Frontal and Parietal Contributions to Proprioception and Motor Skill Learning

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Informed Consent Form

June 13, 2023

INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH
Frontal and Parietal contributions to proprioception and motor skill learning
IRB Protocol 17096
National Institutes of Health

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in the study.

STUDY SUMMARY

The purpose of this research study is to better understand how the different brain regions help us in improving our hand position sense and movement. It will take approximately 3 – 3.5 hours (consisting of up to three study visits) for the study to be completed depending on your group assignment. During the study, you will be given painless brain stimulations and perform movements holding a robotic handle. There are no significant risks associated with these procedures at this time. The main potential risk is fatigue or boredom. There will be no personal benefits from taking part in this study. Your participation in the study is voluntary and you will be compensated for your time.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to understand how the different areas of the brain work together and help us in improving our hand position sense and movement. We hope this information may be useful one day to improve rehabilitation techniques in patients with brain lesions.

You were selected as a possible participant because you contacted the investigator in response to an advertisement and have provided information which indicates you are able to safely participate. The study is being conducted by Dr. Hannah Block and Manasi Wali (Department of Kinesiology and Program in Neuroscience, Indiana University Bloomington). It is funded by the National Institutes of Health.

HOW MANY PEOPLE WILL TAKE PART?

You will be one of 72 participants taking part in this study.

WHAT WILL HAPPEN DURING THE STUDY?

The study involves two experimental sessions (about 3 hours in total) at the Sensorimotor Lab, PH 079 (1025 E. 7th St, Bloomington IN). Depending upon the group you are randomly assigned to (like flipping a coin), you might also be asked to get an MRI scan of your brain, which involves a 20-minute visit to the IU Imaging Research Facility (IRF) at 1101 E 10th St, Bloomington IN (PY 159). Both these visits will ideally take place within a two-week period of time, depending upon study staff and your availability.

Familiarization session: about 1 hour.

First you will be asked to fill out a screening form for the transcranial magnetic stimulation (TMS, which is mild brain stimulation) to ensure you are still eligible to participate in the study, and a

questionnaire which will determine which hand you prefer to use to complete basic everyday tasks. If you meet the criteria to participate, you will sit in a comfortable chair while a non-invasive brain stimulation device (the TMS coil) is held over your head. You will be asked to wear glasses that help us identify the appropriate spots of your brain for stimulation. We will attach small adhesive sensors on your skin over one of your hand muscles (Index finger and thumb) to record the response to brain stimulation. We will stimulate your brain several times and record the responses in the muscles. With each stimulus, you will hear a "click" and you may feel like someone has lightly tapped your head. Once the location has been determined, we will start off with a low intensity setting and we will deliver stimulation with the TMS to your brain, gradually increasing the intensity until we have found the lowest setting needed to consistently produce a result in your dominant hand's finger muscle. This is called your "resting motor threshold".

Most people are not bothered by the sensation of TMS, but some find it uncomfortable. Also, everyone's brain is different and occasionally we are unable to find the right spot to stimulate. If this happens, your participation will conclude with this session. Otherwise, you will be randomly assigned (like flipping a coin) to one of three groups, and we will schedule a time for your next session. The groups differ in what will happen during the main session: whether you will receive real or sham (inactive) TMS stimulation, and what brain region will be targeted.

You will then perform a motor skill task and a position sense task. There will not be any TMS stimulation during this part. During the motor skill task, you will make arm movements while holding on to a handle in order to guide a visual cursor through a maze-like track. During the position sense task, you will hold on to a handle that is connected to a robotic arm and judge where the handle is (i.e., your hand) in relation to a visual target. This will take approximately 60 minutes. If you are comfortable with all procedures and can follow task instructions, you have the option of continuing with the procedures of the first experimental session on the same day or return on a separate day.

Some groups require an MRI scan of your brain before the main session. If you are assigned to one of these groups, we will schedule the scan for you after you complete the familiarization session. The scan involves a 20-minute visit to Indiana University Imaging Research Facility (IRF) at 1101 E 10th St, Bloomington, IN. This will be scheduled at least 1 day before the main session. The IRF technician will ask you to complete a separate MRI safety screening checklist to make sure you are eligible. The actual scan takes about 6 minutes, during which you will be asked to lie still.

MRI uses a strong magnetic field and radio waves to obtain images of body organs and tissues. There is no radiation exposure involved. The MRI scanner is a cylinder surrounded by a strong magnetic field. During the scan you will be required to lay still on a bed that slides in and out of the cylinder. When the scanner takes pictures, you will hear loud knocking and clicking noises. You will wear ear protection to decrease the noise. You will be able to communicate with the experimenter throughout the scan by talking in a normal voice. In addition, you will hold a red ball in your hand, and you can squeeze it at any time to be removed from the scanner. Also, at any sign of discomfort or claustrophobia, we will end the session.

Main session: about 2 hours*.*

For the main experimental session, you will begin by filling out a screening questionnaire to confirm you are eligible to receive TMS that day. Next, you will perform the position sense and motor assessment tasks similar to the familiarization session. This will take about 20 minutes. Then you will be moved to another chair and asked to wear goggles that help us in identifying the appropriate

spots for brain stimulation. We will attach small adhesive sensors on your skin over some of your hand muscles to record the response to brain stimulation, just as was done during the familiarization session. We will stimulate your brain several times and record the responses in the muscles. Then we will apply low-intensity TMS pulses for 40-seconds. Depending upon which of the three groups you are randomized to, you will either receive a stimulation, or you will not receive stimulation. Both the active and sham stimulation feel similar. After stimulation, you will be asked to perform the position sense and motor assessment task again which will take approximately another 20 minutes. This will be followed by about 20 minutes of motor training. The motor training consists of the same maze-tracing task you did during the motor assessment task, except you will practice it over and over. Partway through the motor training, we will stop and do the motor skill assessment task again (about 5 minutes). The experiment will end with performing another set of position sense and motor skill assessment tests, taking about 20 minutes.

Regardless of the group you assigned to, you will be in this study for about two weeks.

Your involvement in the study will end once you have completed your main session. You will get a break approximately every 15 minutes to avoid fatiguing your arms.
You will not receive the results of any of these tests or procedures because they are being done only for research purposes.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?
There are no known significant risks associated with these procedures at this time. The main potential risk is fatigue or boredom, which is why you will be asked to take frequent breaks. There is a small risk of discomfort when placing the adhesive sensors on the skin which might cause skin irritation due to the adhesive, and when the robot moves the handle you're holding onto. The robot will not generate enough force to hurt you and cannot extend far enough to touch any part of your body except your hand. In addition, the robotic arm is locked in place unless someone is grasping the handle; so, if you are uncomfortable at any point, you can simply let go of the handle and the robot will automatically freeze in place. The experimenter will be present throughout the experiment and has a stop button that he or she will press in the event of any problems. If you feel discomfort at any point, please tell the experimenter. If you need a rest during the task just let go of the handle.

In order to ensure confidentiality, all data collected will be under a numerical code which will be kept separately from any identifiable information. Additionally, all the physical documents will be locked in a cabinet in the lab.

TMS has been used safely in humans for decades. It is commonly used in both research and clinical applications. The magnetic fields at the strengths used are thought to be without harm. The exception is if you have a cardiac pacemaker, or a certain type of metallic clip in your body (an aneurysm clip in your brain). Magnetic stimulation will not be performed in people who have pacemakers, implanted pumps or stimulators, or who have metal objects inside the eye or skull. Please inform the investigators if you have any of these. Most people do not find the stimulation painful, but sometimes strong contractions of scalp muscles can cause some discomfort or headache. Neck pain, toothache, and prickling sensations on the skin have also been reported in the literature. If you find the procedure too uncomfortable, you may discontinue it at any time. Headache, if it occurs, is usually mild and only lasts a few minutes beyond the end of the test.

Out of thousands of people studied with brief TMS of the brain, three patients with stroke have had a seizure due to the scar tissue in the brain. There has been only 0.02% of seizure reported using theta burst stimulation. There has also been no seizure reported using TMS in normal healthy people, as we are doing in this study. To minimize the risk of such an event you will not be eligible to participate in this study if you yourself have a history or your family has a history of epilepsy. Fainting has been reported very rarely in association with TMS. With TMS there is an audible 'click' when the magnet discharges. Although studies have found no hearing impairments as a result of this sound, some participants experience a mild temporary effect on their hearing. To minimize the possibility that this clicking sound will affect your hearing, you will be offered protective earplugs. Safety standards for the application of TMS have been published and will be followed during this study to minimize the risks.

There are no known significant risks associated with MRI procedure. The procedures themselves are painless and not uncomfortable except that you must lie still. The MRI machine is confining, and some people may feel claustrophobic when lying in the machine. Such individuals would be removed immediately. You may also be uncomfortable completing the MRI screening checklist. For instance, there are questions about methods of birth control and the existence of tattoos and piercings.

The magnetic field and radio waves of MRI are considered too weak to do any biological damage. There are no long-term risks or consequences of MRI scans. In extremely rare cases (about one in a million), the radiofrequency energy used in MRI has produced burns (most of them minor). If you feel any heat or burning sensation you should notify the staff immediately and we will safely terminate the procedure. The Food and Drug Administration has recently made recommendations for exposure to MRI during studies. The MRI machine that will be used in this study satisfies these safety guidelines. If you wish to retain a copy of these guidelines, please ask the experimenter.

The MRI scan is not a medical test. It is designed to address research questions and it is not a complete scan for any clinical purpose. If there is an abnormality in the scan, the MRI technician, or the researcher may not detect it. If the technician or researcher suspects a possible abnormality, the scan will be sent without any participant identifiers to a neuroradiologist for further review. If the neuroradiologist recommends further action, you will be notified.

MRI may be harmful to an unborn child. If you are of childbearing potential (that is, if you are a woman with sexual partner(s) and do not use an adequate birth control method), you must be excluded. Adequate birth control methods (e.g., oral, implanted, or barrier methods) should be used by all participants and/or their sexual partner to prevent pregnancy while participating in this study. If you become pregnant while participating in this study, you should notify you physician. If you use an IUD for birth control, you must be excluded.

While there is no evidence of increased risk with multiple scans, the risks associated with multiple scans are not known. The IUB imaging center is adopting an arbitrary maximum of 40 hours of scanning time per individual per year and the time involved in the present study is well below limit. There is also a risk of loss of confidentiality.

WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?

We don't think you will have any personal benefits from taking part in this study, but we hope to learn things that will help other people in the future.

HOW WILL MY INFORMATION BE PROTECTED?
Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. No information which could identify you will be shared in publications about this study. Your personal information may be shared outside the research study if required by law and/or to individuals or organizations that oversee the conduct of research studies.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use any information, documents, or specimens that could identify you in any legal action or lawsuit unless you say it is okay. However, there are some types of sharing the Certificate does not apply to. The Certificate does not stop reporting required by federal, state, or local laws, such as reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate does not stop a government agency who is funding research from checking records or evaluating programs. The Certificate also does not prevent your information from being used for other research when allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may still give them permission to release information to insurers, medical providers, or others not connected with the research.

HOW WILL MY INFORMATION BE USED?
The following individuals and organizations may receive or use your identifiable information:

1. The researchers and research staff conducting the study
2. The Institutional Review Boards (IRB) or its designees that review this study
3. Indiana University
4. Data safety monitoring boards and others authorized to monitor the conduct of the study
5. State or Federal agencies with research oversight responsibilities, including but not limited to:
    - Office for Human Research Protections (OHRP)
    - National Institutes of Health (NIH)

Information collected for this study may be used for other research studies or shared with other researchers for future research. If this happens, information that could identify you, such as your name and other identifiers, will be removed before any information is shared. Since identifying information will be removed, we will not ask for your additional consent.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL I BE PAID FOR PARTICIPATION?
Yes. You will receive a $60 Kroger or Amazon gift card after completing the main session. If you attend the familiarization session but we terminate your participation at that point, you will receive a $15 gift card.

WILL IT COST ME ANYTHING TO PARTICIPATE?
There is no cost to you for taking part in this study.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?
In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled by signing this Informed Consent form.

If you are participating in research that is not conducted at a medical facility, you will be responsible for seeking medical care and for the expenses associated with any care received.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?
For questions or problems related to the study or a research-related injury, please contact the researcher Manasi Wali at 732-314-8384. If you cannot reach the researcher during regular business hours (i.e., 8:00AM-5:00PM), please call Dr. Hannah Block at 812-855-5390.
For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

WHAT IF I DO NOT PARTICIPATE OR CHANGE MY MIND?
After reviewing this form and having your questions answered, you may decide to sign this form and participate in the study. Or you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your usual medical care or treatment or relationship with Indiana University.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw during an experimental session, simply tell the researcher. If you decide to withdraw in between sessions, you may notify whichever researcher you have been in contact with by phone or e-mail.

Your participation may be terminated by the investigator without regard to your consent if the researcher is unable to find a good response or signal with TMS, or if you are unable to perform the tasks, or if you have developed a medical condition that would prevent you from participating.

PARTICIPANT'S CONSENT
In consideration of all of the above, I agree to participate in this research study. I will be given a copy of this document to keep for my records.

_____ **Participant's Printed Name** **Date**	_____ **Printed Name of Person Obtaining Consent** **Date**
_____ **Participant's Signature**	_____ **Signature of Person Obtaining Consent**