Information Letter

STRENGTHENING CONNECTIONS IN THE MOTOR CORTEX TO IMPROVE MOTOR FUNCTION FOLLOWING STROKE

THIS STUDY HAS BEEN APPROVED BY MURDOCH UNIVERSITY RESEARCH ETHICS (2017/026)

This information sheet is intended to provide you with sufficient information to make an informed decision about participating in this study. If there is any aspect that is not clear to you, please discuss this with one of the investigators.

Nature and purpose of the study

The human brain is capable of undergoing reorganisations throughout life. These reorganisations are the basis for modifications in behaviour. For example, when you learn a new movement (known as a motor skill), such as playing the piano, the areas of the brain that control movement (motor areas) are reorganised. These modifications allow you to improve your performance.

With stroke, damage in motor areas of the brain can result in weakness or loss of movement on one side of the body. Even with damage to the motor areas of the brain, reorganisation can occur and movements relearnt. In two experimental sessions, we will use non-invasive brain stimulation known as transcranial magnetic stimulation (TMS) to assess responsiveness of motor areas of the brain in stroke survivors and in healthy adults. In each experimental session we will measure the connectivity between two motor areas of the brain involved in voluntary movement. One experimental session will focus on the hand and forearm area, and the other experimental session will focus on the lower leg area. We invite you attend the TMS laboratory at Murdoch University to participate in the two experimental sessions, however you are not required to complete both sessions.

What will the study involve?

During experimental sessions you will sit in a comfortable chair in the laboratory at Murdoch University. Transcranial magnetic stimulation (TMS) will be applied by placing a small, hand-held device over the scalp. The hand-held device generates a brief magnetic field to activate the brain; you will feel a slight 'tap' on your head under the hand-held device and may experience a brief twitch in a muscle in your hand and arm or lower leg. During the TMS protocols you are simply required to sit in the comfortable chair with the muscles of your arms completely relaxed while you look at a computer screen in front of you. An experimental session will take approximately 2 hours and you will be given rest breaks throughout the session as required.

Personal and Medical Information

Participants will be asked to provide the following personal information: date of birth and contact details (telephone and/ or email address).

You will also be asked to provide the following medical information about your stroke: approximate date of stroke incidence, age at time of stroke, whether it is the first stroke you have had, whether the stroke was a block or a bleed and the location in the brain where the stroke occurred.

If you are unsure of any of the information regarding your stroke, with your approval we can contact your general practitioner to obtain the information. Personal information provided will be accessible to study investigators only and your privacy protected. During publication of the studies stroke and

personal information provided will not identify you, but will be used to describe the groups (e.g. average age, average time post-stroke, etc).

Assessment for inclusion

Before participating, screening tests will be conducted to assess your suitability and to ensure your safety. Initially, you will be asked to complete a Safety Screen Questionnaire for transcranial magnetic stimulation (TMS) to identify any possible contraindications and ensure your safety.

Upon receipt of the completed screening questionnaire, if it safe for you to continue, you will be asked to attend the laboratory at Murdoch University where you will be shown the laboratory equipment and hand-held TMS device will be held over your scalp to see if you respond to the technique, which you may feel as a brief twitch in your forearm.

During the screening stage, two additional tests will be conducted, one to assess your cognitive function and the other the movement in your stroke-affected arm and hand or leg.

The cognitive assessment involves a variety of tasks compiled on an A4 piece of paper. The investigator will guide you through the tasks including memorising words and number sequences and connecting words by similarity. The cognitive assessment will take approximately 10 minutes to complete and will be used to determine inclusion to the study.

Movement in your arm and hand or lower leg will be examined using a standard movement assessment. The assessment will examine reflex activity, movement patterns and coordination and speed of your arm and hand or leg. You will be asked to perform various movements against gravity and to grasp different shaped objects. This test will take approximately 10 minutes to complete.

The results of these tests will inform the decision on whether you will be suitable for and included for participation.

Balance and Movement Tasks

There will be a range of simple movement tasks. These tasks involve simple activities like walking for 10 meters, standing still on a platform for 30 seconds, placing one foot on a step, and picking up small objects with your hands.

Recording from the hand, forearm and lower leg muscles

Muscle activity will be recorded from muscles in your arm (hand/forearm) or from muscles in your lower leg (below the knee). The muscle activity will be measured by sticking small recording electrodes to the skin with tape.

Transcranial Magnetic Brain Stimulation

The technique of TMS is painless and non-invasive. It has been in use for more than 30 years and is used routinely to investigate activity of the motor system. Two different TMS protocols will be used in this study, each described in detail below. During an experimental session, you will undergo both of these TMS protocols. The investigator will demonstrate the non-invasive brain stimulation, and you will hear the click that the device makes when discharged, before the stimulation is delivered to you. Initially, stimulation will be at a very low intensity and be increased in small increments until a small muscle response is produced your stroke-affected hand and forearm or lower leg. The investigator will notify you each time the stimulation intensity is increased and after delivering a single pulse at the new intensity they will check with you to see how you are feeling and if you are comfortable to continue.

Single-pulse transcranial magnetic stimulation

Single-pulse TMS will be used to measure the activity of a motor area of the brain. Single-pulse TMS delivers a single pulse to the motor area of the brain to be measured. The stimuli can be felt as brief mechanical 'taps' on your scalp and you will also hear a click when the pulse is discharged through the coil. Small muscle movements may be felt in your dominant arm and forearm or lower leg.

Paired-pulse transcranial magnetic stimulation

Paired-pulse TMS will be used to examine the connectivity between two motor areas of the brain. Paired-pulse TMS consists of two pulses separated by very short time intervals (6 ms). The two pulses will be delivered by two TMS coils to different motor areas of the brain (approximately 2-4 cm apart). The stimuli can be felt as brief mechanical 'taps' on your scalp and you will also hear a click when the pulse is discharged through the coil. Small muscle movements may be felt in your dominant arm and hand or lower leg.

As a matter of policy we exclude any persons for our study who have a history of epilepsy, or who have metal implants in the skull, or cardiac pacemakers. If you have any of these, please inform the investigators prior to commencing the study. If you have any doubts about whether you should participate, please discuss them with one of the investigators. Additionally, you will be required to complete a safety questionnaire that will identify any possible contraindications for the use of TMS.

What are the risks?

We wish to make it clear that although these techniques are used both diagnostically and in research laboratories around the world, all experiments involve a small but finite risk. Very occasionally it has been reported by other groups that subjects may experience a mild and temporary headache, nausea, muscular problems, or dizziness during or after TMS. In our experience this is very rare. It is our policy to exclude any subjects with cardiac pacemakers, metal implants in the skull or a history of epilepsy.

Additional information regarding TMS can be found on the following websites:
http://www.mayoclinic.org/tests-procedures/transcranial-magnetic-stimulation/details/risks/cmc-20163840
http://www.hopkinsmedicine.org/psychiatry/specialty_areas/brain_stimulation/tms/faq_tms.html

A video that shows the use of TMS to elicit responses from major muscles of the body can be seen here:
https://www.youtube.com/watch?v=qkNbYHu_STU

All participants' details will remain confidential except as required by law. Although we plan to publish the results of this study, participants will only be identified by a participant number.

You are free to withdraw from this study at any time without having to explain your reasons for doing so.

If you have concerns either before or following the experiment, please contact:

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This study has been approved by the Murdoch University Human Research Ethics Committee (Approval 2017/026). If you have any reservation or complaint about the ethical conduct of this research, and wish to talk with an independent person, you may contact Murdoch University's Research Ethics Office (Tel. 08 9360 6677) or e-mail ethics@murdoch.edu.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.