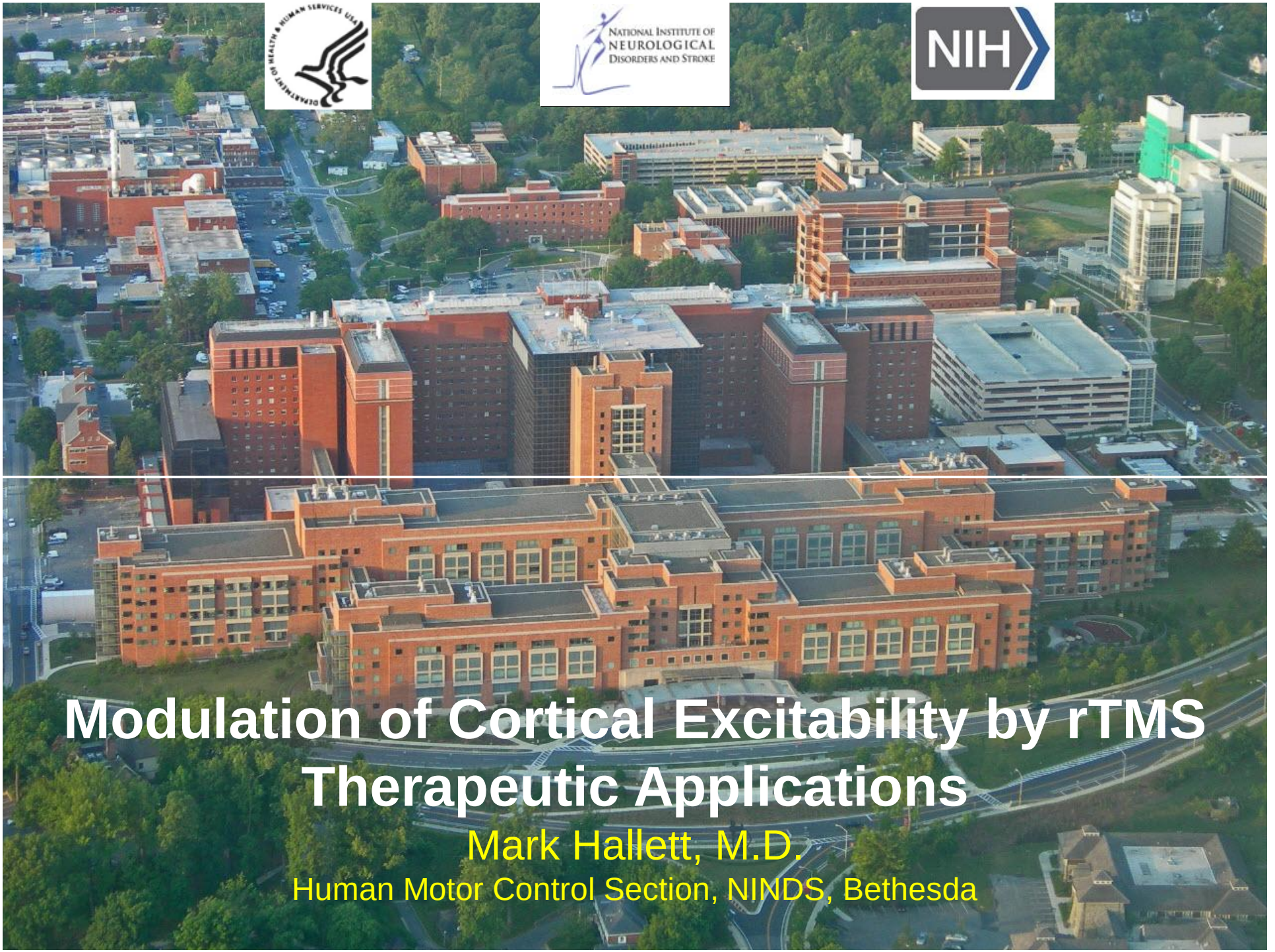


Modulation of Cortical Excitability by rTMS
Therapeutic Applications

Mark Hallett, M.D.
Human Motor Control Section, NINDS, Bethesda

Disclosures

- Conflicts of interest
  - NIH holds the patent for the H-coil and I am one of the co-inventors
- Off-label use
  - rTMS with “NeuroStar TMS Therapy®” and for the Brainsway H-coil is indicated for treatment of major depressive disorder; all other uses are off-label

The possibility of therapy with rTMS depends on its ability to use plasticity to change the brain.

Early Electric Treatments

- Ancient Greeks and Romans used electric ray fish to treat pain from headache, childbirth, gout, and operations
- Electric ray generates electrical current up to 220 V, 30 A, and pulse repetition rate of 0.6 Hz => pretty good electrical stimulator!

From Angel V. Peterchev (internet)

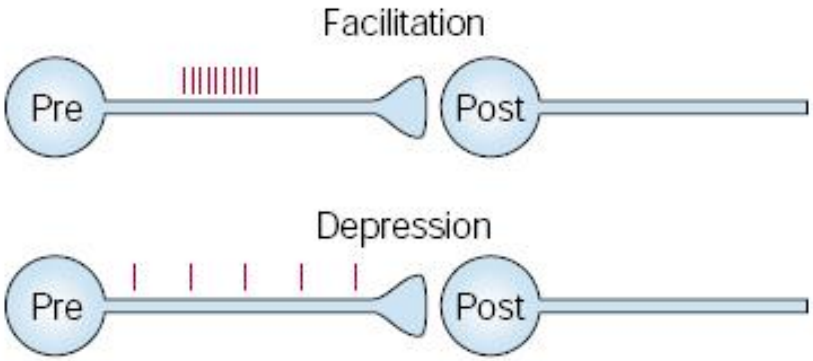
Definitions

- Plasticity: capability for change
- Plastic change: alteration in excitability (or function) of a network
- Metaplasticity (plasticity of plasticity): alteration of plasticity; i.e., alteration in the capability for change
- Homeostatic plasticity: the characteristic that plastic changes (at any one time) can only be within certain limits
- Good plasticity and bad (aberrant) plasticity: plasticity favorable or unfavorable to the organism

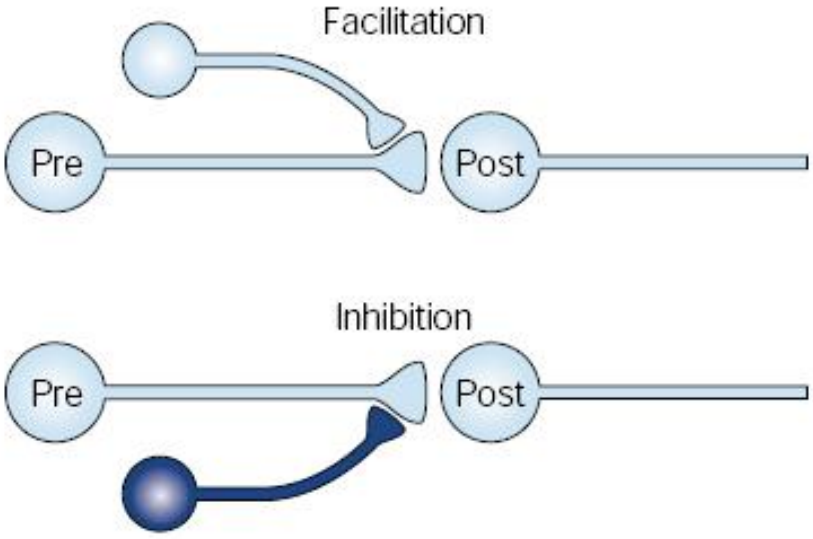
Mechanisms of Plasticity

- Synaptic strengthening/weakening
  - LTP/LTD
  - Homosynaptic & heterosynaptic
    - Spike Timing–Dependent Plasticity
- Anatomical changes
  - Dendritic spines
  - Axonal spouting, new connections
- Turning circuits on and off

a **Homosynaptic (activity-dependent) plastic change**



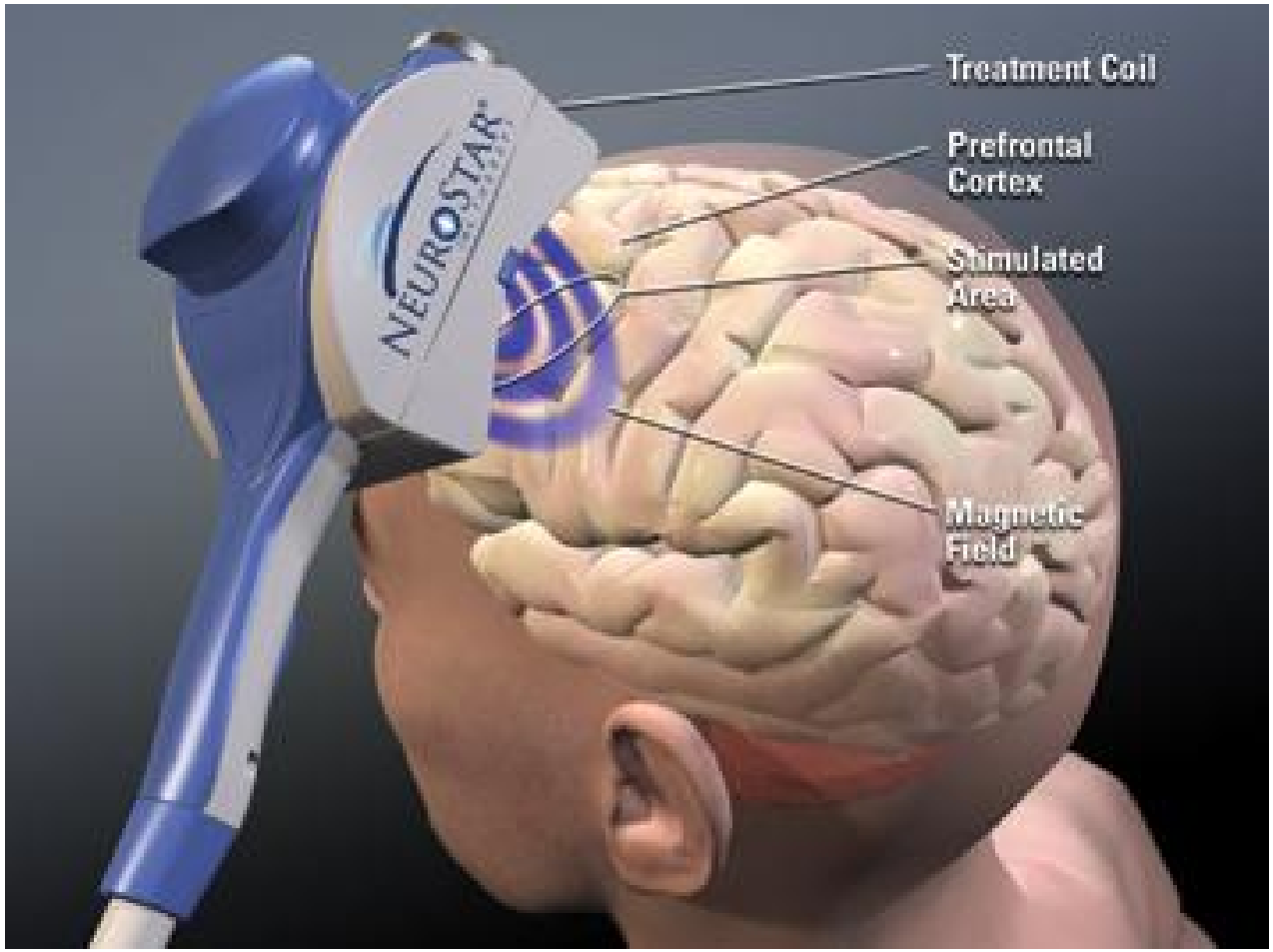
b **Heterosynaptic (modulatory input-dependent) plastic change**



Bailey et al. 2000

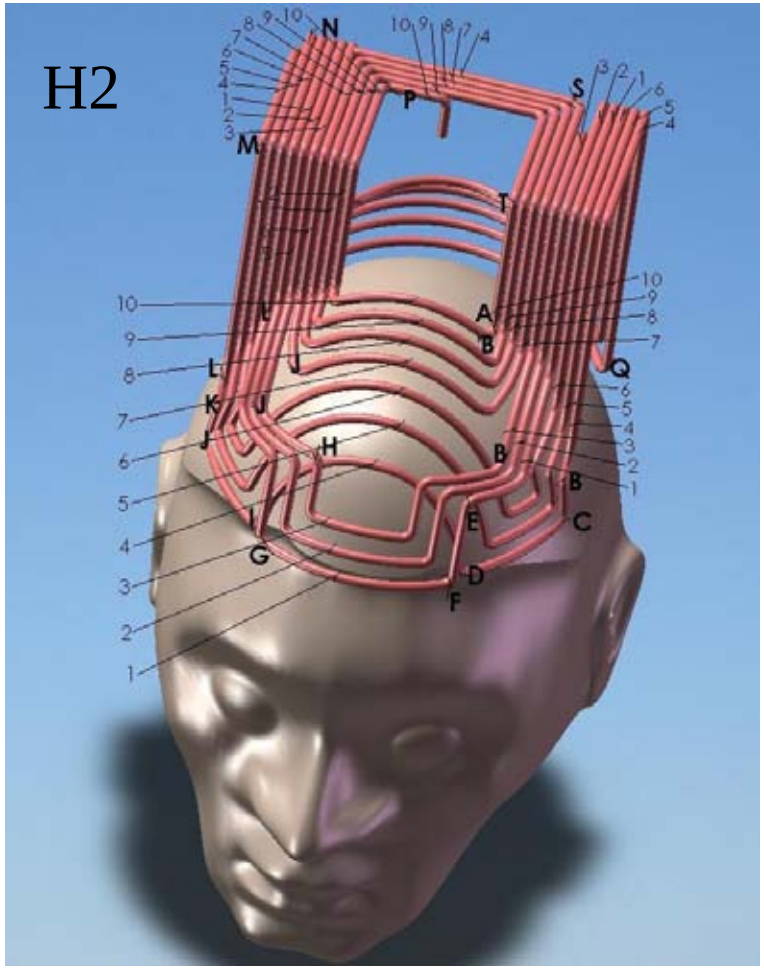
rTMS can modify brain function

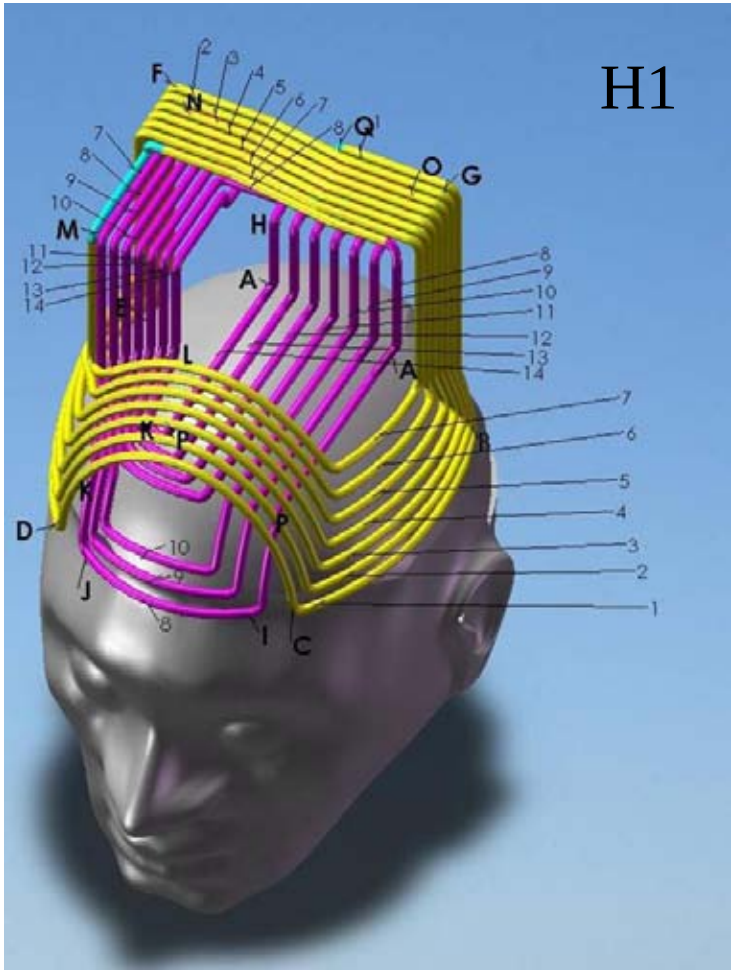
- rTMS has promise for therapy
- There are many possible methods for rTMS and each one will likely have different effects
  - Coil shape, coil current
  - Pattern & time of stimulation
  - Site of stimulation
  - Repetition of treatment



Neuronetics illustration from their website

Versions of the H-Coil from A. Zangen

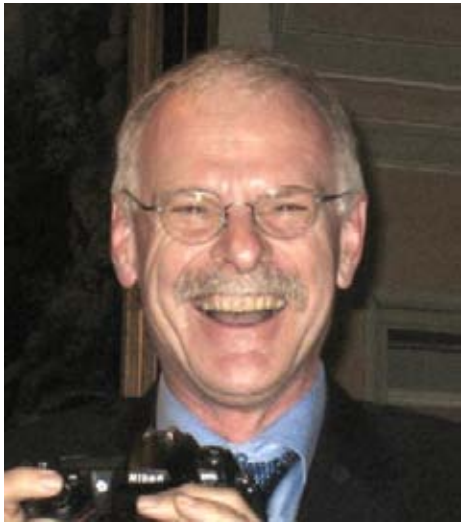




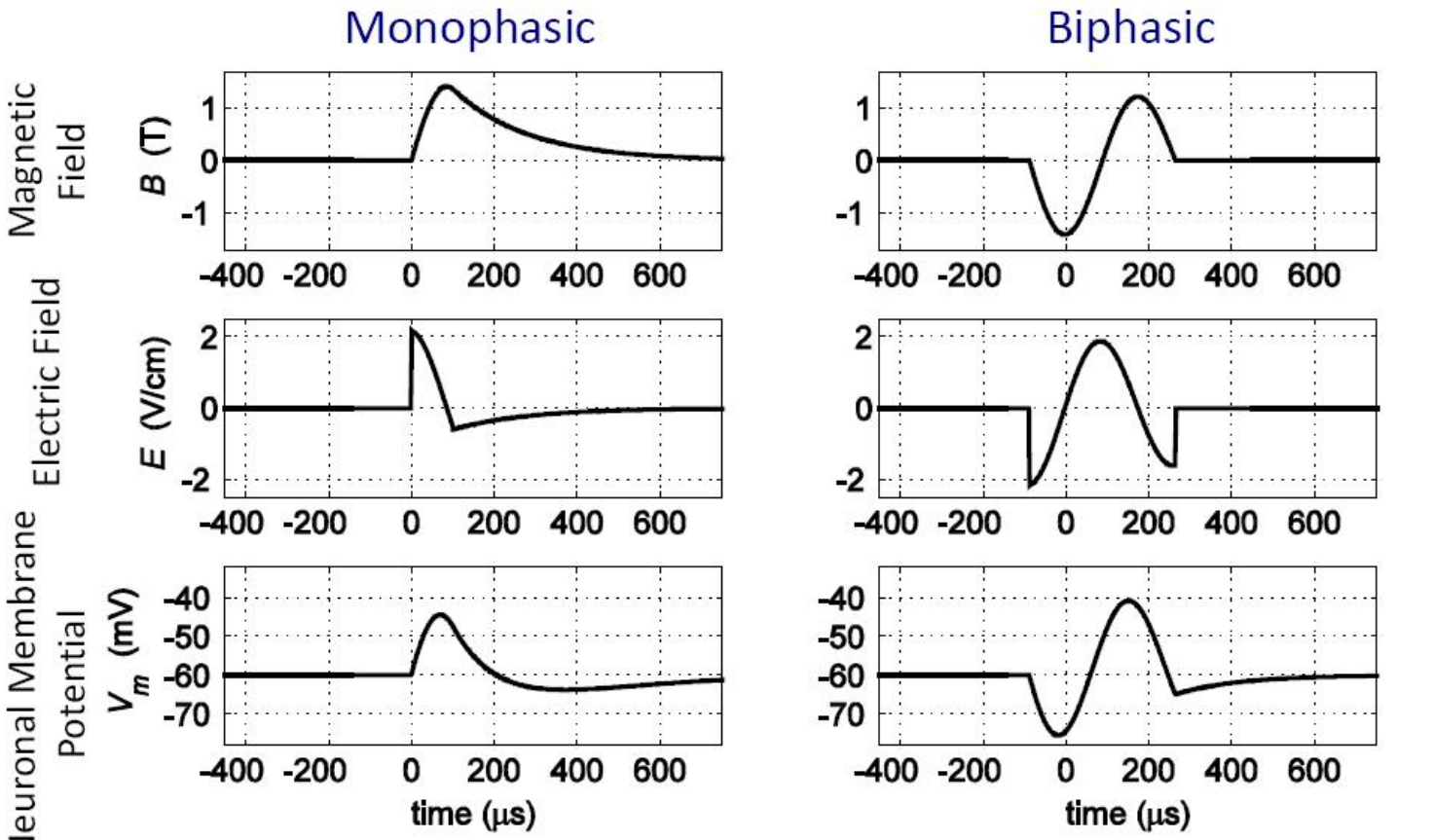
<u>Considerations</u>: Target neuronal structures, directions of axons to be stimulated, increasing depth, decreasing facial pain and other risks or side effects.

Transcranial Direct Current Stimulation (tDCS)

Walter Paulus



Optimizing TMS: Pulse Types



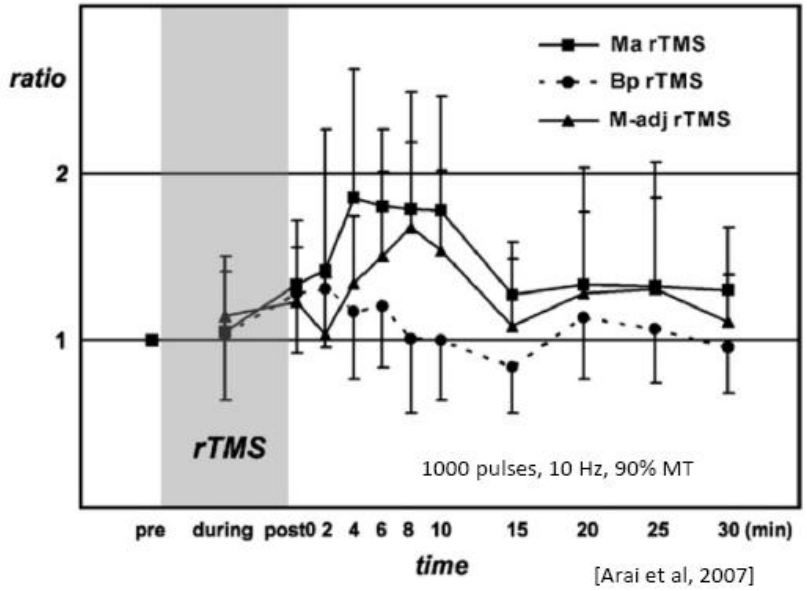
- More selective stimulation
- Single-pulse devices < 1 Hz
- Less selective stimulation
- Rapid-rate devices < 100 Hz

From Angel V. Peterchev (internet)

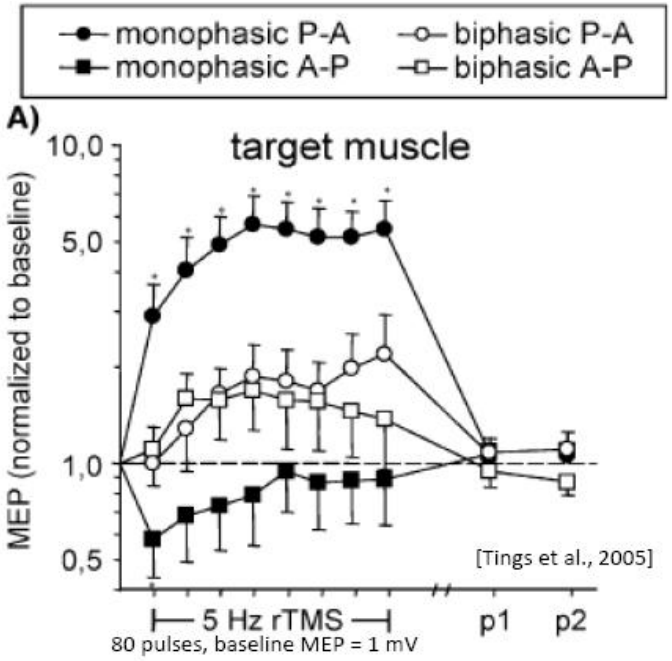
http://psychiatry.duke.edu/wysiwyg/downloads/Grand_Rounds/Duke_Grand_Rounds__Peterchev_March_31_2011.pdf

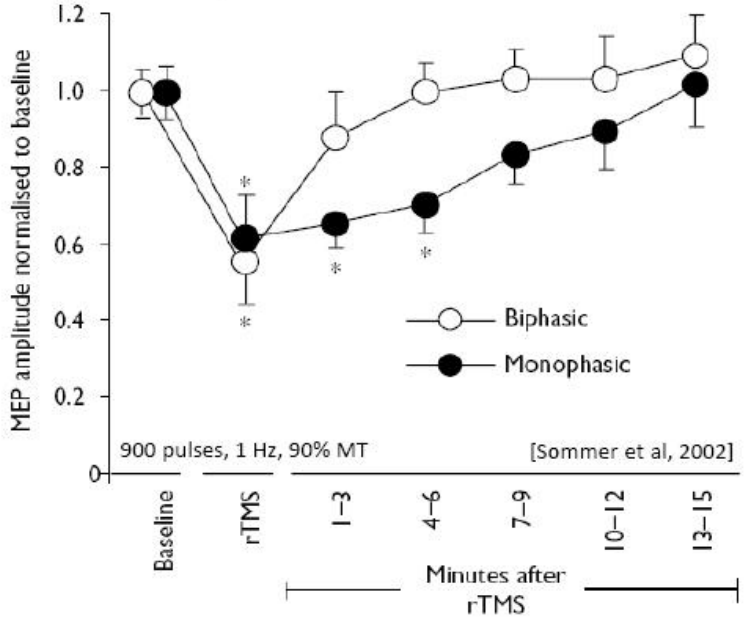
Monophasic vs. Biphasic TMS

- Monophasic (unidirectional) TMS pulses have stronger effect on cortical excitability than biphasic (bidirectional) pulses
  - preferential activation of neuronal populations
  - different inhibition/excitation balance



[Arai et al, 2007]

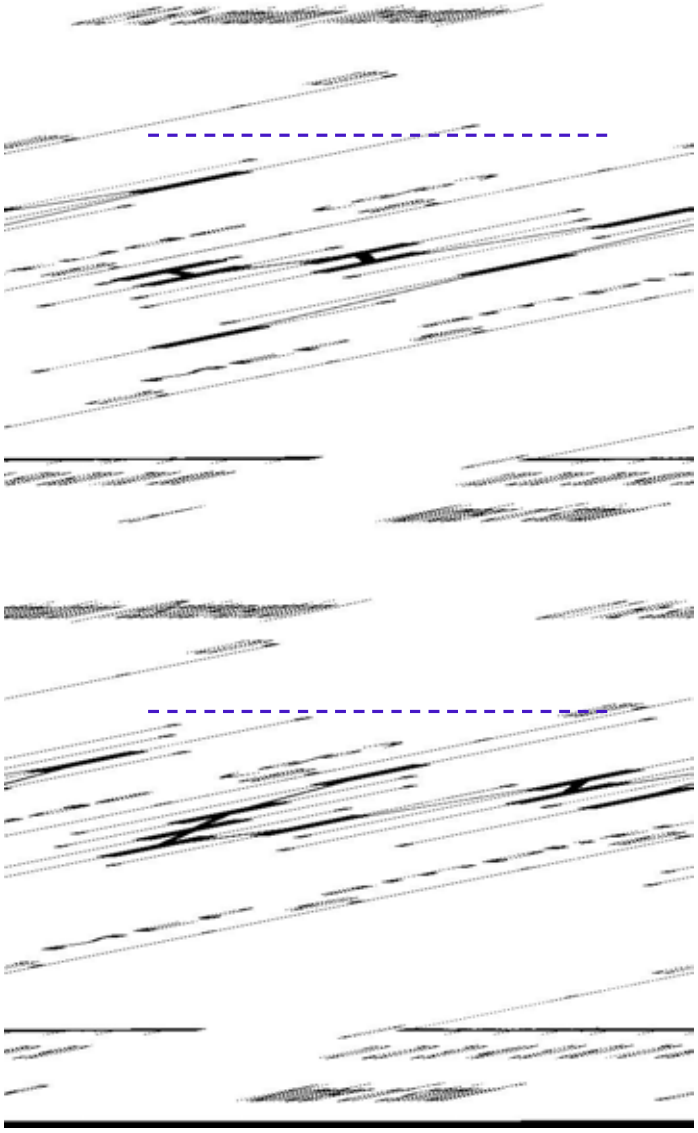




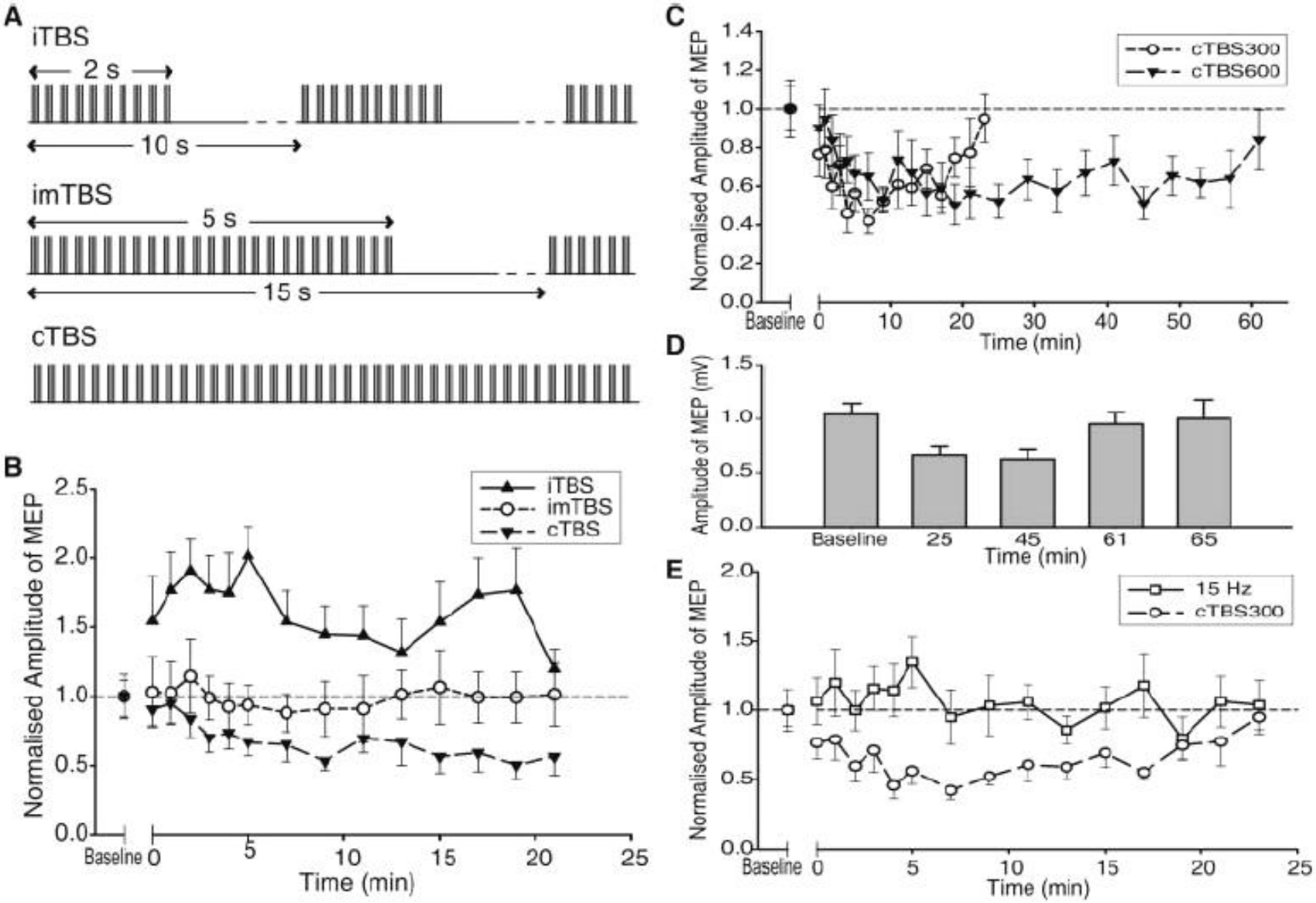
From Angel V. Peterchev (internet)

Rapid rTMS increases brain excitability

Slow rTMS reduces brain excitability

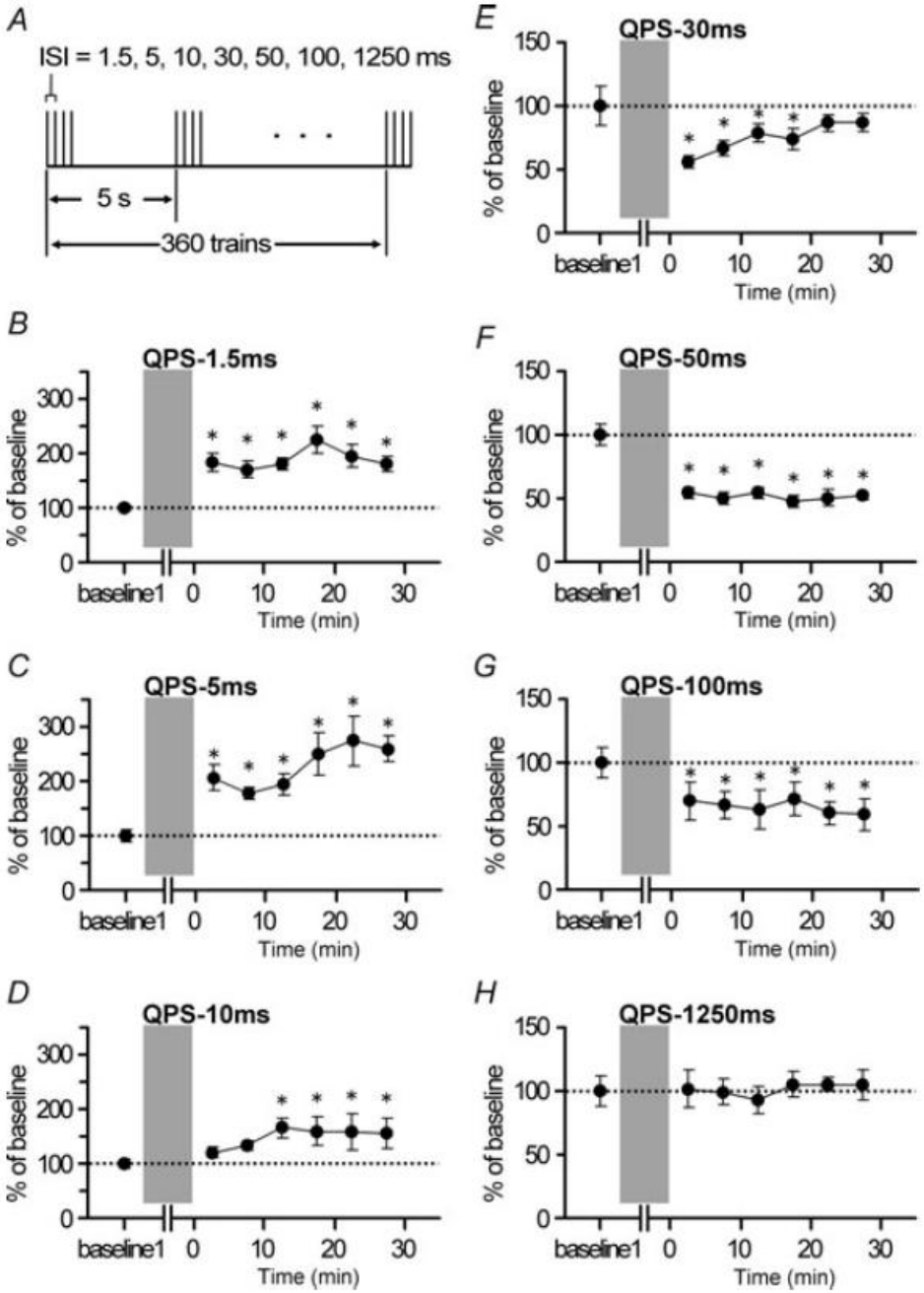


Theta burst stimulation



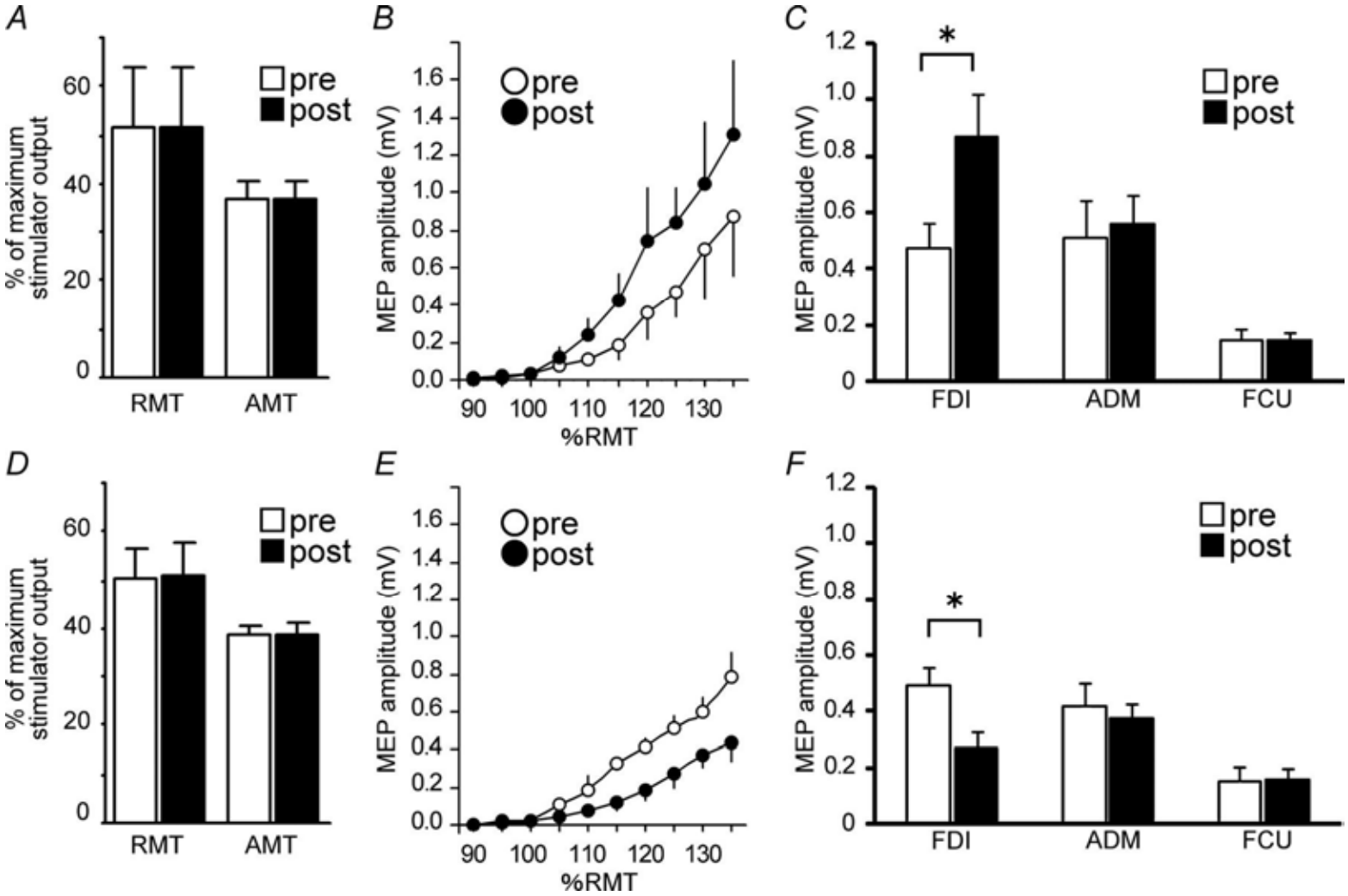
Huang et al. 2005

Quadripulse stimulation



Hamada M et al.
J Physiol 2008;
586:3927-3947

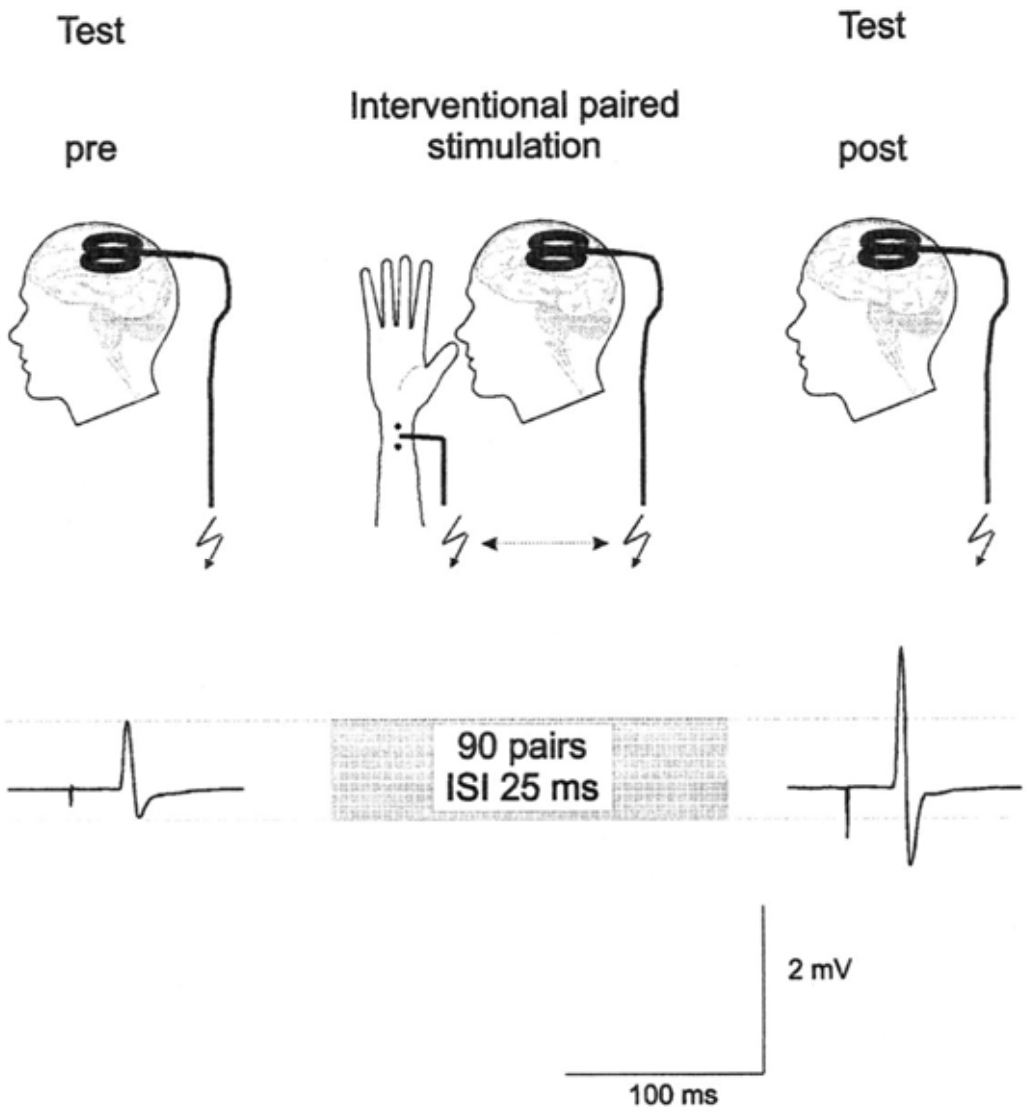
Basic properties of QPS-induced plasticity



Hamada M et al. J Physiol 2008;586:3927-3947

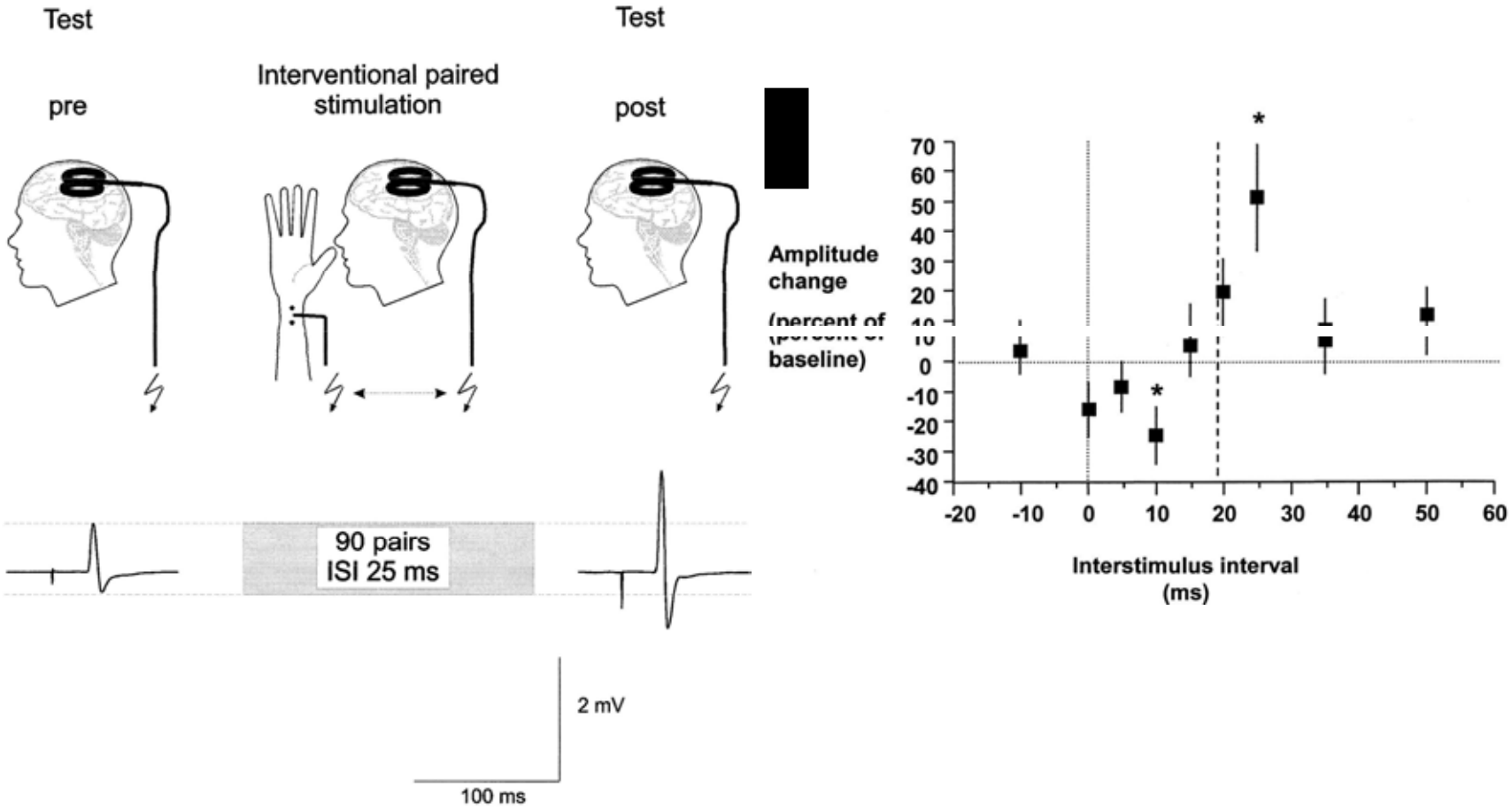
The Journal of Physiology

Technique of Paired Associative Stimulation



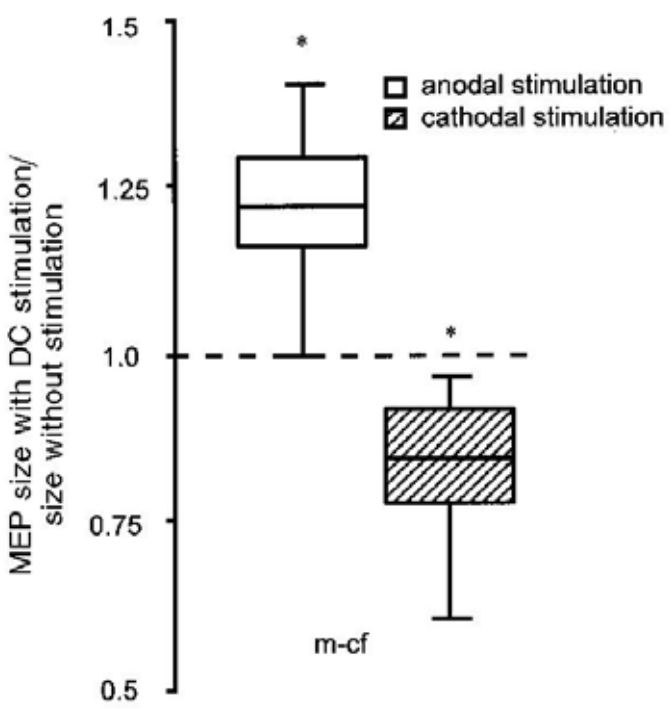
Stefan et al. 2000 (Classen Laboratory)

Paired Associative Stimulation (PAS)

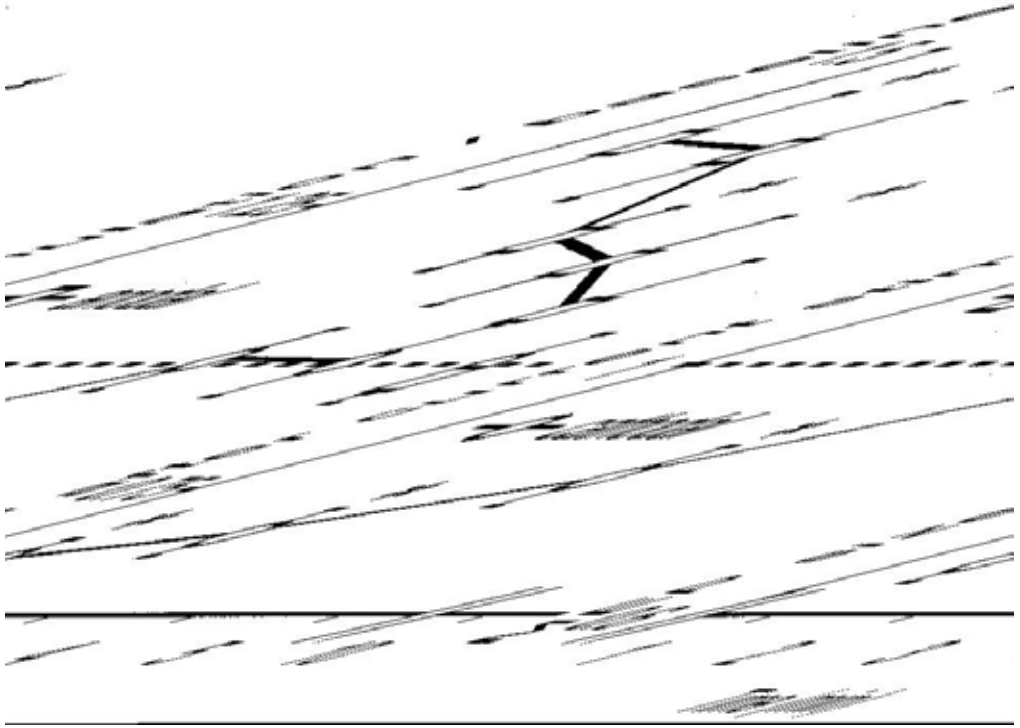


Stefan et al 2000; Wolters et al 2003

Transcranial Direct Current Stimulation (tDCS)



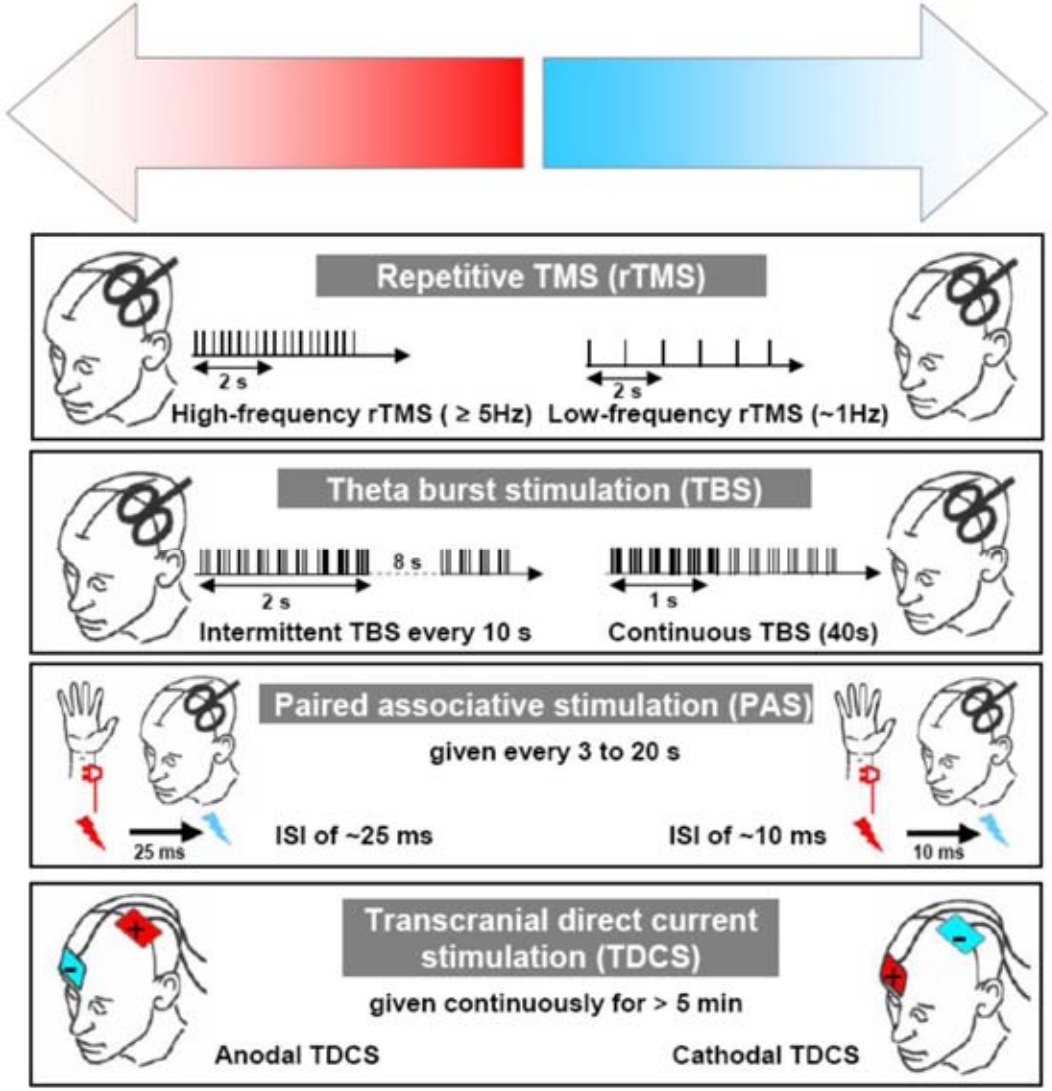
During 1 mA current flow



After 5 min of 1 mA current flow

Nitsche & Paulus 2000

LTP-like and LTD-like changes from brain stimulation



Quartarone et al. 2006

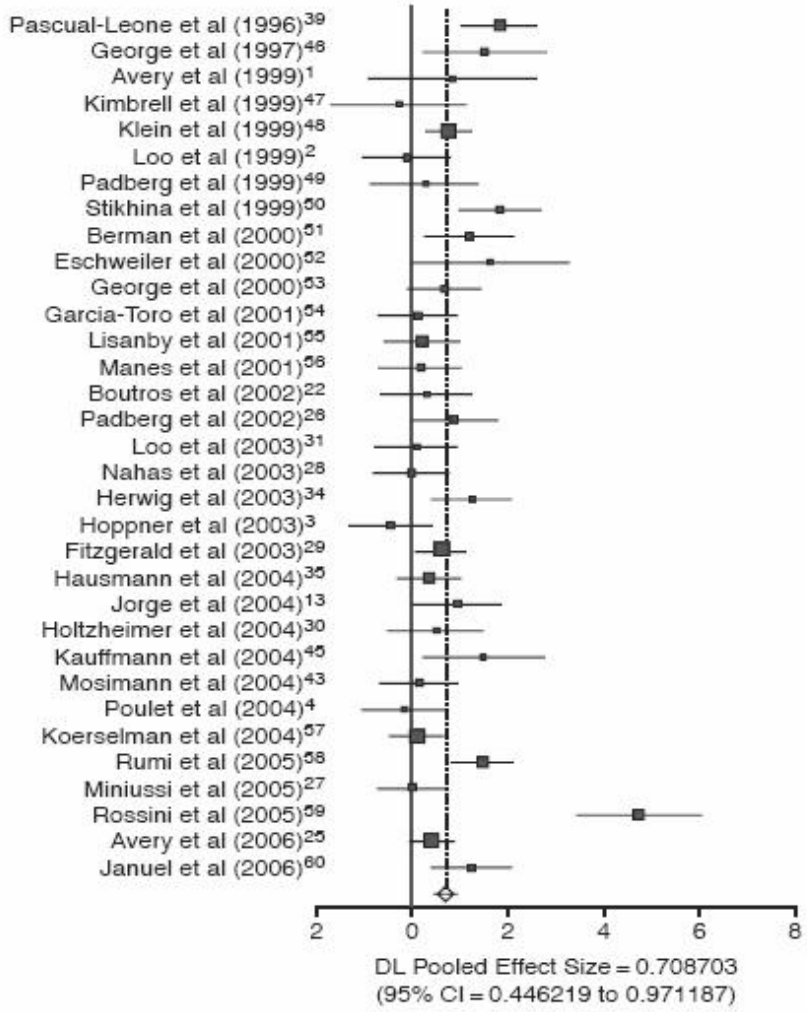
Therapy with rTMS

- Psychiatry
  - Depression (and possibly mania)
  - OCD
  - Suppression of auditory hallucinations
- Tinnitus
- Stroke
- Movement disorders
  - Parkinson’s disease
  - Dystonia
  - Essential tremor?
  - Ataxia?
- Epilepsy
- Pain

Herrmann and Ebmeier
J Clin Psychiatry 2006

rTMS for Depression

Figure 1. Forest Plot of 33 Transcranial Magnetic Stimulation Treatment Studies in Depression[a]



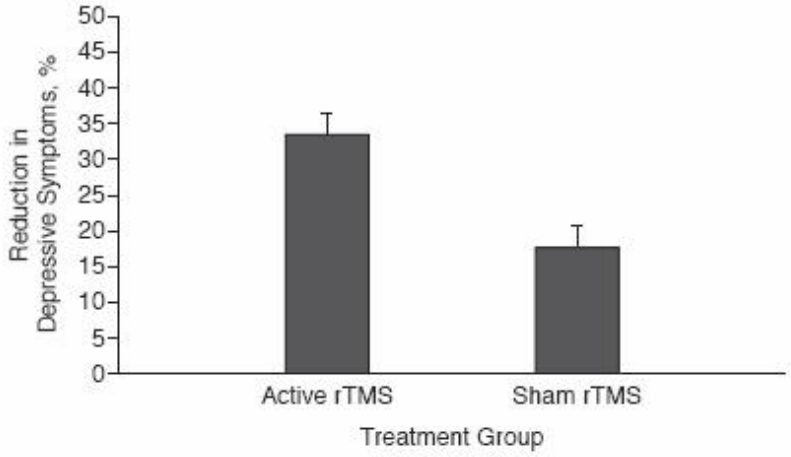
[a]Effect size meta-analysis plot (random effects).
Abbreviation: DL = DerSimonian-Laird.

Table 2. Sample Characteristics of 33 Studies Included in Meta-Analysis

Characteristic	No. of Studies	Active TMS	Sham TMS
No. of patients		475	402
Age, mean (SD), y	27	49.14 (8.19)	48.85 (7.24)
Duration of current episode, mean (SD), mo	16	16.08 (19.61)	17.76 (23.98)
Baseline HAM-D score, mean (SD)	26	27.05 (5.49)	25.86 (5.45)

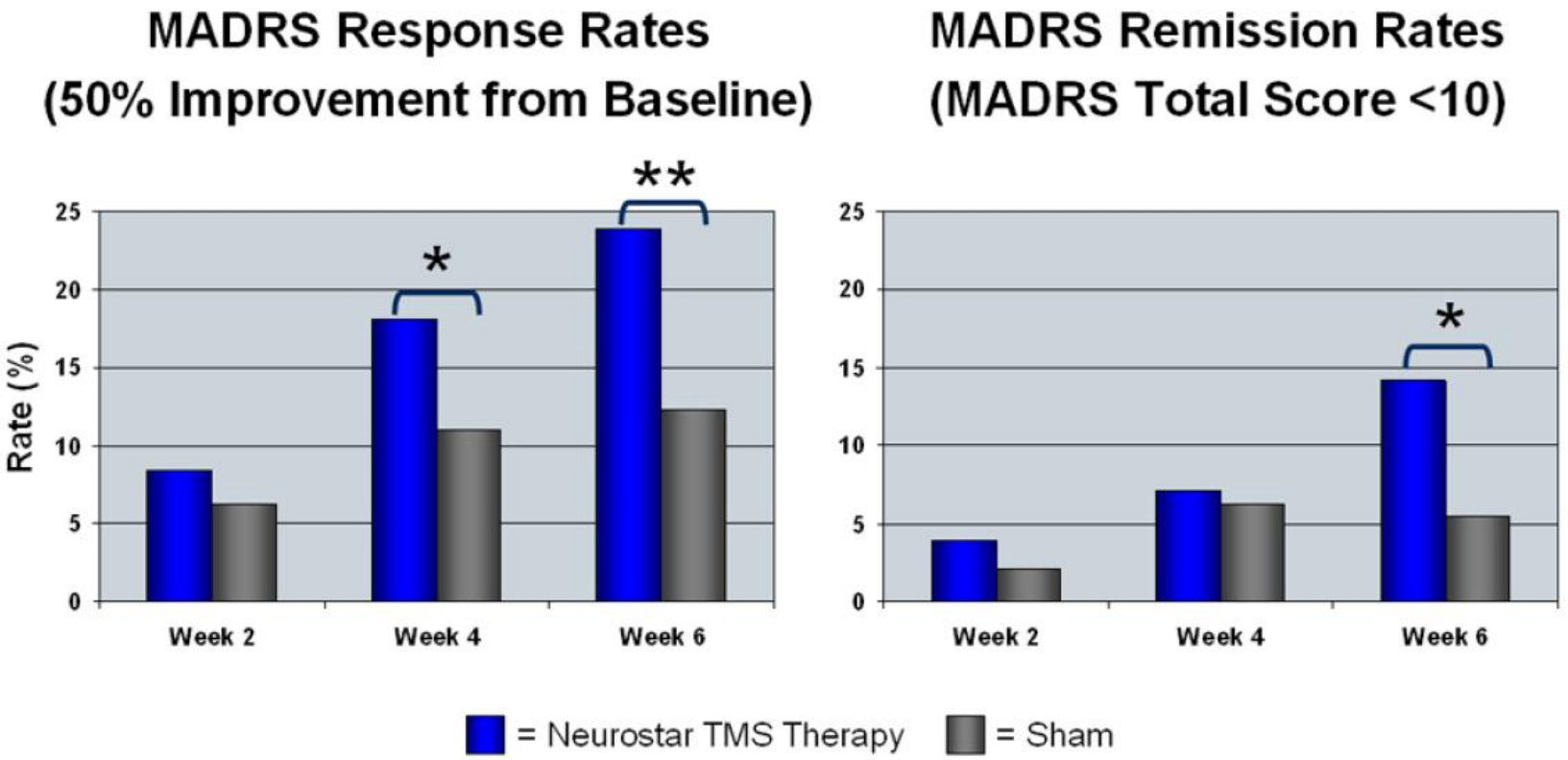
Abbreviations: HAM-D = Hamilton Rating Scale for Depression, TMS = transcranial magnetic stimulation.

Figure 2. Mean Reduction (%) in Depressive Symptoms for Active and Sham Repetitive Transcranial Magnetic Stimulation (rTMS)



TMS for Depression: Limited Efficacy

- Pivotal study that led to FDA approval (325 subjects; 23 sites)



* P < .05 vs sham, ** P < .01 vs sham, LOCF analysis

[Neuronetics, Inc]

From Angel V. Peterchev (internet)

The expanding evidence base for rTMS treatment of depression

Mark S. George, Joseph J. Taylor, and E. Baron Short

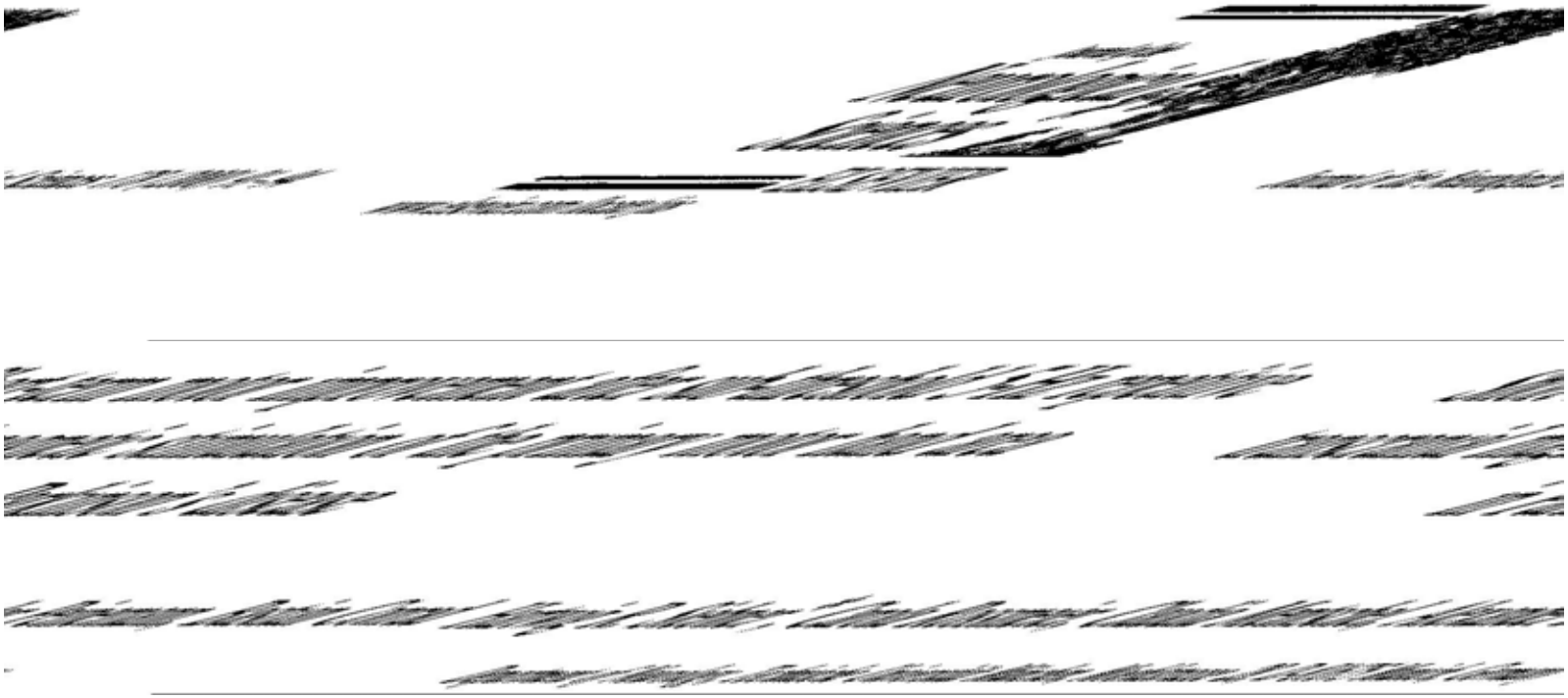
Purpose of review
Daily left prefrontal transcranial magnetic stimulation (TMS) for several weeks was first proposed as an acute treatment for depression in the early 1990s, and was Food and Drug Administration (FDA) approved in 2008. In the past year, several important studies have been published that extend our understanding of this novel treatment approach.

Recent findings
The first round of multisite clinical trials with TMS addressed whether prefrontal rTMS has efficacy and were conducted in carefully selected depressed patients who were antidepressant medication free. Several more recent studies assess the clinical effectiveness of TMS and report that about 35–40% of real-world patients who are commonly taking adjunctive antidepressants reach remission with a modest side effect profile. There are also new studies examining the durability of the TMS-induced antidepressant effect. Fifty-eight percent of TMS remitters remain remitted at 3-month follow-up.

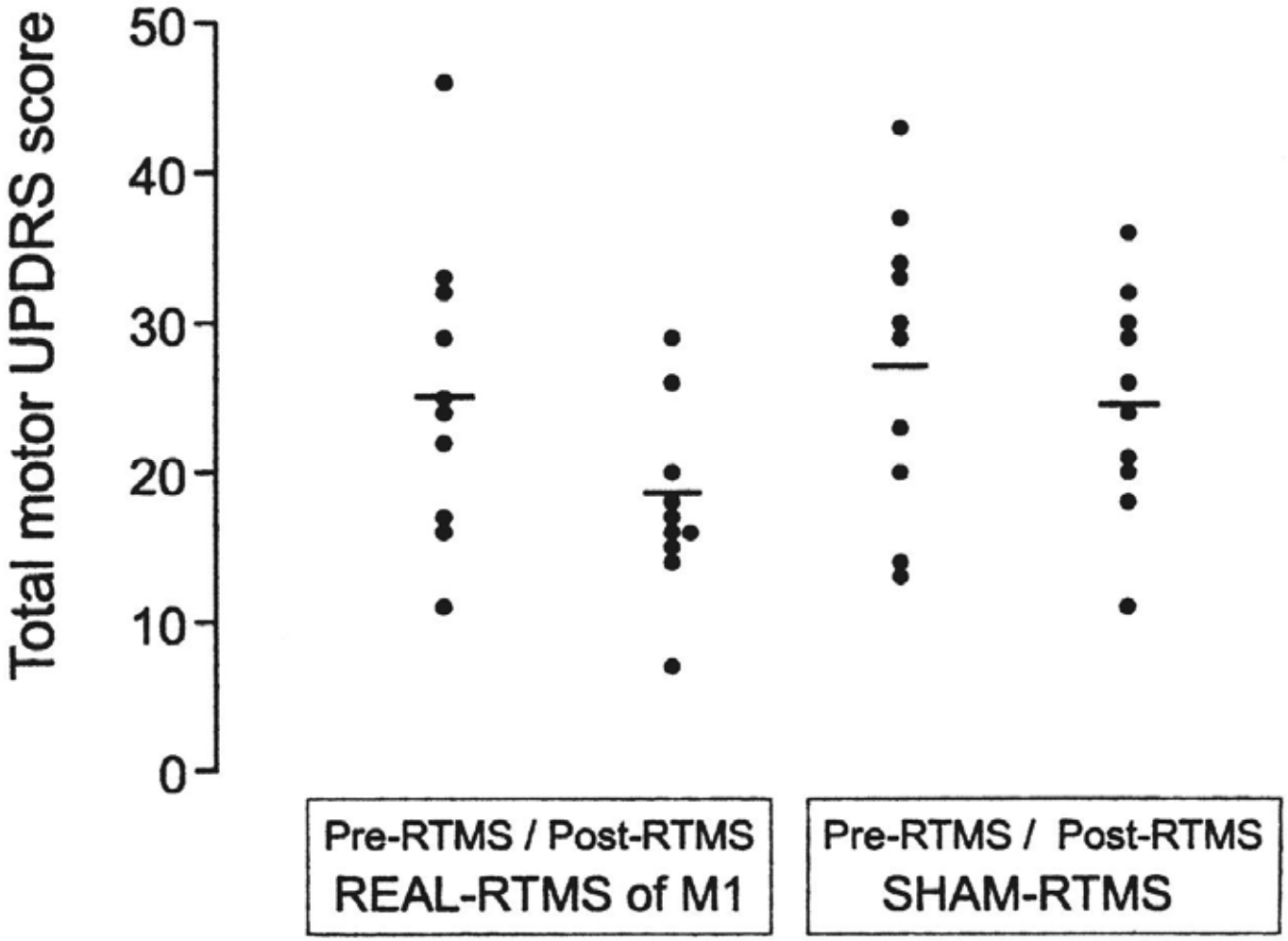
Summary
These recent studies suggest that daily left prefrontal TMS over several weeks as a treatment for depression not only appears to have efficacy in rigorous randomized controlled trials, but is effective in real-world settings, with remission in 30–40% of patients. The TMS antidepressant effect, once achieved, appears to be as durable as with other antidepressant medications or interventions. Much more research is needed, particularly with issues such as the TMS coil location, stimulation intensity and frequency, and dosing strategy.

Curr Opin Psychiatry 2013;26:13

rTMS for Parkinson Disease



rTMS for Parkinson Disease



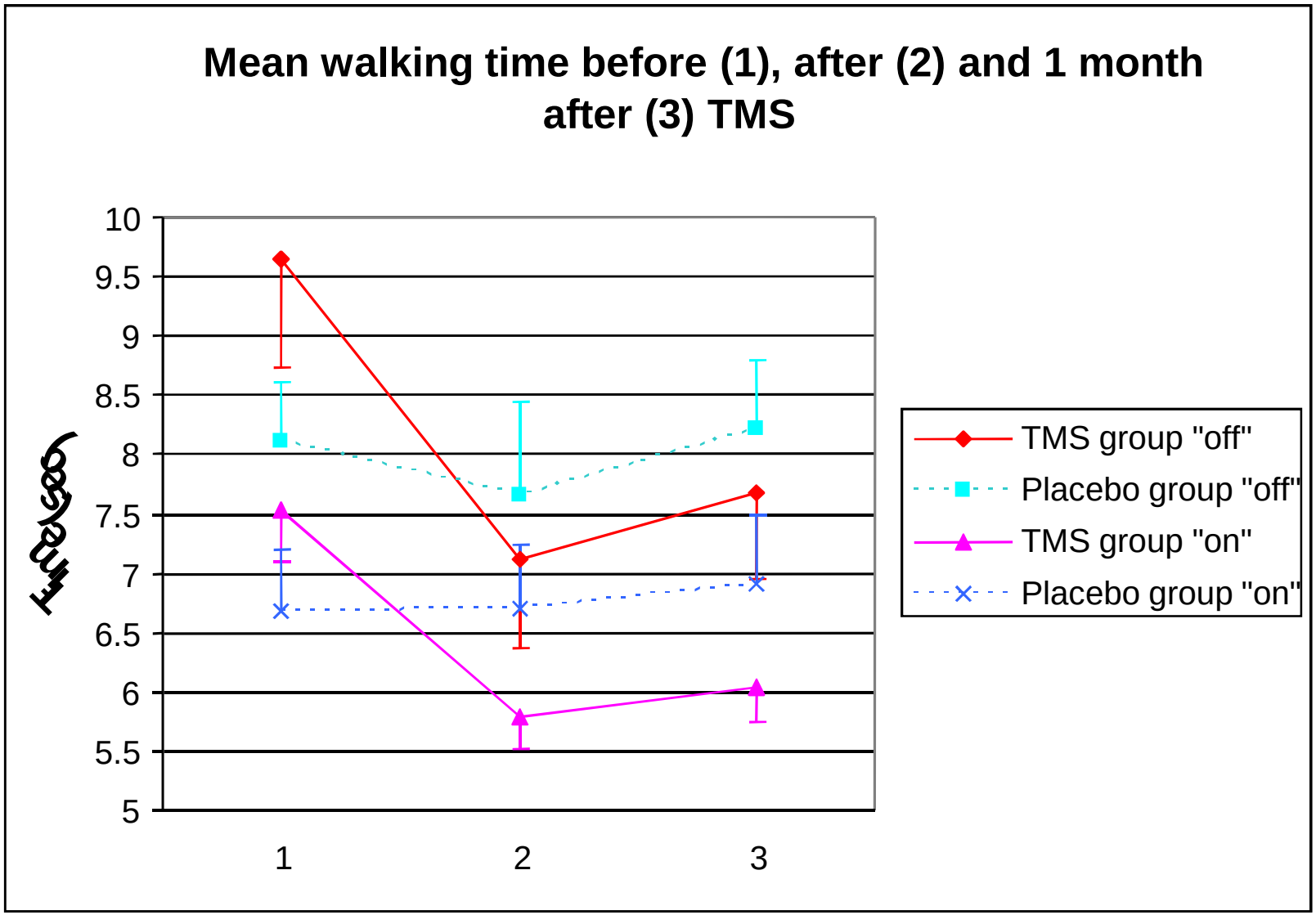
Movement Disorders
Vol. 21, No. 3, 2006, pp. 325–331

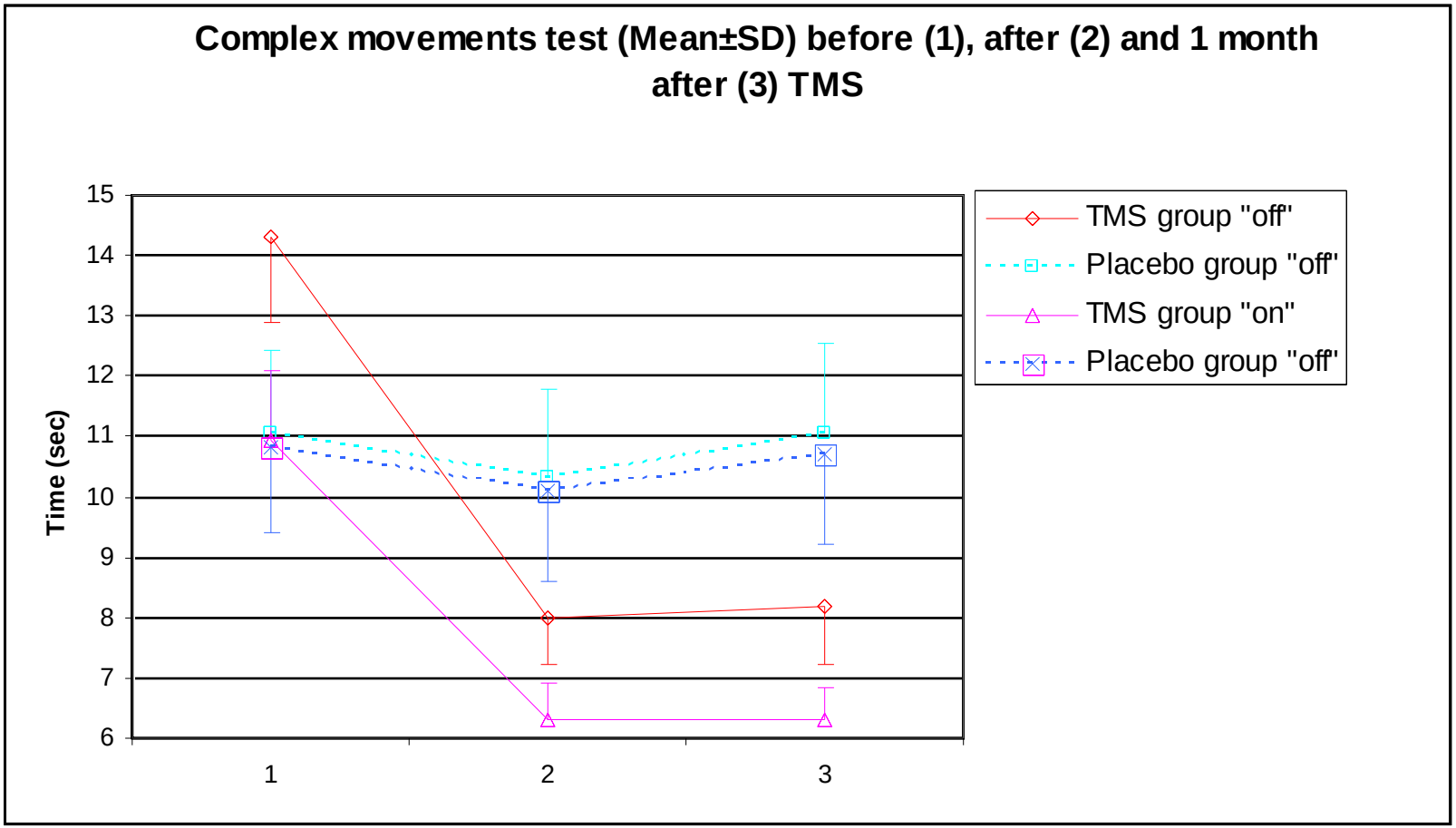
Placebo-Controlled Study of rTMS for the Treatment of Parkinson's Disease

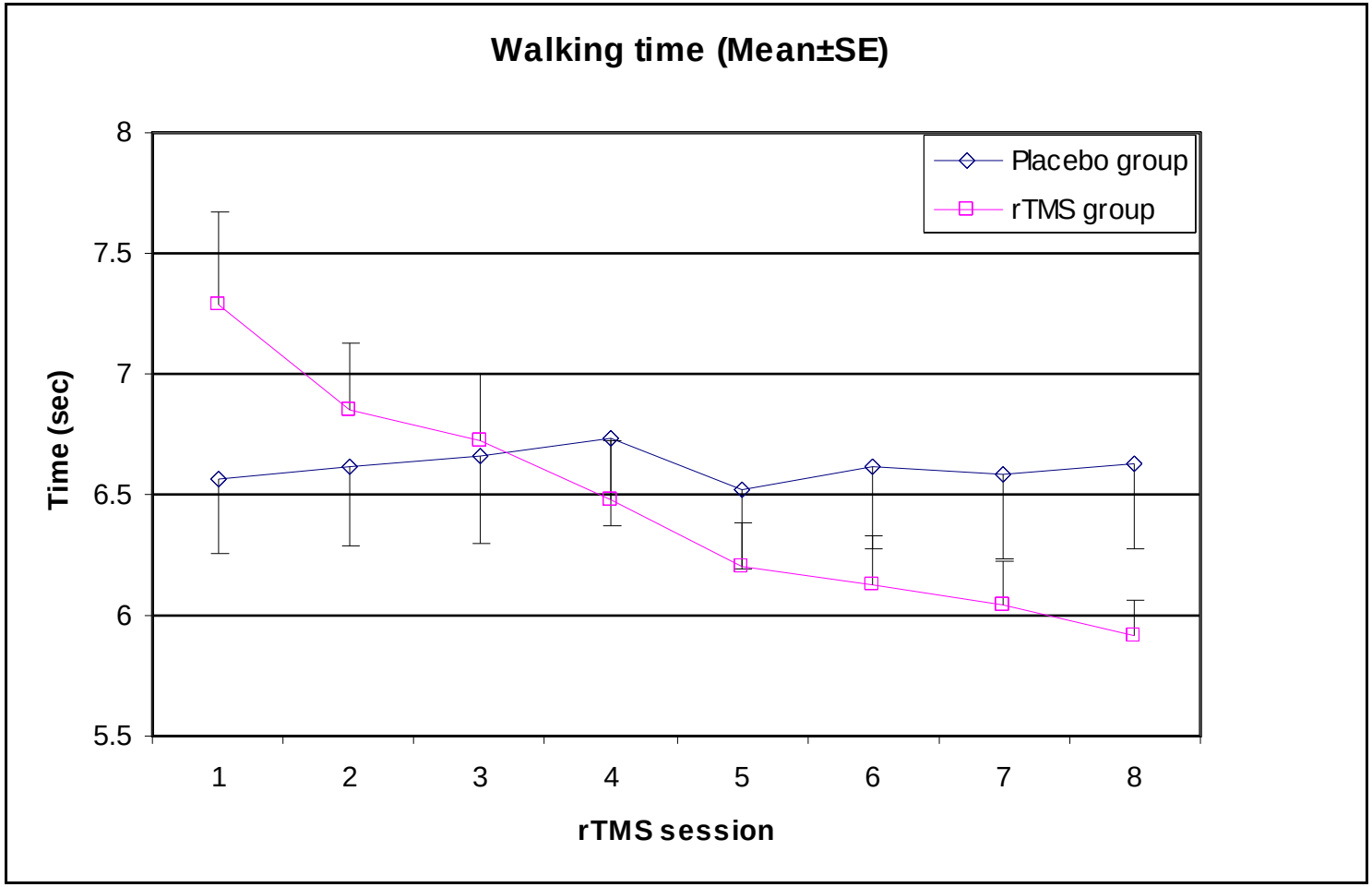
Mikhail P. Lomarev, PhD, MD,[1]* Sulada Kanchana, MD, PhD,[1] William Bara-Jimenez, MD,[2] Meena Iyer, PhD,[3] Eric M. Wassermann, MD,[3] and Mark Hallett, MD[1]

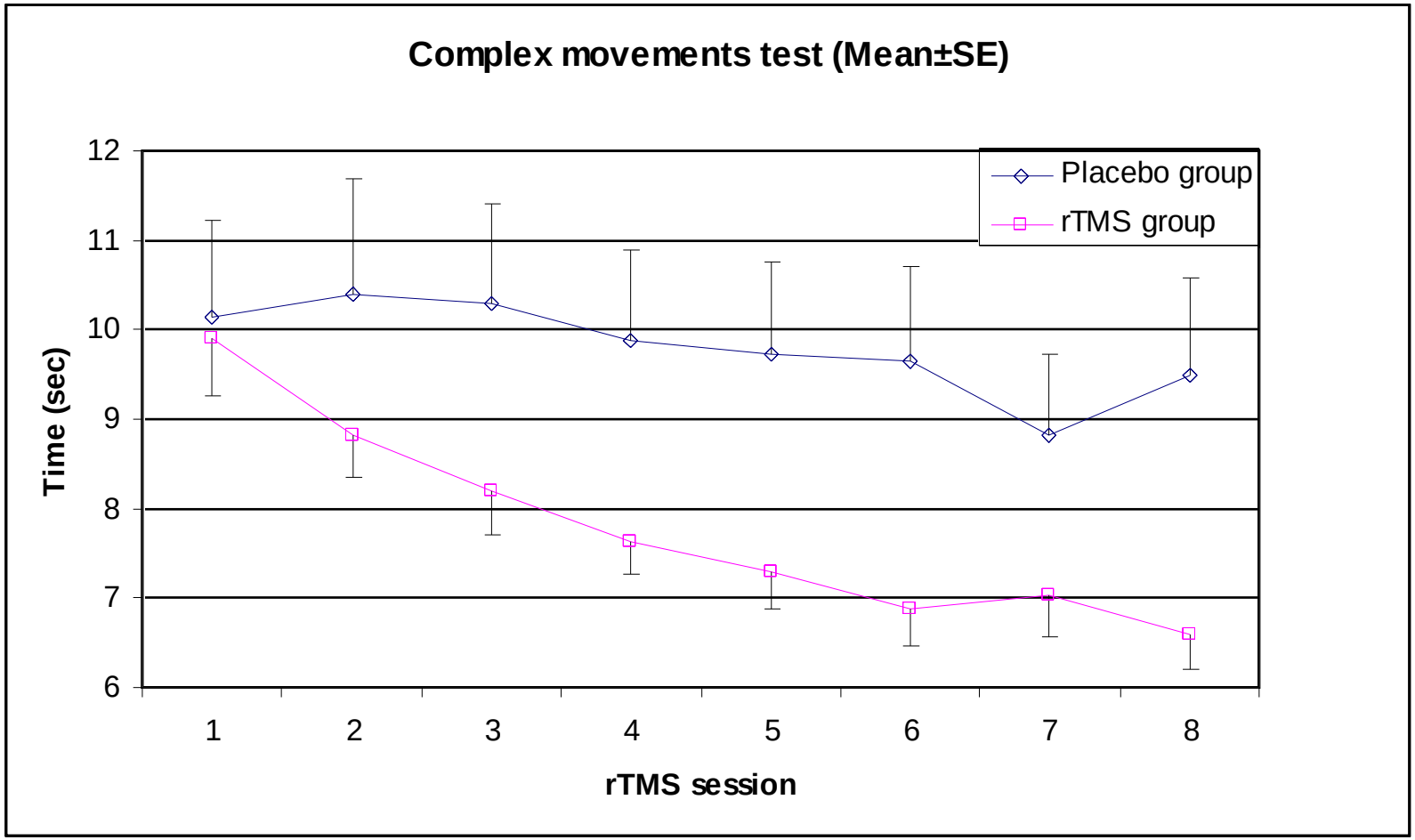
[1]*Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA*
[2]*Experimental Therapeutic Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA*
[3]*Brain Stimulation Unit and Cognitive Neuroscience, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA*

8 sessions over 4 weeks of 25 Hz rTMS at 100% MT delivered to left and right primary motor cortex and dorsolateral prefrontal cortex with 300 pulses each


Mean walking time before (1), after (2) and 1 month after (3) TMS
10
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
1
2
3
TMS group "off"
Placebo group "off"
TMS group "on"
Placebo group "on"


Complex movements test (Mean±SD) before (1), after (2) and 1 month after (3) TMS
Time (sec)
15
14
13
12
11
10
9
8
7
6
1
2
3
TMS group "off"
Placebo group "off"
TMS group "on"
Placebo group "off"


Walking time (Mean±SE)
Placebo group
rTMS group
Time (sec)
8
7.5
7
6.5
6
5.5
1
2
3
4
5
6
7
8
rTMS session


Complex movements test (Mean±SE)
Placebo group
rTMS group
Time (sec)
12
11
10
9
8
7
6
1
2
3
4
5
6
7
8
rTMS session

Thirty-six unmedicated PD patients randomized to

1. Real-rTMS (suprathreshold 5-Hz, 2000 pulses once a day, for 10 consecutive days)
2. Sham-rTMS.

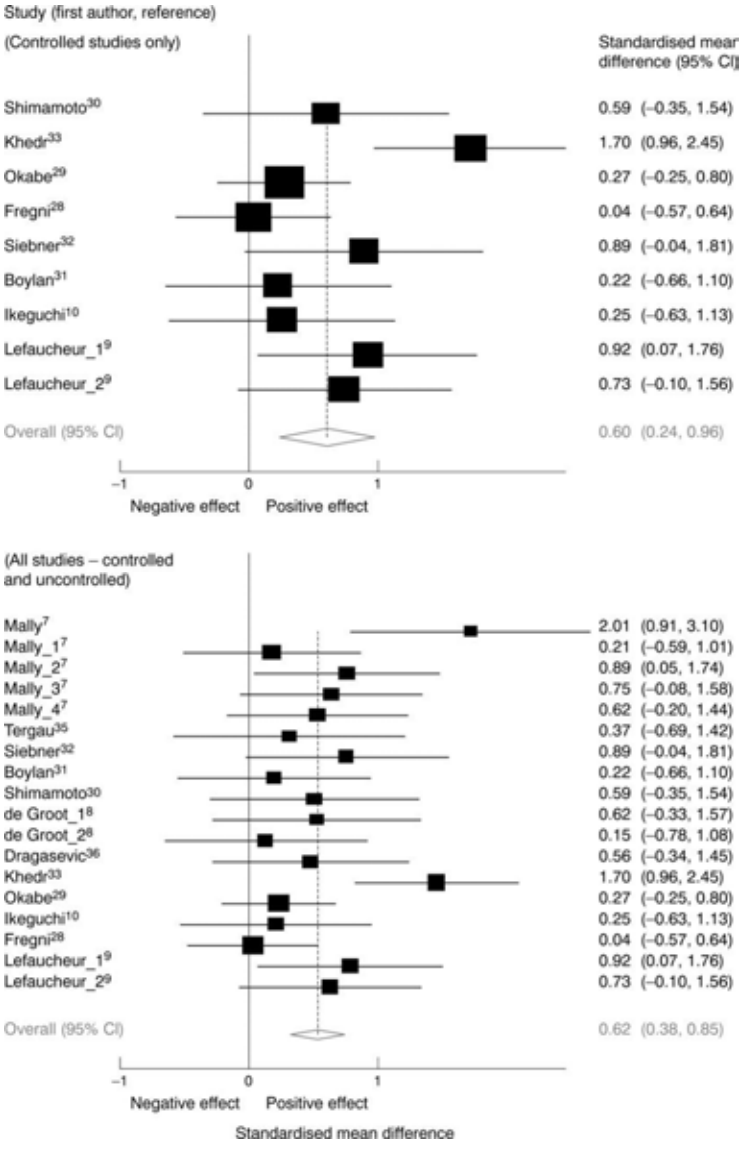
Table 2 Sequential assessment of UPDRS, reaction time, walking speed and self-assessment scale in both groups

Parameters	Baseline assessment	After the first session	After the fifth session	After the 10th session	Follow-up after 1 month
UPDRS					
Real-rTMS	29.5 ± 9.3	26.95 ± 7.9*	19.95 ± 7.2***	14.8 ± 7.9***	15.6 ± 6.5***
Sham-rTMS	24.5 ± 7.8	23.8 ± 7.9	24.05 ± 8.3	24.06 ± 8.0	23.7 ± 7.6
Walking speed (seconds)					
Real-rTMS	83.8 ± 52.2	82.8 ± 61.6*	73.9 ± 61.8**	70.7 ± 63.03***	71.7 ± 53.03***
Sham-rTMS	79.88 ± 60.6	77.9 ± 54.3	75.5 ± 52.3	77.7 ± 65.9	77.5 ± 53.1
Self-assessment					
Real-rTMS	20.1 ± 3.5	19.45 ± 3.4*	15.65 ± 3.7***	13.35 ± 3.8***	14.45 ± 3.5***
Sham-rTMS	19.8 ± 3.6	19.76 ± 3.6	18.88 ± 3.4*	17.65 ± 3.8**	18.56 ± 3.2*

*$P < 0.05$, **$P < 0.001$, ***$P < 0.0001$. The significant versus baseline assessment using paired t-test.

Khedr et al. 2003

Effect sizes (motor UPDRS) for the sham controlled studies only (at the top) and for all TMS studies (controlled and uncontrolled) (at the bottom).

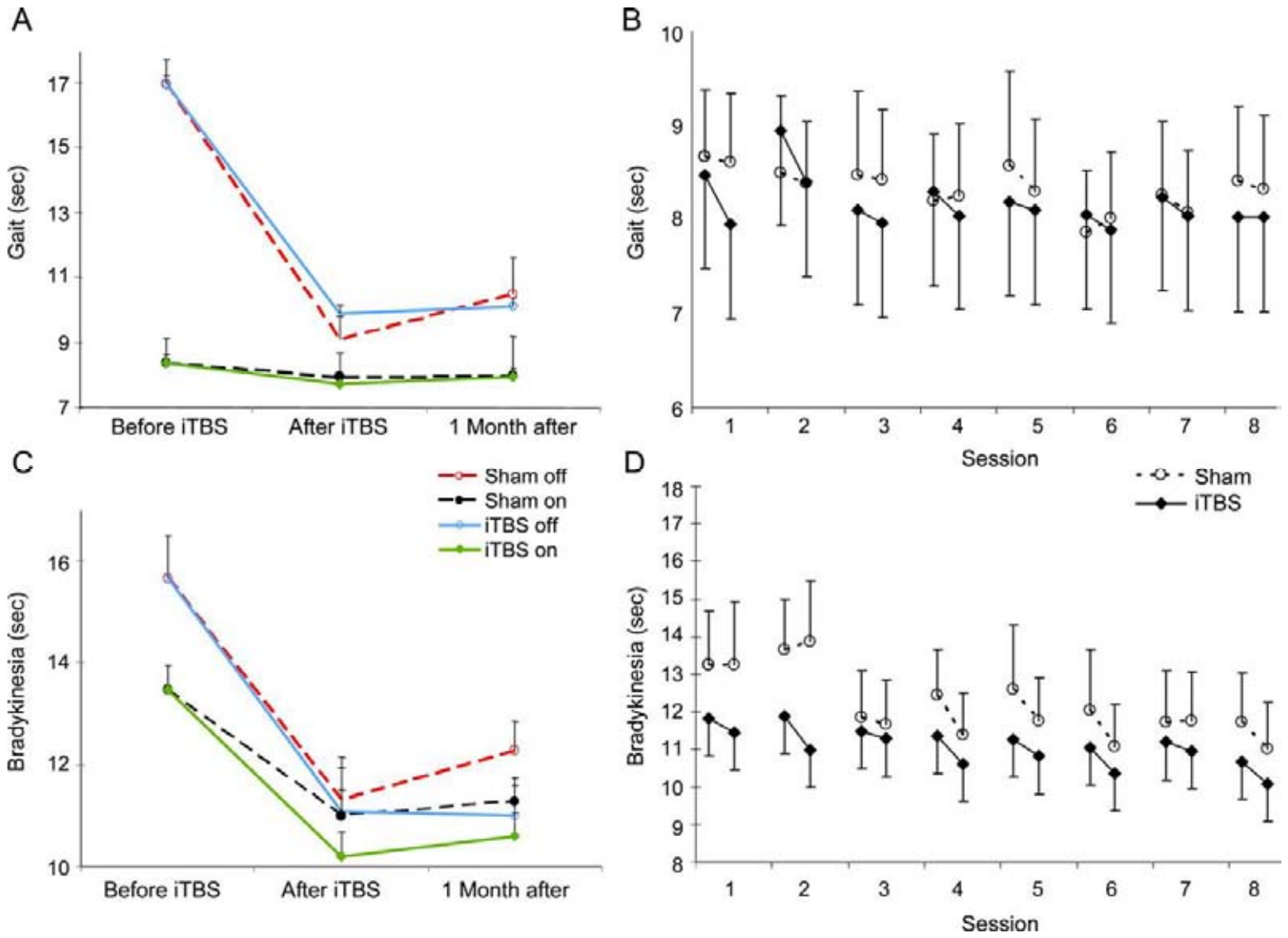


Fregni, F et al. J Neurol Neurosurg Psychiatry 2005;76:1614-1623

Intermittent theta-burst transcranial magnetic stimulation for treatment of Parkinson disease

D.H. Benninger, B.D. Berman, E. Houdayer, et al.

Neurology 2011;76;601-609



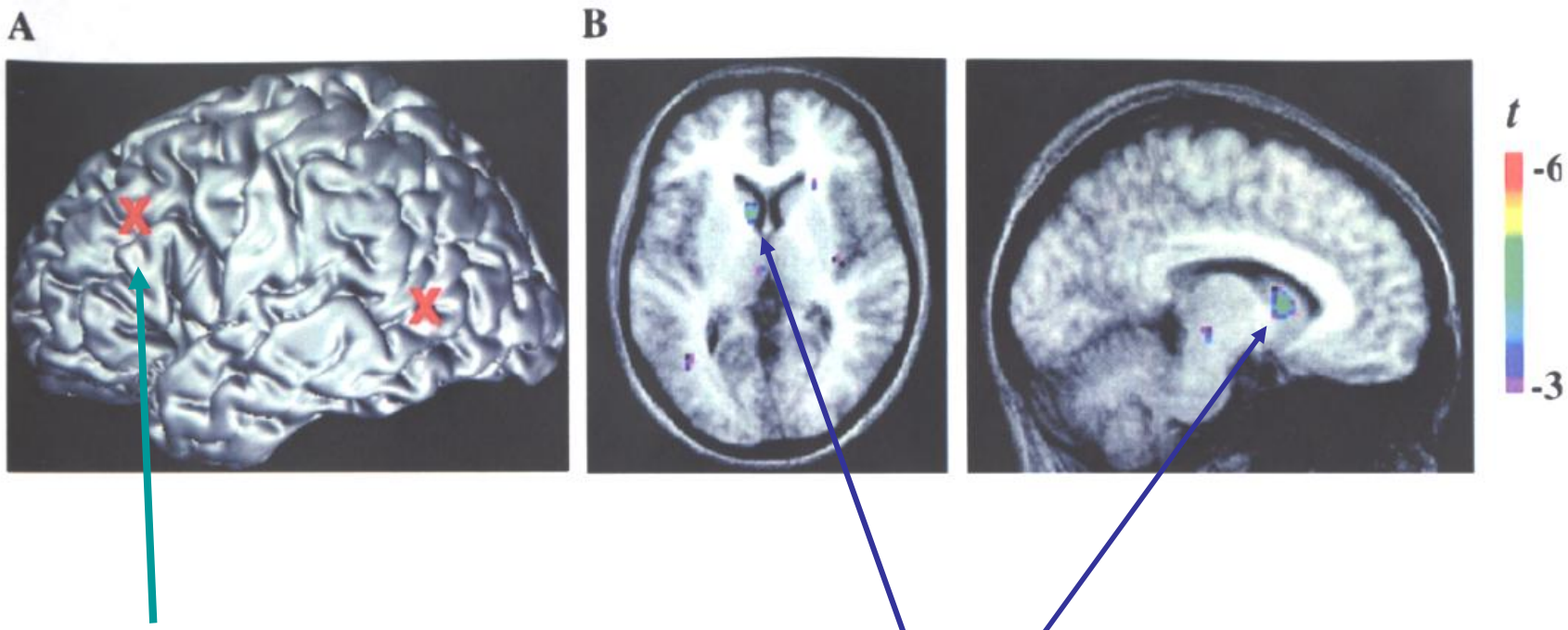
rTMS releases dopamine

Strafella et al. 2001

- rTMS of prefrontal cortex causes release of dopamine in ipsilateral caudate nucleus as measured by raclopride binding PET
- 15 10-pulse trains of 1 sec duration at 10Hz at interval of 10 sec composed 1 block and 3 blocks were delivered with an interval of 10 min.

rTMS releases dopamine

Strafella et al. 2001



Stimulation site

Decrease in raclopride binding

Combination of rTMS and Treadmill Training Modulates Corticomotor Inhibition and Improves Walking in Parkinson Disease: A Randomized Trial

Neurorehabilitation and
Neural Repair
27(1) 79–86

DOI: 10.1177/1545968312451915
http://nnr.sagepub.com
SAGE

Table 3. Comparison of Clinical Measures[a]

Measures	Control (n = 10)		Experimental (n = 10)		Time Effect, *P*	Time × Group, *P*
	Pretest	Posttest	Pretest	Posttest		
Comfortable walking speed, cm/s	108.25 ± 28.42	114.11 ± 25.24	107.86 ± 31.17	122.90 ± 30.48	.000	.062
Fast walking speed, cm/s	147.70 ± 45.29	159.29 ± 51.38	140.85 ± 38.75	162.54 ± 40.18	.000	.049
Timed up and go, s	10.00 ± 3.56	9.06 ± 3.42	11.78 ± 5.36	8.85 ± 3.24	.000	.019

[a]Values are mean ± standard deviation.

experimental group and a control group. Participants received rTMS (experimental group) or sham rTMS (control group) followed by treadmill training (30 minutes) for 12 sessions over 4 weeks. Repetitive TMS was applied at a 5-Hz frequency over the leg area of the motor cortex contralaterally to the more affected side for 6 minutes. Outcomes, including corticomotor inhibition and walking performance, were measured before and after training. *Results*. The results showed significant time effects on almost all corticomotor and functional variables. There are significant interaction effects between group and time of evaluation on the motor threshold, duration of the cortical silent period, and short interval intracortical inhibition of the contralateral hemisphere relatively to the more affected side as well as on the fast walking speed and timed up and go. *Conclusions*. The findings suggested that combination of rTMS and treadmill training enhances the effect of treadmill training on modulation of corticomotor inhibition and improvement of walking performance in those with PD.

Treatment of Pain

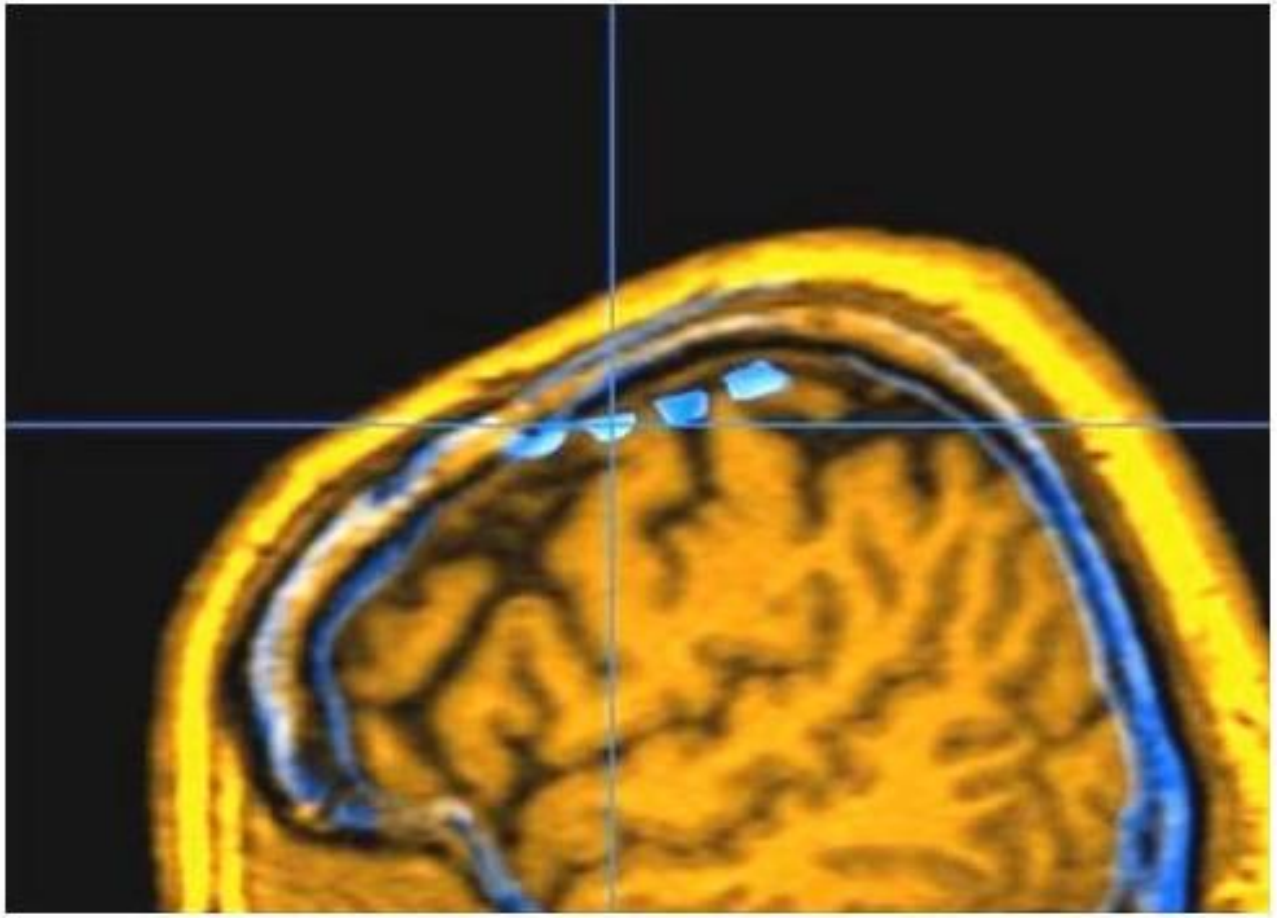
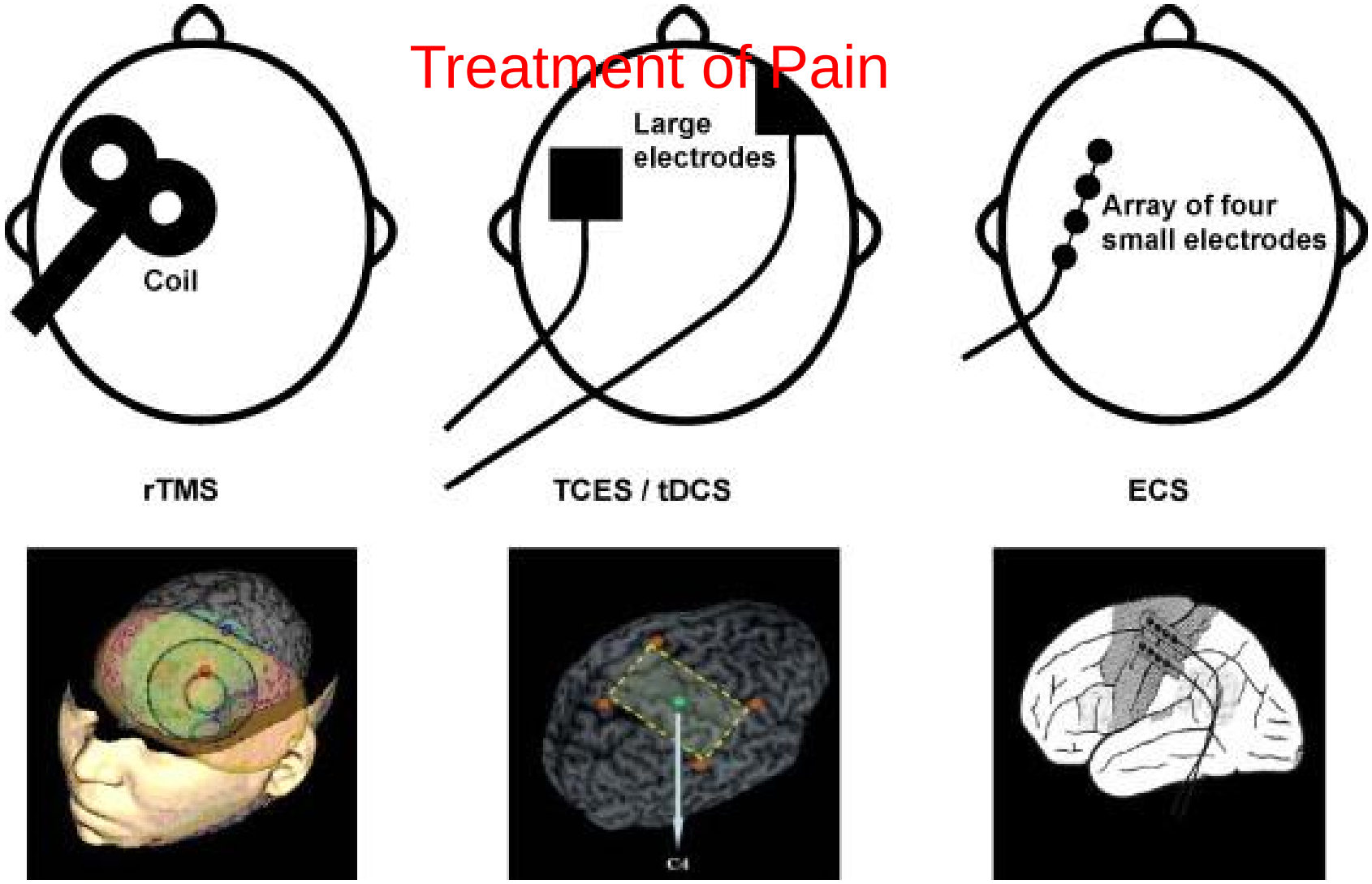


Figure 4. Motor cortex stimulation (MCS): position of the electrode on the postoperative scanner. MCS is a relatively safe invasive stimulation therapy for the treatment of refractory central neuropathic pain, particularly neuropathic facial pain and post-stroke pain.

Nizard et al. Discovery Medicine 2012

Treatment of Pain



J.-P. Lefaucheur

Methods of therapeutic cortical stimulation

Neurophysiologie Clinique/Clinical Neurophysiology Volume 39, Issue 1 2009 1 - 14
http://dx.doi.org/10.1016/j.neucli.2008.11.001

Pain

Repetitive transcranial magnetic stimulation

Primary motor cortex (precentral gyrus)	Contralateral to pain side, low frequency* (?Ý1 Hz), low intensity (80-90 % RMT), parallel to midline	Lack of efficacy proved in chronic neuropathic pain
Primary motor cortex (precentral gyrus)	Contralateral to pain side or left hemisphere, high-frequency* (?ν5 Hz), low intensity (80-90 % RMT), parallel to midline	Efficacy proved in chronic neuropathic pain. Possible efficacy in fibromyalgia and CRPS
Primary somatosensory cortex (postcentral gyrus)	Contralateral to pain side, high-frequency* (? 5 Hz), low intensity (80-90 % RMT)	Possible lack of efficacy in chronic neuropathic pain
Secondary somatosensory cortex	Right hemisphere, low frequency* (?Ü1 Hz), medium intensity (70 % MSO)	Possible efficacy in chronic visceral pain
Dorsolateral prefrontal cortex	Right hemisphere, low frequency* (?ñ1 Hz), high intensity (110 % RMT)	Possible efficacy in fibromyalgia and chronic neuropathic pain
Dorsolateral prefrontal cortex	Left hemisphere, high-frequency* (?ν5 Hz), low intensity (100 % RMT)	Possible efficacy in various pain syndromes (postoperative pain, fibromyalgia, chronic neuropathic pain, migraine)

From Lefaucheur, In Lozano & Hallett *forthcoming*

American Pain Society
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Predictive Value of rTMS in the Identification of Responders to Epidural Motor Cortex Stimulation Therapy for Pain

Jean-Pascal Lefaucheur,*,† Isabelle Ménard-Lefaucheur,† Colette Goujon,*,‡ Yves Keravel,‡ and Jean-Paul Nguyen*,‡

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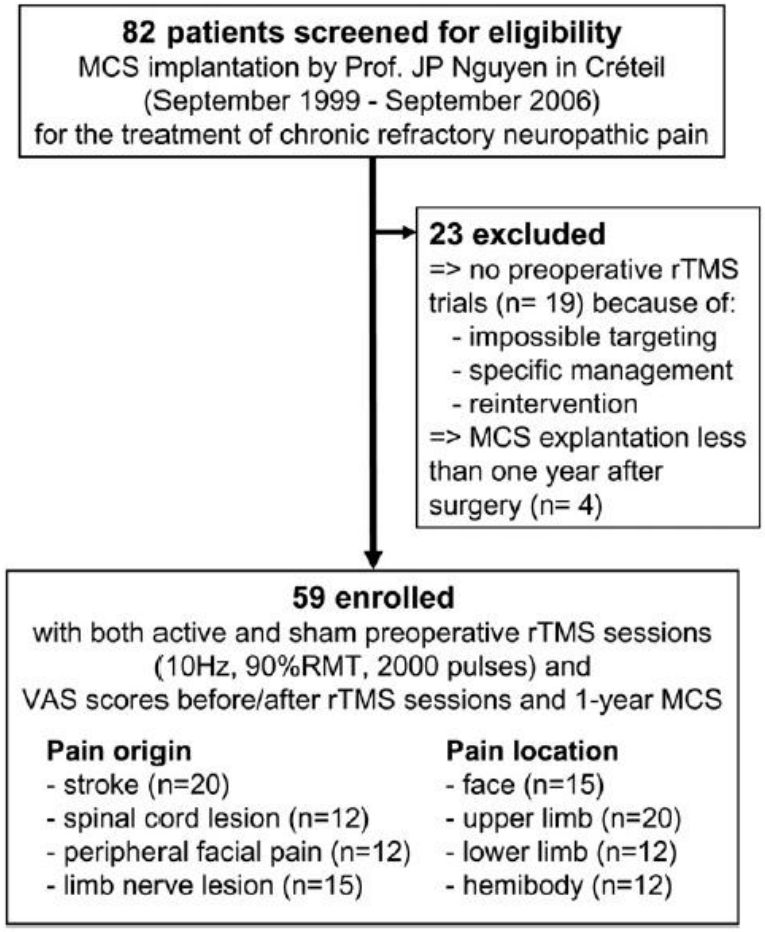
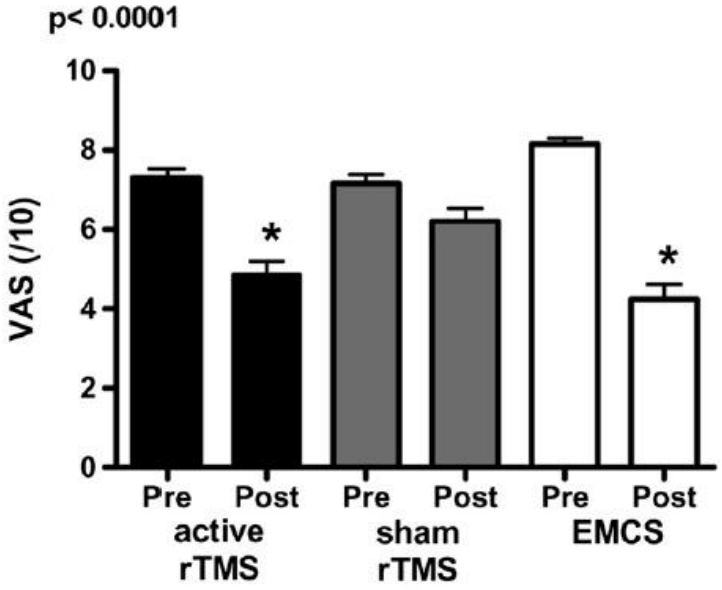
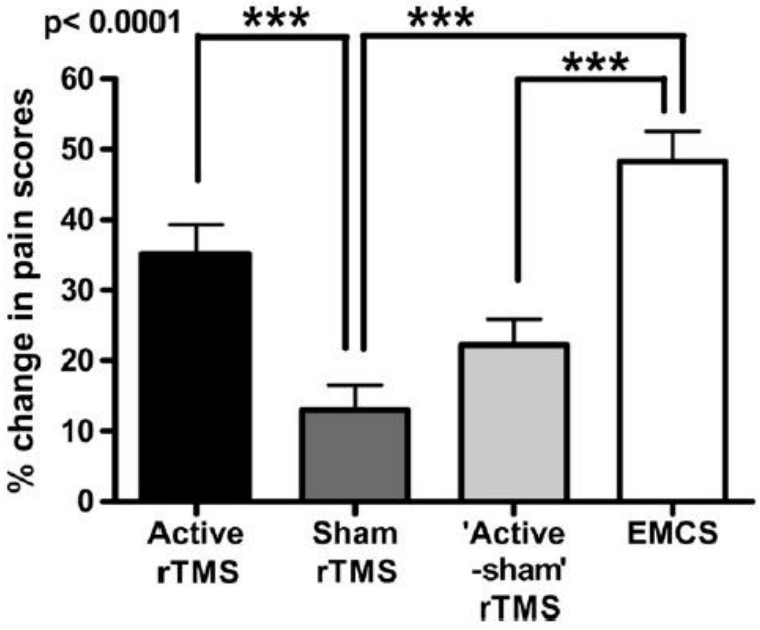
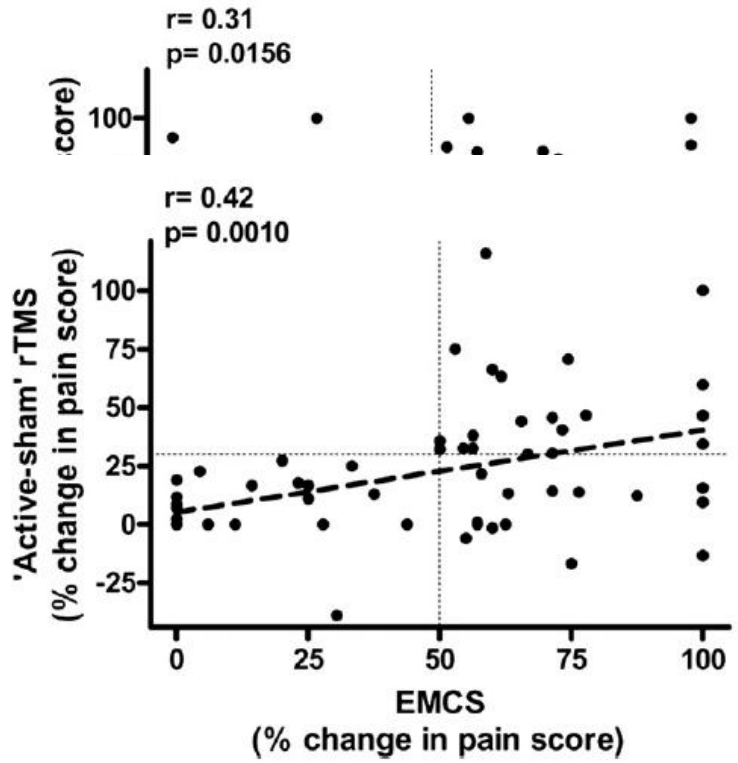
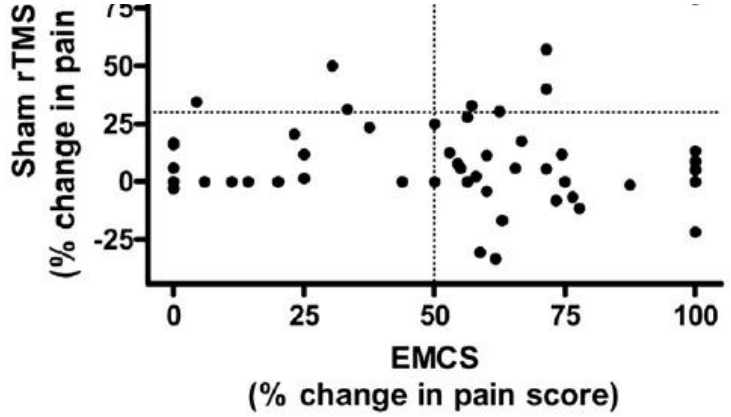
†Service de Physiologie – Explorations Fonctionnelles, Hôpital Henri Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France.
‡Service de Neurochirurgie, Hôpital Henri Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France.

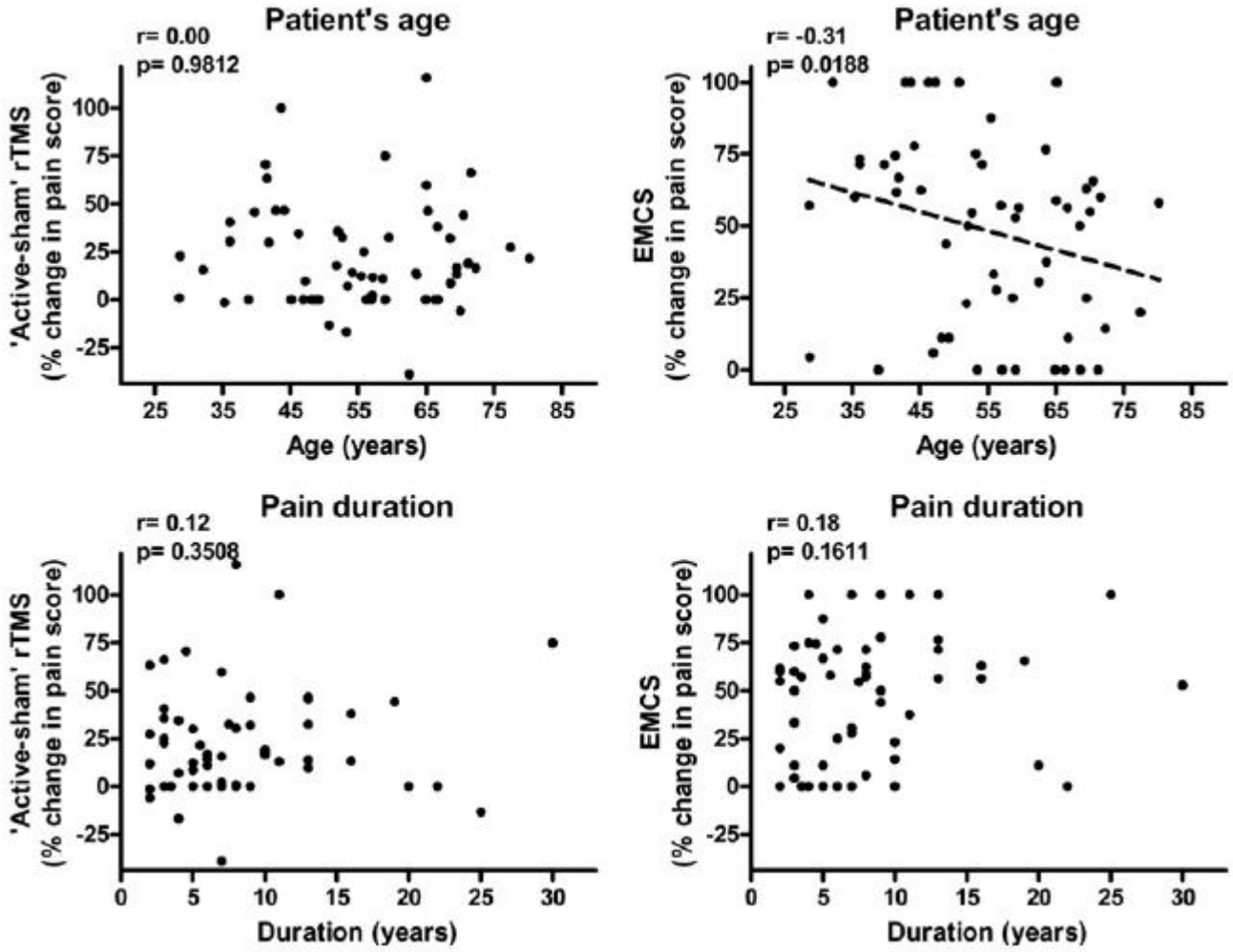


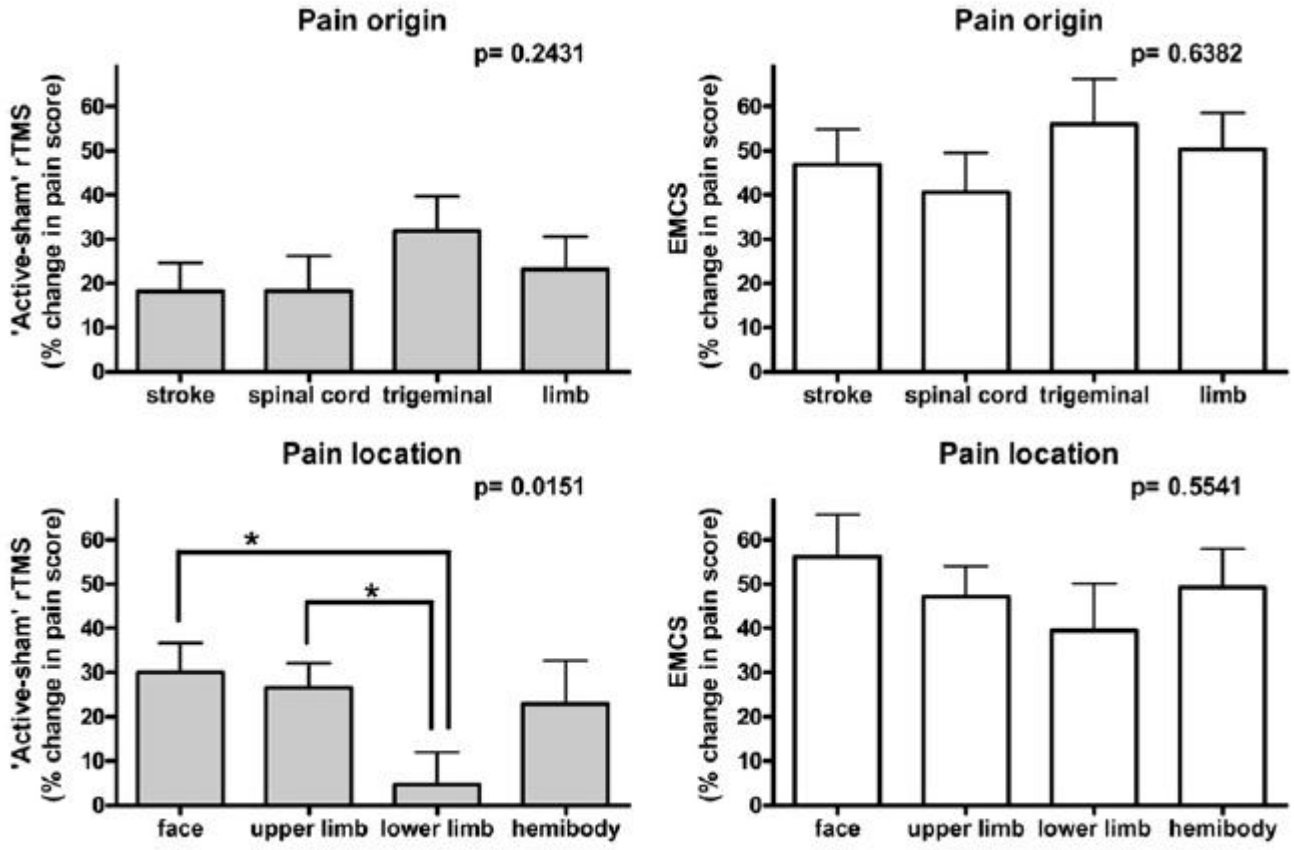

p< 0.0001
VAS (/10)
10
8
6
4
2
0
*
*
Pre
Post
Pre
Post
Pre
Post
active rTMS
sham rTMS
EMCS


p< 0.0001
***
***
***
% change in pain scores
60
50
40
30
20
10
0
Active rTMS
Sham rTMS
'Active -sham' rTMS
EMCS


r= 0.31
p= 0.0156
r= 0.42
p= 0.0010
'Active-sham' rTMS (% change in pain score)
100
75
50
25
0
-25
0
25
50
75
100
EMCS
(% change in pain score)


Sham rTMS (% change in pain
50
25
0
-25
0
25
50
75
100
EMCS
(% change in pain score)


Patient's age
r= 0.00
p= 0.9812
'Active-sham' rTMS
(% change in pain score)
Age (years)
Patient's age
r= -0.31
p= 0.0188
EMCS
(% change in pain score)
Age (years)
Pain duration
r= 0.12
p= 0.3508
'Active-sham' rTMS
(% change in pain score)
Duration (years)
Pain duration
r= 0.18
p= 0.1611
EMCS
(% change in pain score)
Duration (years)


Pain origin
p= 0.2431
'Active-sham' rTMS
(% change in pain score)
0
10
20
30
40
50
60
stroke
spinal cord
trigeminal
limb
Pain origin
p= 0.6382
EMCS
(% change in pain score)
0
10
20
30
40
50
60
stroke
spinal cord
trigeminal
limb
Pain location
p= 0.0151
'Active-sham' rTMS
(% change in pain score)
*
*
0
10
20
30
40
50
60
face
upper limb
lower limb
hemibody
Pain location
p= 0.5541
EMCS
(% change in pain score)
0
10
20
30
40
50
60
face
upper limb
lower limb
hemibody

The Journal of Pain, Vol 10, No 12 (December), 2009: pp 1205-1216
Available online at www.sciencedirect.com

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Review Article

rTMS for Suppressing Neuropathic Pain: A Meta-Analysis

Albert Leung,* Michael Donohue,† Ronghui Xu,‡ Ryan Lee,§ Jean-Pascal Lefaucheur,¶ Eman M. Khedr,‖ Youichi Saitoh,** Nathalie André-Obadia,†† Jens Rollnik,‡‡ Mark Wallace,§§ and Robert Chen¶¶

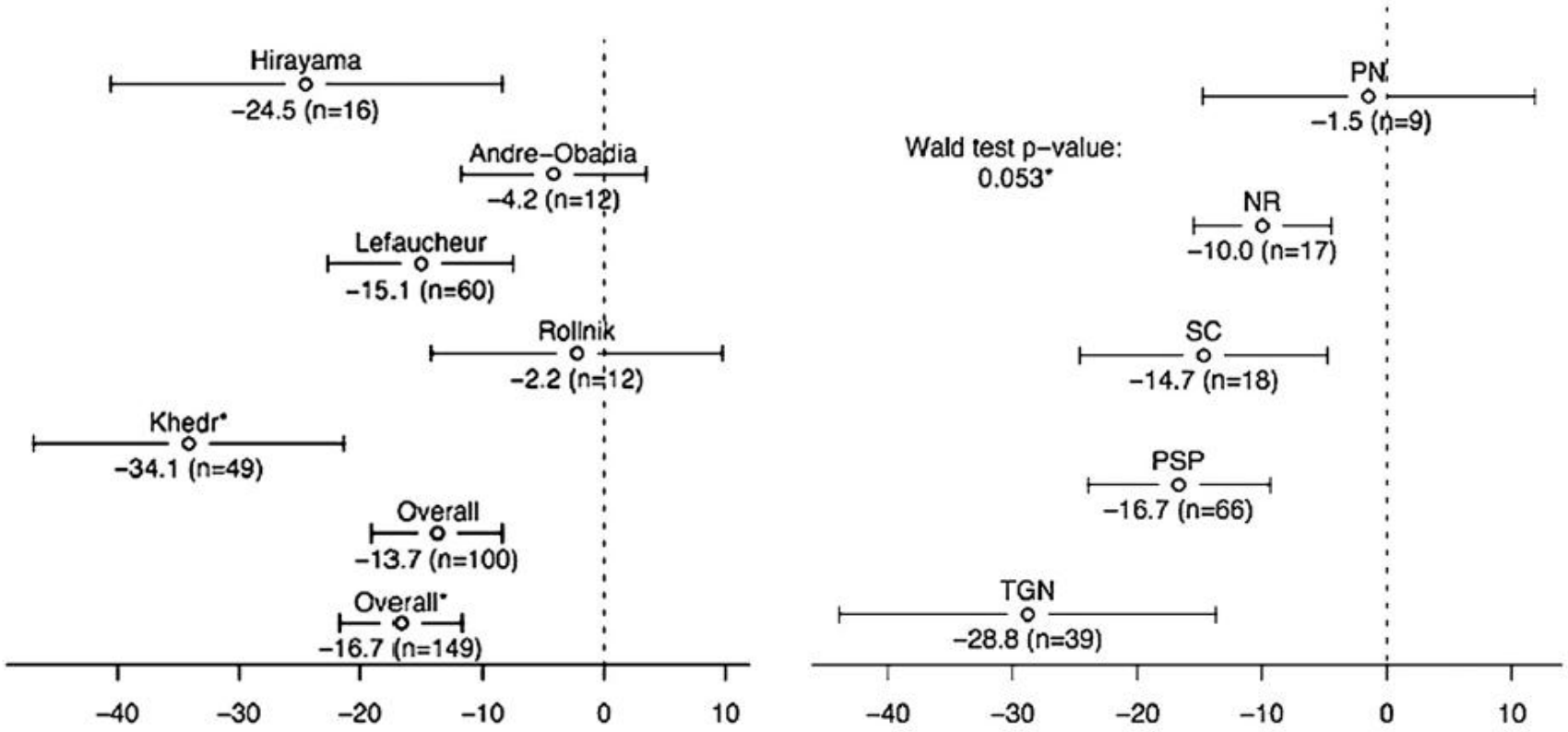
Table 3. Summary of Studies and Neuroanatomical Etiologies for Pain

	NR	PN	PSP	SC	TGN	Total
Khedr et al (2005)[22]	None	None	25 (51.0%)	None	24 (49.0%)	49
Rollnik et al (2002)[24]	3 (25.0%)	7 (58.3%)	None	2 (16.7%)	None	12
Lefaucheur et al (2004)[19]	12 (20.0%)	None	24 (40.0%)	12 (20.0%)	12 (20.0%)	60
Andre-Obadia et al (2006)[25]	1 (8.3%)	1 (8.3%)	9 (75.0%)	1 (8.3%)	None	12
Hirayama et al (2006)[21]	1 (6.2%)	1 (6.2%)	8 (50.0%)	3 (18.8%)	3 (18.8%)	16
Total	17 (11.4%)	9 (6.0%)	66 (44.3%)	18 (12.1%)	39 (26.2%)	149

Abbreviations: NR, nerve root; PN, peripheral nerve; PSP, post-stroke supraspinal related pain; TGN, trigeminal nerve or ganglion.

Table 4. Summary of Treatment Parameters

Study	Design	Pulses/Session	Coding for Pulses	Frequency	Coding for Frequency	Sessions	Coding for Sessions
Khedr et al (2005)[22]	Parallel	2000	High	20 Hz	High	5	Multiple
Rollnik et al (2002)[24]	Cross-over	800	Low	20 Hz	High	1	Single
Lefaucheur et al (2004)[19]	Cross-over	1000	Low	10 Hz	Low	1	Single
Andre-Obadia et al (2006)[25]	Cross-over	1600	High	20 Hz	High	1	Single
Hirayama et al (2006)[21]	Cross-over	500	Low	5 Hz	Low	1	Single


Hirayama
−24.5 (n=16)
Andre−Obadia
−4.2 (n=12)
Lefaucheur
−15.1 (n=60)
Rollnik
−2.2 (n=12)
Khedr*
−34.1 (n=49)
Overall
−13.7 (n=100)
Overall*
−16.7 (n=149)
−40
−30
−20
−10
0
10
PN
−1.5 (n=9)
Wald test p−value:
0.053*
NR
−10.0 (n=17)
SC
−14.7 (n=18)
PSP
−16.7 (n=66)
TGN
−28.8 (n=39)
−40
−30
−20
−10
0
10

Clinical Neurophysiology 120 (2009) 2008–2039

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journal homepage: www.elsevier.com/locate/clinph

Guidelines

Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research ☆

Simone Rossi [a,*], Mark Hallett [b], Paolo M. Rossini [c,d], Alvaro Pascual-Leone [e] and The Safety of TMS Consensus Group [1]

[a] Dipartimento di Neuroscienze, Sezione Neurologia, Università di Siena, Italy
[b] Human Motor Control Section, NINDS, NIH, Bethesda, USA
[c] Università Campus Biomedico, Roma, Italy
[d] Casa di Cura S. Raffaele, Cassino, Italy
[e] Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA

Outline

- Principles of TMS
- Safety concerns
- Side effects
- Patient selection
- Patient dosing
- Safety table
- Where TMS should be done
- Who should do TMS
- Ethical and regulatory concerns

Safety Concerns

- Heating
- Forces and magnetization
- Induced voltages
- TMS in patients with implanted stimulating/recording electrodes
- Magnetic field exposure for subjects/patients
- Magnetic field exposure for operators

Side effects

- Hearing
- EEG issues
- State-dependency of TMS effects
- Seizures
- Syncope
- Local pain, headache, discomfort
- Psychiatric changes
- Cognitive/neuropsychological changes
- Other biological effects (in humans and animal models) possibly related to safety concerns
- Endocrinological after-effects
- Histotoxicity
- Effects on neurotransmitters and immune system
- Autonomic function

Side effect	Single-pulse TMS	Paired-pulse TMS	Low frequency rTMS	High frequency rTMS	Theta burst
Seizure induction	Occasional	Not reported	Occasional (usually protective effect)	Possibile (1.4% crude risk estimate in epileptic patients; less than 1% in normals)	Not reported
Transient acute hypomania induction	no	no	Rare	Possible following left prefrontal stimulation	Not known
Syncope	Possible as epiphenomenon (i.e, not related to direct brain effect)				Not reported
Transient headache, local pain, neck pain, toothache, paresthesia	Possible	Likely possible, but not reported/addressed	Frequent (see para. 3.3)	Frequent (see para. 3.3)	Not reported
Transient hearing changes or tinnitus	possible	Likely possible, but not reported	possible	Possible (avoid rTMS in cochlear implants)	Not known
Transient cognitive/ neuropsychologial changes	Not reported	No reported	Overall negligible (see para. 3.5)	Overall negligible (see para. 3.5)	Not known
Burns from scalp electrodes	no	no	Not reported	Occasionally reported	Not known, but likely possible
Induced currents in electrical circuits	Theoretically possible, but described malfunction only if TMS is delivered in close proximity with the electric device (pace-makers, brain stimulators, pumps, intacardiac lines)				
Histotoxicity/Structural brain changes	Not reported	Not reported	Inconsistent	Inconsistent	Not known
Other biological transient effects	Not reported	Not reported	Not reported	Transient hormone changes (Prolactin, TSH)	Not known

Safety tables

ELSEVIER

Electroencephalography and clinical Neurophysiology 105 (1997) 415–421

Safety of different inter-train intervals for repetitive transcranial magnetic stimulation and recommendations for safe ranges of stimulation parameters

Robert Chen, Christian Gerloff, Joseph Classen, Eric M. Wassermann, Mark Hallett, Leonardo G. Cohen*

Human Cortical Physiology Unit, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bldg. 10, Room SN226, 10 Center Drive, MSC 1428, Bethesda, MD 20892–1428, USA

Accepted for publication: 23 May 1997

Safety tables

Table 3

Table of safe train duration (s)/number of pulses for single trains of rTMS in normal volunteers currently in use at NINDS

Frequency (Hz)	rTMS intensity (% of motor threshold)												
	100	110	120	130	140	150	160	170	180	190	200	210	220
1	>270/270[a]	>270/270[a]	180/180[b]	50/50[c]	50/50[c]	50/50[c]	50/50[c]	20/20	8/8	8/8	6/6	5/5	4/4
5	10/50[c]	10/50[c]	10/50[c]	10/50[c]	5.7/28	3.9/19	2.7/13	1.95/9	1.8/9	1.2/6	1.1/5	1.2/6	0.9/4
10	5/50[c]	5/50[c]	3.2/32	2.2/22	1.0/10	0.6/6	0.7/7	0.6/6	0.4/4	0.5/5	0.3/3	0.2/2	0.2/2
20	1.5/30	1.2/24	0.8/16	0.4/8	0.3/6	0.2/4	0.2/4	0.1/2	0.2/4	0.2/4	0.2/4	0.1/2	0.1/2
25	1.0/25	0.7/17	0.3/7	0.2/5	0.2/5	0.2/5	0.2/5	0.1/2	0.1/2	0.1/2	0.1/2	0.1/2	0.1/2

The maximum safe train duration (s) is shown followed by the number of pulses. See also Wassermann (1997).
[a]Based on Chen et al. (1997a).
[b]Based on Wassermann et al. (1996b).
[c]No spread of excitation or post-TMS EMG activity was observed at these train durations. Based on Pascual-Leone et al. (1993).

- Frequency
- Stimulus intensity
- Train duration

Chen et al, Electroencephalogr. Clin Neurophysiol 1997

Safety tables

Table 4

Safety recommendations for inter-train intervals for 10 trains of rTMS at < 20 Hz

Inter-train interval (s)	Stimulus intensity (% of MT)			
	100%	105%	110%	120%
5	Safe	Safe	Safe	Insufficient data
1	Unsafe (3)	Unsafe[a]	Unsafe (2)	Unsafe (2)
0.25	Unsafe[a]	Unsafe[a]	Unsafe (2)	Unsafe (3)

- Inter-train interval
- 120% or higher – 1 min

Chen et al, Electroencephalogr. Clin Neurophysiol 1997

Conclusions

- rTMS can modify brain function and may be therapeutic in some circumstances
  - BUT – treatment must be repetitive
  - AND – combination with behavior or drugs might be useful/necessary
  - Other than for depression, other indications are experimental
- rTMS might also be used to test whether epidural stimulation would be worthwhile

Thank you!

Save the date!

30th International Congress of Clinical Neurophysiology of the International Federation of Clinical Neurophysiology (IFCN)

21–24 March 2014, Berlin/Germany

58th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN)
20–23 March 2014, Berlin/Germany

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