Austin Health

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Participant Information and Consent Form (Person Responsible)

Version 15.0, Dated 17 May 2018

Project No. H2007/02961

Full Project Title: Genetic Basis of Epilepsy

Principal Researchers: Prof Ingrid Scheffer and Prof Sam Berkovic

1. Introduction

You are invited to consider a study into the genetics of epilepsy on behalf of the participant. This is because they, or someone in their family, has experienced seizures, or a related condition such as intellectual disability, a speech and language problem or a structural abnormality of the brain. This research project aims to gain a better understanding of the genetic relationships between different types of epilepsy and these related conditions, and improve understanding of the mechanisms that cause epilepsy.

This Participant Information and Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you consent to the participant taking part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is entirely voluntary. If you don't wish the participant to take part, they don't have to. They will receive the best possible care whether they take part or not.

If you do want the participant to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- understand what you have read;
- consent to the participant taking part in the research project;
- consent to the research processes that are described;
- consent to the use of the participant's personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research project?

Epilepsy affects at least 5% of the population at some time in their lives. We know that some types of epilepsy are inherited or have a genetic cause, some types may be the result of an illness or injury, while in some people it is not clear what has caused the seizures. Our previous studies have identified specific genes causing epilepsy. However inheritance of epilepsy often involves many genes.

In many families there is only one person with epilepsy, while in others, a number of people may have seizures. By studying individuals with no family history of epilepsy and also families where more than one person has experienced seizures, we hope to gain a better understanding of the genetic relationships between different types of epilepsy and improve understanding of the mechanisms that cause seizures. This may eventually help with new treatments, better genetic counselling and better diagnostic tests. Studying twins is also a very important part of epilepsy research, because they can help us understand the role of genetic and other factors in the development of epilepsy.

In some individuals or families structural abnormalities of the brain (where parts of the brain have not formed normally) or speech and language disorders may occur with or without seizures. In these families it is thought that there may be a connection between epilepsy and these disorders. We now know of some families where the main finding is a structural abnormality of the brain, or a speech and language difficulty, rather than seizures. We will also study these families as part of this project to further explore how these disorders are related.

So far several thousand people with epilepsy or a related disorder and their family members have participated in this project. We hope that many more will participate over the coming years as each individual adds more to our understanding of epilepsy.

This research has been initiated by Professor Ingrid Scheffer & Professor Sam Berkovic and has been funded by research grants.

3. What does participation in this research project involve?

If you agree to the participant participating in this research project we will contact you and arrange to interview you and them (if appropriate) either over the telephone or in person. We are interested in checking the details of any seizure or seizure-like events experienced. Birth history, a history of any head injury and other neurological disorders is also taken as this may be relevant. The interview usually takes between 20 minutes and 1 hour for each person. We would also like to know the results of any genetic testing the participant has had. With your permission the researchers will access their medical records to obtain relevant information.

Blood samples of up to 2 tablespoons (40ml) will be requested with the aim of looking for the genes that cause epilepsy. For twins who are the same sex, some of the blood will be used to test whether or not they are identical. This sample is separate from any routine blood tests requested by other doctors and it can be collected at a time and location convenient for the participant. It can be collected when the participant visits the hospital for a clinic appointment or we can arrange for it to be taken at a local pathology collection centre. In some cases a repeat sample may be requested for additional tests.

If it is not possible to collect a blood sample from the participant we may request a sample of saliva instead. This is collected by spitting into a tube that we will provide. There are some tests that can only be performed from a blood sample so a saliva sample is not suitable in all situations. In rare cases where blood or saliva would be difficult to collect a scraping of cheek cells may be used.

You do not have to agree to a blood or saliva sample being collected. Some people will still be able to participate in other parts of the research, such as completing an interview, however in other cases (for example if the participant is the only person in their family who has had seizures) this may mean that they are unable to participate in the study.

You and the participant will not be paid to participate in the research project and you do not stand to gain financially from participation even if useful scientific discoveries are made.

Family studies

In family studies both affected and unaffected family members may be interviewed. If the participant has not had seizures, we check to ensure they have not experienced any subtle, unrecognised seizure activity (some types of seizures are very quick, or do not involve convulsions). Sometimes an unaffected person may also be asked to have one of the additional tests described below. This is because occasionally abnormal findings can be seen in a person who has never had a seizure or the family member may serve as a control for comparison with affected family members.

We may ask to involve the participant's extended family as part of this research. If so, we will ask you to speak with their relatives about the study first. When we contact the relatives, we will discuss the study in detail, then send them a copy of this information sheet and our consent forms for them to consider. The participant family can still participate in the study, even if their extended family does not wish to. If you are not happy to contact the participant's relatives, we may contact them directly with your permission.

Twin studies

If the participant is a twin we would like to interview both twins and their parents (if available) to obtain a developmental and birth history and a family tree. In addition we would like to see the twins to conduct a neurological examination and EEG. We will also take a photograph which will be used to compare their features. Photographs will not be published under any circumstances without your written permission.

Possible additional tests

In rare instances, we may ask the participant to have additional tests done to help us fully understand the seizures or related disorder in their family. If any of these tests are required, they will be explained to you in detail at the time and you can decide whether or not you agree to have them done. Any tests the participant has for research will be paid for from our research grants. Additional time will be necessary depending on which tests are involved, generally less than two hours.

We may ask the participant to have an EEG (electroencephalogram - a brain wave reading), and a neurological examination. The neurological examination will include checking reflexes and strength and a screening examination of the eyes.

Some participants may be asked to have a Magnetic Resonance Imaging scan (MRI), where pictures of the brain are taken, or an EEG-fMRI. This is where an EEG is recorded whilst having an MRI.

If the participant or a family member has experienced difficulty with their speech or language, we may ask them to have a speech and language assessment. This may involve an assessment of their understanding of language, their spoken language, and a hearing screen. In specific cases neuropsychological testing may be requested. This involves completing some written and verbal tasks so that different aspects of the participant's learning can be assessed. We may ask to record the participant's doing some of the tasks on a video. If you are happy for us to do this, you will be asked to sign a separate consent form.

In some cases the underlying problem causing the seizures may also affect how messages are passed along nerves in other parts of the body (for example to arms and legs). We may ask the participant to have specialised neurophysiology tests of the nerve function to their arms and legs, or an ECG (heart trace). Some people with epilepsy may also experience difficulties with sleep, which may be due to changes in their breathing or heart rate. To help understand this further we may ask to measure the oxygen level in the participant's blood while they sleep. This is done by wearing a small plastic clip on their finger and will usually be done over one or two nights in the participant's home. The clip will be given to you at the participant's clinical appointment where you will be shown how to clip it to their finger. We may also ask the participant to wear a wrist band for several days that monitors physical activity and gives us further information regarding quality and quantity of sleep. Once completed we would appreciate if you return the clip and/or wrist band to us.

4. What will happen to the participant's test samples?

The participant's blood, saliva or cheek cell sample, labelled with their name, date of birth and diagnosis will be sent to our laboratory and the DNA (genetic material) extracted. The DNA sample will be stored in a coded form with the key to the code kept on a password-protected database that is only accessible to members of the research team. In some cases the serum from the blood sample may also be used to look for specific antibodies and be used in other biochemical tests that might help us understand the cause of the participant's seizures.

In specific cases we may ask if you are happy for us to use some of the participant's blood sample to grow a culture of cells. This will enable us to do more tests than we can with a single blood sample. We may use some of the participant's blood sample to make "induced pluripotent stem cells" (iPS cells). iPS cells are a new technology that allows us to produce specific cell types such as brain cells in a laboratory dish. This allows us to study the participant's genetic variation in cells relevant to epilepsy. We will tell you if we would like to grow some cells from this blood sample and what we would like to use the cells for, and this will only be done with your consent.

The DNA sample will be stored by:

Professor Sam Berkovic & Prof Ingrid Scheffer
Department of Medicine
University of Melbourne
Austin Health
Heidelberg VIC 3084
Telephone: (03) 9035 7330
Fax: (03) 9035 7307

The participant's DNA sample will be used to investigate changes in genes that may be causing the seizures or related disorder in them or their family. This may involve looking for changes in specific genes, or it may involve looking at a large number of genes and comparing the information in the participant's genes with other people in their family or other people with similar types of epilepsy.

As this is an ongoing research study, we would like to store the participant's DNA sample for the duration of the study so we can test it when new genes for epilepsy are identified. However, if this

project ceases the DNA sample will be destroyed. Also, you can request that the participant's DNA sample be destroyed at any time by contacting us.

We work closely with other research groups within Australia or internationally who are also trying to identify genes that cause seizures or related disorders, or who are trying to understand how the genetic changes cause seizures. This means we may send some of the participant's DNA sample to another research group. We would routinely send their name with the DNA sample to ensure sample identification so that we can tell you if there are any important results. We may also send details about the type of seizures they have had and other relevant medical history or test results to assist interpretation of further testing. All collaborators are strictly bound by confidentiality requirements.

In recent years, large databases of genetic sequences have been set up to help researchers. For some of our collaborating projects, the funding bodies (such as the National Institutes of Health in the US) prefer that de-identified genetic data obtained be shared with other researchers to bring greater benefits to society. In some cases, de-identified genetic information from the participant's DNA sample may be made available to researchers working separately from us at other hospitals or universities for use in research investigating the genetic causes of epilepsy and related conditions. There is unlikely to be any direct benefit to the participant from this. Their age, gender and brief information about the participant's seizures may be included with the genetic data, but no identifying information will be included. However, their genetic information is unique to them alone and therefore there is some risk of lack of confidentiality. For example, people not involved with our study who have information about their DNA (e.g. researchers from another study they have taken part in) could potentially identify them by comparing the genetic data they have to the information we make available. We believe this is unlikely to happen, but you do not have to agree to the participant's de-identified genetic information being released to researchers who are working independently from us, and you have the option to indicate this specifically on the consent form.

The participant's DNA will not be used for any purpose other than for the study of genes thought to be relevant to epilepsy and related conditions and to determine the zygosity of same sex twins (whether the twins came from the same or different eggs) and their sample will not be released for other uses, except as described above, without your specific written consent.

Rarely, genetic analyses on families reveal unexpected results, such as the discovery that a person thought to be a parent is not the true biological parent. This information would not be revealed to the participant or their family.

If the participant would like to discuss any personal issues or requires independent genetic counselling before deciding whether to participate in this study, or as a result of their participation in this study, this can be arranged by speaking to one of the research staff. The independent counselling would be free of charge and is provided by specially trained staff from the Genetic Health Services Victoria or the equivalent service interstate.

5 . What are the possible benefits?

We cannot guarantee or promise that the participant will receive any benefits from this research, however possible benefits may include identifying the genetic cause of seizures in their family which could assist in their diagnosis and treatment, or helping to understand the risk of future generations developing seizures or related disorder. In most cases this will not change the treatment the participant receives from their doctor, so it is possible that there will be no clear benefit from their participation in this research. Genetic results may take many years and in some cases we may never find meaningful results.

6. What are the possible risks?

Possible risks, side effects and discomforts include:

- Having a blood sample taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel, or the spot from which blood is taken could become inflamed. Rarely, there could be a minor infection or bleeding. If this happens, it can be easily treated.
- Magnetic Resonance Imaging (MRI) is a computerised scan that provides a 3-dimensional picture of the inside of the body using a strong magnetic field. A MRI scan is performed like a CT scan. It is

performed in a large, tunnel-shaped machine but it does **not** use X-rays. The MRI uses radio frequency waves, like those in an AM/FM radio, and a powerful magnet. The space inside the MRI scanner is quite confined and consists of a long, open cylinder that may produce feelings of claustrophobia or unease from being in a confined space. The MRI scanner is noisy while it is operating so the participant will wear earplugs or earphones to minimise the noise, the examiners talk with them via an intercom throughout the procedure in case they require anything. These scans are painless and the participant is required to remain still during the procedure. **The participant must not have any metal objects on or in their body, for example, brain aneurysm clips or a pacemaker to be able to have a MRI scan.**

- Some people may find it distressing to receive information about their genetic make-up and future health, or the risk of having a child with seizures or a related condition in the future.
- There is the potential that genetic information given to families could affect their ability to obtain life and health insurance or employment opportunities.

There may be additional risks that the researchers do not expect or do not know about.

7. Can the participant have other treatments during this research project?

Participation in this research project will not affect any treatments or medications recommended to the participant by their doctor.

8. Does the participant have to take part in this research project?

Participation in any research project is voluntary. You do not have to agree to the participant taking part. If you decide to allow them to take part and later change your mind, you are free to withdraw the participant from the project at any stage. Your decision whether to consent to the participant taking part or not taking part, or to taking part and then withdrawing, will not affect their routine treatment.

9. What if I withdraw the participant from this research project?

If you decide to withdraw the participant from the study, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to inform you if there are any health risks or special requirements linked to withdrawing.

If you decide to leave the project, the researchers would like to keep the personal and health information about the participant and their blood or saliva samples that have been collected. This is to help them make sure that the results of the research can be measured properly. If you do not want them to do this, you must tell them when you notify a member of the research team that you would like to leave the project.

10. Could this research project be stopped unexpectedly?

We expect this research project will continue for many years. However it may be stopped unexpectedly or some aspects of the project may be stopped if we are unable to obtain ongoing research funding.

11. How will I be informed of the results of this research project?

If we find a change in the participant's DNA that is thought to cause seizures, we will write to you to let you know we have some results, then you have the option to contact us for further information. If you choose to receive the results, we will explain what the results mean and give you the opportunity to ask any questions you may have. It is important to remember that we may not always know what the results mean. If you or the participant would like to discuss the results further with someone separate from the study we can arrange for you to see an independent genetic counselor.

Any changes found in the participant's DNA sequence may not be the only cause of their seizures or related disorder and we may not be able to predict accurately if their epilepsy could be passed on to other generations of their family. It may take years of research before we can be clear about the nature of the genetic change and its effects. If you would like to have results from the research passed on to others, for example the participant's local doctor, this can be arranged. We will not pass personal information between family members.

In family studies, if the participant is found to be an unaffected carrier of a genetic change associated with seizures, or have an unusual EEG or MRI result, we will decide whether to disclose these results on a case-by-case basis. We will not automatically tell you of these results, as their significance in an

unaffected person may not be understood. If any such findings are likely to have health implications for the participant or their family, we can arrange for them to see a neurologist associated with this study or we can refer them to see a specialist in your local area who can discuss the results.

Each year we send a newsletter to all of our research participants with general information about the results obtained from this project and about the work we are doing. These results may not be directly applicable to the type of seizures seen in the participant's family.

12. What else do I need to know?

What will happen to information about the participant?

Any information obtained in connection with this research project that can identify the participant will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law. The information will be stored in a locked facility under the supervision of Prof Scheffer and Prof Berkovic, and/or in a digital form on a secure computer network. We are obliged to store the participant's records safely for at least 7 years, but they may be stored for longer if this project continues beyond that time.

Information about the participant may be obtained from their health records held at this, and other, health services for the purposes of this research.

In any publication and/or presentation, information will be provided without any identifying details such as names or dates of birth. However, when our research findings are published in medical and scientific journals we may include family trees and detailed medical information. Such information may make it possible for someone who knows the participant well, such as a family member, to identify them and their medical information. This is unlikely but the possibility needs to be acknowledged.

Information about the participant's involvement in this research project may be recorded in their health records.

How can I access the participant's information?

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about the participant. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named at the end of this document if you would like to access the participant's information.

What happens if the participant is injured as a result of participating in this research project?

If the participant suffers an injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost if they elect to be treated as a public patient.

Is this research project approved?

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Austin Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

14. Who can I contact?

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctors on (03) 9035 7330 or (03) 9035 7344 or any of the following people:

Clinical contact:

Prof Sam Berkovic	Role: Principle Researcher	Telephone: (03) 9035 7093
Prof Ingrid Scheffer	Role: Principal Researcher	Telephone: (03) 9035 7344
Dr Saul Mullen	Research Fellow/Neurologist	Telephone: (03) 9035 7330

Research Assistants:

Rosie Burgess	- (03) 9035 4199	Caitlin Bennett	- (03) 9035 7205
Alix McDonald	- (03) 9035 7132	Anne Harbison	- (03) 8344 3663
Katja Boysen	- (03) 9035 7136	Amy Schneider	- (03) 9035 7349
Olivia Henry	- (03) 9035 7298	Georgie Hollingsworth	- (03) 9035 7104
Allison Hinchcliffe	- (03) 9035 7299		

For complaints:

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Complaints contact person

Position	Complaints Officer
Telephone	(03) 9496 4090 or (03) 9496 3248
Email	ethics@austin.org.au

Austin Health

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Human Research Ethics Committee

LIST OF QUESTIONS FOR POTENTIAL PARTICIPANTS TO ASK INVESTIGATORS ABOUT RESEARCH INVOLVING GENETIC TESTING

You have been invited to participate in research involving genetic materials.

You may be interested in asking the researcher these questions after you have looked over the written information, and before you consent to be involved in the research project.

1. What do you think you might find out in this research?
2. Will I be able to get my results?
3. Who else will get a copy of my results?
4. If I choose to find out the results, what will this mean to me?
5. If I agree to participate what arrangements have been made for my independent counselling and who is the independent counsellor?
6. How might the results affect my family?
7. If I choose to get the results, how long will it be before I get them?
8. If I choose to get the results, who will help me to understand what they mean for my family and I?
9. What will happen to my specimen or sample? Will it be used in other studies?
10. Will my results have any effect upon my job, my being able to get insurance, or my status in legal matters?
11. What will happen if this research leads to the manufacture of commercial products?

For more information about ethical issues concerning this research you may contact

Complaints contact person

Position	Complaints Officer
Telephone	(03) 9496 4090 or (03) 9496 3248
Email	ethics@austin.org.au

There is more general information about research ethics issues at:
http://www.nhmrc.gov.au/your_health/egenetics/index.htm