Supplemental material for:

Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines

A Consensus Statement from the IFCN Workshop on "Present and Future of TMS: Safety and Ethical Guidelines", Siena, October 17-20, 2018 *

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Table S1. Studies using TMS in patients with implanted stimulating/recording electrodes.

Authors	Year	Patients or ex vivo setup	Type of electrode	Electrodes location	Electrode connections	Parameters of stimulation for implanted electrodes	TMS	Results
				Ex-vivo studies				
Kumar et al	1999	Ex vivo magnetic stimulation over DBS leads and implanted pulse generator (IPG)	Model 3387, Medtronic (Minneapolis, MN, USA)	Conductive gel phantom; 3 lead loops (5 cm diameter)	Leads not connected; leads connected to Medtronic Itrel Model 3625 IPG; only IPG	Usual parameters for stimulation of GPI, stimulation on and off	Figure-8 coil or circular coil,single or pairedmonophasic pulses, 100% intensity (Magstim 200, Whitland, Wales, UK); coil–IPG distance 2–30 cm	Maximum induced voltage of 0.08 V differentially between two electrode contacts at proximal end of lead (IPG not connected). TMS–IPG distances < 10 cm and < 2 cm altered and damaged IPG operation, respectively.
Kühn et al	2003	Ex vivo magnetic stimulation over	Kinetra, Medtronic	Skull phantom			Figure-8 coil with monophasic	Maximum induced voltage of 0.7 V (likely

		DBS electrode in skull phantom					pulses (Magstim 200)	differentially between two electrode contacts). TMS–IPG distances < 10 cm and < 2 cm altered and damaged IPG operation, respectively.
Schrader et al	2005	Ex vivo magnetic stimulation directly over VNS leads and IPG	Cuff VNS electrodes	Conductive gel phantom	Leads connected to stimulator Model 102 IPG(Cyberonics, Inc., Houston, TX, USA)	Stimulation off	Figure-8, single biphasic pulses, 100% intensity (Magstim 220)	Maximum induced current of 200 nA differentially between electrode contacts. No effect on IPG operation.
Shimojima et al	2010	Ex vivo magnetic stimulation over DBS electrode in gel and in phantom	Model 3389 electrode, Medtronic	Conductive gel phantom; no lead loop or 2 lead loops (3 cm diameter)	Soletra IPG, Medtronic		Figure-8 and double cone coil,monophasic pulses,5–100% intensity (Magstim 200), single pulses to 0.2 Hz rTMS	No electrode displacement; no heating; maximum induced peak-to-peak amplitude of 7.7 V with no lead looping and 34 V with double loop at 50% output; charge density of 30 μC/cm^2/phaseexceeded for 75% intensity with 2 loops or for more loops
Deng et al	2010	Ex vivo magnetic stimulation of DBS electrode lead connected to IPG	Libra electrodes (St. Jude Medical, Plano, TX, USA)	1.2 kΩ resistor to IPG case; 0–3 loops in lead (5 cm diameter)	Libra IPG (St. Jude Medical)	Stimulation off or on (0 mA or 4 mA)	Figure-8 coil, single monophasic pulses, up to 100% intensity (Magstim 200); circular coil, single biphasic pulses up to 20% intensity (Magstim Theta)	At 100% intensity of Magstim 200, maximum induced peak voltage of 17 V and 100 V with 0 and 3lead loops, respectively. In on state IPG conducts for any induced voltage; in off stateIPG conducts for induced voltage > 5 V.
Kühn et al	2011	Ex vivo magnetic stimulation over DBS electrode lead with IPG	Model 3389, Medtronic	Air, no load, IPG 15 cm away from TMS coil	Activa PC and Activa RC, Medtronic	4 V (contacts 0–, 3+), 90 µs, 10 Hz	Figure-8 coil, single monophasic pulses, 100% intensity (Magstim 200),	Maximum induced voltage of 2.8 V differentially between two contacts at distal end of leads. No changes to IGP settings or battery

							every 3 s, 200 pulses	state.
Phielipp et al	2017	Ex vivo magnetic stimulation over subdural cortical electrode in gel and in phantom	Resume II subdural cortical electrode model 3587A Metronic	Electrodes in conductive gel and phantom, with and without 1 lead loop	Lead not connected or connected to IPG Medtronic-Itrel II 7424	0–6 V, 90 µs, 90 Hz	Figure-8 coil, single biphasic pulses, 10–100% intensity (Magstim Super Rapid Plus); rTMS, 80% intensity, 20 Hz, 2,300 pulses	No electrode displacement; induced heating near electrode likely insignificant; no IPG malfunction; maximum induced voltage of 25 V and 41 V with 0 and 1 lead loop, respectively; maximum charge density of 30.4 $\mu C/cm^2$/phase
				Spinal Electrodes				
Kofler et al	1991	In vivo evaluation in 4 patients	Neuromed 1980JF lead, Medtronic Pisces Quad lead, Neuromed 1994JF lead	Spinal level: T11, T12, C3	Medtronic Itrel II, model 7424	Stimulator on and off	Focal TMS	
Di Lazzaro et al	1998	2 conscious patients with intractable pain	Model Quad 3487A Medtronic	High cervical epidural space	Not connected to IPG	No stimulation	Focal single and paired pulse TMS	
Di Lazzaro et al	1998	3 conscious patients with intractable pain	Model Quad 3487A Medtronic	High cervical epidural space	Not connected to IPG	No stimulation	Focal single pulse TMS	
Chen R et al	1999	1 conscious patient	Resume Lead 3587A, Medtronic	C5-C7 epidural space	Not connected to IPG	No stimulation	Single pulse TMS, circular coil	
Tokimura et al	2000	5 conscious patients with intractable pain	Model Quad 3487A Medtronic	High cervical epidural space	Not connected to IPG	No stimulation	Focal single pulse TMS	
Di Lazzaro et al	2001	4 conscious patients with intractable pain	Model Quad 3487A Medtronic,	High cervical epidural space	Not connected to IPG	No stimulation	Focal monophasic and biphasic single pulse TMS	
Di Lazzaro et al	2001	6 conscious patients with intractable low-back pain	Model Quad 3487A Medtronic	Thoracic epidural space	Not connected to IPG	No stimulation	Focal single and paired pulse TMS. Anodal electric stimulation	
Di Lazzaro et al	2002	2 conscious patients with intractable dorso-	Model Quad 3487A Medtronic	High cervical epidural space	Not connected to IPG	No stimulation	Focal and non focal monopulse TMS and focal	

		lumbar pain					paired pulse TMS; Anodal electric stimulation
Di Lazzaro et al	2002	2 conscious patients with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	rTMS: 5 Hz, Focal single and paired pulse TMS
Di Lazzaro et al	2003	3 conscious patients with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	Single pulse TMS
Di Lazzaro et al	2005	4 conscious patients with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	rTMS: ctbs; focal single pulse TMS
Di Lazzaro et al	2006	6 conscious patients with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	Focal single and paired pulse TMS
Di Lazzaro et al	2007	1 patient with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	rTMS: repetitive paired pulse stim. Focal single pulse TMS
Di Lazzaro et al	2009	4 patients with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	Repetitive focal TMS paired with peripheral stimulation
Lefaucheur et al	2010	2 patients with intractable pain	Quadripolar Pisces Quad Lead Model 3487A Medtronic+ 2 quadripolar Resume II Lead Model 3587A Medtronic	Cervical spine epidural space (Pisces Quad electrode) + motor cortical epidural space (Resume electrodes)	Not connected to IPG	No stimulation	Focal single-pulse TMS
Ni et al	2011	2 patients with intractable pain	Resume Lead Model 3587A Medtronic,	High cervical epidural space	Not connected to IPG	No stimulation	Focal single and paired pulse TMS
Weise et al	2013	1 patient with intractable dorso-	Quadripolar Medtronic	High cervical epidural space	Not connected to IPG	No stimulation	Focal single and paired pulse TMS

		lumbar pain	electrode				
Hamada et al	2014	1 patient with intractable dorso-lumbar pain	Quadripolar Medtronic electrode	High cervical epidural space	Not connected to IPG	No stimulation	Repetitive focal TMS paired with peripheral stimulation
			Deep Brain Stimulation Electrodes				
Chen et al	2001	7 PD patients	Model 3387, Medtronic	Globus pallidus int.	Connected to IPG	Optimal parameters, half amplitude, off	Focal single and paired pulse TMS
Cunic et al	2002	12 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Optimal parameters, half amplitude, off	Focal single and paired pulse TMS
Dauper et al	2002	8 PD patients	Medtronic	Subthalamic nucleus	Connected to IPG	On at 2.8 V, 60 µs, 130 Hz and off	Focal single and paired pulse TMS
Kühn et al	2002	5 dystonia patients	Medtronic	Globus pallidus internus, ventral intermedius (VIM) nucles of thalamus	Connected to IPG Kinetra	Stimulator off	Focal single pulse TMS
Pierantozzi et al.	2002	4 PD patients	Model 3389 for STN Model 3387 for GP1	Subthalamic nucleus and globus pallidus internus	Connected to an external stimulator	STN 2-3.5 V, 90 µs, 165 Hz; gpi 2-5 V, 210 µs, 185 Hz; Stimulator on and off	Focal single and paired pulse TMS
Kühn et al	2003	9 dystonia patients	Medtronic	Globus pallidus int	Connected to IPG Kinetra;	130 Hz, 1.2-5.5 V; 210 µs	Focal single and paired pulse TMS
Kühn et al	2004	10 dystonia patients	Medtronic	Globus pallidus int	Connected to IPG Kinetra	Frequency 5 Hz, pulse width 450 µs	Focal single and paired pulse TMS
Molnar et al	2004	6 patients with essential tremor	Model 3387, Medtronic,	Unilateral ventralis intermedius (VIM) nucleus of thalamus	Connected to IPG	Optimal therapeutic setting, half optimal frequency, off	Focal single and paired pulse TMS over the motor cortex and cerebellum
Hanajima et al	2004	14 PD, 1 pain, 2 dystonia patients	Model 3387, Medtronic, 3-7 days after implantation with leads externalized	Subthalamic nucleus, Sensory thalamus, Globus pallidus int	Connected to an external stimulator (model A360D-B, World	Single stimuli just below the threshold for current spread to the corticospinal pathway	Focal single and paired pulse TMS

					Precision Instruments,)		
Wagner et al	2004	1 epileptic patient	Eight depth electrodes	Bilaterally within the cingulum, orbital frontal cortex, amygdala, and hippocampus	Connected to IPG	No stimulation	Focal single pulse TMS
Strafella et al	2004	6 PD patients undergoing DBS surgery	5 tungsten bipolar microelectrodes	Subthalamic nucleus	Connected to electrophysiological recording system, not connected to IPG	No stimulation	Single pulse TMS, 9 cm circular coil
Molnar et al	2005	7 patients with essential tremor	Model 3387, Medtronic	Ventralis intermedius (VIM) nucleus of thalamus	Connected to Xtrel or Itrel II IPG, Medtronic	Optimal parameters, half optimal amplitude, off	Focal single and paired pulse TMS
Hidding et al	2006	8 PD patients	Model 3389, Medtronic	Subthalamic nucleus	Connected to Kinetra IPG, Medtronic	IPG OFF	Focal single and paired pulse TMS
Molnar et al	2006	5 epileptic patients	Model 3387, Medtronic	Anterior nucleus of thalamus	Connected to IPG	Contacts 1 and 2 -; case +, 4 V, 100 Hz, 90 µs, cycling mode (1 minute on, 5 minutes off) and continuous stimulation	Focal single and paired pulse TMS
Tisch et al	2007	10 patients with primary generalised dystonia	Model 3389 Medtronic	Globus pallidus int.	Connected to IPG Kinetra model 7428, Medtronic	3.5-3.9 V, 90 µs, 130 Hz, DBS on and off in separate sessions	rTMS, PAS+, and single pulse TMS
Sailer et al	2007	7 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Optimal stimulator setting, stimulator off	Focal single pulse TMS paired with median nerve stimulation
Gaynor et al	2008	9 PD patients	Model 3389, Medtronic	Subthalamic nucleus	Not connected to IPG	No stimulation through the electrode	Focal single pulse TMS

Potter-Nerger et al	2008	10 PD patients		Subthalamic nucleus	Connected to IPG	3.1±0.2 V, 64 µs, 148.8±9.2 Hz, stimulation on and off	Focal single pulse TMS
Fraix et al.	2008	15 PD patients	Model 3389, Medtronic	Subthalamic nucleus	Connected to IPG Kinetra, Medtronic	2.9±0.5 V and 4.4±1.1 V, 90 µs, 130-185 Hz, stimulation on and off	Focal single and paired pulse TMS
Ayache et al.	2009	1 Multiple Sclerosis patient with action tremor	Model 3387, Medtronic	Ventralis intermedius (VIM) nucleus of thalamus	Connected to IPG	3 V, 90 µs, 130 Hz, stimulation on and off	Double TMS pulses on the cerebellum (double cone coil) and primary motor cortex (focal coil)
Kuriakose et al.	2010	8 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Clinical parameters except frequency was at 3 or 30 Hz	Focal single pulse TMS
Ruge et al	2011	10 DYT 1 gene-positive dystonic patients	Model 3389 Medtronic,	Globus pallidus int.	Connected to IPG Soletra Kinetra model 7428, Medtronic	0.5-2.1 V, 450 µs, 130 Hz, stimulation on and off	Focal single and paired pulse TMS
Wagle Shukla et al	2013	11 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Clinical DBS parameters, stimulation on and off	Focal single pulse TMS paired with median nerve stimulation
Kim SJ et al	2015	8 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Clinical DBS parameters, stimulation on and off	Repetitive focal TMS paired with peripheral stimulation
Kobayashi et al	2016	9 PD patients		Subthalamic nucleus	Connected to IPG	2-3 V, 60-90 µs, 130 Hz, stimulation on and off	Focal single and paired pulse TMS over motor cortex
Udupa et al.	2016	10 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Connected to IPG	Repetitive STN DBS (1.5-4 V, 60 µs, 3 Hz) paired with focal TMS at 167 ms	Focal TMS

						interstimulus interval	
Wessel et al	2016	9 PD patients	Model 3387, Medtronic	Subthalamic nucleus	Not connected to IPG	No stimulation through the electrode	Single pulse, focal TMS
Ni Z et al	2018	8 dystonia patients	Model 3387, Medtronic	Globus pallidus int.	Cnnected to IPG	Repetitive gpi DBS (2.1-4.5 V, 60-120 µs, 0.1 Hz) paired with focal TMS at 10-25 ms interstimulus intervals, 180 stimuli	Focal TMS
Wagle Shukla et al	2018	10 dystonia patients	5 patients, model 3387, 5 patients, model 3389, Medtronic	Subthalamic nucleus	Connected to IPG	Clinical DBS parameters, stimulation on and off	Focal single pulse TMS paired with median nerve stimulation
Miron et al	2018	1 patient with obsessive compulsive disorder and depression	Model 3387, Medtronic	Bilateral nucleus accumbens and anterior arm of the internal capsule	Connected to IPG Activa AC, Medtronic	Stimulation off	1 Hz rTMS to right orbitalfrontal cortex, 100% motor threshold, 300 pulses, > 12 sessions; 10 Hz rtms to DLPFC, 3000 pulses, 30 sessions
			Vagus Nerve Stimulation Electrodes				
Di Lazzaro et al	2004	5 patients with medically refractory epilepsy	-	Vagus nerve	Connected to stimulator device Kinetra, Medtronic	30 seconds on and 5 minutes off, 30 Hz,	Focal single and paired pulse TMS
Bajbouj et al	2007	10 patients with treatment resistant depression	-	Vagus nerve	Connected to IPG Prosthesis System, Cyberonics	Amplitude: 1.1 ± 0.4 mA, pulse width: 300 ± 105.4 ms, frequency: 19.5 ± 1.6 Hz, stimulation on and off	Focal single and paired pulse TMS over motor cortex
Philip et al	2014	20 patients with		Vagus nerve		Stimulation off in	rTMS

		treatment resistant depression				most of the patients	
				Cortical Electrode			
Lefaucheur et al	2010	2 patients with intractable pain (CRPS-II and brachial plexus injury)	Medtronic Pisces Quad electrode (model 3487A)+ 2 quadripolar Resume II Lead Model 3587A Medtronic	Cervical spine epidural space (Pisces Quad electrode) + motor cortical epidural space (Resume electrodes)	Not connected to IPG	No stimulation	Focal single-pulse TMS
Phielipp et al	2017	1 patient with pain (postherpetic neuralgia)	Medtronic Resume II subdural cortical electrode (model 3587A)	Subdural electrode over right motor cortex	Connected to pulse generator Medtronic Itrel II 7424	Stimulation off	rTMSto R motor cortex, 20 Hz, 90% resting motor threshold, 2000 pulses, 10 sessions
				Cardiac Pacemaker			
Hizli Sayer et al	2016	1 patient with depression	Cardiac pacemaker, Symphony DR 2550; Ela Medical Inc			Stimulation on	rTMSto L DLPFC, 10 Hz, 110% motor threshold, 1000 pulses, > 6 sessions
Wei et al	2018	1 patient with migraine	Cardiac pacemaker, Symphony DR 2550, Sorin Biomedica			Dual chamber rate responsive cardiac, pacemaker, patient remained in atrial paced rhythm, stimulation on	Single pulse TMS to occipital cortex

Legend of abbreviations: CPRS: Complex Regional Pain Syndrome; DBS: Deep Brain Stimulation; DYT: Dystonia; GPi: Globus Pallidus Internus; IPG: Internal Pulse Generator; PD: Parkinson's Disease; STN: Subthalamic Nucleus; VNS: Vagal Nerve Stimulation.

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Table S2. Randomized controlled multicenter trials investigating safety of rTMS in psychiatric disorders.

Authors	Disorder Number of subjects per condition (n)	rTMS coil, stimulator, target region Conditions	rTMS parameters	Adverse events (%) Active rTMS	Adverse events (%) Comparator#	SAE (n) Active rTMS	SAE (n) Comparator#	Outcome of SAEs	Significant differences between active and sham groups	Comment
O'Reardon et al.	MDD Active TMS: n=165 Sham TMS: n=158	Neuronetics Model 2100 Therapy System Left DLPFC Active TMS: iron core coil Sham TMS: sham coil	10 Hz, 120% RMT, 30 sessions/6 weeks, 3000 stimuli/day, 4 sec trains, 26 sec ITI, session duration 37.5 min	Eye pain 10 (6.1) Toothache 12 (7.3) Application site discomfort 18 (10.9) Application site pain 59 (35.8) Facial pain 11 (6.7) Muscle twitching 34 (20.6) Pain of skin 14 (8.5)	3 (1.9) 1 (0.6) 2 (1.3) 6 (3.8) 5 (3.2) 5 (3.2) 1 (0.6)	n = 9 disease-related exacerbation: Suicidality 1 (0.6%) exacerbation of depression 1 (0.6%) suicide gesture 0 Increase of suicidality on HAMD: n = 1	n = 7 (3) 1.9% (3) 1.9% (1) <1% n = 10	-	There was a higher incidence of scalp discomfort and pain with active than sham rTMS. The incidence of headache did not differ between active and sham TMS conditions.	In this study, rTMS was well tolerated and safe. Adverse events reported were principally limited to scalp discomfort or pain within the confines of the rTMS session itself and were mostly transient phenomena in the first weeks of the rTMS course. Despite rTMS being administered here at 120% of motor threshold and 3000 pulses/session, an elevated rate of serious adverse events relative to sham was not detected.
Herwig et al.	MDD Active TMS: n=62 Sham TMS: n=65	Magstim Rapid, Medtronic Maglite r25 or Medtronic Magpro Active TMS: 70 mm figure-8 coil Sham TMS: 5 cm lateral to F3, above the left temporal muscle; coil angled at 45°, touching the skull with the anterior rim, stimulation intensity at 90% RMT	10 Hz, 110% RMT, 15 sessions/3 weeks, 2000 stimuli/day, 2 sec trains, 8 sec ITI, 100 trains	Headache 3 Dizziness 0 Painful local sensations 1 Nausea 1	1 1 2 0	none	none	NA	no statistical information	This was the only study where rTMS was applied together with a new antidepressant medication, i.e. either mirtazapine (mean dosage: 34 and 32 mg) or venlafaxine (mean dosage: 164 and 161 mg). However, only adverse events "related to rTMS" were reported.
George et al.	MDD Active TMS: n=92 Sham TMS: n=98	Neuronetics Inc. Target: left DLPFC Active TMS: solidcore coil Sham TMS: sham coil with metal insert blocking magnetic field, scalp electrodes delivering matched somatosensory sensations	10 Hz, 120% RMT, 15 sessions/3 weeks, 3000 stimuli/day, 4 s trains, 26 s ITI; sham treatment with identical parameters no sufficient improvement after 3 weeks: cross over to open treatment Improvement: Continued treatment for up to 3 weeks Improvers but nonremitters continued treatment for 3	Headache 29 (32) Discomfort at stimulation site 17 (18) Insomnia 7 (7.6) Worsening of depression/ anxiety 6 (7) Gastrointestinal 6 (7) Fatigue 5 (5) Muscle aches 4 (4) Vertigo 2 (2) Skin pain 1 (1) Facial muscle twitching 0 Other 18 (20)	23 (23) 10 (10) 10 (10) 8 (8) 3 (3) 4 (4) 4 (4) 2 (2) 1 (1) 1 (1) 15 (15)	n=1 syncope (unlikely related to the study)	n=1 paranoid ideation (possibly related to the study)	no long-term sequelae	adverse events did not significantly differ by treatment arm	The treatment was relatively well tolerated, with no difference in adverse events between the active sham and the active TMS treatment arms. There were no seizures, and retention was high.

			weeks if showing progressive improvement							
Levkovitz et al.	MDD Active dTMS: n=89 Sham dTMS: n=92	Brainsway dTMS system Target: left DLPFC active dTMS: H1-coil sham TMS: sham coil	20 sessions/4 weeks, 24 sessions in following 12 weeks (min. 48h pause), 18 Hz, 120% RMT, 2 s trains, 20 s ITI, 55 trains/session, 1980 stimuli/session	application site discomfort 3 (3.0) application site pain 5 (5.0) headache 27 (26.7) muscle twitching 2 (2.0) back pain 2 (2.0) insomnia 2 (2.0) anxiety NR	2 (1.8) 0 21 (18.9) 0 3 (2.7) 4 (3.6) 2 (1.8)	n=3 elbow fracture (1) cluster headache (1), generalized seizure following excessive consumption of alcohol on the night before treatment (1)	n=4 suicidality (2) nausea and vomiting (1) nephrolithiasis (1)	seizure with no additional medical intervention	significant difference between study groups regarding application site pain (p=0.02) The incidence of headache did not significantly differ between active and sham TMS conditions.	dTMS was well tolerated by the majority of patients and the main side effect was pain during application, usually not requiring any special care. There was one seizure induced by dTMS in this study, which may have been related to alcohol consumption the night before treatment.
Wobrock et al.	predominant negative symptoms in schizophrenia Active rTMS: n=76 Sham rTMS: n=81	MagPro X100 (Medtronic A/S), passively cooled MCF-B65 figure-8 coils (Medtronic A/S) Target: left DLPFC Sham TMS: magnetic coil tilted over one wing (45 degrees)	15 sessions/ 3 weeks, 10 Hz, 110% RMT , 20 trains with 50 stimuli per train, 30 s ITI, 1000 stimuli/ session	headache 12 facial muscle twitching 3 fatigue 1 psychotic ideation 1 discomfort at stimulation site 1 general discomfort 1	4 3 1 1 0 0	Without withdrawal from study: n=1 (suicidality) With withdrawal from study: n=1 (acute deterioration in symptoms) extension phase: n=2 (hospitalizations owing to deterioration in symptoms)	Without withdrawal from study: n=1 (event requiring hospitalization) With withdrawal from study: n=2 suicidality (1) unspecified (1) extension phase: n=4 hospitalizations (2), suicidality(1), melperone intoxication (1)	no information given	no statistical information	In terms of side effects, the active rTMS intervention was well tolerated, and the main challenge for patient acceptance appears to be the need for treatment 5 days per week.
Blumberger et al.	Treatment resistant MDD 10 Hz rTMS: n=205 iTBS: n=209	rTMS: MagPro X100 or R30 stimulator, equipped with a B70 fluid-cooled coil and high-performance cooler (MagVenture) Target: left DLPFC Neuronavigation: ANT Neuro, Enschede, Netherlands	rTMS: 120% RMT; 10 Hz; 4 s on and 26 s off; 3000 pulses per session; total duration of 37·5 min iTBS: 120% RMT, triplet 50 Hz bursts, repeated at 5 Hz; 2 s on and 8 s off; 600 pulses per session; total duration of 3 min 9 s 4 weeks with 20 sessions, no remission – additional 2 weeks with 10 sessions	Headache 31 (64) Nausea 22 (11) Dizziness 8 (4) Unrelated medical problem 47 (23) Fatigue 14 (7) Insomnia 14 (7) Anxiety or agitation 8 (4) Back or neck pain 7 (3) Unrelated accidents 2 (1) Vomiting 1 (<1) Tinnitus 1 (<1) Migraine aura 3 (1) Abnormal sensations 2 (1)	136 (65) 14 (7) 18 (9) 46 (22) 16 (8) 10 (5) 9 (4) 6 (3) 3 (1) 1 (<1) 3 (1) 4 (2) 4 (2)	1/205 (<1%): myocardial infarction (not rTMS related)	3/209 (1%): agitation that led to hospital admission, worsening of suicidal ideation, hospital admission due to worsening of depression	SAE: no significant difference (Fisher's exact test, p=0·6232)	Numbers of adverse events: p>0·05 on Fisher's exact tests for each pair of proportions intensity of pain associated with treatment was greater in the iTBS group than in the 10 Hz rTMS group (mean score on verbal analogue scale 3·8 [SD 2·0] vs 3·4 [2·0] out of 10; p=0·011); did not translate into increased discontinuation rates	iTBS showed non-inferior effectiveness and a similar adverse event profile and HRSD-17 score acceptability compared with the standard, FDA-approved 10 Hz rTMS protocol for treatment-resistant depression.
Yesavage et al.	Treatment resistant MDD in US veterans Active rTMS: n=81 Sham rTMS: n=83	MagPro R30 (MagVenture) device, Cool-B65-A/P coil Target: left DLPFC	10 Hz, 120% RMT, 4000 pulses/session 5 session blocks over a period of 5 to 12 calendar days, between 20 and 30 sessions of rTMS in total Remission after initial 20 to 30 sessions - additional 6 taper sessions over 3 weeks	Nasopharyngitis 8 Depression 8 Falls 3 Headache 15 Abnormal results of hearing tests 18	8 3 7 16 18	Suicidal ideation 3	4	No suicides or seizures occurred during the study and there were no deaths	AE/SAE did not differ significantly between treatment groups and were generally consistent with expected background medical issues in this population	Abnormal results of hearing tests believed to be an artifact of frequent, imprecise testing

Legend:
MDD=major depressive disorder, # in the majority of studies sham TMS, serious adverse events (SAE), DLPFC = dorsolateral prefrontal cortex, NR = not reported.

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Table S3. Safety table for QPS parameters.

Target	ISI	Intensity	IBI (sec)	Total pulse number	Duration	Coil
M1	1.5, 5, 10, 30, 50, 100, 200, 1250	90-130% AMT for hand muscle	2.5-5	1440-2880	30min	figure of eight
PM	5, 50	90% AMT for hand muscle	5	1440	30min	figure of eight
S1	5, 50	90% AMT for hand muscle	5	1440	30min	figure of eight
DLPFC	5, 50	90% AMT for hand muscle	5	1440	30min	figure of eight
SMA	5, 50	90% AMT for TA	5	1440	30min	figure of eight

Table S4. QPS studies.

First author	Year	Subjects	Number	Target area	ISI	Intensity	Waveform	IBI (sec)	Total pulse number	duration	side effects
Published papers											
Hamada	2007	N	16	M1	1,5	0.9, 1.3 AMT	M	5	1440, 720	30	No
Hamada	2008	N	10	M1	1.5, 5, 10, 30, 50, 100, 1250	0,9	M	5	1440	30	No
Hamada	2009	N	9	M1,SMA	1.5, 5, 10, 30, 50, 100	0.9 AMT for hand muscles, 0.9 AMT for TA	M	5	1440	30	No
Enomoto	2011	PD	10	M1	5, 50	0.9 AMT for hand muscles, 0.13 AMT for TA	M	5	1440	30	No
Hirose	2011	N	10	M1	5, 50	0.9 AMT for hand muscles, 0.14 AMT for TA	M	5	1440, 288	30, 6	No
Nakamura	2011	N	12	M1	5, 50	0.9 AMT for hand muscles, 0.10 AMT for TA	M	5	1440	30	No
Nakatani-Enomoto	2011	N	8	M1	5, 50	0.9 AMT for hand muscles, 0.11 AMT for TA	M	5	1440	30	No
Groiss	2012	N	10	M1, S1	5, 50	0.9 AMT for hand muscles, 0.15 AMT for TA	M	5	288	6	No
Groiss	2012	N	10	M1	5,50	0.9 AMT for hand muscles, 0.16 AMT for TA	M	OPS: 5, QPS: 2.5, 5	OPS:2880, QPS:2880, 1440	30	No
Nakatani-Enomoto	2012	N	11	S1, M1, PM	5, 50	0.9 AMT for hand muscles, 0.12 AMT for TA	M	5	1440	30	No
Tsutsumi	2014	N	10	M1	5, 50	0.9 AMT for hand muscles, 0.18 AMT for TA	M	5	1440	30	No
Watanabe	2014	N	6	M1	5, 50	0.9 AMT for hand muscles, 0.17 AMT for TA	M	5	1440	30	No
Enomoto	2015	N	10	M1	5, 50	0.9 AMT for hand muscles, 0.21 AMT	M	5	1440	30	No

						for TA					
Kadowaki	2015	N	13	M1	5, 50	0.9 AMT for hand muscles, 0.20 AMT for TA	M	5	1440	30	No
Tanaka	2015	N	24	M1	5	0.9 AMT for hand muscles, 0.19 AMT for TA	M	5	1440	30	No
Watanabe	2015	N		SMA	5, 50	0.9 AMT for hand muscles, 0.22 AMT for TA	M	5	1440	30	No
Nakamura	2016	N	35	M1	5, 50	0.9 AMT for hand muscles, 0.24 AMT for TA	M, Bi	2.5, 5, 7.5, 10	720, 1440	15, 30	No
Nakatani-Enomoto	2016	N, ME	10N, 6ME	M1, S1	5, 30, 50, 100, 500	0.9 AMT for hand muscles, 0.23 AMT for TA	M	5	1440	30	No
Simeoni	2016	N	20	M1	5, 50	0.9 AMT for hand muscles, 0.25 AMT for TA	M	5	1440	30	No
Hanajima	2018	N	107	M1	5	0.9 AMT for hand muscles, 0.26 AMT for TA	M	5	1440	30	No

Table S5. TBS studies.

Reference	Stimulation site	Pulse number	Intensity	Number of subjects	Remarks
Hanlon et al. 2017b	L MPFC	two 1800-pulse trains of cTBS (120 s on, 60 s off, 120 s on; 3600 pulses over a total of 5 min)	110%RMT	78	Cocaine (and alcohol) abuse protocol
Smith et al. 2018	M1	iTBS	80%AMT	19	Healthy
Berkay et al. 2018	SMA	cTBS	80% AMT	15	Healthy
Sasaki et al. 2018	M1	cTBS	80% AMT	31 (twice each)	Healthy
Ulrich et al. 2018	VLPFC	cTBS + ITBS sep sessions	80% AMT	15 (twice each)	Healthy
Chung et al. 2018	PFC (F1)	iTBS	50, 75, 100 RMT	16 (3x each)	Healthy
Gedankien et al. 2017	M1	iTBS	80% AMT	17	Healthy
Wilkinson et al. 2017	M1	cTBS	80% AMT	20	Healthy
Giboin et al. 2017	M1	cTBS	80% AMT	17	Healthy
Koc et al. 2017	M1 M1 then cbllm	cTBS	80% AMT	15	Idiopathic Generalized Epilepsy (drug free)
Gomes-Osman et al. 2017	M1	iTBS	80% AMT	14 (twice each)	Healthy sedentary
He et al. 2017	RMPFC RLPFC vertex	cTBS	80% AMT	18 (3x each)	Healthy
Kahan et al. 2017	M1	iTBS + cTBS (each hemisph)	80% RMT	10; 10 (twice each)	Stroke; healthy
Fried et al. 2017	M1	iTBS	80% AMT	9; 15; 12 (twice each)	Probable AD; diabetes T2; healthy
Hilt et al. 2017	M1	cTBS	80% AMT	15	Healthy
Curtin et al. 2017	DLPFC (f3)	iTBS	80% AMT	17	Healthy
Kleinmintz et al. 2018	IFG	cTBS (900)	100% AMT	23	Healthy
Heidegger et al. 2017	M1	cTBS (2 trains separated 10min)	80% AMT	31	Healthy
Hanlon et al. 2017a	VMPFC	cTBS (6 trains; 1min interval (3600 pulses)	110% RMT	25; 24	Cocaine users; alcoholics

Rastogi et al. 2017	Lateral Cbllm	cTBS	80% AMT	12	Healthy[25]
Diekhoff-Krebs et al. 2017	M1; parieto-occipital	iTBS	80% AMT	14 (twice each)	Stroke
Chung et al. 2017	F3	cTBS; iTBS	80% RMT	10 (twice each)	Healthy
Colnaghi et al. 2017	Cbllm vermis	cTBS	100% RMT	20 (half nemantine)	Healthy
Esterman et al. 2017	Cbllm (2 sites DAN; DMN))	iTBS	80% RMT or 100% AMT	15 (twice each)	Healthy
Shirota et al. 2017	M1	iTBS (unidirectional)	80% AMT	19 (3x each; one lower intensity AP)	Healthy
Mancini et al. 2017	Precuneus	cTBS	80% distance adjusted RMT	15	Healthy
Valchev et al. 2017	M1; S1; SPL	cTBS	80% RMT	16; 34; 17 (once per site)	Healthy
Ponzo et al. 2017	M1	iTBS	80% AMT	10; 8; 10	PD; LRRK; Healthy
Meehan et al. 2017	M1	iTBS	80% AMT	16; 15	Adolescents normal; post concussive
Schilberg et al. 2017	M1	iTBS	80% AMT	27 (twice)	Healthy
Hordacre et al. 2017	M1	cTBS	70% RMT	34 (twice)	Healthy
Pitcher et al. 2017	STS or vertex	cTBS (900)	80% AMT	17 (twice)	Healthy
Pellicciari et al. 2017	R&L DLPFC	cTBS (1800) + iTBS (1800) daily for 10 sessions	30% & 32% output	1	Depression
Lin et al. 2017	M1	cTBS; iTBS	80% AMT	35 (twice)	Healthy
Iwabuchi et al. 2017	DLPFC	iTBS	80% RMT	27	Healthy
Ticini et al. 2018	IPL	cTBS; imTBS	80% AMT	16	Healthy
Lenoir et al. 2018	Operular-insular	Deep cTBS; double cone v flat	80% RMT for TA; 80% RMT FDI	17 (twice)	Healthy NB TWO SEIZURES double cone cTBS
Weintraub-Brevda et al.	VLPFC; R;	cTBS	80% AMT	18 (3 times)	Healthy

2018	L; Vertex				
Gilligan et al. 2018	Cbllm	cTBS	80% RMT	41	Healthy
Rocchi et al. 2018	M1	cTBS	80% AMT	13	Healthy
Bogdanov et al. 2018	iLPFC	cTBS; iTBS; imTBS	80% RMT	17, 16, 16	Healthy
Tambini et al. 2018	pIPC; S1	cTBS	80% AMT	25	Healthy
Huang et al. 2018	premotor	cTBS	80% AMT	12	Healthy
Agnew et al. 2018	Premotor; vertex	cTBS	40% ouptut	16	Healthy
Stubbeman et al. 2018	L & R BA46	cTBS (20 Hz; 3600-4800 pulses) + iTBS (20 Hz; 4950 pulses)	90 - 95% RMT	57 daily for 5 days	Depression
Otero-Millan et al. 2018	SMGp	cTBS	55% output	12	Healthy
Vilidaite et al. 2018	Occipital	cTBS	30% ouput	6	Healthy
Guerra et al. 2018	M1	iTBS + TACS (gamma; beta)	80% AMT	14	Healthy
Gaertner et al. 2018	M1	iTBS (600) + 10 Hz rTMS (2000)	80% RMT	21	CRPS
van Holstein et al. 2018	aPFC; DLPFC; PM	cTBS	80% AMT	27 (three times)	Healthy
Marin et al. 2018	DLPFC	cTBS	80% AMT	15	Healthy
Chung et al. 2018	F1	iTBS; iTBS (2 blocks 15min interval)	75% RMT	18 (twice)	Healthy
Ross et al. 2018	PPC; SMA; M1	cTBS	80% AMT	25	Healthy
Allen-Walker et al. 2018	Cbllm (left/right)	cTBS	55% output	18 (twice)	Healthy

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