

Appendix 2: Stimulation parameters for TMS studies

Tables from the Rossi et al., Clinical Neurophysiology 120 (2009): 2008-2039.

Consensus has been reached for safe stimulation parameters for the high and low frequency repetitive TMS used at intensities detailed below in Tables 3-5.

Table 3

Summary of the most employed average stimulation parameters in online interaction rTMS protocols and found to be safe. Consensus has been reached for this table.

rTMS frequency	Number of studies	Average train duration	Average inter-train interval	Average number of trials
4-9 Hz	>10	Variable (see Supplemental material, Table S3)		
10 Hz	>50	5-6 pulse-trains for 400-500 ms	3.2 s	250
20-25 Hz	>20	10 pulse-trains for 400-500 ms	17.1 s	80

Table 4

Maximum safe duration (expressed in seconds) of single trains of rTMS. Safety defined as absence of seizure, spread of excitation or afterdischarge of EMG activity. Numbers preceded by > are longest duration tested. Consensus has been reached for this table.

Frequency (Hz)	Intensity (% of MT)				
	90%	100%	110%	120%	130%
1	>1800 ^a	>1800	>1800	>360	>50
5	>10	>10	>10	>10	>10
10	>5	>5	>5	4.2	2.9
20	2.05	2.05	1.6	1.0	0.55
25	1.28	1.28	0.84	0.4	0.24

^a In Japan, up to 5000 pulses have been applied without safety problems (communication of Y. Ugawa).

Table 5

Adapted from Table 4 (Part A) and Table 3 (part B) of Chen et al., 1997, with permission from the authors. Safety recommendations for inter-train intervals for 10 trains at <20 Hz. The maximum duration of pulses for individual rTMS trains at each stimulus intensity should not exceed those listed in the Part B of the table. A consensus has been reached in adopting this table at this point. However, there is a need to extend these investigations and provide more detailed guidelines that may apply also to non-motor areas.

Inter-train interval (ms)	Stimulus intensity (% of MT)							
	100%		105%	110%	120%		130%	
<i>Part A</i>								
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)			
<i>Part B</i>								
Frequency (Hz)	100%		110%	120%	120%		130%	
	Duration (s)/pulses		Duration (s)/pulses	Duration (s)/pulses	Duration (s)/pulses		Duration (s)/pulses	
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

^a These stimulus parameters are considered unsafe because adverse events occurred with stimulation of lower intensity or longer inter-train interval, but no adverse effects were observed with these parameters.

For patterned rTMS, such as theta-burst stimulation (TBS), the lack of safety studies means that safety guidelines are not currently available. The Rossi et al., (2009) paper summarizes the TBS protocols published up to 2009 in Table 6 below. Based on our previous approvals for TBS from the NRES committees and this table, we propose that protocols involving TBS should follow the standard parameters described by Huang et al., (2005) for continuous (cTBS) and intermittent (iTBS) as detailed below in Table 6. Stimulation intensities for TBS (biphasic stimulation) should be no greater than 60% of maximal stimulator output or 80% of resting motor threshold.

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) Silvanto et al. 2007	3 at 50 Hz, repeated at 5 Hz	600 (40 s)	80% of active MT	Motor cortex, PFC ^c
	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 protocols (following Huang et al. 2005)	3 at 50 Hz, repeated at 5 Hz for 2 s	600	80% of active MT	Motor cortex, PFC ^c
QPS ^b (following Hamda et al., 2008)	4 (ISI ranging 1.5 ms–1.25 s), repeated every 5 s	1440	90% of active MT	Motor cortex

^a Also repeated TBS in the same session (at 5, 15, 60, 75 min).

^b 2000 maximal total pulse number per day; highest intensity used resting MT (Y. Ugawa, personal communication).

^c PFC = prefrontal cortex (Grossheinrich et al. 2009).