University of Kent
School of Psychology

Version 1.**5**, **06 Nov 2014**

TMS Safety & Lab Access Policy

Transcranial Magnetic Stimulation (TMS) is a powerful method for establishing causal relationships between brain activity and behaviour However, TMS also carries some inherent risks to participants. This policy is aimed at minimizing those risks and ensuring that researchers are prepared to recognize and deal with adverse consequences that occur. All of these are very unlikely when appropriate screening and precautions are taken.

PRIMARY TMS RISKS

- Seizure (both focal and generalized)
    - Extremely unlikely when parameters are within safety guidelines. When abiding by the safety guidelines seizures in healthy participants have been non-existent or extremely rare amongst many tens of thousands of participants.
- Syncope (Fainting)
    - Rare but can occur mostly when participant is nervous and can be minimized by experimenter providing reassurance.
- Mild muscle pain/twitching
    - Can occur if TMS is delivered near neck or face muscles. Stimulation can be stopped if too painful or intensity reduced.
- Headache
    - Can occur due to muscle stimulation as described above and can be treated with painkillers or by reducing muscle stimulation
- Burns/Heating
    - Very rare unless inducing currents in metal attached to the head. EEG electrodes should be monitored if applying rTMS over them repeatedly. TMS coil temperature is monitored by machine and automatically stops when above 40 degrees C.
- Hearing disturbance from auditory artefact (minor)
    - Unlikely especially when using foam earplugs during experiment
- Physical Injury
    - TMS involves positioning a heavy coil near a participant's head. Care must be taken to ensure that it is positioned securely and the participant's head is not hit in the process of positioning it.
- ANY serious adverse reactions should be reported to the TMS Lab Manager and the Psychology Ethics Panel as soon as possible after the event.

ELIGIBLE PARTICIPANTS

- All participants must be between 18 and 60 years of age unless specifically authorized by the TMS Lab manager and ethics panel

- Neurological or psychiatric patients are NOT eligible for participation at this time. Any participation of such patients will require further consideration in conjunction with the university's insurance policy. If the patients are recruited via the NHS then approval of an NHS ethics panel may be required. Discuss with TMS Lab Manager to assess feasibility.
- See screening section below for other factors related to eligibility.

MANAGING RISKS – SCREENING

- **ALL** participants must pass a screening before they can participate in a TMS experiment. See the official Kent screening form and scoring guide at the end of this document.
- Any uncertainty about screening results should be brought to the attention of the TMS Lab Manager for a second opinion.
- Screening forms with the participant's name and/or anonymous data label should be stored as participant consent forms would be stored. Because these forms may contain sensitive medical information they must be stored securely within the TMS Laboratory.
- Screening is ideally done BEFORE scheduling an appointment to ensure that the participant will not be disappointed and time will not be wasted. This can be done through an online (Qualtrics) survey. The link can be sent to participants in advance of their participation. Screening data MUST be treated confidentially. In the event of online pre-screening, the screening should be repeated/verified in person before testing begins on the day of the experiment.
- Screening must be conducted carefully and it must be made clear to the participant that honest answers are CRITICALLY important. While TMS is safe for most people we must ACCURATELY assess whether each participant has any risk factors that may cause an adverse reaction.
- Items marked "C" on the screening form are absolute contraindications to TMS. Items marked "O" are possible contraindications to TMS and may require further information for the experimenter to make a decision. Some guidance is provided on the page after the form to indicate how to deal with "O" items. Any drugs being taken should be checked against the list at the bottom of the sheet. Participants may only know the trade-name of a drug whereas the list contains the medical name (e.g. fluoxetine = Prozac).

MANAGING RISKS AND EMERGENCIES – SEIZURE AND SYNCOPE MANAGEMENT

- Participants should be monitored continuously via video and audio link from the control room or by an experimenter in the stimulation room. If stimulating motor cortex, then EMG can also be monitored. EEG can be monitored as well in other cases but this is not required. Any visual signs of seizure (localized or widespread convulsions) or signs of spiking/abnormal activity in EMG/EEG should lead to immediate removal of the TMS stimulus.
    - NOTE: Be sure to know how to stop the stimulation safely in the middle of the experiment. This would usually involve exiting (often using ESC button) your stimulus presentation software that controls the TMS. However, in cases of repetitive stimulation the pulse train may be controlled by a sustained TTL signal on the parallel port. If the program is ended in the middle of the pulse train, the TTL signal may not be taken back to zero and thus the stimulation could continue until you are able to reset the TTL signal to zero. In this case, you may need to urgently enter the stimulation room and physically remove the coil from the participant's head.
- Participants should be informed that if they have any feeling that something is wrong that they should notify the experimenter immediately and the experiment should be stopped immediately.

- The largest risk from seizure or syncope is potential for the participant to injure themselves when they lose consciousness.
- Ideally, participants will be seated such that they will not injure themselves on sharp edges or bring heavy equipment onto themselves when falling.
- Syncope should be managed by carefully laying the participant down supine and elevating the legs. Ensure that the participant can breathe normally.
- Seizures should be managed by carefully laying the participant down on their left side (recovery position) and ensure that their breathing is maintained and that they do not injure themselves by hitting obstacles in the room.
- The lab is equipped with a working telephone line and the emergency line is clearly indicated at the top of the direct dial list. This button will dial 3333, campus watch. Explain the situation to them and where you are. Campus watch will contact emergency services and direct them to KS8. This is better than contacting 999 direct as they will not be familiar with the location of the lab.

TMS PARAMETER LIMITS FOR DESIGNING rTMS EXPERIMENTS

- The following tables from Rossi et al (2009) identify limits on various TMS parameters such as frequency, intensity, inter-train intervals, etc. All parameters should be kept within these safe limits. If your experiment requires going beyond these limits, then you will need to seek special permission from the TMS Lab Manager and the Psychology Ethics Committee with justification and an assessment of the balance of risks and benefits for the participants.

Inter-train interval (ms)	Stimulus intensity (% of MT)			
	100%	105%	110%	120%
Part A				
5000	Safe	Safe	Safe	Insufficient data
1000	Unsafe (EMG spread after 3 trains)	Unsafe[a]	Unsafe (EMG spread after 2 trains)	Unsafe (EMG spread after 2 trains)
250	Unsafe[a]	Unsafe[a]	Unsafe (EMG spread after 2 trains)	Unsafe (EMG spread after 3 trains)

Table 5: Part A from Rossi et al (2009).
The minimum safe inter-train interval as a function of TMS intensity for frequencies below 20 Hz.

Frequency (Hz)	100%		110%		120%		130%	
	Duration (s)/pulses		Duration (s)/pulses		Duration (s)/pulses		Duration (s)/pulses	
Part B								
1	>270	>270	>270	>270	>180	>180	50	50
5	10	50	10	50	10	50	10	50
10	5	50	5	50	3.2	32	2.2	22
20	1.5	30	1.2	24	0.8	16	0.4	8
25	1.0	25	0.7	17	0.3	7	0.2	5

Table 5: Part B from Rossi et al (2009).
The maximum safe duration/pulses in each pulse train for rTMS at frequencies from 1-25 Hz and intensities of 100-130% of resting motor threshold (rMT).

Table 6

Published TBS (biphasic pulses) and QPS (monophasic pulses) protocols on normal subjects. No significant side effects reported, apart vagal reactions after prefrontal cortex stimulation. Consensus reached for this table.

	Pulses in the burst	Total train pulses	Intensity	Stimulation site
"Standard" cTBS (following Huang et al. 2005)	3 at 50 Hz, repeated at 5 Hz	600 (40 s)	80% of active MT	Motor cortex, PFC[c]
Silvanto et al. 2007	8 at 40 Hz, repeated every 1.8 s	200	60% of the maximal stimulator output	Visual cortex
Nyffeler et al. 2006 [a]	3 at 30 Hz, repeated at 10 Hz	200	80% of resting MT	Frontal eye fields
"Standard" iTBS	3 at 50 Hz,	600	80% of active	Motor

Table 6 from Rossi et al (2009).
Examples of theta-burst stimulation protocols found to be safe.

Theta-Burst Stimulation: A seizure has been reported after theta-burst at 120% of active motor threshold in a healthy participant who may have been suffering from some lack of sleep. The Kent TMS lab will strictly limit continuous TBS intensity to 80% of active MT following the Huang et al 2005 protocol. Repeated sessions of TBS have been safely administered with only 15 minutes separation but we will generally aim for separation of at least 24 hours out of an abundance of caution. Other protocols can be considered on a case-by-case basis by the TMS Lab Manager and the Psychology Ethics Committee but should not exceed the parameters in Table 6 above.

TRAINING

All researchers who plan to use TMS unsupervised (students and staff) must either have previous experience using TMS (to be approved by TMS Lab Manager) or be trained by an already-experienced member of staff. Training should generally involve the following:

- Familiarization with TMS Safety Screening procedures and screening sheet
- Familiarization with TMS machine parameters and controls
- Familiarization with detecting adverse effects (e.g. pre-seizure) and procedures for managing them and contacting emergency help.
- Familiarization with procedures for determining motor threshold and dosing.
- Familiarization with coil placement and cooling
- Familiarization with exposure limits and Rossi, et al (2009) or more recent guidelines for limits on frequency, intensity, and other parameters.

TMS & ETHICS

- Participants must be made aware of the risk of seizure and other minor risks
- Despite the above, undue worry should not be induced in participants regarding the procedure. This can lead to complications like syncope (fainting). Complications are possible but rare. Our screening procedure and adherence to safety guidelines makes this very rare. This should be emphasized.
- Example Information Sheets and Debriefing forms are included at the end of this document as a guide. However, your information sheet must also address any additional non-TMS features/risks associated with your experiment.
- Your application should also include details of the TMS parameters for assessment by the ethics panel. These can all be covered easily by completing the "TMS PROTOCOL FOR ETHICAL REVIEW" form at the end of this document and attaching it to your application:
    - Single pulse or repetitive
    - For repetitive, Frequency (in Hz), length of pulse trains, and time between pulse trains
    - Intensity of stimulation (as % of motor or phosphene threshold) OR if not using threshold dosing, then a justification and safety analysis for using a certain % of machine output.
    - Total duration of experiment and number of pulses
    - Location of stimulation on scalp and whether this is likely to generate muscle pain/discomfort.
    - Who will do the stimulation, their training, and whether they will be supervised by a member of staff or have been exempted from this.
    - It is the responsibility of the researcher to state explicitly in the ethics application whether the procedures being used fall within or outside of the current TMS Safety Guidelines (currently Rossi, et al 2009). If they fall outside of the Rossi guidelines, this should be discussed in advance with the TMS lab manager, insurance office, and be justified in the ethics application and the applicant should detail how these risks with be minimized or prepared for.
- All TMS studies should be subject to Full review procedures. The studies should select the following checklist items in their ethics application:
    - The study could induce psychological stress or anxiety or cause harm or negative consequences beyond the risks encountered in normal life.
    - Drugs, placebos or other substances (e.g., food substances, vitamins) are to be administered to the participants or the study will involve invasive, intrusive or potentially harmful procedures of any kind.
- The Ethics panel should consider carefully and perhaps take advice from the TMS Lab Manager regarding any studies which have parameters that fall outside of the current published TMS safety guidelines. Extra safety pre-cautions or stronger screening should be considered for such studies to ameliorate the risk.
- Under no circumstances should a participant be given TMS without prior informed consent.
- Criteria for the ethics committee: Ethics applications should ensure that the following criteria are met
    - Are the stimulation parameters within the safety guidelines? The researchers should submit the TMS Parameters Form which allows them to check this and provides information in an organized manner for the committee
    - If the parameters are outside of the safety guidelines then further review may need to be taken and advice taken about whether the risks can be minimized. This will need to

be done on a case-by-case basis and the committee may want to take advice from the TMS Lab Manager or other TMS experts or request more information from the researchers.

INSURANCE

- John Buckingham at the UoK Insurance Office has been notified (by Dr Joseph Brooks in early 2013) of the use of TMS and has confirmed that use of TMS under the safety guidelines and with healthy participants is covered by the University's existing liability insurance policy. This insures the TMS research team and University in the event that there was negligence on their part.
- Any claim brought against the university or team by a participant will be defended by the university's insurers. If negligence is found, then the liability insurance will pay out. If no negligence is found then obviously, no payment will be made.
- Non-negligence coverage. It was decided that additional non-negligence coverage was NOT needed. This would allow settlements to be paid to participants without the university admitting negligence. This would cost an additional premium and is not necessary.
- Any complaint's should be brought to the immediate attention of the Psychology Ethics Committee and the TMS Lab Manager

ACCESS POLICY

- All researchers using TMS must read and abide by the latest published TMS safety guidelines. As of Jan 2014, these can be found in Rossi et al. (2009). Full reference below.
- The TMS Lab Manager or Experimental Officers (in tech office) will keep a list of approved TMS Authorized Users (TAUs) - trained staff members who may supervise and train other staff and students.
- Academic & Research Staff
    - **Academic, research, and technical staff** are allowed unsupervised access to TMS equipment for stimulation experiments and programming/setup. However, before using TMS, these staff should have:
        - Either previous experience with TMS or training from an experienced member of staff (TAUs). If the staff member has never used the Mag & More device, it is recommended that the staff member access the manual or seek assistance from experienced staff
        - RECOMMENDED: Emergency first aid certification with section about seizure (available through the University), equivalent training, or medical/EMT/nursing training.
    - **PhD Students** are allowed unsupervised access to TMS for stimulation experiments once they have been trained sufficiently (to the satisfaction of their supervisor and/or the TMS lab manager).
        - RECOMMENDED: emergency first aid training.
        - First sessions should be observed by trained member of staff or another trained PhD student.
        - First TMS experiment must be approved after Project Presentation at Cognitive Group meeting or Brooks CogNeuro Lab meeting. Approval can be granted by TMS Lab Manager.

- **MSc Students**
  - Must be supervised at all times unless specifically granted exemption by the TMS Lab Manager. Exemption will only be granted after project presentation, TMS-specific training, and observed testing sessions.
  - Any exempted students who are testing without supervision must test during office hours 900-1700 weekdays.
  - For supervised testing sessions, it is acceptable if the supervisor is not immediately present (i.e. not in the room) but must be in Keynes College and accessible by phone in case of emergency or problem. Direct supervision is required for the first 2-3 testing sessions.
- **Undergraduate Students**
  - Must be supervised at all times unless specifically granted exemption by the TMS Lab Manager. Exemption will only be granted after project presentation, TMS-specific training, and observed testing sessions. For supervised sessions, a trained-TMS user must be immediately present during testing.
  - Any exempted students who are testing without supervision must test during office hours 900-1700 weekdays and a trained TMS user must be on call within Keynes College and available.
- **Non-affiliated/Visitors**
  - Must have approval of TMS Lab Manager and be directly supervised by a TMS trained person at all times. TMS trained person must be present in the lab for all sessions unless exempted by the TMS Lab Manager.

REFERENCES

Rossi et al. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120(12), 2008-39.

School of Psychology
Transcranial Magnetic Stimulation Laboratory
PI: Dr Joseph Brooks, J.L.Brooks@kent.ac.uk

Safety Screening Questionnaire for Transcranial Magnetic Stimulation (TMS)

(Version 1.5, 06 Nov 2014)

Participant Name/ID: _____ **Date:** _____

Current Age: _____ (in years) **Handedness:** Left Right Ambi **Sex:** M F Other

ALL INFORMATION WILL BE TREATED CONFIDENTIALLY

(1) Have you ever had an adverse reaction to TMS? If so, please describe _____	☐Yes	☐No	C
(2) Do you have epilepsy or have you ever had a seizure/convulsion?	☐Yes	☐No	C
(3) Have you ever had a fainting spell or syncope? If yes, describe.	☐Yes	☐No	O
(4) Have you ever had a stroke?	☐Yes	☐No	C
(5) Have you ever had a serious head injury (with loss of consciousness)?	☐Yes	☐No	C
(6) Have you ever had neurosurgery of any type (including brain or spinal cord)?	☐Yes	☐No	C
(7) Do you have hearing problems or ringing in your ears?	☐Yes	☐No	O
(8) Do you have any metal in your body such as shrapnel, surgical clips, or fragments from welding or metalwork?	☐Yes	☐No	C
(9) Do you have any implanted devices such as cardiac pacemakers, aneurysm clips, cochlear implants, medical pumps, deep brain stimulators, or intracardiac lines?	☐Yes	☐No	C
(10) Do you have a medication infusion device?	☐Yes	☐No	C
(11) Do you suffer from frequent or severe headaches?	☐Yes	☐No	C
(12) Have you ever had any other brain-related condition (including Psychiatric diagnoses)?	☐Yes	☐No	C
(13) Have you ever had any illness that caused brain injury?	☐Yes	☐No	C
(14) Are you taking any psychiatric or neuroactive medications? For instance, anti-depressants, anti-anxiety, anti-psychotics, anti-convulsants, or anything else with nervous system effects? (please list) _____	☐Yes	☐No	C
(15) Are you taking any other medications or other drugs/substances? Please list. If any of these substances are illegal, please do still mark "yes" but do not write the name. We will contact you to confidentially discuss this in person to see whether TMS will be safe for you. _____	☐Yes	☐No	O
(16) Are you pregnant or do you have any reason to believe that you may be?	☐Yes	☐No	C
(17) Do you, or does any family member, have epilepsy/history of seizures?	☐Yes	☐No	C
(18) Do you hold a heavy goods vehicle driving license or bus license?	☐Yes	☐No	C
(19) Have you consumed alcohol in the past 24 hours?	☐Yes	☐No	C
(20) Did you have adequate sleep last night?	☐Yes	☐No	C
(21) Have you participated in a TMS study within the past 24 hours?	☐Yes	☐No	C

Potential Contraindication Drugs

Strong Potential Hazard: imipramine, amitriptyline, doxepine, nortriptyline, maprotiline, chlorpromazine, clozapine, foscarnet, ganciclovir, ritonavir, amphetamines, cocaine, (MDMA, ecstasy), phencyclidine (PCP, angel's dust), ketamine, gamma-hydroxybutyrate (GHB), alcohol, theophylline

Relative Potential Hazard: mianserin, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, reboxetine, venlafaxine, duloxetine, bupropion, mirtazapine, fluphenazine, pimozide, haloperidol, olanzapine, quetiapine, aripiprazole, ziprasidone, risperidone, chloroquine, mefloquine, imipenem, penicillin, ampicillin, cephalosporins, metronidazole, isoniazid, levofloxacin, cyclosporin, chlorambucil, vincristine, methotrexate, cytosine arabinoside, BCNU, lithium, anticholinergics, antihistamines, sympathomimetics.

Withdrawl Hazard: alcohol, barbiturates, benzodiazepines, meprobamate, chloral hydrate.

Guidance on Using the Screening form

- All items marked “C” in right column are absolute contraindications to TMS and, if a participant ticks YES to any of these (“no” for the sleep question), then the participant should not be allowed to participate unless explicit justification is given by the experimenter on why the screening does not apply in this case and this is approved by the TMS lab manager
- For items marked “O” some discretion can be used as follows:
    - Item 3 – Fainting: A one of spell of fainting due to a clear cause that would cause anyone to faint is permissible. A history of regular fainting episodes should be taken as contraindication.
    - Item 7 – Ringing in ears: Transient, one-off experiences of this arefine but persistent tinnitus or problems with this can indicate a neurological problem and should preclude participation
    - Item 15 – drugs/substances: check against list at bottom of screening form. Generally, we will avoid participants taking any of the drugs/substances on this list. If the participant is on any unknown drugs/substances or you have reason to believe that they are not sober or under the influence of a substance, this should be taken as a contraindication.
- Item 20 – Sleep: Participants should say YES to this item in order to participate. If you have a reason to believe that the participant has not slept or is significantly sleep deprived, this can be a reason for exclusion. They can be rescheduled for another day. It often helps to remind participants a day beforehand to get a good night of sleep and not drink (or take other substances) the night before the session.
- When doing the screening, it is important to emphasize that honest and complete responses are critical for safety. TMS is safe as long as they allow us to accurately assess their risk. If people fail the screening on the day that they attend, they should be paid/given credit for the time that they do spend there.

School of Psychology
Keynes College
University of Kent
Canterbury, CT2 7NP

Study Information Sheet

Title of Project:		**Ethics Approval Number:**	
Investigator(s):	YOUR NAME HERE Dr Joseph Brooks, TMS Principal Investigator	**Researcher Email:**	YOUR EMAIL j.l.brooks@kent.ac.uk

The researcher should address the following points and any other relevant issues that are required by the participant to make an informed decision about participation. This statement can be deleted from the final version of your information sheet.

Aims of the Study:

This study involves Transcranial Magnetic Stimulation (TMS). TMS is a method of stimulating the brain and changing its activity. This involves using brief magnetic pulses which affect the activity of the cells of the brain. TMS can be used to study the causal effect that brain activity has on behaviour and cognition and is also sometimes used for treatments.

Eligibility Requirements:

All participants must be aged 18-60 and pass the TMS Safety Screening. Any participants having a history of seizure or other neurological or psychiatric illness may not eligible. Participants should also have not consumed alcohol or had TMS in the last 24 hours and should not be sleep deprived. Use of some drugs/medications can also be contraindications to participation and this will be assessed in the safety screening on a case-by-case basis.

What you will need to do and time commitment:

Risks/Discomforts involved in participating:

In rare instances Transcranial Magnetic Stimulation (TMS) has induced a seizure. This risk is extremely low, and is minimised in our research because of our adherence to the safety guidelines established by a consensus of experts on TMS. Nevertheless, it is important that you tell us now if you have ever experienced a seizure yourself, or if there is any history of seizures in your family. To help us determine whether you are eligible to have TMS, you will be asked to complete a safety questionnaire. If you have any of the known risk factors for seizure, you may not be eligible to participate in this research.

In the unlikely event that you do experience a seizure induced by TMS, this has never led to the development of epilepsy or posed any risk for subsequent unprovoked seizures. In addition, any TMS induced seizure would occur during stimulation or immediately after and we have procedures in place to deal with this. Overall, only a small number of seizures have been caused by TMS and have been reported in the world's scientific literature and most of these have occurred by using stimulation beyond the safety guidelines. The parameters that we will use have been used safely in many studies and are consistent with the established safety guidelines for TMS. Neither animal nor human studies have shown any risks of long-term adverse effects to the brain or its functions after TMS, but, as with any intervention, this cannot be absolutely ruled out.

Other potential adverse effects associated with TMS may include a muscle tension headache or a neck ache. These are generally mild discomforts that respond promptly to commonly available painkillers. Also, the audible click produced by the stimulating coil. You will be offered foam earplugs to reduce the noise. You can read more about the risks and safety guidelines for TMS in Rossi, et al. (2009) Clinical Neurophys: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3260536/

Confidentiality of your data:

Details of any payments/RPS credits (*must be approved by ethics committee):*

General Disclaimers and Contact Information:

Remember that participation in this research study is completely voluntary. Even after you agree to participate and begin the study, you are still free to withdraw at any time and for any reason.

If you would like a copy of this consent form to keep, please ask the researcher. If you have any complaints or concerns about this research, you can direct these, in writing, to the Chair of the Psychology Research Ethics Committee by email at: psychethics@kent.ac.uk. Alternatively, you can contact us by post at: Ethics Committee Chair, School of Psychology, University of Kent, Canterbury, CT2 7NP.

School of Psychology
Keynes College
University of Kent
Canterbury, CT2 7NP

TMS PROTOCOL FOR ETHICAL REVIEW

Title of Project:		**Ethics Application Number:**	
Investigator(s):		**Researcher Email:**	

The purpose of this form is to systematically organize the information relevant to a TMS ethics application. This allows the researcher(s) and committee to ascertain whether the parameters of the proposed TMS study fall within the latest TMS safety guidelines. If parameters fall outside of the safety guidelines further information may be needed.

General Parameters/Checklist	
Dosing Procedure?	☐ % Resting Motor Threshold (rMT) ☐ % Active Motor Threshold (aMT) ☐ % Phosphene Threshold (PT) ☐ % Machine Output (MO) ☐ Other (describe):
Standard Screening Form to be used?	☐ Yes ☐ No (explain):
Experimenter(s) delivering TMS:	☐ Trained Academic ☐ Trained PhD Student ☐ Trained MSc Student (with direct supervision) ☐ Trained MSc Student (without direct supervision; requires approval of TMS Lab Manager) ☐ Trained Undergraduate or Visitor (with direct supervision) ☐ Trained Undergraduate or Visitor (without direct supervision; requires approval of TMS Lab Manager)
Experiment will recruit only healthy participants:	☐ Yes ☐ No. Will require further consideration for safety and insurance purposes. May require NHS approval if involving NHS patients.
Participants will give informed consent for stimulation	☐ Yes ☐ No. This study cannot be permitted. Explicit consent is required for all TMS studies.

☐ **Single Pulse TMS**	
There are no particular restrictions for single pulse studies, but as a guide, intensities should be below 140% rMT and pulses should be separated by at least 2 seconds (ideally variable ITI). The total number of pulses in a session should generally not exceed 400.	
Stimulation Locations (approx. brain area):	
Total Number of Pulses:	
Intensity:	
Notes:	

☐ Repetitive TMS (rTMS)

Please complete the table below to indicate parameters of your rTMS study. For each frequency of stimulation being used, please check the nearest frequency in the left-most column and then complete the parameters in columns to the right. Where multiple intensities, locations, etc. are being used, please list all of them. Use "notes" section at end to add any further information to clarify what is being done. Please confirm whether parameters fall within the safety guidelines using the table at the bottom of the table.

Frequency	Amplitude (%MT, %PT, %MO)	Stimulation Location(s)	Total number of pulse trains	Duration per train (in pulses)	Inter-Train Interval (in sec)	Within Safety Limits?
☐ ~1 Hz						Yes/No
☐ ~5 Hz						Yes/No
☐ ~10 Hz						Yes/No
☐ ~20 Hz						Yes/No
☐ ~25 Hz						Yes/No
☐ Other (list frequencies)						Yes/No

Notes:

The maximum safe duration/pulses in each pulse train for rTMS at frequencies from 1-25 Hz and intensities of 100-130% of resting motor threshold (rMT).

Frequency (Hz)	100%		110%		120%		130%	
	Duration (s)/pulses		Duration (s)/pulses		Duration (s)/pulses		Duration (s)/pulses	
Part B								
1	>270	>270	>270	>270	>180	>180	50	50
5	10	50	10	50	10	50	10	50
10	5	50	5	50	3.2	32	2.2	22
20	1.5	30	1.2	24	0.8	16	0.4	8
25	1.0	25	0.7	17	0.3	7	0.2	5

The minimum safe inter-train interval for frequencies below 20 hz as a function of amplitude. This shows that generally inter-train intervals should be greater than 1 second and not significantly less than 5 seconds.

Inter-train interval (ms)	Stimulus intensity (% of MT)			
	100%	105%	110%	120%
Part A				
5000	Safe	Safe	Safe	Insufficient data
1000	Unsafe (EMG spread after 3 trains)	Unsafe[a]	Unsafe (EMG spread after 2 trains)	Unsafe (EMG spread after 2 trains)
250	Unsafe[a]	Unsafe[a]	Unsafe (EMG spread after 2 trains)	Unsafe (EMG spread after 3 trains)

Patterned rTMS Parameters

Please complete the table below to indicate parameters of your patterned rTMS study. For each frequency of stimulation being used, please check the nearest frequency in the left-most column and then complete the parameters in columns to the right. Where multiple intensities, locations, etc. are being used, please list all of them. Use "notes" section at end to add any further information to clarify what is being done.

Frequency	**Intensity %aMT**	**Stimulation Location(s)**	**Duration (in pulses)**	**Within Safety Limits?**
☐ Continuous Theta- Burst				Yes/No
☐ Intermittent Theta-Burst				Yes/No
☐ Other (describe in detail below including previous published uses)				Yes/No

Notes:

Examples of patterned TMS shown to be safe. Protocols should largely conform to these aside from the locations which are open to change in studies.

Table 6

Published TBS (biphasic pulses) and QPS (monophasic pulses) protocols on normal subjects. No significant side effects reported, apart vagal reactions after prefrontal cortex stimulation. Consensus reached for this table.

	Pulses in the burst	**Total train pulses**	**Intensity**	**Stimulation site**
"Standard" cTBS (following Huang et al. 2005)	3 at 50 Hz, repeated at 5 Hz	600 (40 s)	80% of active MT	Motor cortex, PFC[c]
Silvanto et al. 2007	8 at 40 Hz, repeated every 1.8 s	200	60% of the maximal stimulator output	Visual cortex
Nyffeler et al. 2006 [a]	3 at 30 Hz, repeated at 10 Hz	200	80% of resting MT	Frontal eye fields
"Standard" iTBS	3 at 50 Hz,	600	80% of active	Motor