TMS: a Window into Brain Physiology

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We will talk about:

1. A **very** brief history of TMS
2. How TMS helped in the discovery of brain plasticity
3. Central motor conduction time
4. Motor cortex excitability threshold
5. Motor cortex mapping
6. Cortical silent periods
7. Intracortical facilitation and inhibition
8. Final remarks

History

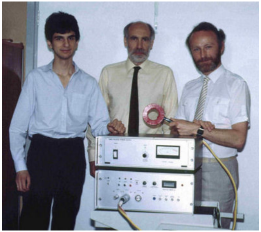
The underlying principles of electromagnetic induction were first discovered by Michael Faraday in 1831 and there were a number of attempts to utilise it to stimulate nerves and the brain around the turn of the 20th century

History

Thompson trying to stimulate his own brain- 1910

History

The first transcranial magnetic stimulator: 1985



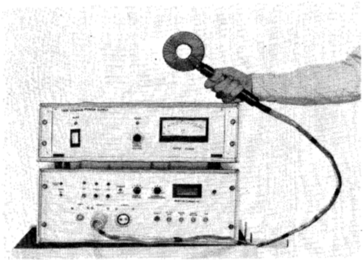


Fig 1—Magnetic stimulator and coil.

Electrical stimulation of the cortex requires careful placement of the surface electrodes and attention to other details of the technique to reduce discomfort to a level acceptable to patients. However, magnetic stimulation of the cortex is pain-free, requires no direct contact with the scalp, is non-invasive, and is easy to use.

Magnetic stimulation of peripheral nerves was reported by Polson et al.[5] The stimulator used on the cortex is similar in concept, but operates with a higher repetition rate of up to one pulse every 3 s and a delivered stimulus of up to twice the intensity. The stimulus is

The magnetic stimulator will also excite peripheral nerves (fig 2, lower) with minimal discomfort, although where the nerve is superficial it has little advantage over conventional stimulation. However, where a nerve lies deeper—for example, the median or ulnar nerves in the centre of the forearm—magnetic stimulation is readily achievable, whereas conventional stimulation causes considerable discomfort.

Magnetic stimulation of the cortex is particularly effective because of the ability of the field to pass through high-resistance structures. The skull has 8–15 times the resistivity of soft tissues[6] and so offers a considerable barrier to electrical stimuli. Roughly the same size of magnetic stimulus is needed for the motor cortex as for peripheral nerves.

Magnetic stimulation is rapid and easy to use in the clinical environment because it is not necessary to attach stimulating electrodes to the patient. Additionally the coil may be readily moved over the scalp until the desired stimulation site is located. The ability to stimulate corticospinal motor pathways allows their function to be assessed in many neurological conditions or monitored during surgical procedures. Magnetic stimulation is a major advance in the implementation of such studies.

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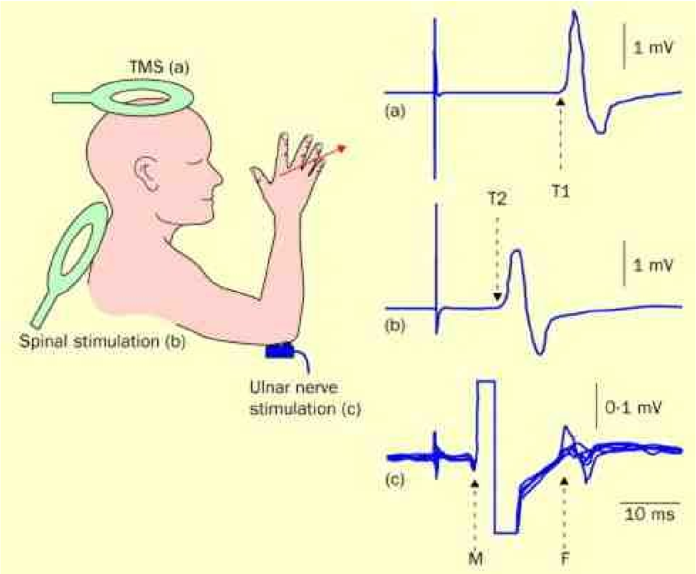
Motor evoked potentials

- First clinical use
- Especially interesting in demyelinating diseases
- Queen Square, 1985 (Barker, Freeston, Jalinous)

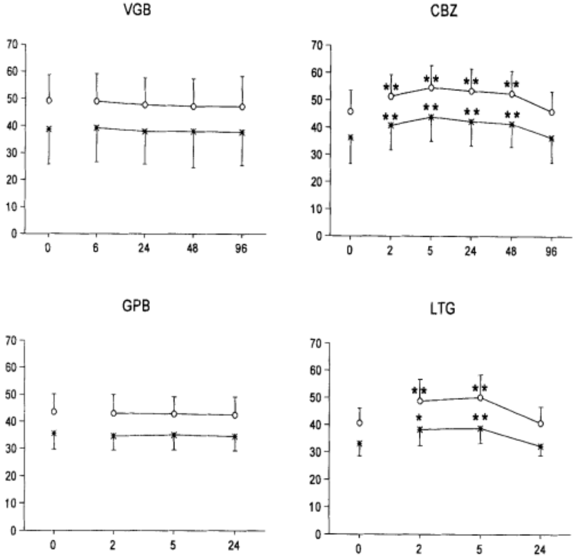
Motor evoked potentials



Motor cortex excitability thresholds

- Useful for studies on central nervous system physiology
- Pathophysiology of central nervous system disorders
- Evaluation of antiepileptic drugs

Excitability thresholds and antiepileptic drugs



Ziemann et al., 1996

TMS and the discovery of brain plasticity

Many studies on the effects of limb amputations, artificial syndactyly, nerve sections, etc. on the somatotopy of the animal brain were carried out in the '80s and '90s by Sanes, Merzenich, Pons and Kaas, among others.

However, almost all these studies involved the sensory cortex, which was much easier to study in animals.

With TMS, it became easy to study plasticity in the human motor cortex in a non-invasive way!

Brain plasticity: animal studies

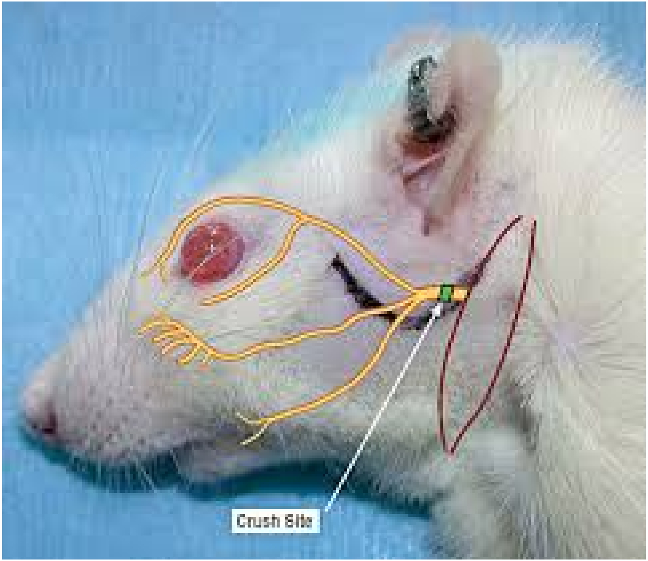
When a limb is amputated, its somatotopic representation on the sensory cortex does not become silent, but becomes part of the representation area of the stump and/or other adjacent body parts

Brain plasticity: animal studies

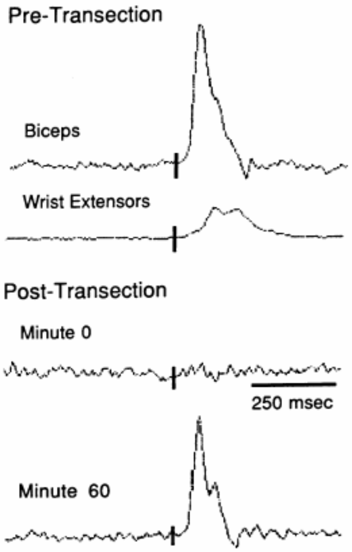
After artificial syndactyly, the digits (e.g. the bat's digits) no longer have separated cortical representation areas, and share a common somatotopic region in the post-central gyrus

Brain plasticity: animal studies

- Most animal studies concentrated on the sensory system
- Exception: Sanes's study on the facial nerve



- motor cortex mapped before and after surgical lesion of the facial nerve
- expansion of the forelimb and eye/eyelid area into the vibrissa area



Sanes et al. 1988

The underlying mechanism probably was unmasking of pre-existing synaptic connections between the vibrissa and the forepaw cortical representation areas

Could this rapid unmasking of pre-existing synaptic connections occur also in humans?

Rapid reversible modulation of human motor outputs after transient deafferentation of the forearm:

A study with transcranial magnetic stimulation

J.P. Brasil-Neto, MD; L.G. Cohen, MD; A. Pascual-Leone, MD, PhD; F.K. Jabir, MD;
R.T. Wall, MD; and M. Hallett, MD

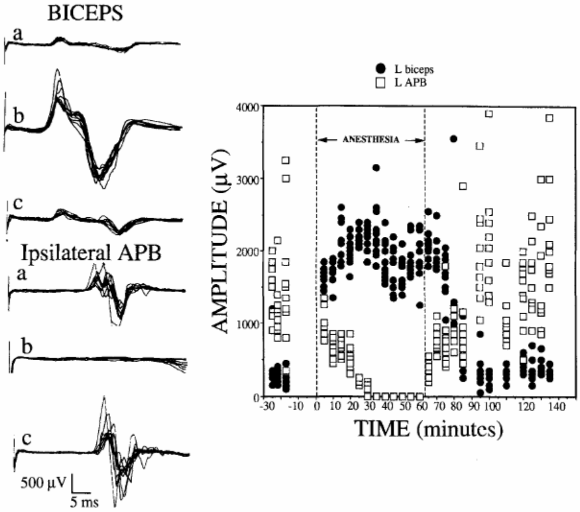


Figure 1. (Left) Ten superimposed MEPs from biceps and ipsilateral APB before anesthesia (a), during anesthetic block (b), and after anesthesia (c) in subject 2. (Right) Amplitudes of MEPs from biceps and ipsilateral APB as a function of the time course of the experiment in the same subject.

The Silver Spring Monkeys

Massive cortical reorganization in adult macaque monkeys

Pons et al, 1991

Massive Cortical Reorganization After Sensory Deafferentation in Adult Macaques

TIM P. PONS,* PRESTON E. GARRAGHTY, ALEXANDER K. OMMAYA, JON H. KAAS, EDWARD TAUB, MORTIMER MISHKIN

After limited sensory deafferentations in adult primates, somatosensory cortical maps reorganize over a distance of 1 to 2 millimeters mediolaterally, that is, in the dimension along which different body parts are represented. This amount of reorganization was considered to be an upper limit imposed by the size of the projection zones of individual thalamocortical axons, which typically also extend a mediolateral distance of 1 to 2 millimeters. However, after extensive long-term deafferentations in adult primates, changes in cortical maps were found to be an order of magnitude greater than those previously described. These results show the need for a reevaluation of both the upper limit of cortical reorganization in adult primates and the mechanisms responsible for it.

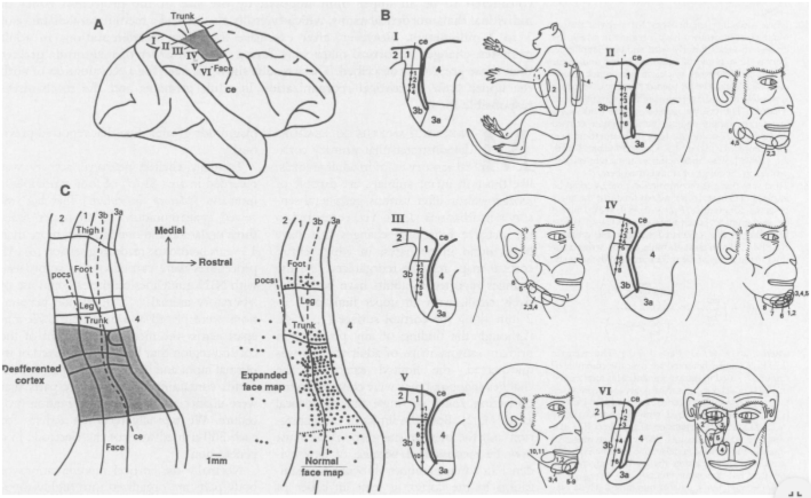


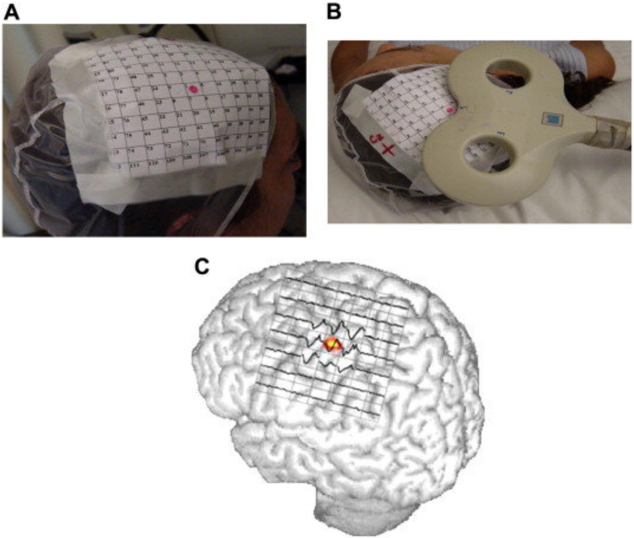
Fig. 2. (A) Lateral brain view showing the portion of the postcentral cortex … represented across the deafferented zone. In section II, located imme

Pons et al., 1991

Motor cortex mapping

- Studies began in 1990
- NIH: several studies
- Amputees: cortical reorganization
- Motor learning
- Cortical reorganization after various peripheral manipulations

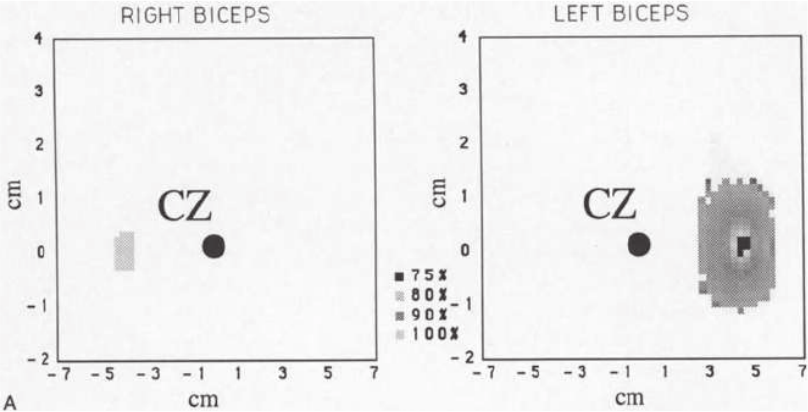
The mapping procedure



Rossini et al., 2015

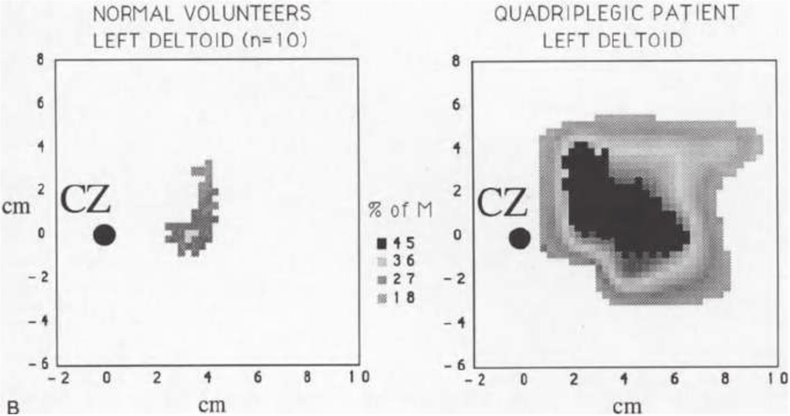
Cortical mapping: limb amputations

- TMS mapping in 78 years old patient 11 months after left arm amputation. The left biceps representation is larger than that of the right biceps.



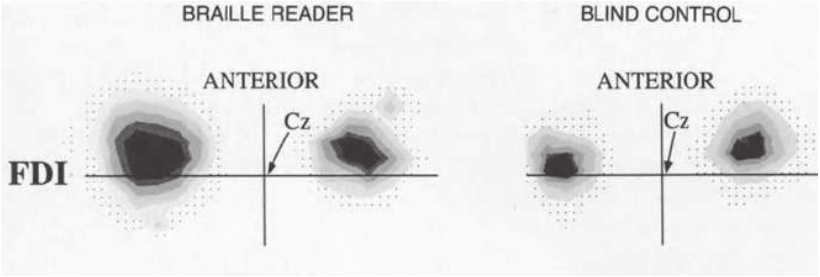
Cortical mapping: Quadriplegia

- Left deltoid cortical representation in 10 normal volunteers compared to that of a quadriplegic patient (lesion at C5).



Cortical mapping: Blind volunteers

- Cortical representation of the right FDI muscle of a blind patient who is a Braille reader with that of a non-Braille reading blind volunteer.



Motor learning

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Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills

A. Pascual-Leone, D. Nguyet, L. G. Cohen, J. P. Brasil-Neto, A. Cammarota, M. Hallett

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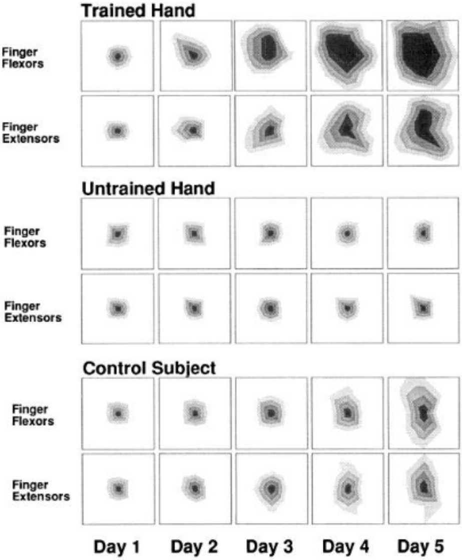
Article Info E-letters PDF

What is LENS?

- The hand cortical representation area expanded after learning of piano scales
- Even imagined practice caused brain plasticity


Trained Hand
Finger Flexors
Finger Extensors
Untrained Hand
Finger Flexors
Finger Extensors
Control Subject
Finger Flexors
Finger Extensors
Day 1
Day 2
Day 3
Day 4
Day 5

Central fatigue

MUSCLE & NERVE 17:713–719 1994

CENTRAL FATIGUE AS REVEALED BY POSTEXERCISE DECREMENT OF MOTOR EVOKED POTENTIALS

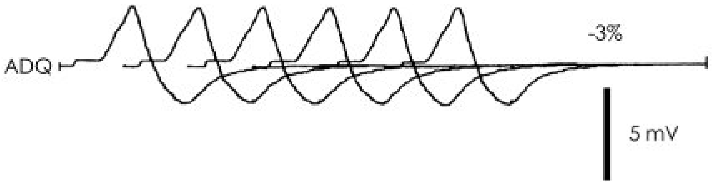
JOAQUIM P. BRASIL-NETO, MD, LEONARDO G. COHEN, MD, and MARK HALLETT, MD

Transcranial magnetic stimulation (TMS) of the human motor cortex provides a noninvasive tool for the study of neurotransmission along central motor pathways. The excitability of these pathways can be easily assessed by calculating the probability of producing motor evoked potentials (MEPs) by a magnetic stimulus, or by studying the amplitude of MEPs elicited by a given stimulus intensity. Moreover, by performing TMS in conjunction with transcranial electric stimulation (TES), recording of H-reflexes, and other neurophysiological techniques, it is possible to demonstrate the level along motor pathways at which events resulting in modulation of MEP amplitudes occur.[3]

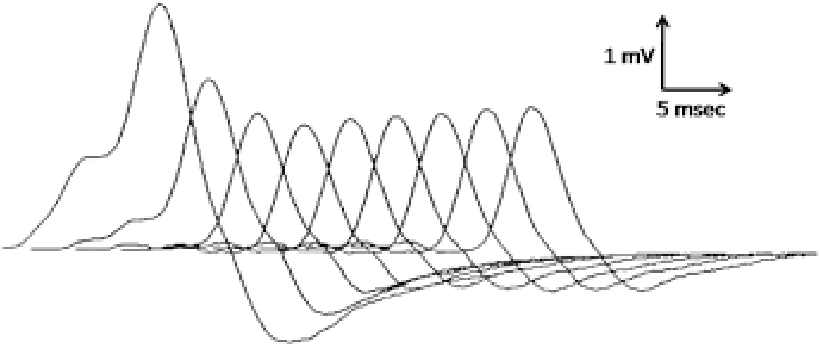
We have reported[3] the attenuation of MEP amplitudes after a single session of exercise performed until the subject felt too fatigued to continue and after successive short (30-s) periods of exercise. Simultaneous recording of maximal M-waves and H-reflexes ruled out changes in neuromuscular transmission or in excitability of the alpha-motoneuron as the cause of this phenomenon. We refer to the generalized decrease in MEP amplitudes after exercise as postexercise depression (PED) of MEP amplitude.

The neuromuscular safety factor

The amount of transmitter released per nerve impulse is normally greater than that required to trigger an action potential on the muscle fiber



- Normal responses to peripheral nerve repetitive stimulation



- Decremental muscle responses in *myasthenia gravis*

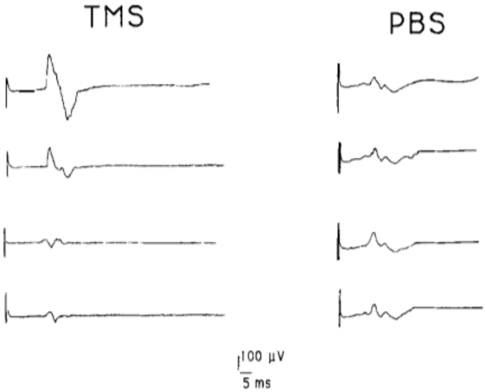


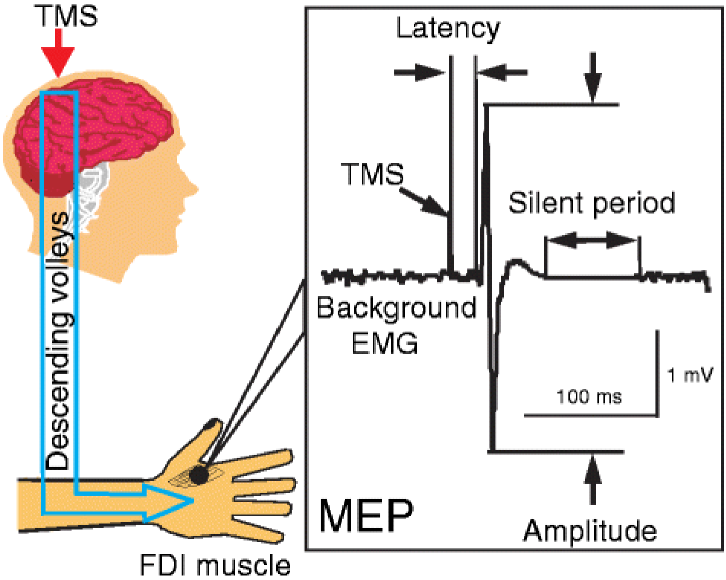
FIGURE 1. MEPs elicited with TMS and PBS at 0.3 Hz after four periods of exercise in 1 subject. The topmost MEP is the first one in a consecutive series. Note the progressive drop (PESD) in MEP amplitude with TMS, and the absence of PESD with PBS.

- Post-exercise decrement of MEPs
- no safety factor in motor cortex synapses

Cortical silent periods

- Seen after an MEP
- Period of supression of background electromyographic activity
- A measure of intracortical inhibitory and excitatory mechanisms

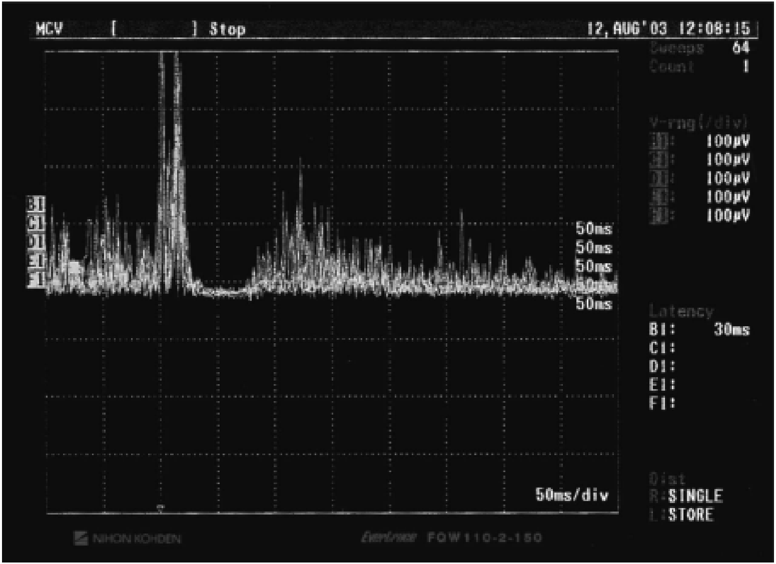
Cortical silent periods



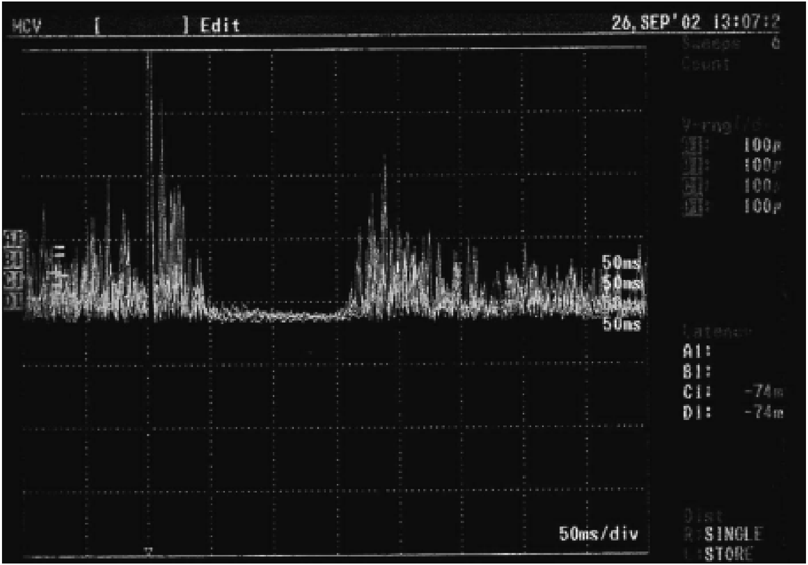
Cortical silent periods

Cortical silent periods in cervical dystonia

- Allam et al., 2015
- 10 patients (39 to 79 years old) with cranial dystonia: 4 with brepharospam and 6 with blepharospasm plus oromandibular dystonia
- Orbicularis oculi silent periods



- Silent periods in the patients

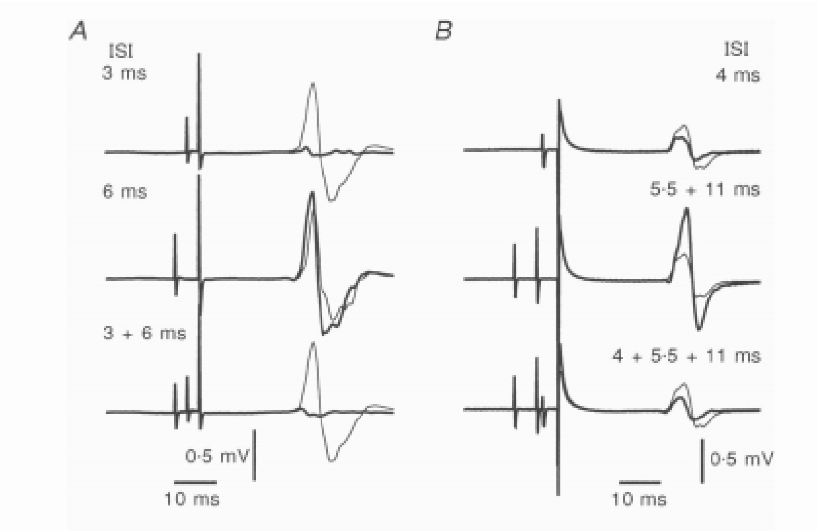


- Silent periods in the controls

Cortical facilitation and inhibition

- paired stimuli
- subthreshold magnetic stimuli may activate inhibitory and excitatory cortical interneurons
- conditioning stimulus 1-4 ms before test stimulus: inhibition
- conditioning stimulus 6-20 ms before test stimulus: excitation

Cortical facilitation and inhibition



Thank You!

References