Relative/spouse of people with Gauchers 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. If you should 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 a relative of yours carries one or two copies of a gene which is associated with a condition called Gaucher disease. This means it is possible that you could be a carrier of this gene.

Part 1 of this information sheet will explain the purpose of the study and our research into Parkinson's, the GBA gene and 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

Gaucher disease is a genetically inherited condition, where the mechanism responsible for getting rid of a waste product of the body's cells called glucocerebroside does not work, leading to its build up in cells at different sites within the body. This can lead to anaemia, fatigue, easy bruising and a tendency to bleed. Enlargement of the spleen and liver may also occur. The condition is present amongst the whole population but is more common amongst the Ashkenazi community. . You may have already have been tested for this gene following the diagnosis of your relative with Gaucher disease.

Only people with two copies of the gene (one from each parent) will develop Gaucher disease, however, those with one copy (known as a carrier) may pass it on to other family members. This means you could be unaffected by the gene as a carrier and still be at risk of passing it on to your children.

In recent years it has emerged that an alteration in one or both copies of the Gaucher gene results in a higher than average risk of developing Parkinson disease. Carriers of the Gaucher gene possess around a 5-30% chance of developing Parkinson disease by the age of 80 compared to 3-4% amongst the general population.

Remarkable progress has been made towards a treatment of Parkinson disease and the understanding of the processes that cause it. Promising potential treatments to slow down or stop the progression of Parkinson disease caused by the Gaucher gene will hopefully emerge in the near future.

Because there is a possibility that you have an alteration in this gene we plan to contact you in the coming weeks to offer you the opportunity to participate in a study we are running. The study is looking at the link between carrying Gaucher gene and developing Parkinson disease. The aim of the study is ultimately to identify those people who carry the Gaucher gene who are at risk of Parkinson disease, so in the future we can give them a drug to prevent Parkinson disease developing.

Your selection to take part in this study does not mean that you have Parkinson's disease or are developing it. You are under no obligation to take part in the study.

Below is some information about Parkinson's disease, Gaucher disease and the study, for you to read if you would like to.

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About Parkinson's disease

What is Parkinson's disease?

Parkinson's disease is a neurological condition.

One person in every 500 has Parkinson's disease. That's about 120,000 people in the UK.

Most people who get Parkinson's are aged 50 or over but younger people can get it too. One in 20 is under the age of 40 when first diagnosed.

People with Parkinson's don't have enough of a chemical called dopamine in their brains, because some of the nerve cells that produce it have been lost.

Without dopamine people can find that their movements become slower so it takes longer to do things.

The loss of nerve cells in the brain causes the symptoms of Parkinson disease to appear, which include tremor, rigidity and slowness of movement.

There's currently no cure for Parkinson's, however, there are effective drugs to control many of the symptoms. As a result many people with Parkinson disease live comfortable and productive lives, and are able to continue working.

How is Parkinson's disease diagnosed?

At present, the diagnosis of Parkinson's is made clinically. This means that the doctor examines the person and takes a detailed history of their symptoms.

Sometimes brain scans are used for uncertain cases but there is currently no conclusive test for Parkinson disease.

The early signs of Parkinson disease may include problems with movement like tremor, stiffness, slowness of movement, difficulties with handwriting and loss of facial expression

and memory problems. Other symptoms, not related to movement, can also be present like loss of sense of smell, depression, and constipation and sleep problems.

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

One reason we don't yet have a cure for Parkinson disease is because the movement symptoms of the condition only appear once >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 disease.

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

Ongoing research suggests that some symptoms may occur several years before the movement problems of Parkinson 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 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 the 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 disease than would normally be expected. These family members were found to be carriers of the Gaucher gene. Research has established that both those affected by Gaucher disease (carrying two copies of the affected gene) and those who possess one copy of this affected gene have a 5-30% chance of developing Parkinson disease by the age of 80.

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

Part 2 - About RAPSODI GDWhat is the RAPSODI GD project?

RAPSODI GD is a study designed to identify the very earliest stages of Parkinson disease associated with the Gaucher 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 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 disease, so when a potential drug to treat Parkinson disease associated with Gaucher disease becomes available, we are able to test its effectiveness on this group.

What will it 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 Gaucher 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 Gaucher disease gene (if you have not already had this done) and another gene known to increase the risk of developing Parkinson

disease called LRRK2, which we know is more common in communities where Gaucher disease is prevalent.

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 GD project?

RAPSODI GD 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?

We are looking for people who have one or two copies of the Gaucher gene or those who are first degree family members (parents, siblings and children) and spouses of people who have one or two copies of the Gaucher gene. Those under the age of 18 cannot participate; however, we may invite the relatives of carriers of the Gaucher gene who are younger than 18 to on enrol the basis that they may be also carriers of the Gaucher gene.

Who cannot take part in the study?

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

2. Certain drugs can contribute to or cause Parkinson 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.

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. Simple log in to our portal using that token and follow the instructions on the website.

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 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.

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

Again upon enrolment 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 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 find out my predicted risk of Parkinson disease?

Ordinarily people involved in this pilot study will not discover their individual risk score.

This is one of the first studies of its kind. So whilst our tests suggest some people may have an increased risk, at this stage we cannot be certain the scores have any meaning.

The only exceptions to this will be if a viable potential treatment for Gaucher associated Parkinson disease needs to be tested and your are deemed to be at risk. In which case we will reveal your risk score in order that you can make an informed decision about whether you want to take part in a clinical trial to test whether the drug works.

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.

If you are contacted, this does not necessarily mean that you are at higher risk. We will contact people with a range of scores to ensure the information we are gathering is accurate.

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 Addenbrookes hospitals. If we ask and you agree to donate cerebrospinal fluid this will be collected by a doctor at the Royal Free or Addenbrookes 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 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 (t tablespoons) of urine will be collected

Saliva will also be used to carry out genetic studies assessing Parkinson 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 in those developing Parkinson disease over time.

Clinical visits

Those participants that are invited to undergo clinical examinations will be contacted after data have been initially analysed. A member of the research team will offer to travel to examine you in your own home or offer to cover travel expenses for you to attend the Royal Free or Addenbrookes hospitals. They will explain all the tests and why we are doing them when we contact you. They may request that the examination be recorded on video, so that a senior movement disorders specialist can verify the examination findings. A sample of handwriting will also be collected.

If during a clinical visit we find that you have a diagnosis or clinically significant signs of Parkinson disease, we will inform you in person and write to your GP so that you can be treated as indicated.

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 disease at the earliest possible stage. This could potentially pave the way to better treatments and a cure.

Should, as we envisage, a viable therapeutic intervention to prevent Gaucher associated Parkinson disease becomes available in the coming years, recruitment for any clinical trial of it is likely to be drawn from participants of RAPSODI GD. 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 the 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 Gaucher association including carriers of the Gaucher gene were involved in design 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 you 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.geneticseducation.nhs.uk/mededu/modes-of-inheritance/single-gene-conditions/autosomal-recessive-conditions

How will you use my information?

Royal Free London NHS Foundation Trust is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Royal Free London NHS Foundation Trust will keep identifiable information about you for up to 25 years.

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

You can find out more about how we use your information by contacting the study team at **rapsodi@ucl.ac.uk**.

Royal Free London NHS Foundation Trust will collect information from you for this research study in accordance with our instructions.

NHS 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 Royal Free London NHS Foundation Trust and regulatory organisations may look at your medical and research records to check the accuracy of the research study.

The Royal Free Hospital will pass these details Royal Free London NHS Foundation Trust along with the information collected from you. The only people in Royal Free London NHS Foundation Trust who will have access to information that identifies you will be people who need to contact you to discuss aspects of the study (e.g. to deliver genetic results) or audit the data collection process.

The Royal Free Hospital will keep identifiable information about you from this study for up to 25 years.

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