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Participant Information Sheet

Study title: **Transcranial Magnetic Stimulation for the treatment of Tremor**

You are being invited to take part in a research study. Before you decide whether you wish to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask the research team if there is anything that is not clear or if you would like more information.

What is the purpose of this study?
Although medications are often used to treat tremor they can be ineffective and cause side-effects like drowsiness and shortness of breath. Deep brain stimulation is another treatment, but this requires surgery that penetrates the brain and can also lead to side-effects such as unsteadiness and slurred speech. This study aims to test new methods for potentially reducing tremor. These methods are based on transcranial magnetic stimulation (TMS) over the part of the surface of the brain that controls your hand. TMS is a technique that allows us to stimulate the brain by rapid switching of a magnetic field in a coil placed over the head. If successful we can then develop direct electrical stimulation to achieve the same effect. Our hope is that we will be able to develop a stimulation treatment technique that is more effective, safer and better tolerated than available medication and surgical treatments for tremor.

Why have I been chosen?
You have been invited to participate because you have tremor and you have shown an interest in taking part in this research study. You are eligible for participating in the study if you are between 18 and 76 years of age, and have been diagnosed as having either Essential or Parkinsonian tremor. In total we are looking to include 20 people with Essential Tremor and 20 people with Parkinson's disease tremor.

Do I have to take part?
No, it is your choice whether or not to take part in the study and you do not need to decide now. If you would consider taking part you should read this information sheet and screening form and discuss with your family and friends. If you consider joining the study then you will have to meet the eligibility criteria in the screening form. We will contact you again by phone or email or you can contact the researcher, and if you decide to go ahead, an appointment will be arranged at the Oxford Centre for Functional MRI of the Brain (FMRIB) at the John Radcliffe Hospital, where you will meet a member of the research team who can answer any further questions and at this point you will be asked to complete the screening questionnaire and sign a consent form. If you decide to take part, you are still free to withdraw from the study at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect any of the standard of care you receive.

What will happen to me if I take part?

If you are taking medication for your tremor you will be asked if you mind missing this out on the day of the study. The study can go ahead regardless, but our results might be slightly easier to interpret should you miss out your tremor medication. Should you miss out your medication you can restart it after the recordings. We will begin by taping some small electrodes and a motion-sensitive device to the skin overlying some muscles in the hand and forearm. The electrodes pick up the electrical activity from the muscles, while the device picks up the physical movement related to the tremor. Next we will record the tremor with your arms in a position that makes the tremor worse. Usually this is with the arms supported at rest in Parkinson's tremor and with the arms outstretched in Essential Tremor.

Following this we will test the effect of TMS, while we record your tremor. During TMS, a magnetic coil is positioned over your scalp as shown in the picture below. We will deliver magnetic pulses through this coil to stimulate the surface of your brain. At first we will ask you to gently pinch your thumb and forefinger together during these pulses. Later we will ask you to hold your arms in a position that makes your tremor worse while we deliver these pulses. You will be able to rest every 40 seconds or so. The effect of stimulation on your tremor will be recorded by the motion-sensitive device and recording electrodes.

At some point you may experience temporary but painless spasm in the hand, or temporary, but painless twitches in the scalp or face. Please tell us if you become aware of these, or any other symptoms, as we may be able to adjust the stimulation to avoid or limit these.

The whole test would take up to one hour to complete. Once we have finished we will remove all the electrodes. That is the end of the study.

What do I have to do?

Before you take part in our research, we ask that you get a good night's sleep the night before, so that you are alert. Also, we ask you to refrain from excessive alcohol consumption (more than 3 units) the day before the visit and not to drink any alcohol on the day. We also ask that you refrain from use of recreational drugs before the visit. If you are taking medication for your tremor we prefer that you omit this on the day of the study, although this is not obligatory. You may drink coffee or tea as normal but we ask that you do not have a coffee for one hour before the visit. If you are unsure about any of the above, please discuss these with the researcher before taking part.

What are the risks and side effects of taking part in the study?

Involvement in the study will not affect the clinical care you receive. The recordings that will be performed during the study are neither invasive nor harmful. Should you omit your medication for tremor on the day of the study (not obligatory in this study) then you can resume it immediately after the study ends. As the study will be complete after about one hour you may only experience a temporary and reversible exacerbation of your tremor, -similar to forgetting a dose.

TMS carries a risk of causing fits in susceptible individuals. In most cases the fits were associated with a family history of epilepsy, existing neurological disease or medication. The risk of a provoked fit occurring in healthy individuals due to TMS has been estimated to be 1 fit per 60,000 TMS sessions. To help ensure safety we will not give TMS to someone with a personal or close family (first-degree relative e.g., parent, sibling, child) history of epilepsy, another significant neurological or psychiatric disorder, or extreme mood fluctuations. If you are taking any medication, you should discuss this with the researcher beforehand.

One of the stimulation devices used in this research has been developed in the Institute of Biomedical Engineering at the University of Oxford and is not CE marked (i.e. it has not yet been officially assessed to ensure it meets EU safety, health and environmental protection requirements). However, the device has been developed and undergone electrical safety testing according to the relevant standards for electrical medical devices and has been used to stimulate healthy volunteers in previous research studies. Other existing TMS systems have limited abilities to adjust the timings of the stimulation pulses. This is an essential part of the therapeutic potential we want to explore in this research and the non-CE marked system provides the required flexibility. The non-CE marked device has already been used to stimulate over 25 sessions to date, without any adverse effects arising from the use of the device. This study has received an ethics approval from an internal University of Oxford Committee (Ethics reference number: R8651/RE001).

It is our policy also not to give TMS to someone who is pregnant. If there is a possibility that you are pregnant, therefore, you must not take part in this research.

Participants may experience some mild discomfort during TMS, in the form of temporary spasm in the hand, or temporary twitches in the scalp or face. In susceptible individuals, TMS may cause headache, which usually responds well to over-the-counter painkillers (e.g. paracetamol).

What happens if something goes wrong?

If you have a concern about any aspect of this study you should ask to speak with the researchers, who will do their best to answer your questions. The University of Oxford, as sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.
If you wish to complain about any aspect of the way in which you have been approached or treated during the course of the study, you should contact Dr Ashwini Oswal on 07930 676 278 or you may contact the University of Oxford Research Governance, Ethics& Assurance Team (RGEA) office on 01865 616480, or the head of RGEA email rgea.complaints@admin.ox.ac.uk.

What are the possible benefits?

The results of the study will be of no direct benefit to you. However, the study may lead to better treatments for tremor in the future.

Is there any possibility of unexpected findings related to my health?
There is no chance for us to have any unexpected finding contributing to any clinical diagnosis. Therefore we are not going to contact your GP for the study.

What information about me will be held?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly.
We will be using information from you to do this research and will use the minimum personally-identifiable information possible. We will keep a basic data set of your age, predominant symptoms and medications. This will be anonymised together with the research data (responses to TMS).
The anonymised basic data set, anonymised research data, consent forms and the TMS questionnaire will be stored for 10 years after the end of the study.

With the exception of signed forms (consent form and the TMS questionnaire), all study data will be entered on a computer within a firewall and password-protected computer system within a secured building. It will be stored on secured university servers and is covered by the Oxford University Data protection register (reference No. Z575783X). Participants will be identified by study-specific subject codes and not by name. Signed forms will be stored in a locked filing cabinet within Oxford Centre for Functional MRI of the Brain (FMRIB) Research Facility, which can only be accessed using a hospital swipe-card.

Responsible members of the NHS Trust and the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations. Data collected may be shared in anonymised form with other researchers upon request, including those working outside of the EU and/or working with commercial companies. This is so that other research studies can benefit.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/. You can find out more about how we use your information by contacting the study investigators whose contact details are at the end of this leaflet.

What will happen to the results?
The results will be analysed and submitted for publication in a scientific journal. It should be emphasized that your name or any other information that would identify you will not be published. We will be happy to provide you with a copy of the completed article for you to keep and in addition, following completion of the study, a short summary of the study findings written in non- scientific language will be made available to participants on request. Some of the research being undertaken will also contribute to the fulfilment of an educational requirement (e.g., a doctoral thesis).

Can I withdraw from the study?
Your participation in the trial is entirely voluntary. You are free to decline to enter or to withdraw from the study at any time, without having to give a reason. If you choose not to enter the trial, or to withdraw once entered, this will in no way affect your medical care. All information about you will be treated as strictly confidential. We will analyse any data that has already been collected. Participation in this study or withdrawal from it will in no way affect your legal rights.

Has the study been approved by an independent body?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by North West - Liverpool Central Research Ethics Committee.

Will I be paid to take part in the study?
Involvement in the study is on a volunteer basis and you will not be paid for taking part. However, we would be pleased to reimburse reasonable travel expenses.

Who is organising and funding the research?
This project is being organised by the Experimental Neurology Group. The University of Oxford is sponsoring the study. The costs of research are being paid by the Medical Research Council and the Rosetrees Trust.

Whom can I contact if I have any questions or concerns?
You can contact the chief investigator:

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