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NRES Committee, South Central, Berkshire Ethics Committee
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OXFORD RBD PARTICIPANT INFORMATION SHEET 1

Study Title: Understanding the early pathological pathways in Parkinson's Disease

Introduction

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of the study, why we have asked you to help us and a brief description of what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study. 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.

Part 1

What is the purpose of the study?

Parkinson's Disease (PD) is a disease affecting the nervous system which causes tremor, stiffness and slowness of movement. Neurologists recognise that there are different forms of PD, and that the way in which the disease spreads is not the same for all patients, but it is not clear why that is the case. The causes of PD are currently largely unknown, but it is likely to be a combination of genetic influences and things in our environment or lifestyle. At present there is no specific test for PD and the diagnosis currently depends on the recognition of typical features by those doctors used to seeing the condition. This can sometimes cause a delay in diagnosis. Furthermore, it is believed that there may be changes in the brain for between 5 to 10 years before someone begins to experience the symptoms of PD. We would like to discover a test to speed up the diagnosis of PD, to understand how the disease spreads, and to monitor its activity. This could result in better treatments which could be given much earlier and hence slow the progression of the disease. It would also allow us to do better trials of new drugs and stop them earlier if they did not seem to be helping. It is now increasingly recognised that having REM sleep behaviour disorder (RBD) may be a risk factor for developing future Parkinson's disease.

We will be recruiting between up to 2000 individuals with PD, 300 relatives of people with PD, 300 people with REM sleep behaviour disorder (RBD) and 300 healthy control subjects without PD. Our objectives are to discover 'biomarkers' such as variations in our genetic code (DNA) and molecules identified in the blood, that are sensitive and specific to PD particularly in the early stages. We will therefore be asking our participants whether they would be willing to volunteer for a special clinic visit where we will examine them and do some tests of memory and attention. In addition we will ask if they are happy to have a blood sample from which we can look at DNA and measure novel proteins, and a brief ultrasound scan of their brain which takes 20-30 minutes. We will explain what these tests involve in more detail in part 2.

Why have I been chosen?
You have been chosen because you have RBD diagnosed through the Oxford sleep clinic at the John Radcliffe Hospital, but do not have Parkinson's disease. In this way we can look for specific changes or biomarkers in individuals with RBD, that may be similar to individuals with Parkinson's disease.

Do I have to take part?
It is up to you to decide whether or not to take part. We have provided you with information in this sheet which will enable you to make a decision and are very happy to discuss this further either in person or over the phone if you still have questions or concerns. If you decide to take part you are still free to withdraw at any time and without giving a reason.

Part 2

What would happen to me if I take part?
If you decide to take part then we will arrange a mutually convenient time to meet you and go through all the study procedures to make sure you understand them. We will then get you to sign a consent form to show you are happy to take part. You can still take part even if you only want to do some of the tests and not all of them. The visit would take place at your local District General Hospital (DGH) in the first instance. This research project does not require any lifestyle restrictions (e.g. dietary, drive, drink, taking part in sport).

Before the clinic visit we will send you a postal questionnaire which takes approximately 30 minutes to complete in your own time at home and bring with you to clinic. During the clinic visit which will last about 2 hours, we will take a short clinical history and do a standard examination. The physical examination will not require you to undress fully, and will be the same as what a neurologist would do in their everyday practice. We will get you to do some cognitive tests. This will involve some reading and writing tasks. We will also perform a smell test in a sample of participants as mild changes in the ability to smell can give us clues as to how the brain is working. After these are done, we will take a blood sample using a sterile needle from a vein in your arm and removes approximately 20-35ml (four to six teaspoons) of blood. This will be stored in our freezers to allow us to do the genetic and protein testing in the future. You will also be asked if you are willing to consider having an ultrasound scan of your brain during the clinic visit. This is a painless procedure and involves placing a plastic probe over your skull to measure changes within the deep part of the brain affected in Parkinson's (substantia nigra). This will take no more than 30 minutes, and it is entirely up to you to decide if you would like to have this done during the clinic visit. During the clinic visit, we will also give you information on how you can make a recording of your voice using a free telephone line or internet at home, and discuss the option of taking some recordings using a smart phone if you have one, to assess your speech and movement over a longer time period.

This is a longitudinal study which means we would like to follow-up all our participants to see if things change over time. We will therefore invite you to come for a repeat clinic visit and blood test after every eighteen months for the 5 year study duration. Ideally, we would also like to repeat the ultrasound scan in eighteen and thirty-six months time. However, this is entirely your decision, and if you agree would be done during your repeat clinic visits. We may continue to invite you back after this time if we can get further funding to continue with the study. Depending on results, some participants may also be contacted by a member of our research team following their clinic visit, and invited to take part in either a telephone interview or a face to face interview with the study doctor.

What are the potential risks of taking part?
The blood test is painful for a few seconds. There may be minor temporary bruising at the site.

There is always a possible risk of introducing infection into the skin or blood with any invasive procedure, but in practice the use of sterile single-use equipment makes this risk extremely remote. Any infection would be treated immediately with antibiotics in hospital. There are no risks associated with having the brain ultrasound scan.

What if you found an unexpected abnormality?
We do not intend to routinely feedback any of our results as there are no obvious advantages for you and some participants can be made anxious by knowing such information. If there is a strong family history of PD in your family and you would like to pursue the option of genetic testing, we can discuss referral to a local clinical genetics service for you and family members where appropriate. If we found anything of concern on our clinical tests we will discuss this with you so that you can seek appropriate referral and treatment via your GP.

What are the possible benefits of taking part?
There is unlikely to be any particularly direct benefit to you but you may feel that your participation will contribute to a greater understanding of the causes of Parkinson's Disease and why it varies among patients. We hope this will allow us to help PD patients in the future by developing new tests to diagnose PD earlier, designing better treatments and being able to predict the future disease course for someone with PD.

Expenses and payments
We are happy to reimburse any travel expenses that are due to visiting the John Radcliffe Hospital or your local District General Hospital as part of the research project. If you come by car we will use standard mileage costs.

What will happen if I don't want to carry on with the study?
You can withdraw from the study at any time without giving a reason. It will not affect your future care in any way. If for various reasons you feel unable to attend for the future study clinic visits, please let us know and we will also be able to offer you and your carer the alternative option of a brief telephone assessment instead. We would still like to use your blood samples and clinical information we have collected for future research, and, if you agree, we would like to maintain contact with your local GP/specialist to follow up on your progress. Any stored samples, ultrasound images or clinical information that can be identified as yours can be destroyed if you wish.

What if there is a problem?
If you have a concern about any aspect of this study you should speak directly to the study organiser (01865 234337, Dr Michele Hu). If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you can contact the University of Oxford Clinical Trials and Research Governance office on 01865 572221. The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

Will my taking part in this study be kept confidential?
If you agree to take part in this study, the study organiser Dr Michele Hu might occasionally need to see information about your past medical history either from your GP or other doctors

if this may be relevant to the research study. This would be done only with your approval and knowledge of your doctors.

All personal information collected about you would be kept strictly confidential. Your samples and results would be stored using a unique anonymous number so that your personal details can be removed. No one other than the research team will be able to link this number back to you, which we need to do to keep in contact with you. In addition, if you consent, information held by the NHS and records maintained by The NHS Information Centre and the NHS Central Register may be used to help contact you and provide information about your future health status. All results will be stored in a password-protected form. All samples will be stored in special secure premises. Responsible members of the University of Oxford or the Oxford Radcliffe Hospitals NHS Trust may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations.

Will my Doctor know that I will be taking part?
Your GP would be informed about your participation in the study if you agree.

What will happen to any samples, ultrasound images or clinical information I give?
The anonymised blood sample will be analysed by collaborators within the Oxford Parkinson's Disease Centre as part of this study. The blood sample will be processed to derive your DNA (or genetic code), serum which is used to measure specific proteins, and plasma which contains blood cells. You will have the option to consent to your anonymised DNA, serum and plasma being retained and used in future studies into Parkinson's and related degenerative conditions by our centre. You may also choose to consent to your anonymised DNA, serum and plasma being shared with researchers in other academic centres, and used for drug discovery, which may be commercially funded. You will not receive any direct commercial benefit in doing so. You will also be given the option of consenting to the storage and use of anonymised ultrasound images and clinical information we collect from you (for example measures such as your height, blood pressure and movement ability). You may also choose to consent to your clinical information being shared with researchers in other academic centres, and used for drug discovery, which may be commercially funded. You will not receive any direct commercial benefit in doing so.

None of the researchers in other centres will be able to identify you from these samples or clinical information as they will only have an anonymous code. We intend to keep the samples and clinical information indefinitely in case there are new developments that can help us to further understand and treat Parkinson's. However, you can ask us to destroy your samples, images or clinical information at any time.

What would happen to the results of the research study?
We hope that the results of this study will be suitable for scientific publication in biomedical journals, and for communication to patients via the Parkinson's Disease Society. The websites for the Oxford Parkinson's Disease Centre will contain updates about progress. We will also provide you with a summary of our overall results by sending you a regular newsletter.

Who is organising and funding the research?
The research has been organised by Dr. Kevin Talbot (Honorary Consultant Neurologist) and Dr Michele Hu (Consultant Neurologist) with other Oxford University scientists and in collaboration with Prof. Yoav Ben-Shlomo (University of Bristol). It is based in the Oxford University Department of Clinical Neurology. The financial support for the study has come from the Parkinson's Society UK.

Who has reviewed the study?

The Berkshire Research Ethics Committee has reviewed the study. An external review process run by the Parkinson's Disease Society reviewed the scientific basis of the study before we were awarded our funding.

Contact for further information

Please contact the study organiser:
Dr Michele Hu, Consultant Neurologist
Department of Clinical Neurology, West Wing Level 3
John Radcliffe Hospital, Oxford OX3 9DU
Tel 01865 234337 or michele.hu@ndcn.ox.ac.uk

Or
Stephanie Gallehawk, Research Nurse
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Thank you for reading this sheet and considering whether you would like to help our research.