Information Sheet for Healthy Adult Volunteers in Research Studies
Version 1.1, dated 27/04/2017

Title of the Project: **Development of threshold tracking transcranial magnetic stimulation protocols for the assessment of corticospinal excitability**

This study has been approved by the UCL Research Ethics Committee (Project ID Number): 10603/001

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We would like to invite you to participate in a research study that is being performed at the Institute of Neurology and the Division of Neurophysiology. Before you decide 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. Do not hesitate to ask us if there is anything that is not clear or if you would like more information; the contact details can be found at the end of the letter.

What is the purpose of the study?

In simple terms, the cortical excitability (CSE) can be defined as the responsiveness of the human brain to various stimuli that depends on complex relationship between inhibiting and excitating processes within the cortex. The excitability of the motor areas of the brain can be measured by applying transcranial magnetic stimulation (TMS). This is a non-invasive and painless method which has been used routinely for over 25 years. In TMS, a special magnetic coil is held over the participant's head to produce magnetic impulses that in turn induce a current in a small area of the brain. Impulses applied over the motor cortex produce a muscle twitch that can be recorded and analyzed. In this way, the function of the motor pathways as well as the inhibitory and excitatory processes in the brain can be assessed. This can provide important information in studying motor control in healthy individuals as well as in diseases where motor control of the body is impaired. The commonly used TMS protocols produce highly variable results which limits their utility. Nevertheless, new stimulation techniques are being developed that would allow to understand the sources of this variability better and potentially reduce it. The aim of this study is to establish how reliable these new techniques are in healthy volunteers. This could increase the value of TMS so that it can be more reliably applied in studying biology of the human motor control, diagnosis and follow-up of patients with a wide variety of neurological disorders (such as motor neurone disease) and development of new treatments.

Why have I been chosen?

You are an adult in good physical and mental health and willing to participate in the study of 100 participants. Your safety during this study is a priority to us. Therefore we will not be able to include you if:

- You have experienced convulsions or fainting spells in the past;
- You have any metal in your body (other than dental fillings);
- You have had a serious head trauma that was associated with loss of consciousness or brain injury;
- You are taking any medication or recreational drugs that act on the nervous system.
- You are pregnant.

Do I have to take part?

It is entirely up to you to decide whether or not to take part. You will have the opportunity to ask us any questions before deciding if you want to participate. If you do decide to take part, you will be asked to sign a consent form, of which you will keep a copy. You will still be free to change your mind at any time and you will not need to give a reason.

What will happen to me if I take part?

If you agree to take part in this study, it will involve participation for **one day or two days**, at least one week apart. We will arrange an appointment for you, usually by telephone or email, to attend the department of Clinical Neurophysiology at the National Hospital for Neurology and Neurosurgery. The study will take approximately **1 to 2 hours**. After you have given your consent, we will ask you about your medical history and current medication. If you meet the selection criteria, we will perform TMS. You will be seated comfortably in an armchair and we will apply magnetic pulses to your head to produce small twitches of a muscle in your hand. We will record these twitches with easily removable stick-on-electrodes placed over your hand muscle to analyse them later. There is a clicking noise associated with the magnetic pulse. You will be provided earplugs if needed.

As we want to test how reproducible the results are and determine the optimal test settings, we will repeat the TMS procedure on the same day and may ask you to come back for further testing at least one week later.

Expenses and payments

You will receive a financial compensation for your time and travel after the completion of scheduled study assessments (£10 per study hour).

What are the possible disadvantages and risks of taking part?

Although we administer TMS according to strict safety guidelines, there are some risks associated with this technique. In rare instances TMS has induced a seizure even in participants without any predisposing illness. This risk is extremely low, and is further minimized in our protocol because of our adherence to the safety guidelines. If you have ever experienced a seizure, you will not be enrolled in the study. It is important to note that experiencing a seizure induced by TMS has never led to the development of epilepsy or posed any risk for subsequent unprovoked seizures. In addition, any TMS induced seizure would occur during stimulation or immediately after; it would not be expected to affect a participant hours or days after the TMS. Overall, less than 10 seizures caused by TMS have been reported in the world's scientific literature, and most of these occurred in the setting of early studies designed to evaluate the safety of TMS.

In the unlikely event of a seizure during the experiment, the magnetic stimulation will be stopped immediately. The medical staff of the Division of Neurophysiology where the study will take place are well experienced in

the management and treatment of seizures as they treat patients with suspected epilepsy as part of their clinical duties.
Other potential adverse effects associated with TMS include the induction of a muscle tension headache or a neck ache in approximately 3 of every 100 participants. These are generally mild discomforts and generally do not require medication. If you feel any pain or discomfort during the procedure please alert the researcher immediately so that testing can be discontinued. The audible click produced by the stimulating coil can rarely cause transient ringing or disturbance of hearing.

What are the possible benefits of taking part?
Participation in the study will have no direct benefits to you, but you may find it a positive altruistic experience to contribute to research. Information that we get from this study will contribute to scientific knowledge and might help improve care of patients with certain neurological diseases such as motor neurone disease or dystonia.

Will my taking part in this study be kept confidential?
If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically under the provisions of the 1998 Data Protection Act. Your name will not be passed to anyone else outside the research team. You will be allocated a study identification number, which will be used as a code to identify you on all study forms. Records with your name and other personal identifiable data (for example, signed informed consent form) will be held in a locked cabinet in a locked office and will be accessible to the research team only. Electronic data will be stored on password-protected computers and copies transferred electronically for backup to UCL Data Safe Haven (a secure environment designated for storing research data). Any information about you which leaves the research site will have your name and contact details removed so that you cannot be recognized.

If you withdraw consent from further study, unless you object, your data will remain on file and will be included in the final study analysis.

In line with the regulations, at the end of the study your data will be securely archived for a minimum of 5 years. Arrangements for confidential destruction will then be made.

What happens to the results of the research study?
The results of the study will be available after it finishes and will usually be published in a medical journal or be presented at a scientific conference. The data will be anonymous and none of the subjects involved in the trial will be identified in any report or publication. Should you wish to see the results, or the publication, please ask the researcher. All personal data will be destroyed at the end of the study. With your permission, you may be contacted if further research is planned.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [(020) 344 84752]. Every care will be taken in the course of this research study. However in the unlikely event that you are injured by taking part, compensation may be available.
If you suspect that the injury is the result of the Sponsor's (University College London) negligence then you may be able to claim compensation. After discussing with your researcher, please make the claim in writing to Prof Martin Koltzenburg who is the Principal Investigator and has an address at the UCL Institute of Neurology at Queen Square (address: UCL Institute of Neurology, Queen Square, WC1N 3BG London). The Principal

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.
Participants may also be able to claim compensation for injury caused by participation in this research study without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your researcher in the same way as above.

Who is organising and funding the research?

This study is organised by the UCL Institute of Neurology and is funded by the Queen Square Neurophysiology Research Fund held at the UCLH trustees.

Who has reviewed the study?

All proposals for research involving human participants are reviewed by an ethics committee before they can proceed. This project has been reviewed by the UCL ethics committee.

Further Information and contact details

If you, your relatives or friends have any questions about participating in this study, please contact Dr Gintaute Samusyte on 020 344 83379 (email g.samusyte@ucl.ac.uk) or Prof Martin Koltzenburg on 0044 20 3449 4752 (e-mail: m.koltzenburg@ucl.ac.uk).

If you decide you would like to take part then please read and sign the consent form. You will be given a copy of this information sheet and the consent form to keep. A copy of the consent form will be filed with the study records.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider taking part in this study.