Department of Physical Therapy

Informed Consent Form

Title of Study: Investigation of motor control and motor learning principles in individuals with Parkinson's disease and age-matched healthy individuals, using transcranial magnetic stimulation (TMS)

Principle Investigator:	Na-hyeon (Hannah) Ko, PT, DPT, PhD
Co-investigator:	Amy Popp, PT, DPT, NCS
Student Investigators:	Adam Perez, SPT

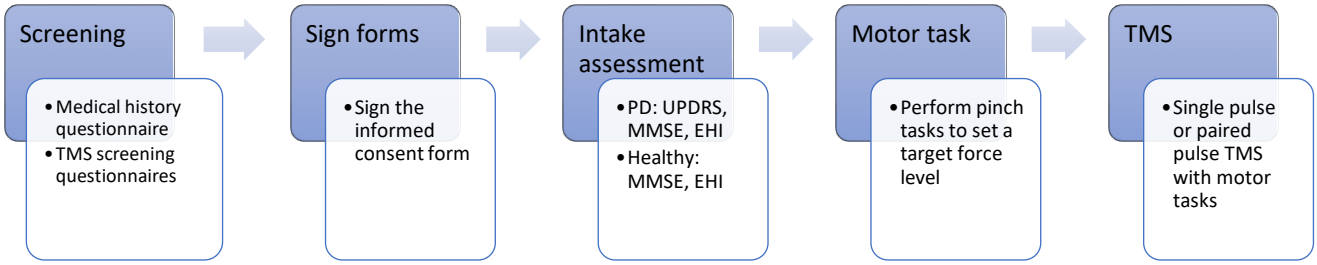
You are invited to participate in this study voluntarily. Please read the following information and ask us any questions you have before you decide to participate in the study.

Why are we doing this?

We would like to understand how brain function changes after a brain damage and how they affect movement. Individuals with Parkinson's disease (PD) suffer from motor impairment such as poor postural control, balance, gait, and fine motor skills (e.g., reaching and grasping). The motor dysfunction ultimately affects patients' independence in daily living and decreases their quality of life. Understanding neuropathology and underlying mechanisms of the way the brain changes when damaged will allow us to develop better rehabilitation strategies. To investigate neurophysiological changes of the brain after damages, we would like to use non-invasive brain stimulation such as transcranial magnetic stimulation (TMS). TMS is widely used in brain research, and the direct functional measurement of the brain, using TMS, will help us understand motor control strategies in PD, which will further assist to develop better intervention for these individuals in the future. This study is an experimental study that compares corticospinal excitability between individuals with PD and age-matched healthy individuals, using TMS while performing a unimanual, challenging motor task. By using the challenging motor task, we can also study how individuals with PD adapt and learn a challenging task by measuring their brain function with TMS.

What are the procedures? What will you be asked to do?

Procedural outline with time



Screening and intake assessment will take place in McLane 111, McLane 104, or Science II Rm 230. All TMS procedures will take place in Science II Rm 230, California State University, Fresno. Upon arrival, a designated parking spot may be provided right behind the Science II building on Barstow Ave. A student investigator will escort the participants from the parking lot to the lab for safety. The entire procedure may take 3-4 hours. Procedures 1-3 may take 1-1.5 hours, and procedure 4-5 may take 2-2.5 hours. Procedure 1-3 and 4-5 may take place in two separate days depending on the participant's tolerance.

1. Screening with previous medical history questionnaire and TMS screening questionnaires
2. Sign the informed consent form
3. Intake assessment with Unified Parkinson's Disease Rating Scales (UPDRS), Mini-Mental Status Exam (MMSE), and Edinburgh Handedness Inventory
4. Perform the pinch task with the unstable object for a few minutes to set a target force level
5. TMS procedure either single pulse or paired pulse TMS

Screening

Upon the agreement to participate in the study, all participants will be thoroughly screened for an eligibility for TMS measurements based on the inclusion and exclusion criteria, medical history and motor function, and TMS screening questionnaires.

The inclusion criteria for healthy individuals

- Age older than 22 years old
- No hand surgeries and arthritis in the thumb and index finger
- An ability to process visual information on a computer screen
- Intact cognition to follow verbal and visual instructions
- An ability to participate in the informed consent process.

The exclusion criteria for healthy individuals

- A medical diagnosis of neurological disorders
- A history of seizure and immediate family member with epilepsy
- Metallic hardware in close contact to the discharging coil such as cochlear implants, an

Internal Pulse Generator or medication pumps
- Individuals with hospitalization or surgery within 3 months
- Pregnancy

The inclusion criteria for individuals with PD
- A medical diagnosis of PD and age older than 22 years old
- No hand surgeries and arthritis in the thumb and index finger
- An ability to process visual information on a computer screen
- Intact cognition to follow verbal and visual instructions
- An ability to participate in the informed consent process.

The exclusion criteria for individuals with PD
- An inability to follow verbal instructions
- A history of seizure and immediate family member with epilepsy
- Metallic hardware in close contact to the discharging coil such as cochlear implants, an Internal Pulse Generator or medication pumps
- Implanted brain electrodes (cortical or deep-brain electrodes)
- Individuals with hospitalization or surgery within 3 months
- Vascular, traumatic, tumoral, infectious, or metabolic lesion of the brain
- Inability to follow verbal instructions
- Pregnancy

Intake Assessment

Once the participant is determined to be eligible, additional clinical assessment will be performed such as the Unified Parkinson's Disease Rating Scales (UPDRS), Mini-Mental Status Exam (MMSE), Edinburgh Handedness Inventory, and previous medical history questionnaires.

Motor behavioral tasks

You will perform motor tasks including but not limited to: precision grip of stable and unstable objects and two magnets against poles with fingers and legs and finger tapping (Figure 1 for an example). We measure your compression force from the objects, using a device and set a target force that you will trace during TMS procedures. These compression force levels will be < 3N, and you will trace a line, displaying on a computer screen for 15-20 times per each condition.

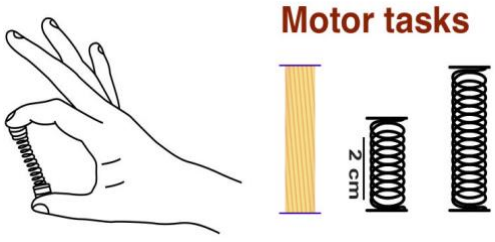


Figure 1. An example of motor tasks: compression of stable and unstable objects

TMS protocols

1. Resting motor threshold measures for the baseline intensity

Each session will begin with determining the intensity of brain stimulation for the experiment. You will wear a swim cap over the head and sit on a chair comfortably with both arms resting on a pillow placed the participant's laps. To record muscle activity, we will place surface EMG electrodes on the muscles after cleaning the area with alcohol wipes. The TMS coil will be placed over your head and single pulses will be delivered to identify areas that induce visible

muscle activity. We call these areas as “hot spots”. We will identify one hot spot that induce muscle activity at the lowest stimulator intensity, which we call as “resting motor threshold, RMT”. Please see figure 2 for the TMS set-up.

2. Single pulse TMS measures

You will sit on a comfortable chair with back support and will be instructed not to move the head. Single pulse TMS will be delivered over the hotspot at 120% of the RMT while you perform the motor task with your dominant hand. The non-dominant hand will be resting on a table comfortably. We will record muscle activity using surface EMG just like the resting motor threshold measures. Single pulse will be delivered 15-20 stimulations for each motor task condition (e.g., rest, stable, unstable condition) for a total of 45-60 single pulse stimulations.

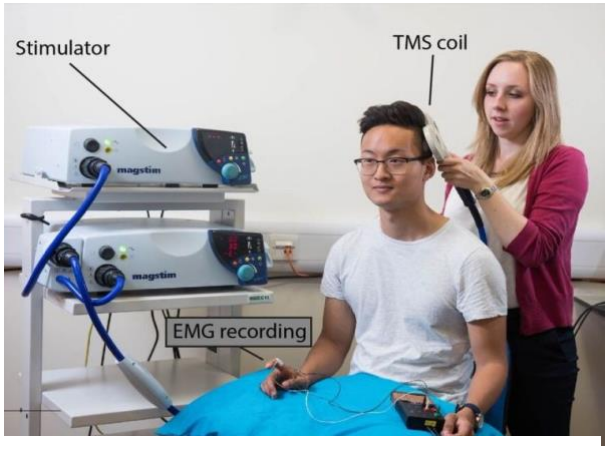


Figure 2. An example of TMS setting (photo from University of Oxford Medical Science Division)

3. Paired pulse TMS measures

For this protocol, you will receive two TMS pulses over your head for each delivery. We call the first pulse as a “conditioning pulse”, which will be lower intensity than your resting motor threshold (80-90% of RMT). The second pulse is a “testing pulse”, which will be delivered at 120% of RMT. Similar to single TMS technique, we will record muscle activity using surface EMG. For each condition (e.g., rest, stable, unstable condition), 15-20 stimulations will be delivered, so in total 45-60 paired pulse stimulations will be delivered.

What are the benefits of the study?

There will be no direct benefit from participation in this study. However, future patients with PD and clinicians may benefit from the knowledge gained through this study.

What are the risks associated with this study?

Potential Risks of TMS

Single and paired pulse TMS protocols are reported to be very safe for research and TMS device is FDA approved for research; however, there are potential risks reported depending on the protocols. These risks are applied to both healthy individuals and individuals with PD. To minimize potential risks, we will strictly follow the guidelines of safety and ethical use of TMS and thoroughly screened the participants with TMS screening questionnaires.

1) Metals near the TMS coil

Because the TMS coil generates a magnetic field, any metals near the head can move or be heated. Therefore, before TMS procedures, all metals around the head will be removed. Also,

any participants with metal implants in their eyes, head, brain or ear, except for dental filling, will be excluded from the study.

2) Risk of seizure

The greatest potential side effect is TMS induced seizure. However, seizure induction with single pulse and paired-pulse TMS is extremely rare, and there has been no report on seizure with paired-pulse TMS. Approximately 1.4% with epileptic patients and less than 1% with healthy individuals are estimated to be at a risk of seizure with a certain protocol (such as repetitive TMS with higher frequency stimulation). However, our TMS protocols for this study do not include such protocol, which minimizes the risk of seizure induction. However, in order to continue preventing and minimizing the risk of seizure in TMS studies, we will be very conservative to screen potential participants.

The investigators are trained to recognize any signs of seizures. If seizure occurs during the TMS procedures, the data collection will be immediately stopped, and the investigators will follow the standardized seizure management. If the participant exhibits seizure symptoms that are not recovered shortly after the occurrence, the investigator will call 911. A seizure may result in disturbance of sensation, loss of consciousness or cognitive function, convulsion movement, or combinations of these symptoms. Short-term effects of stimulation induced seizure are known to be disappeared within 2 days, and longer-term effects of stimulation induced seizure on physical risks are not reported.

3) Headache

Muscles and nerves near the stimulation coil may cause temporary discomfort. Occasional migraine or tension headache may be triggered by TMS. The temporary discomfort and headache can be resolved by over the counter drugs such as Tylenol or Ibuprofen.

4) Temporary hearing loss

The TMS coil generates click sounds during stimulation, which ranges 87-114 dB. We will provide ear plugs if you are not able to tolerate the click sounds during procedures.

5) Single-pulse and paired-pulse TMS are reported to be safe, however, there may be any other risks that are not yet known.

Will I be paid for taking part in this study? Does it cost anything to participate?

You will not be paid for your participation. However, your parking pass will be covered by the department. There is no cost to participate in this study.

How will my information be protected?

For participant privacy and data confidentiality, research procedures including initial screening and the informed consent process will be conducted in person in a private setting. Each participant will be given subject ID number and their biographical and statistical data will be recorded via custom data collection software. An electronic record of the data sheet will be

recorded on the research lab's computers identifiable only by subject ID number. All computers are password protected. The informed consent form and other initial screening and clinical assessment documents will be kept in a locked filing cabinet in the PTIA 112 at California State University, Fresno.

What if I get sick or injured or need emergency care?

If at any point you become injured or sick due to participation in the study, notify the investigator the research as soon as possible. If you need to go to a doctor or see a healthcare professional, you or your personal insurance will be responsible for any related billing. The situation should be handled just like you would if you were to get injured or sick at any other time.

What rights do I have and can I choose to stop participating in the study?

Participation in this study is completely optional and voluntary. If you do not want to participate in this study, for any reason, you do not have to. You can leave the study at any time for any reason without consequences. Consent can be withdrawn at any time if you unable or inadequately perform the tasks associated with the research.

Who can I contact with questions concerning the study?

If you have any questions throughout your decision-making process, or during the study, you are welcome to contact the principal investigators, Dr. Hannah Ko at (559) 278-4862. If you have any questions pertaining to your rights, please contact Dr. Jennifer Randles, the Chair, CSUF Committee for the Protection of Human Subjects, (559) 278-2985.

Department of Physical Therapy

Permission for Participation in a Research Study
California State University, Fresno

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Documentation of Permission:
By signing this document, I am agreeing that I have read this form in its entirety, and voluntarily participate in this study. I understand, or have asked questions to clarify, what I will be asked to do during the duration of this study, the purposes of this study, and the risks involved. I understand that I have the right to discontinue involvement with this study at any time. In addition, my signature below means that I have been offered a copy of this form.

Signature:	Print Name:	Date:

Signature of Person Obtaining Consent (or Principle Investigator)	Print Name:	Date:

☐ **I give permission to show still or video images of me while presenting these data or in a publication**