

Consent Form

Title of Research Study: *Phase-dependent evaluation of motor cortex excitability with TMS in stroke*

Investigator Team Contact Information: *Prof. Alexander Opitz*

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Prof. Alexander Opitz Investigator Affiliation: Dept. of Biomedical Engineering Phone Number: 612-624-1094 Email Address: aopitz@umn.edu	Study Staff (if applicable): N/A Phone Number: N/A Email Address: N/A
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Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because we are looking for adult volunteers who have previously suffered a stroke, as well as healthy adult volunteers.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

What is TMS, MEP, and EEG?

Transcranial magnetic stimulation (TMS) is a non-invasive application of a magnetic field to the head. In this experiment, we will apply TMS over the motor area. The motor area performs movements, by

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sending a signal to the muscle. In this study, the signals to the muscle of the hand will be investigated by looking at its electric activity (motor-evoked potentials, MEP). Further, we will record brain activity with non-invasive electrodes attached to your scalp (electroencephalogram, EEG).

Why is this research being done?

The purpose of this study is (1) to evaluate the effect of TMS on MEP when applied at different time points relative to the brain activity and (2) to examine whether these effects depend on the individual's head anatomy. This study will provide insights into how brain activity relates to effects of TMS. Therefore, this study can lead to a better stroke rehabilitation using TMS.

How long will the research last?

We expect you to come two times for the research sessions. The first visit will take approximately 2.5 hours. The second visit will take up to 3 hours. There will be a time gap of at least 48-hrs between the visits. Depending on your schedule, we expect you to finish both sessions within 1-3 weeks.

What will I need to do to participate?

You will be asked to attend two experimental sessions that will last approx. 2.5 and 3 hours, respectively. In the first meeting we will record your brain anatomy using magnetic resonance imaging (MRI) and measure movement ability of both hands. In the second session we will stimulate you with TMS and use EEG to record the brain responses. You will be asked to fill out short questionnaires at the end of every session.

More detailed information about the study procedures can be found under ***“What happens if I say yes, I want to be in this research?”***

Is there any way that being in this study could be bad for me?

TMS is an FDA approved procedure for depression and is commonly used in therapeutic research studies on stroke rehabilitation. Common side-effects include small contractions in the muscles of the head, neck, forearm and/or hand. These should not provide any discomfort. No long-lasting side effects of the stimulation with the same regime as in this study have ever been reported. Potential adverse effects of TMS include rare cases of: (1) head and neck aches; (2) transient hearing changes. In very rare cases seizure and seizure-like events can occur. You should not participate if you have reasons to believe that you are pregnant. We will follow up-to-date guidelines to minimize TMS intensity and risk of adverse events.

The MRI scanner uses a strong magnet and radiofrequency electromagnetic fields to take images of your head. Possible adverse-effects include (1) cases of claustrophobia inside the MRI machine, (2) twitching or muscle contractions, (3) heating of certain types of fabric and tattoo ink, (4) hearing damage due to the loud noise, and (5) disruption of implanted or wearable devices. The trained personnel will give you necessary hearing protection and will guide your preparation for the scanning procedure to minimize risks.

Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include development of new therapeutic approaches for patients with neurological disorders (such as stroke).

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Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 30 adult stroke volunteers and 30 adult healthy volunteers will participate in this research study.

What happens if I say “Yes, I want to be in this research”?

Two experimental sessions will be scheduled in the following weeks according to your schedule. The research will be performed on the University of Minnesota Twin Cities Campus. The sessions last approximately 2.5 and 3 hours, respectively. We will contact you 24 hours before the session via email or phone to remind you and confirm the session. Please contact the investigator who explained the content of this consent form to you or the principal investigator as soon as possible if you decide to reschedule.

During the first meeting we start with the consent procedure. Afterwards, a trained physical therapist will perform a motor exam on the upper extremities to assess severity of motor function. The therapist will assess upper extremity range of motion and strength. In addition, you will receive a few questions on how you would rate your symptoms subjectively. After the motor exam, we will record your brain anatomy using magnetic resonance imaging (MRI). Specific CMRR (Center for Magnetic Resonance Research) procedures may include: Screening procedures, including testing procedures needed before participation in MRI (e.g. pregnancy testing, x-ray to determine location of shrapnel); MRI screening procedures and duration of scanning (e.g. remove all metallic objects, wear hospital gown, etc.); whether study specific positioners like bite bars will be used or additional devices will be placed to communicate with or monitor the subject (e.g. heart rate or respiration monitoring, headphones); additional procedures subjects will be asked to perform in this study while in the MRI scanner (e.g. perform tasks while lying in the scanner); and procedures associated with completion of the study (e.g. completion of exit questionnaires, etc.). Preparation will for the MRI scan will take about 30 minutes and the scan itself can take up to 1 hour.

In the second session we will stimulate you with TMS in the absence of any test. Before, after, and during TMS stimulation we will record your brain activity with EEG. These recordings will be conducted via electrodes that we will place on your skin on your head before each session. The electrodes will be attached to your skin using conductive gel or paste. The preparation of EEG and TMS equipment lasts approximately 1.5 hours. The TMS measurement will last approximately 1.5 hours. During this time, we will perform 5-minute blocks of TMS, with 5 minute breaks between each block. Electrodes and other equipment will be removed immediately after each session. Please note that the investigator may touch your head in the process. After the end of the session you will have the opportunity to wash your head and hair and remove the rest of the conductive gel or paste. Finally, you will be asked to fill out a questionnaire about your state and possible adverse effects.

You will have the option to receive updates related to appointment reminders and other updates via text message and email message (standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages, but you are not required to provide your cell phone or

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email address to be enrolled in the study. If you choose to receive messages and decide later that you want to stop these messages, you will have the ability to opt-out.

What happens if I say “Yes”, but I change my mind later?

If you take part in this research study, and want to leave, you should tell us. Your choice not to be in this study will not negatively affect your right to any present or future medical care, or your present or future employment. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you decide to leave the research study, contact the investigator so that the investigator can cancel future appointments and arrange the final monetary compensation. You may be asked few questions regarding your reason and potential adverse effects to the experimental procedures.

If you stop being in the research, information about you that has already been collected may not be removed from the study database. See section ***“What happens to the information collected for the research?”***

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

MRI machines use a strong magnet and radiofrequency magnetic fields to take images of your body. The scanning process is similar to an x-ray or CT scan, but MRI does not use ionizing radiation (high-energy radiation that can potentially cause damage to DNA) like x-rays or CT scans. The risks associated with MRI scans are:

Projectiles: Objects with magnetic properties can be pulled into the magnet and turn into projectiles. To minimize this risk we ask that subjects remove all metallic items (watches, cell phones, hair pins, etc.) prior to entering the scanner and by controlling access to the scanner.

Claustrophobia: The scanner is a long narrow tube that may cause some people to feel claustrophobic.

Hearing Damage: The noise generated by the operation of the scanner during a study is loud enough to cause hearing damage if you do not wear hearing protection. Hearing protection is required and is provided by the investigator.

Nerve Stimulation: Some people experience localized tingling, twitching, or muscle contractions during MRI scans. This is expected, but if it is uncomfortable please notify the investigator.

Disruption of Devices: Some devices can be damaged by magnetic fields and should not be brought into the scanner room. This includes some implanted devices such as pacemakers, cochlear implants, insulin pumps, nerve stimulators, etc. If you have any implanted device notify the investigator.

Heating of Devices: The radiofrequency waves used in MRI can heat conductive materials such as metal implants (screws, plates, rods, wires, artificial joints, etc.), certain tattoo inks, certain clothing fabrics, jewelry, medication patches, wigs, etc. You will be asked to remove these items if possible. If they cannot be removed you will be asked to provide more information to allow MRI staff to be able to make determination on the safety of proceeding with the scan.

A thorough pre-scan questionnaire will allow us to minimize the risk of device disruption and heating. You will be in constant contact with the investigator and should notify the investigator immediately, via the squeeze ball, if you notice anything unusual, become claustrophobic, think that your hearing protection is not adequate, or if you experience nerve stimulation that is uncomfortable.

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In addition, there is a risk of unknown effects related to participation in MRI research. Long-term effects of exposure to high magnetic fields are unknown. Most people experience no short-term ill effects from the strong magnetic field, but some people report dizziness, mild nausea, headache, a metallic taste in their mouth, or sensations of flashing lights. These symptoms, if present, subside shortly after leaving the magnet. If any sensations experienced during participation cause discomfort or pain, notify the researcher right away and your participation will stop and you will be taken out of the magnetic field.

TMS uses a magnetic field to briefly stimulate a focal brain area. Common side-effects include small contractions in the muscles of the head, neck, forearm and/or hand. These should not cause any discomfort. No long-lasting side-effects of stimulation within the regime as in this study have ever been reported. Potential adverse-effects of TMS include rare cases of: (1) head and neck aches; (2) transient hearing changes. In very rare cases seizure and seizure-like events can occur. You should not participate if you have reasons to believe that you are pregnant.

Will I receive any imaging results after an MRI?

The pictures created during this study are for research purposes only and are not intended to provide health care to you. The investigator in charge of this study has decided that results from your scan will not be shared with you or your physician.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

The risks of exposure to high magnetic fields are unknown for fetuses. Therefore, if you are a female who is capable of becoming pregnant, and you have any reason to believe that you might be pregnant, you should not participate in this study.

The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You should not be or become pregnant or breastfeed while on this research study.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable, but least effective, methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study it is important that you tell the study doctor or other research team member immediately. You might be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research study it is

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important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

Will I know about any new information about the effects of MRIs on human health?

Notification of Significant New Findings

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance (such as the Quality Assurance Program of the Human Research Protection Program (HRPP)).

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. **What will be done with my data and specimens (if applicable) when this study is over?**

Your identifiable data will not be used for any future research after this study is complete.

Informed consents will be safely secured under lock and key. Experimental data (MRI, EEG, TMS) will be saved on Box (box.umn.edu), which is an internal repository. This data is saved for analysis and only researchers directly involved in this study have access to this data. This data will be destroyed after 6 years. After analysis, de-identified analyzed data and analysis scripts related to scientific publication will be put in the open repositories Zenodo (zenodo.org) and National Institute of Mental Health Data Archive (NDA). Data will remain for 20 years.

Will anyone besides the study team be at my consent meeting?

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You may be asked by the study team for your permission for an auditor to observe your consent meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at [612-625-1650](tel:612-625-1650) (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include repeated non-appearance for the experimental sessions, lack of motivation to participate in the study, disrespectful behavior towards the investigators and university staff, and any legal or medical reasons why you cannot continue participating.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, we will pay you \$35 per hour in the study at the end of the final session. In case you will leave the study after the first session, you will receive compensation for the first session (estimated: \$87.50). When completing both sessions of this study the

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total estimated amount of compensation is \$192.50, not exceeding a maximum of \$250. On top of that, travel costs will be reimbursed.

Payment will be made using a pre-paid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card and each time you receive a payment for participation in this study, the money will be added to the card after each completed visit.

You may use this card at any store that accepts MasterCard or you can use a bank machine to remove cash. However, there may be fees drawn against the balance of the card for cash withdrawals (ATM use) and inactivity (no use for 3 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The debit card system is administered by an outside company. The company, Greenphire, will be given your name. They will use this information only as part of the payment system. Your information will not be used for any other purposes and will not be given or sold to any other company. Greenphire will not receive any information about your health status or the study in which you are participating.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I agree No, I disagree

The investigator may contact me in the future to see whether I am interested in participating in other research studies by Prof. Alexander Opitz.

If yes, provide the following contact information:

Email Address: _____

Phone Number: _____

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Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

Signature of Participant

Date

Printed Name of Participant

Signature of Person Obtaining Consent

Date

Printed Name of Person Obtaining Consent