Principles of Transcranial Magnetic Stimulation

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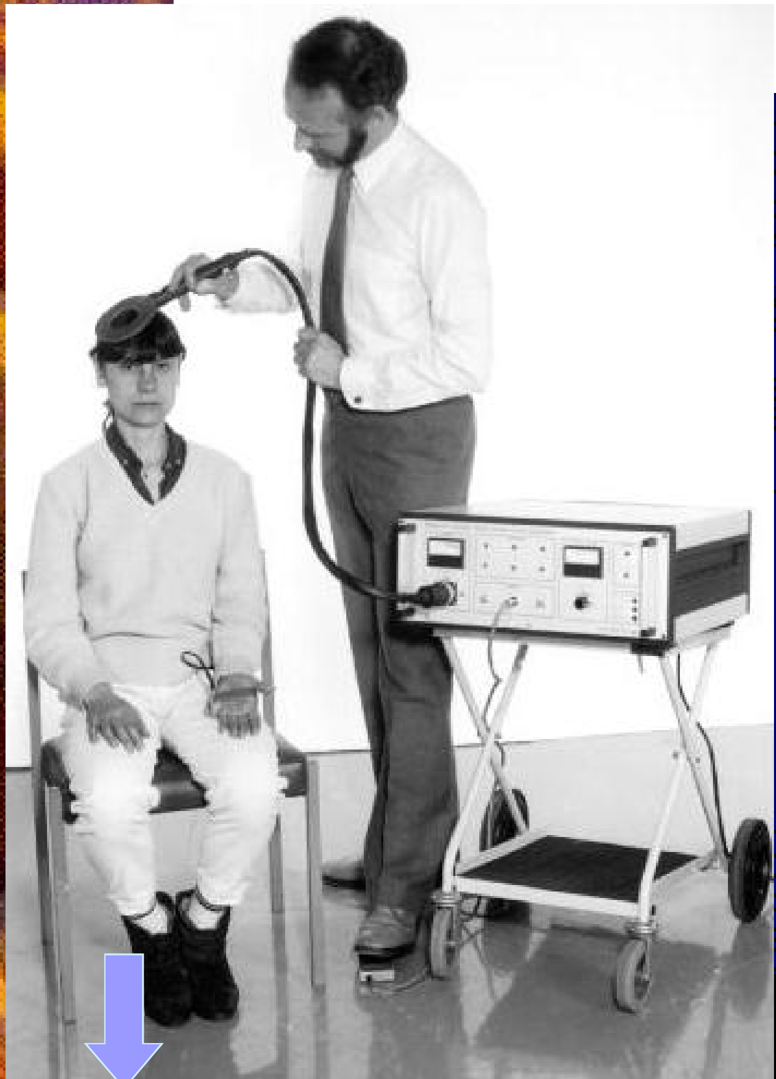
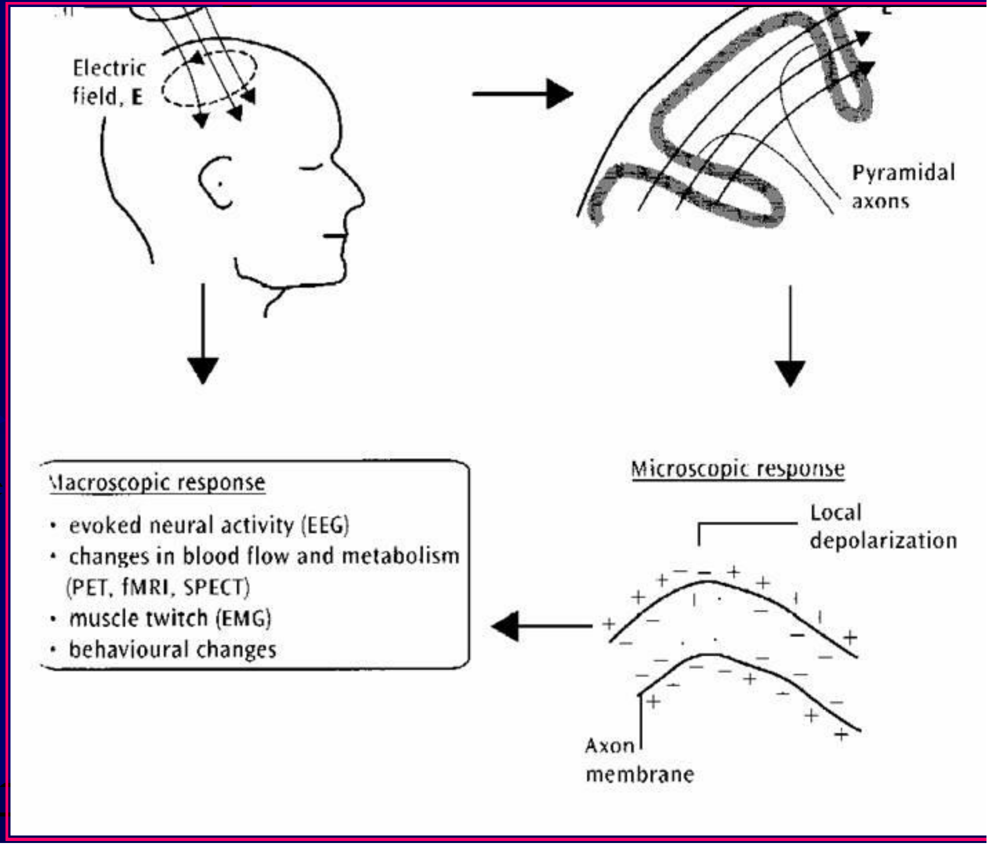
Transcranial magnetic stimulation (TMS)

Transcranial magnetic stimulation (TMS) is performed by placing on the skull, above the motor cortex, an electromagnetic coil that supplies an alternating current generated by a capacitor. This produces a time variable magnetic field of duration of 100-200 us. The intensity of the generated magnetic field is about 2 tesla (value corresponding approximately to 40,000 times the Earth's magnetic field or, roughly, to the magnetic field used in magnetic resonance imaging). The variable magnetic field induces a current flow in the nervous tissue sufficient to produce a neuronal depolarization.



A. Barker, 1985

- Neuroscience Researches
- Clinical Studies



Transcranial Magnetic Stimulation
T.M.S.

Circular Coil

- ü non-focal
- ü 2 tesla along the coil circle
- ü useful for clinical examination

Figure-of-eight Coil

- focal
- 2.2 tesla at the intersection of the two circles
- useful for studies of cortical excitability
- Useful for mapping individual muscles

Transcranial Magnetic Stimulation: A Primer

Neuron
Primer

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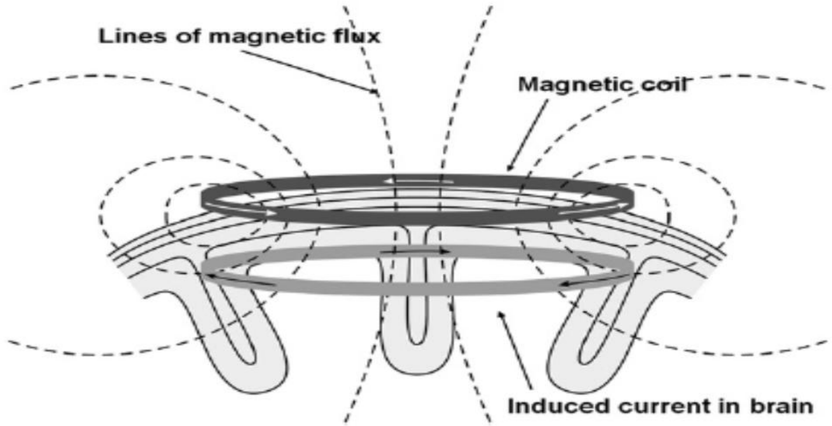


Figure 1. Illustration of Direction of Current Flows in a Magnetic Coil and the Induced Current in the Brain Hallett, 2000

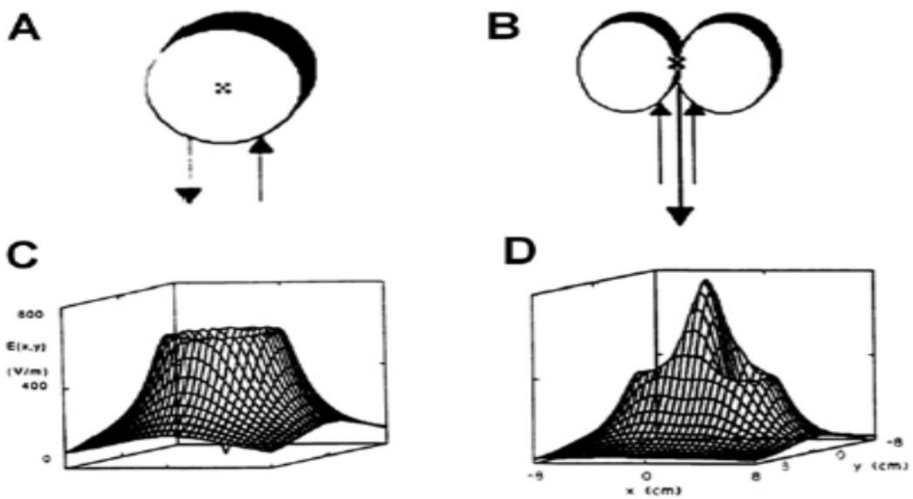
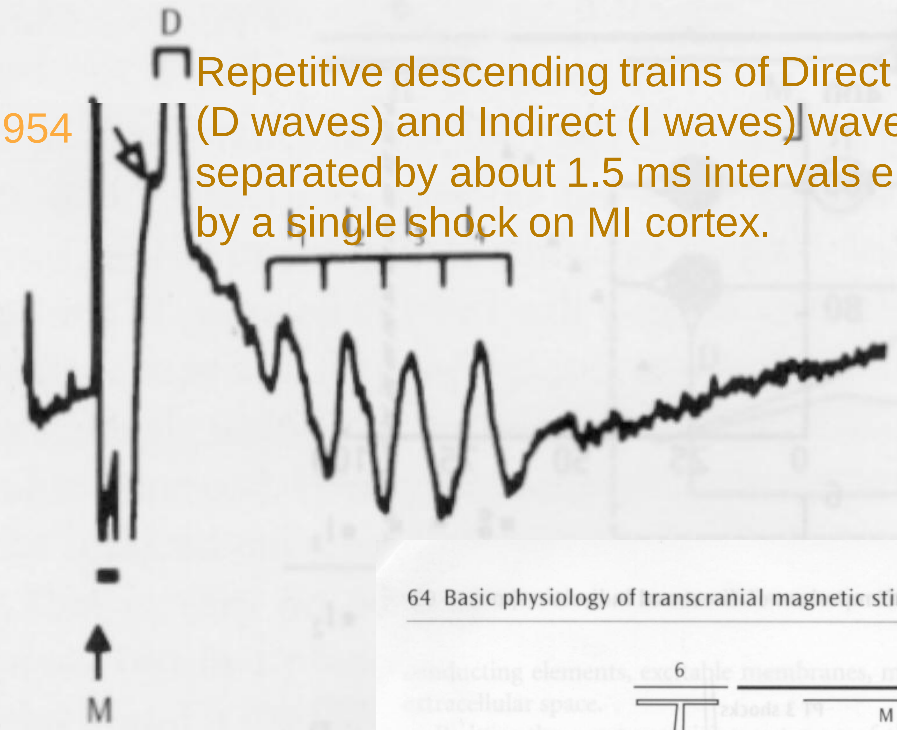
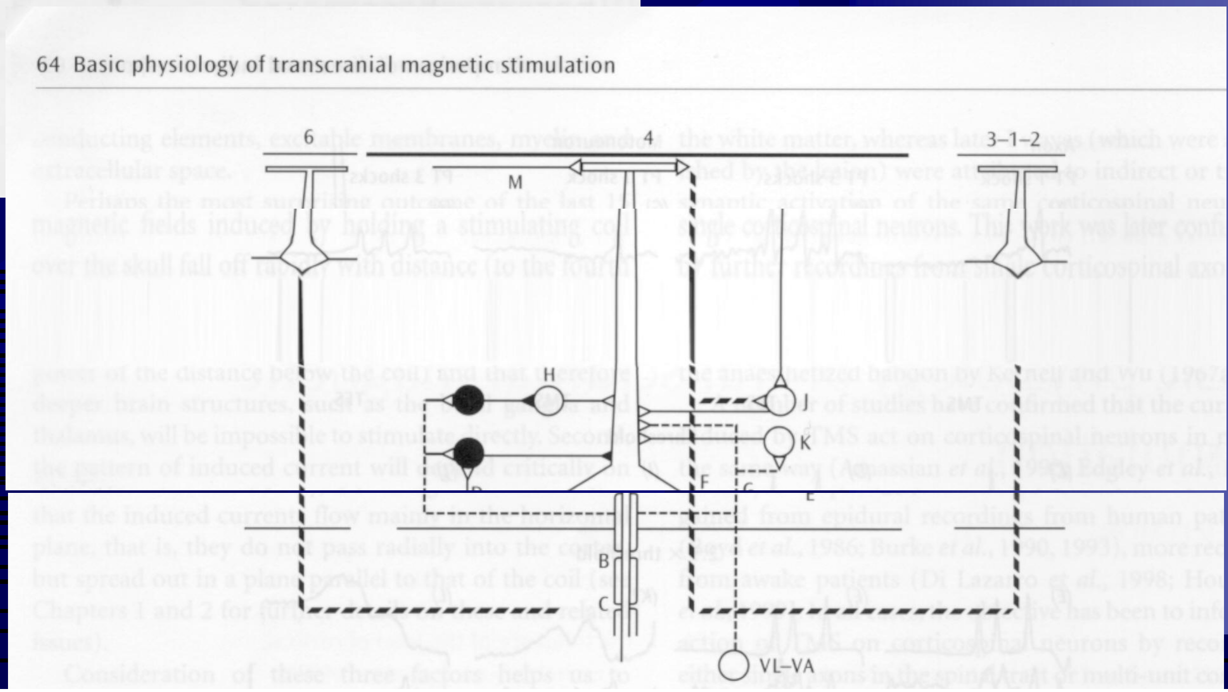


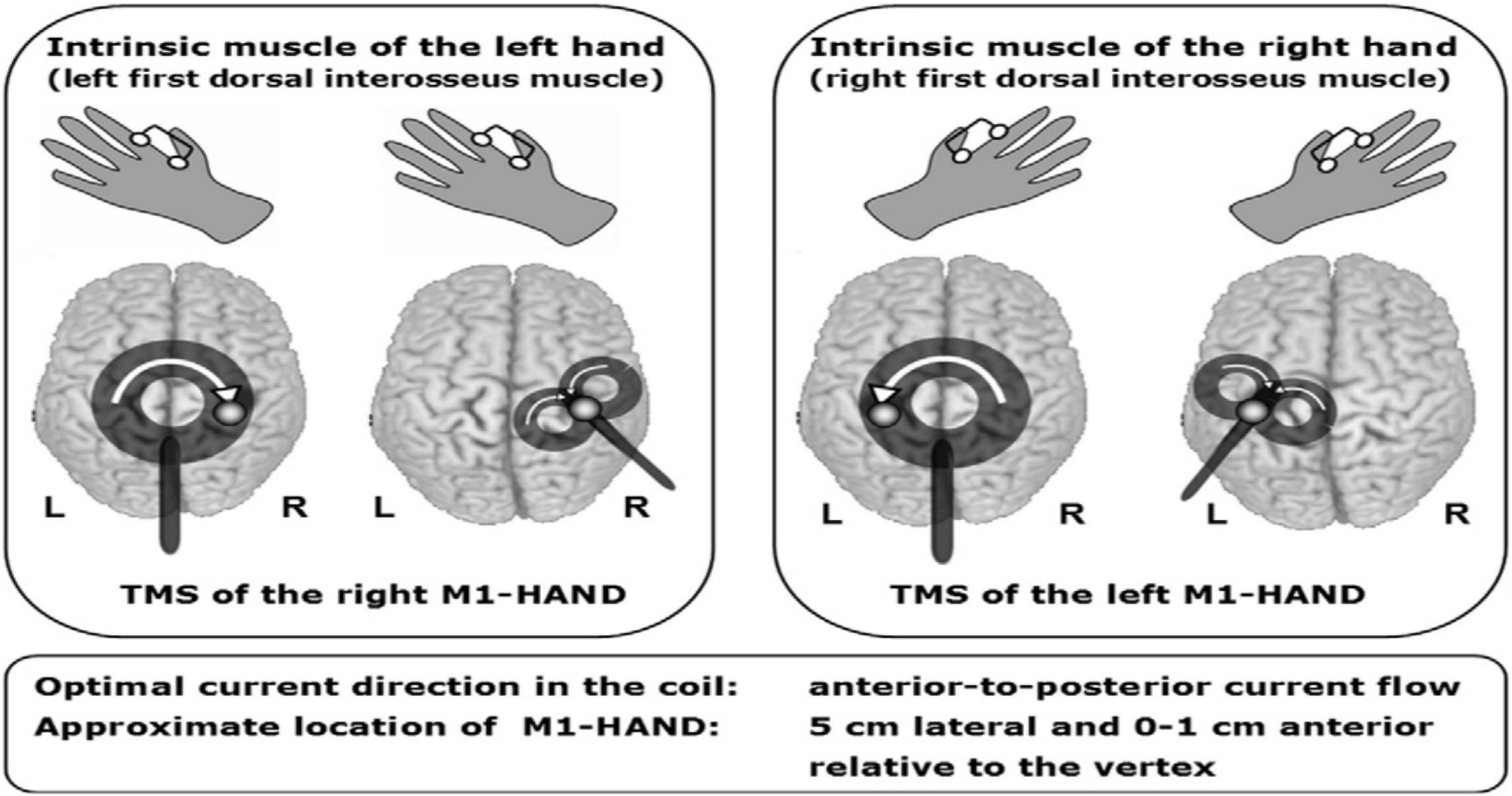
Figure 2. Magnetic Coil Shape Determines the Pattern of the Electric Field

Patton & Amassian 1954

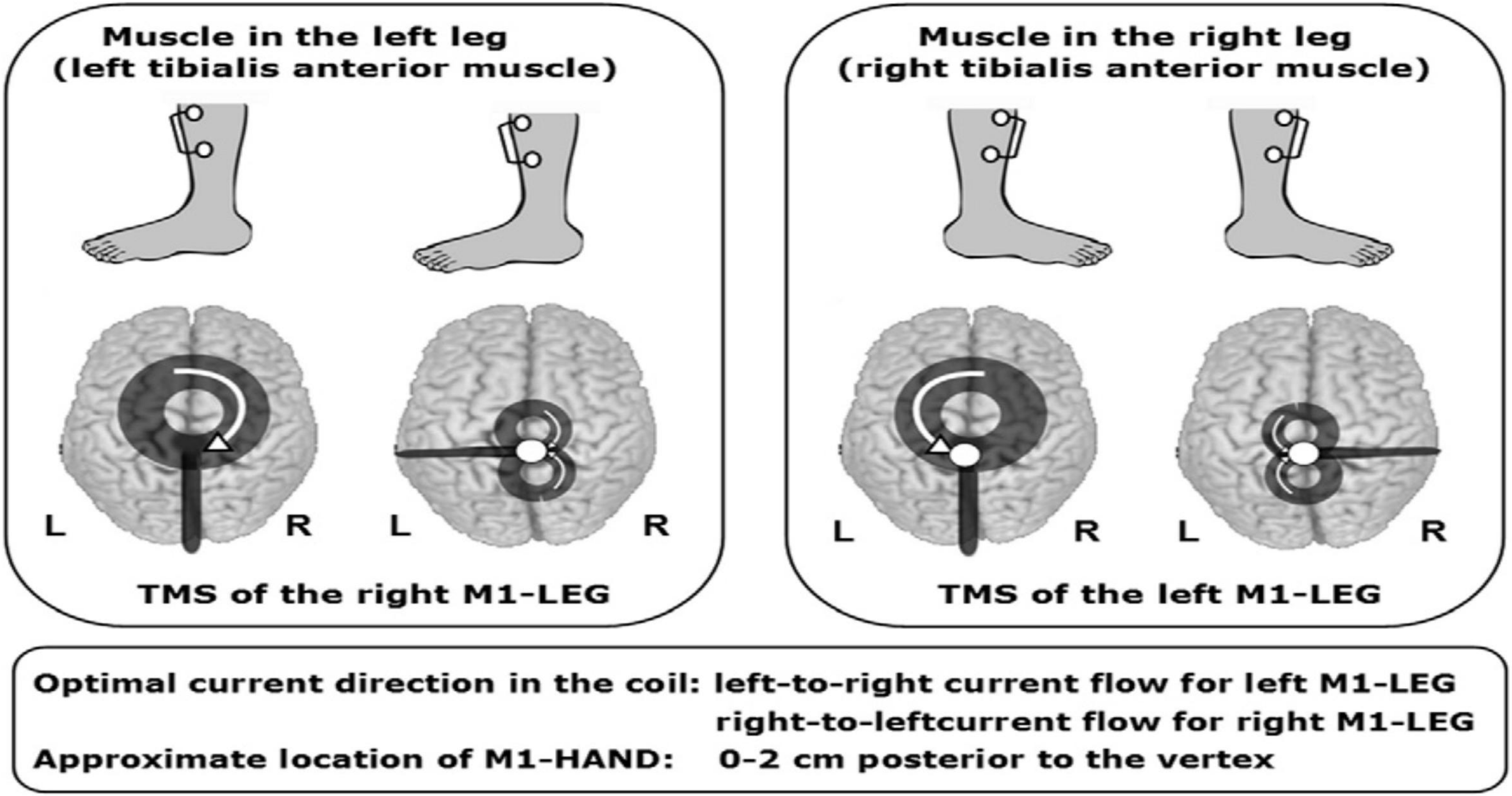


Repetitive descending trains of Direct (D waves) and Indirect (I waves) waves separated by about 1.5 ms intervals elicited by a single shock on MI cortex.





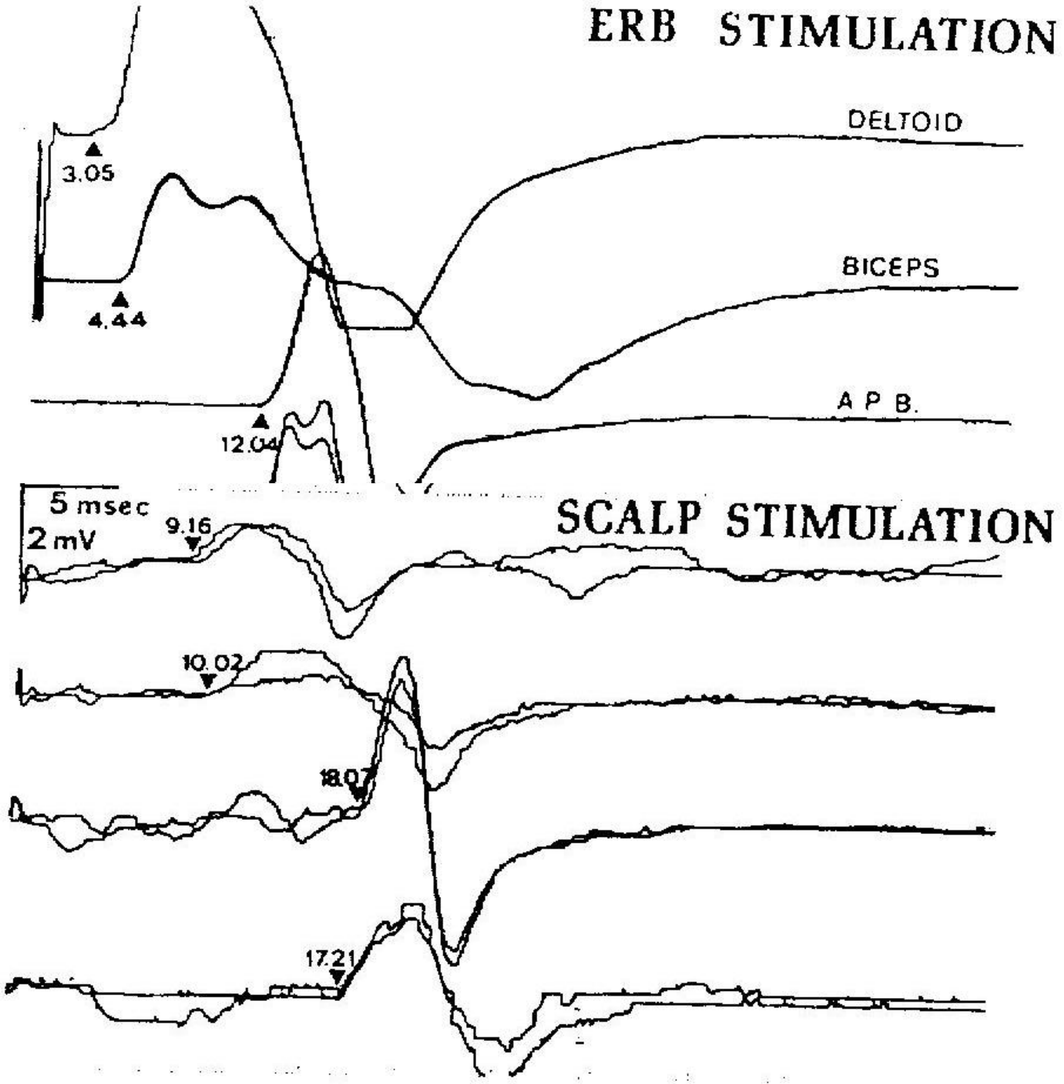
Groppa et al, 2012



Groppa et al, 2012

Braom Research, 567 (1991) 111-119
Brain excitability and electroencephalographyc activation….
PM. Rossini, et al.

…or manipulating (i.e. blocking) the idling, resting EEG rhythms…



By recording MEPs from several muscles with different myelomeric innervation, one can get clinically relevant information on the level of partial or total impulse Propagation block (i.e. by comparing interlatency differences during Erb stimuli with those during brain stimuli).

Electroencephalography and clinical Neurophysiology, 1985, 61: 272-286
Nervous propagation along 'Central' motor pathways in intact man…
PM. Rossini, et al

Plastic cuff (i.e.waterpolo), to avoid any movement between stimulation sites and anatomical landmarks on the skull

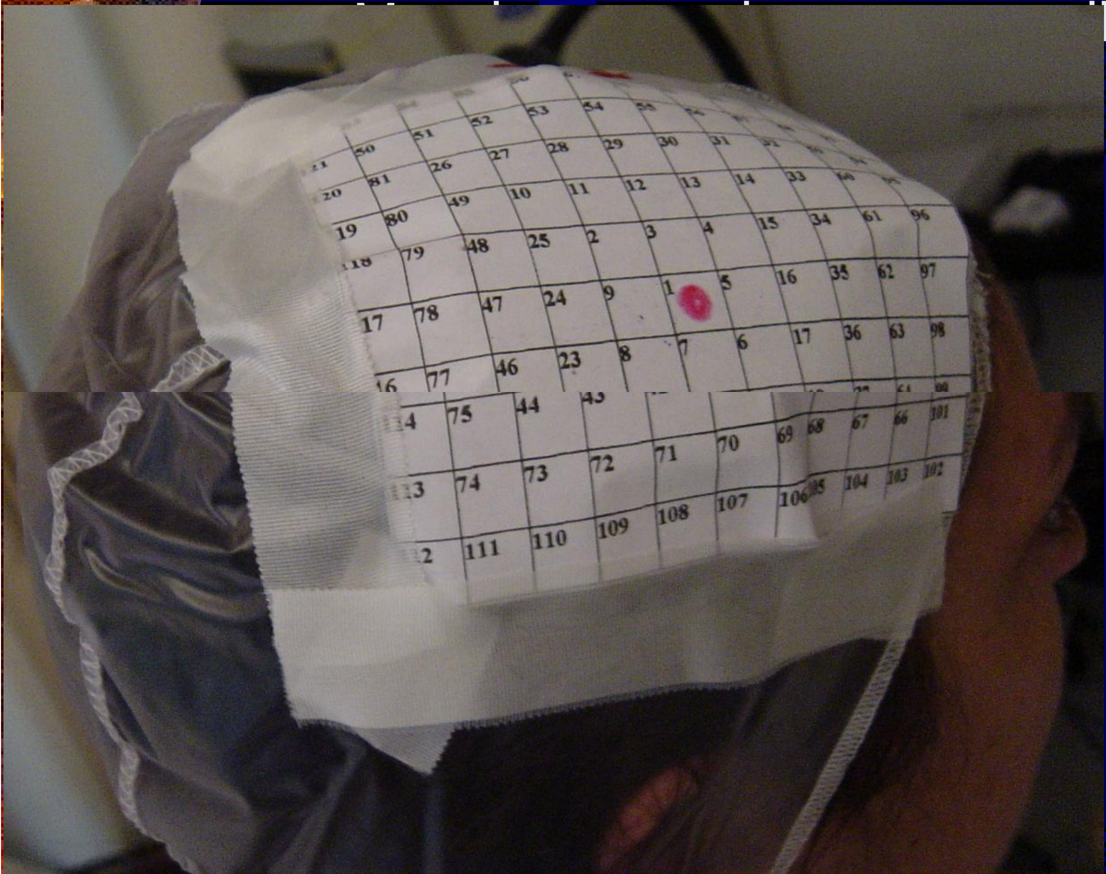
Grid: 121 scalp positions. Point 1 at the centre (hot spot) represents the site with maximal excitability. Number of sites of stimulation progress in a spiral fashion

Figure of 8 focal coil

Surface, disk Ag/AgCL electrodes

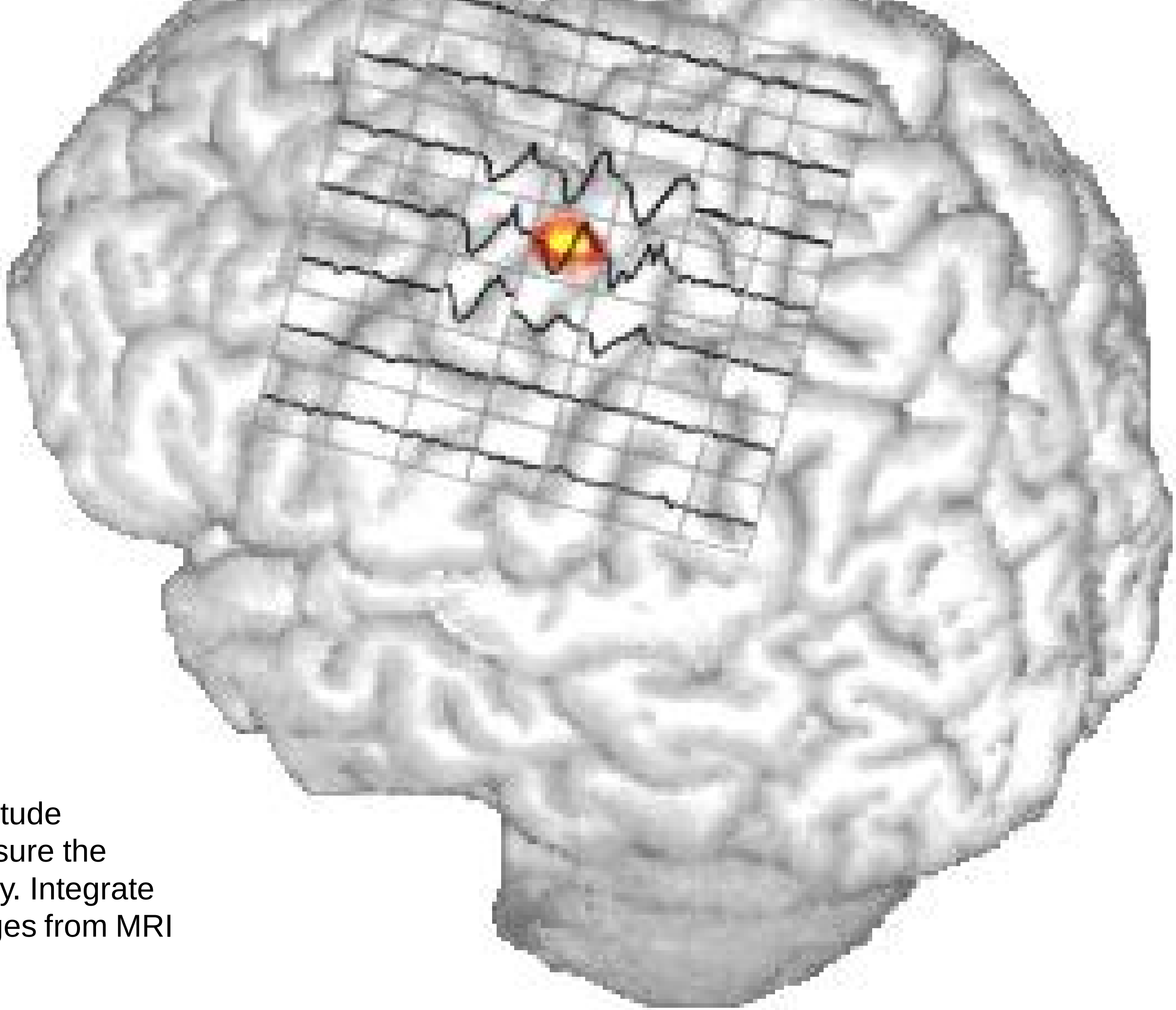
82	83	84	85	86	87	88	89	90	91	92
121	50	51	52	53	54	55	56	57	58	93
120	81	26	27	28	29	30	31	32	59	94
119	80	49	10	11	12	13	14	33	60	95
118	79	48	25	2	3	4	15	34	61	96
117	78	47	24	9	1	5	16	35	62	97
116	77	46	23	8	7	6	17	36	63	98
115	76	45	22	21	20	19	18	37	64	99
114	75	44	43	42	41	40	39	38	65	100
113	74	73	72	71	70	69	68	67	66	101
112	111	110	109	108	107	106	105	104	103	102

…ble with on-line ‘neuronavigation



2) 4 to 8 stimuli for each position at intensity of THR +10%.

1) Threshold defined on the hot spot of the ‘target muscle’



3) Create amplitude
Maps and measure the
Centre of gravity. Integrate
With brain images from MRI

Measured routine parameters of MEP

- ü Excitability threshold
- ü Absolute latencies
- ü Peak to peak amplitudes
- ü MEP amplitude/area and input/output curves (I/O curves)
- ü TMS mapping
- ü Silent period duration
- ü Central conduction time
- ü Interhemispheric and interside differences of the examined parameters
- ü **cMAP/MEP amplitude ratio**

Motor EVoked Potentials =MEPs Clinical Applications

- Multiple Sclerosis
- Myelopathies
- Movement Disorders
- Stroke (examples)
- Post-lesional Plasticity (examples)
- Neurodegenerative Disorders (examples)
- Epilepsy (examples)
- Pain control
- Monitoring
- …Neuropsychophysiology (examples)…
- …Going beyond normal brain performances…
- …Creating SUPERMAN ? (NO EXAMPLE AT ALL !!!)

Motor Threshold

- Rest motor threshold (RMT):

The minimum stimulation intensity needed to elicit a recordable EMG response (Motor Evoked Potential usually 50 to 100 uVolts)) from the target muscle with the muscle at rest with a 50% probability in a cascade of 10 to 20 consecutive stimuli (Rossini et al EEG J. 1994)

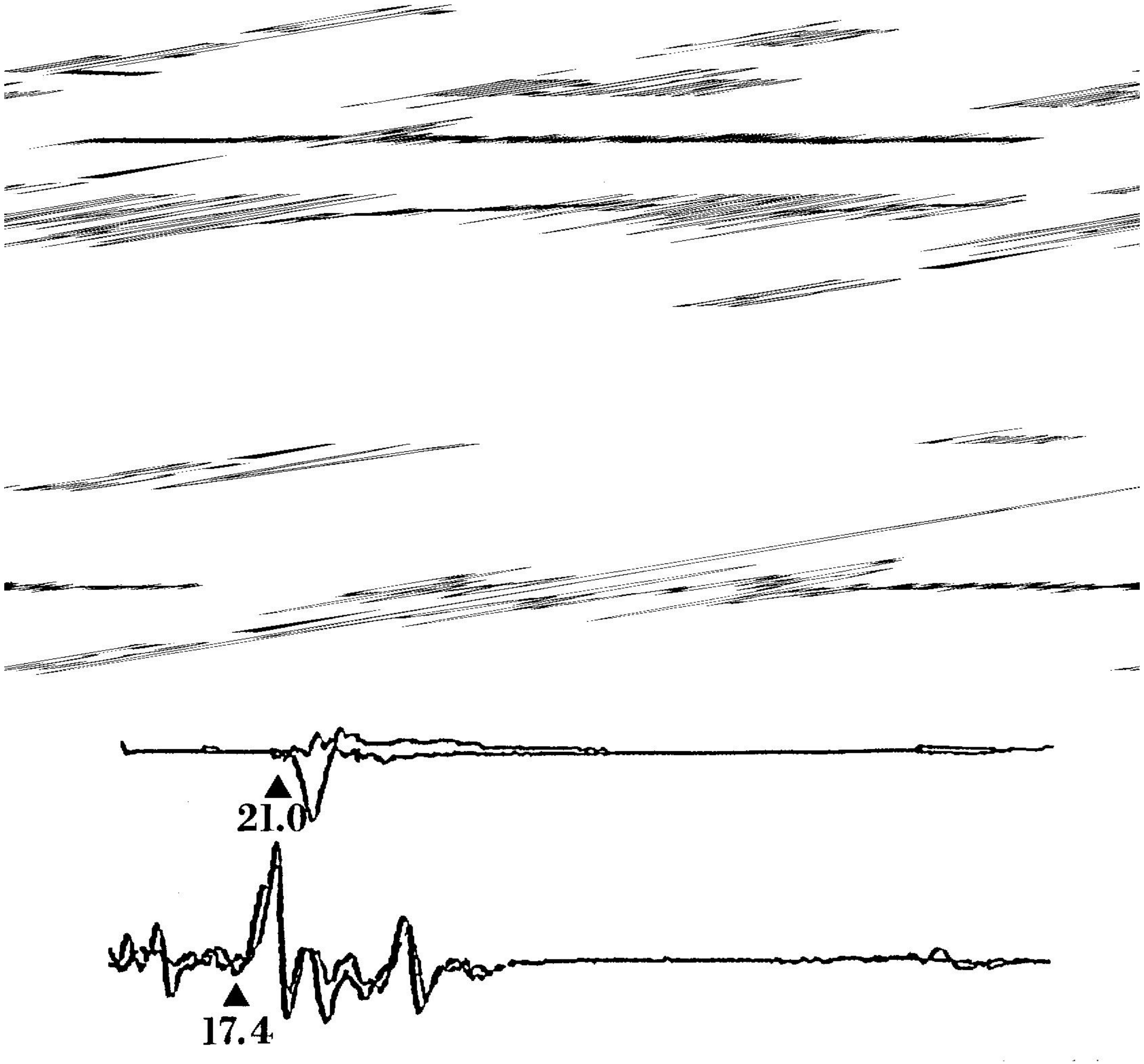
- Active motor threshold (AMT):

The minimum stimulation intensity needed to elicit a recordable EMG response (Motor Evoked Potential) from the target muscle during tonic contraction (usually 10% less intensity needed than for RMT)

<u>Frequent conditions that may alter Excitability Thresholds</u>

- Age
- Wakefulness, drowsiness, sleep
- Body Position and Posture
- Drugs (psicoactive drugs ↓, benzodiazepines, barbiturates, antiepileptic drugs↑)

Latency 'jump' between relaxed and contracted MEPs



Electroencephalography and clinical Neurophysiology, 89 (1993) 61-66
Latency jump of “relaxed” versus “contracted” motor evoked potentials as a marker….
MD. Caramia, et al.

Age effects on absolute latencies and ’latency jump’ between relaxation and contraction

Effects of ‘mental activation’

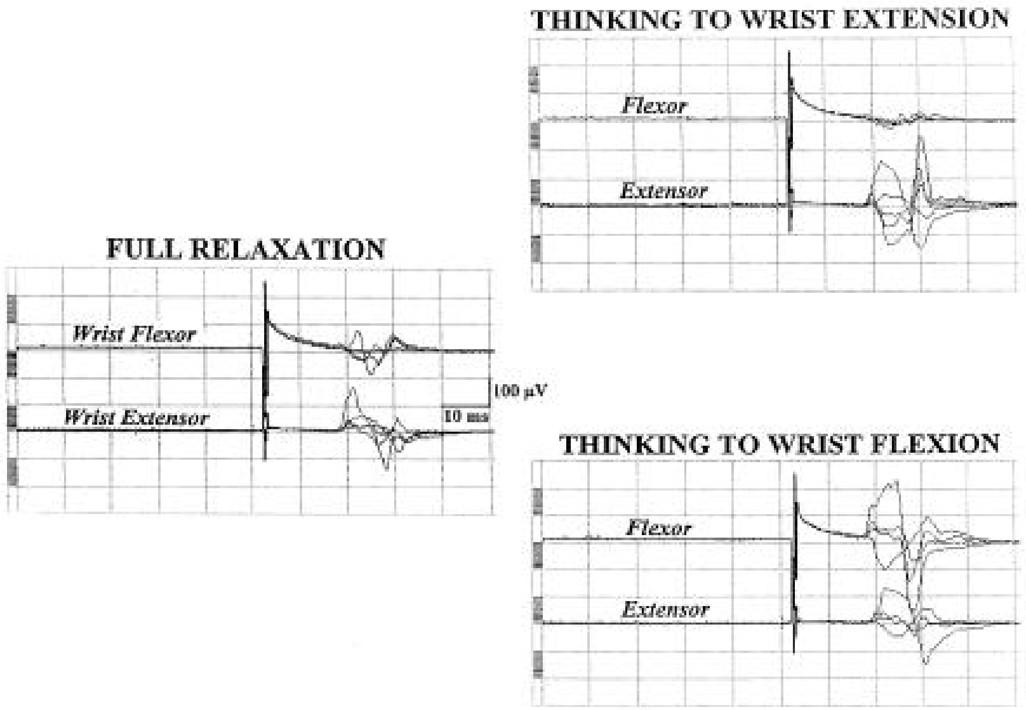


Fig. 2. Original tracings in a representative subject during near-threshold magnetic TCS of the left motor cortex in a task of ‘thinking to move’ the wrist joint. MEPs are recorded simultaneously from right flexor and extensor muscle at forearm. The first 50 ms are a pre-trigger analysis time; 4-5 MEPs are superimposed in each trace. Note that the motor program dispatched, but not executed, is exerting an amplitude facilitation (without latency changes) on the ‘prime mover’ muscle. When the flexor muscle is acting as antagonist (first trace on the right panel) an inhibitory effect is taking place.

P.M. Rossini, S. Rossi / Electroencephalography and clinical Neurophysiology 106 (1998) 180–194

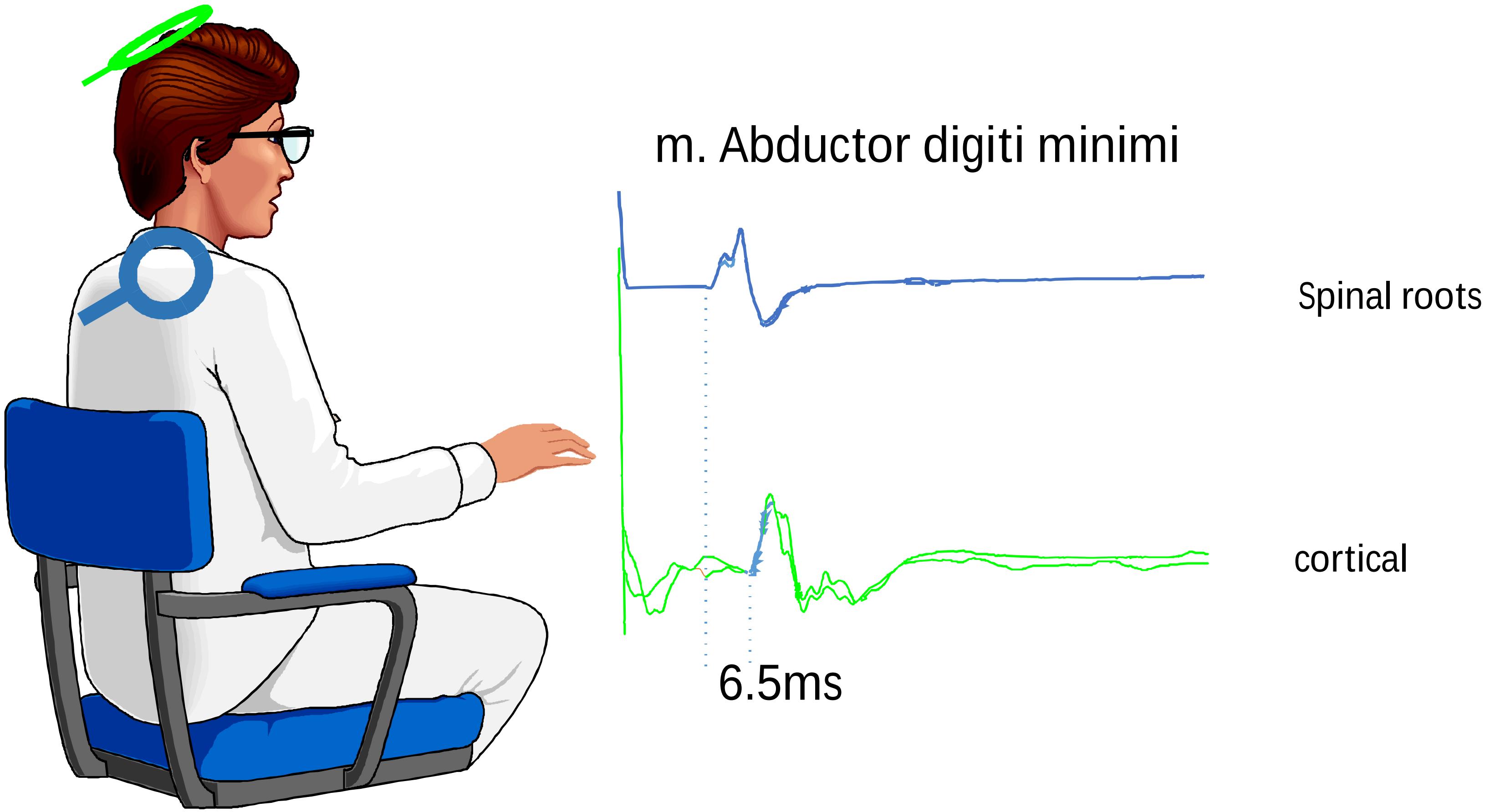
Central motor conduction time

Central motor conduction time (CMCT) can be estimated by subtracting the latency of the response obtained after spinal roots stimulation (peripheral motor conduction time) from the MEP latency obtained after cortical stimulation during voluntary contraction of the target muscle.
CMCT mainly provides information on conduction velocity of the activated fibres. Usually around 6 msec for upper limb and 12 msec for lower limb.

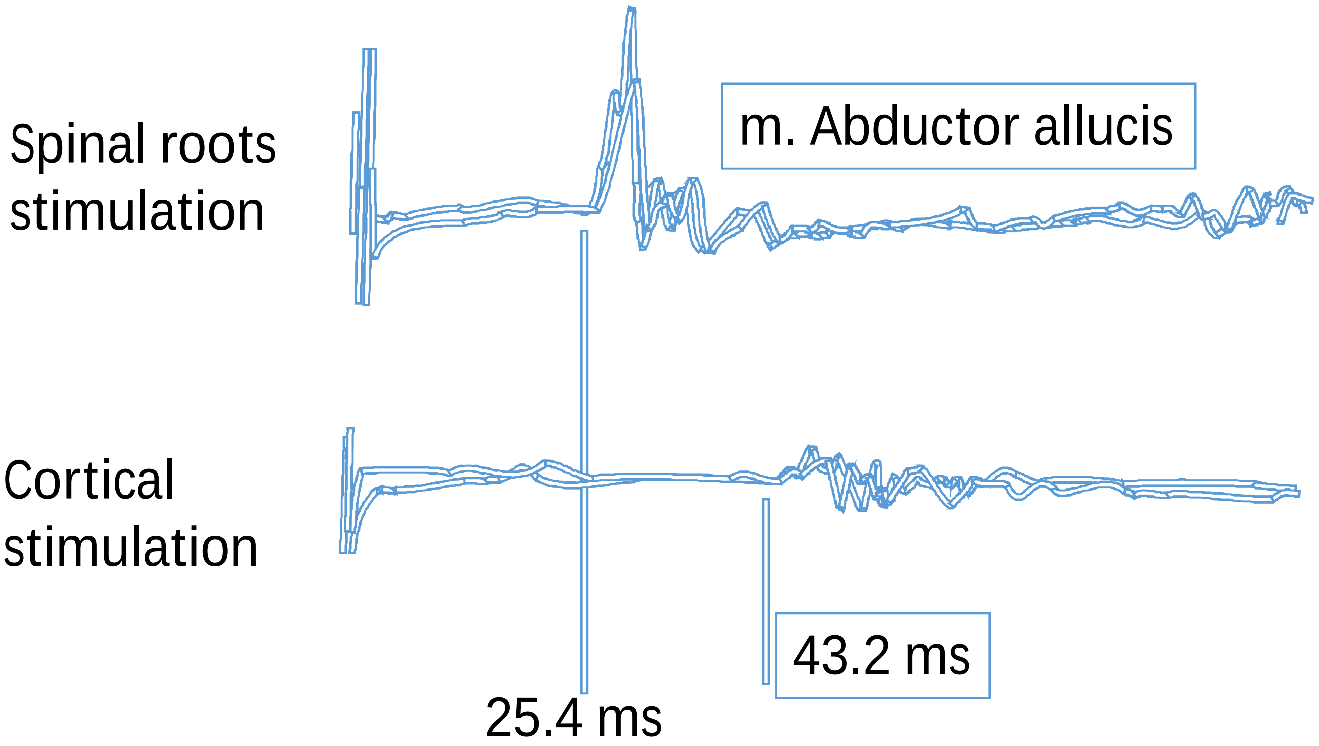
Central motor conduction time

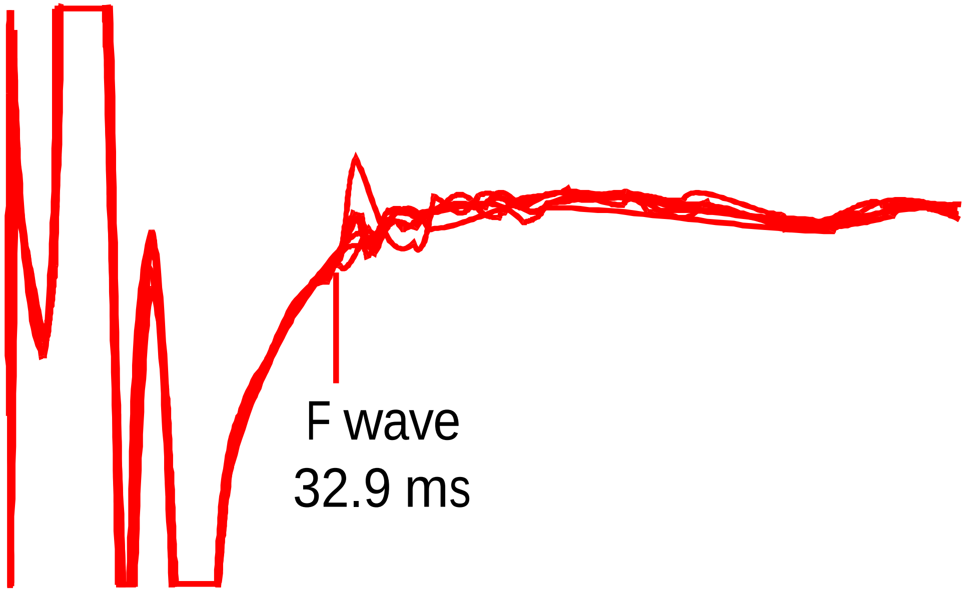
- For the study of the upper limb the center of the circular coil is placed on Cz, while for the study of the lower limb the coil is positioned 6-7 cm more anteriorly.
- The paravertebral stimulation should be performed with muscle to be studied at rest, the cortical stimulation should be recorded both at rest that during voluntary contraction.
- The tracks must be analyzed individually; it is not encouraged to make the averaging (especially for the cortical response during tonic contraction)
- In approximately 20% of individuals without any pathology, a magnetic stimulation of a muscle of the lower limb can not show any response at rest condition. The absence of a response at rest for the upper limb must always be considered pathological.

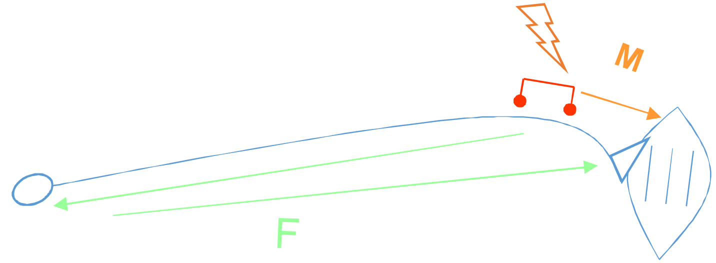
Central motor conduction time



Central motor conduction time





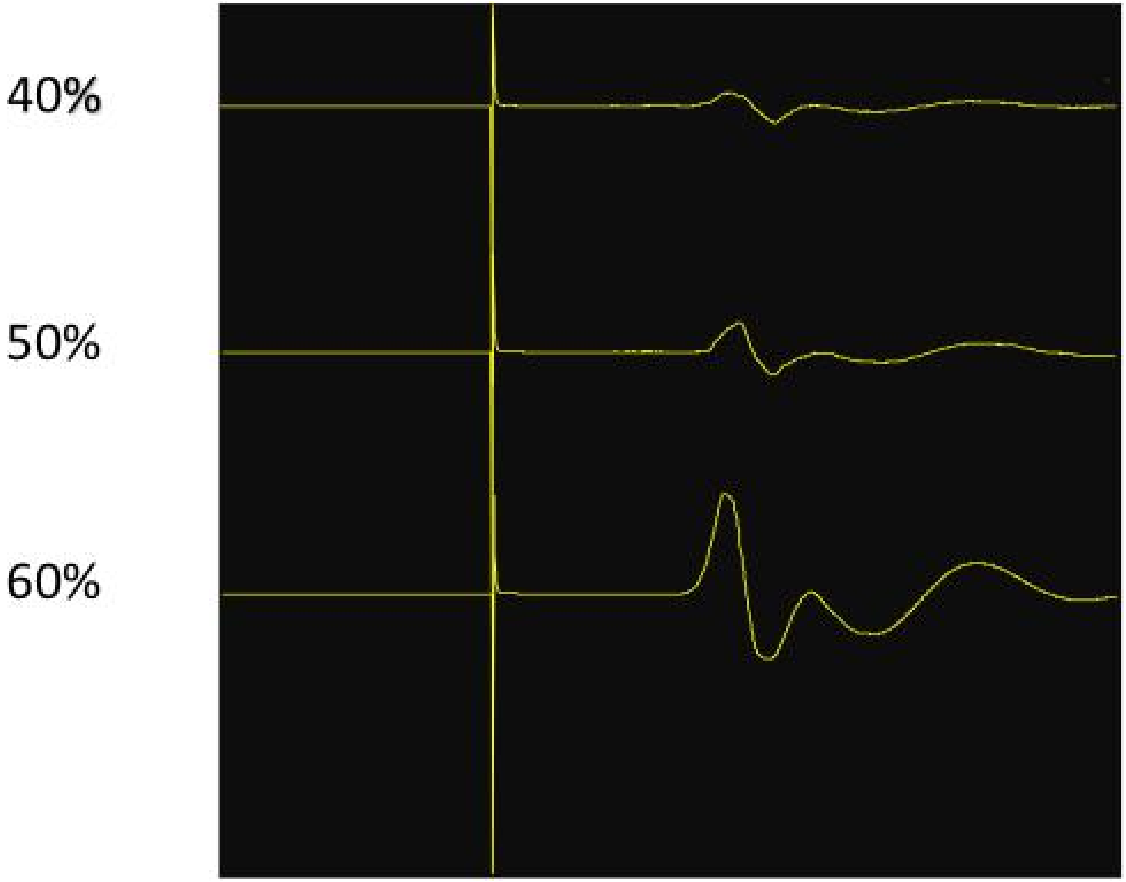


Formula of Kimura $\frac{F+M-1}{2}$

I/O Curves

Measures of the size of the EMG response evoked by a standard intensity of TMS pulse, expressed as peak-to-peak amplitude or area, are equivalent to taking a single point in the input–output curve (I/O curve) that relates stimulus intensity to size of response.

In healthy subjects, the I/O curve for small hand muscles is usually sigmoidal with a steeply rising segment followed by a plateau



SILENT PERIOD

NeuroReport 11: 701-707 (2000)
Transcranial magnetic stimulation reveals an interhemispheric asymmetry….
P. Cicinelli, et al.

Short interval intracortical inhibition (SICI)

The MEP evoked by a single suprathreshold pulse (test stimulus at 120% RTM) is suppressed if preceded by subthreshold stimulus (conditioning stimulus at 80% of RMT) given 1–5 ms earlier. Inhibition produced at these interstimulus intervals is referred to as short interval intracortical inhibition (SICI). Longer interstimulus intervals (> 5 ms) result in facilitation.

ournal of Physiology (1993), 471, pp. 501–519
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Prin

OCORTICAL INHIBITION IN HUMAN MOTOR CORTEX

CORTI

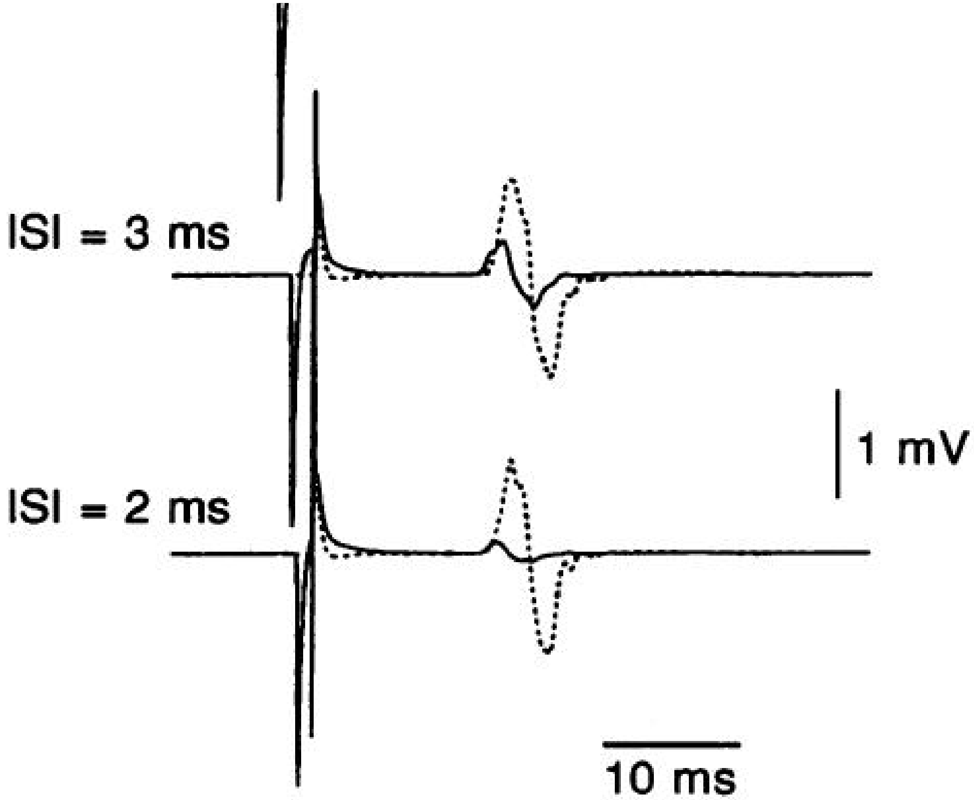
RAI*, M. D. CARAMIA†, J. C. ROTHWELL‡, B. L. DAY,
OMPSON, A. FERBERT§, S. WROE, P. ASSELMAN
AND C. D. MARSDEN

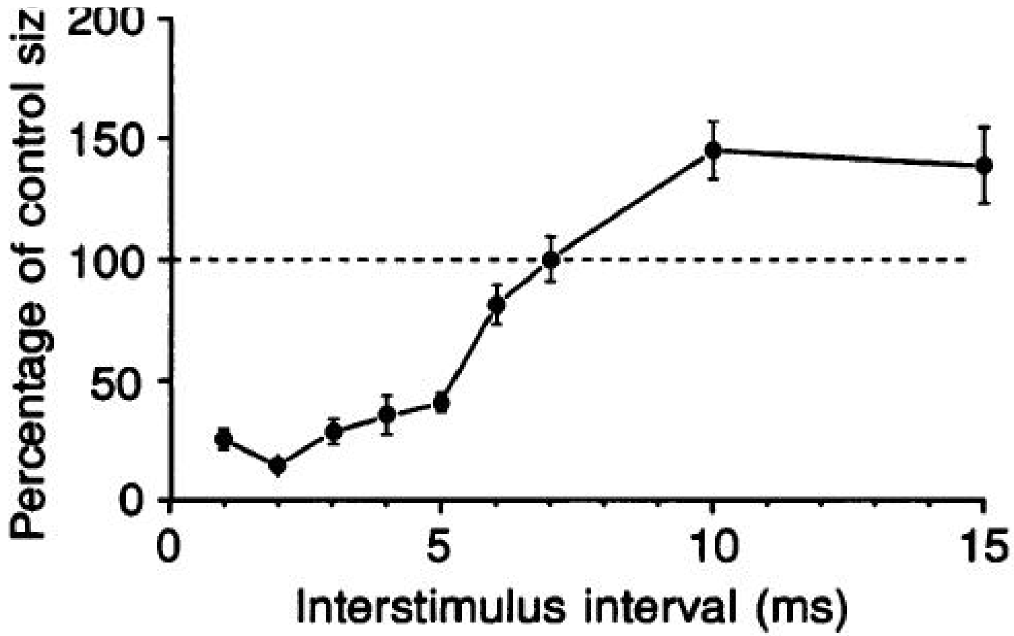
BY T. KU
P. D. TH

Movement and Balance Unit, Institute of Neurology,
n Square, London WC1N 3BG

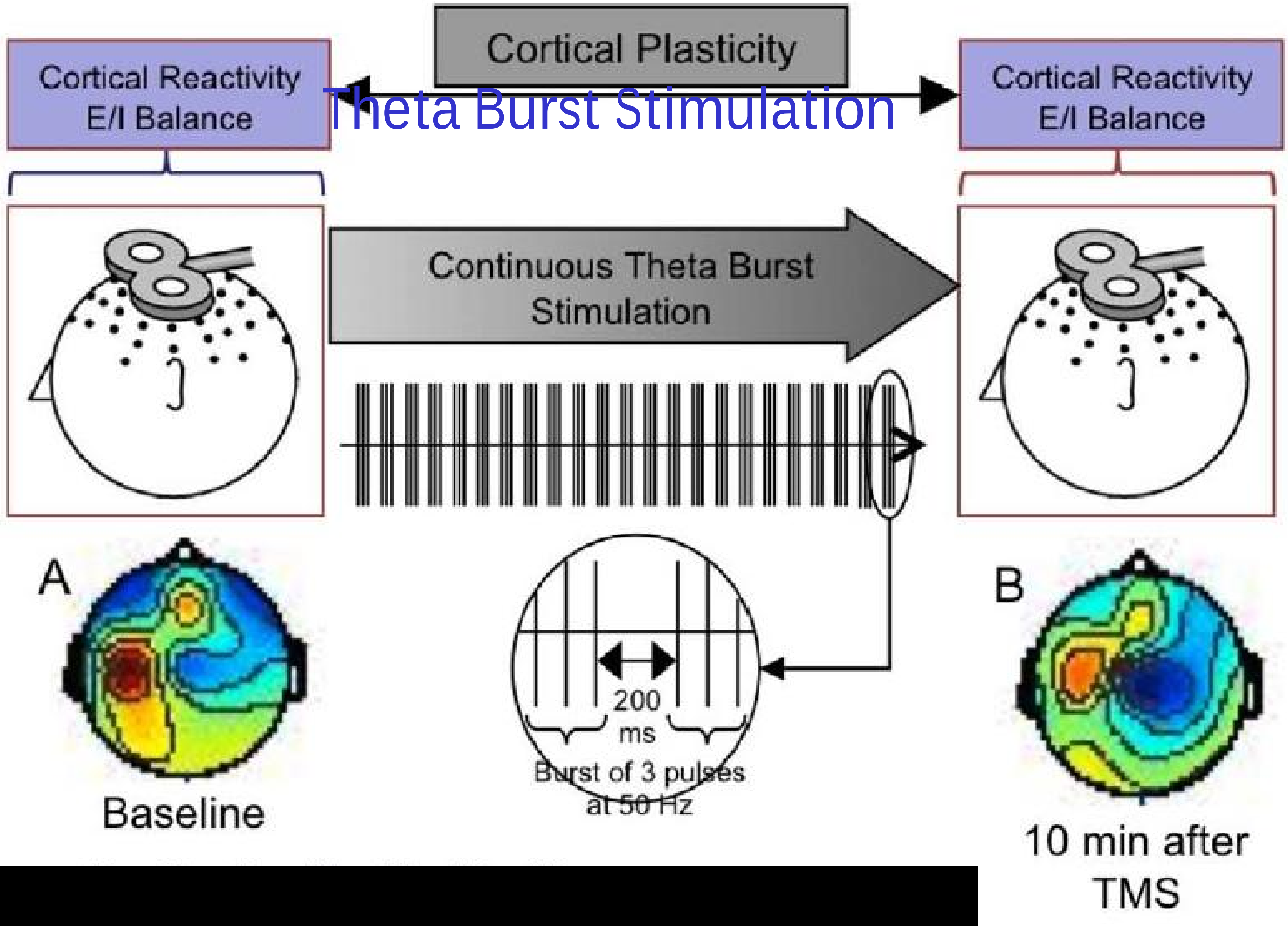
From the MRC Human
Queen

EMG responses to magnetic cortical stimulation in relaxed first dorsal interosseous are inhibited by a prior, subthreshold, magnetic conditioning stimulus. The lower two records have two superimposed traces, the response to the test stimulus given alone, and the response to the test stimulus when given 3 (middle traces) or 2 ms (lower traces) after a conditioning stimulus. The larger of the two traces (dotted line) is the response to the test stimulus alone. It is dramatically suppressed at these two interstimulus intervals (ISI).



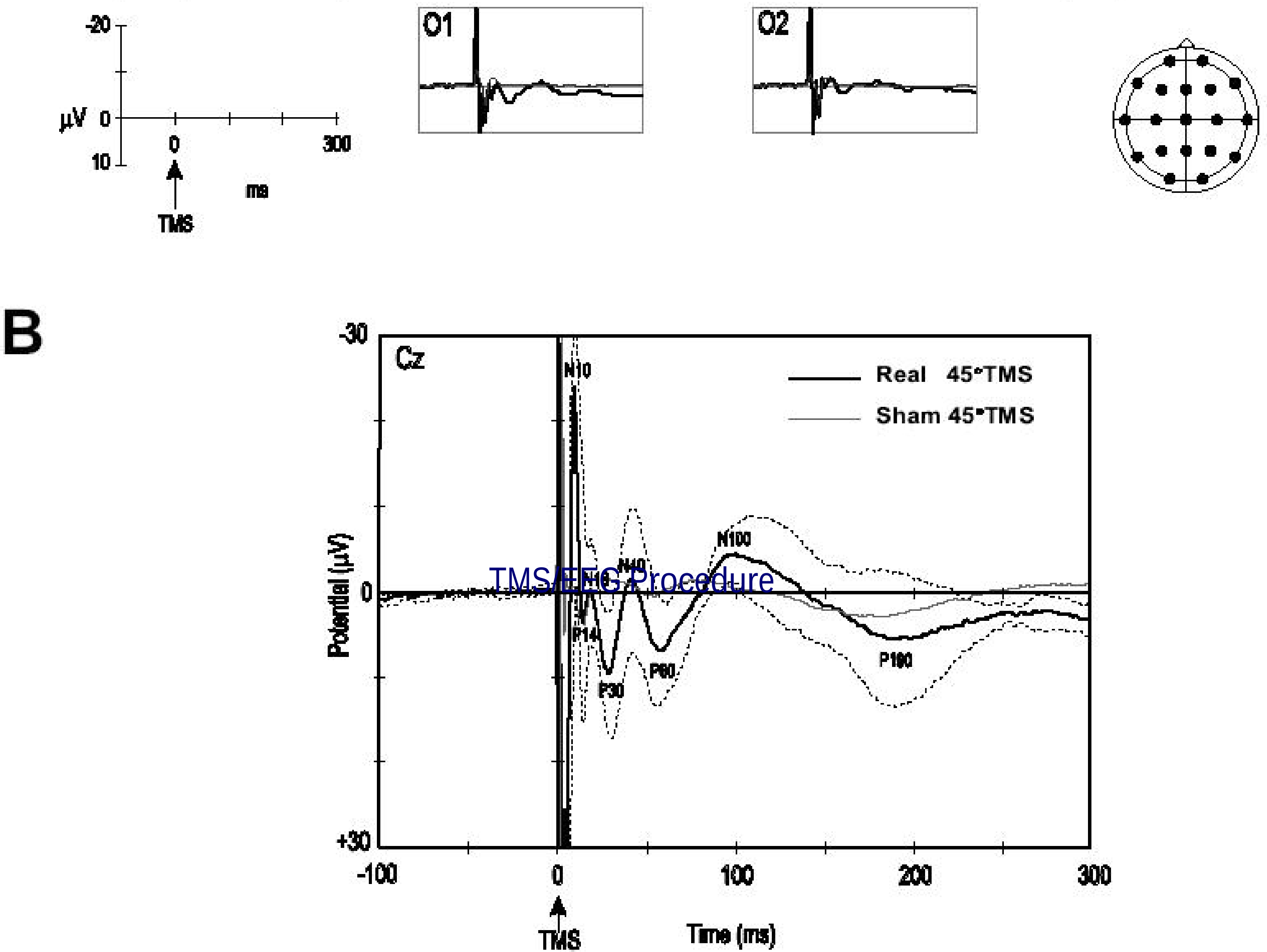


Theta Burst Stimulation

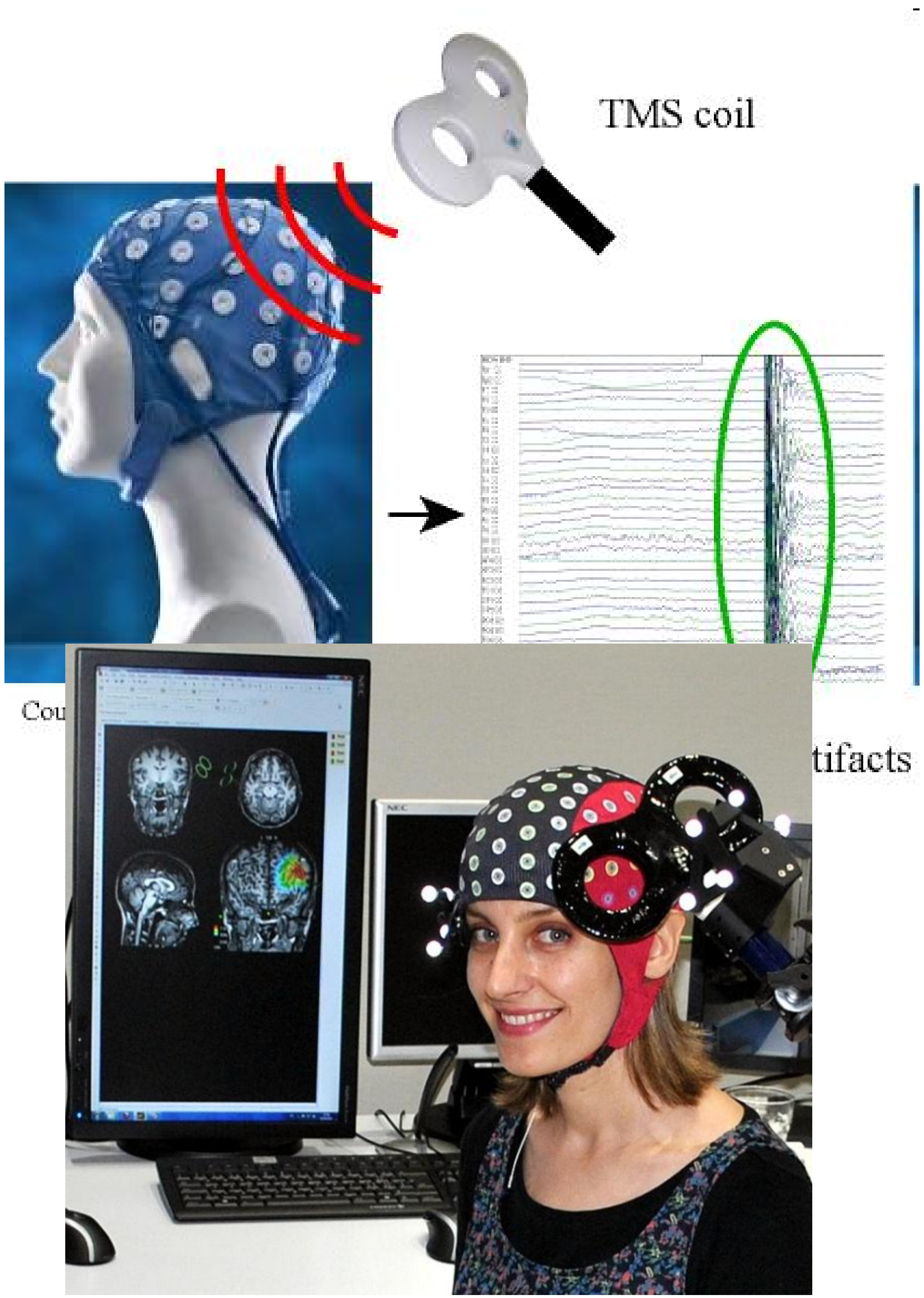


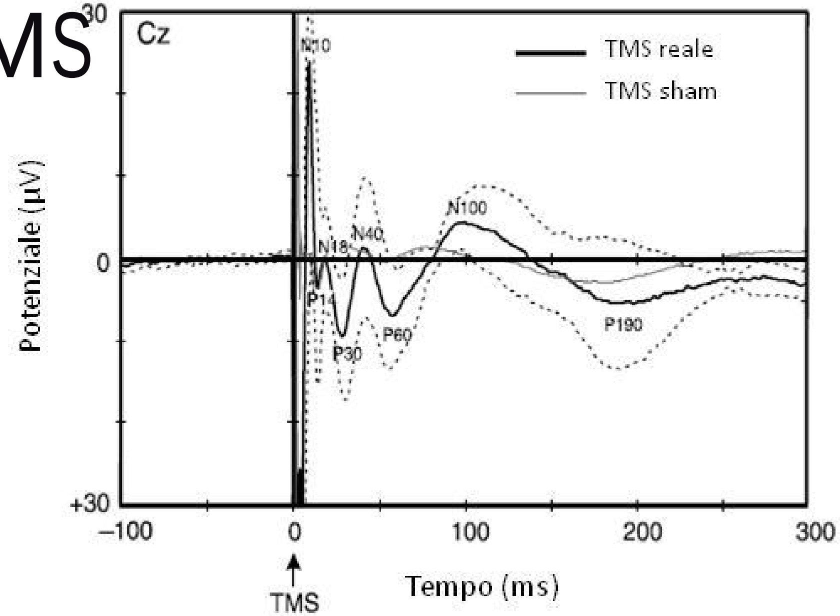
[redacted]

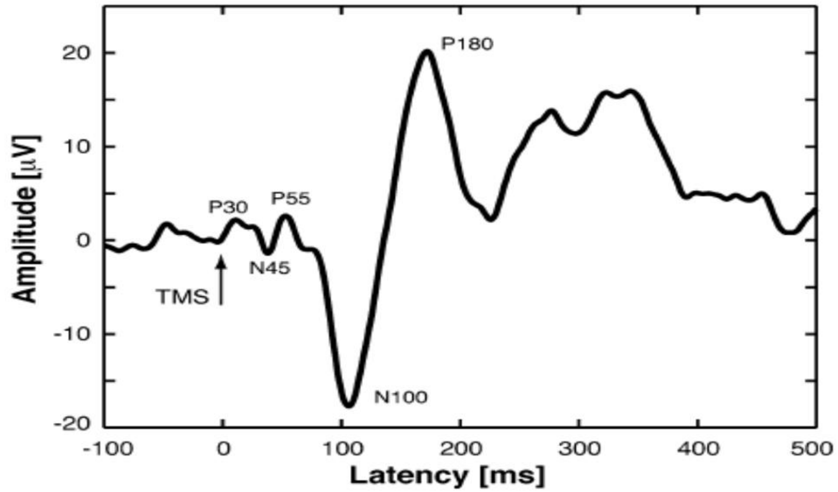
TMS/EEG Procedure



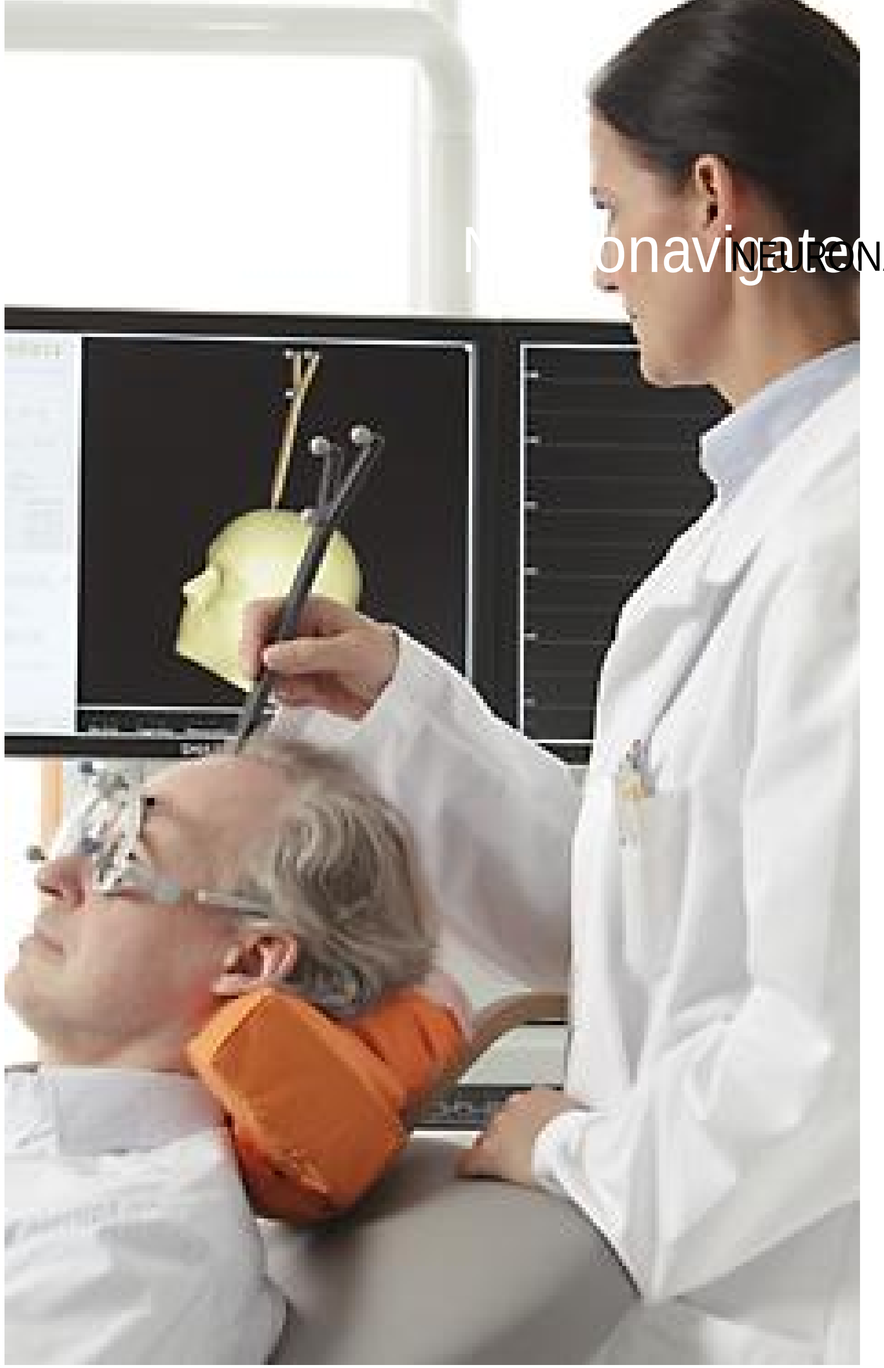
EEG-TMS

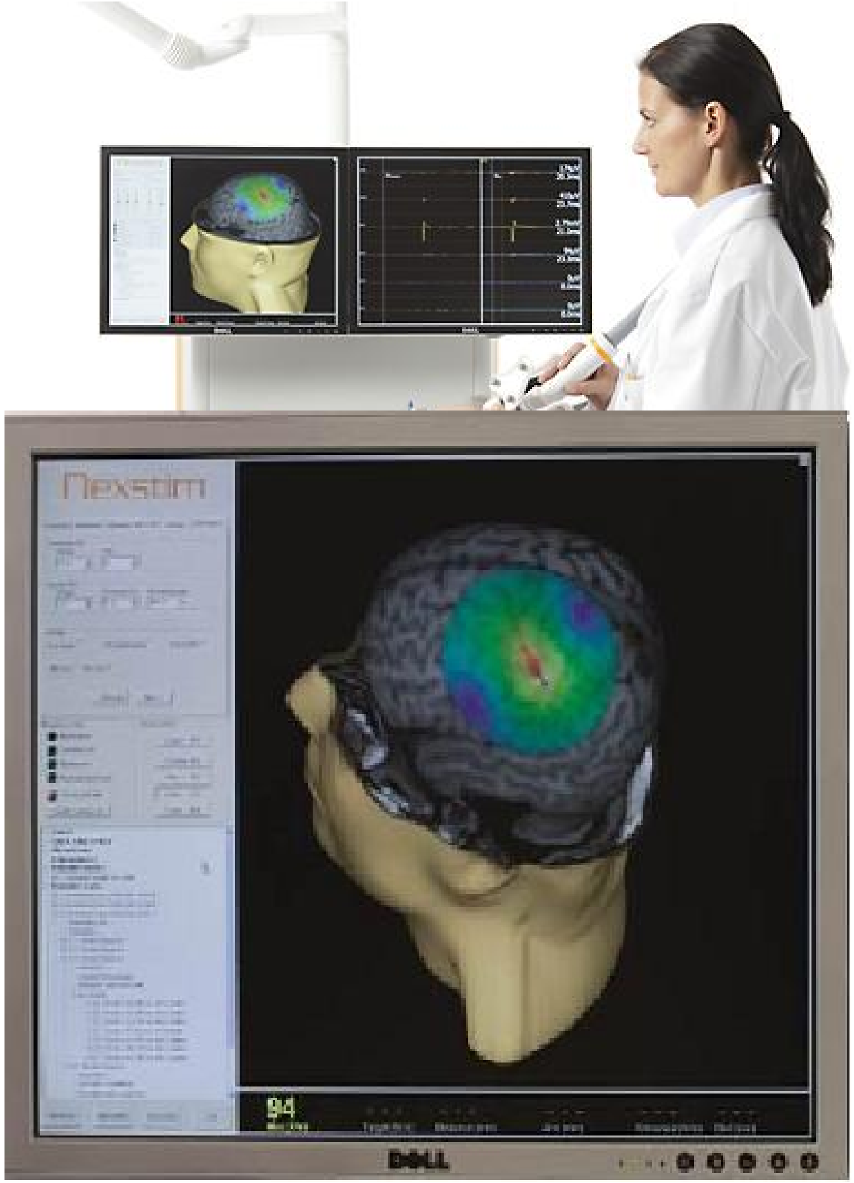

TMS coil


Cz
TMS reale
TMS sham
N10
N18
N40
N100
P14
P30
P60
P190
Potenziale (µV)
30
0
+30
–100
0
100
200
300
TMS
Tempo (ms)


P180
P30
P55
N45
N100
TMS
Amplitude [µV]
20
10
0
-10
-20
-100
0
100
200
300
400
500
Latency [ms]

NEURONAVIGATION





Ø Suggested check-list for a routine TMS clinical examination:

1) take a note about age, height, current therapy, and relevant clinical information and check-list for safety
2) electrode application and lower skin-electrode impedance to <10 KHoms
3) Supine position (= full muscular relaxation) or seated, with open eyes in a relatively soundproof environment (any sudden noise can modify threshold parameters)
4) demonstrate a few stimuli in the air or on the examiner at wrist in order to familiarise the subject with stimulus
5) stimulate the scalp, scanning in search for the 'hot spot'
6) define the excitability threshold during relaxation and contraction
7) collect and superimpose some reproducible MEPs in relaxation/contraction
8) perform sustained contraction for silent period measurements, collect and superimpose some traces
9) collect M wave of maximal amplitude during supramaximal peripheral nerve stimulation and calculate the cMAP/MEP amplitude ratio
10) collect and superimpose some MEPs during spinal root stimulation
11) collect and superimpose the 'F-waves' during supramaximal nerve stimulation
12) repeat on the other side and note the interside differences of the measured parameters
13) ask and take a note for any side effect.

30th International Congress of Clinical Neurophysiology

20-24 March, 2014 in Berlin, Germany (www.ICCN2014) of the IFCN

We would be happy to meet you all in Berlin in 2014 !!!