Harvard University

# **Detailed Guidance for Human Subject Research: Transcranial Magnetic Stimulation (TMS)**

This is specific guidance for preparing, operating, and cleaning in-person Transcranial Magnetic Stimulation systems. If scientifically feasible, investigators are encouraged to consider novel non-invasive brain stimulation paradigms which can be administered by the participant and supervised by the investigator remotely (e.g. at-home transcranial direct current devices).1 In addition to the device specific procedures illustrated below, general human subject research guidance and research lab specific guidance will be followed during all research activities. These guidelines were partially informed by consensus guidelines in press.1 Lastly, these guidelines are meant to be temporary, and are to be used until more concrete or permanent recommendations (including a return to pre-Covid guidelines) are provided by supervising agencies or commissions.

**Pre-Visit Screening Procedures**

* Call the participant and complete the Coronavirus Pre-Visit Screening Form using the participant script prior to visit. Potential participants who are presumed to be at higher risk for Covid-19 infection (e.g. elderly individuals, individuals on immunosuppressive drugs, individuals with cancer or with a pulmonary condition (COPD, asthma, smoking) are strongly discouraged from participation.1
* All study team members complete Coronavirus Screening Form.
* Participants will be given explicit instructions (including diagrams and/or videos) about how to properly put on surgical masks.

**General Procedures**

* All study team members and the participant wash their hands upon arrival and after any physical contacts with other people.
* All study team members and the participant wear university-supplied surgical-grade facemasks at all times. Anyone who wants to take off the mask (for taking breaks or drinking water) does so at least 6 ft away from others and in advance notifies all the others present in the testing location to ensure adequate distancing during the break.
	1. Additional PPE such as face shields, goggles, and/or sterile gloves may be used for the participant and/or the study team members in any part of the study visit, e.g. when there is close contact (less than 6 ft apart).
	2. After every use of reusable PPE (e.g. face shields), they are cleaned and sanitized using Lysol Disinfecting Wipes/Spray or equivalent.
		1. Note: See [EPA (US Environmental Protection Agency) website](https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2) for the full list of disinfectants for use against SARS-CoV-2.
* During the study visit, one study team member should be in the testing room at any time to the degree possible. Up to two study team members can be present at the testing location, but no close contact occurs between them (i.e. the two persons cannot work on the same task together) and they should maintain a 6 ft distance at all times.
* During the study visit, only one designated study team member can make close contact (less than 6 ft apart) with the participant for all procedures that require close contact. Close contact should be minimized, and only occurs as outlined in **red** below and when otherwise required to ensure the participant’s safety.
	1. During close contact, the designated study team member wears a face shield in addition to a surgical mask, and if possible, the designated study team member face away from each other (e.g., experimenter should stand behind rather than in front of the seated participant).
	2. When additional PPE (e.g. face shields) are used during close contact, the designated study team member (i) first puts on his/her own PPE while maintaining 6 ft distancing, (ii) approaches to the participant and dons PPE for the participant, (iii) carries out the close contact tasks, (iv) doffs the PPE from the participant, and (v) takes 6 ft distancing from the participant and then takes off his/her own PPE.
* The participant’s personal belongings are placed in a designated storage space, and the study team members should not touch them.
	1. The participant may be asked to bring their own bottle of water. It will be placed near the testing site where the participant can access during breaks, and same with the other belongings, the study team members should not touch the water bottle.
* All materials are handled on a clean/sanitized surface, e.g. desks or benches. Anything below the waist level is considered as unclean surfaces.
* After every study visit, all non-disposable items used in the testing should be cleaned/sanitized and stored in sealable containers. Each container will have a label and a log to track when and who cleaned the contents, and the containers shouldn’t be re-open until the next use; otherwise, the contents should be cleaned/sanitized again.

**Specific Procedures for Transcranial Magnetic Stimulation (TMS)**

* **Preparation**
	1. One person sanitizes the entire TMS system. This includes using Lysol Disinfecting wipes/spray or equivalent as approved by the equipment manufacturer on the stimulator, the TMS coil and attached tubing, the subject trackers (e.g. headband, glasses), neuronavigation pointer, calibration block, the TMS subject chair, the neuronavigation computer, the coil holder apparatus (e.g. arms) and the electromyography (EMG) apparatus. Particular emphasis will be placed on equipment which comes in direct contact with the subject (e.g. the coil, the chair and the subject trackers).1 Whenever possible, single use items should be used (e.g. disposable electrodes instead of reusable electrodes). These items should be properly disposed of in waste repository.1
	2. In addition to the room cleaning log, investigators should fill out a log of who was in the TMS room and times these individuals entered and left the room. To protect participant confidentiality, only study IDs should be recorded. This information will only be used to trace contacts/exposure in the event that an investigator or participant is identified as being Covid-positive.
* **Operation**
	1. General Guidelines:
		1. Participant-investigator interactions will be limited to no more than 15 minutes. The duration for allowable interactions will increase at later phases of re-opening.
		2. Only one investigator is permitted in the TMS room with the participant. The other TMS investigator (required for all TMS studies) will be present in the hallway at least 10 feet away from the TMS room. During an emergency (e.g. a seizure), the investigator in the room will institute the seizure protocol. The second investigator will be responsible for getting assistance (e.g., calling Emergency Medical Services (EMS)) in the event of a seizure or other emergency.
		3. The investigator is to wear single-use gloves for all TMS sessions.1
		4. Talking should be kept to a minimum when the investigator and participant are in the same room, especially talking at a loud volume. Experimental instructions should be reviewed with participants prior to them coming in through remote video platforms.
		5. To increase ventilation, in physical situation where appropriate, the door to the TMS room should remain OPEN. A fan will be placed in the TMS room to circulate air out into the hallway.
		6. Privacy/confidentiality will be maintained by the presence of a room divider.1
	2. Room preparation: Prior to data collection, one person will prepare the TMS system for use prior to the subject entering the TMS room. *While these procedures are routinely done prior to the subject’s entrance, emphasis will be placed on performing ALL procedures which do not require the subject’s physical presence and readying the system for rapid execution of experimental procedures.* This includes powering up the stimulator and neuronavigation system, calibrating the TMS coil, preparing the subject trackers, attaching the reusable sterile EMG electrodes to the EMG leads, positioning the TMS coil in the arm (if applicable) and loading the subject’s neuronavigation session.
	3. During the experiment:
		1. *Registration:* The designated investigator will apply the subject tracking apparatus (e.g. headband, glasses) to the participant. Following this, the participant will be registered to anatomical landmarks by pacing the pointer on the subject’s ears, nasion and nose tip. This procedure requires very brief (a few second) face-to-face interactions, during which time the investigator and subject will be encouraged to briefly hold their breath and the participant will be asked to close their eyes.
		2. *Motor Threshold (MT) assessment:* To the extent permissible with the experimental design, studies involving multiple TMS visits should endeavor to check the MT only once. If MT assessment and TMS application occur during the same subject visit, these procedures should be separated by at least a 15-minute break to limit the time that the investigator and subject are in the same room/proximity. Investigators are encouraged to use the “3 out of 6” rule (as opposed to the 5 out of 10 rule).
		3. *TMS administration:* No stimulation should be performed with the investigator and participant facing one another (at a minimum the investigator should be behind the participant). Until further notice, ONLY protocols less than seven minutes will be permitted. Theta Burst protocols are encouraged over fixed frequency protocols, as they are shorter in duration (e.g., 190 seconds for intermittent TBS and 60 seconds for continuous TBS).1 Other protocols, including single pulse and brief fixed frequency protocols, will be permitted provided the stimulation duration is less then 5 minutes. If possible, investigators are encouraged to use the coil holder and step out into the hallway where they can clearly see the subject and the navigation computer, as opposed to standing behind the participant and holding the coil themselves on the patient’s scalp. However, if the investigator anticipates that precisely positioning the arm will take time, it may be faster to hold the coil. After TMS, subjects should rapidly remove their subject tracker when the TMS protocol and exit the room without passing within 6 feet of the investigator. Investigators should wait 30 minutes before re-entering the room to collect data (e.g. from the navigation software) and clean.
* Cleaning
	1. When cleaning, study team members wear disposable gowns and sterile gloves per CDC recommendation.
	2. One person cleans and sanitizes all TMS equipment using Lysol Disinfecting Wipes/Spray or equivalent as described above.
	3. After cleaning, store the equipment in its prior locations. Also clean the receptacles in which they are stored. Add a time and date to the cleaning log.
	4. Investigators are encouraged to contact the equipment manufacturer (e.g., Magventure, Brainsight) with questions about how different equipment is properly cleaned (e.g. alcohol-based products should not be used with some electrodes.1

References:

* + - 1. Bikson et al. “Guidelines for TMS/tES Clinical Services and Research through the Covid-19 pandemic” *Brain Stimulation*, 2020 (*in press*).