Stimolazione Magnetica Trancranica ripetitiva e craving

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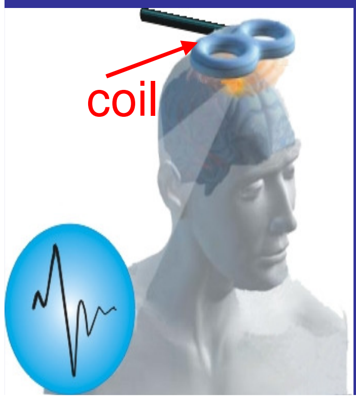
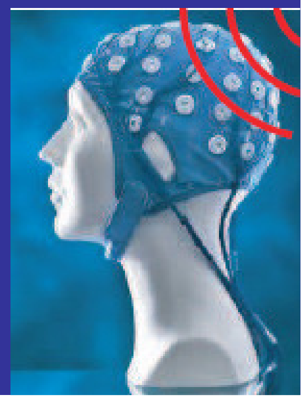
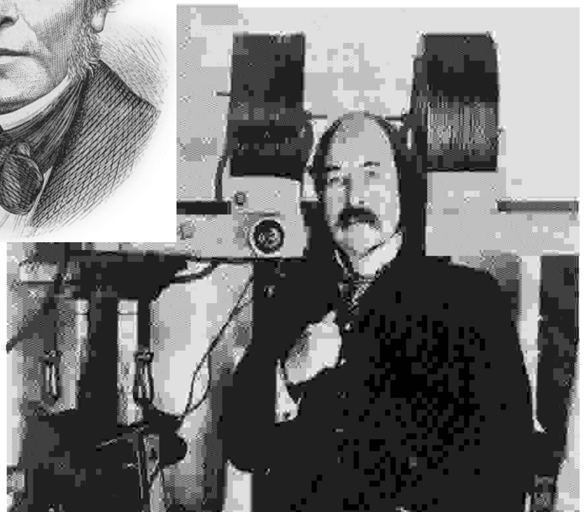




LA STIMOLAZIONE MAGNETICA TRANSCRANICA



London.)

NATURE 2007

OPINION

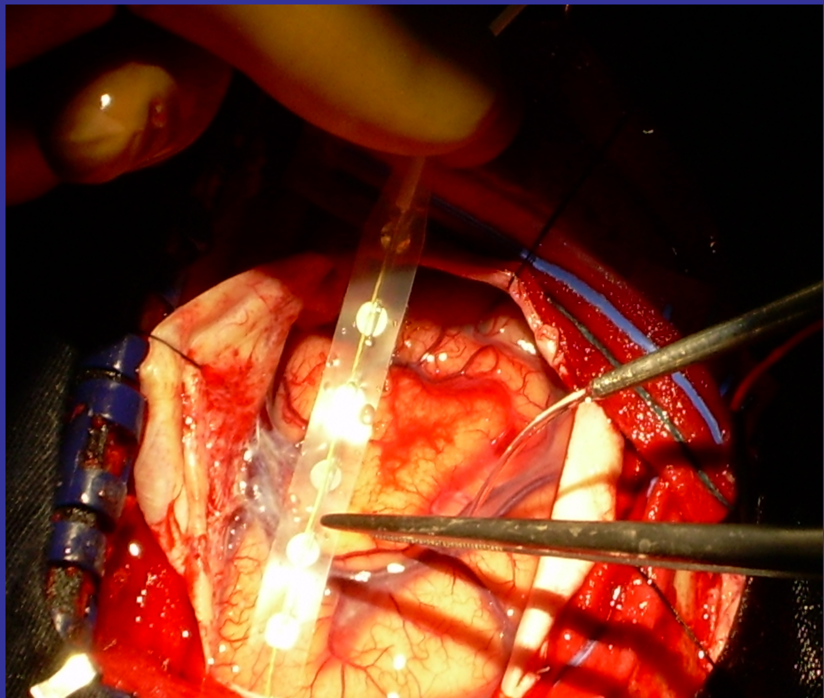
Is there a future for therapeutic use of transcranial magnetic stimulation?

Michael C. Ridding and John C. Rothwell

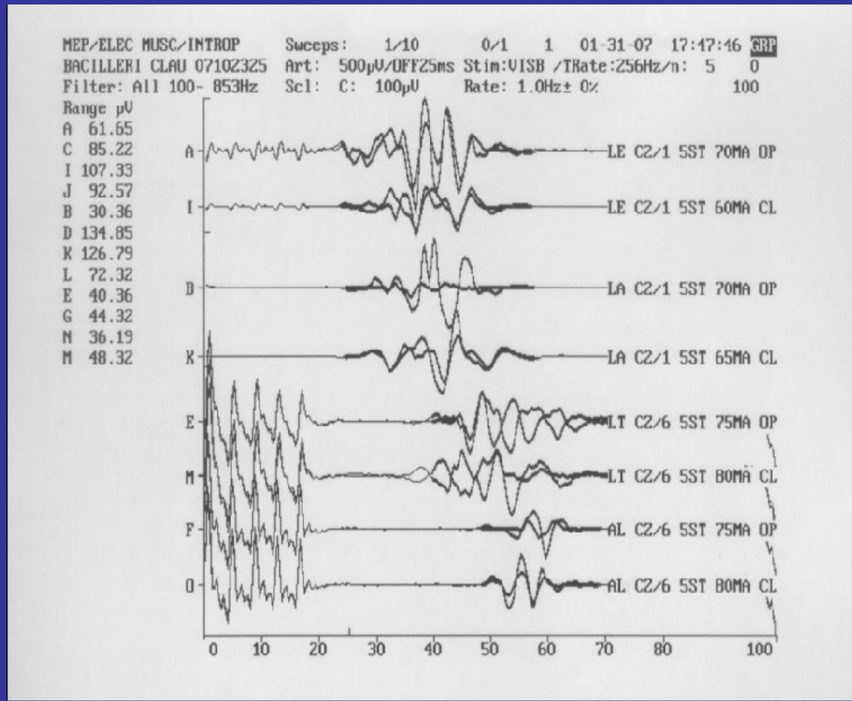
- The past year have seen a remarkable number of paper on the therapeutic effects of rTMS from stroke to addiction

- After 10 years there is still debate wether rTMS has any greater effects than placebo

Corticografia in awake surgery.

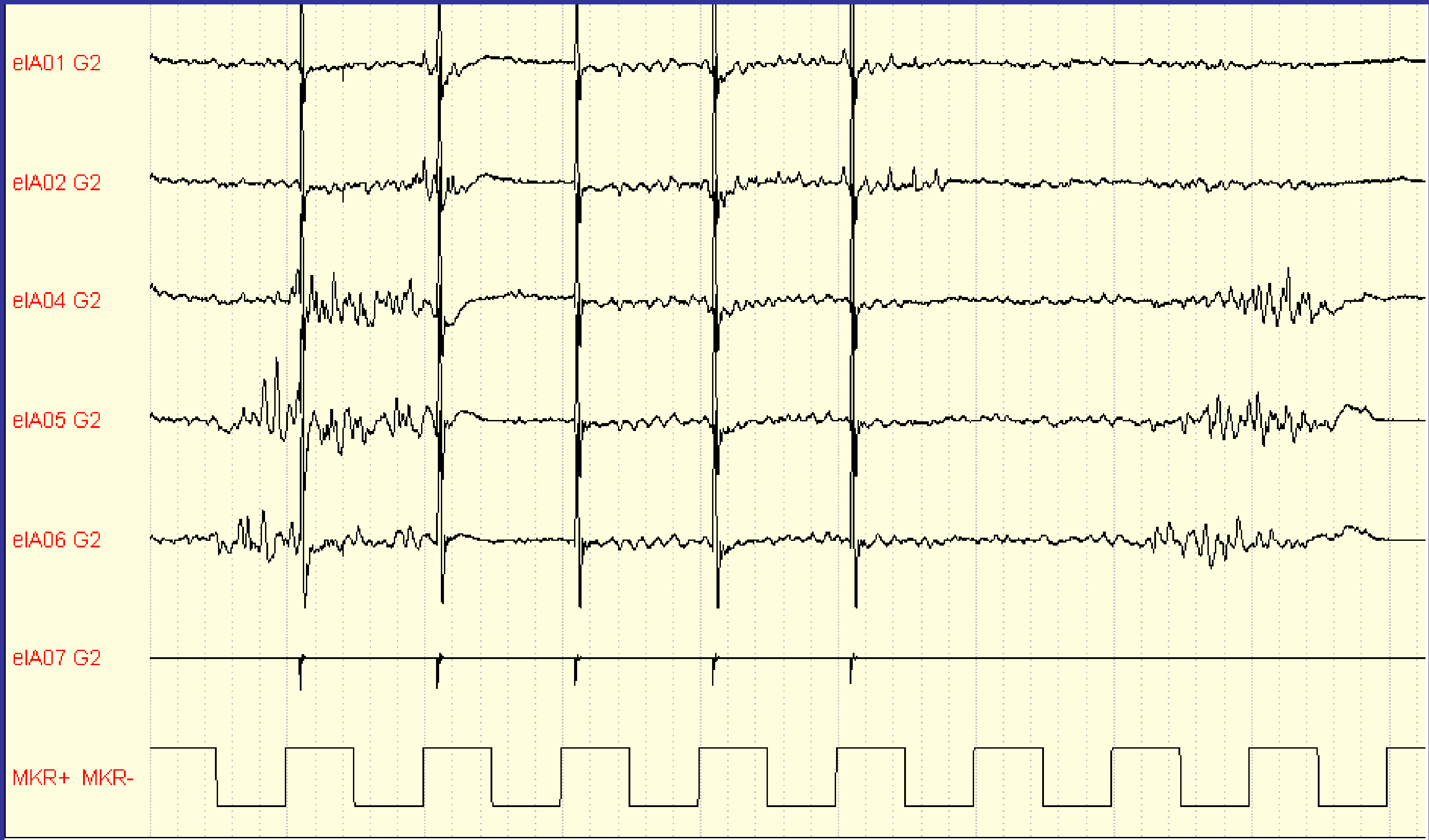


Posizionamento strip



Potenziali motori evocati

Extradischarges after train of stimulation



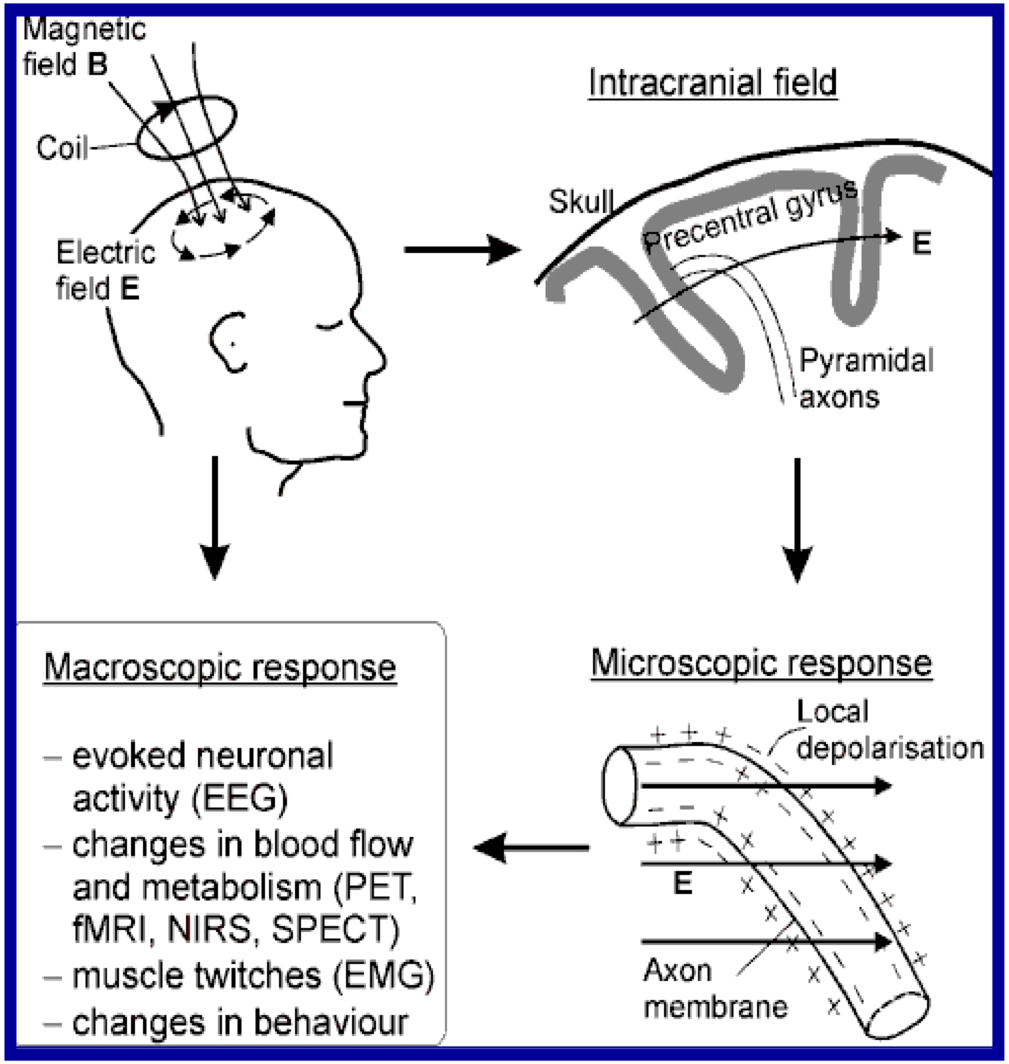
LA STIMOLAZIONE MAGNETICA TRANSCRANICA

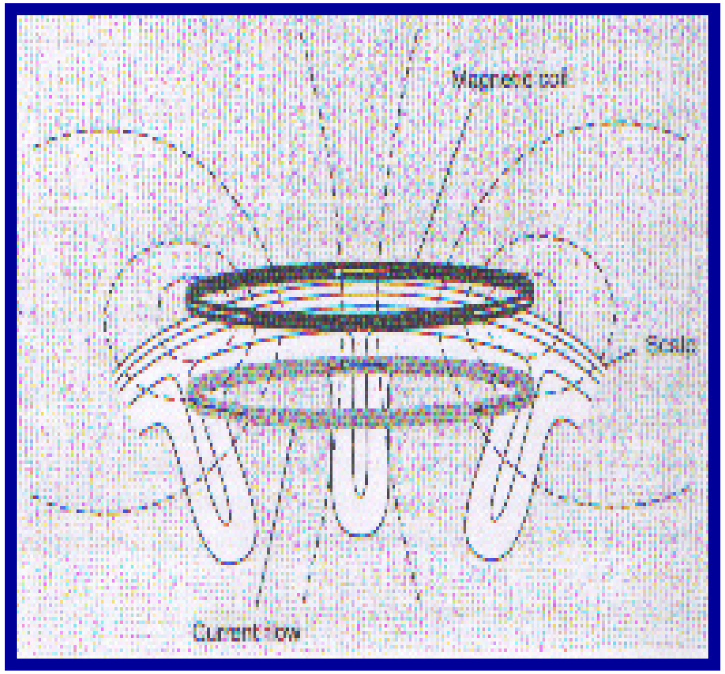
I. **STIMOLO SINGOLO (SINGLE PULSE-TMS)**
   → Conduzione fascio cortico-spinale
   → Eccitabilità corticale (soglia)
   → Periodo silente
   → Rappresentazione corticale (mappaggio)

II. **STIMOLO DOPPIO (PAIRED-TMS)**
   → Eccitabilità intracorticale

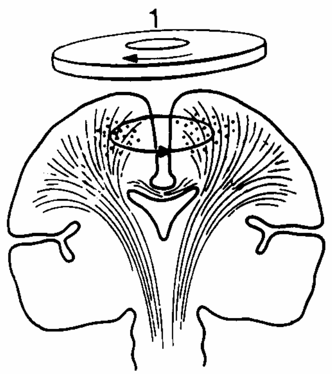
III. **STIMOLO RIPETITIVO (REPETITIVE TMS)**

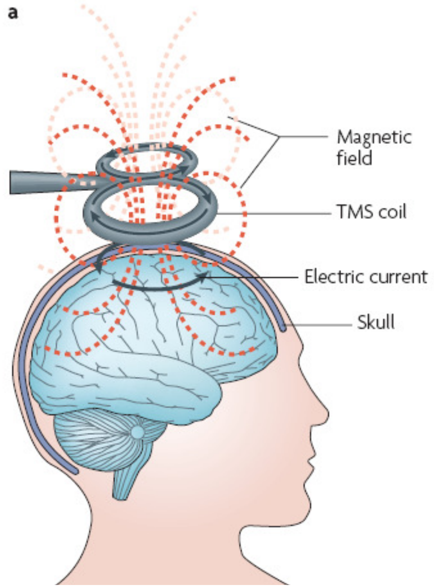
MECCANISMO D'AZIONE AREA MOTORIA

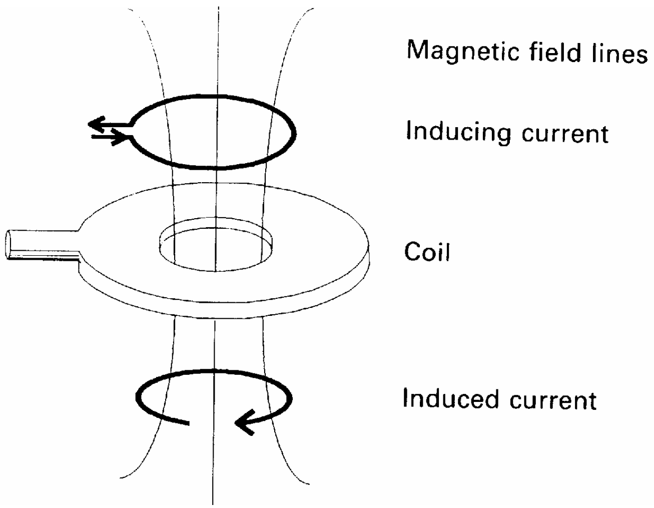


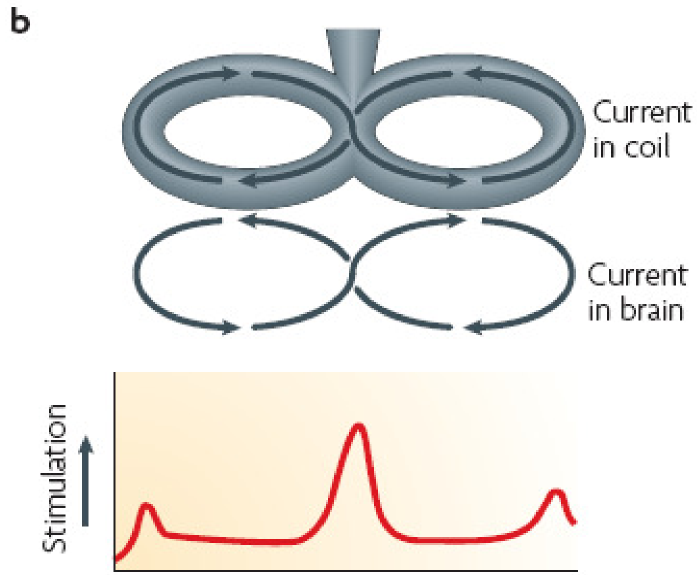


Area di stimolazione e coil









1 – 2 cm di area di stimolazione

TMS

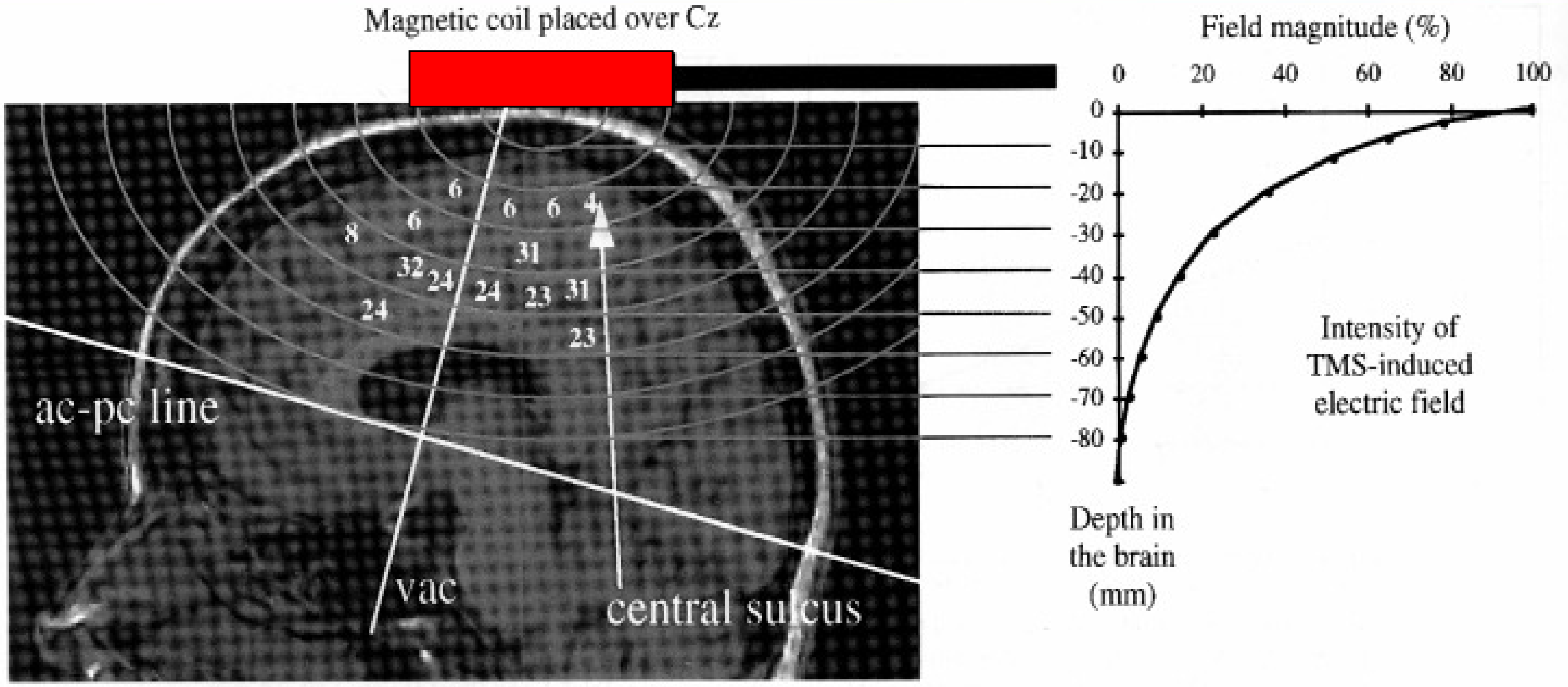
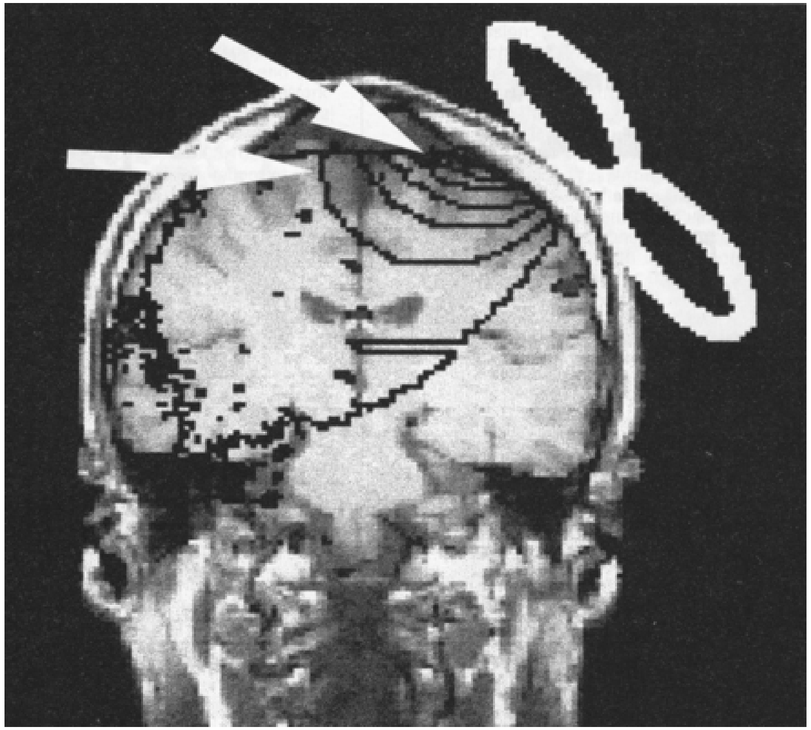
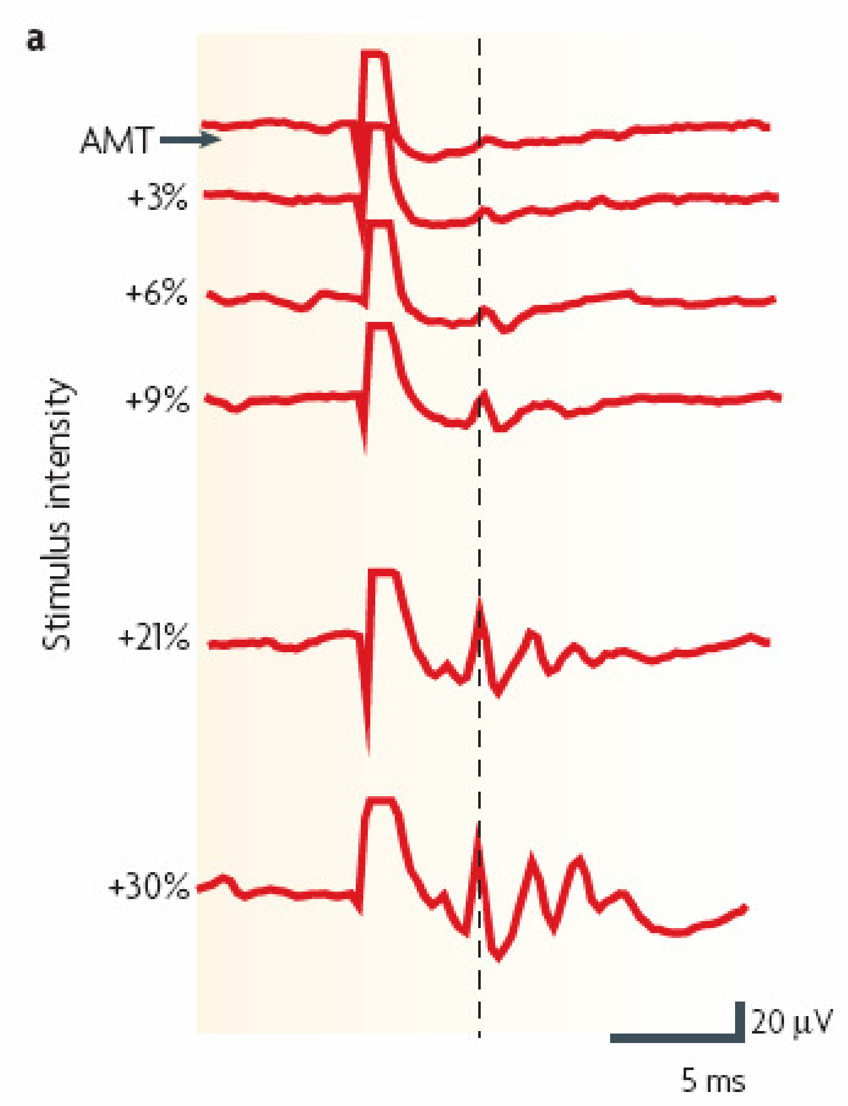


Fig. 8 The relationship between the anatomy of the mesial cortex and the shape of the magnetically induced electric field as estimated on the basis of model measurements (Roth *et al*., 1991). T_1-weighted conventional magnetic resonance image (sagittal slice, 1.5 Tesla) of a normal subject. The numbers refer to Brodmann areas. Area 6 represents the supplementary motor area, areas 24, 32, 23, 31 the cingulate cortex, area 4 the primary motor cortex representation of the leg, and area 8 the prefrontal association cortex. The vertical anterior commissure line (vac) crosses the anterior commissure and is orthogonal to the anterior commissure–posterior commissure (ac-pc) line. The vac line roughly separates pre-supplementary motor area (anterior to vac) and the supplementary motor area proper (posterior to vac). The arrow marks the central sulcus. The magnetic coil is positioned over Cz in this figure, and the concentric lines represent electric field lines of different field magnitudes. The field magnitudes for each line can be identified in the graph on the right side where the field magnitudes are plotted as a function of the depth inside the brain. Note the substantial difference in estimated field magnitudes between the supplementary motor area and the cingulate cortex (3–5 times greater field magnitudes in the more superficially located supplementary motor area). According to these considerations, even taking into account inter-individual anatomical variability, the supplementary motor area is the most likely target region when rTMS is applied over Cz.

Meccanismo d'azione



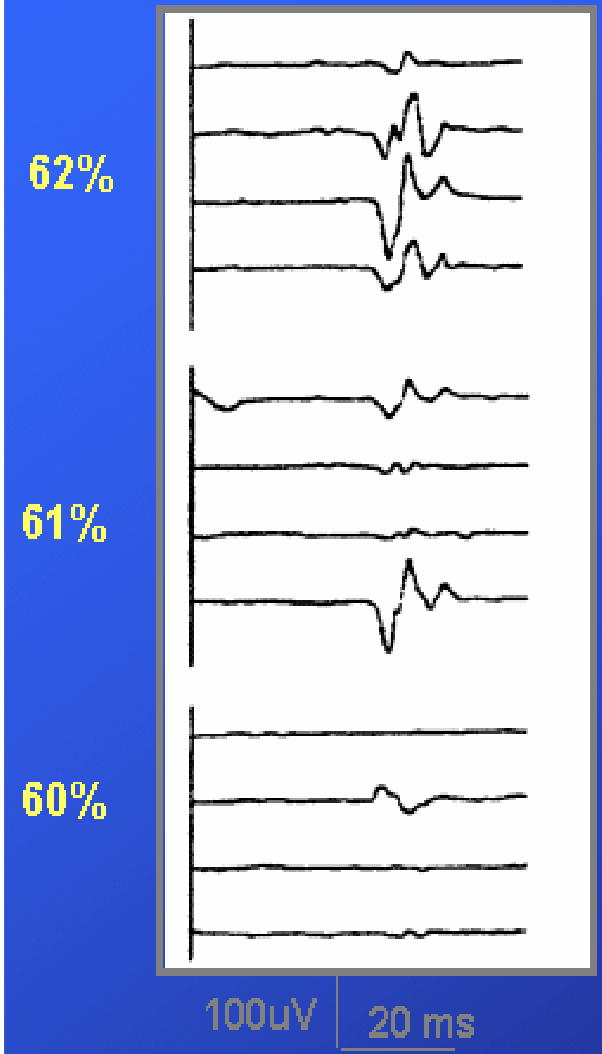


D wave
stimolazione diretta assonale

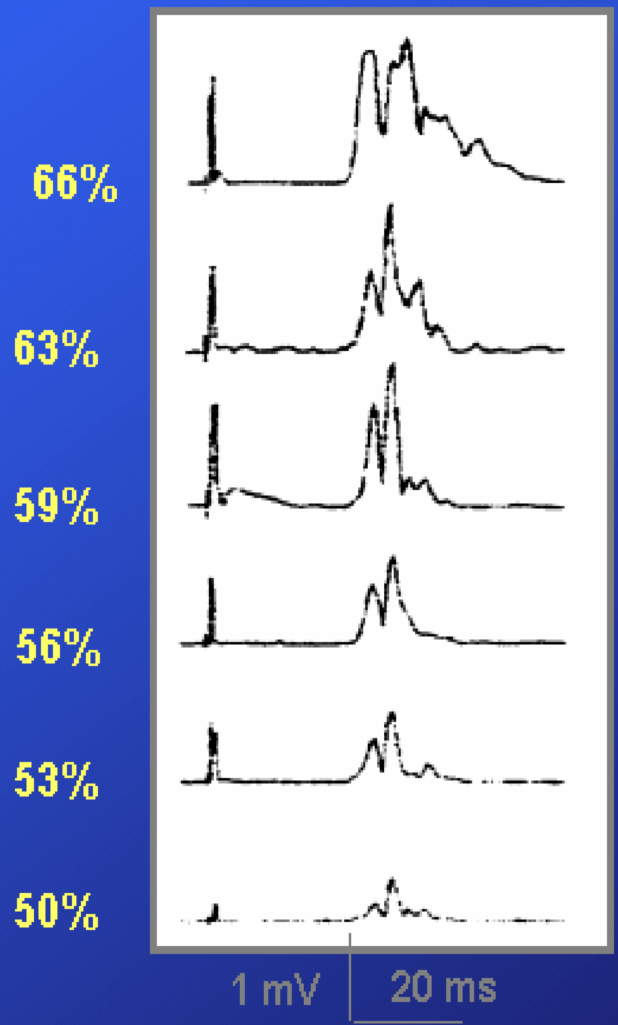
I wave
stimolazione indiretta transinaptica

TMS

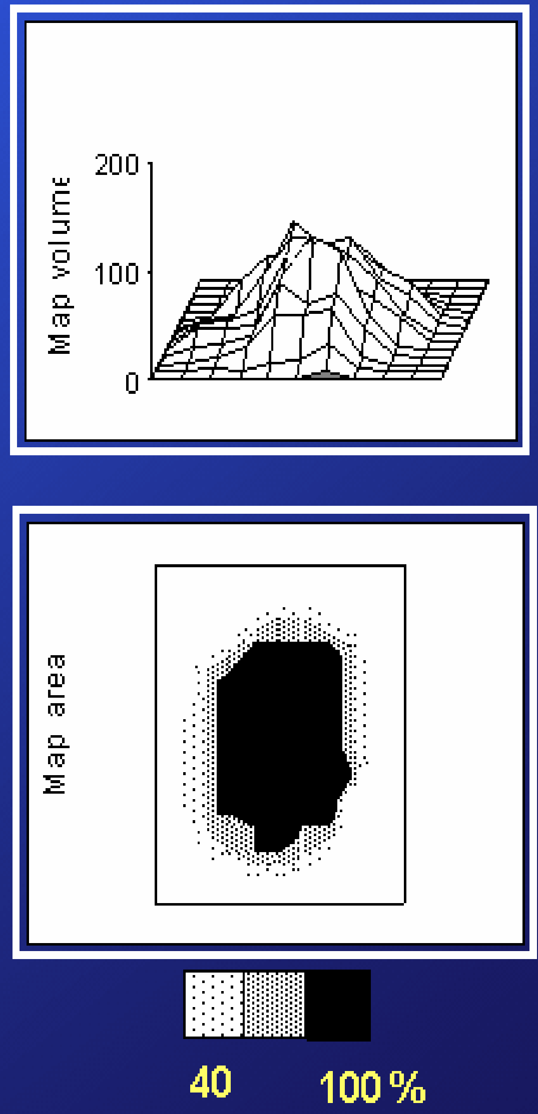
SOGLIA MOTORIA



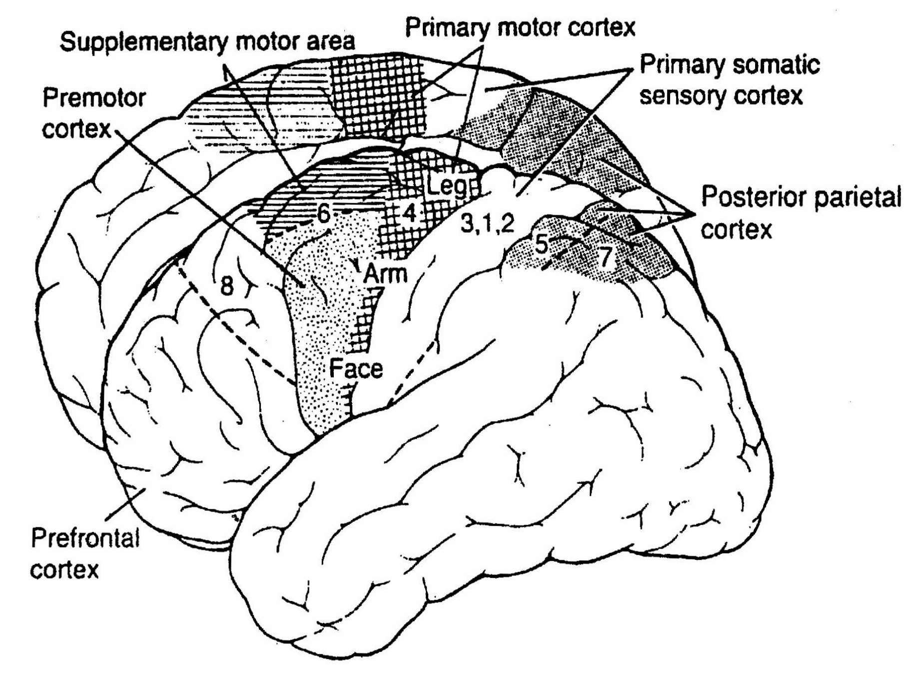
CURVA I/A



MAPPAGGIO



A


Supplementary motor area
Primary motor cortex
Primary somatic sensory cortex
Premotor cortex
Leg
6
4
3,1,2
Posterior parietal cortex
5
7
8
Arm
Face
Prefrontal cortex

B

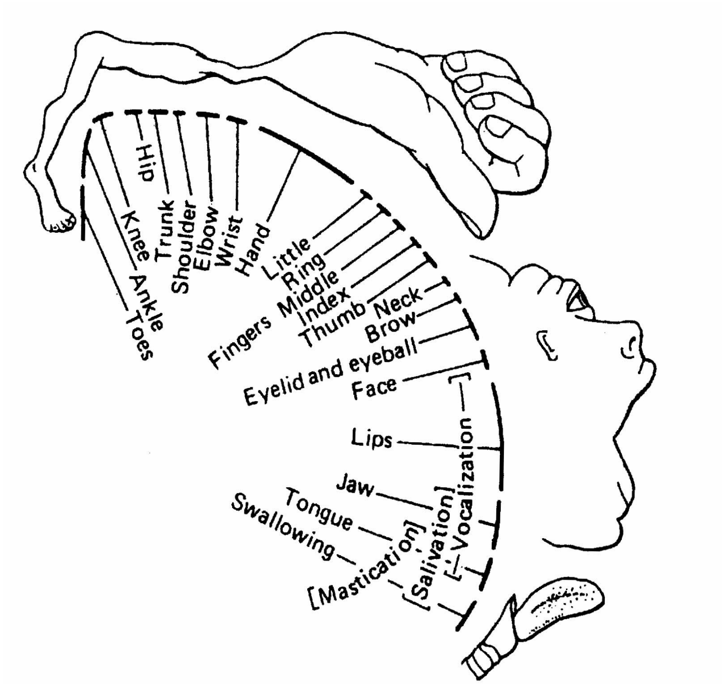

Hip
Knee
Ankle
Toes
Trunk
Shoulder
Elbow
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Fingers
Neck
Brow
Eyelid and eyeball
Face
Lips
Jaw
Tongue
Swallowing
[Mastication]
[Salivation]
[–Vocalization–]

Figura 2

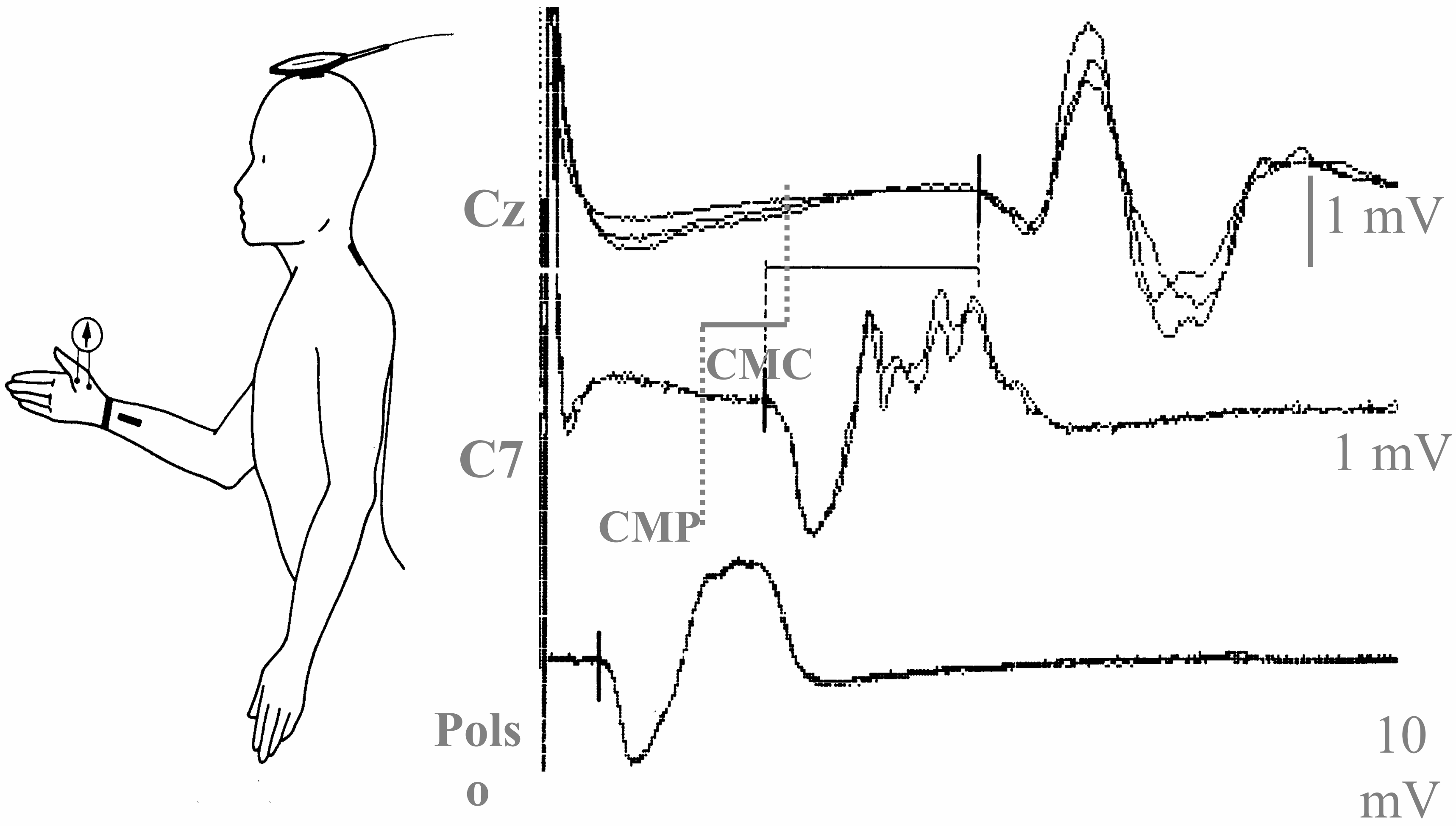
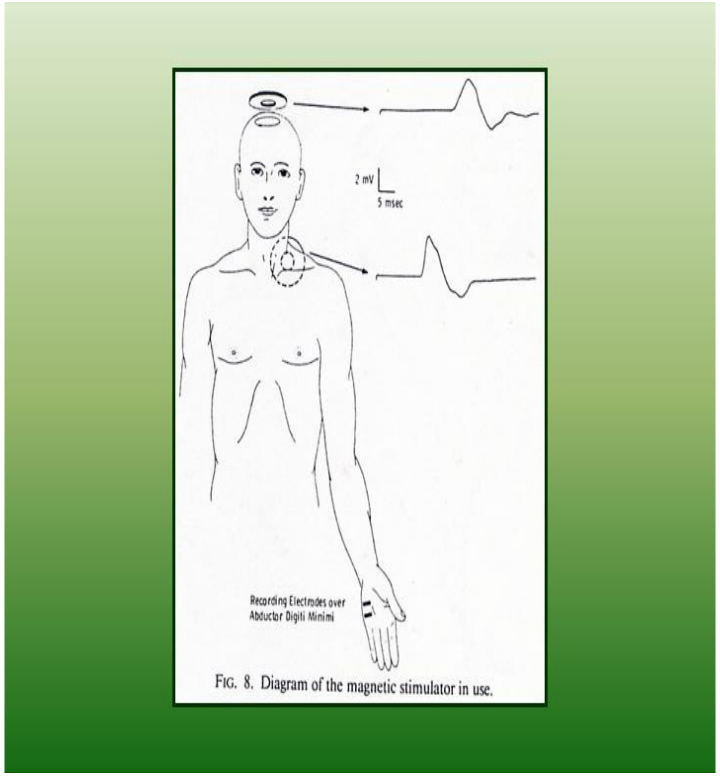


Figura 5

A


2 mV
5 msec
Recording Electrodes over
Abductor Digiti Minimi
FIG. 8. Diagram of the magnetic stimulator in use.

B

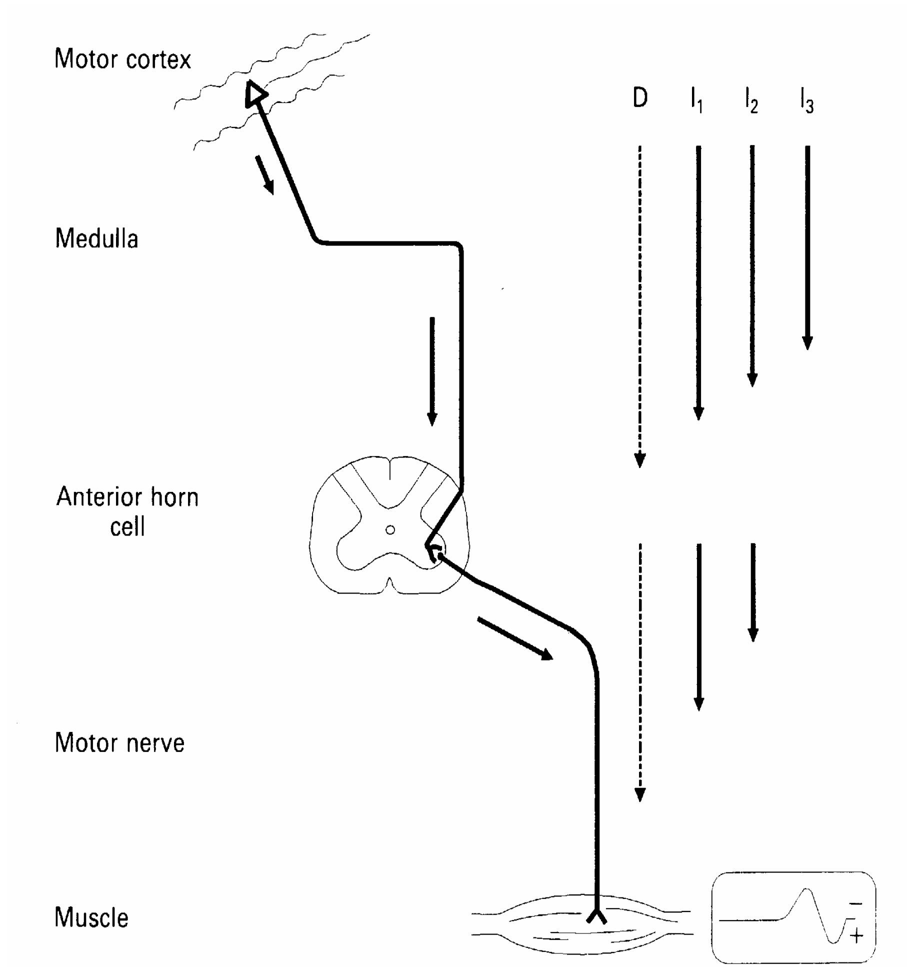

Motor cortex
Medulla
Anterior horn
cell
Motor nerve
Muscle
D
I_1
I_2
I_3
−
+

Figura 1

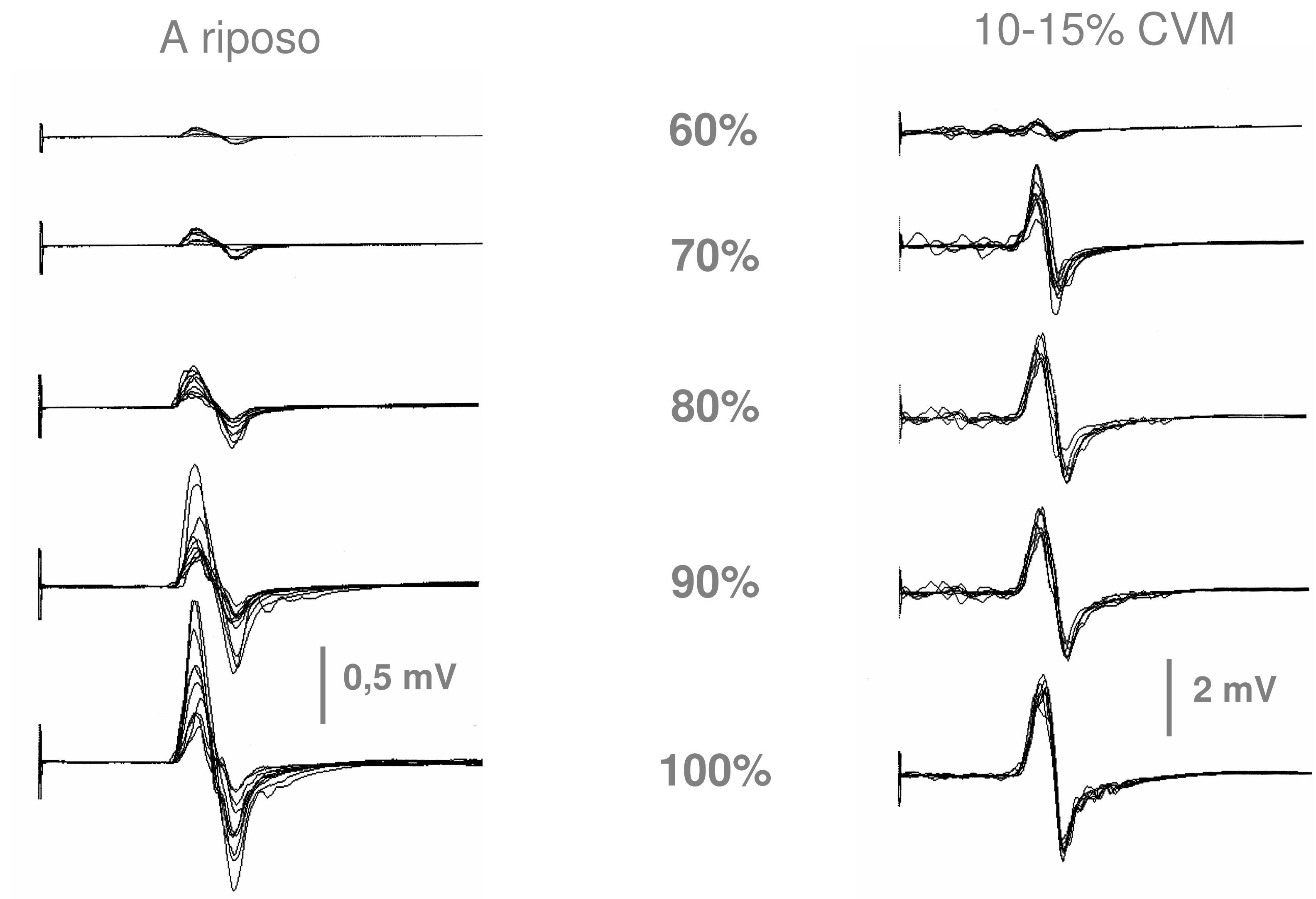


Figura 3: curva intensità-ampiezza del PEM ottenuta a riposo e durante modesta attivazione muscolare. A riposo si assiste ad un incremento graduale dell'ampiezza del PEM che presenta una elevata variabilità per stimolazioni successive.
Durante attivazione, il PEM raggiunge già a bassa intensità l'ampiezza massimale ed è più stabile.
La latenza del PEM è 2,4 msec più precoce durante attivazione rispetto a quella registrata a riposo.

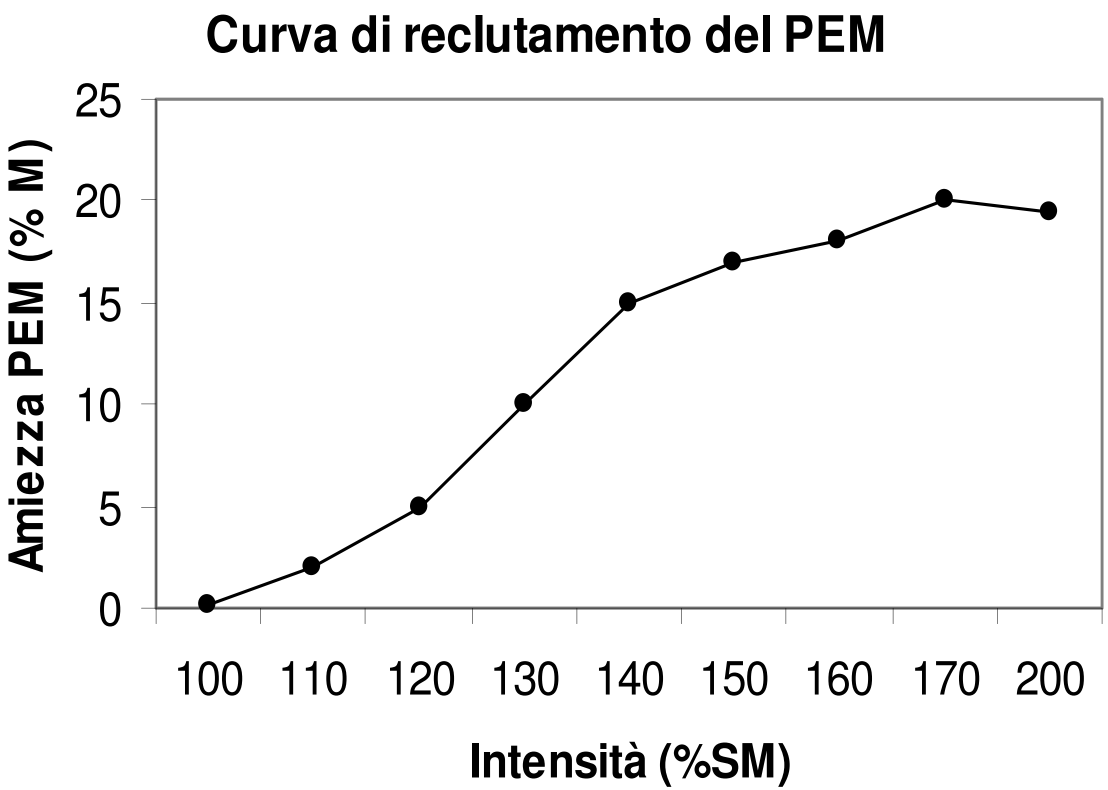


Figura 4: registrazione effettuata dal m. abduttore breve del pollice

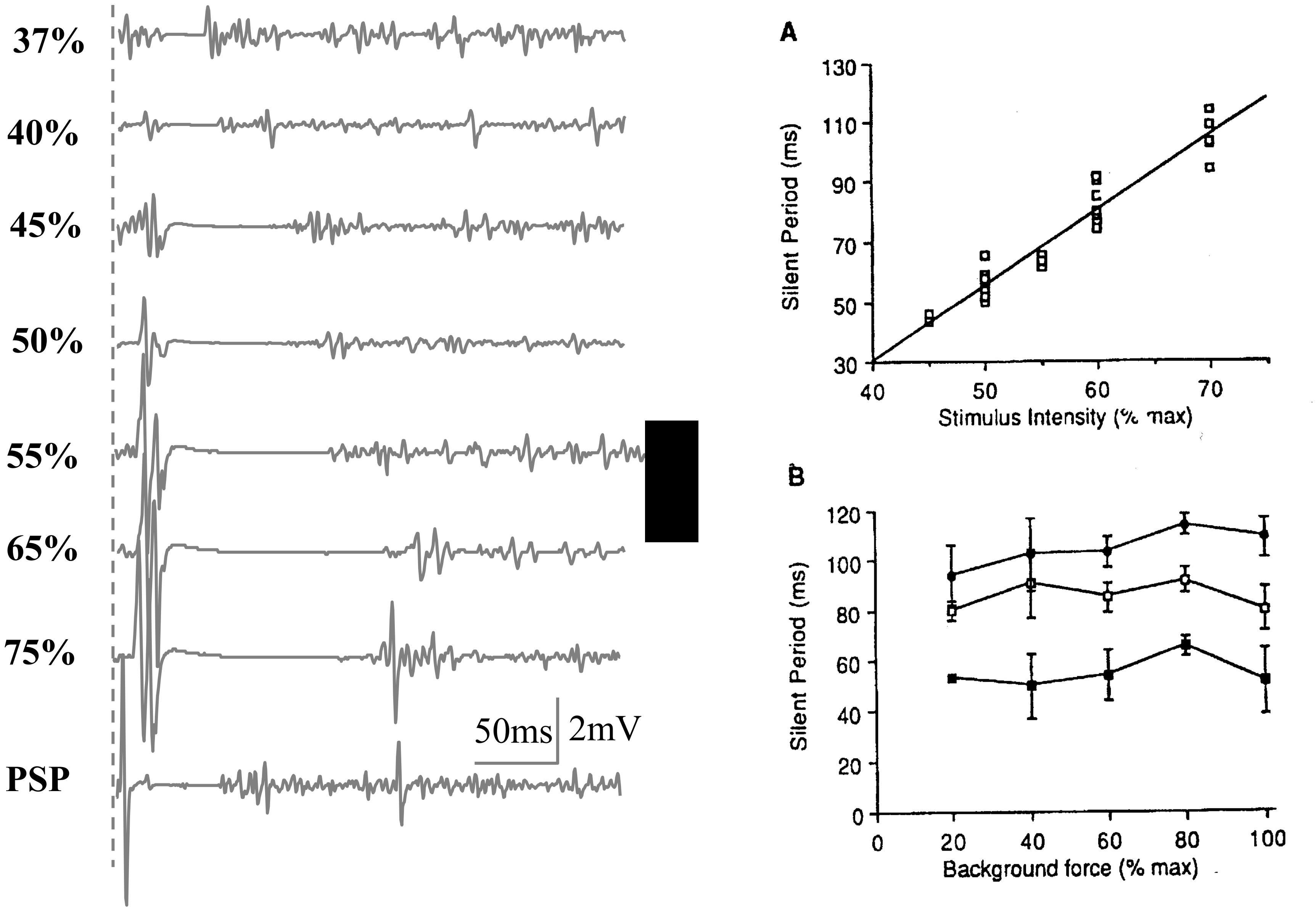


Figura 7: a sinistra registrazione dal m. APB durante contrazione del 30%. Si nota un incremento progressivo della durata del PS all'aumentare dell''intensità di stimolazione. Nella traccia inferiore è illustrato il PS periferico (PSP) che occupa la parte iniziale del PS da stimolo corticale. A destra, il PS si incrementa linearmente in relazione all'intensità di stimolazione (A), mentre non viene modificato dalla variazione della forza muscolare (B).

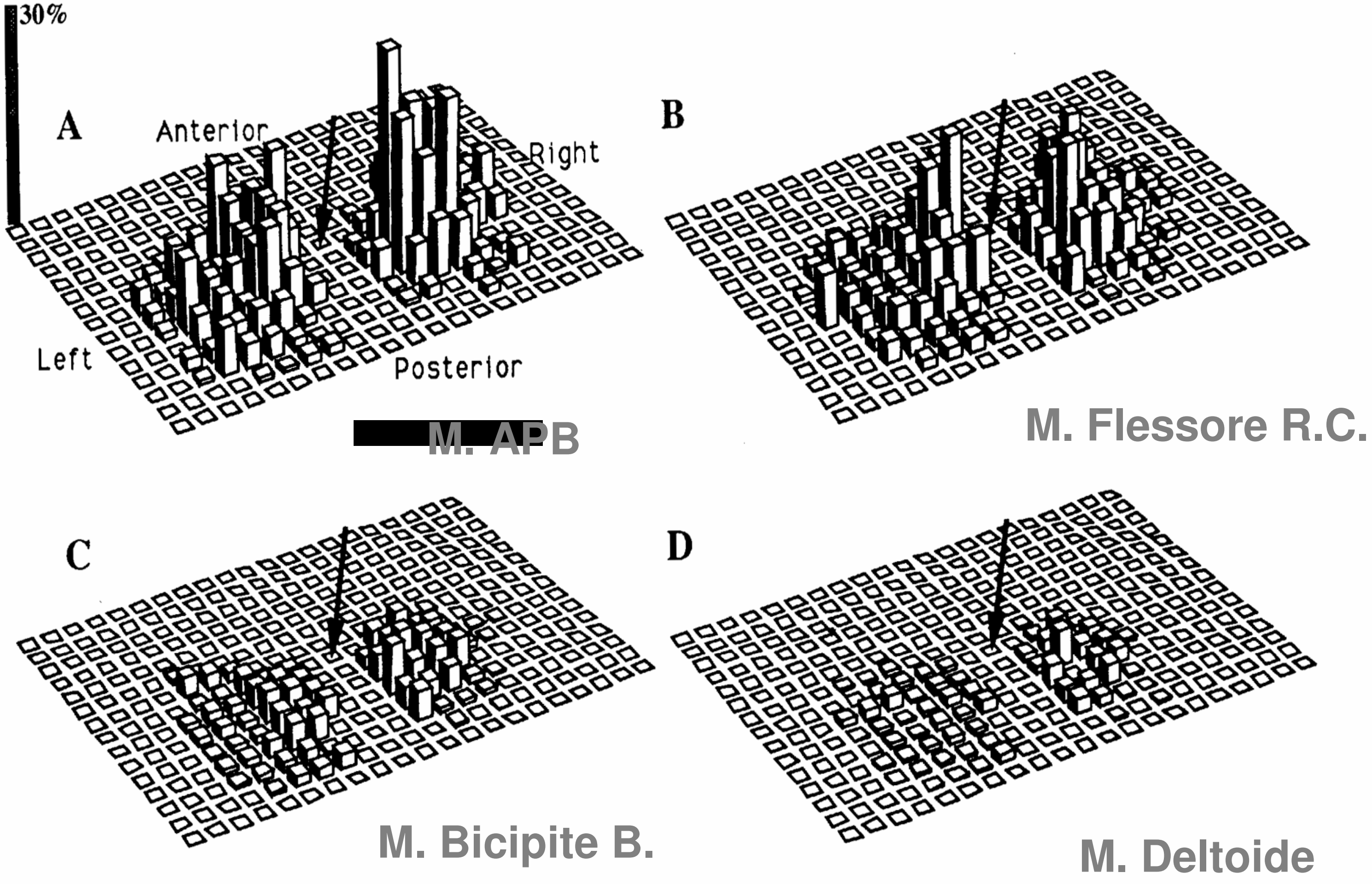
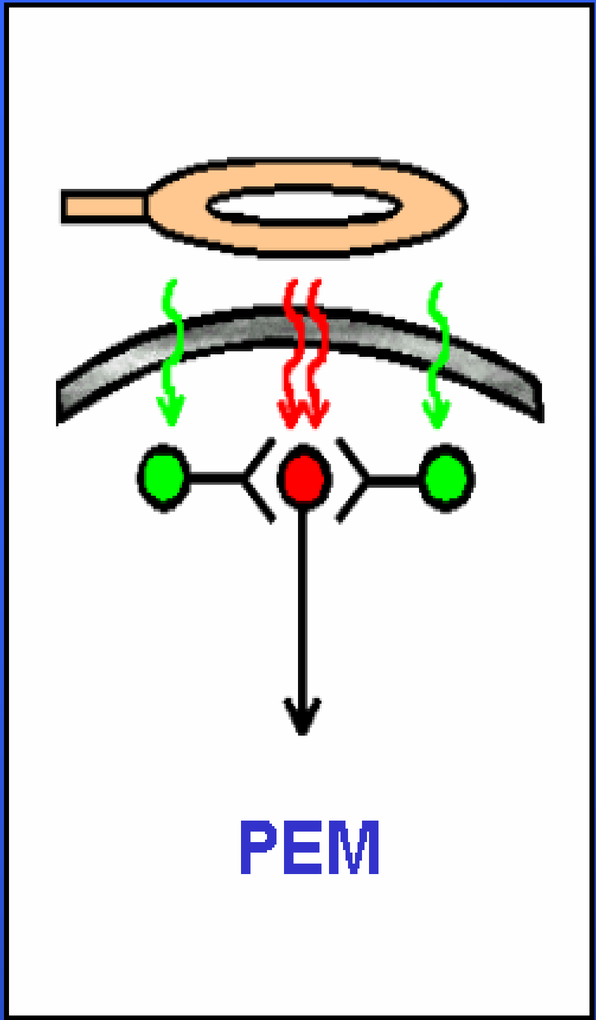
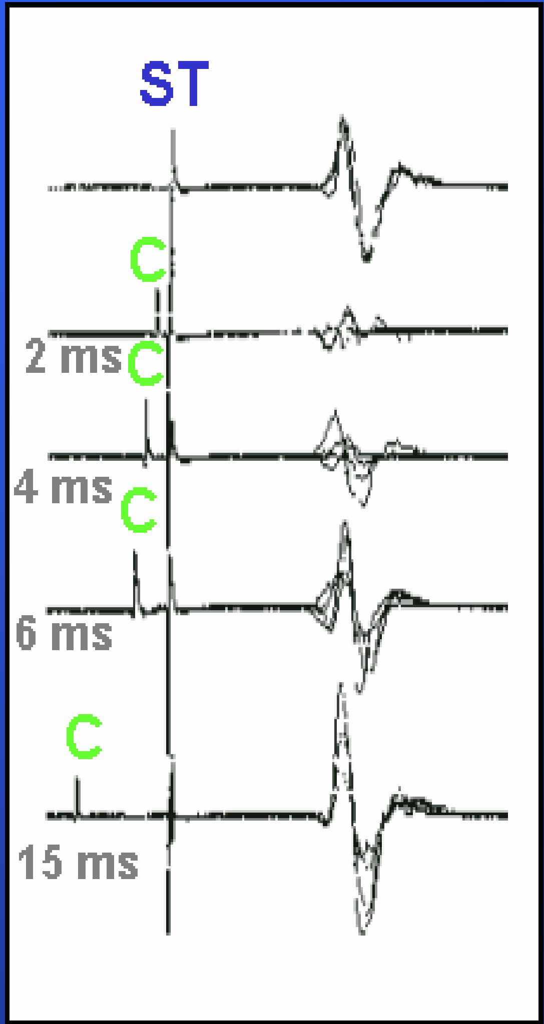


Figura 6: rappresentazione corticale di 4 muscoli dell'arto superiore che, in senso disto-prossimale, sono l'abduttore b. pollice, il flessore radiale del carpo, il m. bicipite brachiale e il m. deltoide. Si noti la più ampia rappresentazione in termini di area e la maggiore ampiezza del PEM nei muscoli distali rispetto ai prossimali. La soglia motoria dei muscoli della mano è significativamente più bassa rispetto ai muscoli prossimali come il deltoide.

Curva Inibizione/Facilitazione intracorticale da doppio stimolo





Inibizione Gabaergica

Facilitazione Glutamatergica

STIMOLAZIONE MAGNETICA TRANCRANICA RIPETITIVA

PROLONGED EFFECTS ON BRAIN

- **30 – 60 MIN**
- **DEPENDS ON :**
- **NUMBER OF PULSES**
- **FREQUENCY**
- **INTENSITY**

CONVENTIONAL RTMS

- BELOW MOTOR THRESHOLD
- TO AVOID SENSORY INPUT
- TO SAFETY CRITERIA

- LOW FREQUENCY $<$ 1 HZ (0.5 HZ)

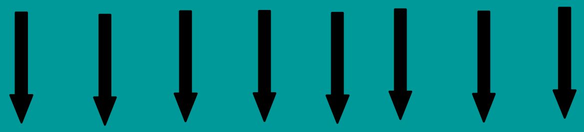
- HIGH FREQUENCY $>$ 1 HZ (5-10-20 HZ)

rTMS e MODULAZIONE DELL'ECCITABILITA' MOTORIA

Frequenza, Intensità e Durata

A **DURANTE LA STIMOLAZIONE**

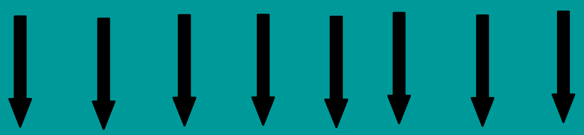
TMS - impulsi



millisecondi

B **DOPO LA STIMOLAZIONE**

TMS - impulsi

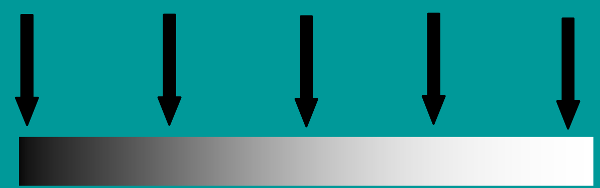


millisecondi

MODULAZIONE LONG-LASTING

LTP - LTD

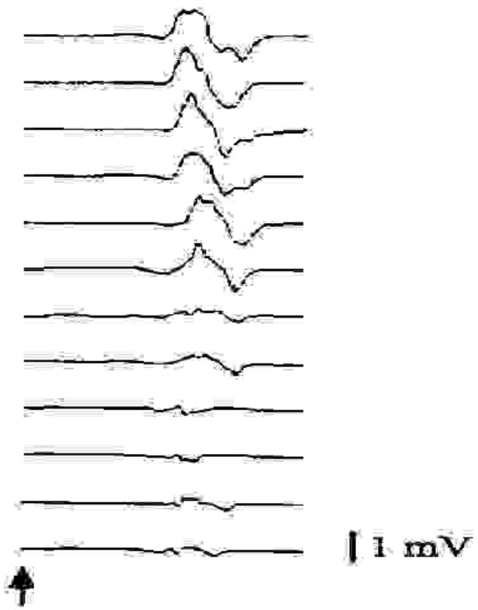
TMS - test



Minuti

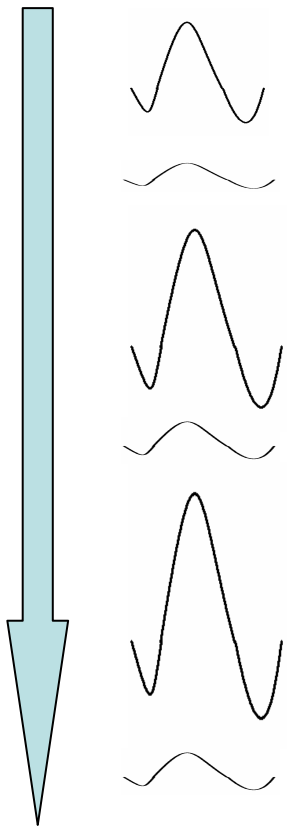
LOW FREQUENCY STIMULATION DECREASE OF MEP AMPLITUDE DURING STIMULATION

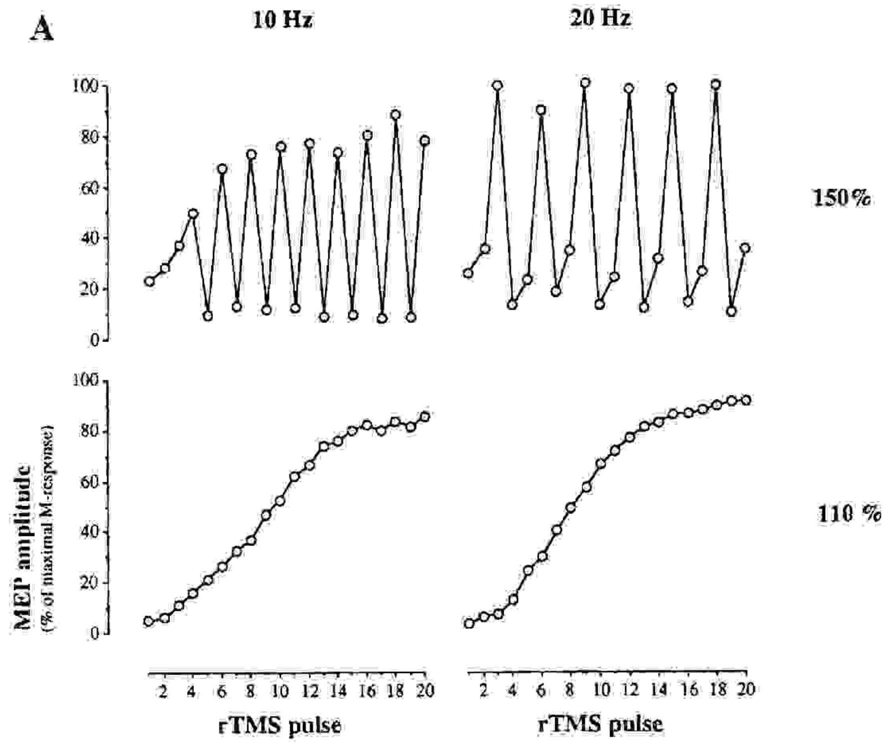
1 HZ rTMS



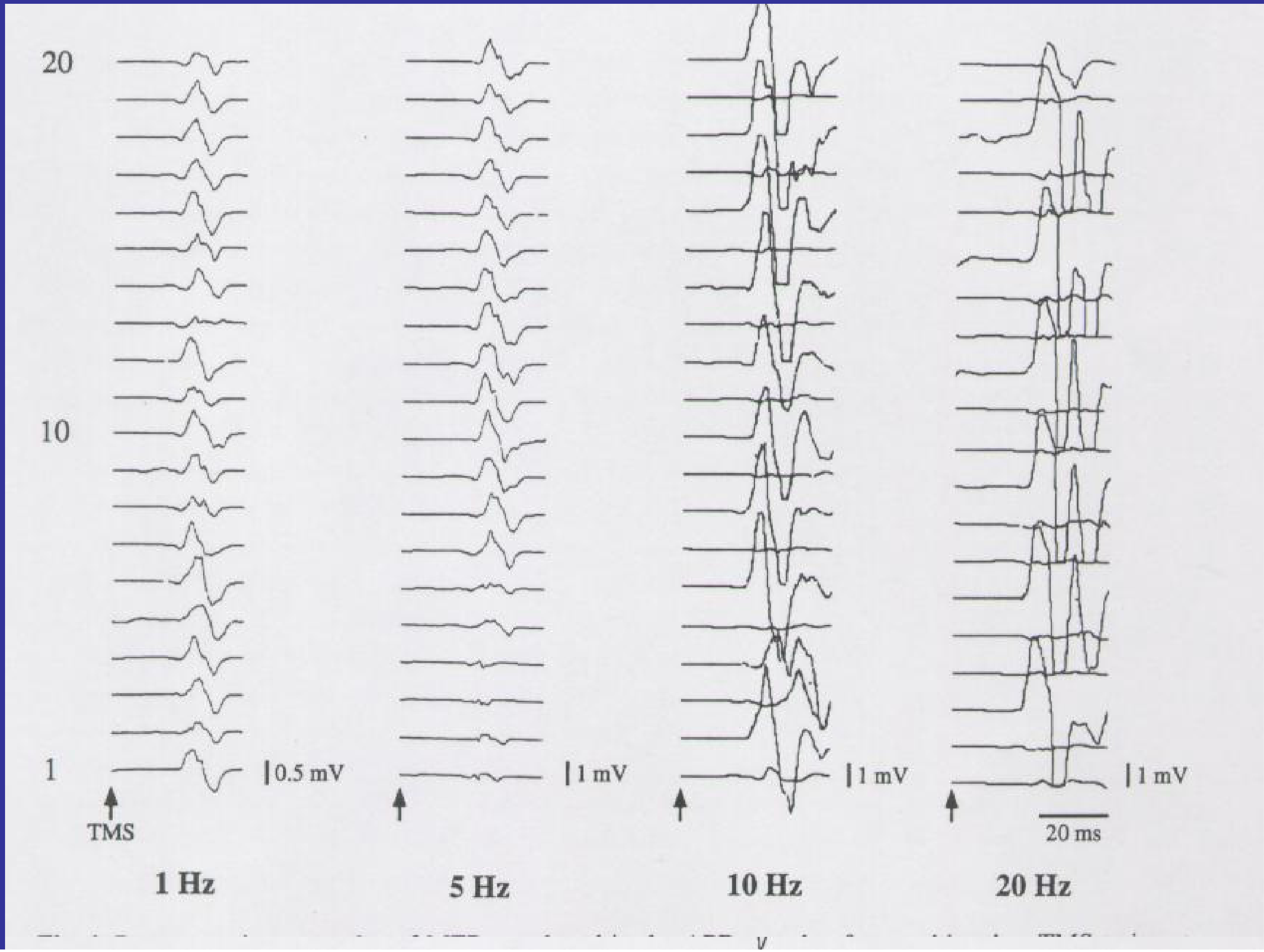
HIGH FREQUENCY STIMULATION SALTATORY INCREASE OF MEP AMPLITUDE DURING STIMULATION

10 Hz

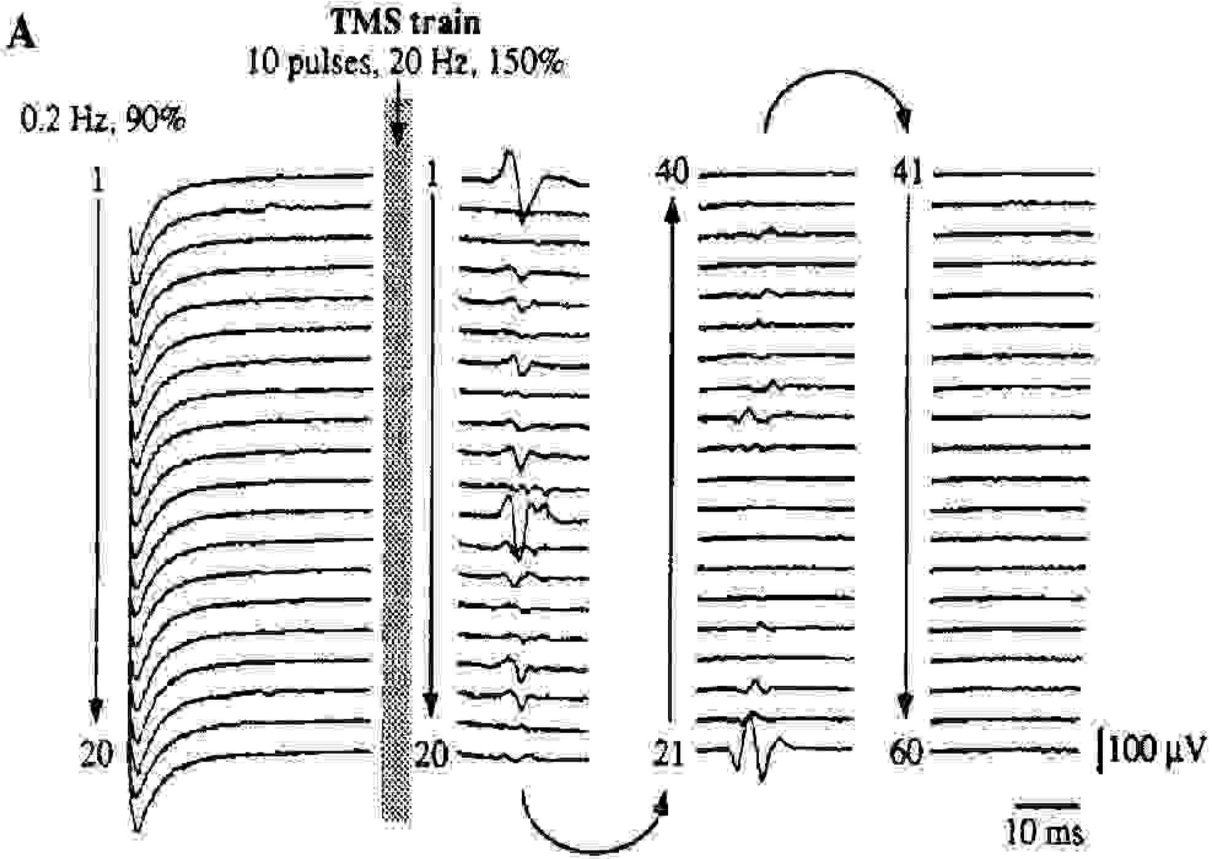




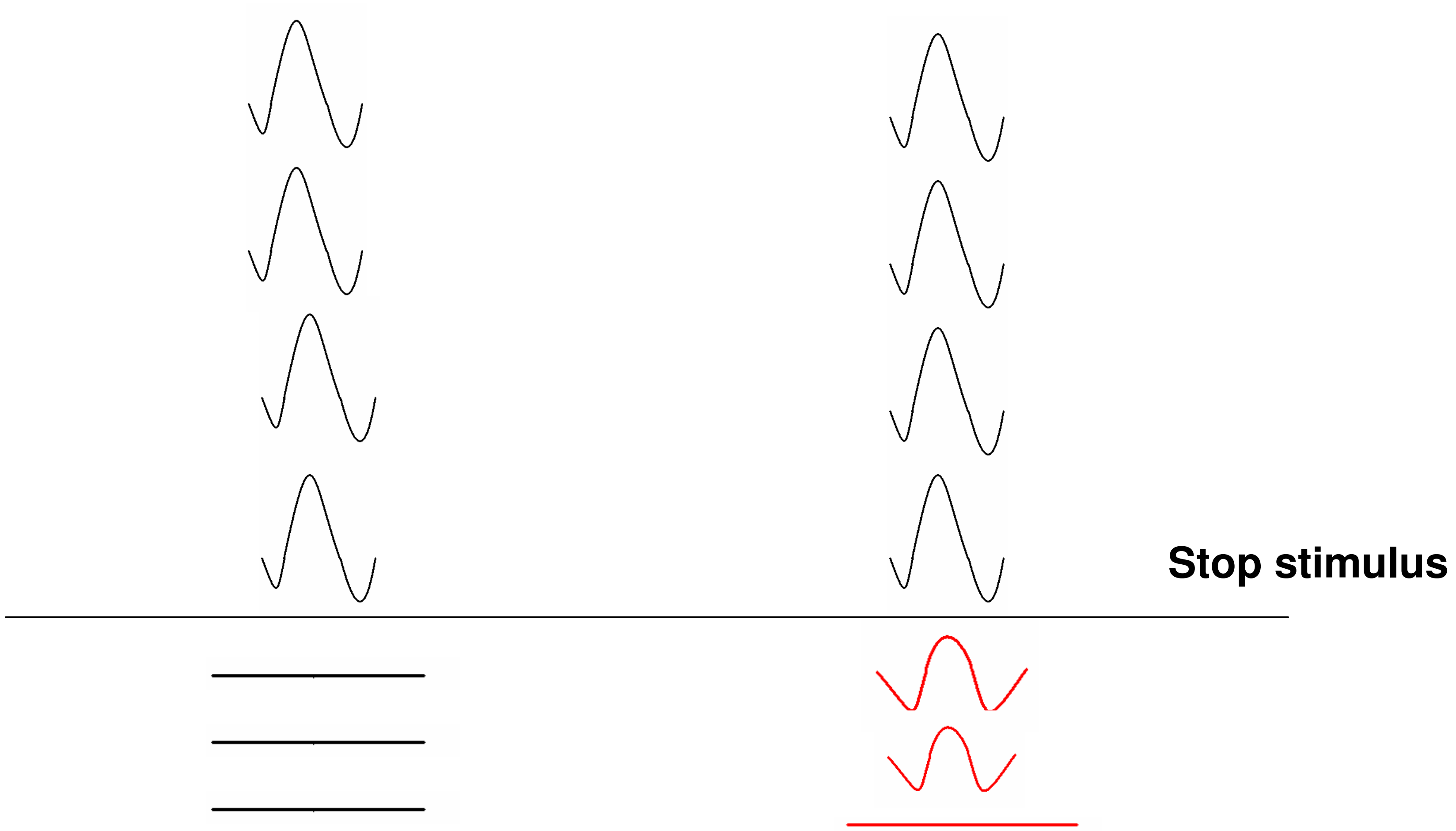
Aumento dell'eccitabilità durante rTMS ad alta frequenza PATTERN ALTERNANTE



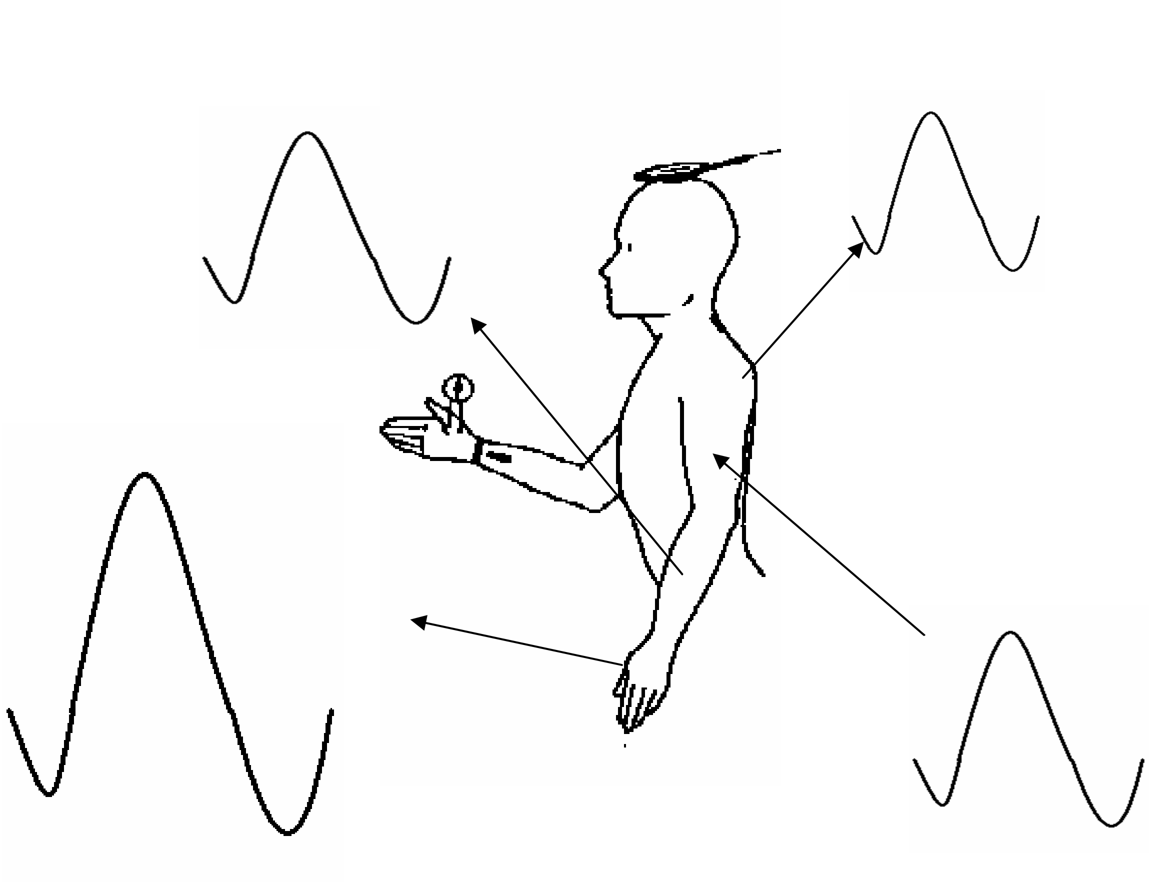
Aumento dell'eccitabilità dopo rTMS



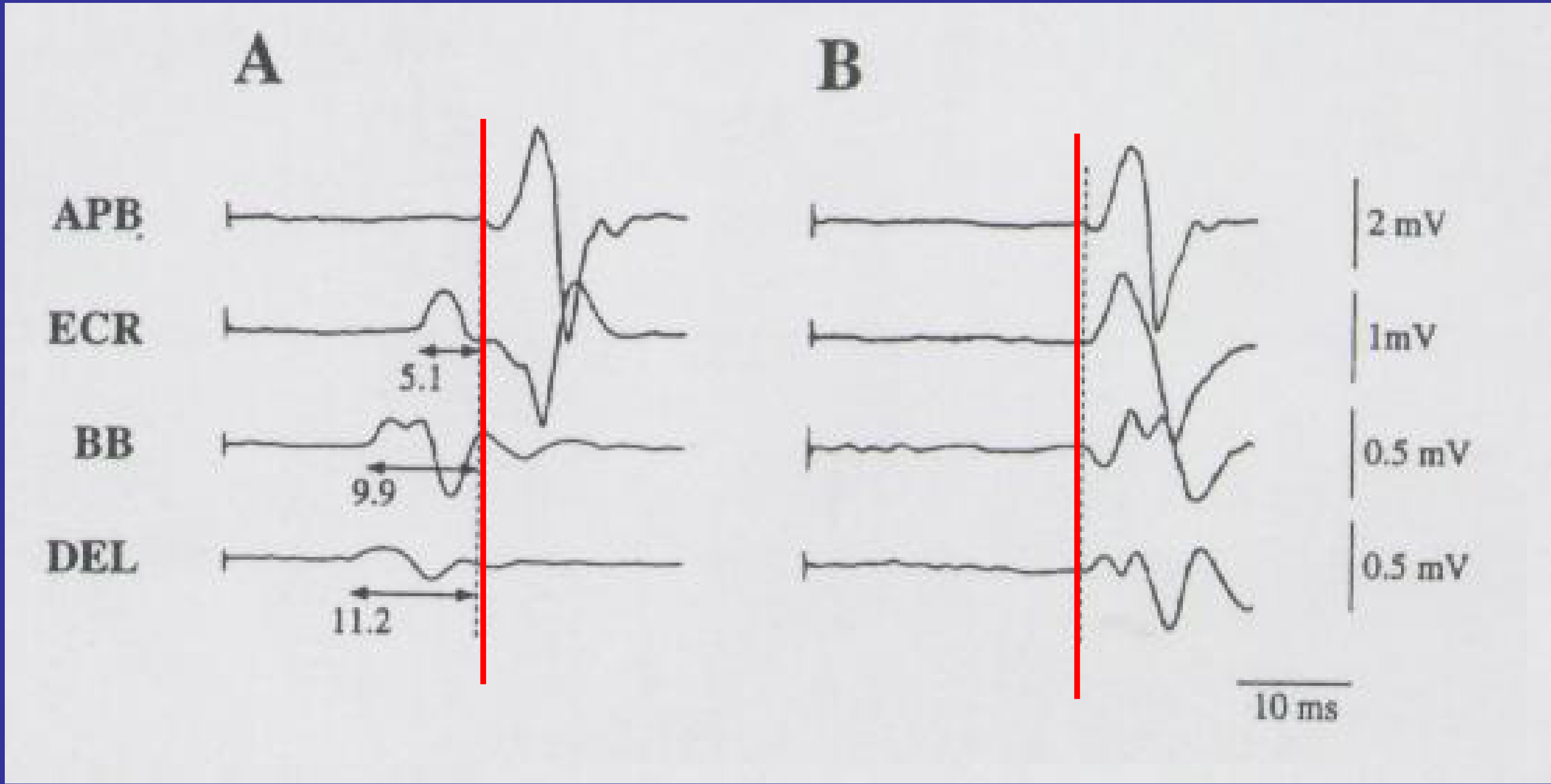
Extra discharges after rTMS on motor areas



Spread during and after rTMS



Aumento dell'eccitabilità durante rTMS ad alta frequenza la diffusione su ouput motori non contigui: SPREAD

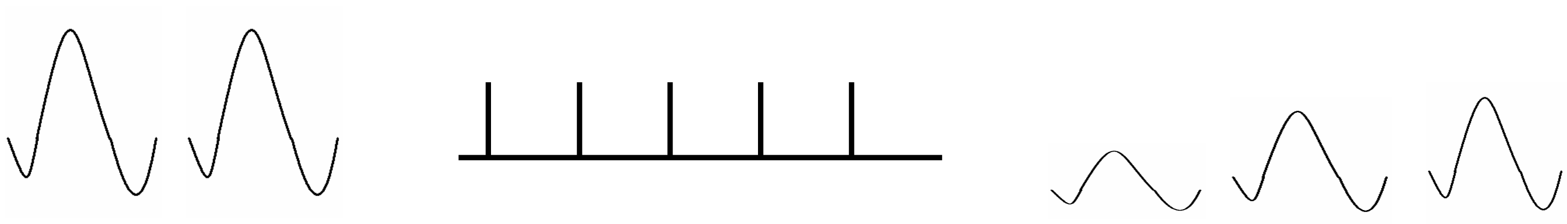


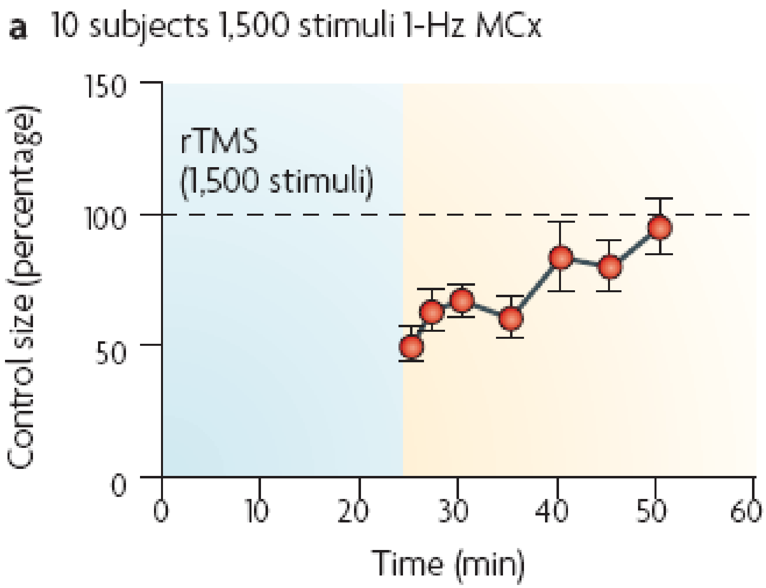
Sincronizzazione delle latenze dopo stimolazione 5 Hz (150%) tra muscoli distali e prossimali

Meccanismi della modulazione dell'eccitabilità corticale

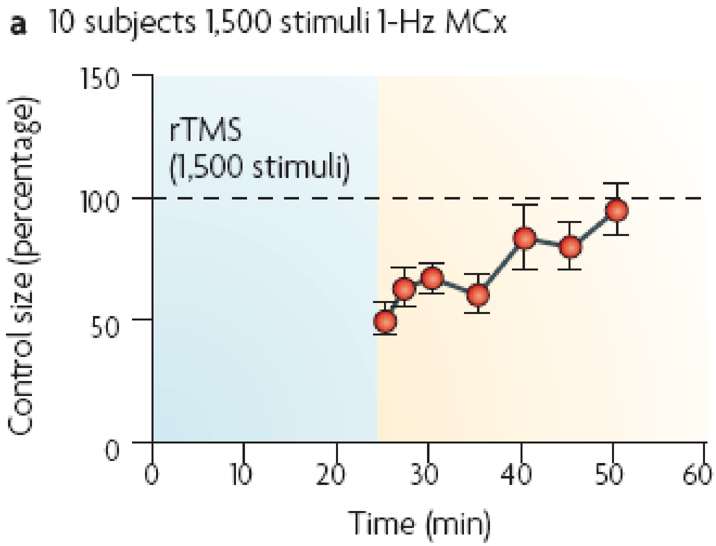
1. Long-term potentiation (facilitazione, >5 Hz)
2. Long-term depression (inibizione, < 1Hz)
3. Long-term depotentiation ? (normalizzazione,< 1Hz)
4. Modificazione dei neurotrasmettitori (↑dopamina)
5. Modificazione del metabolismo

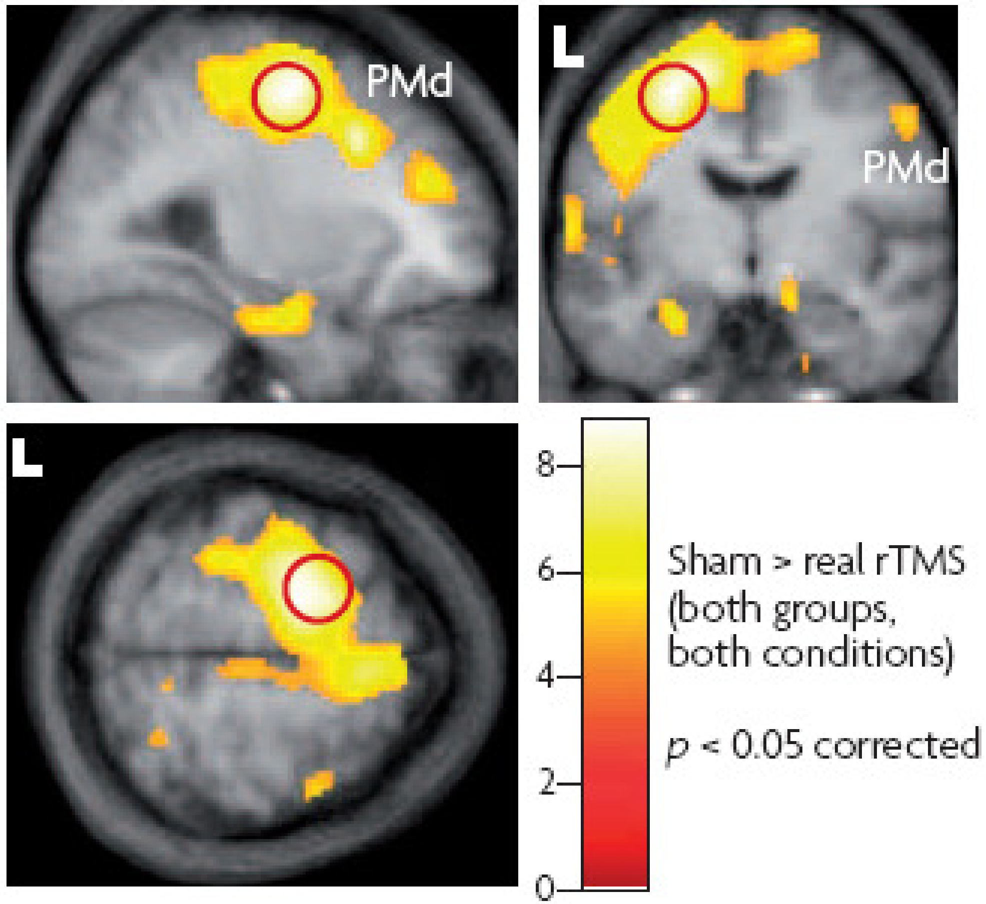
Decrease in mep amplitude after 1 Hz rTMS



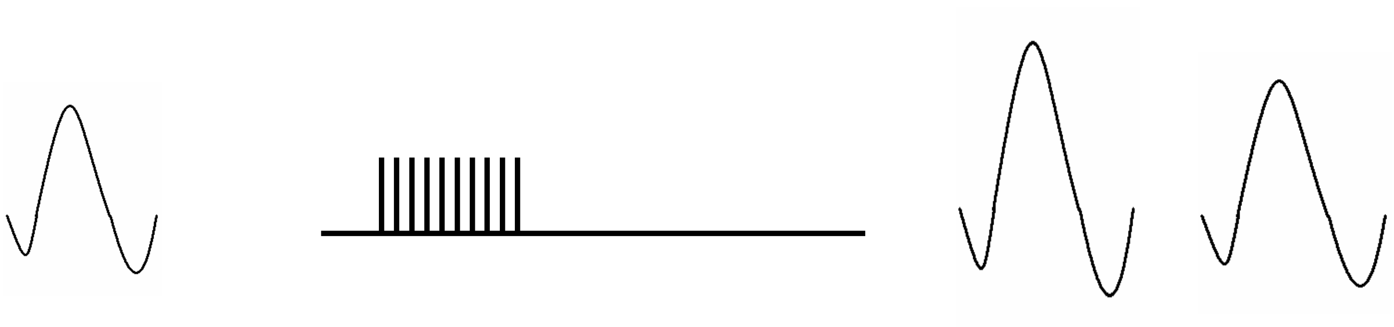


DORSAL PREMOTOR CORTEX 1 HZ RTMS DECREASE OF PET METABOLIC ACTIVITY

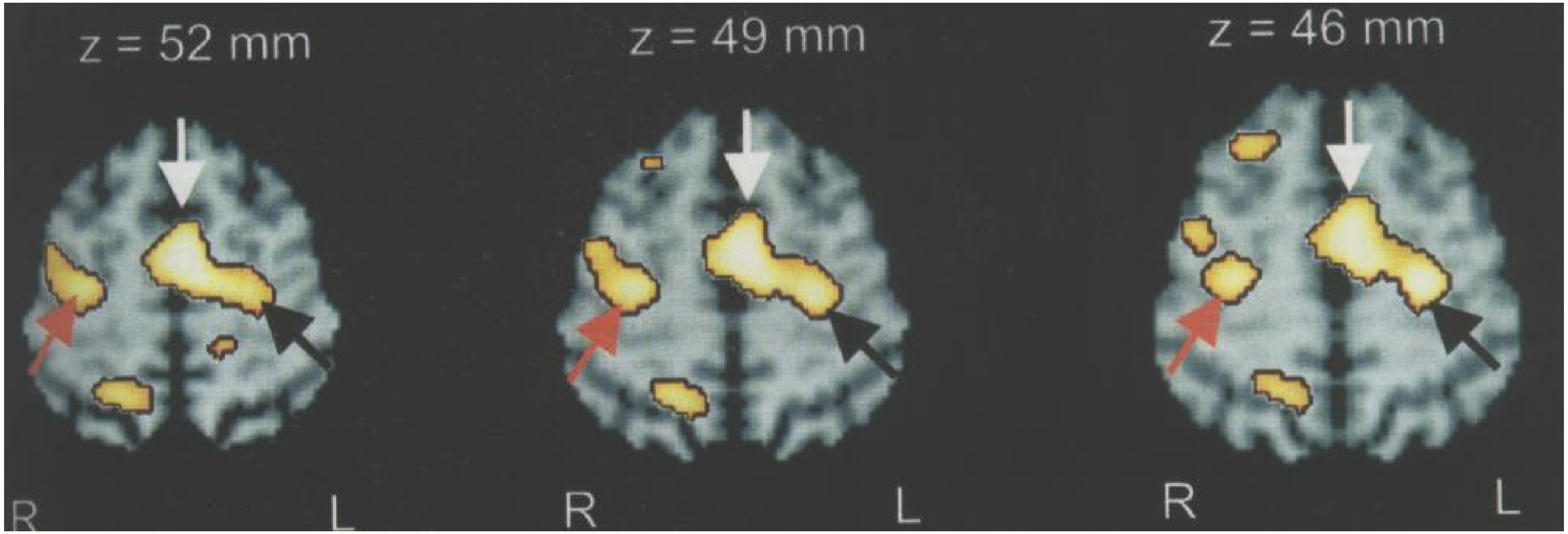




Increase MEP amplitude during and after high frequency rTMS



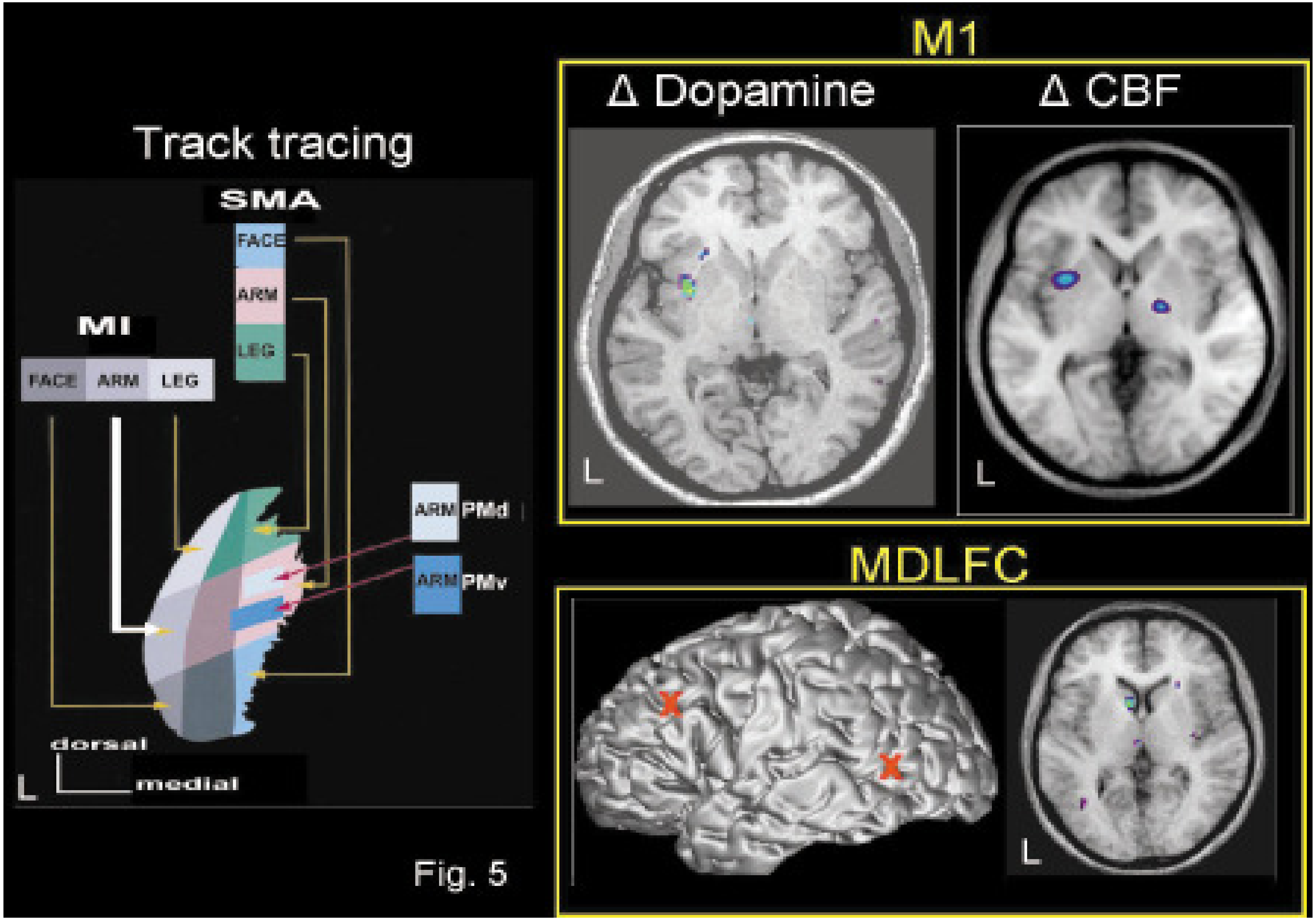
EFFETTO DELLA STIMOLAZIONE RIPETITIVA 5 HZ E NEUROIMAGING FUNZIONALE : STUDI PET
EFFETTO SU AREE LONTANE



AUMENTO DEL METABOLISMO DEL GLUCOSIO A LIVELLO DELL'AREA MOTORIA PRIMARIA E DELLA SUPPLEMENTARE MOTORIA DOPO 5 Hz

EFFETTO PIU' GRANDE PIU' LUNGA E' LA DURATA DEI TRENI DI STIMOLO

Siebner et al 2000 Neurology

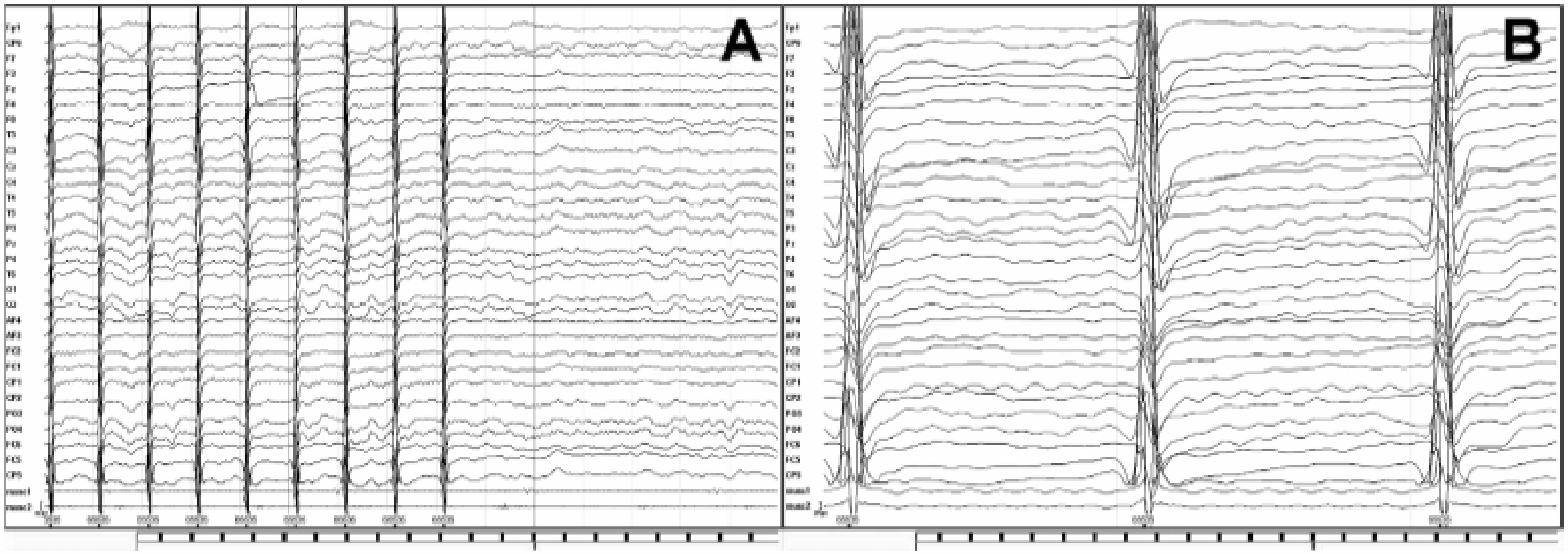


PAUS STRAFELLA 2001

Acute Modulation of Cortical Oscillatory Activities During Short Trains of High-Frequency Repetitive Transcranial Magnetic Stimulation of the Human Motor Cortex: A Combined EEG and TMS Study

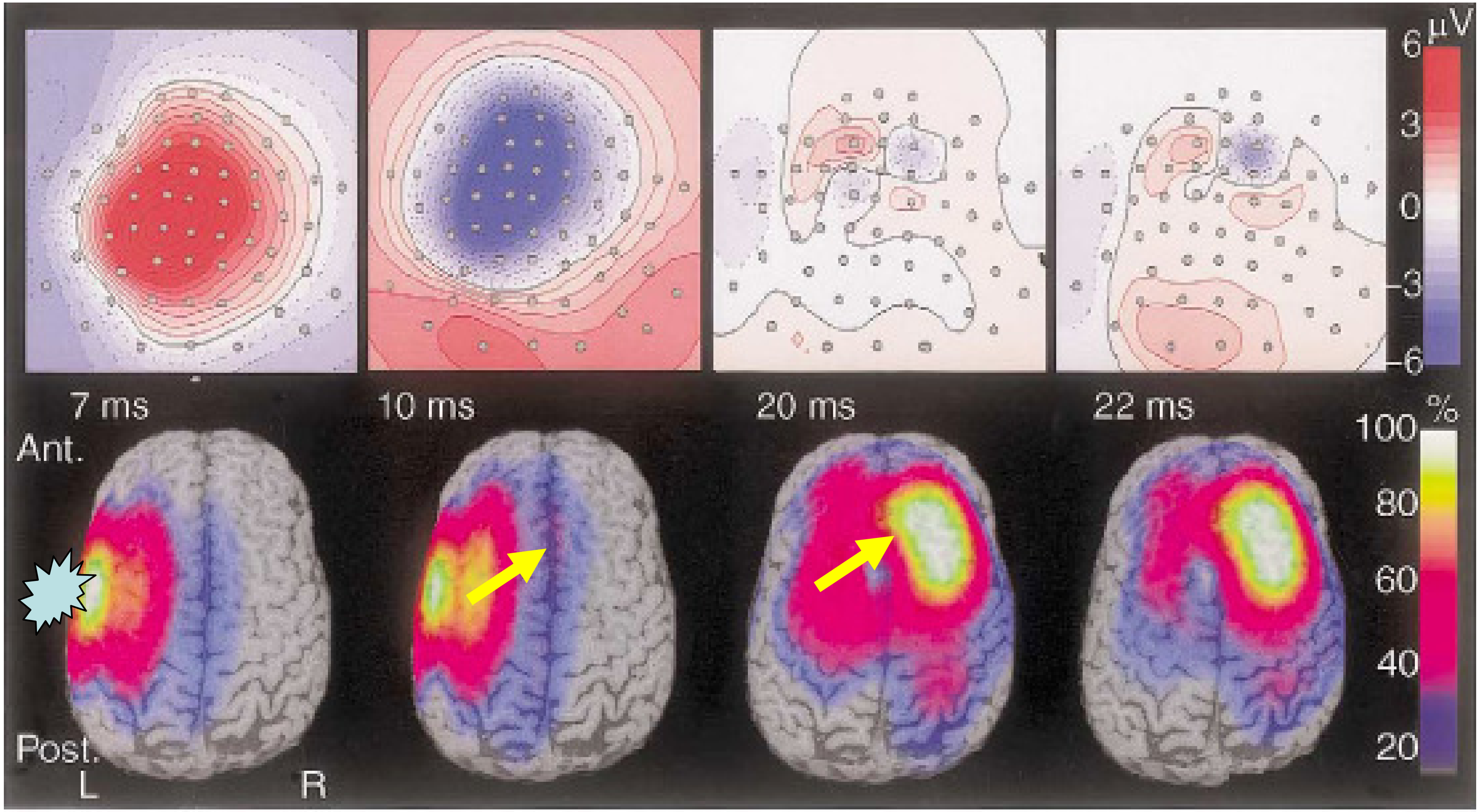
Giorgio Fuggetta,* Enea F. Pavone, Antonio Fiaschi, and Paolo Manganotti

Section of Neurological Rehabilitation, Department of Neurological and Visual Sciences, University of Verona, Verona 37134, Italy



Ipsi- and contralateral EEG reactions to transcranial magnetic stimulation☆

Soile Komssi[a,b,c,d,e], Hannu J. Aronen[b,c,e,f,*], Juha Huttunen[c,e,g], Martti Kesäniemi[c,j], Lauri Soinne[h], Vadim V. Nikouline[c,e], Marko Ollikainen[c,j], Risto O. Roine[h], Jari Karhu[c,i,j], Sauli Savolainen[b,d], Risto J. Ilmoniemi[c,e]



- VARIABILITY OF RTMS EFFECTS

- ANATOMICAL
- INTRINSIC EXCITABILITY
- HORMONES LEVELS (IN FEMALES)
- GENETIC FACTORS (BDNF)
- DRUGS

ELSEVIER

Clinical Neurophysiology 115 (2004) 1063–1068

www.elsevier.com/locate/clinph

Ovarian hormones and cortical excitability. An rTMS study in humans

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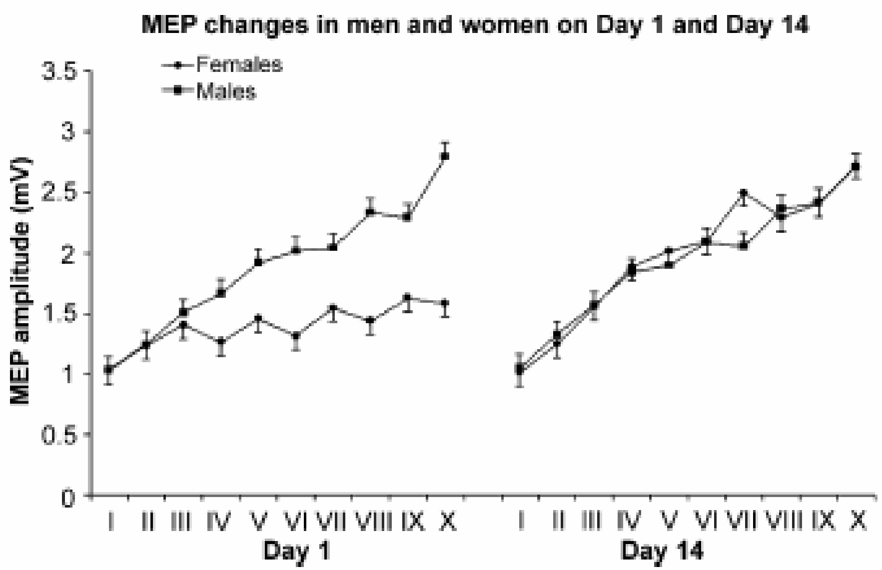
Accepted 5 December 2003



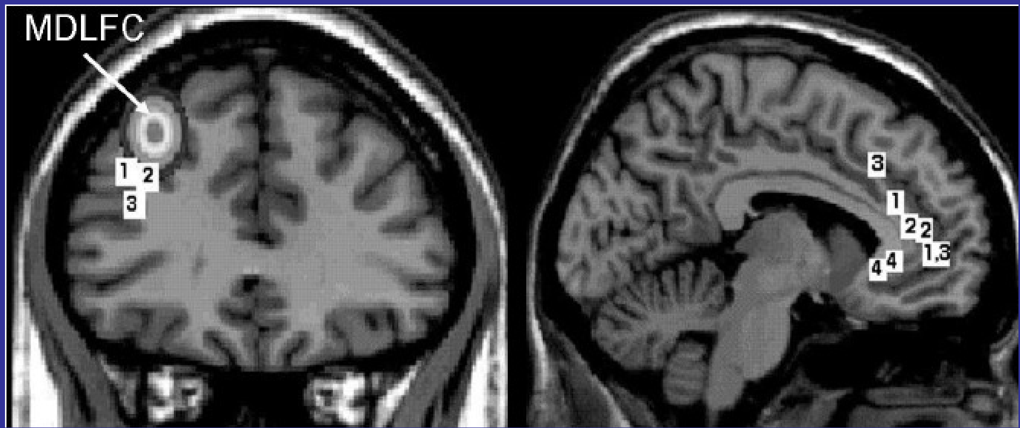
Pharmocological treatement:

- Level of drug induce inhibitory –facilitaroy effects (valproate)
- Parkinson rtms facilitation lost without dopa
- Dextro amphetamine effect on rtms

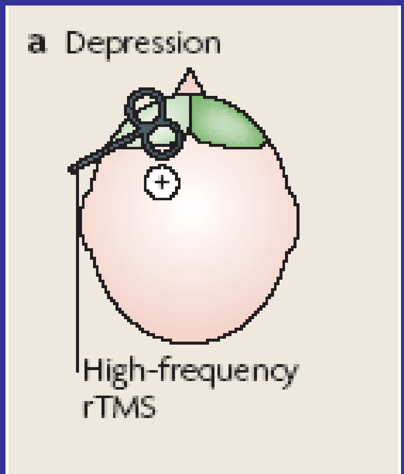
CRSN Symposium: Focus on Depression, Part II
Symposium du CRSN : le point sur la dépression, deuxième partie

Transcranial magnetic stimulation (TMS) of the human frontal cortex: implications for repetitive TMS treatment of depression

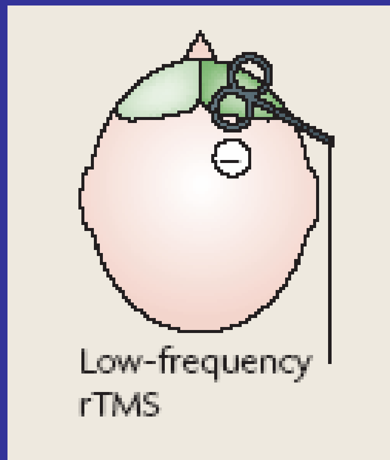
Tomáš Paus, MD, PhD; Jennifer Barrett, PhD



Hypometabolism and hypofunction
Left frontal lobes



FACILITATION
ON LEFT



INHIBITION
ON RIGHT

CRSN Symposium: Focus on Depression, Part II
Symposium du CRSN : le point sur la dépression, deuxième partie

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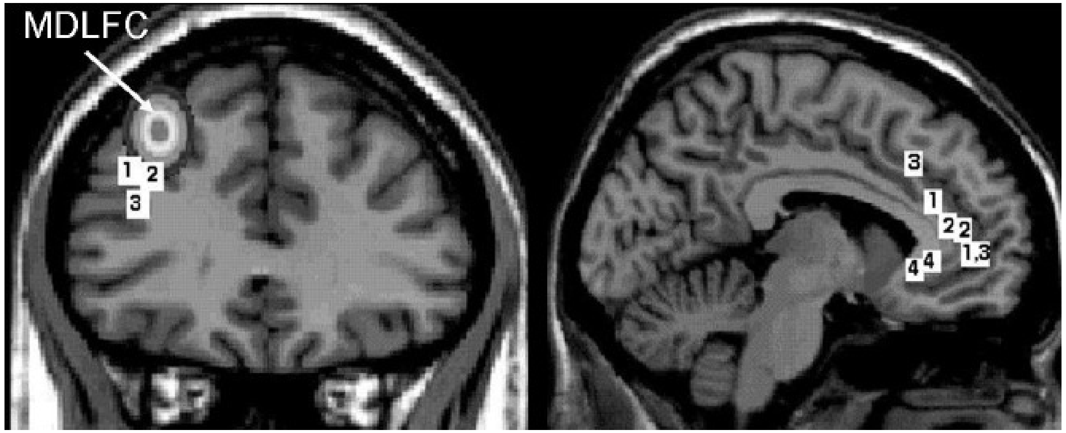
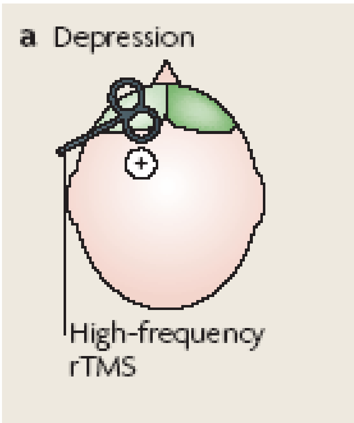
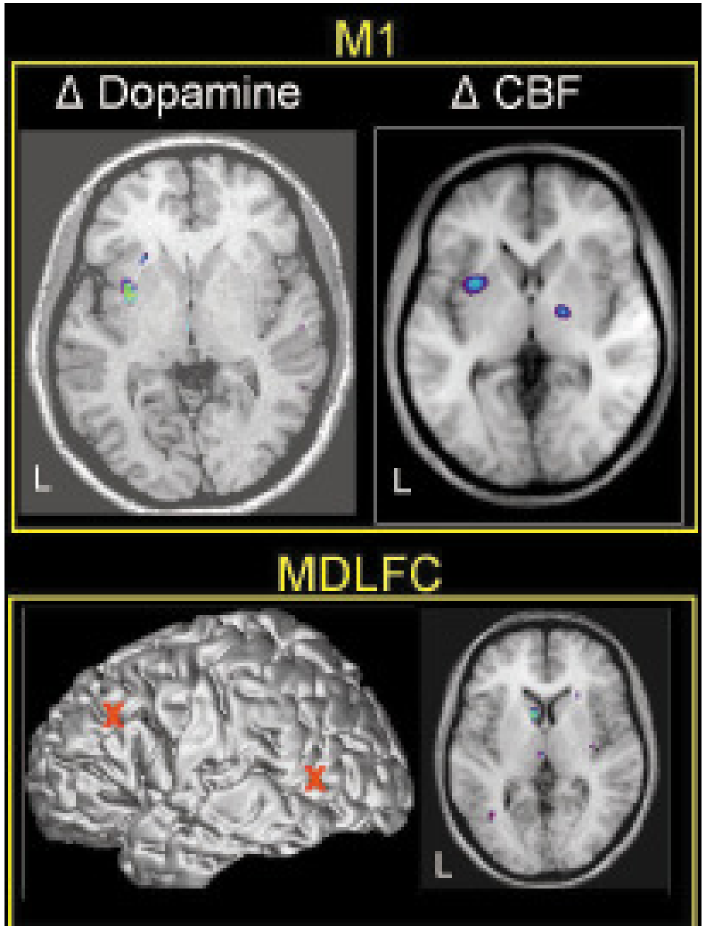
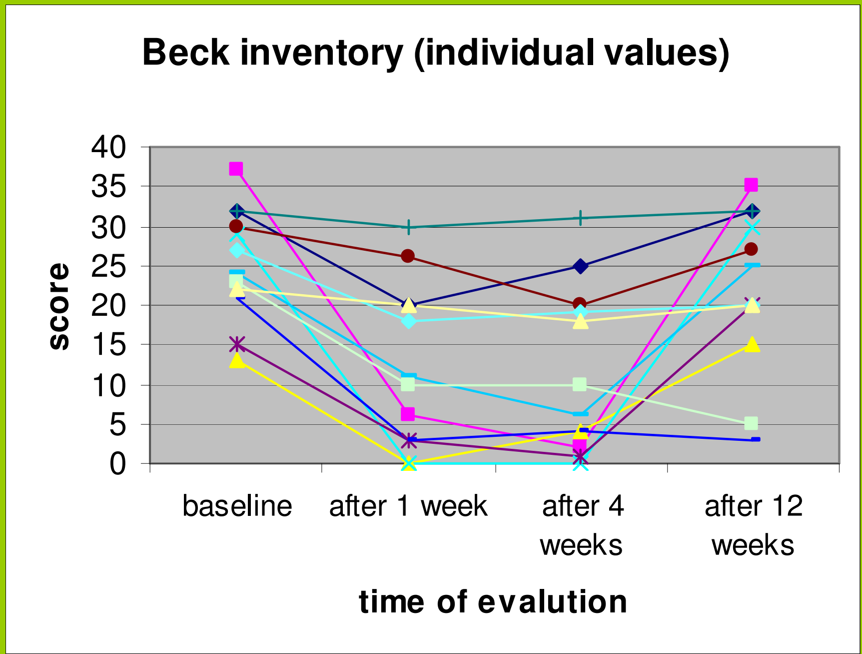


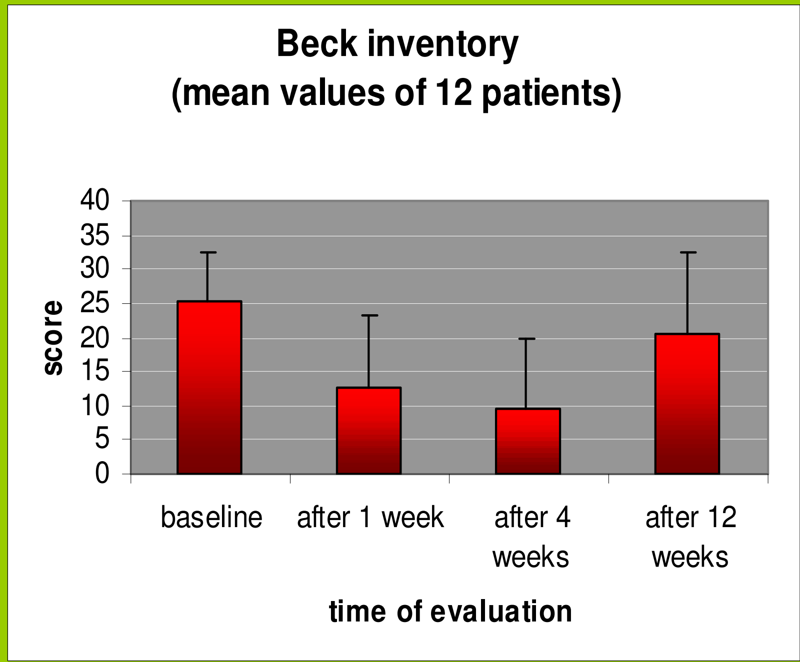


High frequency
On left frontal lobe



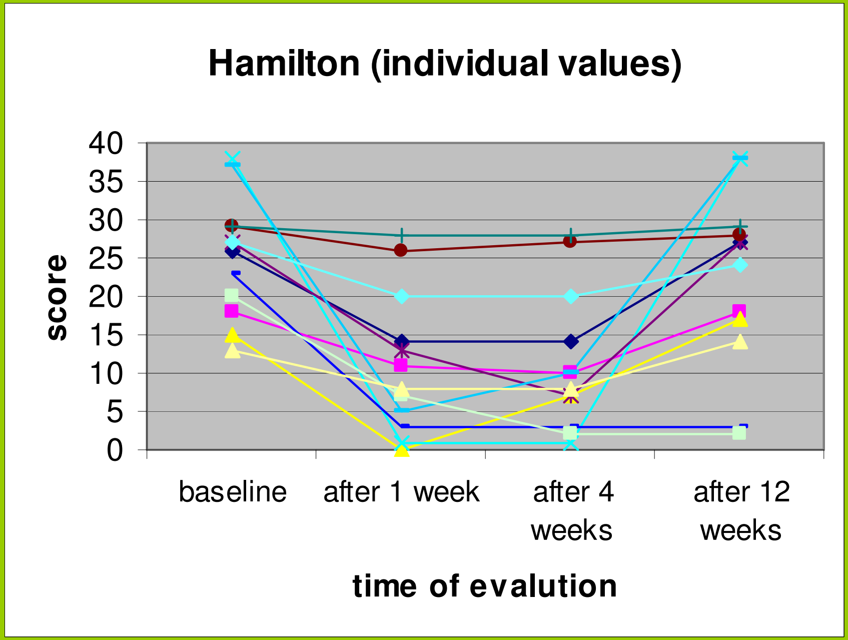
RISULTATI GRUPPO TRATTATO: 8/12 PAZIENTI HANNO MOSTRATO UN SIGNIFICATIVA (P <0.01) RIDUZIONE DELLO SCORE ALLA BDI DELLA DURATA DI UN MESE

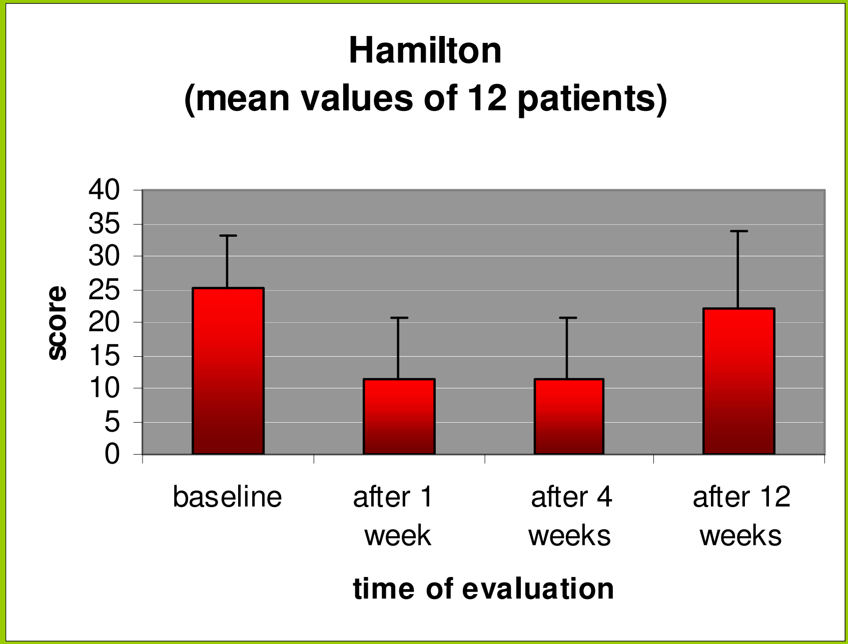




BORTOLOMASI M., MINELLI A. MANGANOTTI P. 2007

RISULTATI GRUPPO TRATTATO: 8/12 PAZIENTI HANNO MOSTRATO UN SIGNIFICATIVA (P <0.01) RIDUZIONE DELLO SCORE ALLA HDRSS DELLA DURATA DI UN MESE





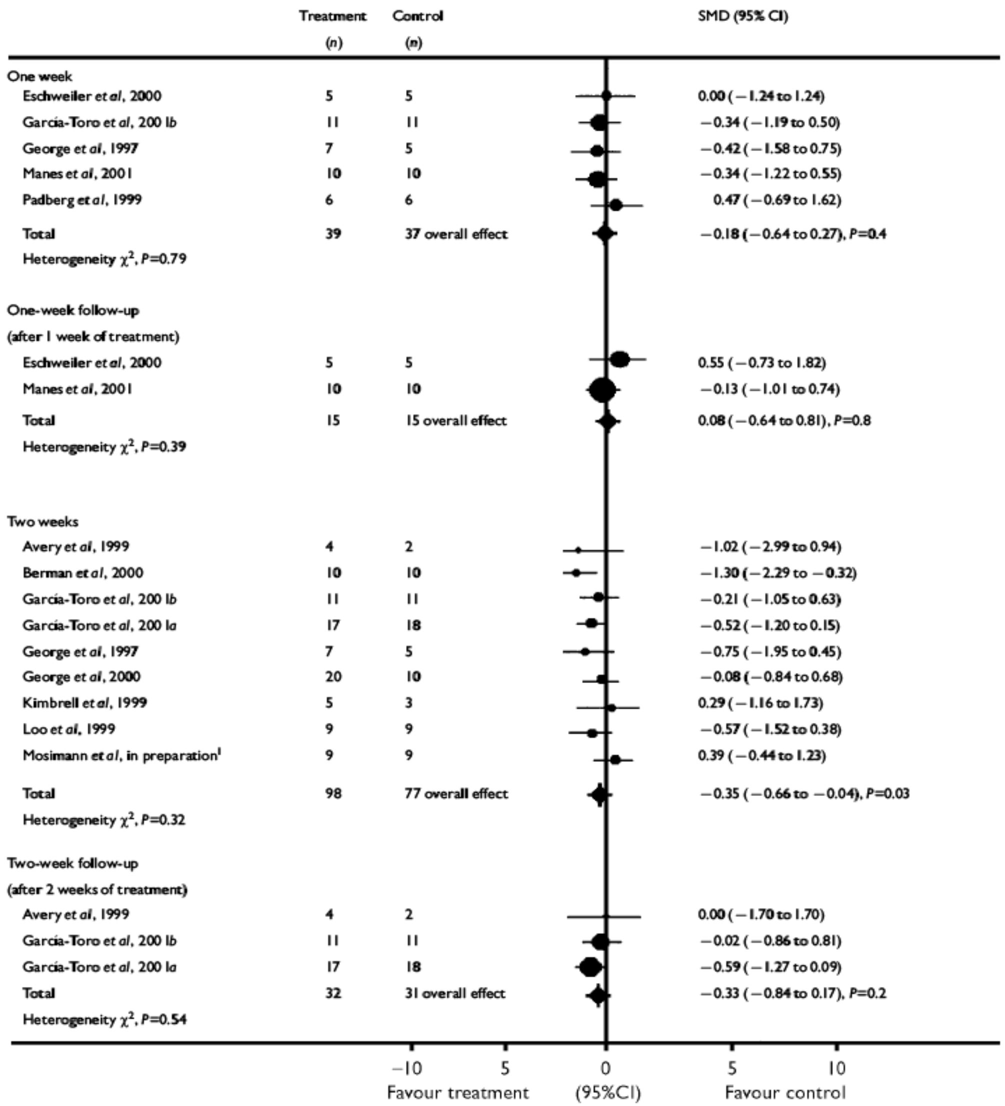
BORTOLOMASI M., MINELLI A. MANGANOTTI P. 2007

BRITISH JOURNAL OF PSYCHIATRY (2003), 182, 480–491

Repetitive transcranial magnetic stimulation for the treatment of depression

Systematic review and meta-analysis

JOSÉ LUIS R. MARTIN, MANUEL J. BARBANOJ, THOMAS E. SCHLAEPFER, ELINOR THOMPSON, VÍCTOR PÉREZ and JAIME KULISEVSKY



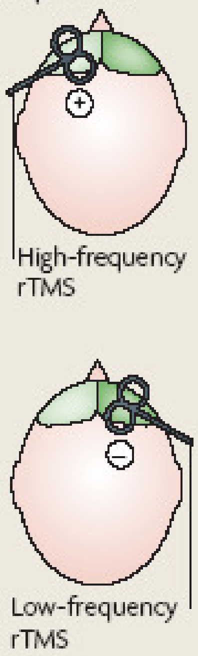
Nature july 2007

OPINION

Is there a future for therapeutic use of transcranial magnetic stimulation?

Michael C. Ridding and John C. Rothwell

a Depression



Meta-analysis	Number of studies included	rTMS approach	Outcome measure	Analysis conclusions
Couturier[2]	6	Randomized sham-controlled trials using LDLPFC rTMS	Change in HAM-D	Suggests rTMS no better than sham
Martin *et al.*[3]	14	Most (13 out of 14 studies) used high frequency LDLPFC and sham control	Change in HAM-D (in all studies) and BDI (7 studies)	Real rTMS significantly greater effect than sham on HAM-D when applied for 2 weeks (but not 1 week) No significant difference for BDI
Kozel and George[4]	12	Randomized sham-controlled trials involving LDLPFC rTMS	Change in HAM-D	Real rTMS led to small but significantly greater effect than sham
Burt *et al.*[6]	16	Randomized controlled (sham or other control) trials predominantly involving LDLPFC/RDLPFC*	Change in HAM-D	Real rTMS significantly better than sham Improvement in HAM-D of ~20% Doubtful clinical significance
Holtzheimer *et al.*[45]	12	Most (11/12) used LDLPFC and sham control	Change in HAM-D	Real rTMS significantly better than sham However, clinical significance considered only modest

Acta Psychiatr Scand 2007: 116: 165–173

DOI: 10.1111/j.1600-0447.2007.01049.x

ACTA PSYCHIATRICA SCANDINAVICA

Review

Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies

Gross M, Nakamura L, Pascual-Leone A, Fregni F. Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies.

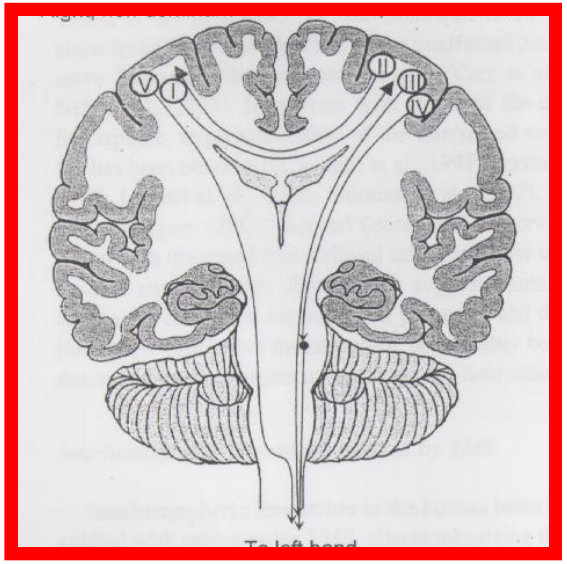
M. Gross[1], L. Nakamura[1], A. Pascual-Leone[2] F. Fregni[2]
[1]Department of Psychiatry, University of São Paulo, São Paulo, Brazil and [2]Center for Noninvasive Brain

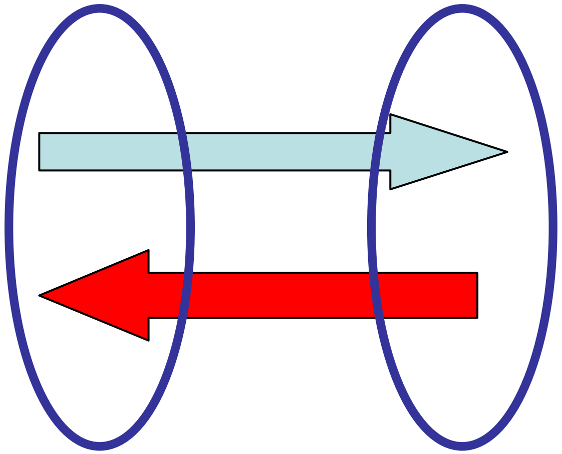
Summations

- The 10-year experience with rTMS for the treatment of major depression has optimized the parameters of stimulation, resulting in improved clinical effects of this technique.
- Recent rTMS trials used novel parameters of stimulation, such as more sessions of rTMS, and had better study designs with larger sample sizes.
- Our findings showing that the recent TMS trials had larger effect sizes when compared with the earlier rTMS studies give additional support for the antidepressant effects of rTMS.

Acta Psych Scandinavica 2007

THE INTERACTION MODEL AND MOTOR STROKE





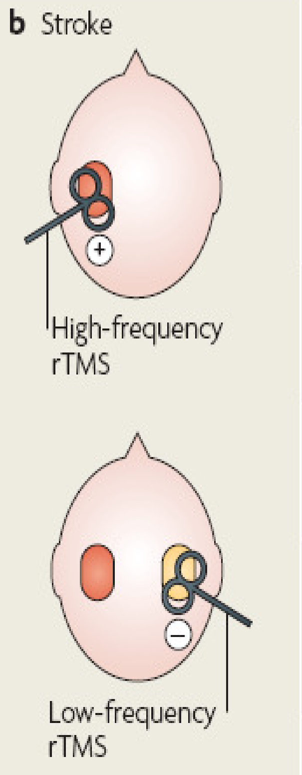
Ridotta inibizione
TRANSCALLOSALE
(sbilanciamento dinamico)

DIASCHISI

VIE IPSILATERALI

AUMENTO DELL'ECCITABILITA' LATO SANO

THE INTERACTION MODEL AND MOTOR STROKE



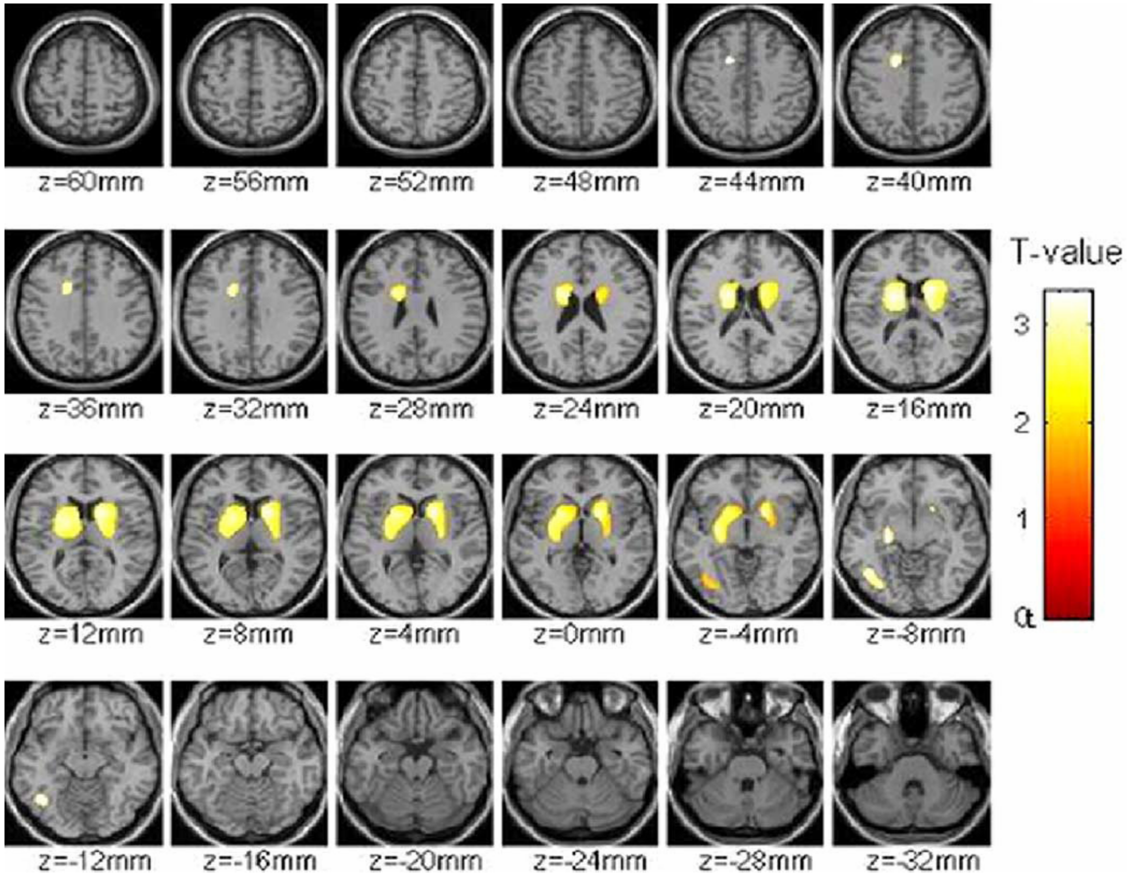
Study	Number of patients	rTMS approach	Functional outcome measures	Results
Mansur *et al.*[83]	8 (< 1 year after stroke)	600 pulses at 1 Hz to contralesional motor cortex	SRT, CRT, PPT, finger tapping speed	M1 stimulation significantly improved performance on RT and PPT
Takeuchi *et al.*[62]	20 (>6 months after stroke) split into two groups, one receiving real rTMS and the other sham	1 Hz for 25 mins to contralesional motor cortex	Pinch task	Real rTMS improved pinch acceleration of affected hand
Fregni *et al.*[55]	15 (>1 year post stroke) randomized into real ($n = 10$) and sham ($n = 5$) groups	5 sessions over 5 days of 1 Hz; 1,200 pulses to contralesional M1	JTT, PTT, SRT and CRT	Improvement on all functional measures for affected hand that lasted for 2/52
Khedr *et al.*[54]	52 (5–10 days post stroke) randomized into real ($n = 26$) and sham ($n = 26$) groups	10 × 10-sec 3-Hz trains for 10 days	SSS, NIHSS and BI	Real rTMS resulted in significantly greater improvements on all measures
Talelli *et al.*[61]	6 (>1 year post stroke)	Excitatory TBS to lesioned M1 or inhibitory TBS to contralesional M1	SRT, CRT and GS	Inhibitory TBS to contralesional hemisphere improved SRT in affected hand

The Journal of Neuroscience, June 14, 2006 • 26(24):6583–6588 • 6583

Brief Communications

Cocaine Cues and Dopamine in Dorsal Striatum: Mechanism of Craving in Cocaine Addiction

Nora D. Volkow,[1] Gene-Jack Wang,[2] Frank Telang,[1] Joanna S. Fowler,[3] Jean Logan,[3] Anna-Rose Childress,[4] Millard Jayne,[1] Yeming Ma,[1] and Christopher Wong[3]
[1]National Institute on Alcohol Abuse and Alcoholism, Bethesda Maryland 20892, [2]Medical Department and [3]Department of Chemistry, Brookhaven National Laboratory, Upton, New York 11973, and [4]Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104



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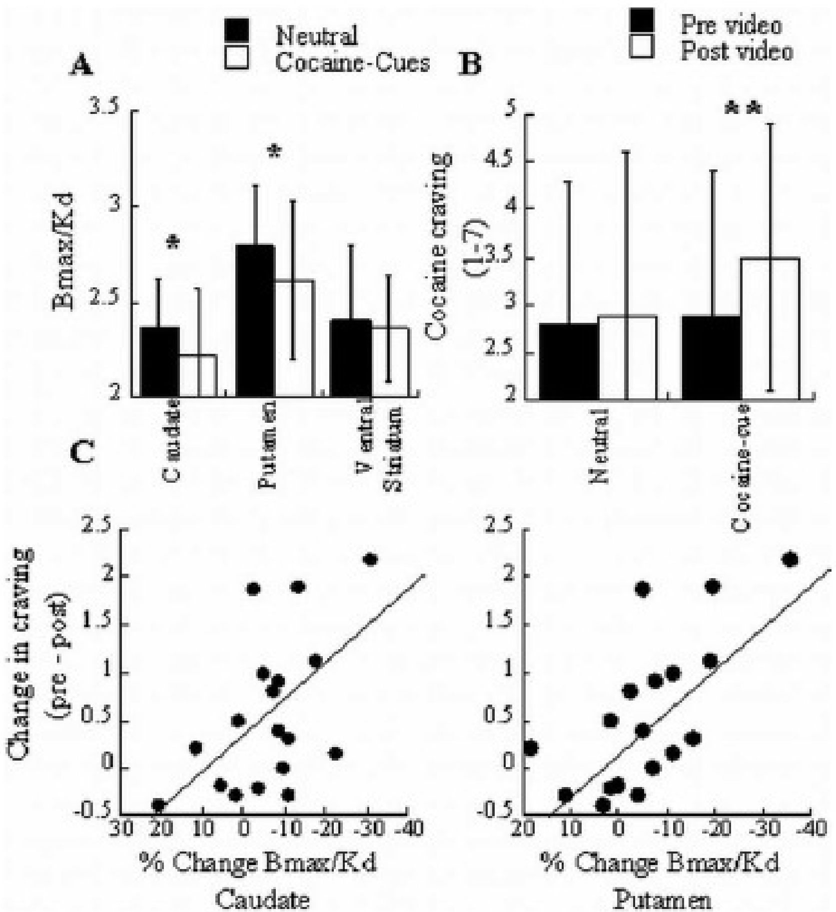
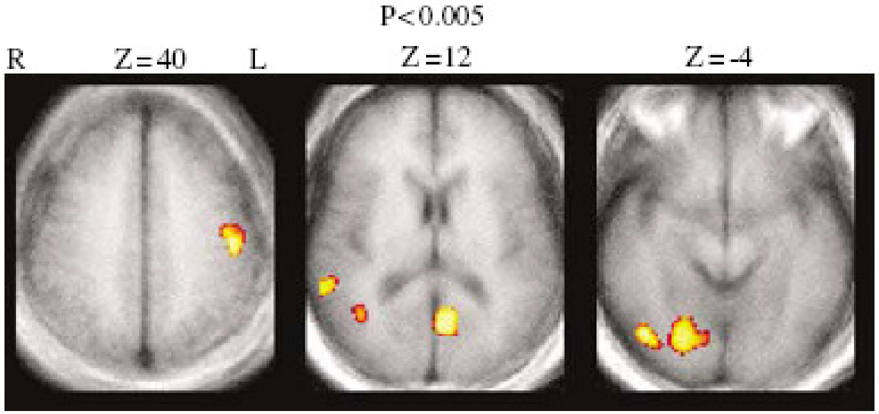


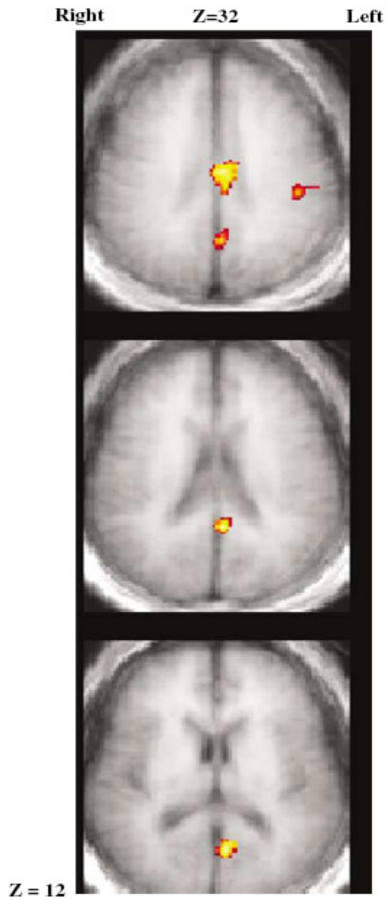
Neuropsychopharmacology (2006) 31, 644–650
 0893-133X/06 $30.00
www.neuropsychopharmacology.org

Cue-Induced Brain Activity Changes and Relapse in Cocaine-Dependent Patients

Thomas R Kosten*[,1], Barbara Ellen Scanley[2], Karen A Tucker[1], Alison Oliveto[1,3], Chekema Prince[4], Rajita Sinha[2], Marc N Potenza[2], Pawel Skudlarski[5] and Bruce E Wexler[2]

[1]Department of Psychiatry, Yale University School of Medicine, VA Connecticut Healthcare System, West Haven, CT, USA; [2]Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, CT, USA; [3]Department of Psychiatry, University of ... of Technology,





Increase brain activity
in cocaine dependent patients

Precentral gyrus
Posterior cingulate gyrus
Superior temporal gyrus
Inferiorior occipital gyrus
Lingual gyrus

Available online at www.sciencedirect.com
ScienceDirect
Drug and Alcohol Dependence 86 (2007) 91–94
DRUG and ALCOHOL DEPENDENCE
www.elsevier.com/locate/drugalcdep

Short communication

One session of high frequency repetitive transcranial magnetic stimulation (rTMS) to the right prefrontal cortex transiently reduces cocaine craving

Joan Albert Camprodon[a], José Martínez-Raga[b], Miguel Alonso-Alonso[a], Mei-Chiung Shih[c], Alvaro Pascual-Leone[a,*]

[a] *Center for Noninvasive Brain Stimulation, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, KS 452, Boston, MA 02215, USA*

[b] *Instituto de Drogas y Conductas Adictivas (IDYCA), Universidad Cardenal Herrera–CEU, Unidad de Conductas Adictivas Area 11, Agencia Valenciana de Salud, Spain*

[c] *Department of Biostatistics, Harvard School of Public Health and Clinical Research Program, Children's Hospital Boston, 333 Longwood Avenue, Boston, MA 02115, USA*

Received 26 March 2006; received in revised form 2 June 2006; accepted 7 June 2006

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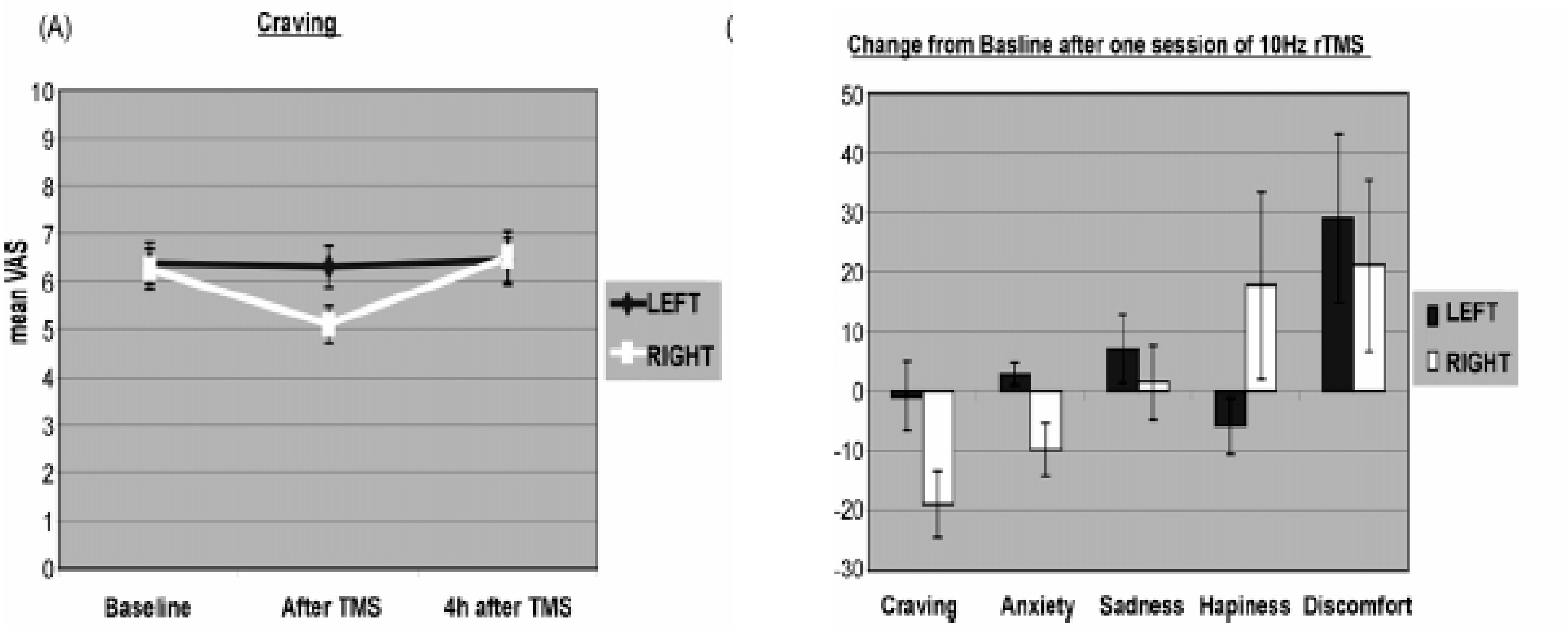


High frequency over RIGHT FRONTAL LOBES DECREASE CRAVING

SIX SUBJECTS CROSS OVER STUDY 20 TRENI 10 HZ DI 10 SECONDI

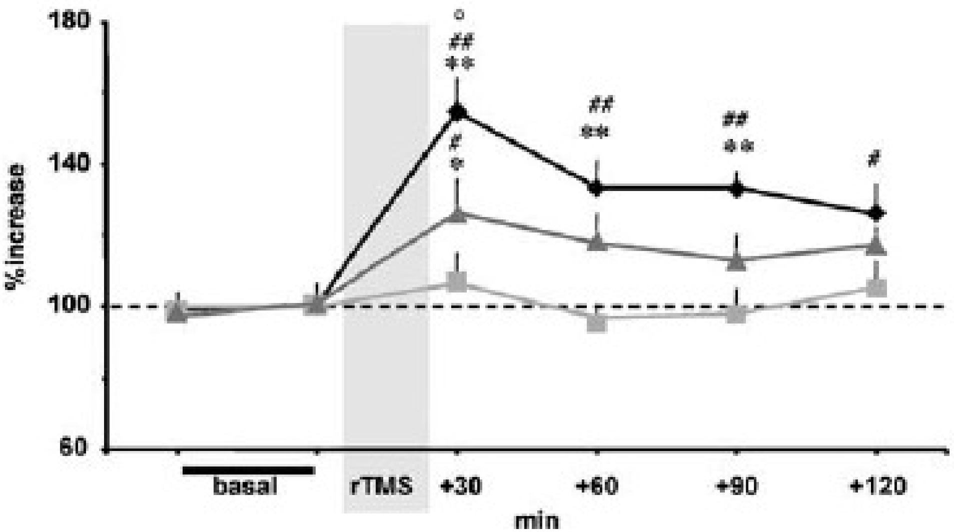
Neuropsychopharmacology (2004) 29, 2074–2080

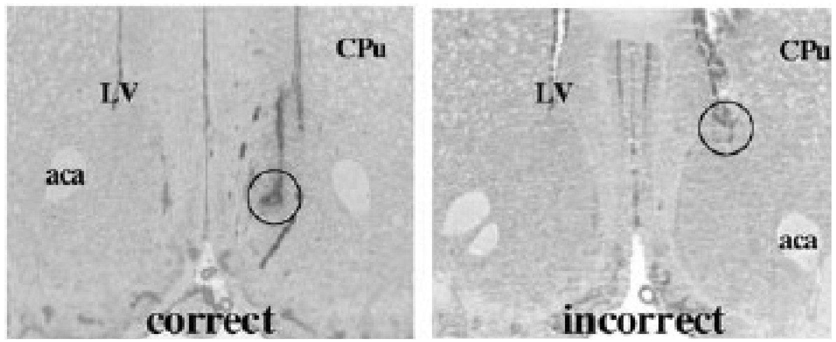
www.neuropsychopharmacology.org

Repetitive Transcranial Magnetic Stimulation Increases the Release of Dopamine in the Nucleus Accumbens Shell of Morphine-Sensitized Rats During Abstinence

A Erhardt[1], I Sillaber[1], T Welt[1], MB Müller[1], N Singewald[2] and ME Keck*[,1]

[1]Max Planck Institute of Psychiatry, Munich, Germany; [2]Department of Pharmacology and Toxicology, University of Innsbruck, Innsbruck, Austria





Microdialyisis in nucleus accumbens

Neuropsychopharmacology (2004) 29, 2074–2080
 0893-133X/04 $30.00
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- Withdrawal in rats with chronic drug abuse
- Is associate to decrease of dopamine in mesolimbic structures

- 10 Hz rtms induced release of dopamine in morphine sensitized rats

High frequency rtms decrease cigarette smoking
P. Eichhammer et al. 2003

J Clin Psychiatry 64; 951-953

- Rtms over the left frontal lobe decrease smoking craving
- Reduced number of sigarettes
- Sham condition
- Vas and number of cigarette

Johan et al. Psych prax 2003 11 patients with similar results

Rtms and craving

- The craving induces metabolic and neurotrasmitter changes
- The hypothesis that Rtms can induce transitory changes in dopamine and excitability in patients can be plausible
- Cross over and sham studies on patients are necessary

Summary

- Rtms is a real instrument of brain stimulation not a placebo brain stimulation
- Safety criteria should be respected
- Terapeutical protocols need a congruent hypothesis (Ridding and Rothwell 2007)
- Transitory effects can be useful and different therapies can be combined