GENERAL STUDY INFORMATION

Use for greater than minimal risk studies and minimal risk studies that fit into one or more expedited categories (see Section 5.3 of our Policies & Procedures for details regarding expedited research).

Do NOT submit this form if the study will qualify for exempt review, instead submit HRP-UT902 IRB Proposal – Exempt Submission Form found in the document Library.

If you are only using secondary data that will not be initially collected solely for this research project, use HRP-UT903 Template IRB Proposal Secondary Use form instead.

For studies following a multi-center or sponsor protocol, please use this guidance to assist in your completion of this form.

For questions regarding definitions, policies, or terms referenced below see the policies and procedures manual.

Please note, Word online does not support Word checkboxes. Please download the file and use your desktop version of Microsoft Word.

1 Review Type (Choose one)

*Click on the check box (or double click and type an "X" if using Google Docs) the **one** review type that applies.*

Please note: Expedited Review does not refer to the timeliness of the review of your protocol, but specific categories of research defined by ORHP. If you would like help determining which type of review is most appropriate for your study please contact the Office of Research Support and Compliance: https://research.utexas.edu/ors/about-ors/contact-us/.

a ☒ **Full Board Review – Greater than Minimal Risk Research**

b ☐ **Expedited Review – Minimal Risk Research**

2 Research Hypothesis

To input text, click in the light grey area below.

Hypothesis 1 (Experiment 1): Transcranial magnetic stimulation (TMS) can be accurately applied during brain states reflecting strong and weak corticospinal tract recruitment.

Hypothesis 2 (Experiment 2): Transcranial magnetic stimulation (TMS) applied during brain states reflecting strong corticospinal tract recruitment will activate more alpha motoneurons than identical TMS applied during brain states reflecting weak corticospinal tract recruitment or random brain states.

Hypothesis 3 (Experiment 3): Delivering paired corticospinal-motoneuronal stimulation (PCMS) during brain states reflecting strong corticospinal tract recruitment will increase (a) corticospinal transmission, (b) voluntary

hand muscle activation, (c) voluntary hand muscle force production, and (d) hand dexterity more than identical PCMS applied during brain states reflecting weak corticospinal tract recruitment or random brain states.

3 Study Background

To input text, click in the light grey area below.

Stroke is the leading cause of long-term disability in the United States (Go et al. 2013) and commonly disrupts the corticospinal tract (Twitchell 1951). The presence of residual corticospinal connections is one of the best prognostic markers of post-stroke motor function and recovery potential (Stinear et al. 2007), indicating that the most serious and long-lasting stroke-related motor deficits are caused by corticospinal tract disruption. Interventions capable of strengthening residual corticospinal connections are thus promising candidates for improving motor function after stroke. Paired cortico-motoneuronal stimulation (PCMS) can strengthen corticospinal connections in healthy adults (Taylor and Martin 2009; Bunday and Perez 2012) and patients with corticospinal tract disruption caused by spinal cord injury (Bunday and Perez 2012). PCMS involves repeatedly delivering precisely-timed pairs of non-invasive peripheral stimuli (via transcutaneous peripheral nerve stimulation) and cortical stimuli (via transcranial magnetic stimulation) such that they induce long-term potentiation via spike-timing dependent plasticity ($STDP_{LTP}$) at corticospinal-motoneuronal synapses, which are essential to human dexterity (Lemon 2008).

For PCMS to maximally enhance motor output and dexterity, it must reliably activate as many corticospinal-motoneuronal synapses as possible. However, corticospinal tract recruitment via TMS varies significantly with the brain state at the exact moment of TMS delivery (Sauseng et al. 2009; Berger et al. 2014; Zrenner et al. 2018; Hussain et al. 2019a, Hussain et al. 2019b; Bergmann et al. 2019). Yet, current approaches deliver PCMS irrespective of the brain state. Delivering PCMS in this way ensures that only a fraction of stimuli occur during brain states that are likely to maximally recruit alpha motoneurons. By delivering PCMS during brain states reflecting strong alpha motoneuron recruitment, $STDP_{LTP}$ could be induced at a greater proportion of corticospinal-motoneuronal synapses, leading to greater PCMS-induced gains in corticospinal transmission and hand function. We recently developed a novel machine learning framework that successfully identifies brain states during which TMS strongly or weakly activates the corticospinal tract. Results of this work show that individually-defined brain states predict TMS-related activation of the corticospinal tract (Hussain and Quentin 2021), suggesting that delivering PCMS during these states could improve PCMS's efficacy.

The long-term goal of this work is to improve voluntary hand muscle activation and manual dexterity in chronic stroke patients with residual corticospinal connections. As first steps towards this goal, the efficacy of brain state-dependent PCMS must be established in the healthy nervous system. The purpose of this project is to establish this efficacy in healthy adults. The aims of this study are to:

1) validate the accuracy of real-time brain state-dependent TMS
2) determine if TMS activates more alpha motoneurons when applied during brain states reflecting strong corticospinal recruitment than during brain states reflecting weak corticospinal recruitment or random brain states.
3) determine if delivering PCMS during brain states reflecting strong corticospinal recruitment enhances the behavioral and neurophysiological effects of PCMS.

Abbreviations:
TMS: transcranial magnetic stimulation
EEG: electroencephalography
EMG: electromyography
PNS: peripheral nerve stimulation
PCMS: paired corticospinal-motoneuronal stimulation
ISI: inter-stimulus interval
TST: triple stimulation technique
RMT: resting motor threshold
M-max: intensity needed to elicit a maximal muscle response using PNS or TMS
FDI: left first dorsal interosseous
MEP: motor evoked potential

4 Design and Methodology

Provide information regarding study design or data collection methodologies. Details regarding protocol specific research procedures will be discussed in a later section.

To input text, click in the light grey area below.

For all experiments, single-pulse TMS will not be applied at a rate that exceeds 0.5 Hz. That is, at least 2 seconds will elapse between individual single TMS pulses.

Experiment 1

Design: within-subjects, single-group
Population: healthy adults (≥ 18 years old)
Conditions:

1. TMS during brain states reflecting strong corticospinal recruitment
2. TMS during brain states reflecting weak corticospinal recruitment
3. TMS may also be applied during random brain states
    a. The order of conditions will be randomized

Session frequency: Up to 2 sessions for <= 6 hours. Each session will involve the same experimental procedures (see below). In the event of technical difficulties, a third session may be performed, during which any combination of the procedures described below may be applied. At least 24 hours will elapse between sessions.
Methodology:
EEG recordings: EEG will be recorded while participants rest quietly with their eyes open and during stimulation procedures. 64 EEG electrodes will be secured to the scalp using a swim-like cap and electrode gel.
EMG recordings: EMG will be recorded from a maximum of 5 hand and wrist muscles while participants rest quietly and during stimulation procedures (see below, *Real-time brain state-dependent TMS*). EMG will be recorded from <= 8 hand and wrist muscles.
Brain state discovery: <= 600 single TMS pulses will be applied to the scalp at <= 120% of scalp RMT during EEG and EMG recordings. These data will be used to identify brain states reflecting strong versus weak corticospinal tract recruitment using machine learning.
Real-time EEG analysis: The EEG system will stream data to a dedicated computer. This computer will analyze the data in real time to identify brain states associated with strong or weak corticospinal tract recruitment (see above), or a random mixture of the two.
Real-time brain state dependent TMS: The real-time EEG analysis algorithm will trigger delivery of a single TMS pulse when it identifies brain states predicted to reflect strong, weak, and/or random corticospinal tract

recruitment. <= 450 single TMS pulses at <=120% RMT during strong, weak and/or random brain states may be delivered.

Experiment 2

Design: within-subjects, single-group
Population: healthy adults (≥ 18 years old)
Conditions:

4. Triple stimulation technique (TST) assessment during brain states reflecting strong corticospinal recruitment
5. TST assessment during brain states reflecting weak corticospinal recruitment
6. TST assessment during random brain states
    a. The order of conditions will be randomized

Session frequency: Up to 2 sessions for <= 6 hours. Each session will involve the same experimental procedures (see below). In the event of technical difficulties, a third session may be performed, during which any combination of the procedures described below may be applied. At least 24 hours will elapse between sessions.
Methodology:
EEG recordings: EEG will be recorded while participants rest quietly with their eyes open and during stimulation procedures. 64 EEG electrodes will be secured to the scalp using a swim-like cap and electrode gel.
EMG recordings: EMG will be recorded while participants rest quietly and during stimulation procedures (see below, *Calculation of ISIs for TST assessment* and *TST assessment*). EMG will be recorded from a maximum of 5 hand and wrist muscles.
Brain state discovery: <= 600 single TMS pulses will be applied to the scalp at <= 120% of scalp RMT during EEG recordings. These data will be used to identify brain states reflecting strong versus weak corticospinal tract recruitment using machine learning.
Real-time EEG analysis: The EEG system will stream data in real-time to a dedicated computer. This computer will analyze the data in real time to identify brain states associated with strong or weak corticospinal tract recruitment (see above), or a random mixture of the two. When desired states are identified, either a single TMS pulse (see *Evaluation of state-targeting* accuracy) or the TST (see *TST assessment*) will be triggered.
Evaluation of state-targeting accuracy: <= 150 single TMS pulses will be applied to the scalp at <= 120% of scalp RMT during EEG recordings.
Calculation of ISIs for TST assessment: The following stimulation procedures will be performed to calculate the ISIs for TST assessment.

1. <= 25 Single-pulse TMS to the scalp at <= 120% of scalp RMT
2. <= 25 Single-pulse PNS to the left wrist at <= 120% of M-max
3. <= 25 Single-pulse PNS to the left Erb's point at <= 120% of M-max

TST assessment: The TST will be applied according to an established protocol (Magistris et al. 1998) using consecutive application of TMS (<= 120% of scalp RMT), PNS at the left wrist (<= 120% of M-max), and PNS at the left Erb's point (<= 120% of M-max). The delays between each stimulus will be individualized based on each participants central and peripheral conduction times (see *Calculation of ISIs for TST assessment*). The TMS portion of the TST will be timed to occur during brain states reflecting strong corticospinal tract recruitment, weak corticospinal tract recruitment, or random brain states, using real-time EEG analysis. <= 50 TST applications will be performed per brain state condition.

Experiment 3

Design: within-subjects, single group
Population: healthy adults (≥ 18 years old)
Conditions: At least 24 hours will elapse between sessions.

1. Active PCMS delivered during brain states reflecting strong corticospinal recruitment
2. Active PCMS delivered during brain states reflecting weak corticospinal recruitment
3. Active PCMS delivered during random brain states

4. Control PCMS delivered during brain states reflecting strong corticospinal recruitment
    a. The order of conditions will be counterbalanced
    b. Participants may complete one, two, three or four of the conditions

Session frequency: Up to 4 sessions for <= 6 hours each. In the event of technical difficulties, <= 3 additional sessions may be requested, during which any combination of the procedures described below may be applied.

Methodology:

EEG recordings: EEG will be recorded while participants rest quietly with their eyes open and during stimulation procedures. 64 EEG electrodes will be secured to the scalp using a swim-like cap and electrode gel.

EMG recordings: EMG will be recorded from a maximum of 5 hand and wrist muscles while participants rest quietly and during stimulation procedures (see below, *Calculation of ISIs for PCMS* and *PCMS*). EMG will be recorded from <= 8 hand and wrist muscles.

Brain state discovery: <= 600 single TMS pulses will be applied to the scalp at <= 120% of scalp RMT during EEG recordings. These data will be used to identify brain states reflecting strong versus weak corticospinal tract recruitment using machine learning.

Real-time EEG analysis: The EEG system will stream data in real-time to a dedicated computer. This computer will analyze the data in real time to identify brain states associated with strong or weak corticospinal tract recruitment (see above). When states are identified, either a single TMS pulse (see *Evaluation of state-targeting* accuracy) or PCMS (see *PCMS*) will be triggered.

Evaluation of state-targeting accuracy: <= 150 single TMS pulses will be applied to the scalp at <=120% of scalp RMT during EEG recordings.

Calculation of ISIs for PCMS: The following stimulation procedures will be performed to calculate the ISIs for both control and active PCMS.

1. <= 25 Single TMS pulses to the scalp at <= 120% of scalp RMT
2. <= 25 Single PNS pulses to the left wrist at <= 120% of M-max

PCMS: PCMS will involve <= 150 pairs of scalp TMS and wrist PNS, applied repeatedly with >= 10 seconds between pairs. The TMS aspect of PCMS will be timed to occur during brain states reflecting strong corticospinal recruitment, brain states reflecting weak corticospinal recruitment, or random brain states, and the ISI between TMS and PNS will be based on individual peripheral and central conduction times (see *Calculation of ISIs for PCMS)*.

Corticospinal excitability measurements: <= 25 single TMS pulses to the scalp at <= 120% RMT. Measurements will be taken immediately before PCMS and at 0, 20 and 40 minutes after PCMS.

Spinal excitability measurements: <= 25 single PNS pulses to the left wrist at <= 120% of M-max. Measurements will be taken immediately before PCMS and at 0, 20 and 40 minutes after PCMS.

Voluntary motor output measurements: <= 5 maximum voluntary contractions of the FDI, each lasting <= 5 seconds. Measurements will be taken immediately before PCMS and at 0, 20 and 40 minutes after PCMS.

Manual dexterity measurements. <= 5 attempts of the 9-hole peg test. Measurements will be taken immediately before PCMS and at 0, 20 and 40 minutes after PCMS.

5 Data Analysis

Describe the data analysis plan, including any statistical procedures or power analysis.
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Experiment 1:

1. Primary outcome: Amplitude of MEPs evoked during brain states reflecting strong, weak, and/or random corticospinal tract recruitment
    a. This outcome will be evaluated using linear-mixed effects models (fixed effect of state, random effect of subject) with alpha equal to 0.05.

Experiment 2:

1. Primary outcome: amplitude of FDI muscle response after TST application during brain states reflecting strong, weak, and random corticospinal tract recruitment.
2. Secondary outcome: area under the curve of FDI muscle response after TST application during brain states reflecting strong, weak, and random corticospinal tract recruitment.
    a. Both outcomes will be evaluated using linear mixed-effects models (fixed effect of state, random intercept of subject) with alpha equal to 0.05.

Experiment 3:

1. Primary outcomes: Maximum FDI force output, FDI activation (calculated using the root-mean-square of EMG signals obtained during FDI contractions)
2. Secondary outcome: Number of pegs placed per attempt at the 9-hole Pegboard test.
3. Exploratory outcomes: Amplitudes of MEPs produced by scalp TMS, amplitudes and persistence of F-waves evoked by wrist PNS
    a. All outcomes will be evaluated before and after PCMS. Outcomes will be analyzed using linear-mixed effects models (fixed effects of condition and time point, random intercept of subject). Main effects will be evaluated using likelihood ratio tests, and p-values from post-hoc contrasts will be corrected for multiple comparisons. Alpha will be equal to 0.05.

STUDY ELEMENT IDENTIFICATION

6 Study Elements

Click on the check box (or double click and type an "X" if using Google Docs) each procedure included in your study.

A full description of all study procedures should be provided in the Procedures (Details) section below and/or the applicable supplement form.

☐	Bio-specimens	☒	Biometrics	☐	Registry or Repository
☐	Focus Group	☐	Genetic Analysis	☐	Genomic Data Sharing
☐	International Research	☐	Interview/Survey	☐	MRI
☐	Protected Health Information	☒	Observation	☐	Record Review
☒	Sensors (Externally Placed)	☐	Sensors (Inserted)	☐	Video/Audio Recording
☐	X-Ray				

7 Study Intervention

Click on the check box (or double click and type an "X" if using Google Docs) if you will implement any of the following interventions.

A full description of all study interventions should be provided in the Procedures (Details) section below and/or the applicable supplement form.

☐	Behavioral	☒	Device	☐	Drug/Biologic

8 Clinical Trial

Click on the following check box (or double click and type an "X" if using Google Docs) if the research meets the below definition of a clinical trial.

☐ **This study meets the definition of a clinical trial according to clinical trials.gov in that it involves one or more human subjects who are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.**

9 Additional Oversight

Click on the check box (or double click and type an "X" if using Google Docs) each activity that requires oversight from additional UT committees.

☐	Biohazards, Recombinant DNA, or Gene Transfer	☒	Energy introduced to the subject (electrical, magnetic, light)	☐	Human embryonic, human induced pluripotent, or human totipotent stem cells; or human gametes or embryos
☐	Radiation exposure without direct clinical benefit				

10 Alternatives to Participation in This Study

To input text, click in the light grey area below.

Participants are not expected to benefit from this study, and this study is not designed to treat any medical condition. The alternative is to not participate.

11 Procedure Description

Describe all study procedures, including a step-by-step outline of what participants will be asked to do or how data will be used. Be sure to describe all of the following in detail, as applicable:

- Provide a description of all research procedures being performed and when they are performed, in sequential order.
- All research measures/tests that will be used and state if questions or measures are standardized or published (upload copies of all surveys, scripts and data collection forms)
- Secondary data or specimens that will be obtained, how they will be collected, and how they will be used
- Where each activity will take place, the duration of each, and who will perform each activity
- Include time commitment of participants

To input text, click in the light grey area below.

All procedures will take place in BEL 546F. All procedures will be carried out by trained research staff listed on this protocol. Participants may participate in any or all experiments described under this protocol. If participants choose to participate in more than one experiment, an informed consent document will be signed for each experiment. There is no specific mechanism for determining which participants participate in each experiment. The only requirement for participation is willingness to participate and eligibility. Prior to enrollment, participants will be pre-screened using RedCap to determine potential study eligibility.

Experiment 1:

- The participant and research team member will review and discuss the informed consent document.
- Eligibility will be formally determined by the research team member by reviewing a list of the inclusion and exclusion criteria with the participant (see attachments).
- Participants will complete a short demographics survey.
- The EEG cap will be positioned on the participants head according to the 10-20 International EEG system (Seeck et al. 2017). The scalp beneath each electrode may be cleaned with alcohol, and an electrolytic gel will be applied beneath each electrode. Afterwards, the scalp may be lightly abraded using a blunt needle.
- The skin on the left hand and wrist will be cleaned using isopropyl alcohol. EMG electrodes will be attached to a maximum of 5 hand and wrist muscles using medical grade adhesive. A ground electrode will attached to the dorsum of the hand in the same manner.
- The scalp TMS hotspot will be determined as the site of the scalp producing the most reliable focal muscle twitch within the left FDI. The scalp RMT will be determined using an automatic threshold tracking tool (Awiszus and Borckhardt 2011) as the minimum stimulation intensity needed to elicit an MEP of 50 microvolts in peak-to-peak amplitude in response to 50% of stimuli. EMG and EEG signals may be recorded for offline quality control analysis.
- <= 600 single-pulse TMS pulses will be delivered during EEG and EMG recordings. Immediately afterwards, EEG and EMG data will be analyzed using machine learning. The brain states identified using machine learning will be used for all subsequent real-time EEG analysis.
- The real-time EEG algorithm will be used to deliver <= 150 single TMS pulses during brain states associated with strong corticospinal recruitment, <= 150 single TMS pulses during brain states associated with weak corticospinal recruitment, and/or <=150 single TMS pulses during randomly selected brain states, for a total of <= 450 single TMS pulses. During this time, participants will rest quietly with their eyes open (Zrenner et al. 2018; Hussain et al. 2020).

- We may also record EEG signals at any time point during testing while participants rest quietly with their eyes open.
- The EEG cap and EMG electrodes will be removed and participants will leave the laboratory.
- If participants are asked to complete two sessions, the same experimental procedures described above may be used during the second session. The second session may be used to evaluate between-day reliability of the measurements made during the first session. At least 24 hours will elapse between sessions.

Experiment 2:

- The participant and research team member will review and discuss the informed consent document.
- Eligibility will be formally determined by the research team member by reviewing a list of the inclusion and exclusion criteria with the participant (see attachments).
- Participants will complete a short demographics survey.
- The EEG cap containing will be positioned on the participants head according to the 10-20 International EEG system (Seeck et al. 2017). The scalp beneath each electrode may be cleaned with alcohol, and an electrolytic gel will be applied beneath each electrode. Afterwards, the scalp may be lightly abraded using a blunt needle.
- The skin on the left hand, left wrist, and left Erb's point will be cleaned using isopropyl alcohol. EMG electrodes will be attached to a maximum of 5 hand and wrist muscles using medical grade adhesive. PNS electrodes will be attached to the left wrist and left Erb's point using medical grade adhesive. A ground electrode will attached to the dorsum of the hand in the same manner.
- The scalp TMS hotspot will be determined as the site of the scalp producing the most reliable focal muscle twitch within the left FDI. The scalp RMT will be determined using an automatic threshold tracking tool (Awiszus and Borckhardt 2011) as the minimum stimulation intensity needed to elicit an MEP of 50 microvolts in peak-to-peak amplitude in response to 50% of stimuli. EMG and EEG signals may be recorded for offline quality control analysis.
- Single-pulse TMS pulses will be delivered during EEG and EMG recordings. Immediately afterwards, EEG and EMG data will be analyzed using machine learning. The brain states identified using machine learning will be used for all subsequent real-time EEG analysis.
- M-max following PNS at the wrist and Erb's point will be determined by increasing stimulation intensity until a larger FDI response cannot be obtained. Either bipolar stimulation with both the cathode and anode positioned over the left clavicle or monopolar stimulation with a cathode positioned over the left clavicle and an anode positioned in the internal region of the suprascapular fossa will be used to evoke a muscle response in FDI from Erb's point. EMG and EEG signals may be recorded for offline quality control analysis.
- Single-pulse TMS, wrist PNS, and Erb's point PNS will be performed to calculate ISIs needed for the TST (see Design and Methodology). EMG signals will be recorded to enable ISI calculation. EEG may be recorded for offline quality control analysis.
- The real-time EEG algorithm will be used to deliver <= 50 single TMS pulses during brain states associated with strong corticospinal recruitment, <= 50 single TMS pulses during brain states associated with weak corticospinal recruitment, and <=50 single TMS pulses during randomly selected brain states. During this time, participants will rest quietly with their eyes open (Zrenner et al. 2018; Hussain et al. 2020). EEG and EMG signals will be recorded to allow offline verification of accurate state targeting identification as a quality control procedure (Zrenner et al. 2018; Hussain et al. 2020).
- The participant will take a break while ISIs required for TST application are calculated using the following formulas:
    - Delay 1 = latency of MEP evoked by TMS – latency of FDI muscle response evoked by wrist PNS
    - Delay 2 = latency of muscle response evoked by Erb's point PNS – latency of FDI muscle response evoked by wrist PNS

- The TST will be applied during brain states reflecting strong corticospinal recruitment, brain states reflecting weak corticospinal recruitment, and randomly selected brain states according to an established procedure (Magistris et al. 1998), with details below. EMG data will be recorded and processed offline to calculate the primary and secondary outcomes. EEG data will be recorded and processed offline to ensure accurate state identification as a quality control procedure (Zrenner et al. 2018; Hussain et al. 2020).
    - TMS will be timed using the real-time EEG analysis algorithm
    - After an interstimulus interval equal to delay 1, Wrist PNS will be applied.
    - After an interstimulus interval equal to delay 2, Erb's point PNS will be applied.
- The EEG cap, EMG electrodes, and PNS electrodes will be removed and participants will leave the laboratory.
- If participants are asked to complete two sessions, the same experimental procedures described above may be used during the second session. The second session may be used to evaluate between-day reliability of the measurements made during the first session. At least 24 hours will elapse between sessions.

Experiment 3

Days 1-4 (at least 24 hours will elapse between sessions)

- The participant and research team member will review and discuss the informed consent document.
- Eligibility will be formally determined by the research team member by reviewing a list of the inclusion and exclusion criteria verbally with the participant (see attachments).
- Participants will complete a short demographics survey.
- The skin on the left hand and wrist will be cleaned using isopropyl alcohol. EMG electrodes will be attached to a maximum of 5 hand and wrist muscles using medical grade adhesive. PNS electrodes will be attached to the left wrist using medical grade adhesive. A ground electrode will also attached to the dorsum of the hand in the same manner.
- The scalp TMS hotspot will be determined as the site of the scalp producing the most reliable focal muscle twitch within the left first dorsal interosseous muscle. The scalp RMT will be determined using an automatic threshold tracking tool (Awiszus and Borckhardt 2011) as the minimum stimulation intensity needed to elicit a MEP of 50 microvolts in peak-to-peak amplitude in response to 50% of stimuli. EMG signals may be recorded for offline quality control analysis.
- Single-pulse TMS pulses will be delivered during EEG and EMG recordings. Immediately afterwards, EEG and EMG data will be analyzed using machine learning. The brain states identified using machine learning will be used for subsequent real-time EEG analysis.
- The M-max following PNS at the wrist will be determined by increasing stimulation intensity until a larger response cannot be obtained. EMG signals may be recorded for offline quality control analysis.
- Electrode positions may be marked on the skin using a skin-safe surgical marker to ensure consistent electrode placement across sessions.
- Single-pulse TMS to the scalp and wrist PNS will be performed to calculate delays needed for PCMS (see Design and Methodology). EMG signals will be recorded to enable delay calculation.
- Delays for PCMS application will be calculated using the following formulas (units are milliseconds; Bunday and Perez 2012; Urbin et al. 2021):
    - Peripheral Conduction Time (PCT) = (F-wave latency –M-wave latency) * 0.5
    - Central Conduction Time (CCT) = MEP latency – (PCT + M-wave latency)
    - Active PCMS Delay = (PCT – CCT) – X ms (where X = 1 – 5 ms)
    - Control PCMS Delay = (PCT – CCT) + X ms (where X = 5 – 30 ms)
- The real-time EEG analysis algorithm will be used to deliver TMS pulses during the target brain state for that session. The order of brain states targeted per session will be counterbalanced across subjects. During this time, participants will rest quietly with their eyes open (Zrenner et al. 2018; Hussain et al. 2020). EEG and EMG data will be recorded for offline quality control analysis.

- Participants will complete pre-PCMS measurements of corticospinal excitability, spinal excitability, voluntary motor output, and manual dexterity (see Design and Methodology). EMG signals will be recorded during all measurements and processed offline to obtain outcome measures. EEG may recorded for offline quality control analysis.
- The PCMS intervention will be delivered (see Design and Methodology) during the target brain state for that session. The order of brain states targeted per session will be counterbalanced across subjects. EEG and EMG signals will be recorded for subsequent quality control analysis.
    - Active PCMS during brain states reflecting strong corticospinal recruitment, with the delay between scalp TMS and wrist PNS equal to the Active PCMS delay.
    - Active PCMS during brain states reflecting weak corticospinal recruitment, with the delay between scalp TMS and wrist PNS equal to the Active PCMS delay.
    - Active PCMS during random brain states, with the delay between scalp TMS and wrist PNS equal to the Active PCMS delay.
    - Control PCMS during brain states reflecting strong corticospinal recruitment, with the delay between scalp TMS and wrist PNS equal to the Control PCMS delay.
- Participants will complete post-PCMS measurements of corticospinal excitability, spinal excitability, voluntary motor output, and manual dexterity (see Design and Methodology) immediately, 20 minutes, and 40 minutes after PCMS is complete. EMG signals will be recorded during all measurements and processed offline to obtain outcome measures. EEG may recorded for offline quality control analysis.
- EEG, EMG and PNS electrodes will be removed and participants will leave the laboratory.

SUBJECT POPULATION

12 Protected Subject Populations

Click on the check box (or double click and type an "X" if using Google Docs) each population, if they are specifically studied for this research.

☐ Active military personnel	☐ Children	☐ Decisionally impaired adults
☐ Emancipated minors	☐ Fetuses	☐ Individuals with limited English proficiency
☐ Neonates	☐ Pregnant Woman	☐ Prisoners
☐ UT Students	☐ UT or Seton Staff/Employees	

13* Research Participant Information

Describe the research population.

**For multiple research populations (e.g., teachers, students, and parents), copy this section as necessary to describe your population.*

a Participant Group Name

To input text, click in the light grey area below.

Healthy adults

b Minimum Age

To input text, click in the light grey area below.

18

c Maximum Age

To input text, click in the light grey area below.

none

d Inclusion Criteria

To input text, click in the light grey area below.

Right-hand dominance
Willingness to participate
Ability to provide informed consent

e Exclusion Criteria

To input text, click in the light grey area below.

History of major neurological, orthopedic, psychiatric, or cardiovascular disease
Presence of contraindications to TMS or PNS (Keel et al. 2000), including:

1) history of adverse reactions to TMS or PNS
2) history of stroke or head injury
3) metal in head, eyes, neck, chest/trunk, or arms, including but not limited to shrapnel, surgical clips, fragments from metalworking, fragments from welding
4) implanted devices
5) history of frequent and severe headaches or migraines
6) immediate family history of seizure or epilepsy
7) personal history of seizure or epilepsy
8) current, suspected, or planned pregnancy
9) current or recent (within the last 3 months) use of medications acting on the central nervous system, including but not limited to: antipsychotic drugs, antidepressants, benzodiazepines, prescription stimulants

f Additional Population Information

To input text, click in the light grey area below.

none

14 Total Sample Size

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Experiment 1: target N=20, maximum N=30
Experiment 2: target N=20, maximum N=30

Experiment 3: target N=20, maximum N=30

Maximum N values are increased compared to the target N to account for subject drop-out and withdrawal. Participants may participate once in each experiment.

15 Sample size rationale

To input text, click in the light grey area below.

Experiments 1 and 2: Previous work examining brain state-dependency of corticospinal transmission achieved adequate power with N=17 (Hussain et al. 2019; Hussain and Quentin 2021) and N=12 (Zrenner et al. 2018). The expected effect sizes of Experiments 1 and 2 are predicted to be very similar to that observed in these two studies. To be conservative in our effect size estimates, we have increased the sample size from N=12-17 to N=20 to ensure adequate power.

Experiment 3: Previous work examining PCMS in healthy adults identified a significant effect of this intervention with N=14 (Bunday and Perez 2012). More recent work examining the impact of voluntary contraction of PCMS efficacy identified significant enhancement of PCMS efficacy with N=14. The expected effect size in Experiment 2 is predicted to be very similar to that observed in these two studies. To be conservative in our effect size estimates, we have increased the sample size from N=14 to N=20. A maximum of N=30 will be recruited to account for subject withdrawal.

SCREENING AND RECRUITMENT

16 Identification and Screening

Click on the check box (or double click and type an "X" if using Google Docs) if true.

☒ **This study involves obtaining information or biospecimens for the purpose of screening, recruiting or determining eligibility of prospective subjects prior to informed consent by either:**

1. Oral or written communication with the prospective subject or LAR
2. By accessing records containing identifiable private information or stored identifiable biospecimens.

17 Identification and/or Screening Procedures

Describe the identification and/or screening procedures below.
To input text, click in the light grey area below.

Screening procedures will involve preliminary determination of eligibility (using eligibility checklist, see attachments) in person, by telephone, or via email. Eligibility will also be formally assessed in-person after participants provide their informed consent.

18 Recruitment Overview

Click on the check box (or double click and type an "X" if using Google Docs) all recruitment methods utilized for this research.

☒	E-mail	☒	Flyer
☐	In-Person	☐	Letter
☒	Social Media	☒	Research Pool
☒	Telephone/Text	☐	Snowball Sampling
☒	Web-post	☒	Word of Mouth

19 Describe the recruitment process, including where recruitment will take place.

Describe the recruitment procedures below.
To input text, click in the light grey area below.

Email: Emails may be sent to UT students and staff via existing list-servs. All emails will be approved by the list-serv manager. See attachments.

Social media: We may post a short description of the study on social media (i.e., Twitter, Craigslist, Facebook, etc). See attachments.

Redcap: Redcap surveys will be used for recruiting and pre-screening. Once potential participants have completed the Redcap survey, they may be contacted via phone or email.

Web-post: We may post a short description of the study on UT websites. All web-posts will be approved by the website manager. See attachments.

Research pool: Participants may be recruited from existing lists and/or registries of individuals interested in participating in research that maintained by the Texas Aging and Longevity Center. These individuals may be contacted by telephone or email. See attachments.

Flyers: Flyers with a brief description of the study and the eligibility criteria may be posted on-campus at the University of Texas at Austin and at community locations throughout the greater Austin metropolitan area. See attachments.

Word of mouth: Researchers involved in this study may describe the study and eligibility criteria in-person to potential participants. If interested, participants will be invited to email or visit the laboratory (546F BEL) in-person to express interest prior to initiating the preliminary determination of eligibility. That is, potential participants must make first contact prior to enrollment after learning of the study via word of mouth.

OBTAINING INFORMED CONSENT

20 Consent Overview

Click on the check box (or double click and type an "X" if using Google Docs) all applicable items.

☒ Obtaining Written Informed Consent	☐ Requesting a Waiver of Documentation of Informed Consent
☐ Requesting a Waiver of Informed Consent	☐ Requesting an Alteration of the Required Elements of Informed Consent
☐ Obtaining Child Assent	☐ Obtain Consent Using a Short Form with a Witness

21 Consent and Assent Processes

Provide a detailed description of the consent process including who will obtain consent, where, and when consent will occur in such a manner that participants have sufficient time for adequate consideration.

To input text, click in the light grey area below.

A member of the research team trained by the PI in informed consenting procedures will explain the study to the participant verbally while reviewing the informed consent document with the participant. All pertinent information will be provided, including the purpose of the study, procedures, risks, and potential benefits for participation. The research team member will encourage the participant to ask any questions about the study. Following the verbal explanation, the participant will be allowed to review the informed consent form and be given sufficient time to review this document, and to decide whether or not to participate. The research team member will answer any questions the participant may have and obtain both verbal agreement and a signed consent form. The consent process will take place in BEL 546F.

22 Consent and Translation

Click on the check box (or double click and type an "X" if using Google Docs) to indicate that consent will be translated.

☐ The study population will likely include participants whose limited English speaking status requires translation of the consent form.

Translation Process

Click on the check box (or double click and type an "X" if using Google Docs) that best describes the translation process, either 21 or 22.

23 ☐ The consent documents will be translated by a certified translator.

24 ☐ A non-certified translator will translate the consent documents.

If selected, complete the next two questions below.

i Describe the translator's qualifications

To input text, click in the light grey area below.

n/a

ii ☐ **Another individual will confirm that the translation is accurate and appropriate.**

Waiver of Documentation of Informed Consent

To approve a waiver of documentation of informed consent, one of the following options below must be justified by the researcher.

Only complete the sections below if requesting a waiver of documentation of informed consent. *If not requesting a waiver of documentation of consent, skip to 27.*

Please choose one waiver option and provide additional information as prompted. The Office of Research Support and Compliance recommends using Waiver Option 2 in most cases.

25 **Waiver Option 1**

Provide confirmation for the following criteria and follow the additional instructions.

Additional Instructions:
1. Include this choice in the informed consent form.
2. Articulate the destruction process for signed consent forms in the privacy and confidentiality section.

Click on the check box (or double click and type an "X" if using Google Docs).

a ☐ **The only record linking the subject and the research would be the consent document.**

b ☐ **The principal risk would be potential harm resulting from a breach of confidentiality.**

c ☐ **Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.**

26 **Waiver Option 2**

Provide confirmation for the following criteria and follow the additional instructions.

Click on the check box (or double click and type an "X" if using Google Docs).

a ☐ **The study is minimal risk.**

b ☐ **Written consent would not be required outside the research context.**

27 **Waiver Option 3**

Provide confirmation for the following criteria and provide additional information as requested.

Click on the check box (or double click and type an "X" if using Google Docs).

a ☐ **The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm**

b **Describe the cultural group or community.**

To input text, click in the light grey area below

n/a

c ☐ **The research presents no more than minimal risk of harm to subjects.**

d ☐ **There is an appropriate alternative mechanism for documenting that informed consent was obtained.**

e **Describe mechanism for documenting that informed consent was obtained**

To input text, click in the light grey area below

n/a

Waiver or Alteration of Informed Consent

To approve a waiver or alteration of informed consent all of the following criteria below must be justified by the researcher.

Only complete the sections below if requesting a waiver of informed consent. *If not requesting a waiver or alteration of consent, skip to 31.*

28 **The research involves no more than minimal risk to the subjects.**

To input text, click in the light grey area below

n/a

29 **The waiver or alteration will not adversely affect the rights and welfare of the subjects.**

To input text, click in the light grey area below

n/a

30 **The research could not practicably be carried out without the waiver or alteration (it is impracticable to perform the research if obtaining informed consent is required and not just impracticable to obtain consent).**

To input text, click in the light grey area below

n/a

31 **If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.**

To input text, click in the light grey area below.

n/a

Deception and Debriefing

Only complete the sections below if requesting an alteration of informed consent that involves deceiving research participants. *If this study does not involve deception, skip to 35.*

See IRB Policies and Procedures Section 15 for a description of deception.

Click on the check box (or double click and type an "X" if using Google Docs).

32 ☐ **It is appropriate to provide additional pertinent information to the subject after research activities are complete (e.g., the researcher needed to deceive to subject to the nature of the study).**

33 ☐ **Research participants will have the opportunity to withdrawal their data during the debriefing.**

34 **Describe the nature of deception and why it is necessary to conduct the research.**

To input text, click in the light grey area below.

n/a

35 **Describe debriefing procedures.**

To input text, click in the light grey area below.

n/a

BENEFITS

36 **Benefits to Society**

Describe the scientific and societal benefit(s) below.

To input text, click in the light grey area below.

The research described in this protocol will benefit society by establishing the validity and efficacy of brain state-dependent PCMS in healthy adults, which may lead to better treatments for motor impairments after neurological diseases like stroke or spinal cord injury.

Benefits to Participants

Click on the applicable check box (or double click and type an "X" if using Google Docs).

37 ☒ **There is no anticipated direct benefit to participants.**

38 ☐ **There are anticipated benefits to participants.**

39 **If applicable, describe the potential direct benefits to participants.**

To input text, click in the light grey area below.

none

RISKS

40 **Describe the risks associated with each activity in this research**

To input text, click in the light grey area below.

The research described in this protocol is minimal risk.

EEG: EEG poses no known medical risk. Participants may experience scalp discomfort during application of the EEG electrodes. Participants may be annoyed by any remaining gel in their hair after completion of EEG procedures.

EMG: EMG poses no known medical risk. Participants may experience a mild itching sensation or skin irritation from the adhesives used to attach the EMG electrodes.

TMS: TMS, when applied in individuals without any contraindications (see exclusion critieria), and at a rate <= 1 Hz (as applied in this protocol) is considered to be minimal risk by the international neurophysiology community (Rossi et al. 2020) and the National Institutes of Health. Participants may experience mild muscle contractions (scalp, back, face, arms/hands) during TMS and may find it uncomfortable, but it is not painful. Some participants experience a mild headache after TMS.

PNS: PNS, when applied in individuals without any contraindications (see exclusion criteria), poses no known medical risk but can be painful. Participants may experience a burning or stinging sensation during PNS, and/or mild itching or skin irritation from the adhesives used to attach the EMG electrodes.

Behavioral testing: The behavioral testing procedures used here, including maximum voluntary contractions and manual dexterity assessment via the 9-hole Pegboard Test, pose no known medical risk. Participants may experience mild hand muscle soreness or fatigue during or after the behavioral assessments.

There is a risk of loss of confidentiality.

41 **Describe how each risk is mitigated/minimized.**

To input text, click in the light grey area below.

EEG: The risk of scalp discomfort will be minimized as much as possible by taking care to ensure subject comfort during EEG set-up and communicating with the participant continuously regarding their comfort level. Medical grade supplies will be used at all times.

EMG: Medical grade adhesives will be used at all times to minimize skin irritation and itching.

TMS: Participants will be fitted with earplugs during all TMS procedures to protect hearing. If a participant finds TMS too uncomfortable, they may choose not to continue participation.

PNS: Medical grade adhesives will be used at all times to minimize skin irritation and itching. The lowest possible stimulation intensities will be used to reduce pain experienced during PNS. If a participant finds PNS too uncomfortable, they may choose not to continue participation.

Behavioral testing: To minimize the risk of fatigue and soreness, participants will receive breaks during behavioral testing.

Loss of confidentiality: We will take all steps to minimize loss of confidentiality, including storing all study-related documents on password protected computers and in locked file cabinets behind locked laboratory doors of 546F BEL. Only study personnel will have access to personally-identifiable information.

Data Safety Monitoring

For additional information regarding data safety monitoring boards and data safety monitoring plans, please see Section 21 of our Policies and Procedures.

Click on the check box (or double click and type an "X" if using Google Docs).

42 ☐ **This study is minimal risk and does not require a Data Safety Monitoring Plan (DSMP) or a Data Safety Monitoring Board (DMSB).**

43 ☒ **This study does not have a Data Safety Monitoring Board, but researchers have an internal plan/policy to monitor for safety.**

Complete Data Safety Monitoring Details (44-51).

44 ☐ **This study has a Data Safety Monitoring Board (DSMB).**

Complete Data Safety Monitoring Details (44-51) or upload this study's Data Safety Monitoring Board's charter.

Data Safety Monitoring (Details)

45 **How is safety information collected?**

To input text, click in the light grey area below.

Safety information will be collected weekly as part of research team meetings. Researchers working on this study will provide a verbal report of any and all safety issues encountered during study sessions. If a safety issue is encountered, the PI will create a brief written description of the encountered issue and the steps taken to resolve this issue. Additional monitoring will be conducted by an independent medical monitor, please see Data Safety and Monitoring Plan (attached).

46 **When will safety data collection start (for each participant or for the whole study, as applicable)?**

To input text, click in the light grey area below.

For each participant, safety data collection will begin immediately after informed consent is provided and will continue until each participant completes their participation in the study.

47 How frequently will safety data be collected?

To input text, click in the light grey area below.

Safety data will be collected during every experimental session if a safety issue arises. Safety data will be verbally reported and discussed during weekly research team meetings.

48 Who will review the data for safety?

To input text, click in the light grey area below.

The PI will review the data for safety.

49 How frequently will data be monitored for safety concerns?

To input text, click in the light grey area below.

Data will be monitored for safety concerns weekly at research team meetings.

50 What data will be reviewed?

To input text, click in the light grey area below.

Verbal reports of research team members

51 State the frequency or periodicity of the review of cumulative data?

To input text, click in the light grey area below.

We will review the safety data at the time of continuing IRB review as well as at the time of NIH progress reporting.

52 State any conditions that would trigger an immediate suspension of the research.

To input text, click in the light grey area below.

If a serious adverse event occurs, enrollment and procedures will be suspended until a review can be performed by the IRB and until the IMM provides approval to re-start the study. Depending on the results of consultation with the IRB and IMM, the procedure associated with the serious adverse event may be removed from the project (after obtaining IRB approval) or specific language may be added to the written informed consent document to reflect any changes in risk level.

Early Withdrawal

Only complete this section if there are planned conditions under which a participant will be withdrawn from the study. *If not applicable, skip to 56.*

Include this information in your consent form.

53 **List the criteria for withdrawing individual participants from the study (e.g., safety or toxicity concerns, emotional distress, inability to comply with the protocol, or requirements from study sponsor).**

To input text, click in the light grey area below.

n/a

54 **Describe any necessary procedures for ensuring the safety of a participant who has withdrawn early.**

To input text, click in the light grey area below.

n/a

55 **Describe any pre-specified criteria for stopping or changing the study protocol due to safety concerns.**

To input text, click in the light grey area below.

n/a

REQUIRED DISCLOSURES

Required Consent Disclosures

Identify each element below that may require additional information to be disclosed in the consent form.

Click on the check box (or double click and type an "X" if using Google Docs).

56 ☒ **It is reasonable that researchers could discover or suspect child or elder abuse.**

57 ☐ **It is reasonable that researchers could learn of an incident that could require reporting under Title IX.**

58 ☐ **It is reasonable that researchers could discover incidental findings or other information of medical interest about a participant's previously unknown condition.**

59 **Articulate methods for addressing and reporting incidental findings, if applicable.**

To input text, click in the light grey area below.

n/a

PRIVACY AND CONFIDENTIALITY

60 **Privacy**

Describe how you will protect the identity and privacy of study participants during each phase of research. Privacy focuses on the individual participants rather than data. In this section, researchers should focus on issues such as where research activities take place and how participant involvement is protected from non-participants.

Describe methods to ensure participants' privacy during identification, recruitment, screening, the consent process, the conduct of the study, and dissemination of data.

To input text, click in the light grey area below.

Potential participants will contact the research team either by email, telephone or in-person on an individual basis. Participants may also express their interest in participating by completing a RedCap survey (see attachments). RedCap is a secure database. Surveys associated with this project are only accessible by our research team. This survey will provide the researchers with a preliminary determination of eligibility and allow potential participants to indicate which day/times they are available for participation. All publications obtained from data collected in this protocol will exclude any personally-identifiable information. Consenting and eligibility determination procedures will take place in 546F BEL, a private laboratory space.

Confidentiality and Data Security Plan

Click on the check box (or double click and type an "X" if using Google Docs) that best describes the confidentiality and data security plan and provide additional details regarding how you will protect the confidentiality of data or address confidentiality concerns.

61 ☒ **Identifiers will be coded to protect confidentiality.**

61a **If true, state how data is coded and where identifiers are stored.**

To input text, click in the light grey area below.

Signed informed consent forms will be maintained in a locked file cabinet for laboratory records. All other data will be coded. The key to the code will be maintained on a password-protected computer behind the locked laboratory doors of 546F BEL. Identifiable data downloaded from RedCap will be maintained electronically on a password-protected computer behind the locked laboratory doors of 546F BEL.

Overall, the only document linking names to identifiers will be the key to the subject number code. This document will contain each subject's name and their subject number and will be stored on a password-protected computer behind the locked laboratory doors of 546F BEL.

The subject number will not be listed on the informed consent document but may be listed on other study-related documents that do not list the subjects name or other personally-identifiable information.

All study-related documents will be separated into those that do and do not contain subject names and personally-identifiable information. Documents containing subject names and personally-identifiable information will be stored in a different locked file cabinet than those documents containing subject numbers. All documents will be stored in locked file cabinets behind the locked laboratory doors of 546F BEL.

62 ☒ **Identifiable data will be destroyed.**

62a If true, describe destruction plan and timeline

To input text, click in the light grey area below.

For each experiment, we will maintain this code and documents containing identifiable information until all data acquired as part of that experiment is published in peer-reviewed manuscripts. After publication, we will destroy the key to the code as well as any documents that contain participant's names (i.e., the informed consent document) so that no identifiers remain.

63 ☐ **Identifiable data will not be destroyed.**

63a If true, provide rationale for retaining identifiable data indefinitely.

To input text, click in the light grey area below.

n/a

64 Data Access

Click on the check box (or double click and type an "X" if using Google Docs) for each group of individuals that will have access to study data.

If you plan on creating a repository, complete the repository form as well.

☒ Study Team Members	☐ External Collaborators	☐ Data coordinating center
☒ Sponsor	☒ Future Sharing with other researchers	

☐ **Others**

Describe below. To input text, click in the light grey area below.

n/a

65 Describe data sharing plan for each group checked above and state whether researchers plan on sharing identifiable, coded, or de-identified data

To input text, click in the light grey area below.

All shared data and code will be deidentified and may be shared to an open-access data sharing platform, such as Zenodo.org or OpenNeuro.org, in accordance with the uploaded NIH Data Management and Sharing Plan. After data sharing is complete, PI Hussain will monitor the quality of the data sharing through annual checks of the shared data.

Identifiable data may be shared with or copied by the NIH or representatives of the NIH (study sponsor) for the purposes of managing, monitoring and/or overseeing this study.

Certificate of Confidentiality

Click on the check box (or double click and type an "X" if using Google Docs) to identify each element below that may require additional information to be disclosed in the consent form.

If a Certificate of Confidentiality is not applicable for this study, skip to 68.

66 ☐ **The study requires a Certificate of Confidentiality.**

67 ☒ **NIH has issued a Certificate of Confidentiality for this study.**

68 ☐ **A Certificate of Confidentiality has not been obtained, but there are plans to apply for one.**

COMPENSATION AND COSTS

Compensation

Click on the check box (or double click and type an "X" if using Google Docs).

69 ☒ **Subjects receive compensation.**

70 ☐ **Subject will not receive compensation.**

Skip to question 74 if subjects will not receive compensation.

71 **Total Amount of Compensation**

To input text, click in the light grey area below.

Subjects will receive $15 per hour of participation to reimburse them for their time and inconvenience. The total amount of compensation will depend on the duration of participation for each participant.

72 **Type of Compensation**

Click on the check box (or double click and type an "X" if using Google Docs) for each form of compensation that will be provided.

☒	Cash	☐	Check	☐	Gift Card
☐	Course Credit	☐	ClinCard	☐	Tango Card

☒ **Other**

Describe, To input text, click in the light grey area below.

Direct deposit via venmo

73 **Proration Schedule**

To input text, click in the light grey area below.

Compensation will be pro-rated on a 30 minute basis. For example, in the event of participation lasting 2.5 hours, compensation will equal $37.50.

74 ☒ **Amount of compensation and its form is reasonable for this population for the activities requested of them.**

75 **Costs**

Click on the check box (or double click and type an "X" if using Google Docs) each applicable item regarding costs.

☐ **Participants will have no costs associated with this study**

☐ **Standard of care procedures contributing to study data**

☐ **Research procedures not associated with standard of care**

☐ **Administration of drugs / devices**

☐ **Study drugs or devices**

☒ **Transportation and parking**

76 **Describe all costs below.**

To input text, click in the light grey area below.

Participants are responsible for obtaining their own transportation to the laboratory for testing and paying for parking if necessary.

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