across something that we think may possibly have an impact on your future health or that of your family, and for which there are specific treatments or preventative measures which will help you or your family, we would like to tell you about this. You can choose whether you wish to be informed about this, in advance. If you do chose to be informed we will make sure that you have the appropriate guidance and counselling and this will involve a repeat DNA blood test. This will be discussed with you by Dr Christian Lambert and/or his team during the screening assessment.

17. What will happen to my information?

Your personal details and any data concerning medical problems you may have (where applicable), will be kept using a clinical database on a specialised computer system that is designed to look after confidential information safely. This computer network routinely holds personal details and test results for hospital networks, and is used by several NHS organisations. An anonymised, coded database holding clinical, imaging and genetic data, without any identifying personal details will be held on research computers, may be held by collaborators at other sites and may be made available to other qualified researchers to enable the combined analysis of samples from different, large patient series around the world (see below).

When this study is completed we will store your data (personal information, assessments, scans, blood results) for many years (in accordance with the General Data Protection Regulation: Articles 6a, 6e , 9(2)(j) and 19). We will review all the data we hold about you every 10 years, and only destroy records that are felt to be no longer required for ongoing or potential future scientific projects. At any time you may ask us for details regarding the information we hold about you, and what it has been used for. At any time you may ask for any data about you to be removed (see *22. What happens if I want to withdraw from the study*?).

18. Who will be able to use my data?

Non-identifiable information and samples from qMAP-PD participants may be made available to researchers who apply for access and have the relevant scientific and ethics approval for their planned research. This could include researchers who are working in other countries and in commercial companies looking for new treatments. Allowing more researchers to work with the data we collect may help accelerate scientific discoveries. Any results from this type of research will be put in the qMAP-PD database so that they are available to all approved researchers. There will also be a requirement to publish the results of all research based on this resource so that people can benefit from it. If you do not wish for us to share any of your data, you can opt out of this at any time simply by notifying the qMAP-PD investigators. We will arrange for any copies to be deleted, but it may not be possible to remove your data from analyses that had already been done. We would retain the original dataset and samples for use within the qMAP-PD study only. If you wish all of your data to be removed entirely, see "*22. What happens if I want to withdraw from the study?*".

19. How will you keep my data confidential?

We have strict measures in place to protect your confidentiality. These include the following:

1. We keep any personal information that might identify you (such as your name and address) completely separate from all your other data (assessments, scans, blood results), and stored using high-level computer security (ISO27001 certified) to prevent unauthorised access.

2. We restrict access to personal information as much as possible, and all research staff working on this project will sign confidentiality agreements as part of their employment contracts.

3. We will code your sample, so that a randomly generated number is assigned to your data rather than your name, and this will be used in further analysis. The link between the code and your name will be stored separately and kept confidential.

4. We merge some of your data to make it less unique e.g. only providing month and year of birth,"*defacing*" brain scans to prevent you being identified from MRI data.

5. Only coded-merged de-identified samples (i.e. those without identifying features) may be shared with other research groups for analyses.

6. Any other researcher wanting to use any aspect of the qMAP-PD data will first need to sign a data agreement that strictly prohibits any attempts to re-identify or contact subjects, or to allow any individual who has not signed the data agreement to use the data.

The data controller for this project will be University College London (UCL). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data. If you are concerned about how your personal data is being processed, please contact UCL in the first instance at:

data-protection@ucl.ac.uk

If you remain unsatisfied, you may wish to contact the Information Commissioner's Office (ICO). Contact details, and details of data subject rights, are available on the ICO website at:

https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

20. Can outside bodies like insurance companies access my results?

No. Third parties such as insurance companies and employers will not be given any individual's information, samples or test results, and nor will we allow access to the police, security services, relatives or lawyers, unless forced to do so by the courts.

21. What happens if I want to take part in another study?

You are free to take part in any other studies if you wish. However, some studies may change the measurements we are testing in this work (e.g. MRI results). If you enrol in a study that may alter the progression of the disease and/or symptoms (e.g. drug trials), we would ask that you notify us as soon as possible or discuss with us prior to enrolling. Depending on the scenario, we may choose to bring forward some of your qMAP-PD assessments if possible, so they can be completed prior to you commencing the other study.

22. What happens if I want to withdraw from the study?

Participation in the study is voluntary and you can chose to withdraw your participation at anytime. If you do decide not to take part or to withdraw, this will not affect your current or future treatment in any way.

You can withdraw by emailing **ion.qmap@ucl.ac.uk**, or telling us at one of the assessment visits/telephone calls. A member of the qMAP-PD team will contact you to discuss your concerns and determine the desired level of withdrawal from the following options:

"No further contact": This means qMAP-PD would no longer contact you directly, but would still have your permission to retain and use information and samples provided previously and to obtain and use further information from your health records.

"No further access": We would no longer contact you or obtain any further information from your health records in the future, but would still have your permission to use the information and samples provided previously.

"No further use": This means that, in addition to no longer contacting you or obtaining further information about you, any samples and data collected previously would no longer be available to researchers and it would not be used for any further analysis. We would endeavour to destroy your samples and data, although it may not be possible to trace all distributed sample remnants and it would not be possible to remove your data from analyses that had already been done. We will retain some minimal information as outlined below.

If, having discussed the options and your concerns, you did decide to withdraw then we would send you a Withdrawal Form to confirm your wishes in writing. This form can be completed by you or, if you are not able to do so for some reason by someone able to act on your behalf. You will be asked to confirm your withdrawal with a signature. Your signed consent and withdrawal would be kept as a record of your wishes.

23. What if I am unable to communicate my wishes in the future?

We plan to follow you up regularly with assessments for up to four years (see *10. Study schedule*). If, for some reason, you become unable to communicate your wishes during this time frame, then we would not arrange any further assessments and would withdraw you from the study as *"No further access"* (unless you had previously specified otherwise). Similarly, if in the future (i.e. after 4y) you lose the ability to understand or communicate your wishes about this study, we will continue to hold and study your samples but would withdraw you from the study as *"No further access" (*unless you had previously specified otherwise).

24. What will happen to the results of the study?

We plan to publish any results in scientific journals. Your name would not be mentioned in any publication. We will make regular reports to funding bodies and to patient groups.

25. Who is funding this study?

This study is being funded by the Medical Research Council.

26. What happens if something goes wrong?

If you or your relatives have any concerns about the research study you can speak to a member of the research team who will do their best to answer any questions. If you or your relatives wish to make a formal complaint about the research study you can do this through the NHS complaints procedure. Full details can be obtained from the UCL Hospitals NHS Foundation Trust Complaints Department or from the Patient Advisory and Liaison Service (PALS). You or your relatives can also contact the UCL/UCLH Joint Biomedical Research Unit by writing to the following address and quoting reference **18/0232**. All communication will be dealt with in the strictest confidence.

UCL/UCLH Joint Biomedical Research Unit, R&D Directorate, Maple House, Rosenheim Wing, Ground Floor, 25 Grafton Way, London, WC1E 5DB

Every care will be taken to ensure that your well-being and safety is not compromised. However, UCL has a special insurance arrangement in place (no fault compensation) in the event that something unforeseen happens and on the balance of probabilities, harm or injury is attributed to their taking part in the study. In the event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation.

27. Can I claim travel expenses?

We will reimburse the following travelling expenses for attending the assessment sessions:

A. Train
- Standard tickets only (i.e. not first class)
- Please where possible book in advance to get the best value tickets
- Where possible, avoid booking open return tickets as these tend to be more expensive
- Buying split tickets may reduce the overall price of your fare (see www.splitticketing.com)

B. Other public transport
- Fares for bus, tram, Metro or underground

C. Private transport (car, motorcycle or bicycle)
- An allowance of 25p per mile for car and 9p per mile for motorcycle/bicycle will be paid
- There is no free parking, but you can claim the parking costs (but not any fines)

If you need someone to help you during the journey, you can also claim travel expenses for a companion Please keep all travel receipts to enable us to reimburse you as quickly as possible.

28. How do you find us?

We are located at the Wellcome Centre for Human Neuroimaging, close to Russell Square tube station, on the Piccadilly line.

29. How do I get further information:

If you would like to volunteer or would like to know more about the study, please contact:

Name:	DR CHRISTIAN LAMBERT
Address:	Wellcome Centre for Human Neuroimaging 12 Queen Square, London WC1N 3BG
Telephone:	020 3448 4362 ext 84365
Email:	ion.qmap@ucl.ac.uk

Thank you for taking the time to read this information sheet