Relative of People with Parkinson's Participant Information Sheet

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Study: RAPSODI GD (Remote assessment of Parkinsonism supporting ongoing development of interventions in Gaucher disease)
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Introduction

We would like to invite you to take part in a research study. This is an information sheet which you should read before making a decision on participating in the study. Should you have any further questions please email the research team at rapsodi@ucl.ac.uk or make a request for somebody to call you at a convenient time.

You have been given this information sheet because you may be related so someone who has Parkinson's disease and we would like to offer you the opportunity to participate in a study which we hope will enhance our understanding of the disease. The aim of the study is to understand better the very earliest symptoms of Parkinson's disease so that in the future we can treat those with these early symptoms before the nerve cells are damaged. This does not mean you are at risk of developing Parkinson's, but studying people who are related to individuals with Parkinson's Disease helps us understand how some genes function

We are asking for your help because we would like to understand exactly what these earliest symptoms are and when they occur. We would like to assess you on a yearly basis for these symptoms. We shall then compare these results with a group of people who carry a gene (called *GBA*) who have an increased risk of developing Parkinson's disease, to see if we can predict whether they will develop it. We would like also to test you for this gene and another gene which increases Parkinson's risk, called LRRK2.

Part 1 of this information sheet will explain the purpose of the study and our research into Parkinson's, the GBA gene and a group of people who are known carriers of this gene, who have a condition called Gaucher disease.

Part 2 gives you more detailed information about the process of the study and a brief description of what taking part involves for you and potentially other family members.

Part 1.

Why do we want to diagnose Parkinson's disease earlier?

One reason we don't yet have a cure for Parkinson's disease is because the movement symptoms of the condition only appear when 50% of the nerve cells have already been lost.

We believe the nerve cells begin to be affected many years before symptoms appear but we don't know enough yet about these early stages.

If we could identify people at risk earlier – before the movement symptoms appear – we would be in the best possible position to slow, stop or even reverse Parkinson's disease.

How could we identify people at risk of Parkinson's disease before the symptoms appear?

Ongoing research suggests that some symptoms may occur several years before the movement problems of Parkinson's disease appear.

Many older people probably experience some of these problems at some stage. But finding people who experience several of these issues together may help us identify those at a higher risk of Parkinson's disease.

About Gaucher disease

What is Gaucher disease?

Gaucher disease is a genetically inherited, enzyme deficiency disorder. Symptoms range from mild to severe and can appear at any time, from infancy to old age. They may include anaemia, fatigue, easy bruising and a tendency to bleed. Enlargement of the spleen and liver may also occur as well as bone pain, demineralisation and fractures.

People with Gaucher disease lack sufficient activity levels of an enzyme called glucocerebrosidase. This enzyme helps the body break down worn-out cells and as a result, a fatty substance called glucocerebroside accumulates in the spleen, liver, bone marrow and sometimes in the nervous system.

Effective treatments are available for some manifestations of the disease; however there are currently no treatments available for the damage which Gaucher disease causes to the brain and for some of the other forms of Gaucher disease.

For more information visit the Gauchers Association's website at: www.gaucher.org.uk .

How is Parkinson's disease related to Gaucher disease?

In the 1990s doctors noticed that a larger number of family members of patients with Gaucher disease were developing Parkinson's disease than would normally be expected. These family members were found to be carriers of the GBA gene. Research has established that both those affected by Gaucher disease (carrying two copies of the GBA gene) and those who possess one copy of this gene have a 5-30% chance of developing Parkinson's disease by the age of 80.

2-10% of patients with Parkinson's within the general population carry a copy of the Gaucher gene and this figure may be even higher amongst certain groups such as within the Ashkenazi Jewish community. This makes carrying the Gaucher disease gene the most significant genetic risk factor for Parkinson's disease, across the whole population. At present there is no effective treatment for Parkinson's disease caused by the GBA gene. The aim of this research is to discover more about the disease course so in the future we can give effective treatments as early as possible.

Part 2

About RAPSODI GD

What is the RAPSODI project?

RAPSODI is a study designed to identify the very earliest stages of Parkinson's disease associated with the GBA gene. Our laboratory is in the process of developing a number of potential treatments to stop the early loss of these nerve cells within the brain and so prevent

the disease developing. To test whether these treatments work will require many patients in the earliest stages of developing Parkinson's disease, who will be given the drug to test its effectiveness in a clinical trial. The end objective of the study is to provide information which will allow the identification of those carriers of the Gaucher gene with early signs of Parkinson's disease, so when a potential drug to treat Parkinson's disease associated with Gaucher disease becomes available, we are able to test its effectiveness on this group. We believe that any treatment for Parkinson's caused by the Gaucher gene may also be able to treat Parkinson's disease in general.

What will being in the study involve?

- Once a year we will ask you to log in to our internet portal and complete an assessment. This will take about an hour and will involve answering a number of questions and carrying out some interactive tests which will assess your response times and memory.

- We will ask for permission to access your medical records to discover whether you have been previously tested for the GBA gene and if so what the result was.

- The first time you take these assessments we'll ask you to send us a saliva sample by post. This will be used to carry out genetic testing for the GBA gene and the LRRK2 gene, both of which increase the risk of developing Parkinson's disease. You will be able to choose whether you wish to be told the results of these tests.

- Every two years we will ask you to complete a booklet testing your sense of smell this will be sent through the post with a return stamped address envelope.

What's new about the RAPSODI project?

RAPSODI is innovative because it will be conducted almost entirely online.

This means participants do not even need to leave their homes to take part, and we can process lots of information quickly, cheaply and efficiently.

We hope that using the Internet will mean more people take part and potentially benefit from its results.

Taking part in RAPSODI GD

Who can take part in the study?

In terms of people who have a diagnosis of Parkinson's disease, we are looking to recruit anyone with a diagnosis of Parkinson's within the catchment area of the Royal Free Hospital, their spouses and in some cases their first degree family members (this means where possible, parents, brothers and sisters and children if over the age of 18)

Who cannot take part in the study?

1. People diagnosed with a movement disorder other than Parkinson's disease and those with dementia, stroke or motor neurone disease.

2. Certain drugs can contribute to or cause Parkinson's disease-like symptoms. We may exclude some participants if we think their previous or current medication may affect the results of the study.

Do I have to take part in the study?

No. There is no obligation to take part in the study and the decision to participate rests entirely with you.

You also have the right to withdraw from the study at any point and are not obliged to provide a reason.

If you do choose to participate, please read the information on these pages carefully. You will then be asked to read and complete a consent page before registering on the website www.rapsodi.org.uk

I'd like to take part. What do I have to do?

If we have contacted you directly to ask you to enrol in the study you will have received a 'token' by e-mail. Simply log in to our portal using that token and follow the instructions on the website www.rapsodi.org.uk

If you would like to be considered but have not been contacted by the research team, please fill in the form on the website and you will be contacted by a member of the research team.

Will I discover whether I am a carrier of the Gaucher gene if I don't already know?

This will be up to you. We will ask you upon enrolment in the study whether you would like to be given the result of a genetic test for this gene if you do not already know your status.

You should think carefully about this decision. Those who carry one copy of the gene have a 50% chance of passing it on to their children. If your partner also possesses one copy of the

Gaucher gene (1% risk of the general population and 4% of the Ashkenazi Jewish community) there is 25% chance that your child may develop Gaucher disease, which in many cases is a treatable condition. There is also a 5 – 30 % risk of developing Parkinson's disease associated with carrying one or two copies of the gene. Carriers of the gene may have siblings and parents who are also carriers, therefore the decision may have an impact not just on you but on others in your family. If you would like to discuss any of this we are available to talk to you about this in more detail. The study team can be contacted at rapsodi@ucl.ac.uk

Will I discover whether I am a carrier of the LRRK2 gene if I don't already know?

Again we will ask you whether you would like to know your LRRK2 status upon enrolment in the study.

You should think carefully about this decision. Those who possess the LRRK2 gene have a 70% risk of developing Parkinson's disease by the age of 80. Carriers of the gene have a 50% chance of passing it on to their children. Carriers of the gene may also have siblings and parents who are carriers, therefore the decision may have an impact not just on you but on others in your family.

Will I be contacted directly by the research team when the tests are completed?

Maybe. We will contact certain participants who have taken part in the research by email or telephone. The purpose of this contact is to confirm the information you have provided. We may ask if we can either come and visit you in your home, or pay travel expenses for you to visit a local neurologist, so that a specialist can examine you in order to gather more detailed data

Collection of and storage of biological samples

On the basis of the data we collect, we may ask some participants to provide samples of urine, blood or in a few cases cerebrospinal fluid. We will not ask you to do this any more frequently than once every two years.

Some samples like urine and pin prick samples of blood can be collected by yourself in your own home. Others, like some blood tests will be taken by a nurse, doctor or research associate, either within your home or at our research sites at the Royal Free

or Addenbrooks hospitals. If we ask and you agree to donate cerebrospinal fluid this will be collected by a doctor at the Royal Free or Addenbrooks hospitals.

Not wanting to give any of these samples will not affect your ability to participate in the rest of the study.

Participants may also be invited to donate biological samples to the study in the form of saliva, blood and urine. Increasingly we are recognising that there are chemicals and compounds contained in blood and urine that may further define an individual's risk of future Parkinson's disease.

Taking a blood sample may cause mild pain and carries a small risk of bleeding, bruising, or infection (in less than 1% of people). Members of the research team will collect blood samples. Approximately 30ml of blood will be taken (30ml is equivalent to 2 tablespoons). We may ask participants, by pricking their finger, to collect a very small amount of blood themselves and deposit it on a card.

Participants will collect their own urine. 30ml (two tablespoons) of urine will be collected

Saliva will also be used to carry out genetic studies assessing Parkinson's disease risk.

All samples will be labelled with a unique number so as to not identify the participant. Samples will be transported to the laboratories of University College London for storage and analysis. Additional tests may be requested from external companies and institutions if required.

You will continue to have access to the general results of the study, including analyses of samples and data, when the analyses are reported in the medical literature. We will keep you informed of publications arising from the research.

How long will I be involved in the study?

We envisage that this study will run for up to 25 years. Although you will not be under any commitment to remain in the study for the whole duration, we hope that you will be able to make yourself available for assessments (typically an hour) every year. This is because the primary value of data we collect will be that it shows how these symptoms evolve with the development of Parkinson's disease over time. The overall aim of the study is not to predict each individual's risk of developing Parkinson's but to look for patterns in the bigger community. But by predicting Parkinson's earlier we will be able to offer help to everyone more at risk of developing the condition.

Will my involvement be confidential?

Yes. All information you provide will be kept strictly confidential and will not be personally identifiable.

Our website and all associated web applications used in this study are compliant with the international standards of data protection and data handling.

What are the benefits in taking part?

You will receive no payment for your assistance with this study.

By taking part in this study you will be helping us find ways of diagnosing Gaucher associated Parkinson's disease at the earliest possible stage. This could potentially pave the way to better treatments and a cure.

We envisage a viable therapeutic intervention to prevent Gaucher associated Parkinson's disease should become available in the coming years. We believe this treatment may also be able to treat those with Parkinson's disease not caused by the Gaucher gene. Recruitment for any clinical trial of it is likely to be drawn from participants of RAPSODI. As a study participant you may be eligible for selection in any such trial.

What are the possible risks of taking part?

There are no major anticipated risks in being part of this study. The information we collect will not be personally identifiable and will be entirely confidential.

If we ask you to donate blood there is a risk of bruising at the puncture site. Those who undertake a lumbar puncture are at risk of headache as well as infection and bruising at the entry site. If we would like you to undertake a lumbar puncture these risks will be discussed in more detail at the time: you will be under no obligation to have this procedure and it will not affect your ability to participate in the rest of the study.

What happens if something goes wrong?

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this. In the unlikely event that you are harmed by taking part in this study, compensation may be available.

If you suspect that the harm is the result of University College London or the hospital's negligence then you may be able to claim compensation. After discussing with your research doctor, please make the claim in writing to Prof. Tony Schapira who is the Chief Investigator for the research and is based at Royal Free Hospital. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

How have patients and public been involved in this study?

Representatives of the Gauchers Association and patients with Parkinson's including carriers of the GBA gene were involved in the design and running of this study

Who has reviewed the ethical aspects of the study?

Ethical aspects of this study have been reviewed by the London – Queen Square research ethics committee (reference number 15/LO/155)

Will my GP be notified of my participation in the study?

We will notify your GP that you have participated in the study.

What if I have further questions?

If you would like any further information about patterns of inheritance you can find this at:

http://www.genesinlife.org/genetics-101/how-does-genetics-work/main-inheritance-patterns

Should you have any further questions please request for a research team member to call you, email us at rapsodi@ucl.ac.uk