PATIENT INFORMATION SHEET

We would like to invite you to take part in our research study. Before you decide, we would like you to understand why the research is being done and what it would involve for you. Please read this information sheet carefully – the first part tells you the purpose of our study and what will happen if you take part; the second provides more detailed information about the conduct of the study.

It may take some time to fully digest the information and you might want to talk to others about the study. There’s no rush and you can ask us if there is anything that is not clear. If you do want to get involved, or would simply like some more details before deciding, please get in touch – we’d be happy to answer any of your questions.

STUDYING THE EFFECTS OF LITHIUM ON THE BRAIN

Bipolar disorder is a serious mental illness that affects hundreds of thousands of people in the UK. Episodes of depression and mania have a profound effect on wellbeing, but patients can also struggle with poor memory and concentration. Preventing relapse is really important and we most often advise patients to take long-term ‘maintenance’ medication. Lithium can be very effective but it doesn’t work for everyone. It can also have serious side effects, so it would be really useful to be able to predict who will respond well to lithium before they start taking it.

What is the purpose of the study?
We are trying to understand why lithium is an effective treatment for some patients with bipolar disorder but not others. Lithium responders may differ in their pattern of episodes, family history, genetic make-up and possibly brain structure. It might be that for a given dose, more lithium gets into the brains of those who respond. We don’t know for sure. Finding out if there are differences between lithium responders and other patients is the first step toward being able to predict response.

Why have you been invited?
Mental Health teams across the region have been told about the research and asked to identify suitable patients. You should have received this information pack either directly from your team, or from the staff of the NHS Clinical Research Network on your team’s behalf. The research study team are not aware of the details of your case.
Do you have to take part?
It is up to you to decide to join the study. If you are interested, we will describe the study and go through this information sheet with you. If decide to take part, you are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will the study involve?
We are collecting data from three groups of people: patients with bipolar disorder who are taking lithium, patients with bipolar disorder who have never taken lithium, and healthy volunteers. We aim to recruit 160 people in total. Your involvement in the study will be separate to your usual care and no changes to your treatment will be made.

Meeting the research team
We will invite you to our research centre at the Campus for Ageing and Vitality, which is part of Newcastle University. You are welcome to bring a friend or carer with you. Here we will discuss the study in detail and address any concerns you might have. If you agree to take part, we will ask you to sign a consent form and give you a copy for your records.

Gathering information about your condition
In a structured interview that lasts about an hour, we will talk to you about the nature of your illness, the number of episodes you have had and your response to treatment. You will be asked to fill in some short questionnaires about your current wellbeing and any medication side effects you might be experiencing. We would like you to complete a standard questionnaire about childhood trauma – if this is a topic you don’t feel able to discuss then you can skip this and still take part in the rest of the study.

A brief set of psychological tests
We will ask you to complete a few tasks designed to test your attention and memory. Some tasks are computer-based whilst others just use pen and paper. To make sense of the results we also need to measure your IQ (and yes, we can let you know what it is).

Arranging the next stage
Your first appointment at the research centre should last around two to three hours, depending on how complex your illness has been. We will try to make your visit as relaxed as possible and give you plenty of breaks if you need them. The second part of the study involves you providing a sample of saliva, and then having a blood test and a magnetic resonance brain scan. These are best performed in the morning and so we will arrange an appointment that is convenient for you.
Having a brain scan
You will be invited to Newcastle Magnetic Resonance Centre, again on the Campus for Ageing and Vitality. The staff of the centre will greet you and check that it is ok for you to have a magnetic resonance imaging (MRI) scan. Every volunteer will have a scan that lasts about an hour, during which we will collect data about your brain structure and composition. Patients taking lithium will be asked to have a second hour-long scan on the same day, in order to measure the amount of lithium in their brains. This is an experimental scan using specially designed equipment and we are one of only a few centres worldwide that are capable of performing it. More details about the scans can be found in the second part of this information sheet.

Collecting a sample of your saliva
We would like you to provide a sample of saliva (spit) on the morning of your scan. This sample will be frozen and stored anonymously for later testing. We will use it to measure the levels of stress hormones, linking our findings to treatment response.

A blood test
We will want to take a small sample of blood (10ml; about two teaspoons) for routine measures and medication levels. Experienced staff will take the sample. Blood sampling is a safe, very common and normal part of medical treatment and assessment. Some localised discomfort, bruising, blood clot formation and in rare instances infection may occur in the area where blood samples are taken.

Donating a sample of blood for genetic testing and storage
We will also be asking you to consider donating a sample of blood that we can store and analyse for genetic studies. You do not have to agree to this in order to take part in the main study – we need you to sign a specific consent form before we can take the sample. More details can be found in the ‘BLISS genetics’ information sheet.

We would like to stay in touch
Interview, psychological testing, blood sample and scan – that’s all there is to it. No changes to your medication and no experimental treatments. We would, however, ask you to think about joining our long-term follow up study. To do so, indicate this preference on the main study consent form. We will arrange for you to come back to the research centre once a year for three years. You will simply be asked about whether you have remained well on your medication, to talk about any relapses you might have had and the side effects you might be experiencing. The visit should take no longer than a typical outpatient appointment and no additional investigations would be required.
THE CONDUCT OF THE STUDY

If the information in the first part of this document has interested you and you are considering taking part in the study, please read on. The next section describes the conduct of the study in more depth and provides details of how best to contact the team should you wish to do so.

Who is organising and funding the research?
The research is publicly funded, with no industry involvement. The Medical Research Council (MRC) awarded Dr David Cousins a Clinician Scientist Fellowship, and Newcastle University are administering the award. Northumberland Tyne and Wear (NTW) NHS Foundation Trust are sponsoring the research.

Has the study been reviewed?
A Research Ethics Committee, an independent group of people responsible for protecting your interests, looks at all research in the NHS. Our study has been reviewed and given a favourable opinion by the North East - Newcastle and North Tyneside 1 National Research Ethics Service Committee. An international panel of experts, tasked by the MRC, has reviewed the scientific basis of the research.

How is recruitment being organised?
The research team is not allowed to screen case notes to find suitable patients; doing so would be a breach of your privacy. Instead, we work closely with the North East and North Cumbria Clinical Research Network (CRN), part of the NHS National Institute for Health Research. You can find out about their activities online (www.crn.nihr.ac.uk).

The NTW Trust considers the CRN staff as being part of every patient’s care team. They are bound by the same principles of confidentiality as the professionals you have face-to-face contact with. Members of the CRN will have spoken to those directly involved in your day-to-day care, such as your psychiatrist, community psychiatric nurse or the pharmacist who oversees the monitoring of your prescribed medication. If you have received this information pack, your named Consultant will have felt that it is appropriate for you to be contacted in this way.

The CRN follow an opt-out policy. This means that if they don’t hear from you, they will give you a call in the near future to discuss the study. If you don’t want this happen, drop them a line to let them know. With your permission, they will keep your name on file confidentially so that you are not contacted about the study in the future. Opting out will not be held against you in any way, and you can even ask not to be considered for other research that is happening in the Trust.
**What about confidentiality?**
All information collected about you during the course of the research will be kept strictly confidential. Your local community mental health team will know you are taking part and we will ask your permission to notify your family doctor.

**How will data be stored?**
Instead of your name, we will use a code to identify you. All of the clinical information, brain scan data and blood test results that we store will be labelled with this, and only this, code. The anonymised data collected on paper will be stored in a locked filing cabinet in a locked room, itself in a Newcastle University research facility accessible only to staff with an authorised swipe-card. In previous studies, structured diagnostic interviews were recorded on paper but in this study, we will be entering data directly into the NetSCID, a web-based research tool. This is a more powerful and flexible resource that substantially reduces the length of the interview and improves data management. No identifiable personal information is entered into the NetSCID; the data is coded, password protected and storage is fully HIPAA\(^1\) compliant. Coded data in electronic format will also be stored on secure Newcastle University computer servers. Dr Cousins will be the custodian of the file linking your name to your study code and this file will be held separate to the stored data. The Medical Research Council require us to store the data for a period of ten years after the end of the study, following which it will be destroyed.

**Will data be shared with other research groups?**
The Medical Research Council has invested valuable public resources in this study, believing that it represents excellent science and addresses an important health care need. The Council expect and encourage us to collaborate with other groups, increasing the likelihood of a beneficial research outcome. We intend to share data with known colleagues in centres where we have established useful collaborations, and would consider applications for data access from other bone fide research groups. Use of the data would be restricted to the topic of our proposed research and Dr Cousins would personally review all applications. Data would not be released to scientists in countries with a lower standard of data protection than the UK. In all instances, only coded data will be made available for analysis.

**What will happen to the results of the research?**
We will analyse the results and submit them for publication in a scientific journal. Presentations may also be given at scientific conferences. You will not be identified in any publication or presentation. If you wish to know the outcome of our research, we will be happy to discuss our findings with you once the analysis is complete.

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\(^1\) Health Insurance Portability and Accountability Act (1996)
What if there is a problem?
In the event that something does go wrong and you are harmed during the research, you might wish to pursue a claim. There are no special compensation arrangements to cover non-negligent injury. If you are harmed due to someone’s negligence, then you may have grounds for legal action for compensation against Northumberland Tyne and Wear NHS Foundation Trust, but you may have to pay your legal costs. If you have a concern about any aspect of the study, you should ask to speak to the researchers who will do their best to answer your questions. If you do not feel able to do so, or are unhappy with their response and wish to complain formally, you can do so by following the NHS Complaints Procedure. Details can be obtained from the NTW Foundation Trust website (www.ntw.nhs.uk).

What is it like to have a brain scan?
Magnetic resonance scanners use powerful magnets and radiowaves to gather information about the structure and make-up of the brain. They do not use harmful radiation and are safe, so long as you don’t have loose metal objects in your body or implanted electrical devises such as pacemakers. We would not perform the scan if you are pregnant, or if there is a chance that you might be pregnant. The scanner itself is a large tube that you go into headfirst. It is not uncomfortable but it is enclosed so if you suffer from claustrophobia then you should not volunteer for this study. Some of the scans we perform are noisy, so you will be given headphones to wear. You can listen to the radio or bring some music with you if you prefer. We will keep a close eye on you throughout the scan and we have a two-way intercom system and a buzzer, so if you become uncomfortable, you can let us know and we will stop the scan immediately.

If you are taking lithium, we will ask you to have a second scan where we will chart the distribution of lithium in your brain. This is a new type of scan that we are still developing in Newcastle. We have carefully tested the techniques for safety.

What if ‘something shows up’ on the brain scan?
Almost everyone who has a scan worries that it will show some abnormality – this is unlikely but the anxiety is normal. During the scan, a senior radiographer will see the images of your brain and in the rare instance that they notice something wrong, it will be brought to the attention of Dr Cousins. Further scans and a review by a clinical radiologist may be required. You should be aware, however, that the scans we perform are designed for research studies, not for the purposes of detecting illness. Unlike a clinical scan, they will not be formally reviewed and your GP will not receive a report. The research team do not accept responsibility for detecting or missing abnormalities.
What are the benefits of taking part?
We aren’t paying volunteers for taking part but we will reimburse expenses. Luncheon receipts to the value of £5 will be covered and you can claim for your travel on public transport. If you travel by car, we can refund you the equivalent of the return public transportation costs.

Taking part is unlikely to benefit you directly or immediately; we aren’t going to change your treatment on the basis of the scan, for example. Nevertheless, many people enjoy taking part in research, finding it fulfilling and informative – we do hope that you’ll leave with this impression. What’s more, as a small token of our appreciation, we will even send you a picture of your brain!

What happens next?
If you are interested in taking part in our study, then you should contact the research team for advice on how to proceed. Should you have any unanswered questions about the study or if you want to meet the team before you reach a decision, please let your local CRN know – their contact details can be found below.

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