Applications of TMS in Neuroscience Research and Clinical Practice

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contacts :: Carmelo Vicario

The main non-invasive brain stimulation methods

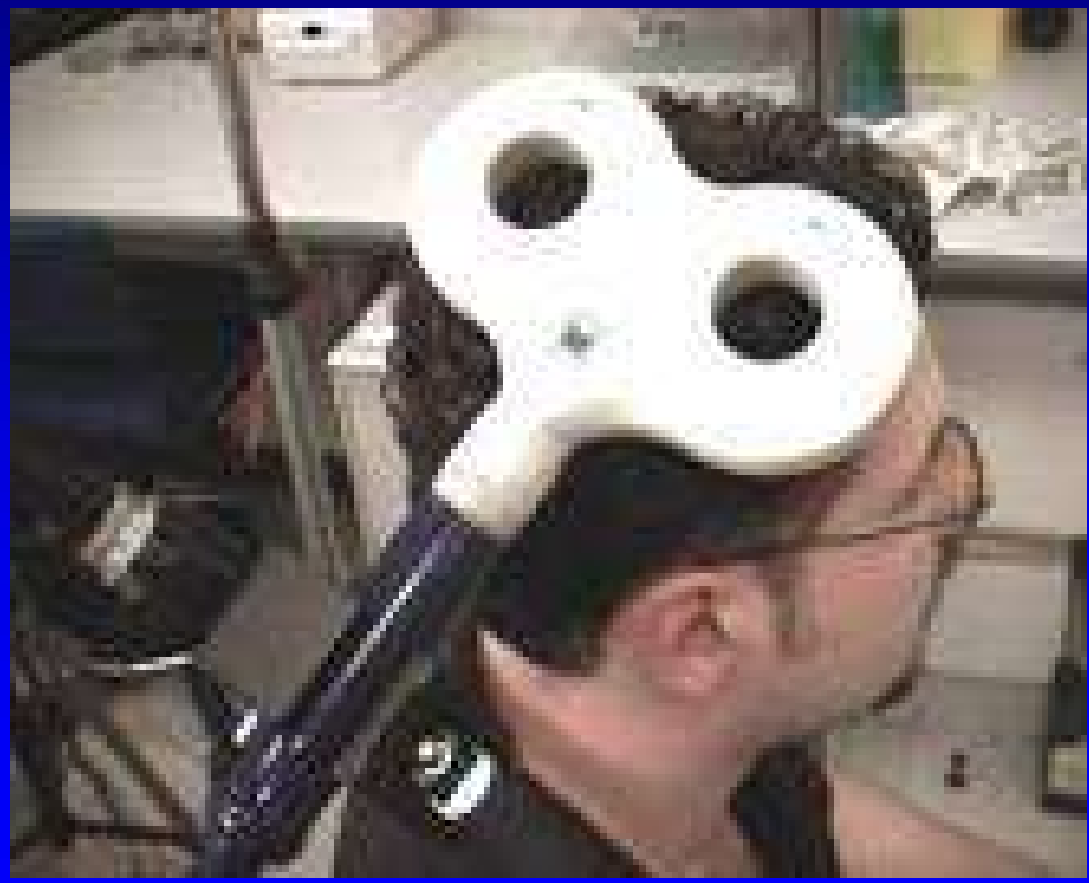
Fields of application:

- **Basic research** (e.g., the study of cognitive and affective processes)
- **Clinical** (neurological / psychiatric treatment through the modulation of neuroplasticity processes and diagnostic applications).

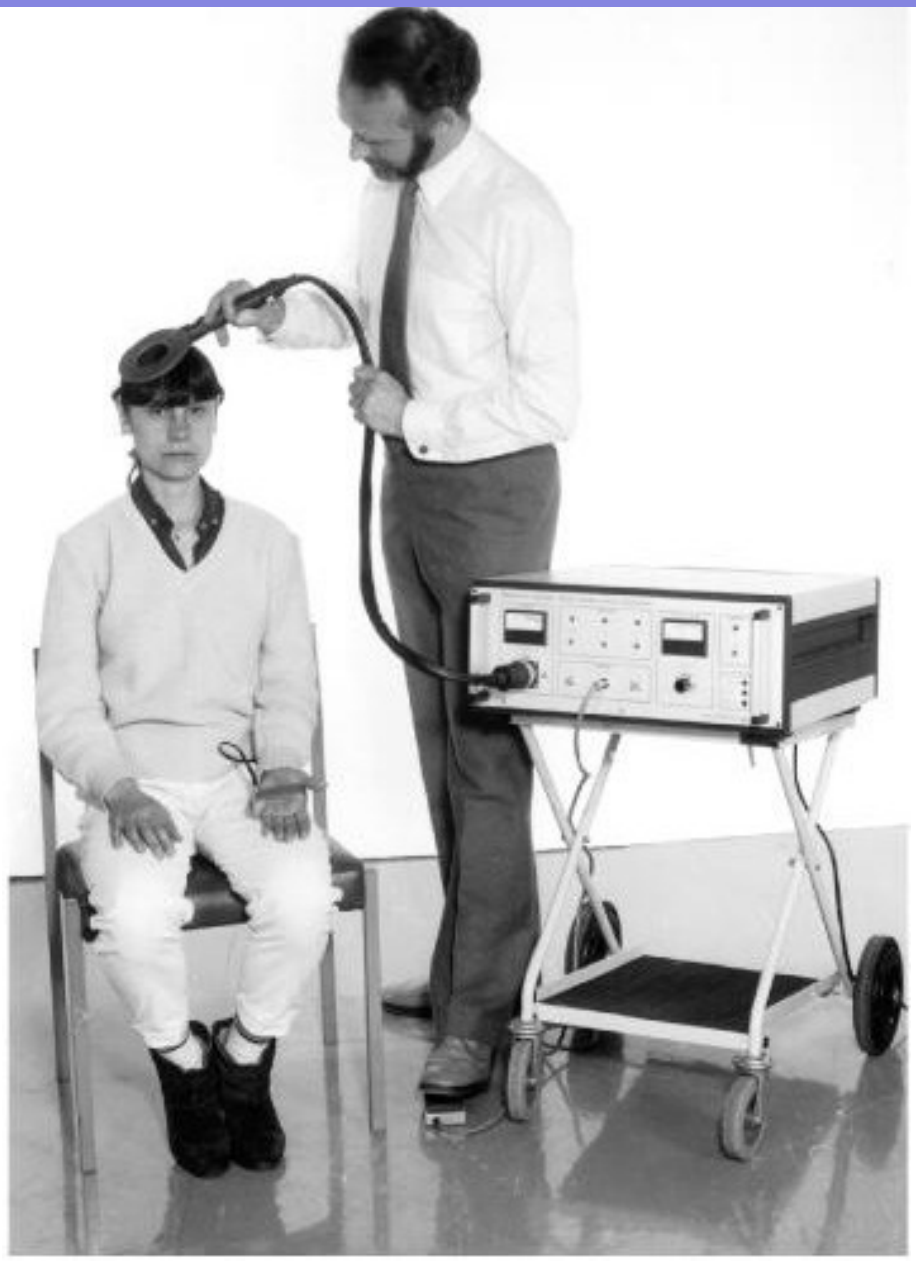
TMS

tES

Transcranial Magnetic Stimulation (TMS)



BARKER INTRODUCED THE MODERN TMS



Barker (1984)

Magnetic stimulation of M1

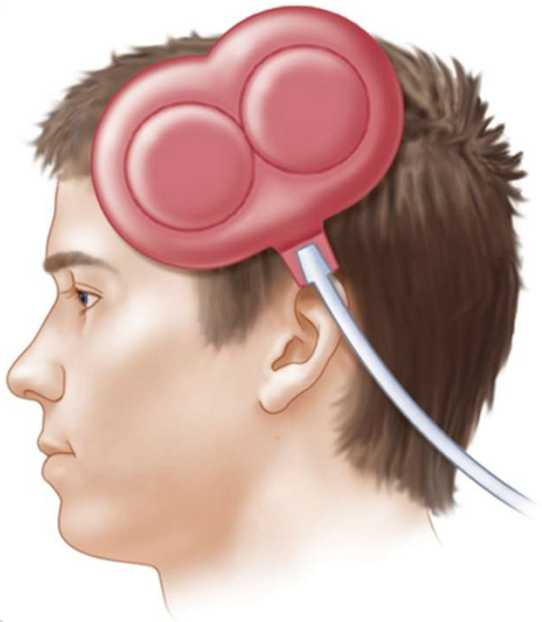
He showed that a short and intense magnetic field (1-3 Tesla, 100-200 ms) evokes fingers movements.

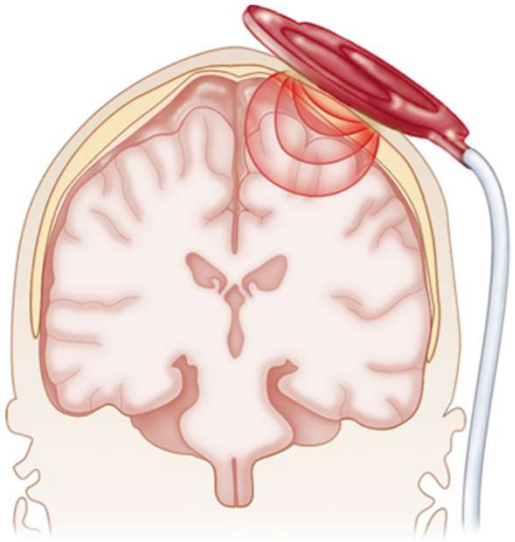
What is TMS?

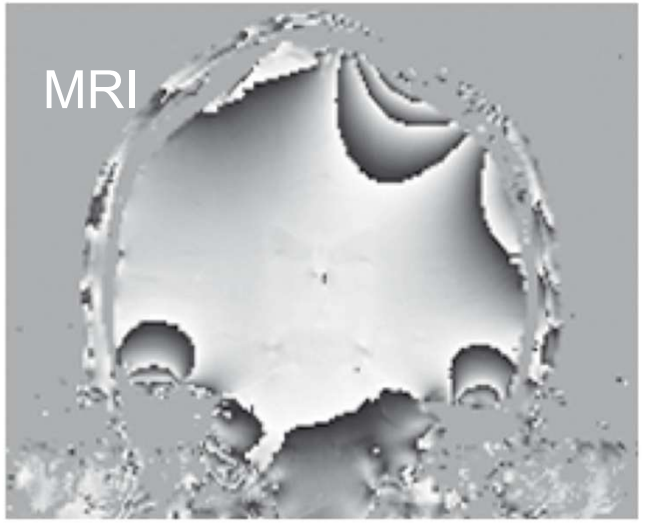
A non-invasive neurophysiological technique that allows to stimulate specific brain areas.

It is based on the application of a transient magnetic field on the scalp using a stimulator (called coil).

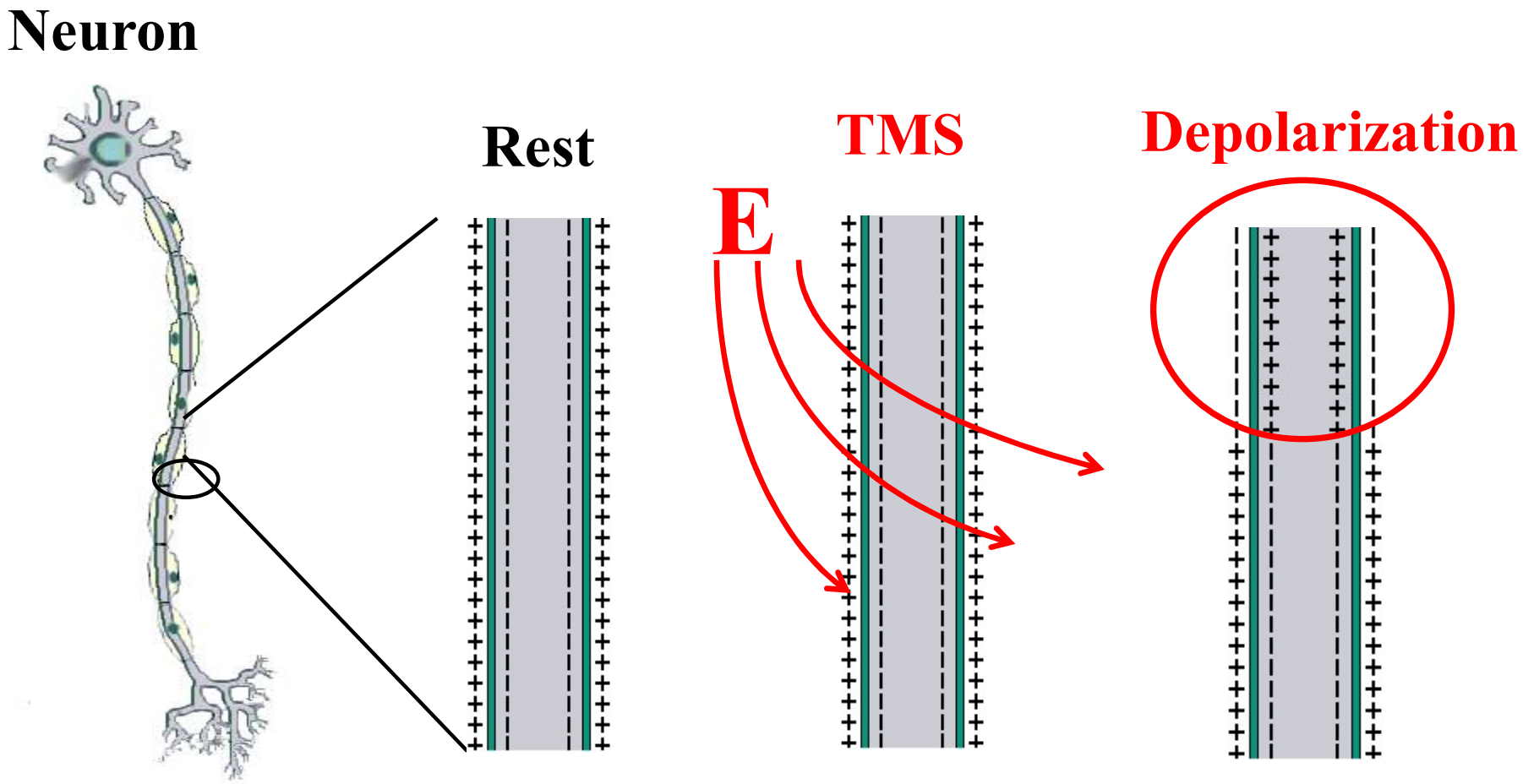
The neural tissue underlying the coil is subject to a current flow that causes neuronal depolarization.







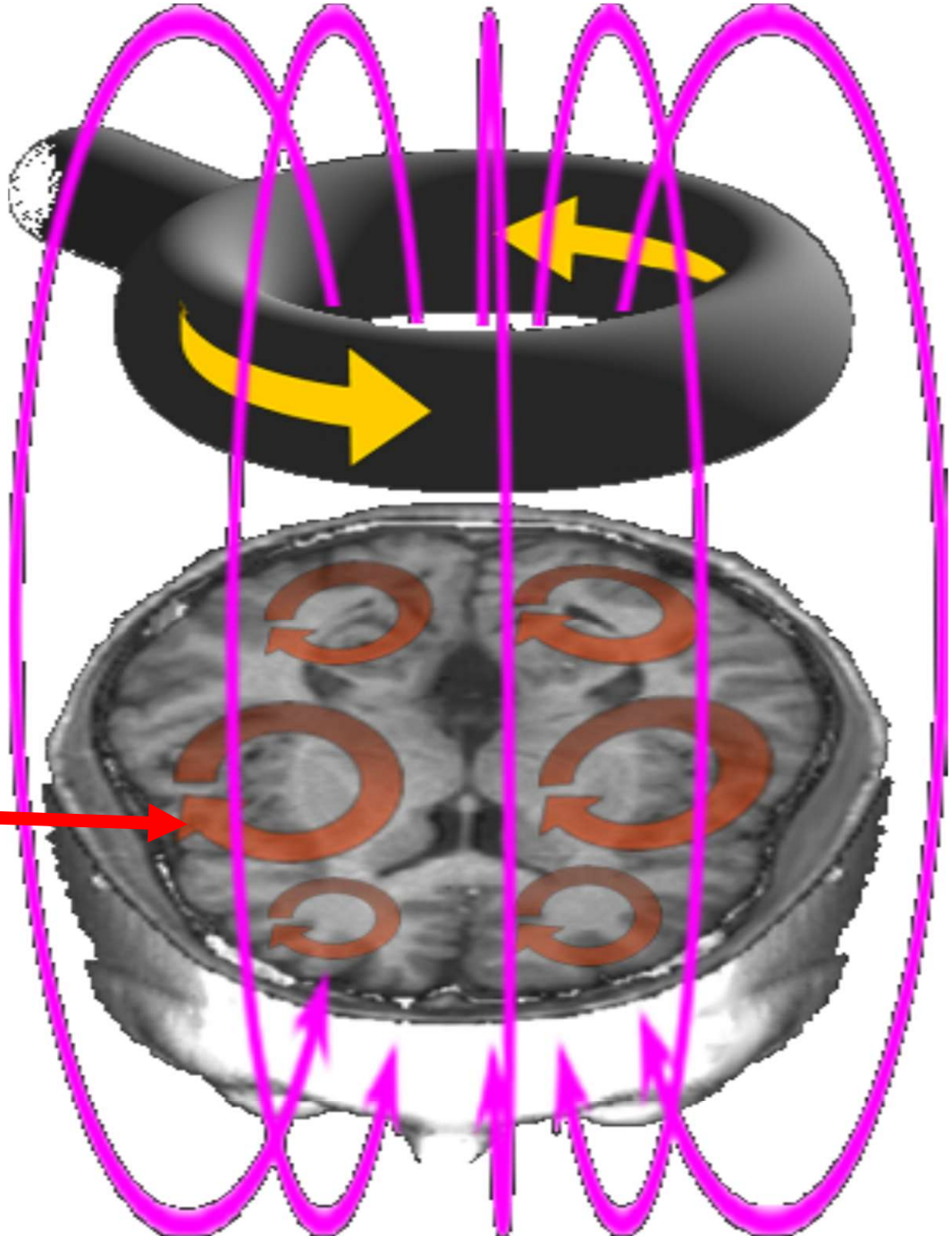
The mechanism of stimulation



Electromagnetic induction

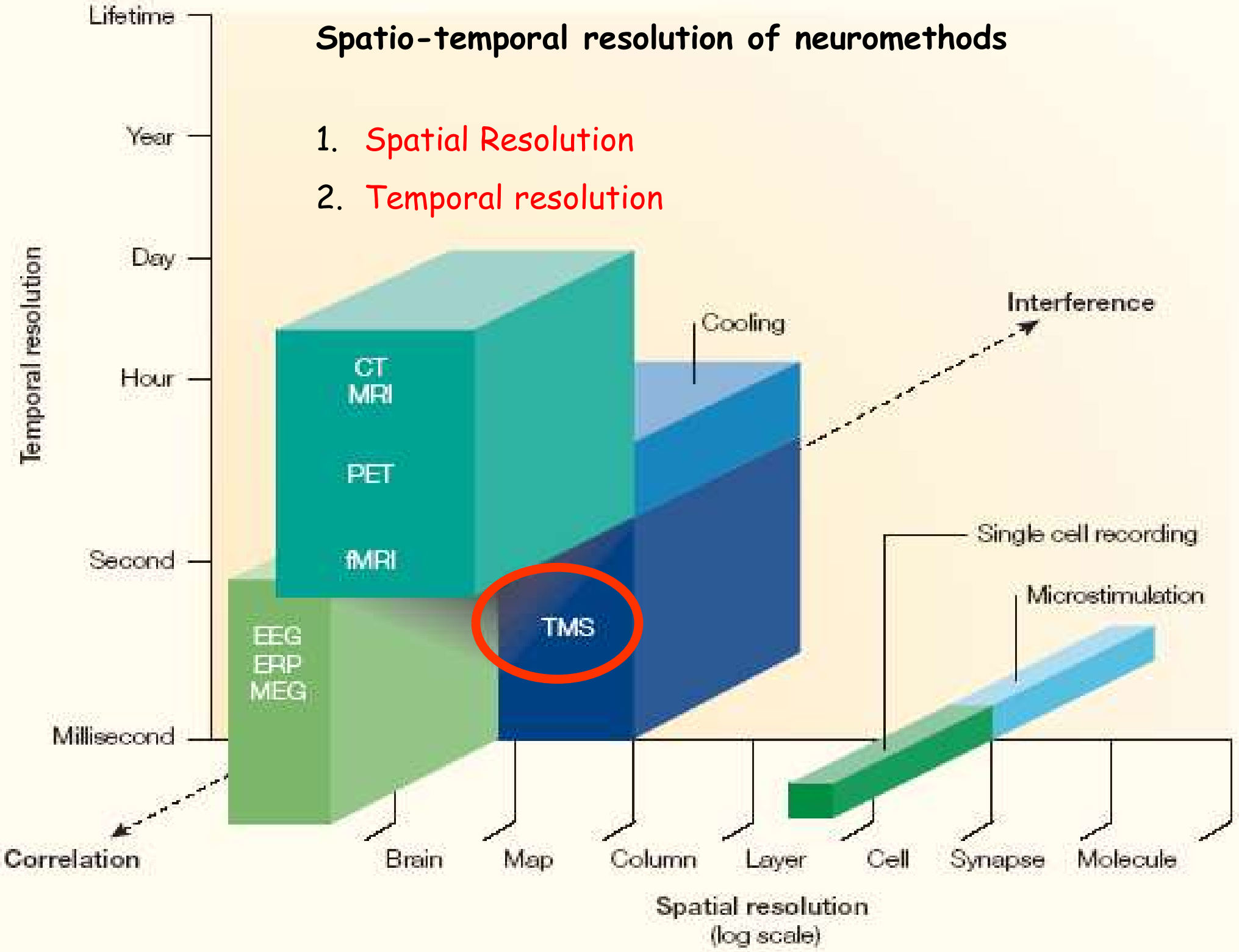
Introduces disorder
into a normally ordered system

The magnetic field cross the scalp and provokes an electrical field into the neural tissue.



Spatio-temporal resolution of neuromethods

1. Spatial Resolution
2. Temporal resolution



Spatial resolution

±1 cm²

Related to:

- Position and orientation of the coil over the scalp
- Intensity and shape of the magnetic field
- Geometry and conductivity of the brain

Temporal resolution

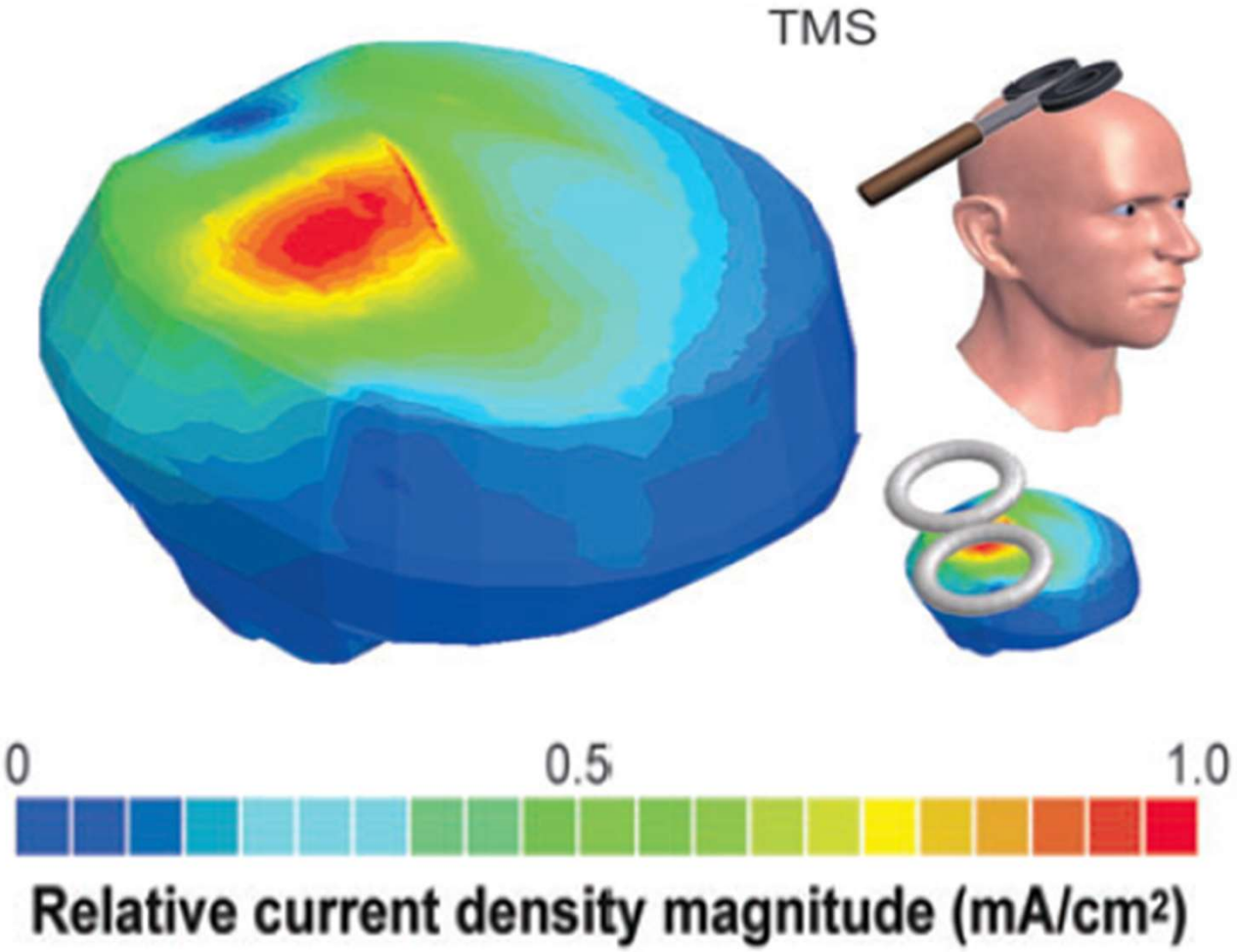
ms

Related to:

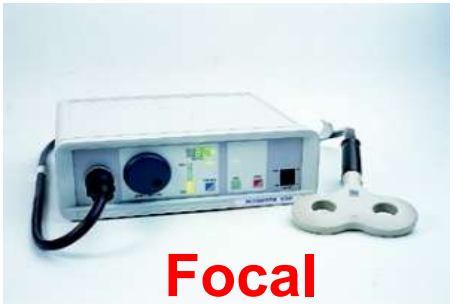
- Duration of impulse effects
- Duration of involvement of the area in the task

Spatial resolution

COIL SHAPE AND THE MAGNETIC FIELD



COIL SHAPE



Focal

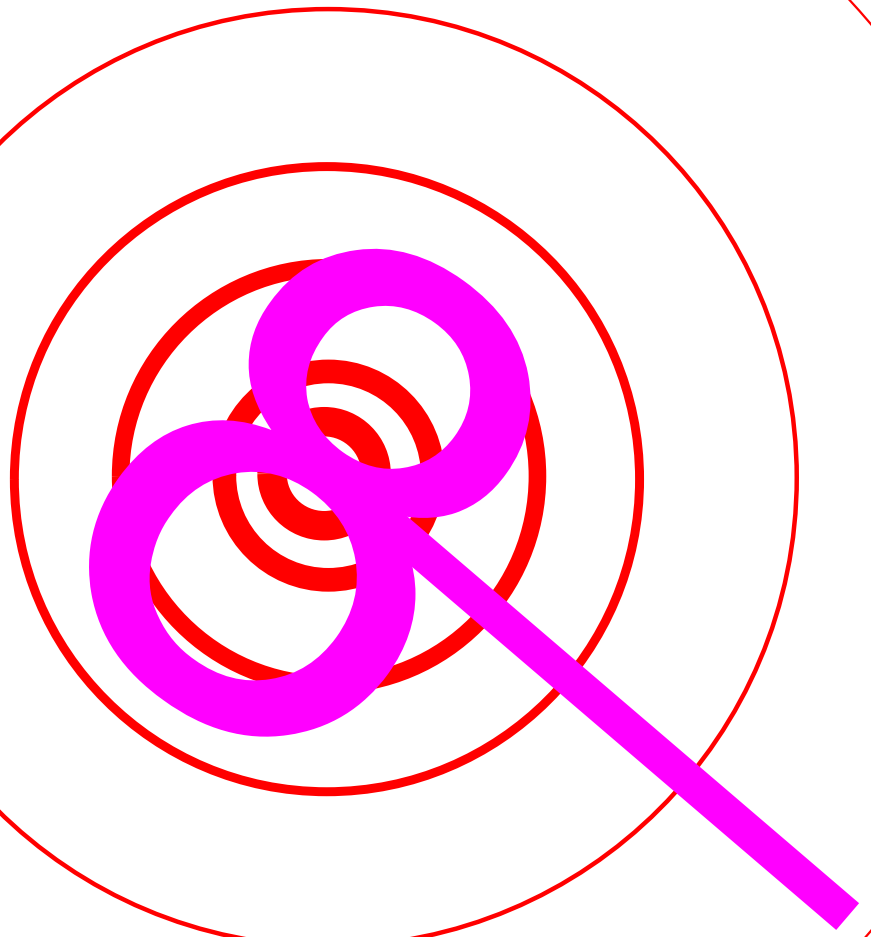
Conic

Circular
(non focal)

Spatial resolution

8 SHAPE COIL

Focal, able to stimulate small portion of the cerebral cortex

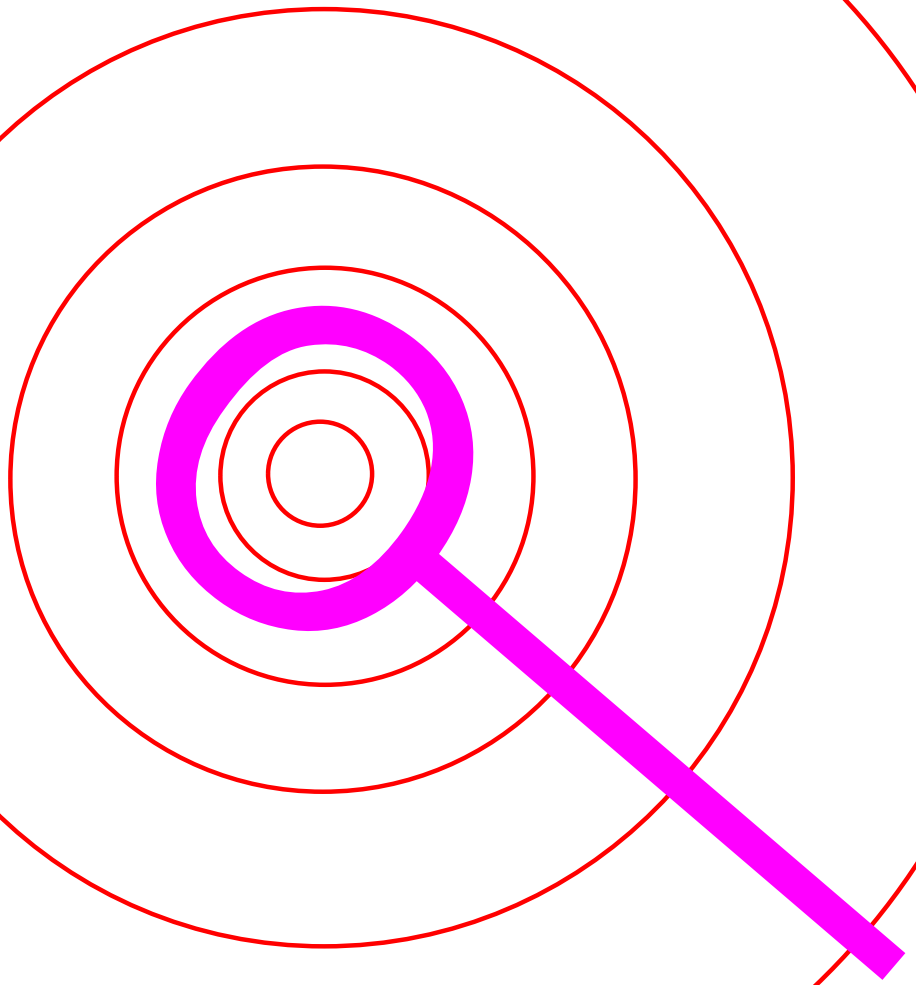


Spatial resolution

CIRCULAR COIL:

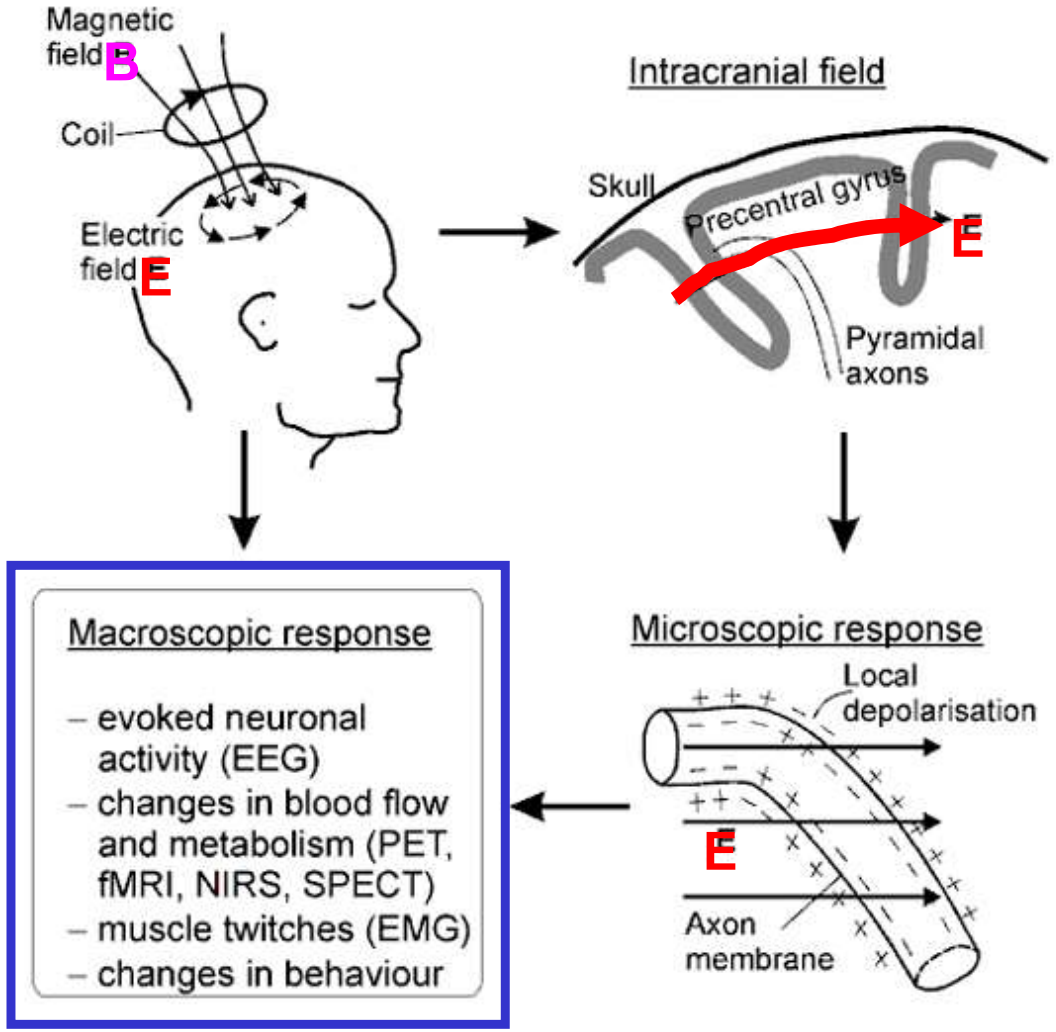
Not focal

(stimulates large portions of the cerebral cortex)



Spatial resolution

PRINCIPLES OF FUNCTIONING



Macroscopic responses can be recorded by means of:

Co-registration

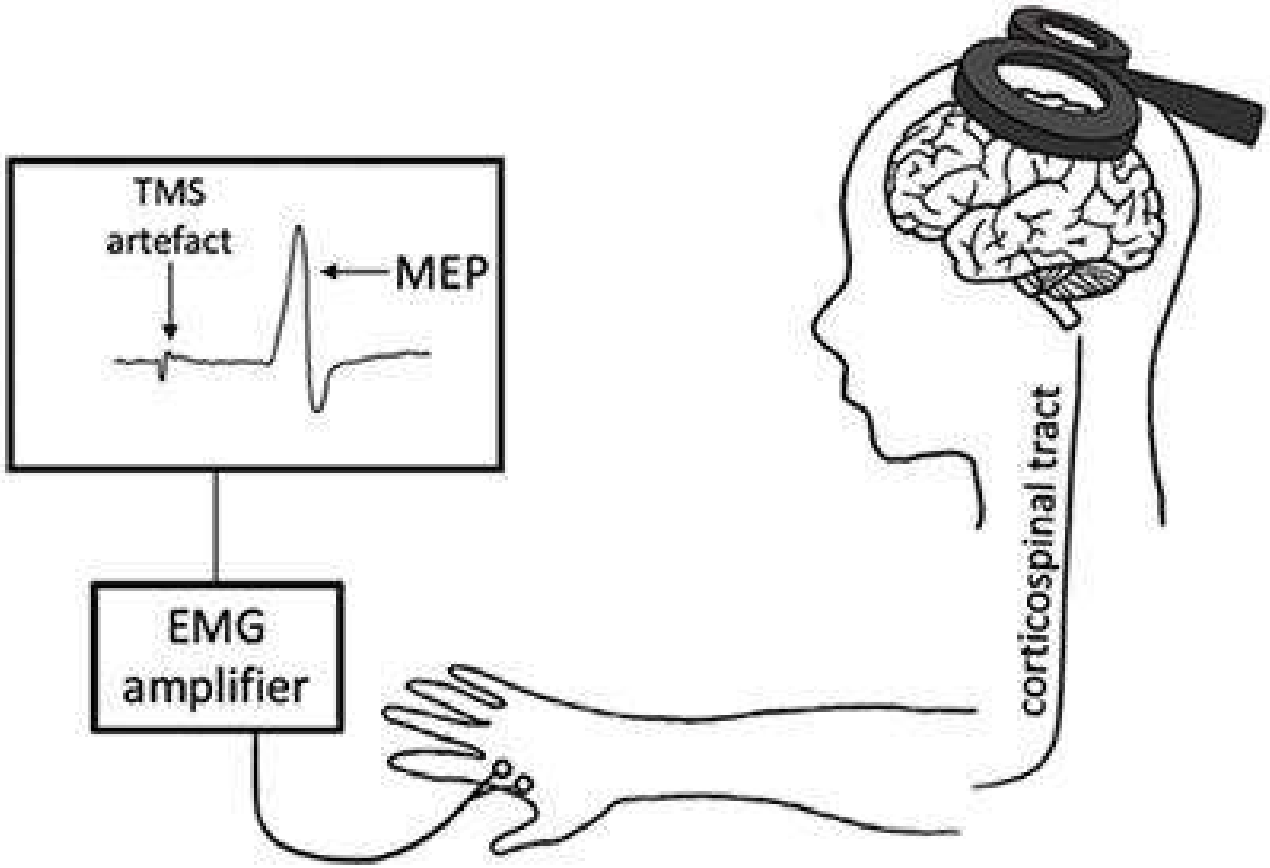
1) EEG
(Evoked neural activity)

2) PET, fMRI
(BOLD signal and metabolism)

3) EMG of Surface
(MEPs)

4) Behavior (perfromance modulation)

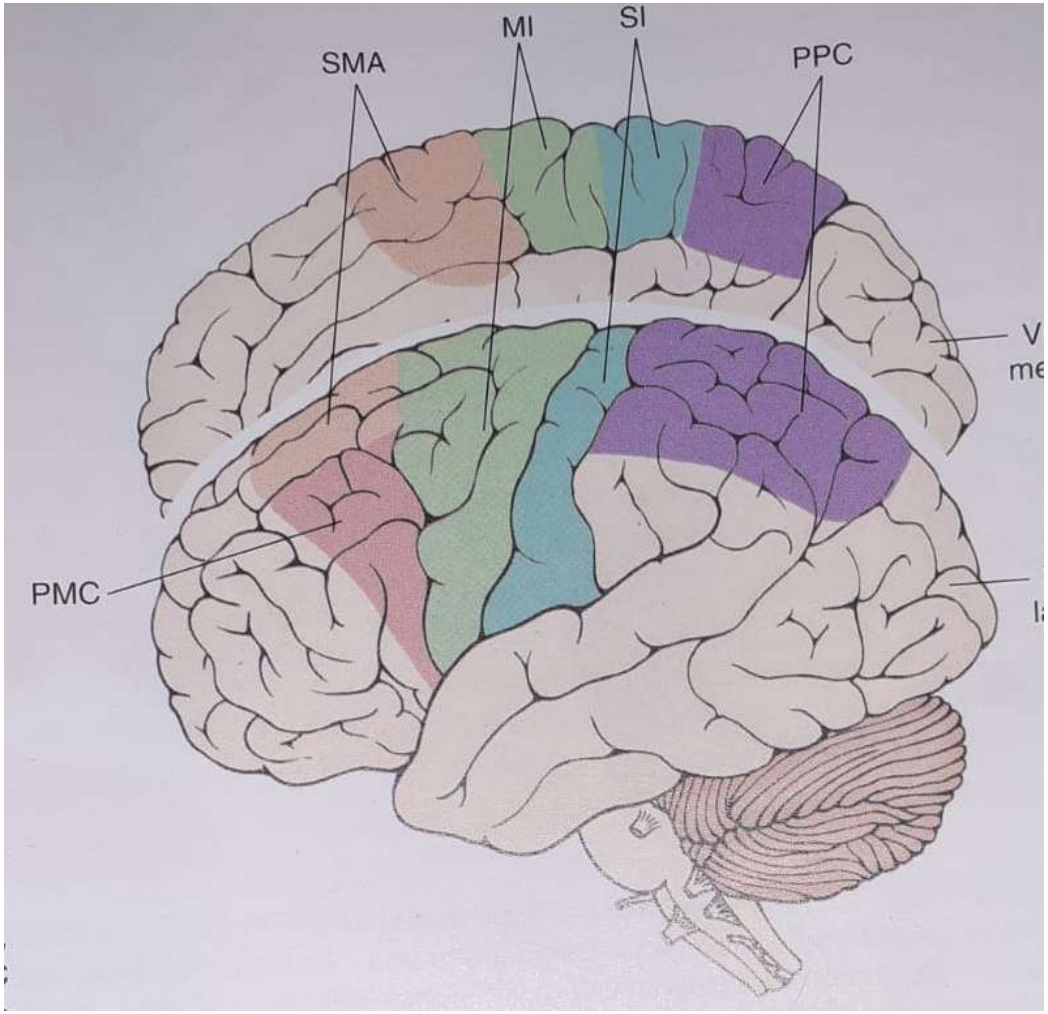
The TMS can be used to study changes in the activity of the motor system in response to external stimuli.



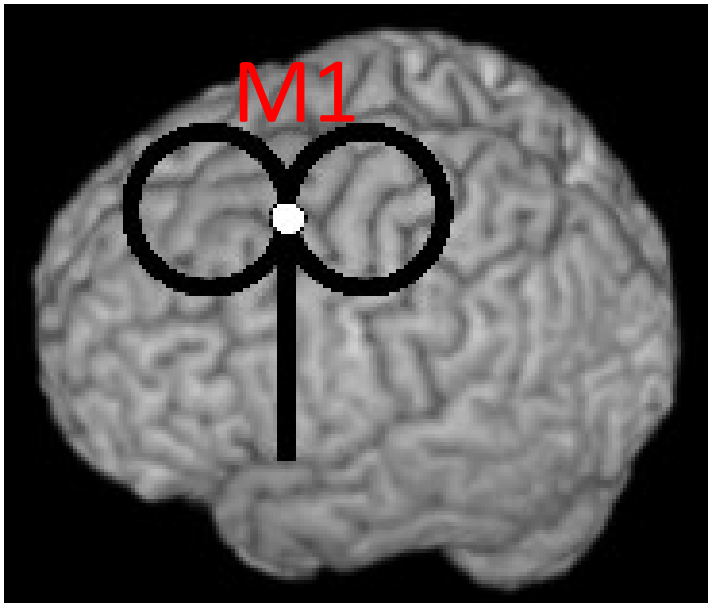
Corticospinal motor tract

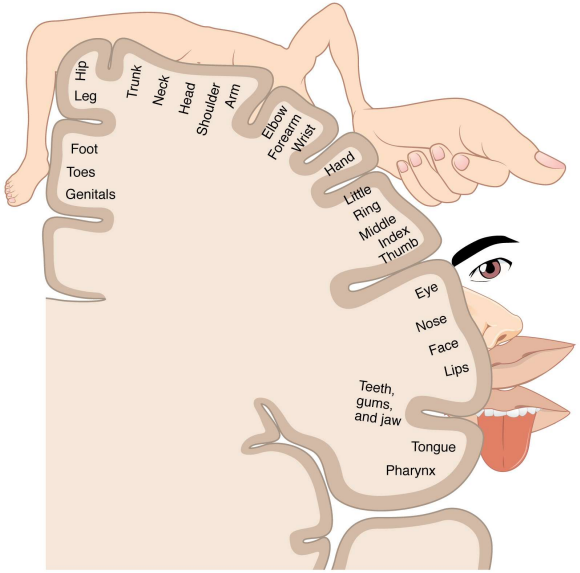
Crucial in the expression of voluntary movement, it includes the motor neurons that project to the spinal cord.

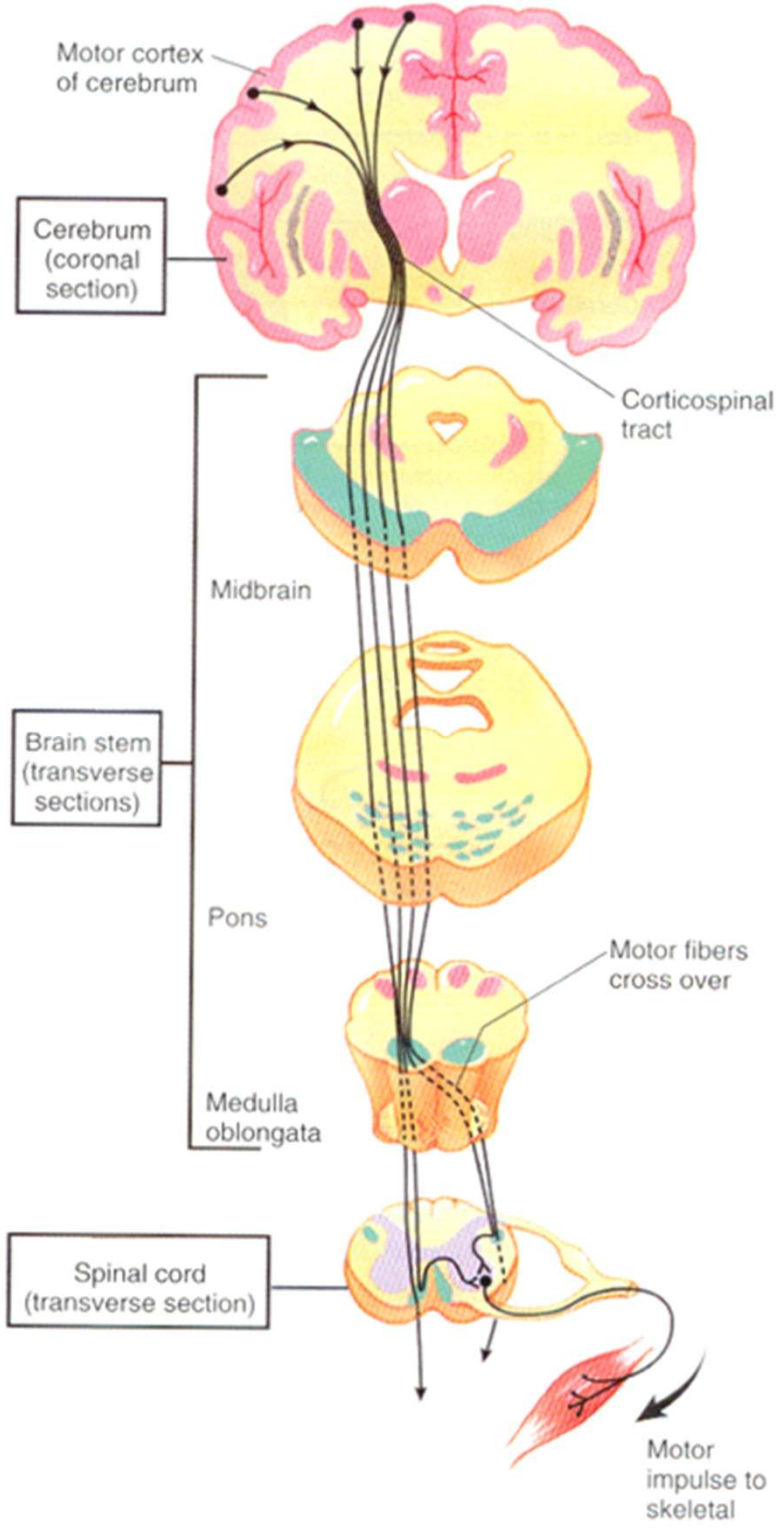
- 30% originates from MI
- 40% originates from the primary somatosensory cortex (SI)
- 30% originates from SMA and PMC



Evoked activity

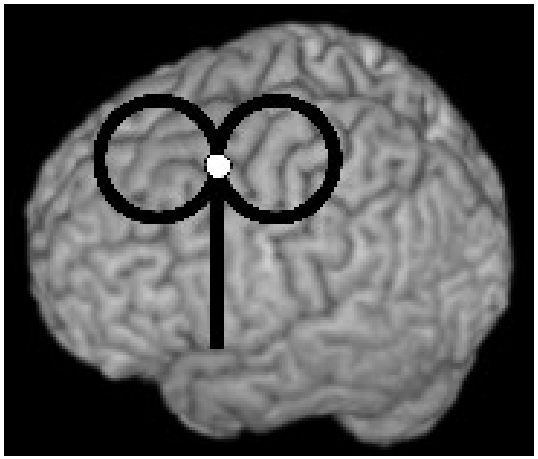






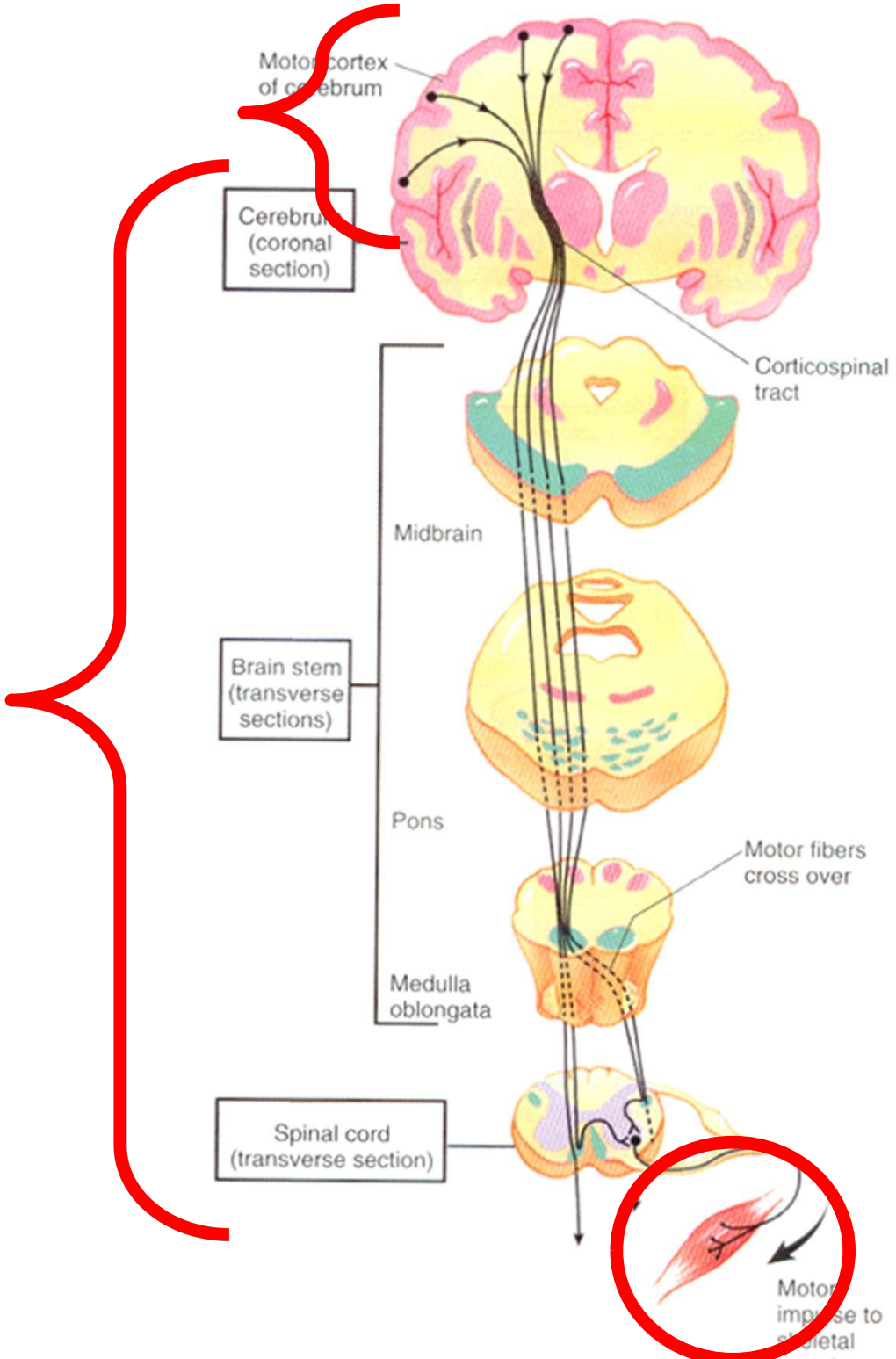
Evoked activity

- Depolarization of motor neurons

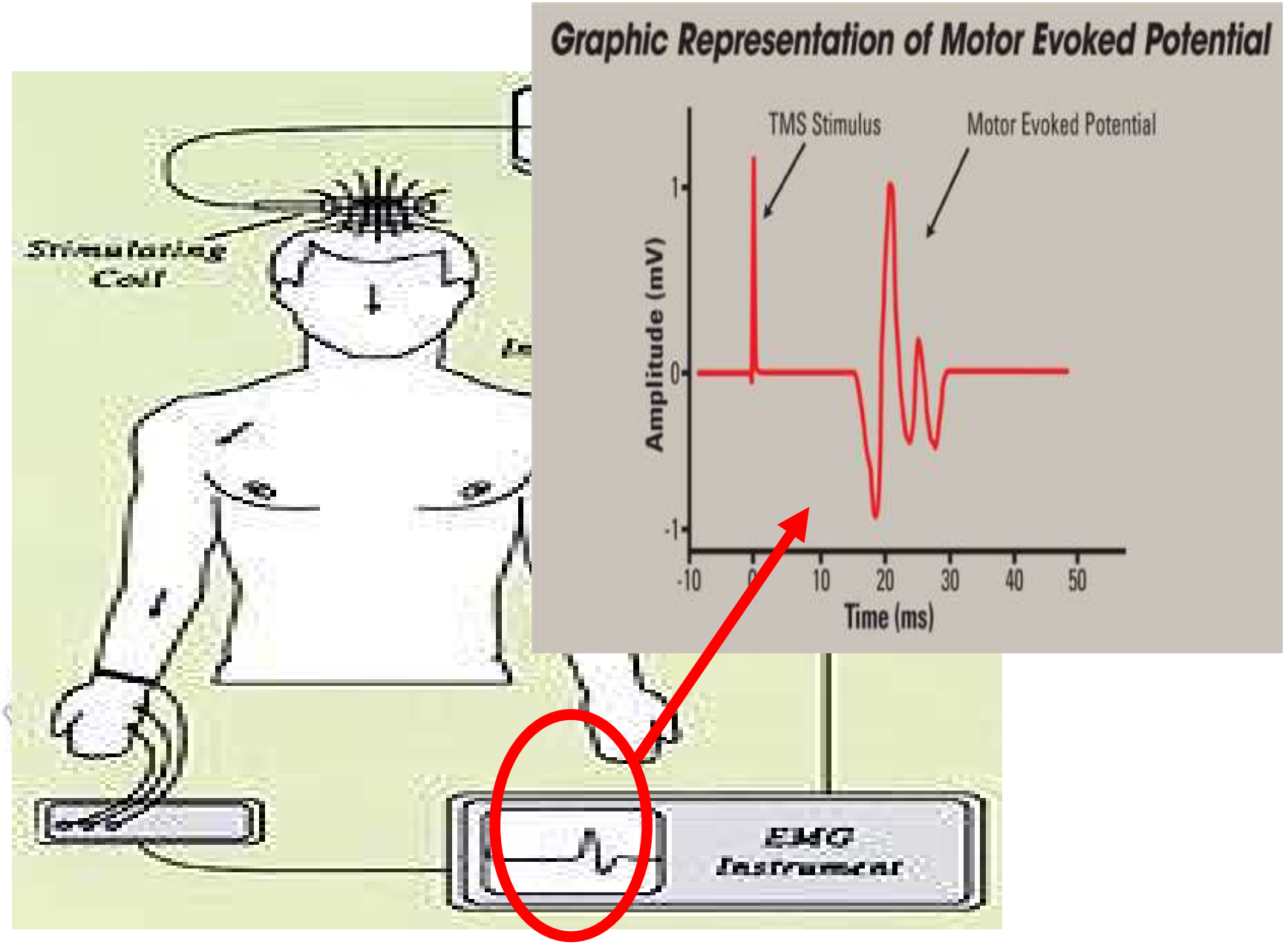


- Activation of the cortico-spinal tract

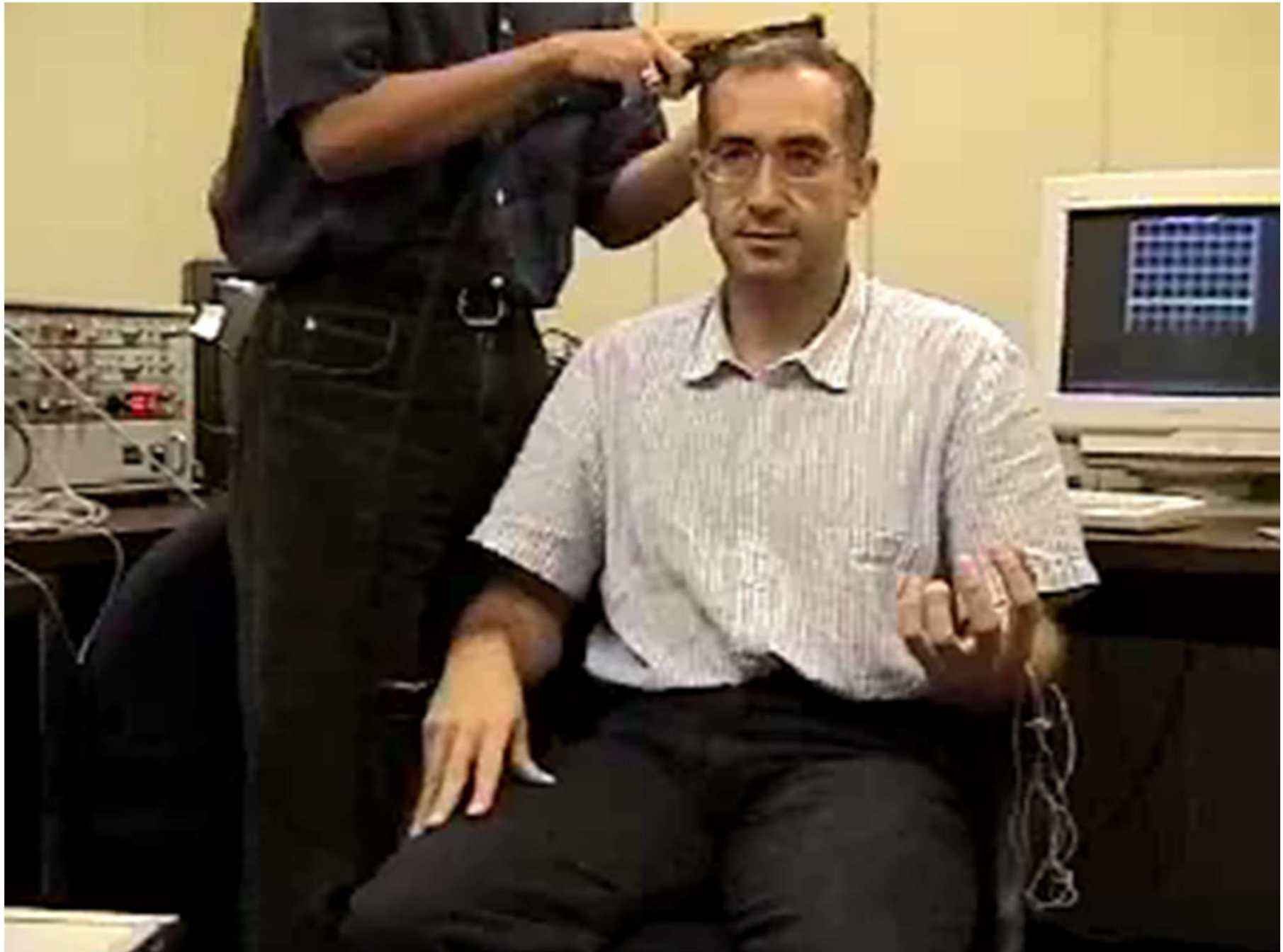
- Motor twiches (and or EMG response)



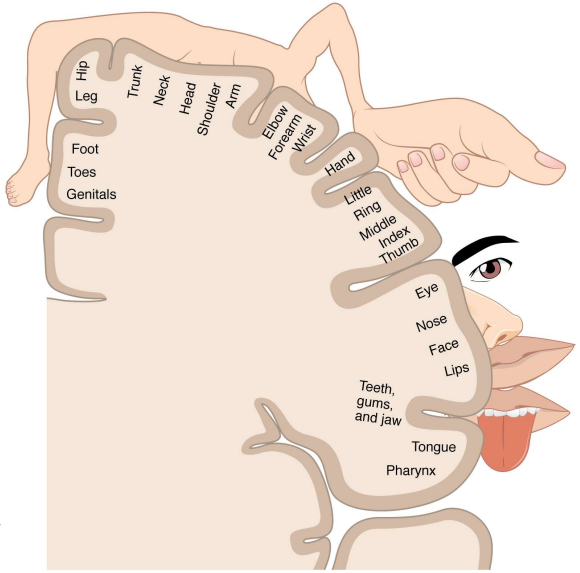
TMS induced MEPs



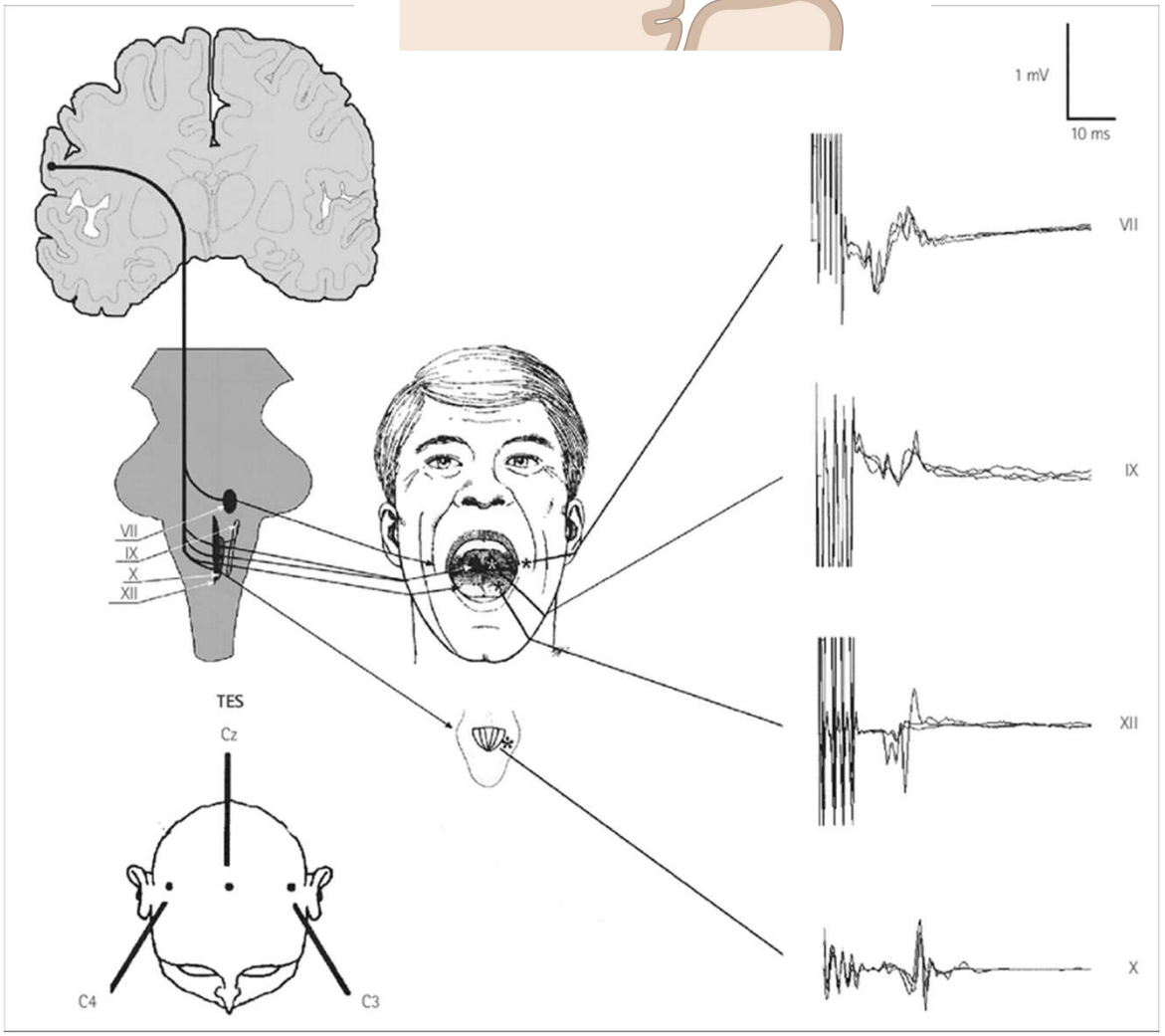
MEPs recording (corticospinal stimulation)



The Corticobulbar motor tract

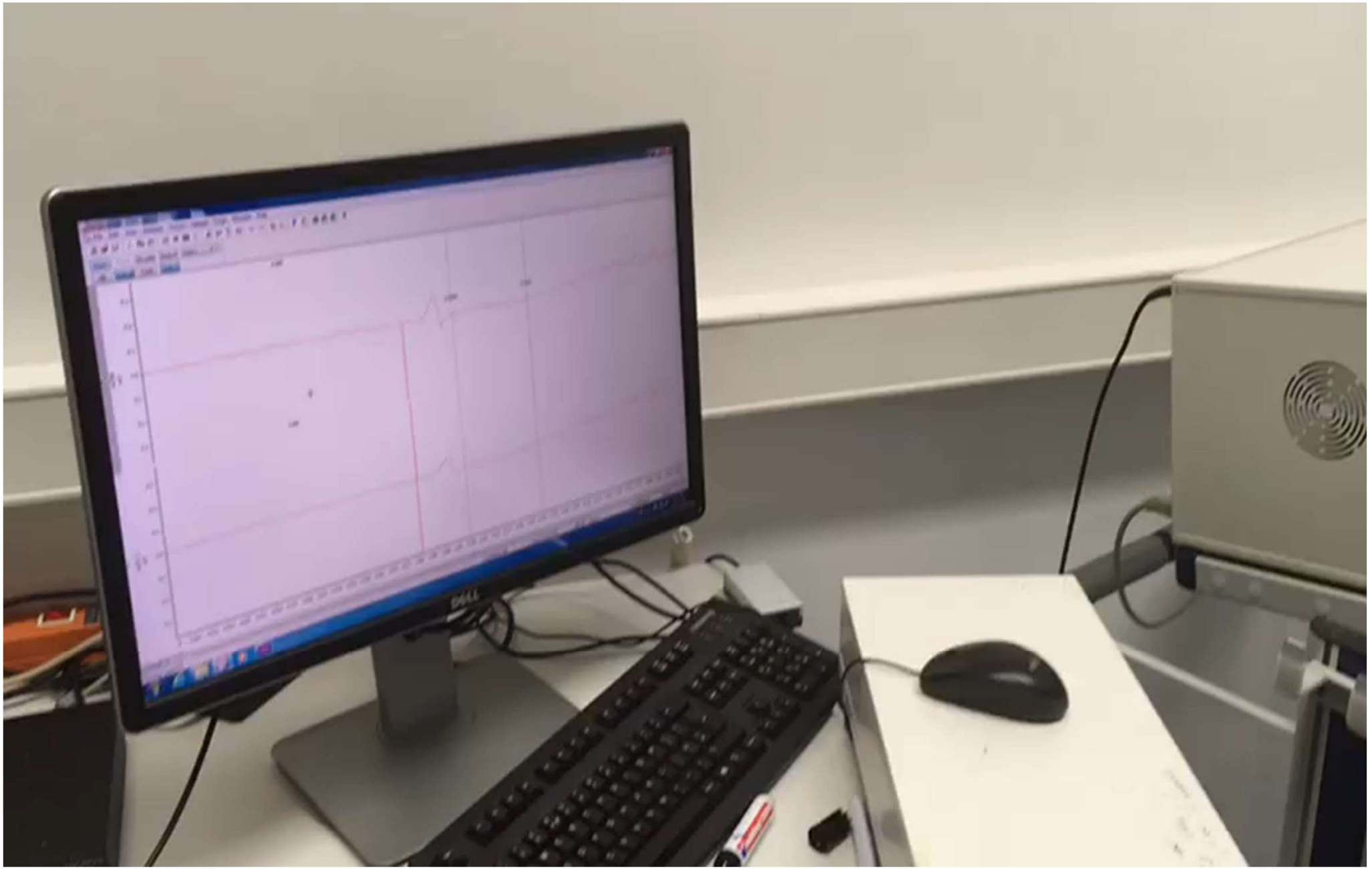


It referes to the control of movements made with facial, ocular, lingual muscles.

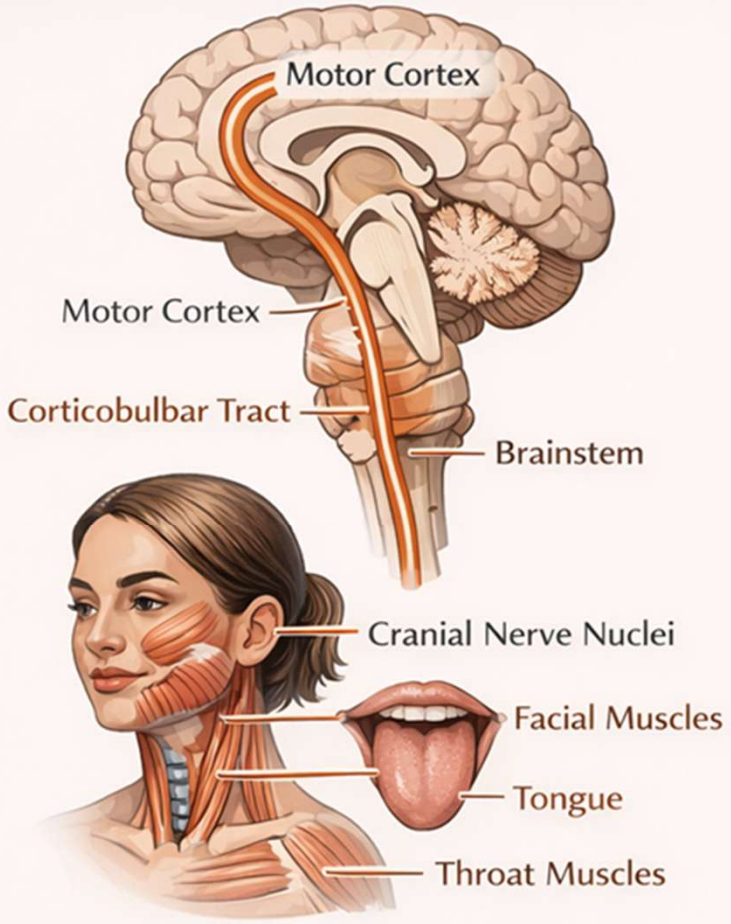


Setting the corticobulbar TMS

Tongue MEPs recording

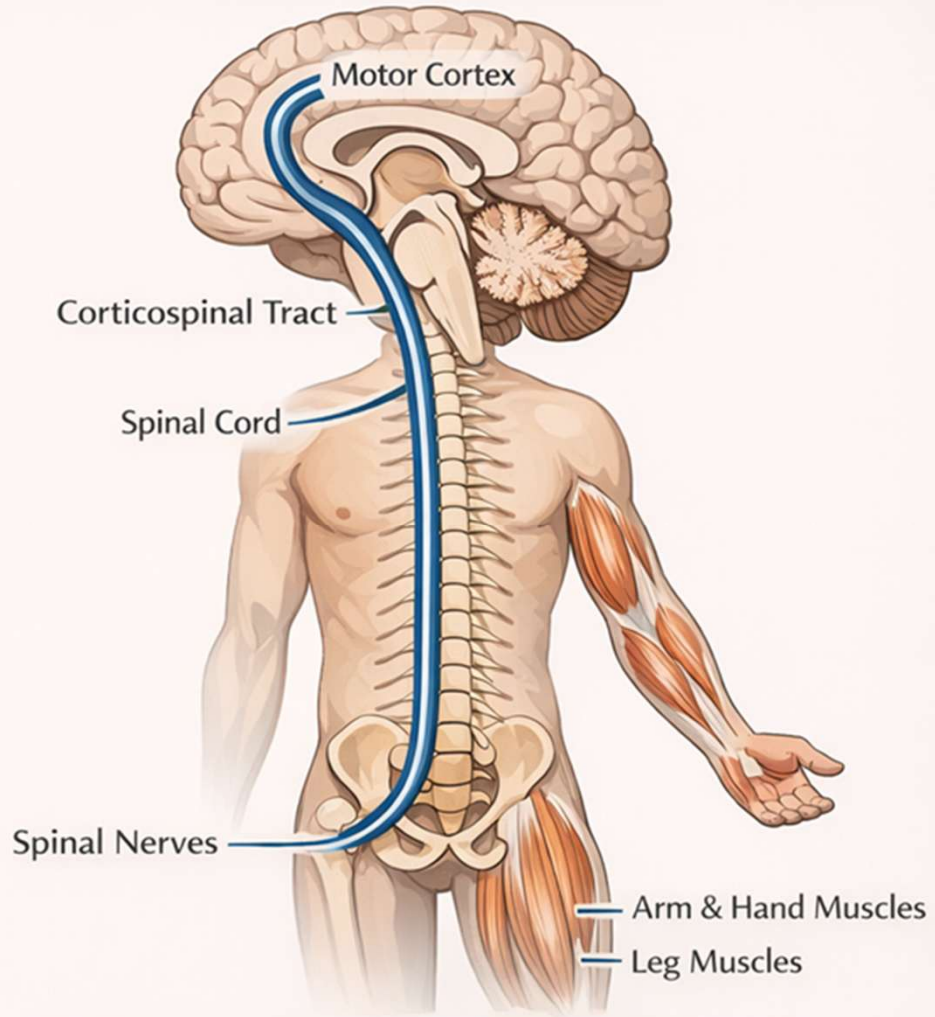


Corticobulbar Tract



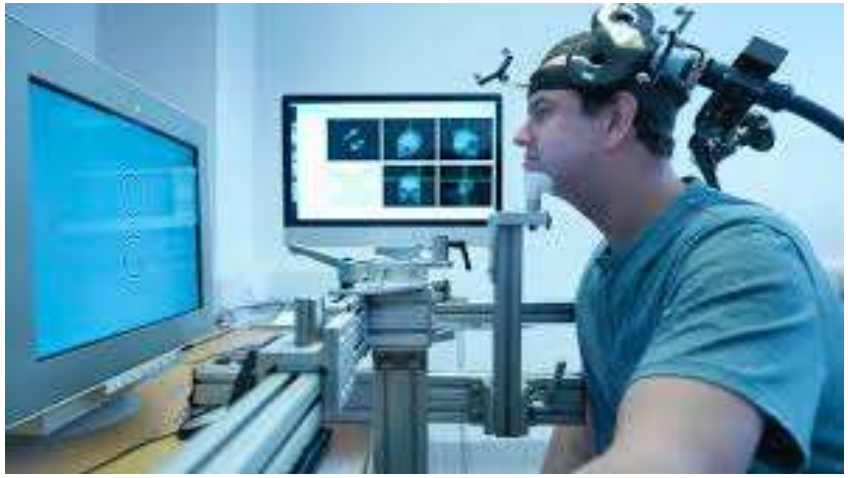
Controls Face, Head & Neck Muscles

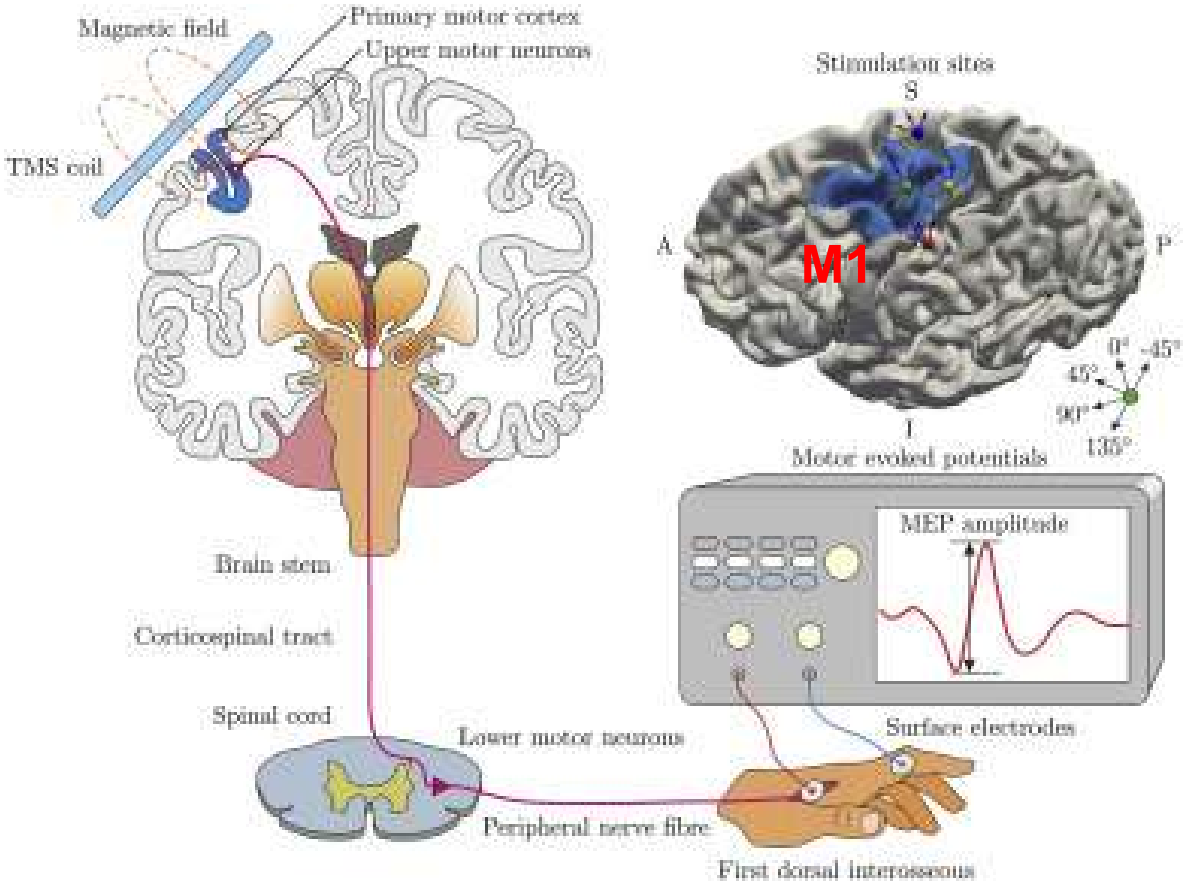
Corticospinal Tract



Controls Body & Limb Movements

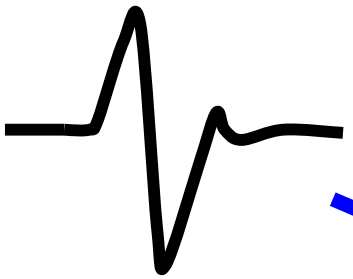
TMS MEPs allow to measure the excitability of the M1 in response to external stimuli



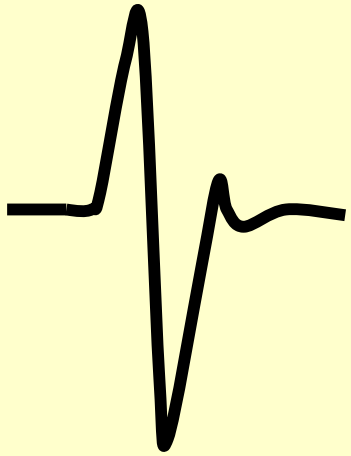


TMS-induced MEPs of the motor cortex measure the excitability of the corticospinal system

The baseline excitability

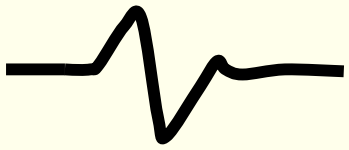


…increases…



Corticospinal facilitation

…decreases…

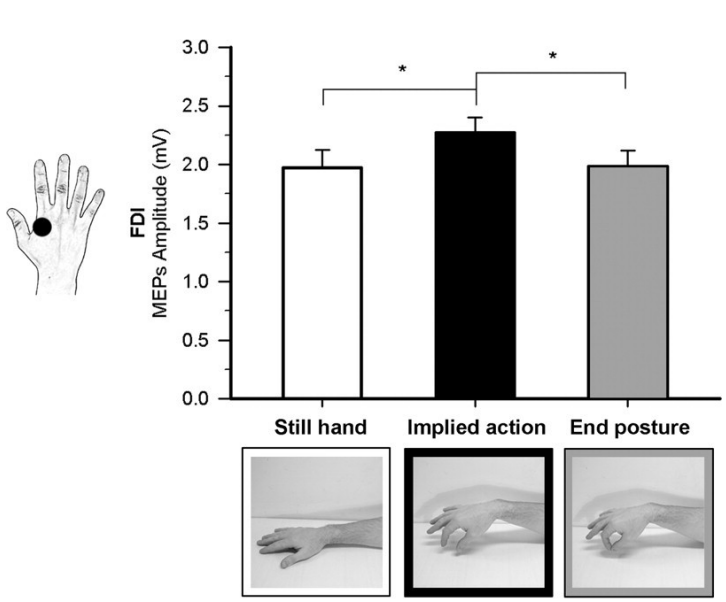


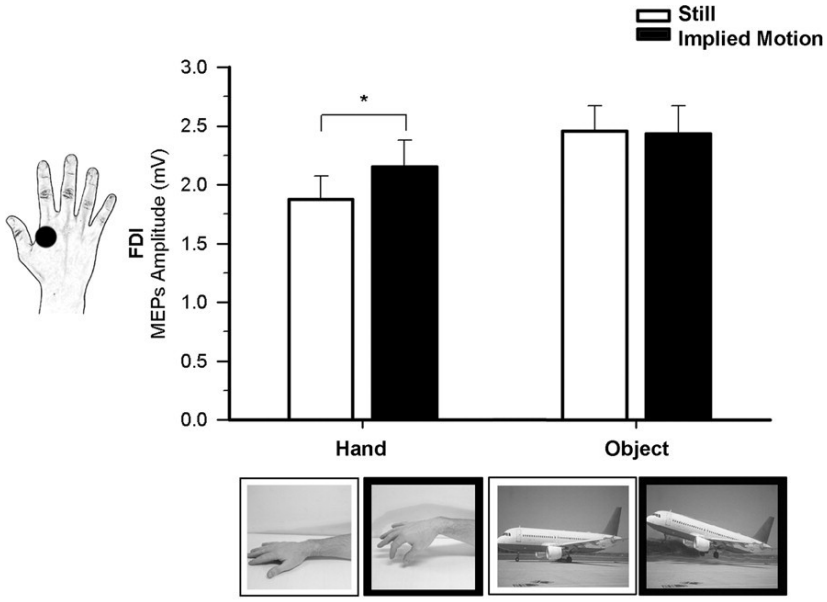
Corticospinal inhibition

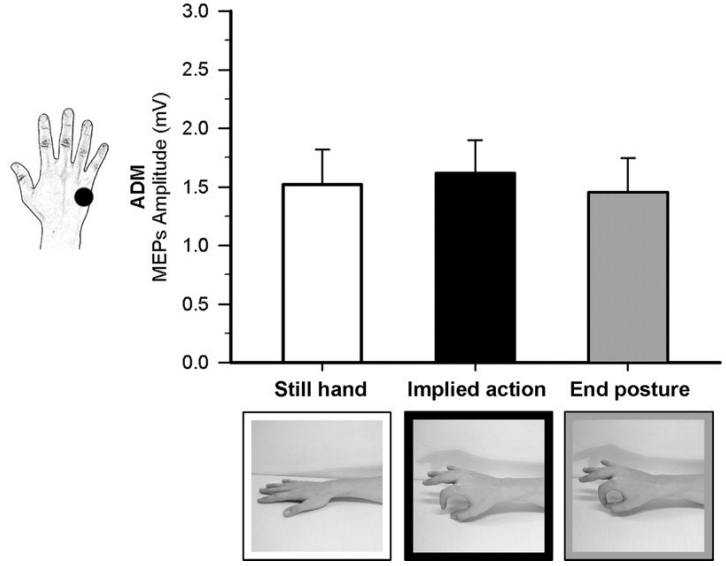
If following an experimental manipulation (e.g., motor and/or cognitive task) the amplitude of the MEP….

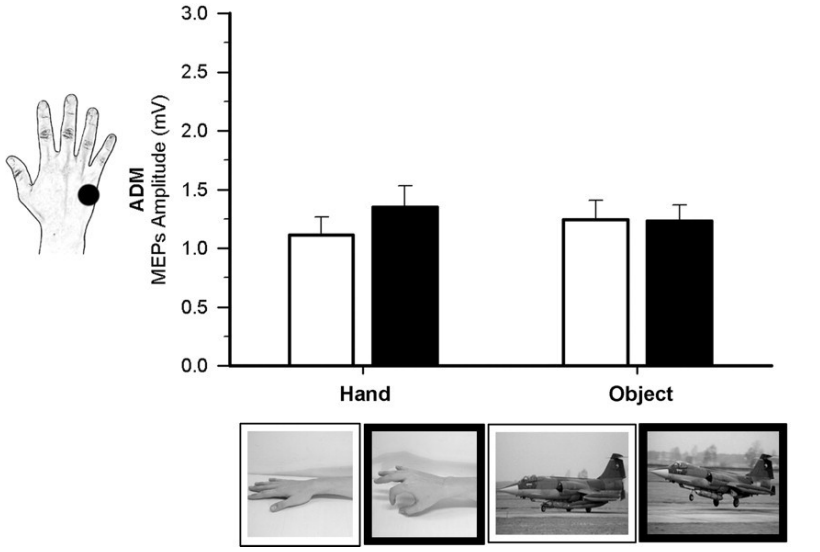
TMS MEPs allows to study the role of M1 in cognitive and affective processing

MEPs during the exposure to body actions





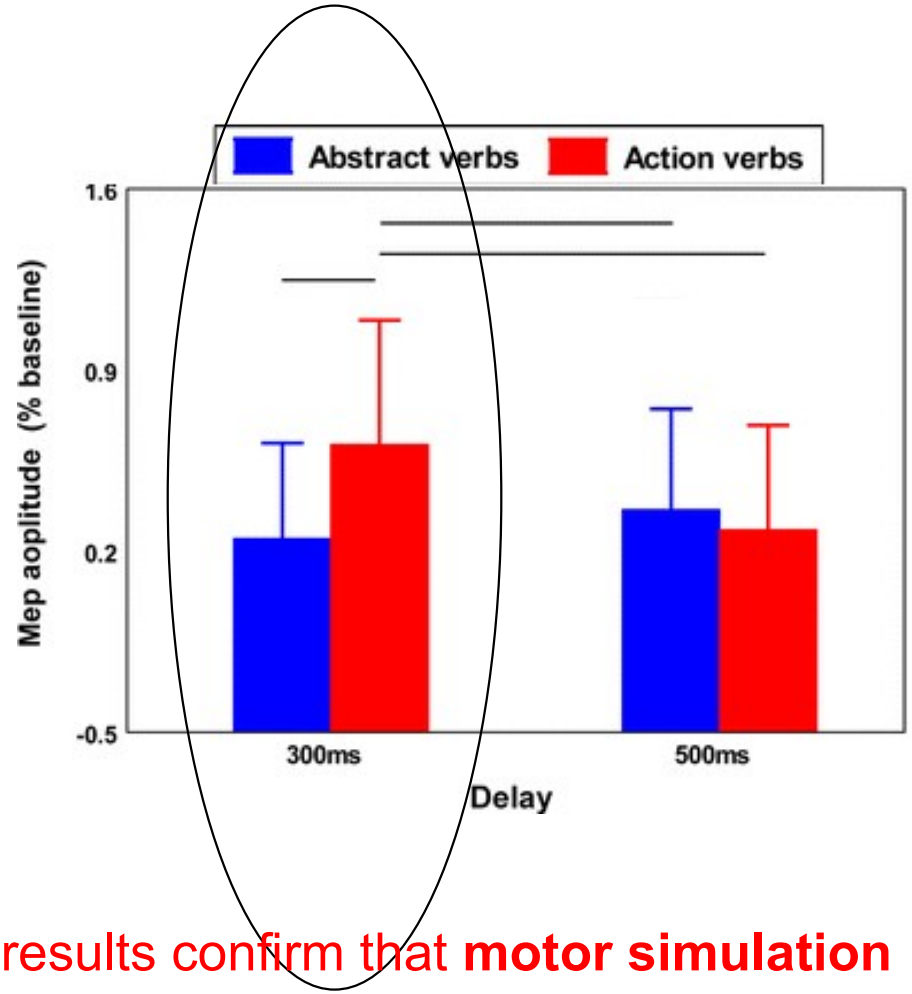




Urgesi et al., 2006 The Journal of Neuroscience,

MEPs and reading of action verbs

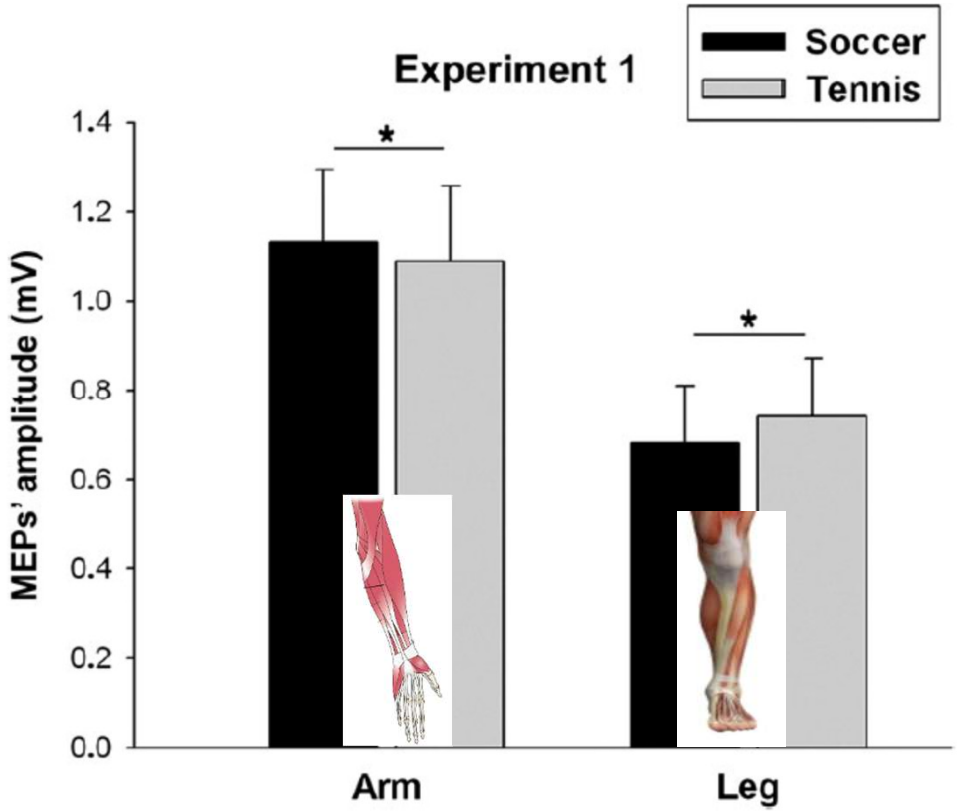
Hand-action-related verbs		Abstract verbs	
Italian	English	Italian	English
1. Cucire	*to sew*	1. Angosciare	*to worry*
2. Martellare	*to hammer*	2. Astrarre	*to abstract*
3. Pettinare	*to comb*	3. Avverare	*to fulfill*
4. Remare	*to row*	4. Fidare	*to trust (in)*
5. Sbucciare	*to peel*	5. Ideare	*to conceive*
6. Scalpellare	*to chisel*	6. Impegnare	*to commit*
7. Stirare	*to iron*	7. Innamorare	*to fall in love (with)*
8. Strofinare	*to scrub*	8. Inquietare	*to trouble*
9. Tagliare	*to cut*	9. Mitizzare	*to mythologize*
10. Trapanare	*to drill*	10. Scordare	*to forget*



These results confirm that **motor simulation** can be used to understand action verb rather than abstract verbs

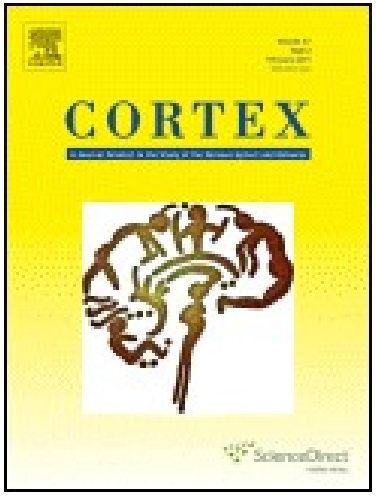
Innocenti et al., 2013, Cogn Process

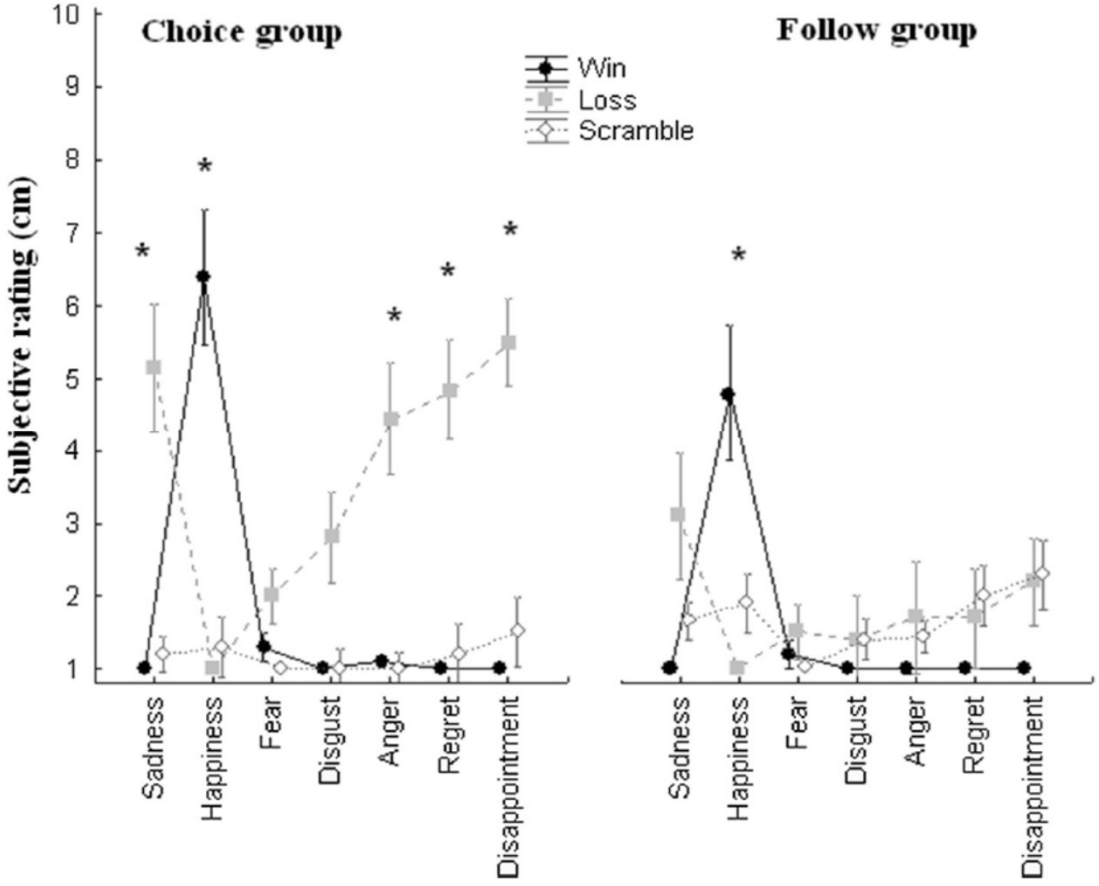
MEPS during the recognition of famous sportsmen



Candidi, Vicario et al., 2010, *Cerebral Cortex*

MEPs, decision making and negative emotions





Vicario et al., 2015 ,*Cortex*

MEPs and the experience of core and social disgust

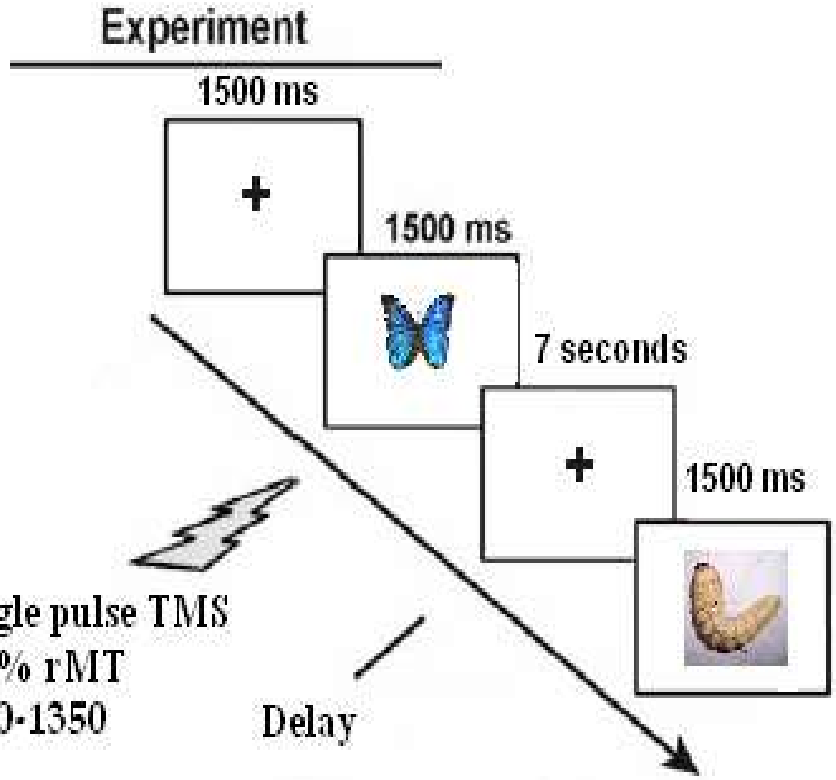
OXFORD

Social Cognitive and Affective Neuroscience, 2016, 1–11

doi: 10.1093/scan/nsw129
Original article

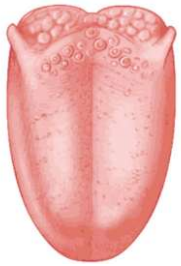
Pictures of disgusting foods and disgusted facial expressions suppress the tongue motor cortex

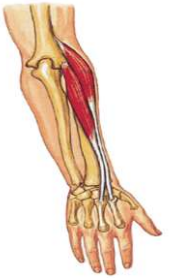
Carmelo M. Vicario,[1,2] Robert D. Rafal,[1] Sara Borgomaneri,[3,4] Riccardo Paracampo,[3] Ada Kritikos,[5] and Alessio Avenanti[3,4]

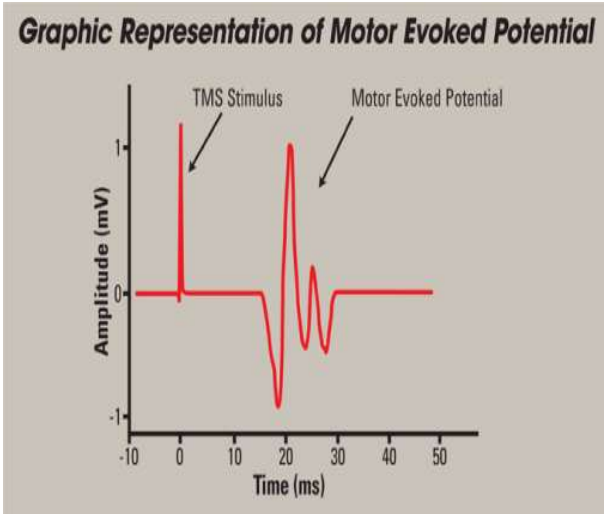


Method

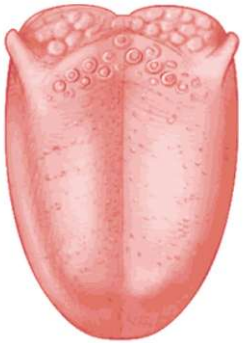
Muscles

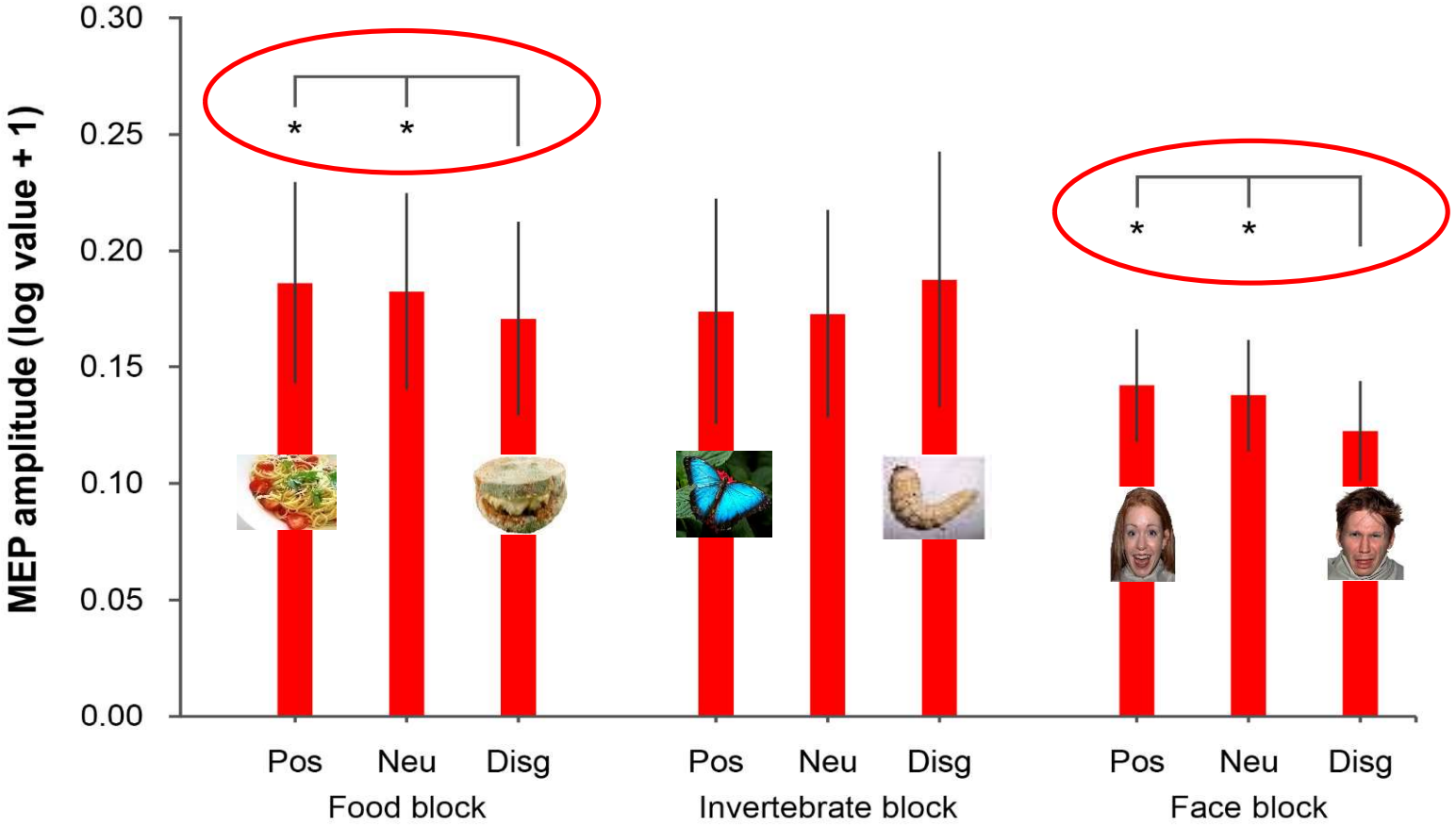




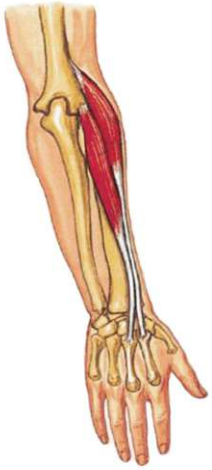


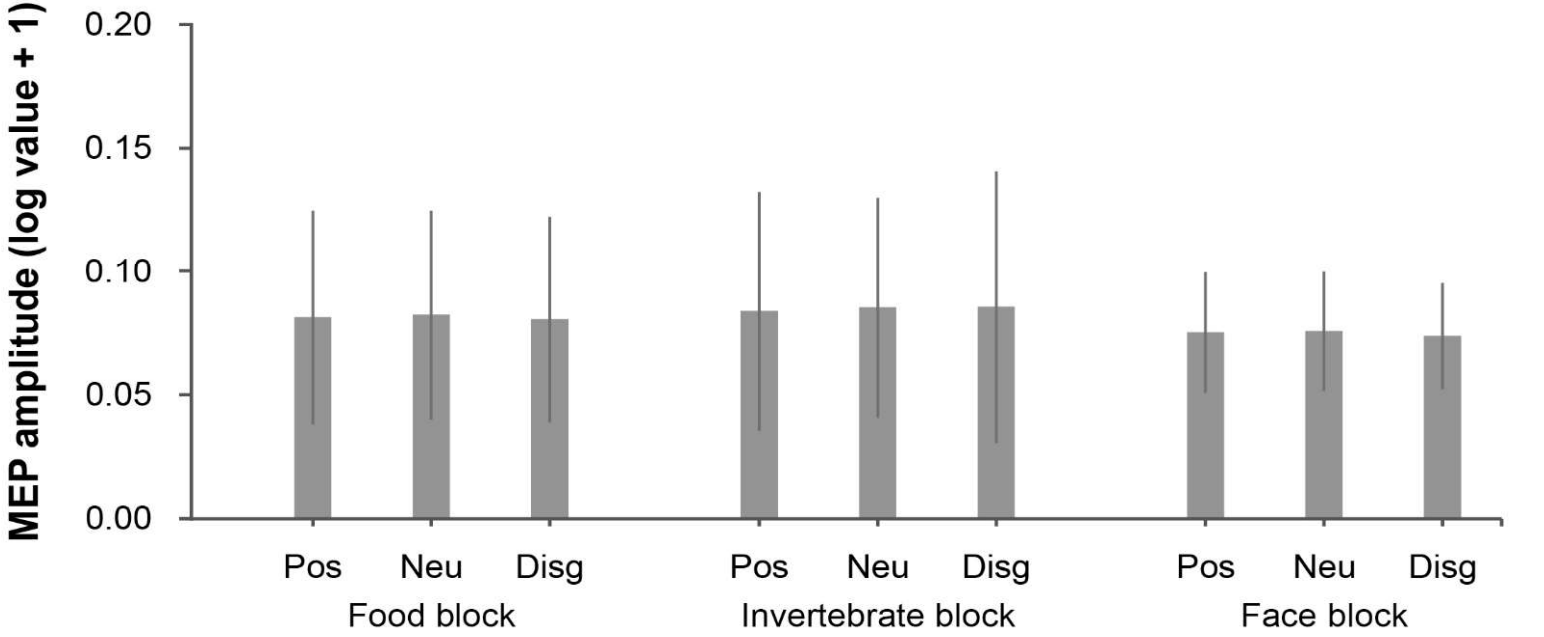
MTA excitability





ECR excitability





OXFORD

Social Cognitive and Affective Neuroscience, 2020, 1–10

doi: 10.1093/scan/nsaa036
Original Article

MEPs and the experience of moral disgust

Neuromodulation Special Issue

Indignation for moral violations suppresses the tongue motor cortex: preliminary TMS evidence

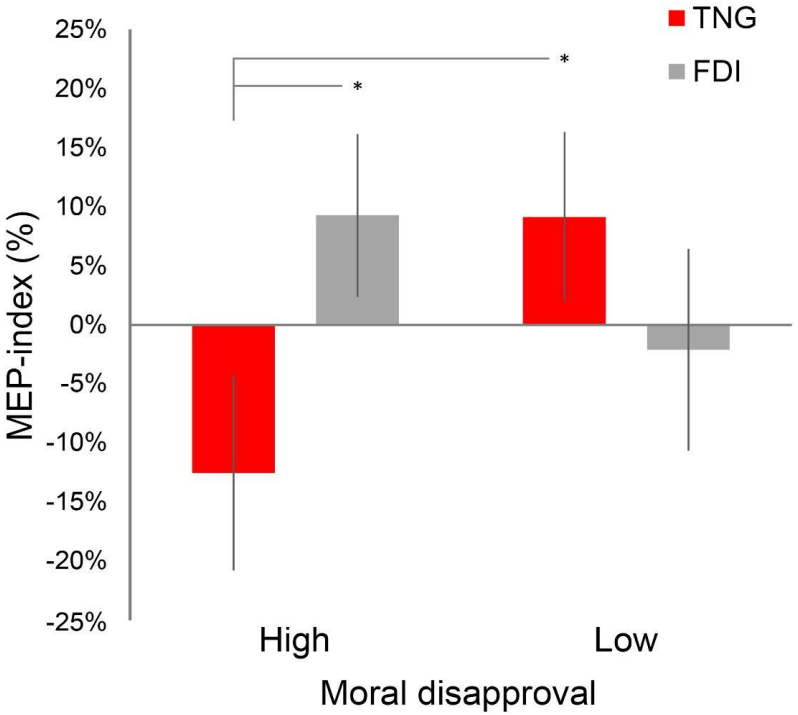
Carmelo M. Vicario,[1,2,3,4,5] Robert D. Rafal,[6] Giuseppe di Pellegrino,[7] Chiara Lucifora,[1,2] Mohammad A. Salehinejad,[3] Michael A. Nitsche,[3] and Alessio Avenanti[5,7]

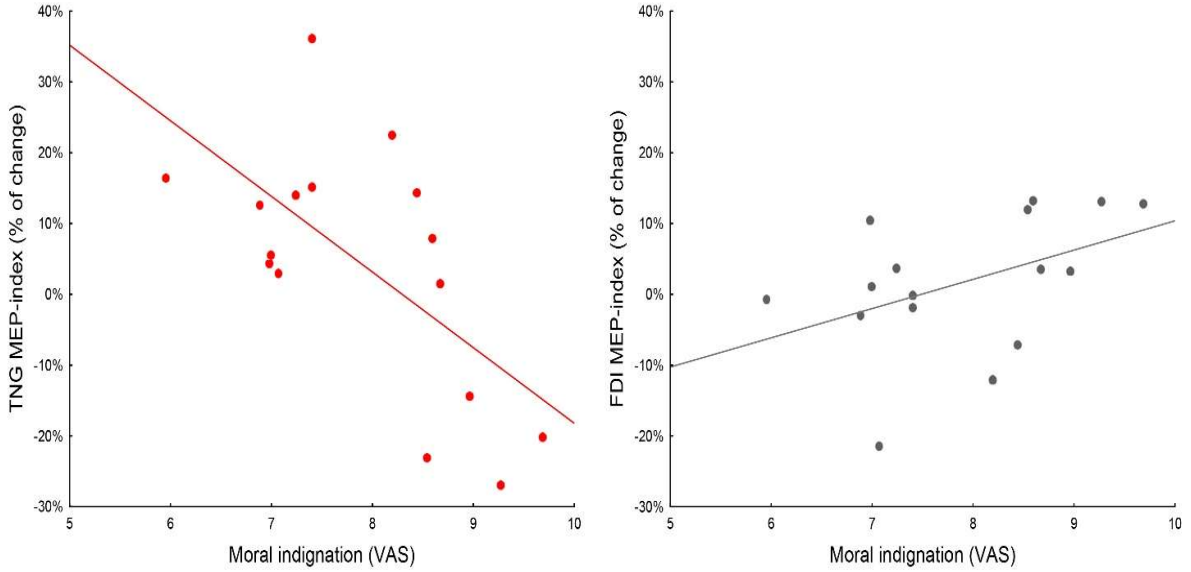
Moral dilemmas

Non moral dilemmas

participants were dealing with 16 standard hypothetical moral dilemmas adapted into short vignettes (e.g., Harrison et al., 2012).

Results


TNG
FDI
25%
20%
15%
10%
5%
0%
-5%
-10%
-15%
-20%
-25%
MEP-index (%)
*
*
High
Low
Moral disapproval


40%
30%
20%
10%
0%
-10%
-20%
-30%
TNG MEP-index (% of change)
5
6
7
8
9
10
Moral indignation (VAS)
FDI MEP-index (% of change)
Moral indignation (VAS)

TMS MEPs allow to measure the excitability of the M1 as a marker of neurological and psychiatric disorders

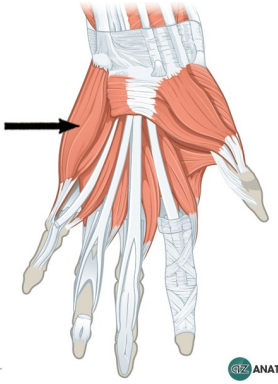
MEASUREMENT OF CENTRAL MOTOR CONDUCTION IN MULTIPLE SCLEROSIS BY MAGNETIC BRAIN STIMULATION

C. W. HESS K. R. MILLS
N. M. F. MURRAY

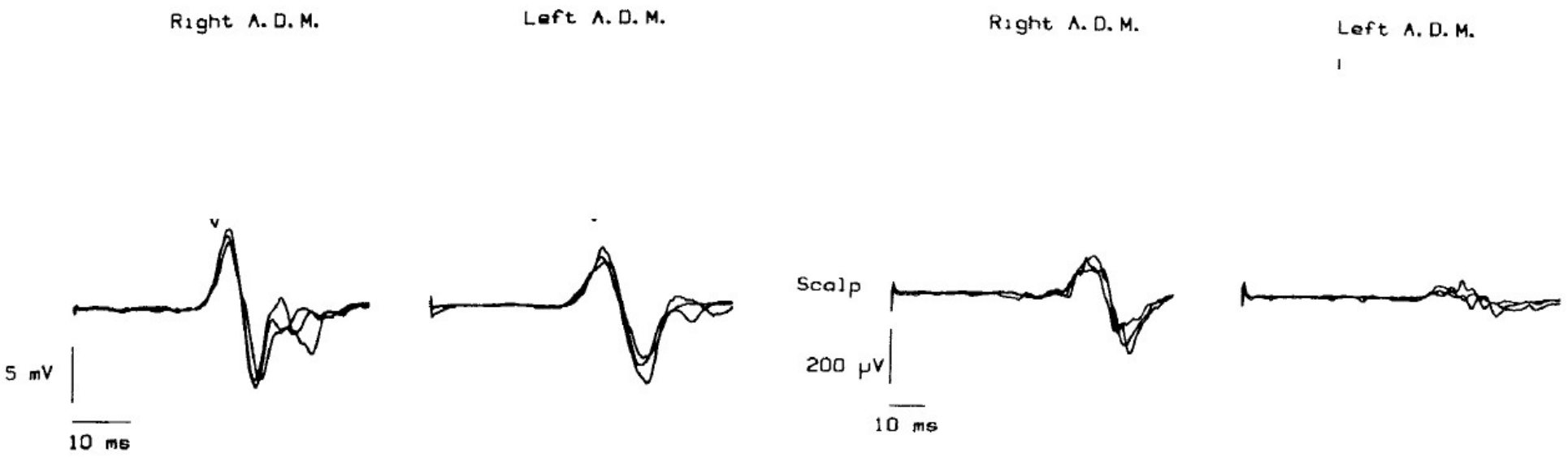
THE LANCET, AUGUST 16, 1986

Difference in amplitude and latency of MEPs

abductor digiti minimi



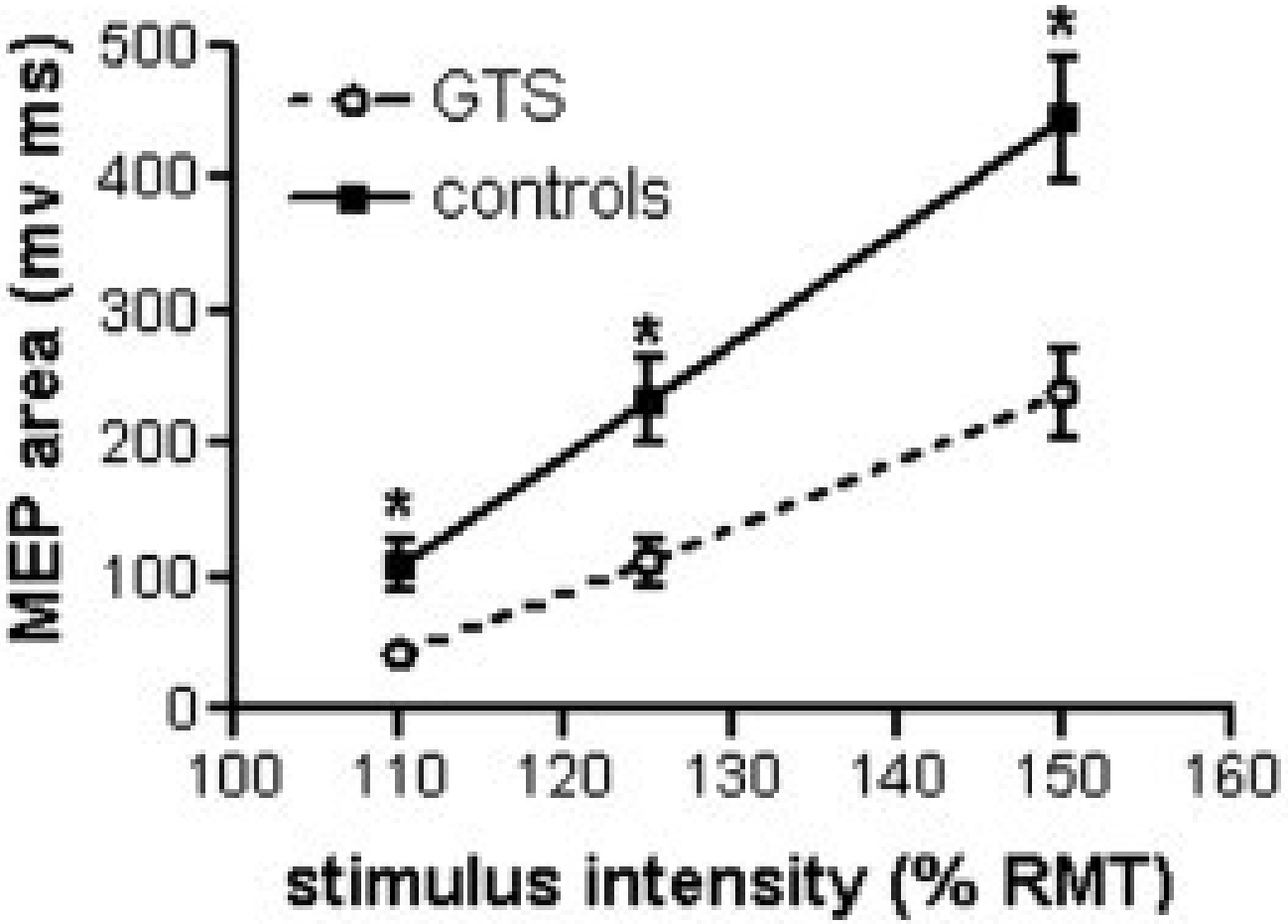
healthy humans **Patients with MS**



Corticospinal System Excitability at Rest Is Associated with Tic Severity in Tourette Syndrome

Michael Orth, Alexander Münchau, and John C. Rothwell

A difference in MEPs area

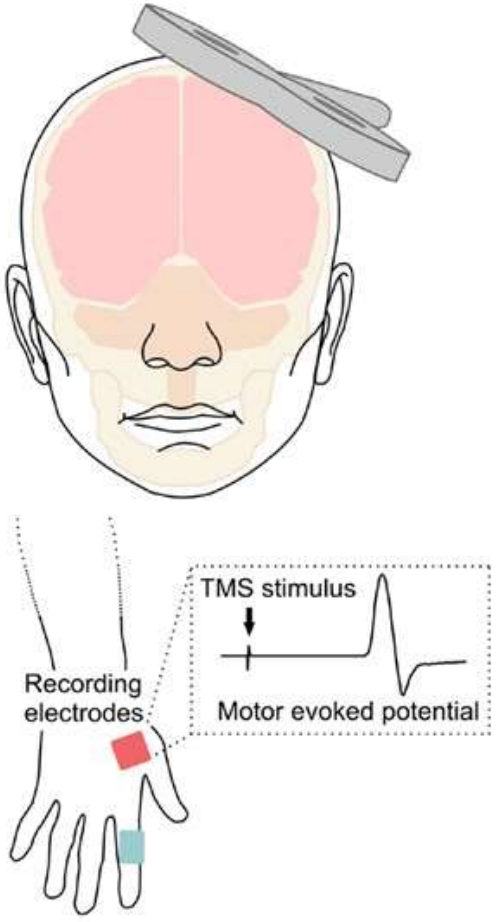


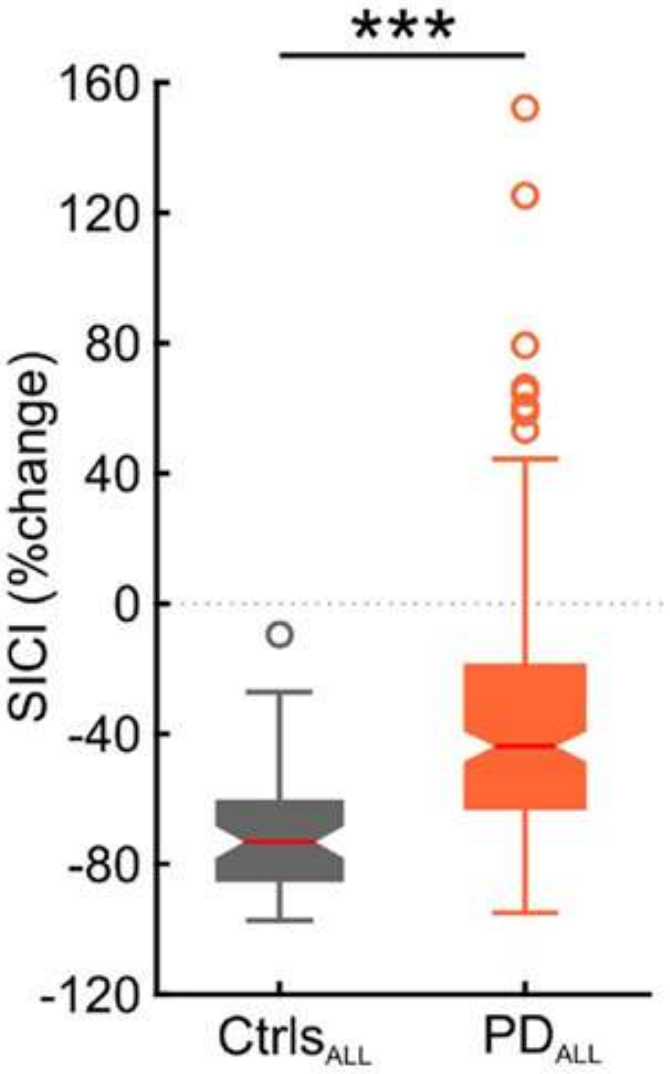
BIOL PSYCHIATRY 2008;64:248–251

Less inhibition in the motor cortex of patients with Parkinson's disease

SICI: short-interval intracortical inhibition

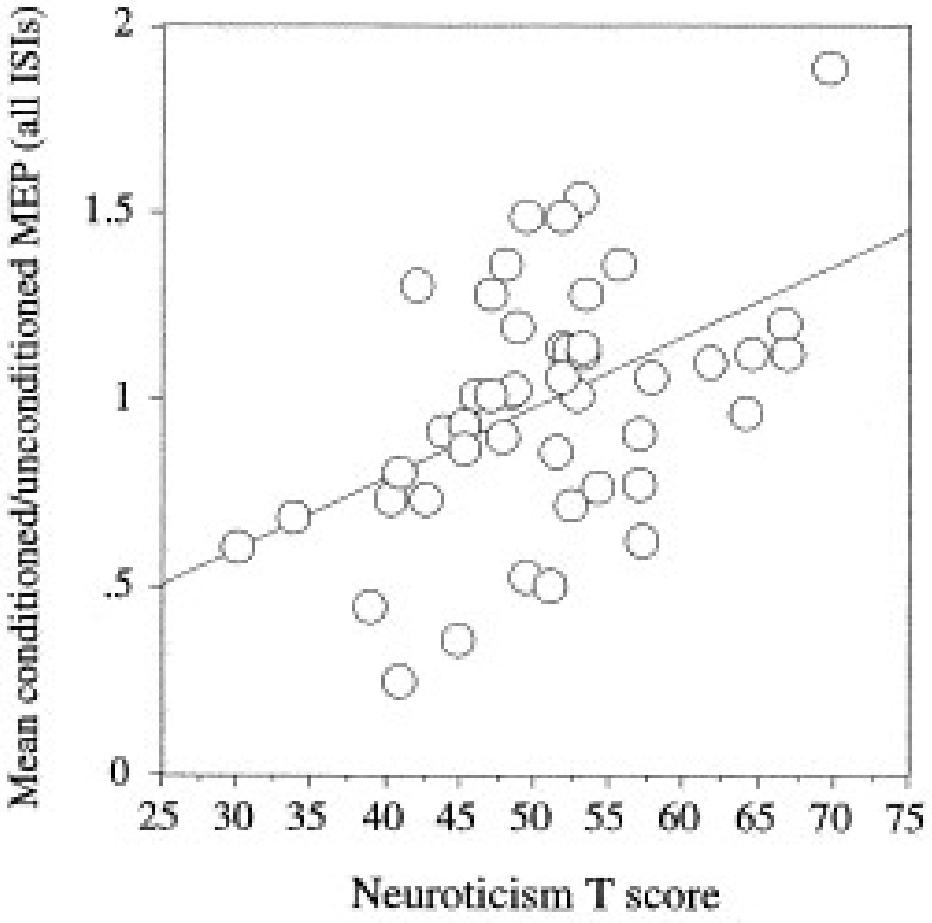
SICI reflects **synaptic inhibition** through the **GABA receptor**





Motor cortex excitability correlates with an anxiety-related personality trait

NEO-PI-R personality inventory.



Biological Psychiatry
Volume 50, Issue 5, 1 2001, 377-382

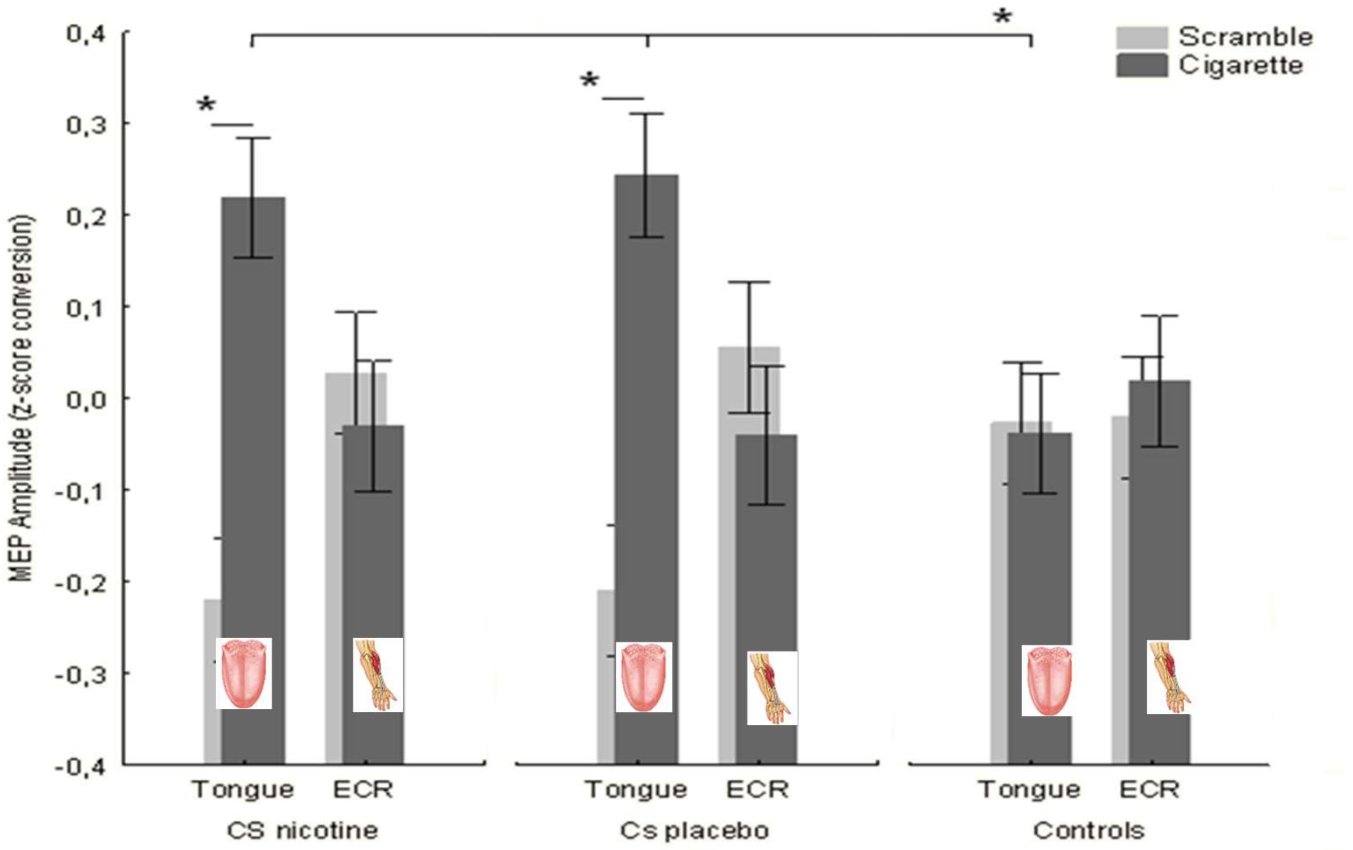
Nicotine Addiction

Research Paper

Enhanced corticobulbar excitability in chronic smokers during visual exposure to cigarette smoking cues

Carmelo M. Vicario, PhD; Naeem Komeilipoor, MS; Paola Cesari, PhD;
Robert D. Rafal, MD; Michael A. Nitsche, MD

J Psychiatry Neurosci



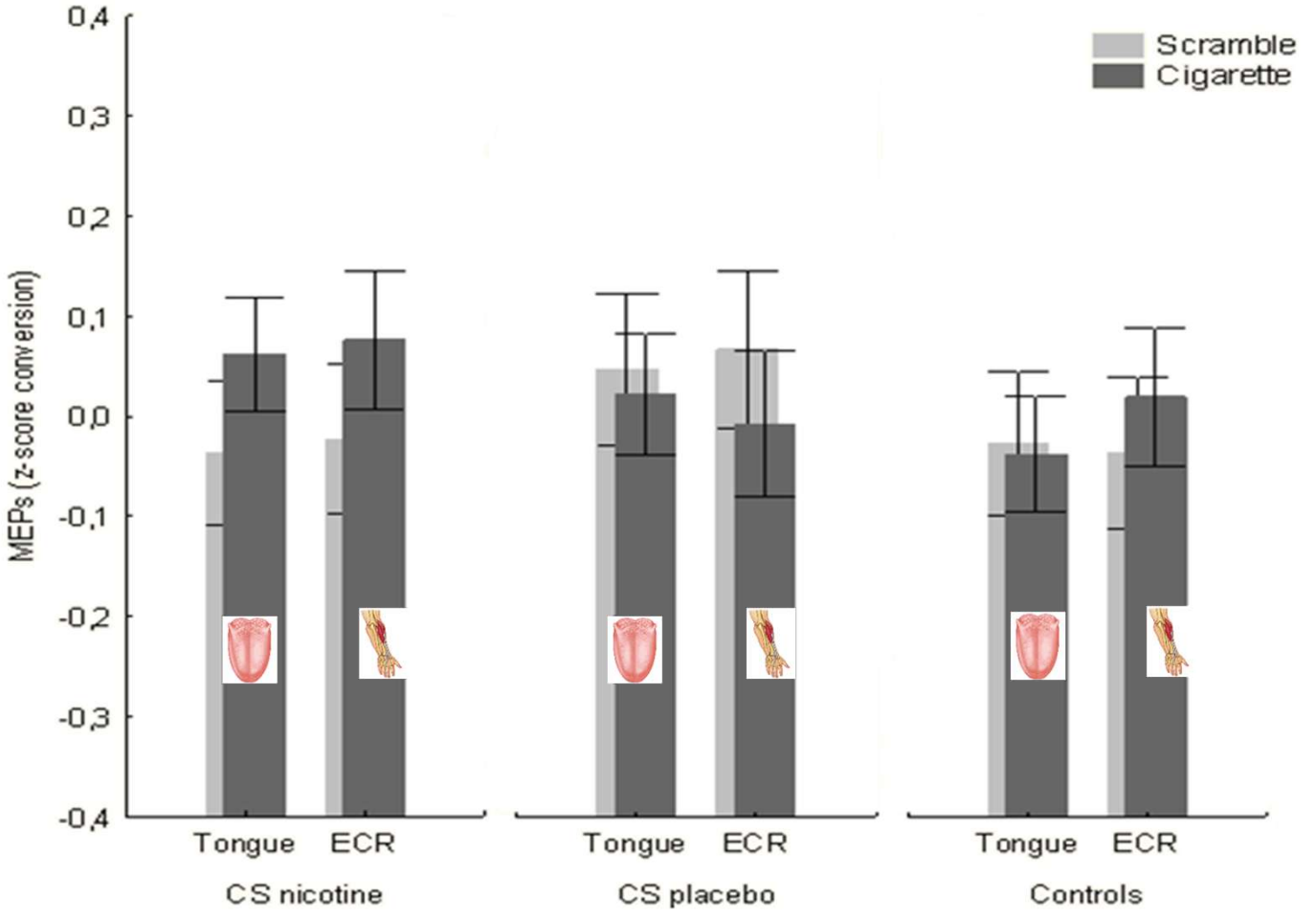
TNG MEPs during tobacco abstinence

Research Paper

Enhanced corticobulbar excitability in chronic smokers during visual exposure to cigarette smoking cues

Carmelo M. Vicario, PhD; Naeem Komeilipoor, MS; Paola Cesari, PhD;
Robert D. Rafal, MD; Michael A. Nitsche, MD

J Psychiatry Neurosci



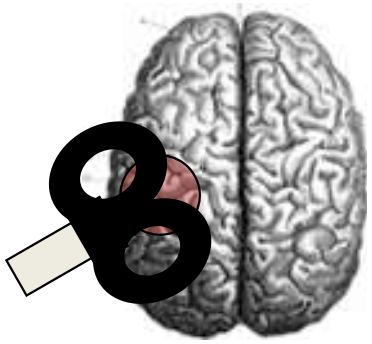
TNG MEPs following the smoking of a real/placebo cigarette

TMS as a tool to interfere with cortical activity.

TMS and causal approach

Interfering with the neural activity during the task execution to map cognitive functions

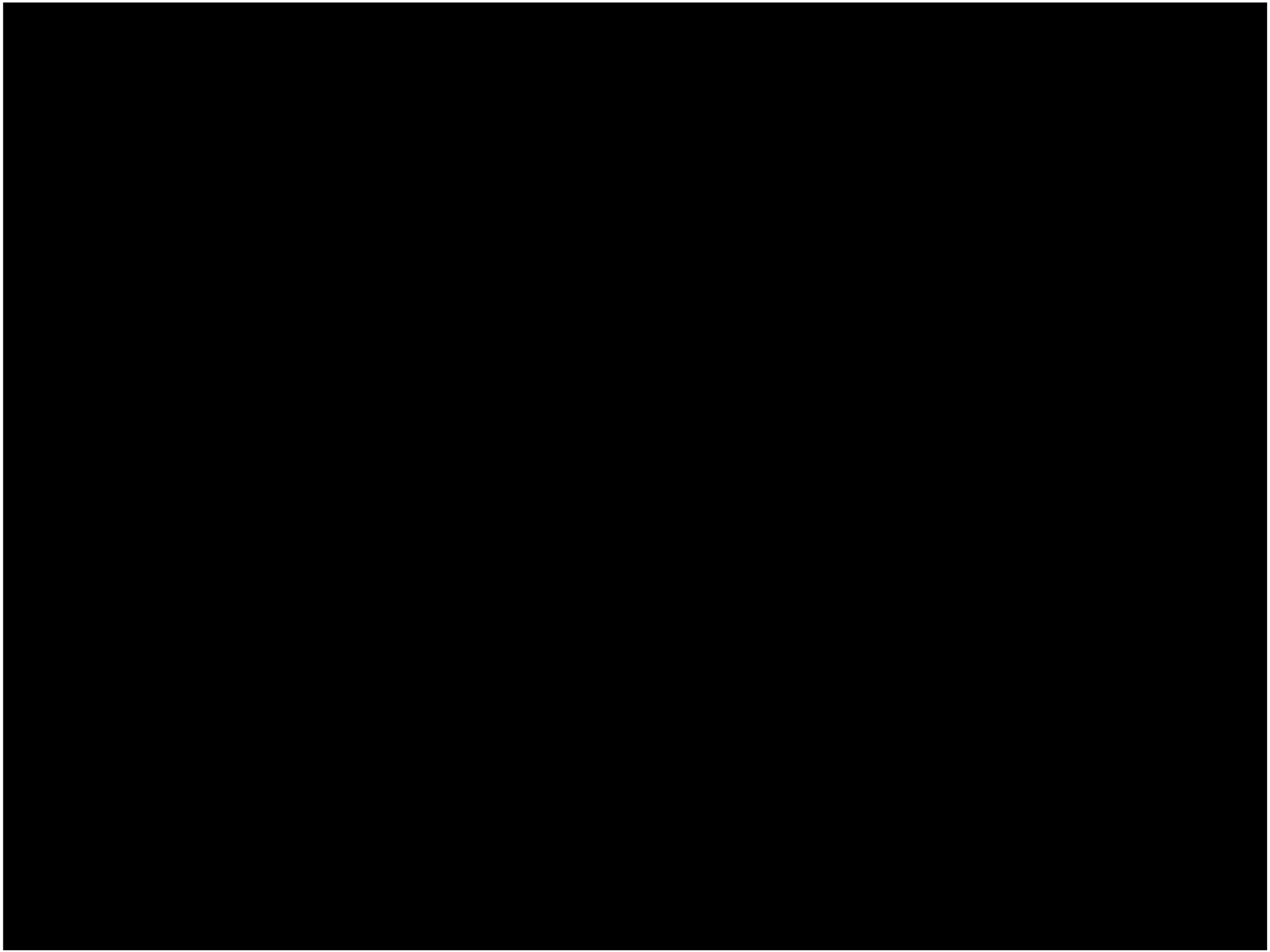
Virtual lesion to map cortical functions



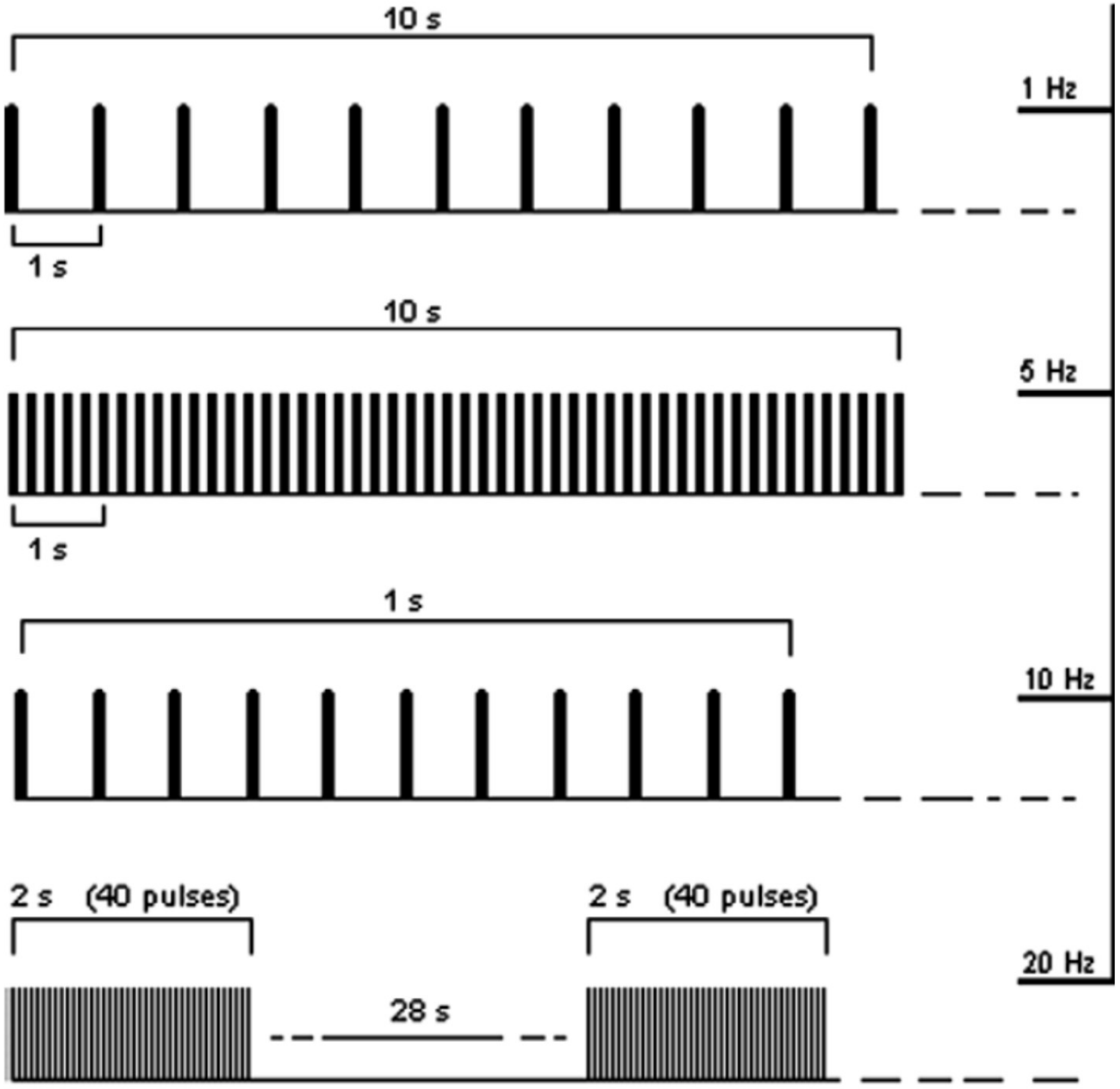
«Virtual Lesion»

Single pulses or trains of pulses (rTMS 5-30 Hz) released over a target area during the execution of a task can interfere with the performance.

Goal: establishing a causal relationship between brain and behavior



rTMS



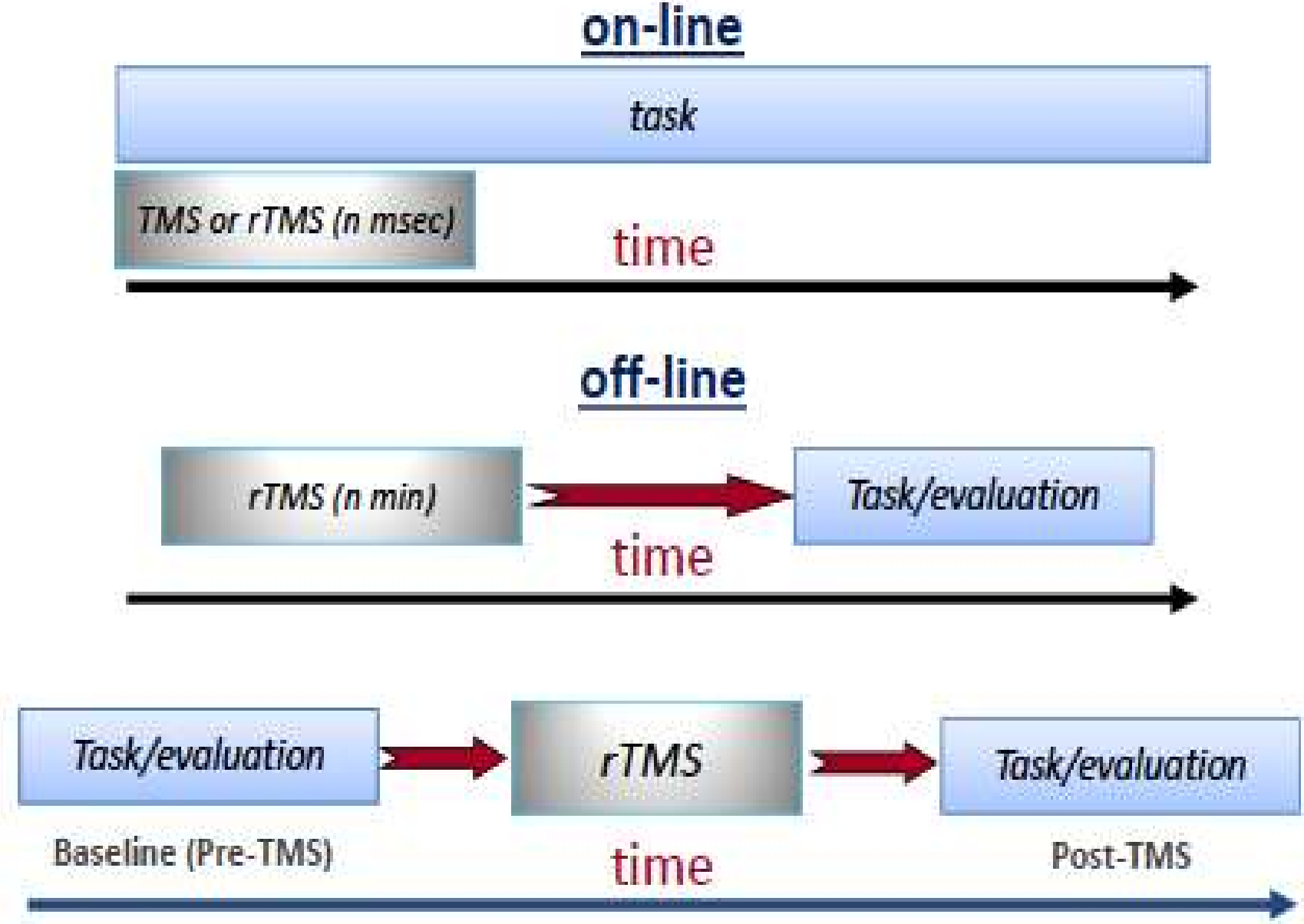
How TMS OR rTMS can be applied

TMS online

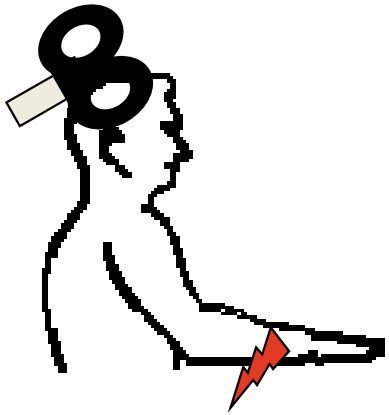
vs

TMS offline

HOW TMS OR rTMS can be applied

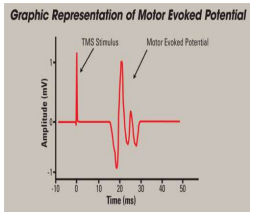


How to localize the region of interest over the scalp to be stimulated?

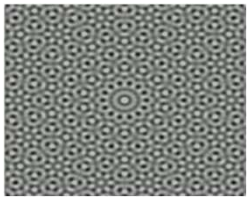


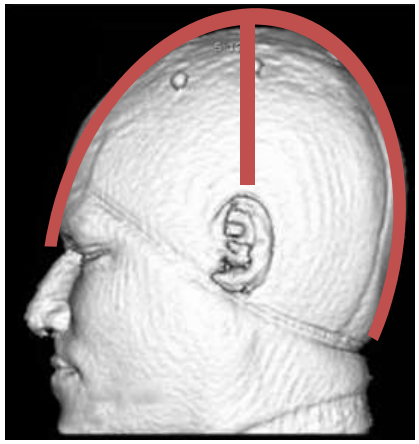
Via functional effect

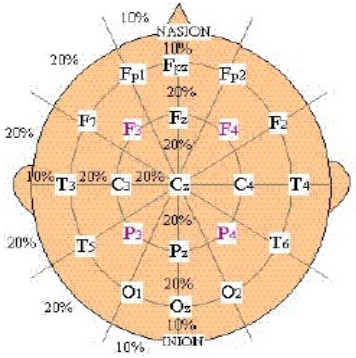
M1 – motor twitch (MEP)



V5 - visual phosphenes







Via anatomical landmark

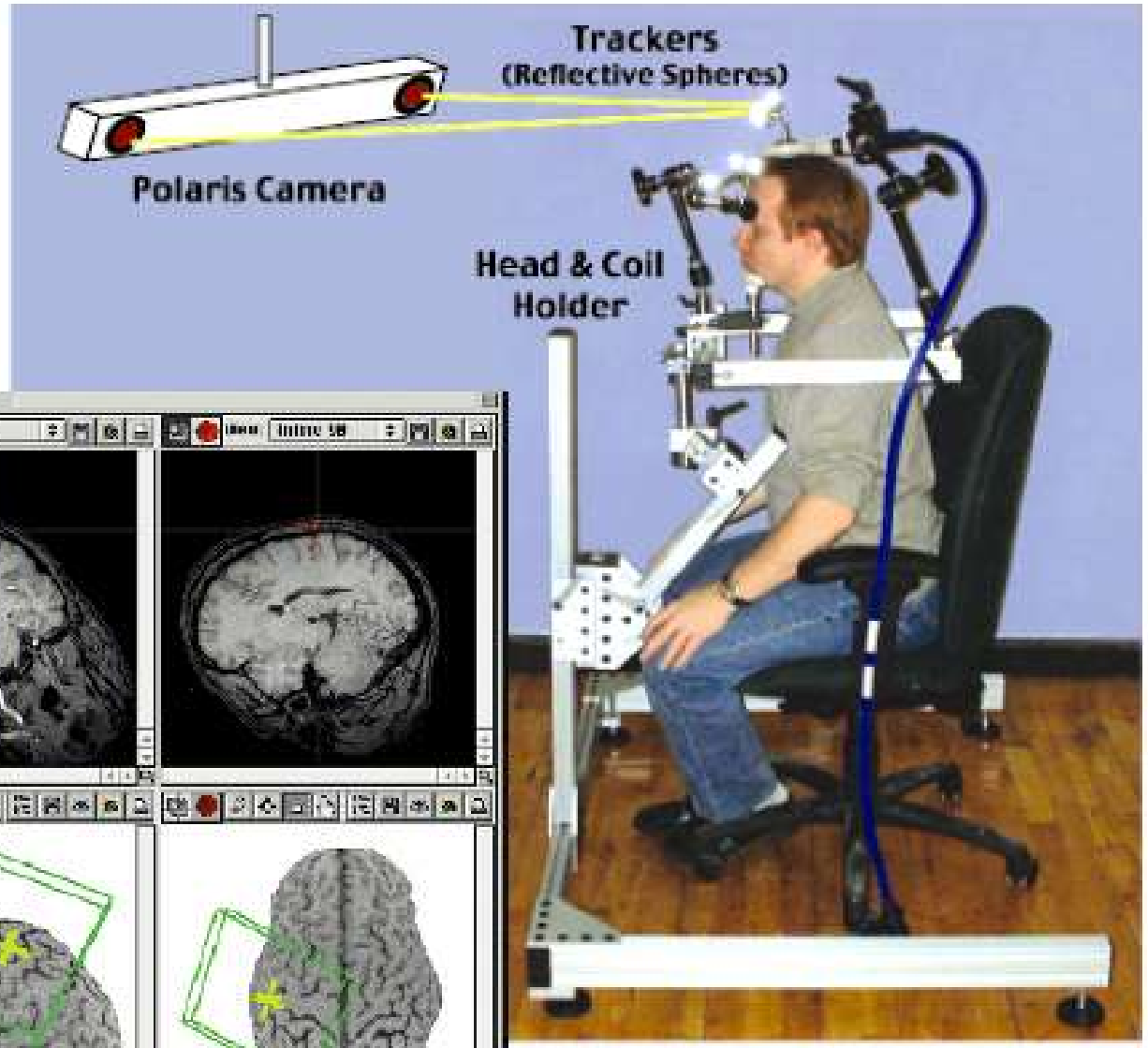
Inion/nasion, vertex system 10-20 (EEG)

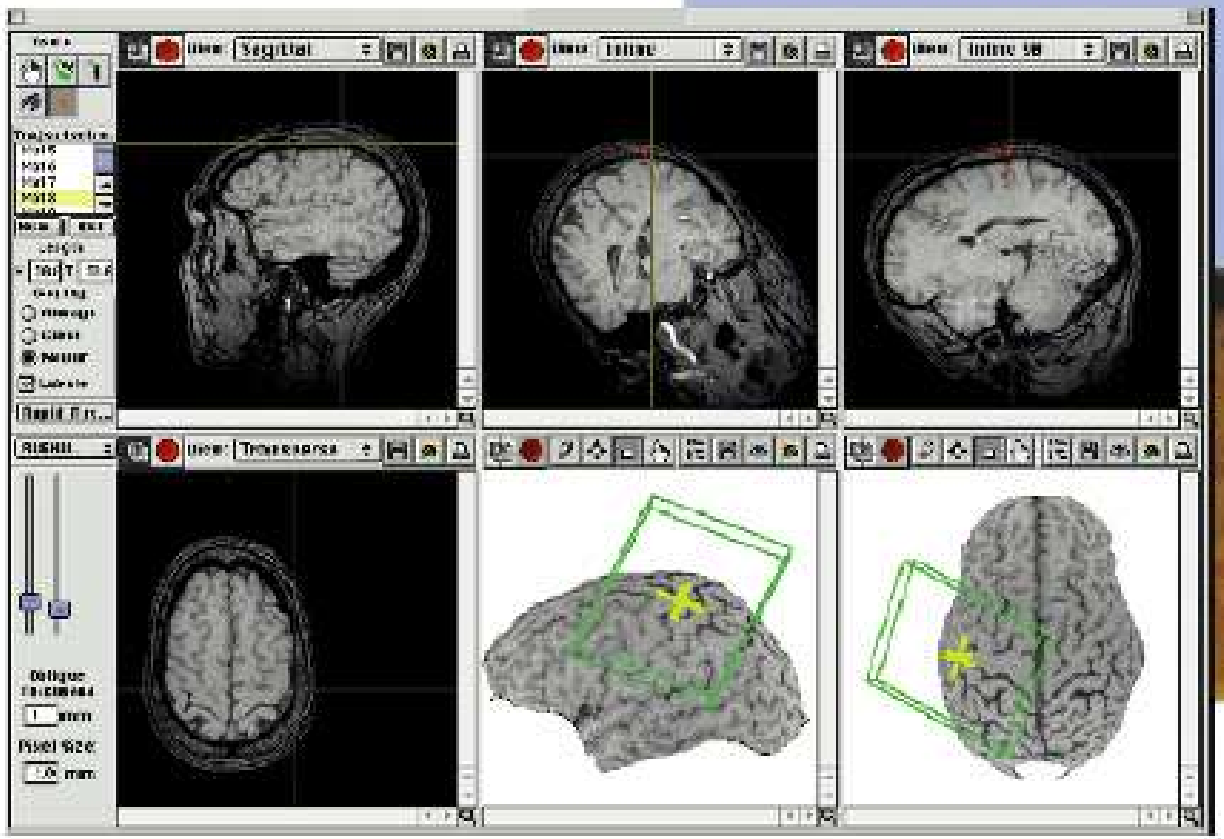
Moving from a specific point of the scalp

(e.g. FEF = 2-4 cm anteriorly and 2-4 cm lateraly from hand area).

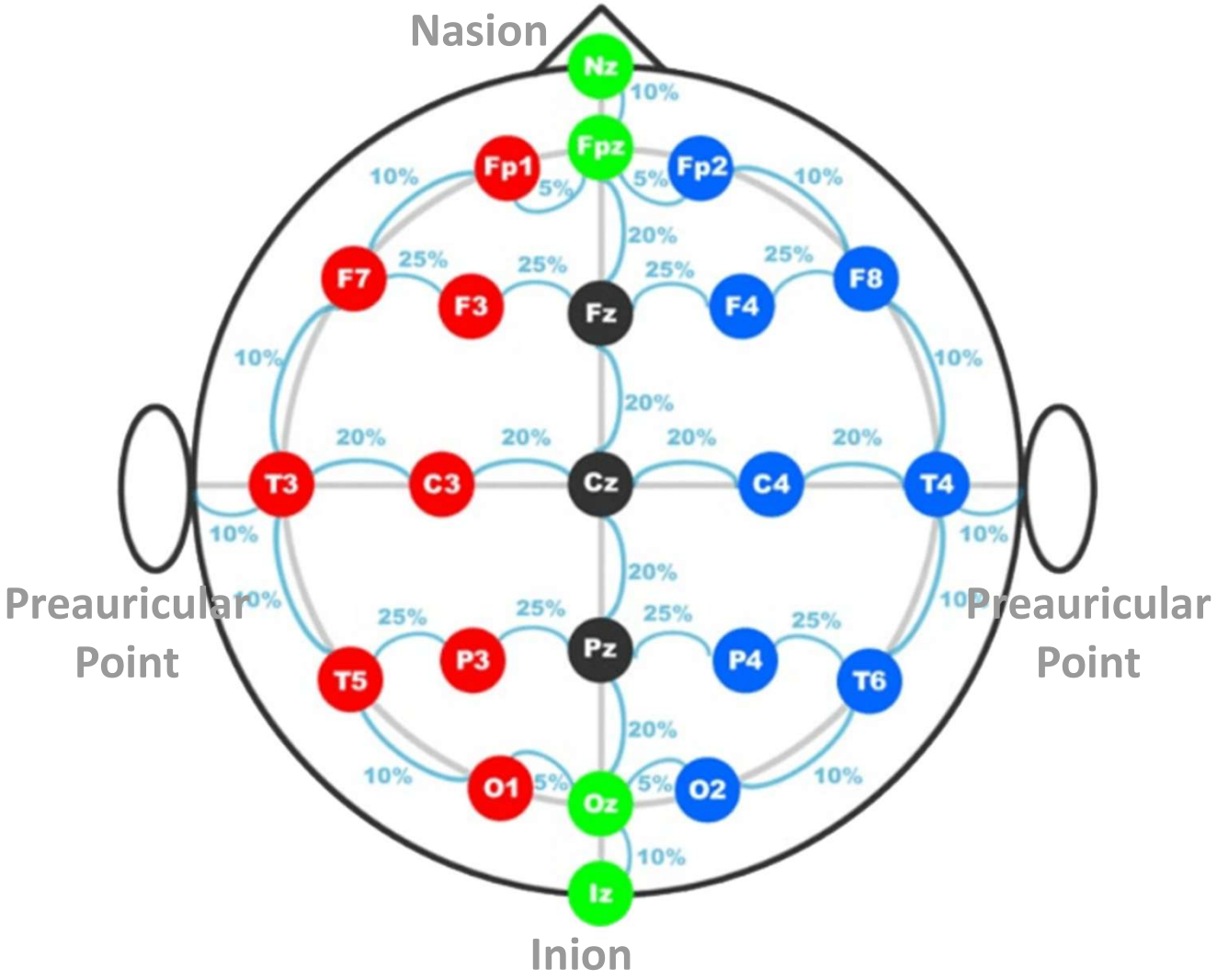
Neuronavigation

Using the MRI of the subject for online placement of the coil on the specific anatomical structure



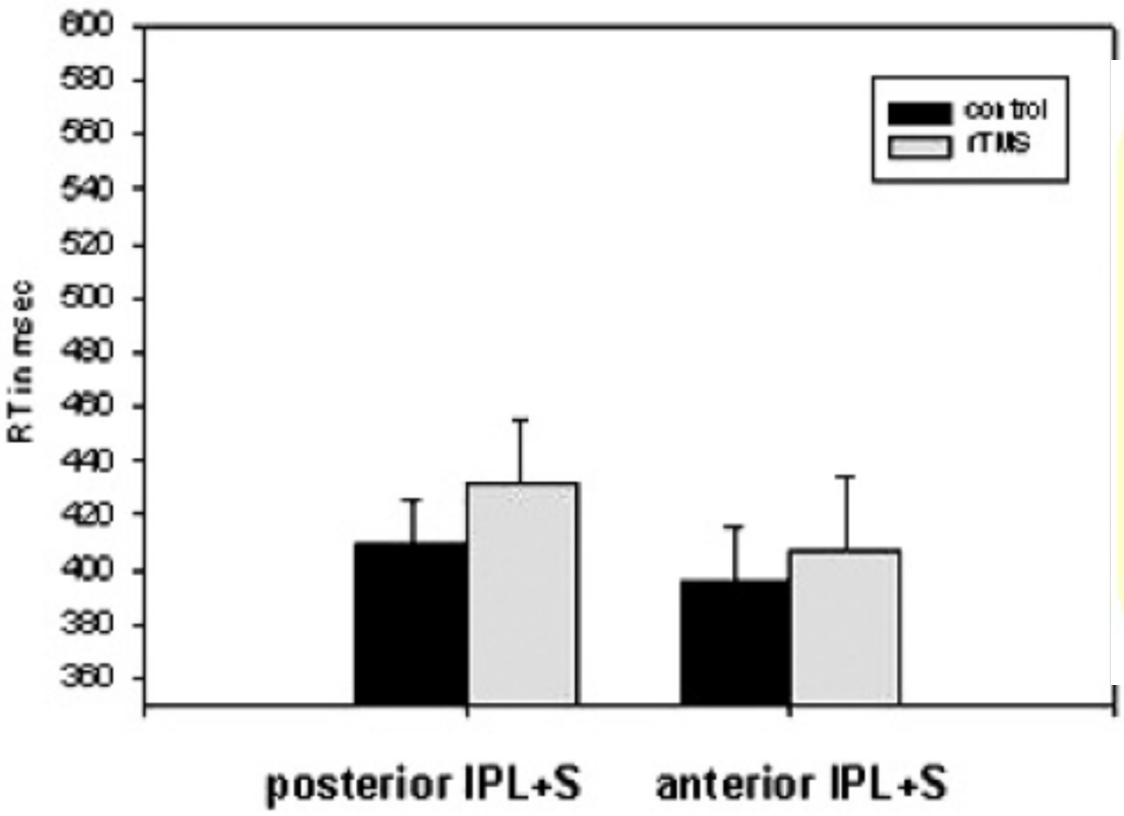


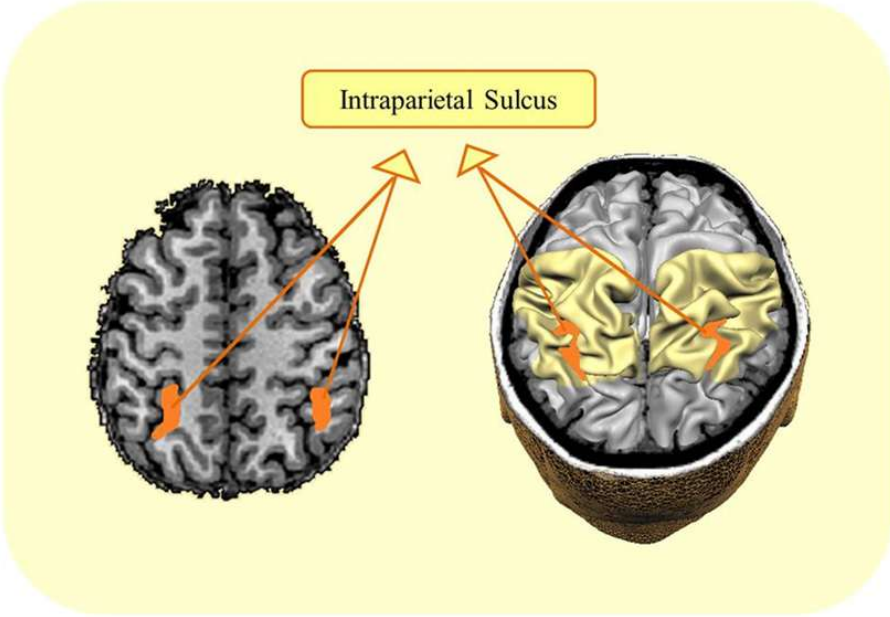
10-20 EEG System



Some example of TMS causal approach from the literature

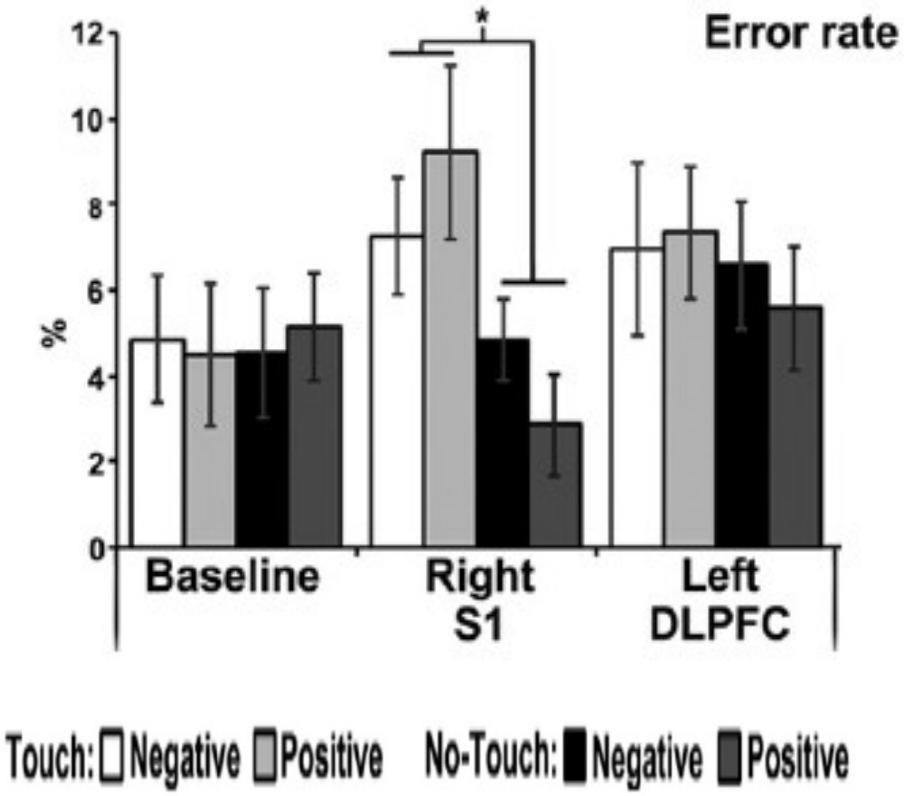
rTMS of the IPS slows down math performance





Göbel et al., 2006, *Cortex*

Offline rTMS of S1 modulates the understanding of affective touch



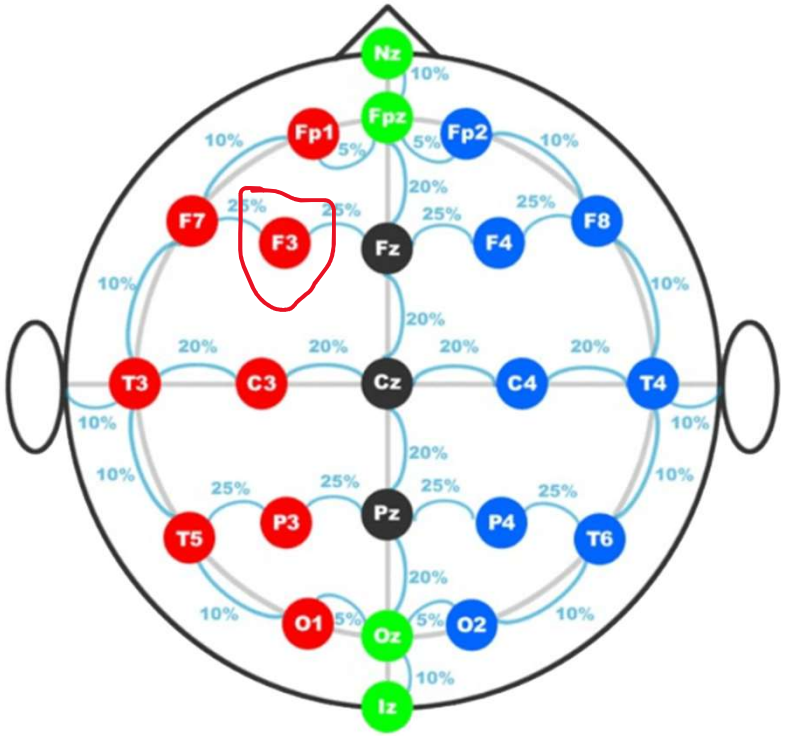
Bolognini et al., 2013, *Journal Neurosci.*

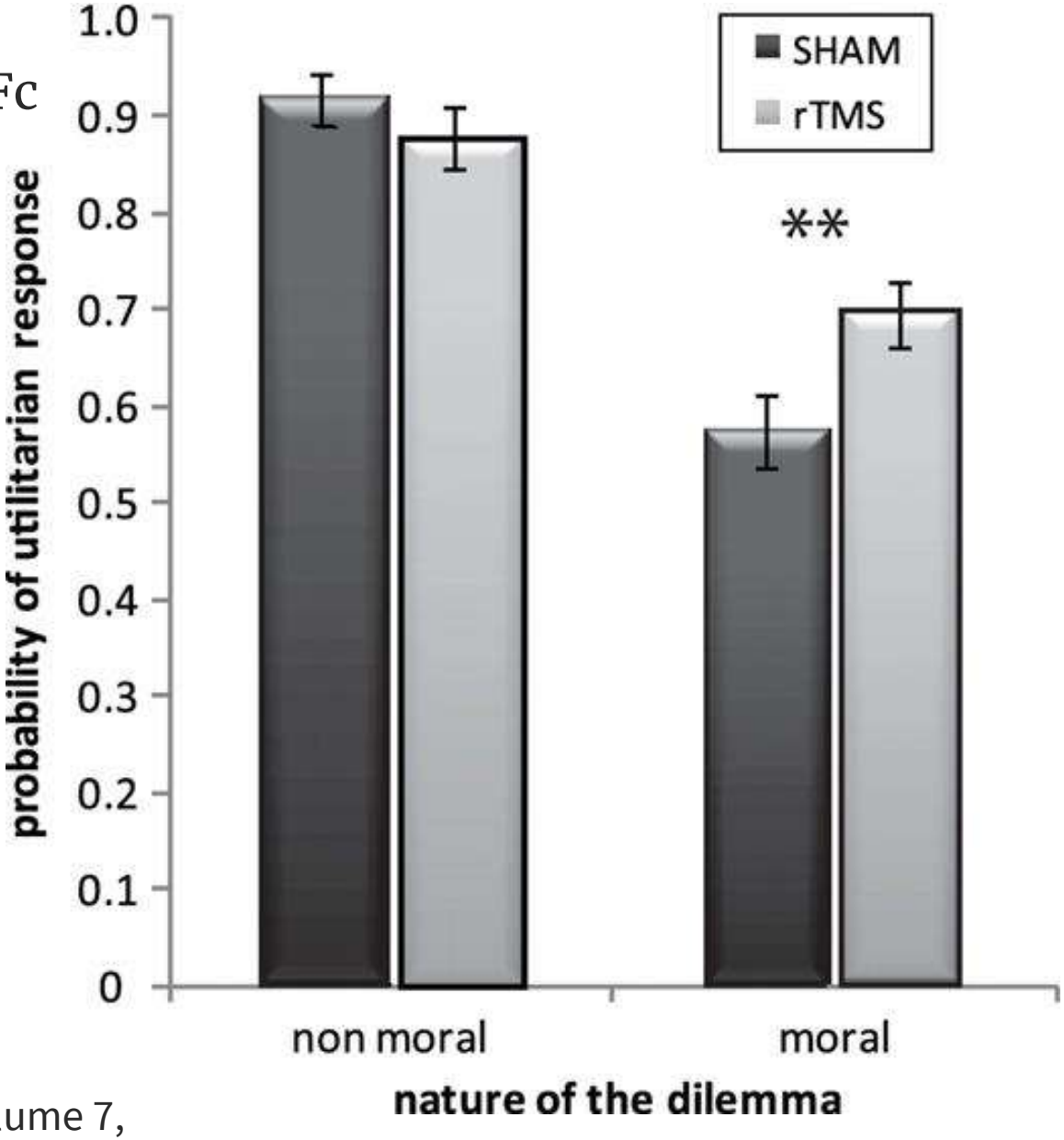
10 minutes of rTMS (1 Hz) on the right somatosensory cortex (**S1**) interferes with understanding the emotional states of others, but only in response to images involving touch.

Utilitarian: more rational and less affective response

Disrupting the right prefrontal cortex alters moral judgement

right DLPFc





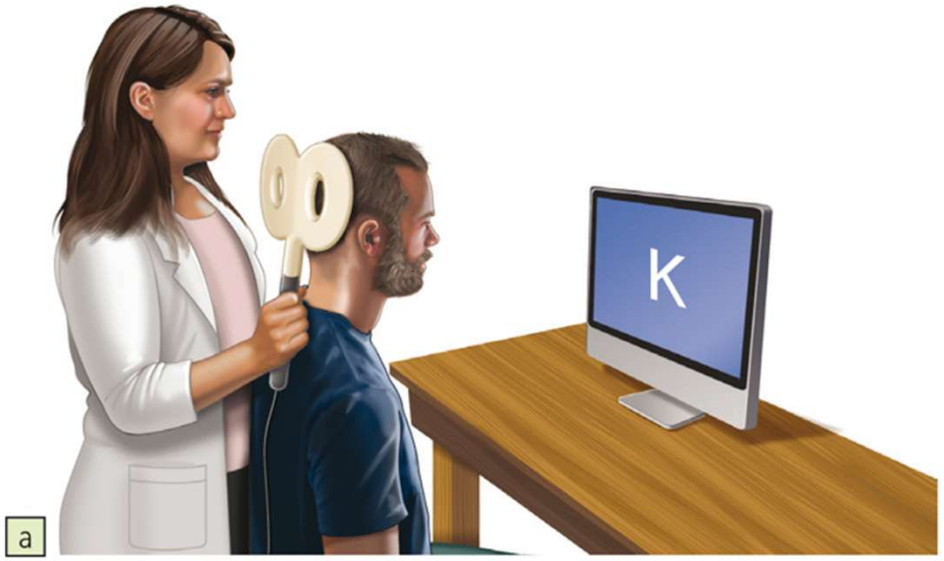
Social Cognitive and Affective Neuroscience, Volume 7, Issue 3, March 2012, Pages 282–288,

Online Interferential stimulation techniques

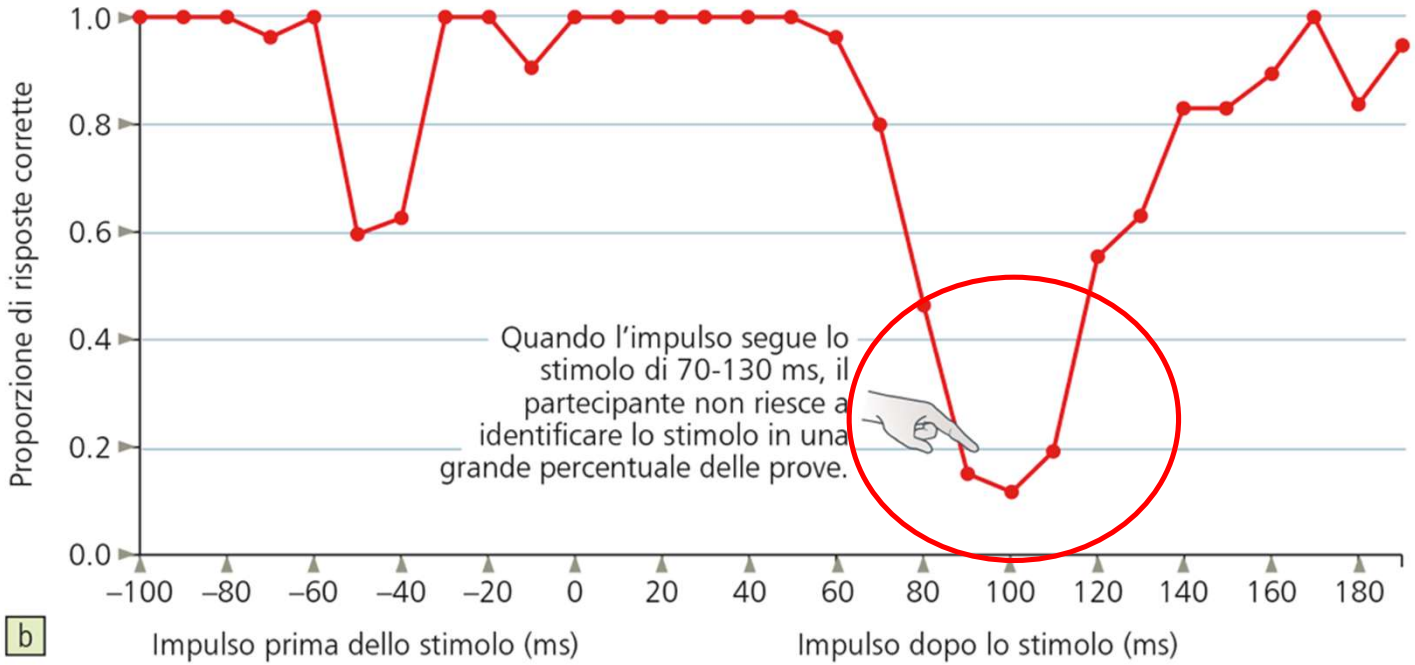
Online single pulse TMS and chronometry

When exactly is the stimulated area required to perform a task?

When: Single pulse TMS and stimulus detection



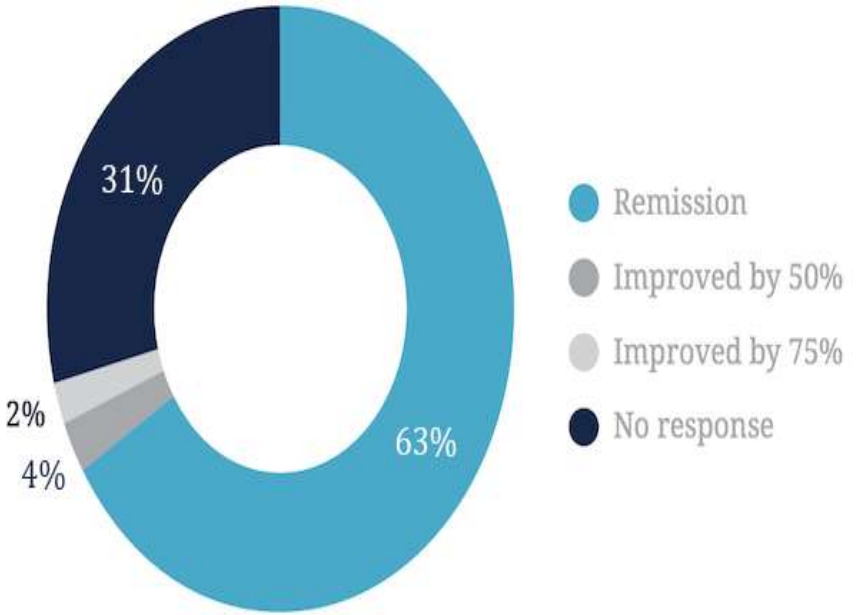
When exactly is the stimulated area required to perform a task?



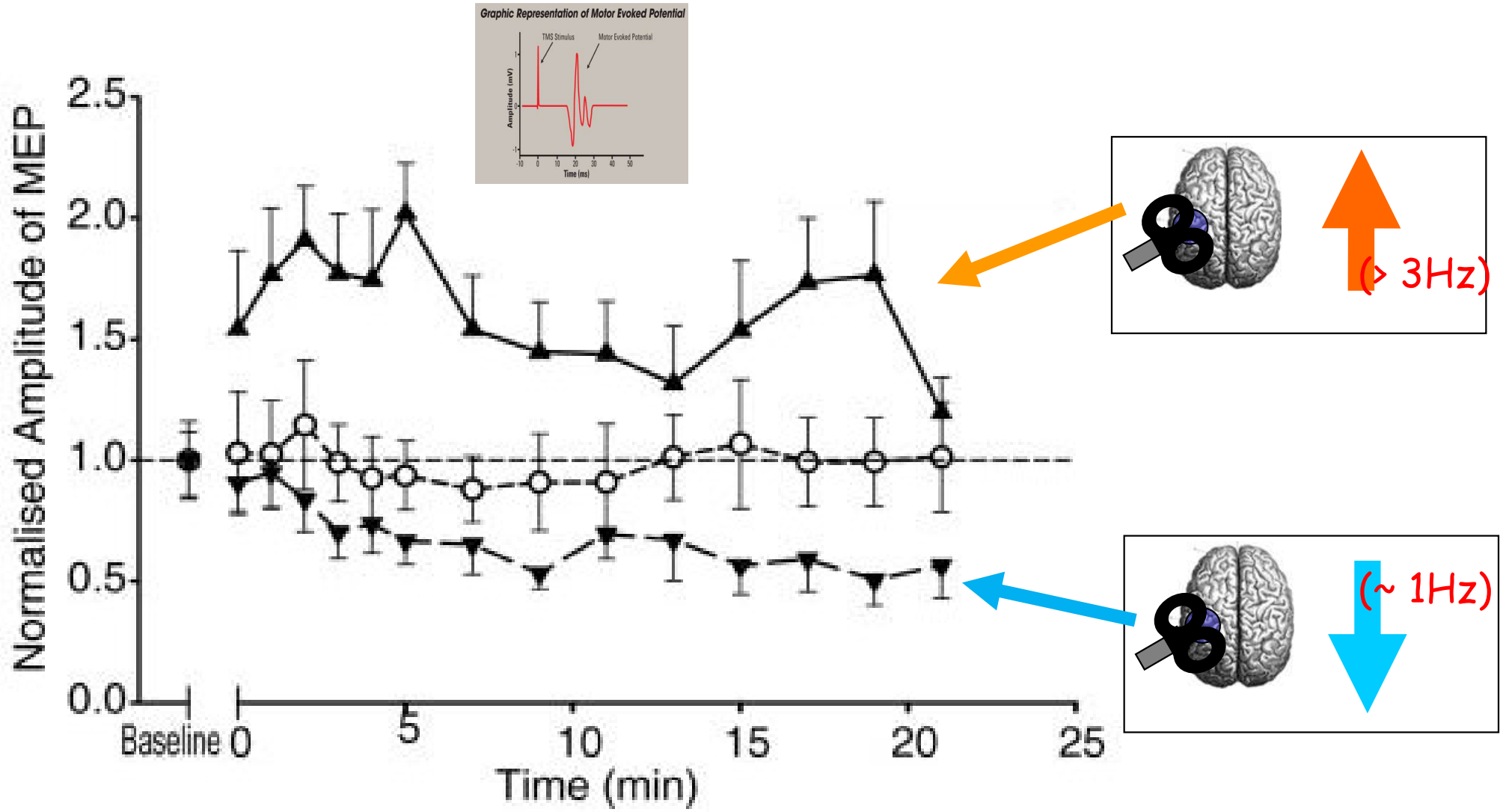
Amassian et al. 1989, *Electroencephalogr Clin Neurophysiol*

TMS and clinical applications

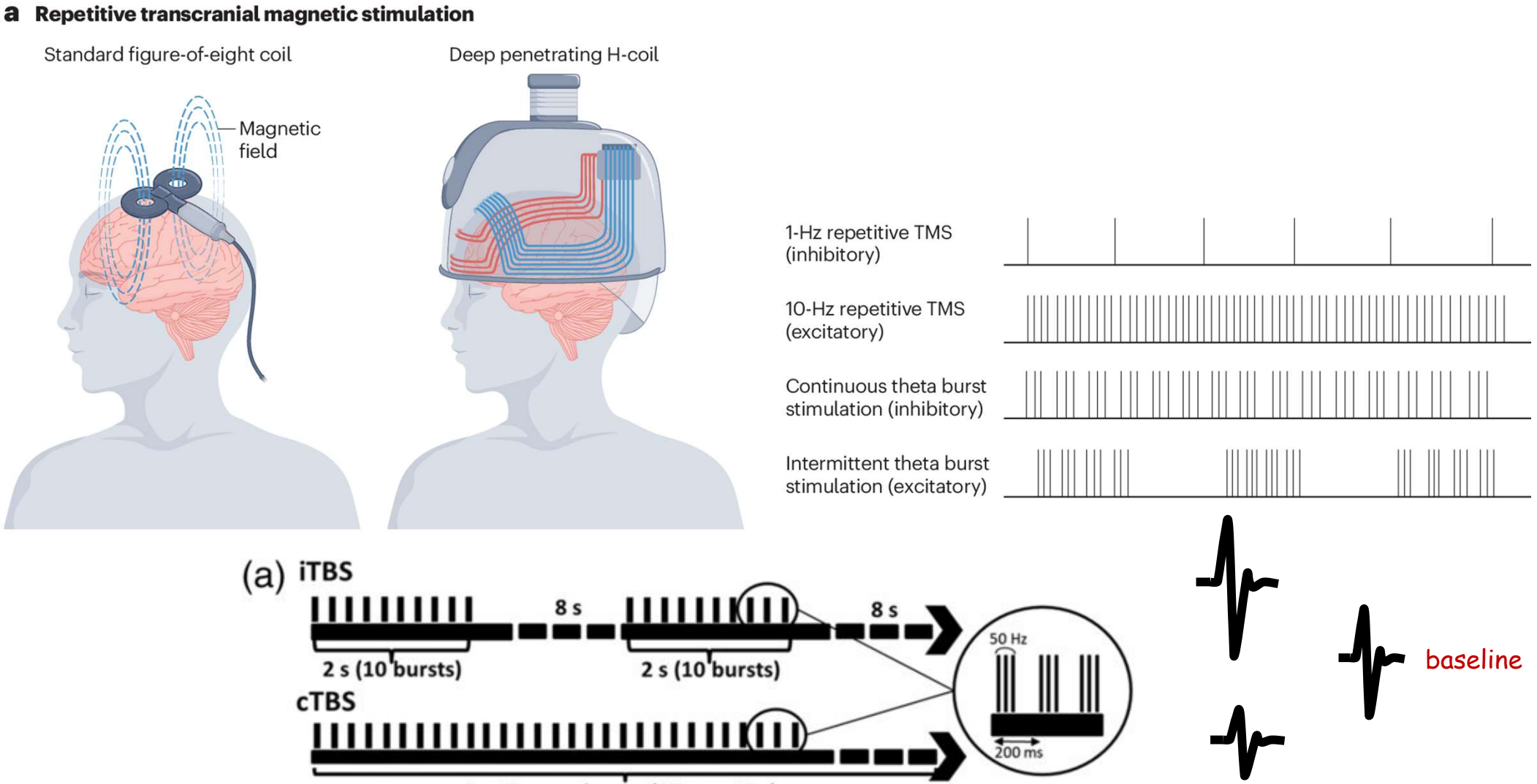
The FDA approved rTMS in 2008



Effects of high e low-frequency rTMS over M1 (measured via MEPs)



A single application of rTMS typically induces effects of the order of a few minutes, probably mediated by **changes in synaptic efficiency** (Long Term Potentiation / Long Term Depression)



Continuous TBS (cTBS) → ~600 impulsi in 40 sec

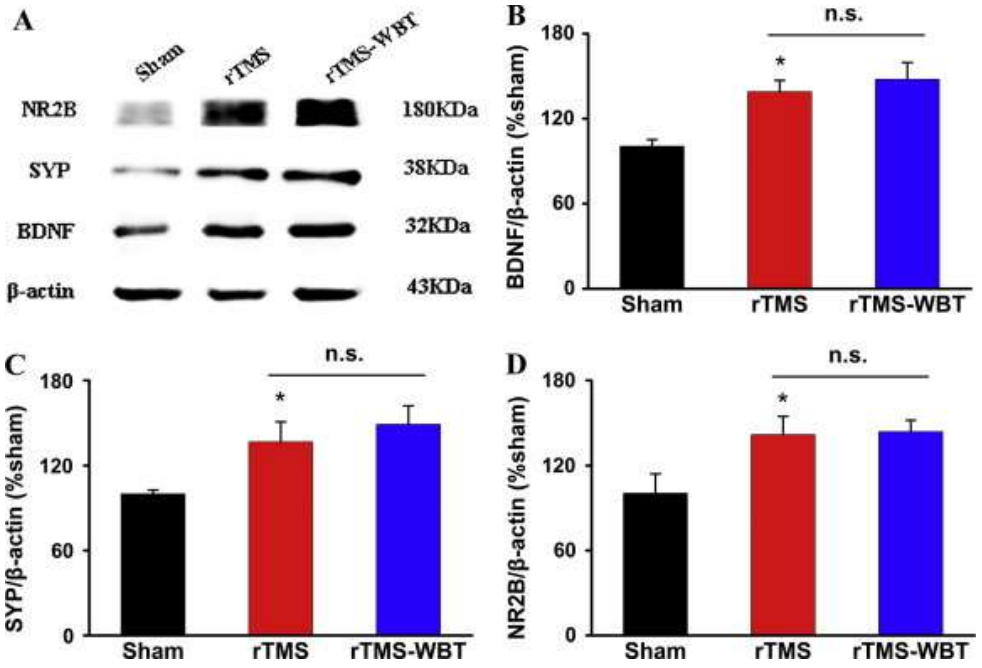
Intermittent TBS (cTBS) → ~600 impulsi con pause2/8 secs per 190 sec

Effects of high frequency rTMS on synaptic plasticity in the hippocampus

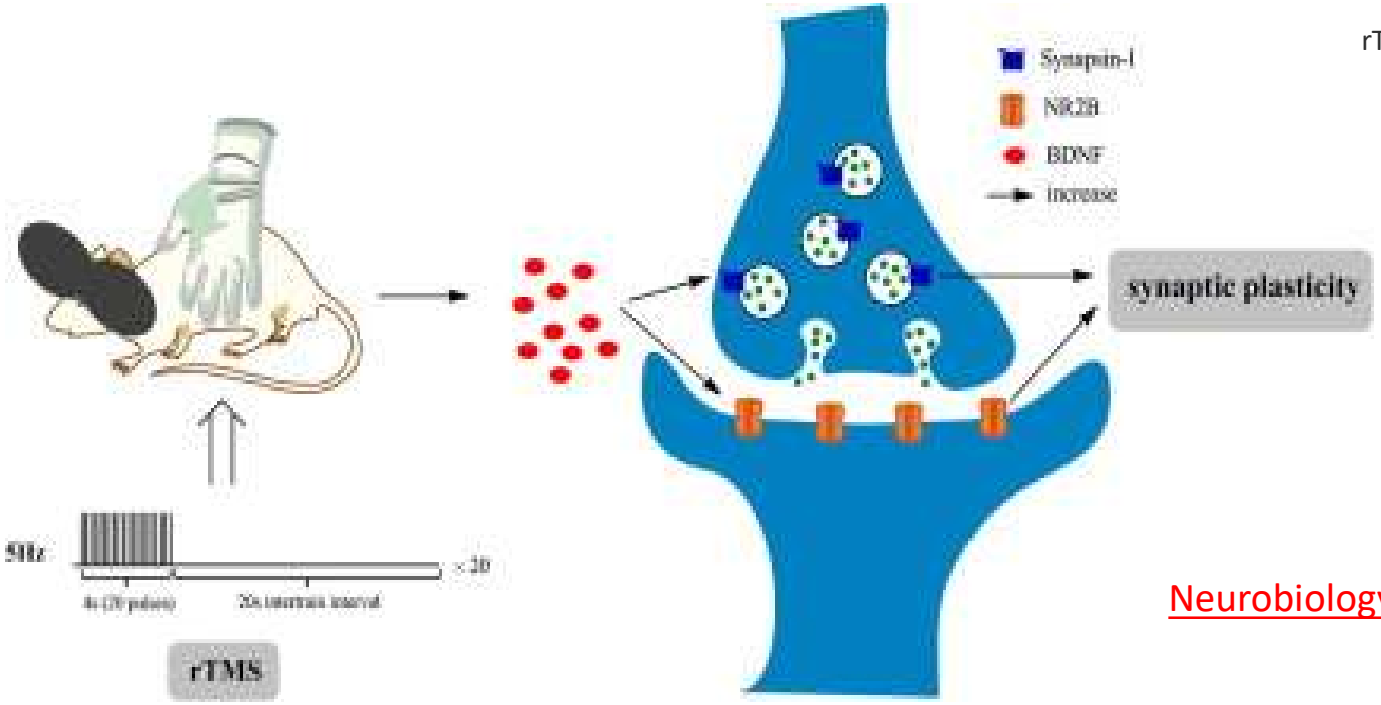
Brain-derived neurotrophic factor (BDNF)

Synaptophysin (SYP)

Postsynaptic protein NR2B (Channel)



rTMS without behavioral tasks group (WBT)



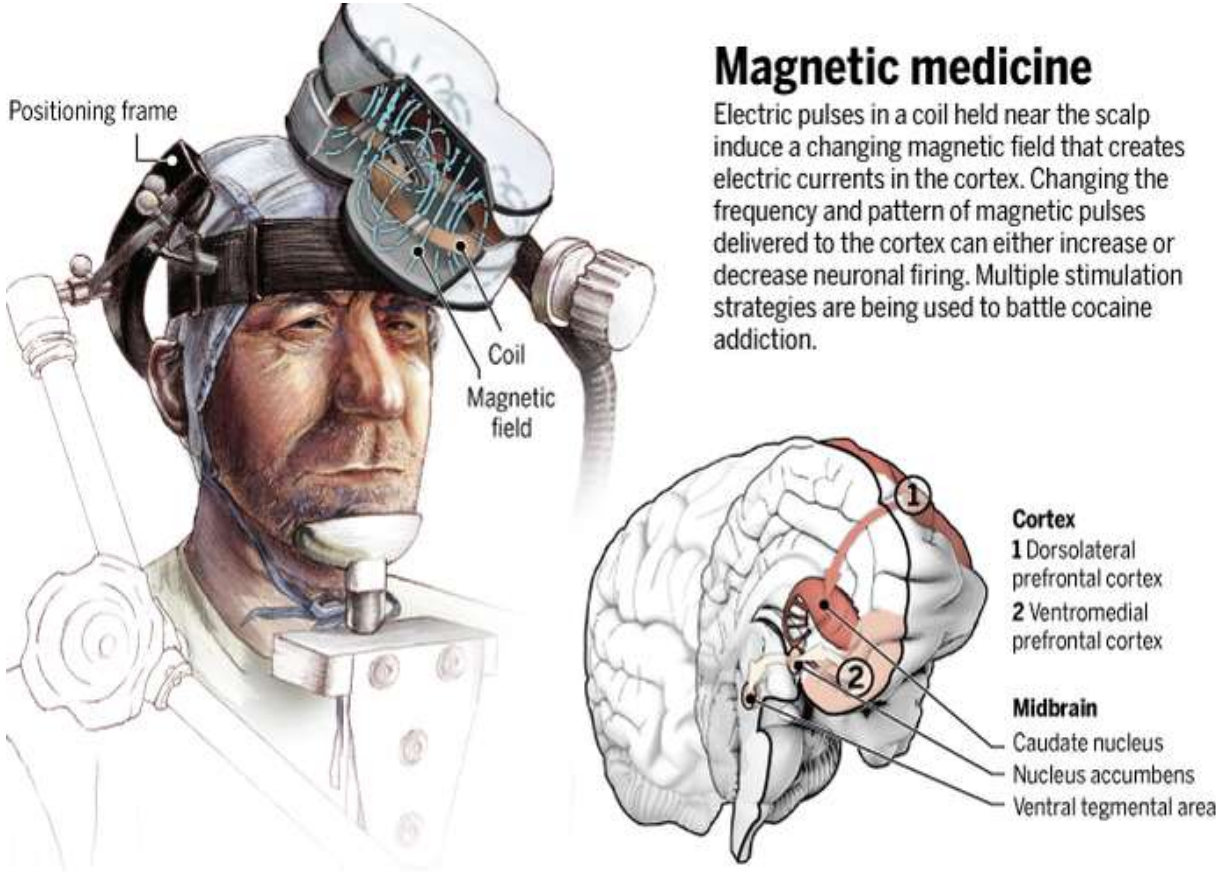
Results suggest that behavioral tasks do not significantly enhance the synaptic transmission in the present study.

Neurobiology of Learning and Memory 134, 2016, 369-378

Early report

Rapid-rate transcranial magnetic stimulation of left dorsolateral prefrontal cortex in drug-resistant depression

Alvaro Pascual-Leone, Belen Rubio, Federico Pallardó, Maria Dolores Catalá



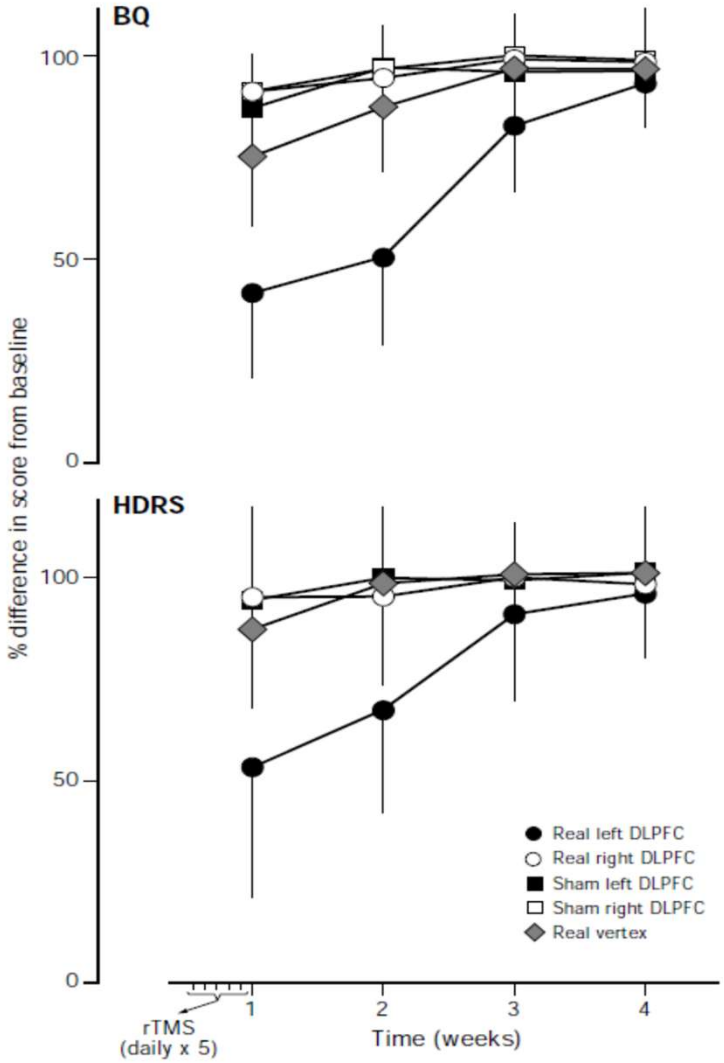


Figure 3: **Scores (mean and standard deviation) in Hamilton depression rating scale (HDRS) and Beck questionnaire (BQ) according to rTMS stimulation condition**
Mean results for all 17 patients are expressed as percentage difference from baseline scores. Baseline score is represented by score on Friday preceding week with daily rTMS—ie, last rating of preceding rTMS condition. Stimulation conditions A–E as in figure 1.

High frequency **(left)-DLPFC**

TMS e depression

Table 9
rTMS studies in depression (target: dorsolateral prefrontal cortex).

Articles	Number of patients	Target, coil type	Control condition	Stimulation frequency and intensity	Number of pulses/session and number of sessions	Results	Class of the study
HF rTMS of the left DLPFC							
Pascual-Leone et al. (1996b)	17	Left DLPFC, F8c	Tilted coil or active coil on irrelevant cortical sites	10 Hz, 90% RMT	2000 pulses, 5 sessions	Positive (24% responders, 48% improvement)	III
George et al. (1997)	12	Left DLPFC, F8c	Tilted coil	20 Hz, 80% RMT	800 pulses, 10 sessions	Positive (8% responders, 16% improvement)	III
Loo et al. (1999)	18	Left DLPFC, F8c	Tilted coil	10 Hz, 110% RMT	1500 pulses, 10 sessions	Negative (0% responders, 23% improvement)	III
Padberg et al. (1999)	18 (active: 12; control: 6)	Left DLPFC, F8c	Tilted coil	10 Hz or 0.3 Hz, 90% RMT	250 pulses, 5 sessions	Negative (6% improvement after 10 Hz, 19% after 0.3 Hz)	III
Berman et al. (2000)	20 (active: 10; control: 10)	Left DLPFC, F8c	Tilted coil	20 Hz, 80% RMT	800 pulses, 10 sessions	Positive (10% responders, 35% improvement)	III
Eschweiler et al. (2000)	12	Left DLPFC, F8c	Tilted coil	10 Hz, 110% RMT	1500 pulses, 10 sessions	Negative (0% responders, 23% improvement)	III
George et al. (2000)	30 (active: 20; control: 10)	Left DLPFC, F8c	Tilted coil	20/5 Hz, 100% RMT	1600 pulses, 10 sessions	Positive (20 Hz: 30% responders, 28% improvement; 5 Hz: 60% responders, 48% improvement)	III
Garcia-Toro et al. (2001a)	35 (active: 17; control: 18)	Left DLPFC, F8c	Tilted coil	20 Hz, 90% RMT	1200 pulses, 10 sessions	Positive (29% responders, 30% improvement); 29% of non-responders to sham rTMS will then respond to active rTMS	III
Garcia-Toro et al. (2001b)	22 (active: 11; control: 11)	Left DLPFC, F8c	Tilted coil and sertraline	20 Hz, 90% RMT	1200 pulses, 10 sessions	Negative compared to sertraline (36% responders, 38% improvement); no additive efficacy to sertraline	III
Manes et al. (2001)	20 (active: 10; control: 10)	Left DLPFC, F8c	Vertex stimulation	20 Hz, 80% RMT	800 pulses, 5 sessions	Negative (30% responders, 37% improvement)	III
Boutros et al. (2002)	21 (active: 12; control: 9)	Left DLPFC, F8c	Sham coil	20 Hz, 90% RMT	800 pulses,, 10 sessions	Negative (25% responders, 29% improvement)	III
Padberg et al. (2002)	31 (active: 20; control: 10)	Left DLPFC, F8c	Tilted coil	10 Hz, 90-100% RMT	1500 pulses, 10 sessions	Positive (20-30% responders, 15-30% improvement)	III
Nahas et al. (2003)	23 (active: 11; control: 12)	Left DLPFC, F8c	Tilted coil	5 Hz, 110% RMT	1600 pulses, 10 sessions	Negative (36% responders, 25% improvement)	III
Fregni et al. (2004)	42 (active: 21; control: 21)	Left DLPFC, F8c	Sham coil and fluoxetine	15 Hz, 110% RMT	3000 pulses, 10 sessions	Negative compared to fluoxetine (43% responders, 38% improvement); improvement for more than 2 months after rTMS as with fluoxetine, but with less adverse events for rTMS	III
Hausmann et al. (2004a)	25 (active: 12; control: 13)	Left DLPFC, F8c	Sham coil	20 Hz, 100% RMT	2000 pulses, 10 sessions	Negative (46% improvement)	III
Jorge et al. (2004)	20 (active: 10; control: 10)	Left DLPFC, F8c	Tilted coil	10 Hz, 100% RMT	1000 pulses, 10 sessions	Positive (30% responders, 38% improvement)	III
Koerselman et al. (2004)	52 (active: 26; control: 26)	Left DLPFC, C	Tilted coil	20 Hz, 80% RMT	800 pulses, 10 sessions	Negative (19% improvement)	II
Mosimann et al. (2004)	24 (active: 15; control: 9)	Left DLPFC, F8c	Tilted coil	20 Hz, 100% RMT	1600 pulses, 10 sessions	Negative (6% responders, 20% improvement)	III
Rossini et al. (2005a)	54 (active: 37; control: 17)	Left DLPFC, F8c	Tilted coil	15 Hz, 80–100% RMT	600 pulses, 10 sessions	Positive (80% RMT: 28% responders; 100% RMT: 61% responders)	II
Rossini et al. (2005b)	99 (active: 50; control: 49)	Left DLPFC, F8c + escitalopram, sertraline, or venlafaxine	Tilted coil	15 Hz, 100% RMT	900 pulses, 10 sessions	Positive (51% responders at 2 weeks; 80% responders at 5 weeks)	II
Rumi et al. (2005)	46 (active: 22; control: 24)	Left DLPFC, F8c + amitryptiline	Sham coil	5 Hz, 120% RMT	1250 pulses, 20 sessions	Positive (95% responders, 57% improvement); rTMS increases and speeds up the efficacy of amitriptyline	II
Su et al. (2005)	30 (active: 20; control: 10)	Left DLPFC, F8c	Tilted coil	20/5 Hz, 100% RMT	1600 pulses, 10 sessions	Positive (20 Hz: 60% responders, 58% improvement; 5 Hz: 60% responders, 54% improvement)	III
Avery et al. (2006), Herbsman et al. (2009)	68 (active: 35; control: 33)	Left DLPFC, F8c	Tilted coil	10 Hz, 110% RMT	1600 pulses, 15 sessions	Positive (20/3% responders between active and sham rTMS). Better response with more anterior and lateral stimulation sites	I
Anderson et al. (2007)	29 (active: 13; control: 16)	Left DLPFC, F8c	Sham coil	10 Hz, 110% RMT	1000 pulses, 20–30 sessions	Positive (43% responders, 55% improvement)	III
Bortolomasi et al. (2007)	19 (active: 12; control: 7)	Left DLPFC, F8c	Tilted coil	20 Hz, 90% RMT	800 pulses, 5 sessions	Positive (significant reduction of HDRS and Beck scores at 1–4 weeks)	III

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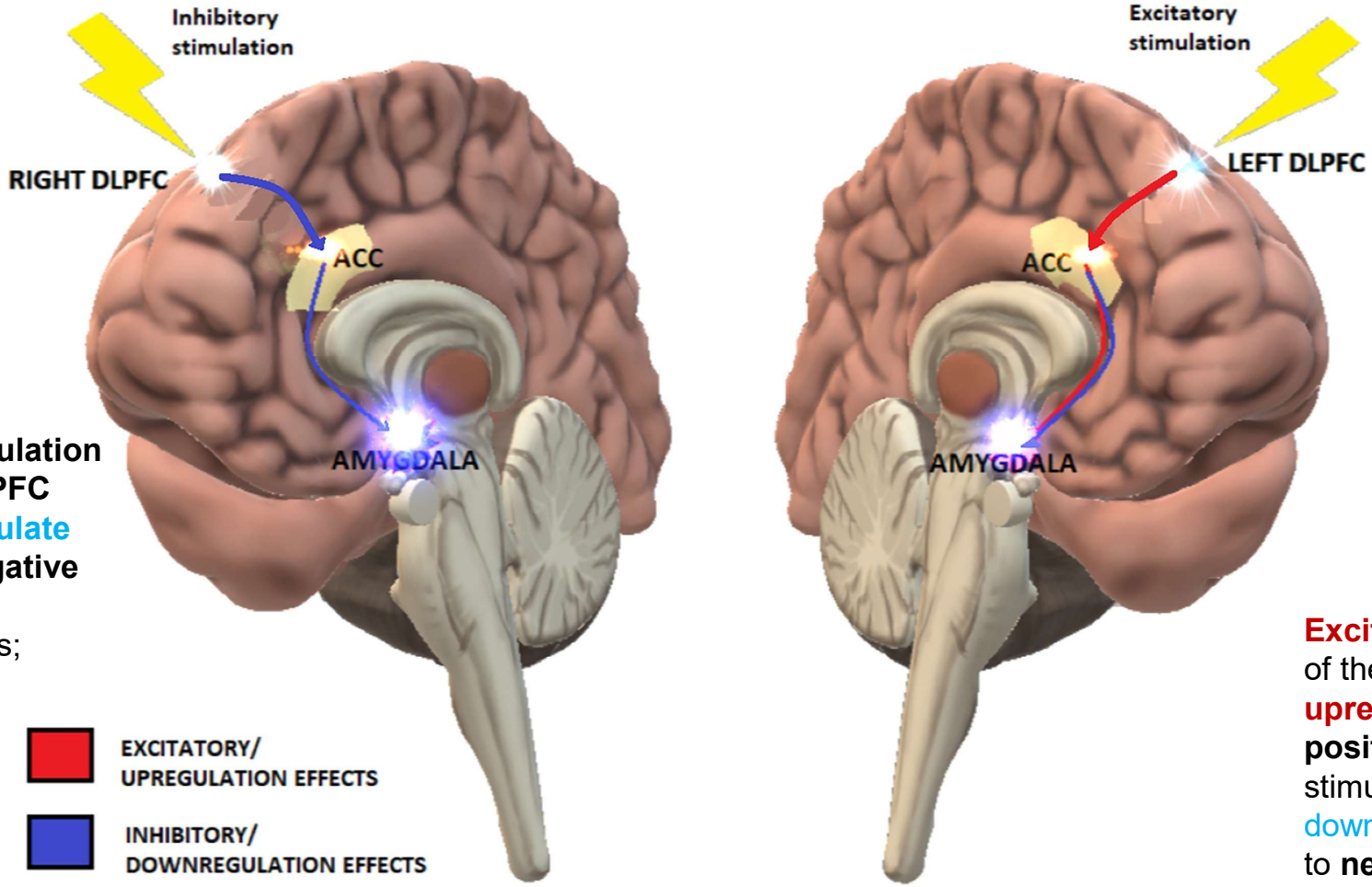
journal homepage: www.elsevier.com/locate/neubiorev

A systematic review on the therapeutic effectiveness of non-invasive brain stimulation for the treatment of anxiety disorders

C.M. Vicario[a,b,f,*], Mohammad Ali Salehinejad[b,c], K. Felmingham[d], G. Martino[a], M.A. Nitsche[b,e]

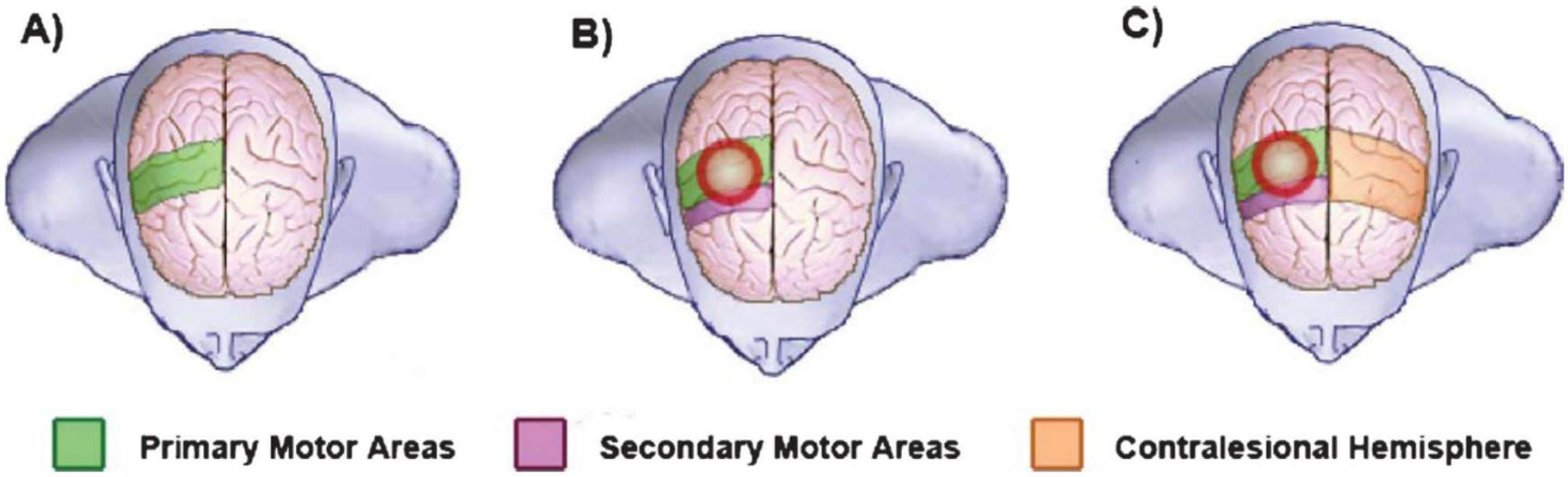


Inhibitory stimulation of the **right DLPFC** might **downregulate** reactions to **negative emotional** stimuli/outcomes;

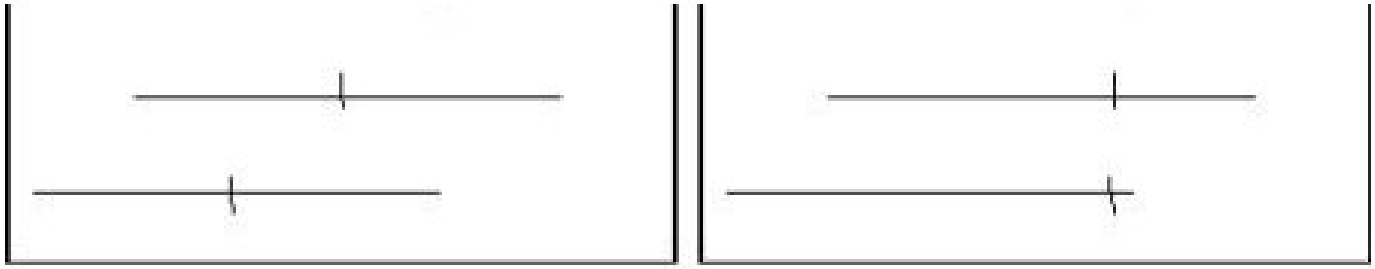
Excitatory stimulation of the **left DLPFC** might **upregulate** reactions to **positive emotional** stimuli/outcomes and downregulate reactions to **negative emotional** stimuli/outcomes.

TMS and stroke

Treatment strategies: inhibition of the health brain hemisphere and/or excitation of the activity of the damaged hemisphere

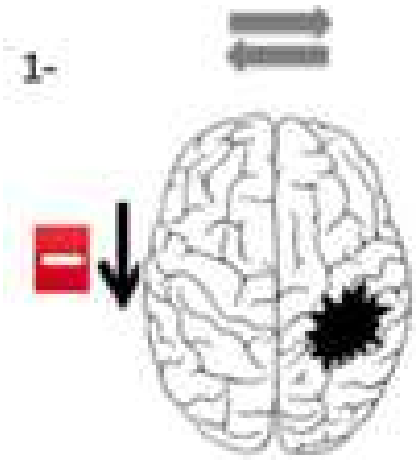


rTMS of the unaffected hemisphere transiently reduces contralesional visuospatial hemineglect



A. Normal line bisection

B. Highly impaired line bisection



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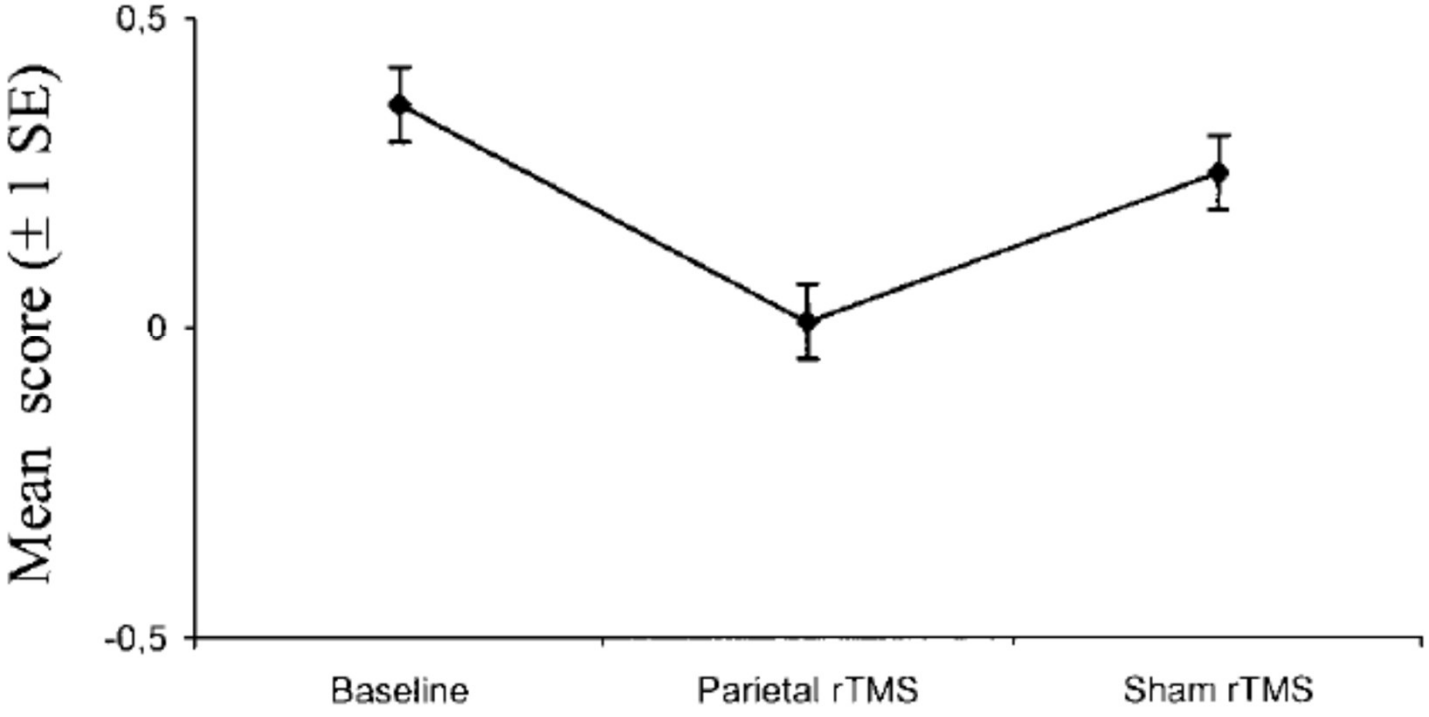


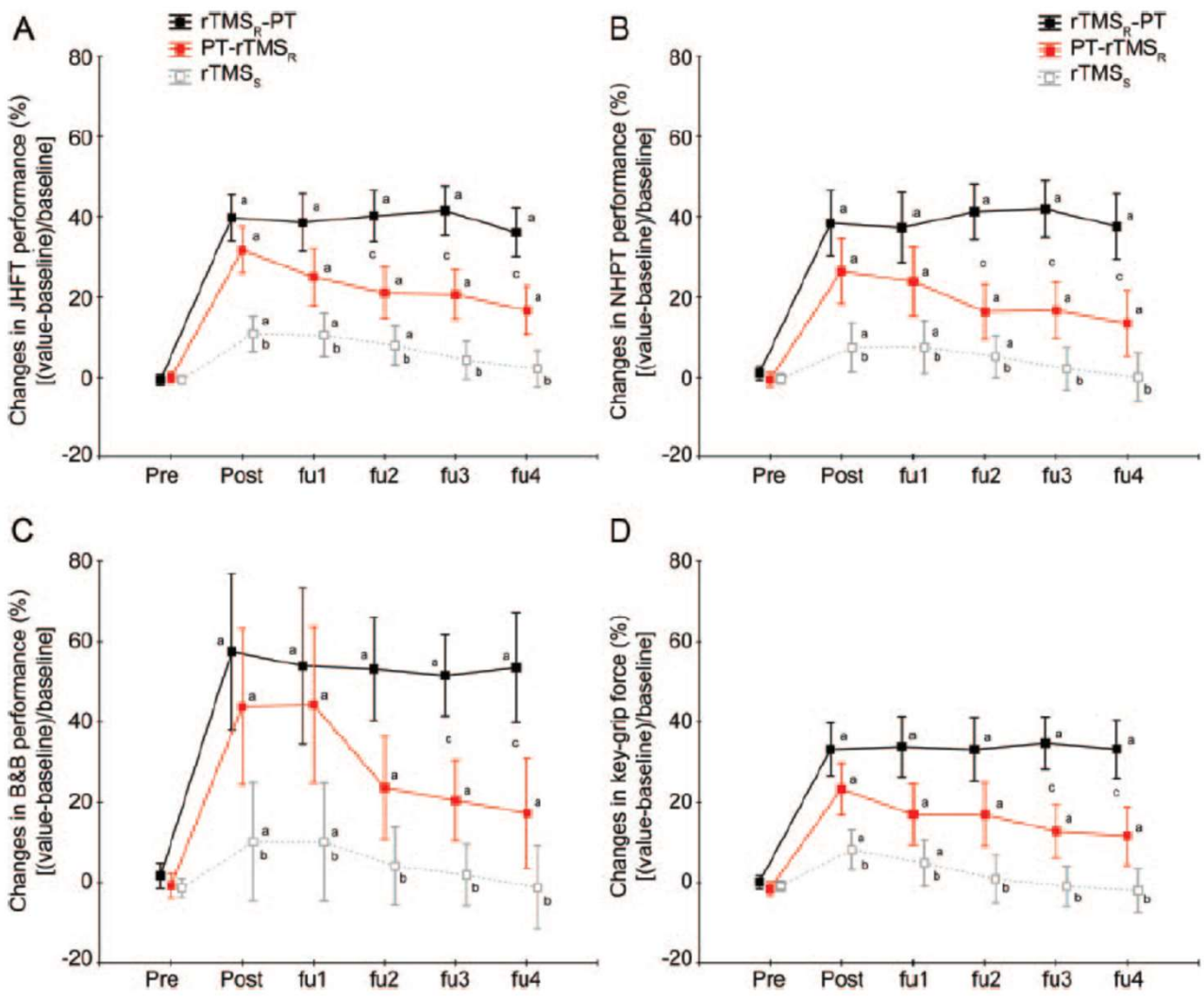
Combining rTMS with physical therapy in chronic stroke

Low-frequency rTMS promotes use-dependent motor plasticity in chronic stroke

A randomized trial

A. Avenanti, PhD
M. Coccia, MD
E. Ladavas, PhD
L. Provinciali, MD
M.G. Ceravolo, MD

Figure 3 Changes in performance in tests tapping trained motor functions



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Psychology Press
Taylor & Francis Group

Improved naming after TMS treatments in a chronic, global aphasia patient – case report

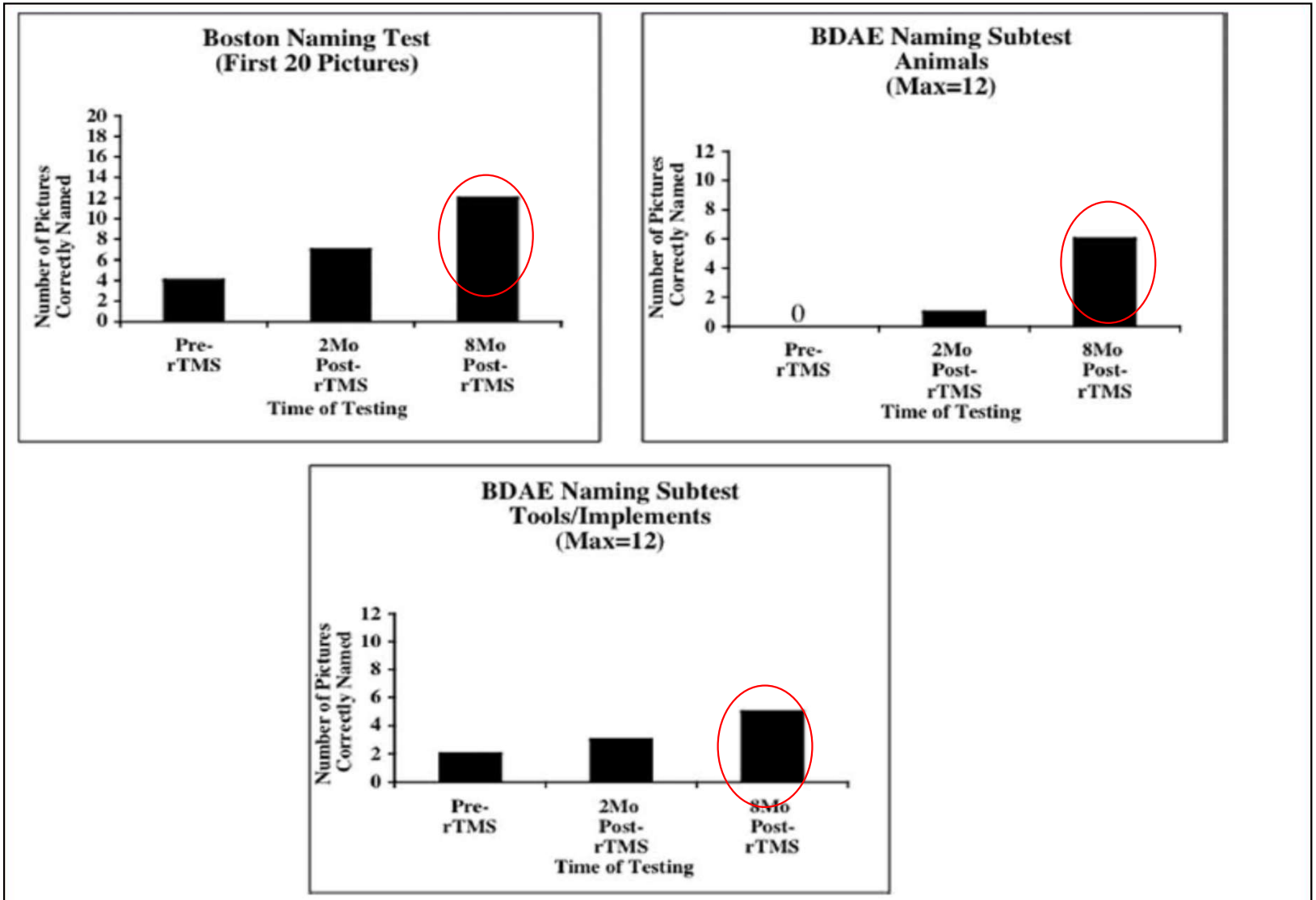

Fig. 4. Phase 2. Graphs showing BNT and BDAE naming scores for this global aphasia patient pre-rTMS (6.5 years poststroke) and at 2 months and 8 months after 10, 20 minute, 1 Hc rTMS treatments to RBA 45.

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Non-invasive brain stimulation for the treatment of brain diseases in childhood and adolescence: state of the art, current limits and future challenges

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Studies	Design		Patients		Stimulation protocol						Outcome	
	Sham controlled	Blinding	Disease	Sample size	rTMS intensity	Stimulation position	Number of sessions/ days	rTMS frequency	Total number of pulses/ session	Duration per session	Effects	Side-effects
VASCULAR DISEASES												
Kirton et al., 2008	Yes	Partially	AIS	10	100% rMT	Controlesional motor cortex	1 session per day/8 days	1 Hz	1200	20 min	Grip strength improvement	None
Valle et al., 2007	Yes	Double blind	CP	17	90% rMT	Motor cortex	1 session per day/5 days	5 Hz	1500	N/A	Reduction of spasticity	None
EPILEPSY												
Brasil-Neto et al., 2004	No	Open	Left front-central slow activity	1	95% rMT	Frontal cortex (Epileptogenic focus)	1 session per day/2 sessions per week/3 months	0.3 Hz	100	N/A	No effects	None
Graff-Guerrero et al., 2004	No	Open	EPC	2	50% of the TMS device power (case 1) 128% rMT (case 2)	Frontal cortex (Epileptogenic focus)	1session/1 day	20 Hz	N/A	N/A	Seizure discharge reduction	None
Fregni et al., 2005a,b,c	No	Open	Cortical mal-formation	3	65% of the TMS device power	Epileptogenic focus vs. Cz	1 session/1 day	0.5 Hz	600	20 min	Seizure discharge reduction	None
Morales et al., 2005	No	Open	EPC	2	N/A	Motor cortex (Epileptogenic focus)	2 sessions/1 day (case 1) 2 session/1 day + 1 session (second day-case 2)	Patient 1: 1–6 Hz Patient 2: 1: 1 Hz-6 Hz-1 Hz	N/A	N/A	No effects	None
Kinoshita et al., 2005	No	Pilot	Extratemporal lobe epilepsy	1	90% rMT	PCz	2 sessions per day/5 days in a week	0.9 Hz	N/A	15 min	No effects	None
ADHD												
Weaver et al., 2008	Yes	Open	ADHD only	4	100% rMT	Right DLPFC	1 session per day/5 days per week/2 weeks	10 Hz	2000 stimuli	N/A	Improved attention in the Sham + active rTMS condition	None
TOURETTE												
Kwon et al., 2011	No	Open	TS only	2	100% rMT	SMA	10 daily sessions/10 days	1 Hz	1200	N/A	Tics reduction	None
Le et al., 2013	No	Open	TS only	25	100% rMT	SMA	1 session per day/5 days per week/4 weeks	1 Hz	1200	20 min	Tics reduction	None
AUTISM SPECTRUM DISORDERS												
Baruth et al., 2010	Control group	Open	Autistic	22	90% rMT	Bilateral DLPFC	1 session per day/1 day per week/12 weeks	•1 Hz	150	N/A	Reduction of irritability and repetitive behavior	None
Sokhadze et al., 2010	No	Open	Autistic	13	90% rMT	Bilateral DLPF cortices	1 session per day/2 day per week/3 weeks	0.5 Hz	150	N/A	Reduced errors % in the oddball task and ritualistic behaviors	None

Advantages and limits of TMS

Advantages:

-Possibility of establishing a causative link between the activity of a cortical region and behavior (Transient virtual injury).

-Excellent temporal resolution (accuracy about 1 msec) Good / fair spatial resolution (0.5-2cm)

-MEPs: Direct measurement of M1 excitability, good spatial resolution (mapping of individual muscles at the level of the primary motor cortex).

- Low cost

Limits/risks

-At high stimulation intensities it loses spatial resolution.

-An appropriate and sensitive task is necessary!

-Online rTMS: It can be distracting or annoying for the subject (auditory 'click', sensation on the skin).

-A high frequency stimulation can trigger epileptic attacks.

Screening questionnaire

1	**Do you have a pacemaker or an artificial heart valve?**	**Y/N**
2	Have you ever had a few metal fragments in your eye?	Y/N
3	Have you ever worked with metal (e.g. welding) without eye protection?	S/N
4	Do you have bits of metal or splinters anywhere on your body?	Y/N
5	Have you ever had a head, eye, spine or chest surgery?	Y/N
6	Do you have implanted electrical devices (eg, hearing aids, cochlea implant, nerve stimulator)?	Y/N
7	Have you ever had an MRI brain scan?	Y/N
8	Do you have any skin changes including eczema or dryness?	Y/N
9	Have you had or do you have heart problems?	Y/N
10	Have you taken part in a brain stimulation experiment (tES or TMS) in the past seven days?	Y/N
11	Have you ever had a neurological or psychiatric condition, including a stroke or severe head injury?	Y/N
12	Do you or any member of your family have a history of seizures, epilepsy or fever seizures?	Y/N
13	Do you suffer from headaches or migraines frequently?	Y/N
14	Are you taking any medications that affect brain function (e.g., antiepileptic drugs, tranquilizers, antidepressants)?	Y/N
15	Have you ever fainted? If YES, are you prone to recurring fainting?	Y/N
16	Have you recently been abusing alcohol or taking recreational drugs?	Y/N
17	Are you well rested?	Y/N
18	Is there any chance you may be pregnant?	Y/N

Transcranial Magnetic Stimulation (TMS) enables the mapping of various cognitive functions, highlighting regions like the parietal lobe for tasks such as calculus.

Additionally, TMS can delineate individual affective states, such as negative emotions following incorrect decisions, and provide valuable clinical or diagnostic insights, for example, by analyzing the **latency** and **amplitude** of motor evoked potentials in patients with various disorders.

Moreover, TMS can influence an individual's performance at both cognitive levels, such as in the timing of calculation processes, and in motivational or decisional aspects.

It can also induce temporary changes in the excitability of stimulated neurons, such as motor neurons, potentially enhancing neuroplasticity, which is crucial for the rehabilitation of neurological and psychiatric disorders.

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Take home message (s)

conclusion

https://carmelovicario.webnode.it/