Application of magnetism: TMS
Resting potential

$$E_{eq,K^+} = \frac{RT}{zF} \ln \frac{[K^+]_o}{[K^+]_i},$$

$$E_m = \frac{RT}{F} \ln \left( \frac{P_{Na^+}[Na^+]_o + P_{K^+}[K^+]_o + P_{Cl^-}[Cl^-]_o}{P_{Na^+}[Na^+]_i + P_{K^+}[K^+]_i + P_{Cl^-}[Cl^-]_o} \right)$$

$E_{eq,K^+}$ is the equilibrium potential for potassium, measured in volts

$R$ is the universal gas constant, equal to 8.314 joules·K⁻¹·mol⁻¹

$T$ is the absolute temperature, measured in kelvins ($= K = \text{degrees Celsius} + 273.15$)

$z$ is the number of elementary charges of the ion in question involved in the reaction

$F$ is the Faraday constant, equal to 96,485 coulombs·mol⁻¹ or J·V⁻¹·mol⁻¹

$[K^+]_o$ is the extracellular concentration of potassium, measured in mol·m⁻³ or mmol·l⁻¹

$[K^+]_i$ is likewise the intracellular concentration of potassium

$E_m$ is the membrane potential, measured in volts
Biology of magnetism

EPSP, IPSP and Action potential

[Diagram showing EPSP, IPSP, and Action potential]

Critical level of depolarization

Stimulus intensity

Na⁺ Outside

Inside

K⁺

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity

0 1 2 3 ms

Critical level of depolarization

0 1 2 3 ms

mV

0 -60

-90

Stimulus intensity
Biology of magnetism

History of EEG:

- Caton R. (1875) Electrical phenomena of the cerebral hemispheres of rabbits and monkeys.
- Pravdich-Neminsky V.V. (1912) First publication on EEG.
- Berger H. (1920) EEG in humans.

Limitations:

- EEG picks up the activity of large groups of neurons.
- EEG has limited anatomical specificity when compared with brain imaging techniques such as fMRI (some anatomical specificity can be gained with the use of EEG topography, which uses a large number of electrodes to triangulate the source of the electrical activity).

Advantages:

- The time resolution is very high (subms).
- EEG is the only method to measure electric activity of the brain directly.
Field distribution by 510 coils at distinct locations. Coils configured into 306 MEG channels.
The coil configuration optimally combines the focal sensitivity of 204 planar gradiometers and the widespread sensitivity of 102 magnetometers.
Accurate geometry and excellent balance of the sensors provided by thin-film technology.
Interference compensation by on-line Signal Space Projection (SSP) using the sensor array as a reference; involves no increase of white noise.
Whole-head design with realistic shape based on standard (EN960:1994).
Biology of magnetism

It's possible to alter the way the brain works by altering the electrical environment.

**Transcranial magnetic stimulation (TMS)** is the use of powerful rapidly changing magnetic fields to induce electric fields in the brain by electromagnetic induction without the need for surgery or external electrodes.

Standard equipment consists of something to generate an electromagnetic signal at a specific frequency, and a coil to focus that magnetic field on specific brain regions.
History of TMS

- Galvani and Volta (18th century) demonstrated the importance of electrical phenomena in nerves and muscles.
- Faraday (1831) discovered the law of electromagnetic induction.
- Maxwell (1860s) mathematically formulated the interrelationship between electricity and magnetism.
- D’Arsonval (1896) induced eddy current in living tissue by strong alternating current.
- Walsh (1946) showed the lower threshold for retina stimulating rather than other tissues.
- Bickford and Freeming (1965) reported non-invasive stimulation of frog, rabbit and human peritheral nerves.
- Cadwell Laboratories Inc. (1988), repetitive stimulation with water-cooled coil.
TMS coils

Magstim Company Ltd, UK

Liebetanz et al., 2003

Medtronic Inc, USA

Thielscher, Kammer, 2004
Limitations for TMS use

There are relative and absolute contraindications to TMS.

- Subjects with **metal anywhere in the head**, excluding the mouth, is generally a contraindication to TMS. This includes shrapnel, and screws and clips from surgical procedures unless the physical properties of the metal object are known and there is a strong reason for using TMS.
- Subjects with **cardiac pacemakers** and implanted medication pumps should not participate in most TMS studies.
- TMS also should not be performed in patients with electrodes inside the heart which might provide a low-resistance current path to electrically sensitive tissue.
- Persons with **serious heart disease** are at increased risk in the event of a seizure, and unless the potential clinical benefit outweighs the risk, they should not participate in TMS studies.
- Persons with **increased intracranial pressure**, as in acute large infarctions or trauma, are also at increased risk in the event of a seizure, and should not receive TMS.
- **Pregnant** women or women in child bearing age that might be pregnant should also be excluded from TMS studies.
- Great caution is needed when applying rTMS to subjects with a history of **seizures**, a family history of **epilepsy**, and patients taking medication that might increase the risk of seizures.
Safety of TMS use

- **Seizure induction**: Single-pulse TMS has produced seizures in patients, but not in normal subjects. rTMS has caused seizures in patients and in normal volunteers.

- **Hearing loss**: During TMS there will be a loud clicking sound from the coil. The peak sound pressure is 120-130 dB 10 cm from the coil. Most sound energy is in the frequency range 2-7 kHz where the human ear is the most sensitive. The noise may exceed criteria limits for sensorineural hearing loss.

- **Heating of the brain**: Heating of the brain is unlikely to cause deleterious effects. Theoretical power dissipation from TMS is few milliwatts at 1 Hz, while the brain's metabolic power is 13 W.

- **Engineering safety**: TMS equipment operates at lethal voltages of up to 4 kV. It is hence important not to keep coffee cups or ice bags on the stimulator. The maximum energy in the capacitor is about 500 J, equal to dropping 100 kg from 50 cm on one's feet. An electrical engineer with experience in low-power electronics only should keep his/her hands behind the back and ask a power electronics expert to do the job.
Safety of TMS use

- **Scalp burns from EEG electrodes:** Mild scalp burns in subjects with scalp electrodes can be easily avoided using, e.g., small low-conductivity Ag/AgCl-pellet electrodes.
- **Effects on pulse rate, blood pressure, serum prolactin and cortisol levels and hormone levels:** Many tests, including blood pressure, pulse rate, hormone levels and serum prolactin and cortisol levels, have revealed no statistically significant changes. The same is true for psychometric tests. Naturally, naming and verbal fluency tasks are disturbed during TMS.
- **Spontaneous EEG:** Spontaneous EEG following TMS has been found to be normal; yet, EEG will fail to uncover transient changes like development of mild or additive cellular dysfunction. Monitoring of the EEG during TMS could, at least in principle, be used to stop the experiment if abnormalities appear.
- **Long-term effects:** It is believed that harmful effects of TMS are related to the induced electric field, since the body tissue is transparent to low-frequency magnetic fields.
Silent period (SP)

*Butler et al., 2005*

*Chistyakov et al., 2001*
Resting motor threshold (MT) for MEP relates to resting membrane potential properties of cortical and spinal motor neurons (Ziemann et al., 1996).

MEP size reflects more globally the corticospinal input–output balance (Devanne et al., 1997).

SP is produced through activation of both spinal and cortical circuits (Cantello et al., 1992), maybe mainly mediated by GABA-B receptors (Werhahn et al., 1999).

SP duration depends on the activity of subcortical structures, mainly basal ganglia, and the integrity of the connections between them and the motor cortex.
Paired pulse paradigm

- Paired pulse experiments are designed to give insight into the nature of the cortical circuitry activated by TMS.
- **Short interval intracortical inhibition** (SICI) was first reported by *Kujirai et al.* (1993).
  
  - The SICI does not modify directly the excitability of pyramidal neurons. It seems more likely that the inhibition is due to activation of other intracortical elements.
- **Long latency** (50-200 ms) **intracortical inhibition** (LICI) was first described by *Valls-Sole et al.* (1992).
  - ICIs are low-threshold GABA-A ergic in origin (*Ilic et al.*, 2002; *Kujirai et al.*, 1993).
- **Short interval facilitation** (ICF) described by *Tokimura et al.* (1996) and *Ziemann et al.* (1998) is due excitatory inputs from high-threshold glutamatergic pathways to the motor cortex (*Ilic et al.*, 2002; *Liepert et al.*, 1997).
  - ICF is observed between ICIs. The second stimulus excites the cell bodies or initial segments of neurones that were excited but not discharged by the first stimulus.

*Di Lazzaro et al.*, 2004
Paired pulse paradigm

Cracco et al. (1989) recorded in man an evoked response from one hemisphere after electrical or magnetic stimulation over the motor cortex of the opposite hemisphere. The potential had a minimum onset latency of 8-9 ms, and a duration of 7-15 ms (magnetic stimulation) or 18-44 ms (anodal electric stimulation).

Interhemispheric inhibition (IHI) appears at ISI of 5-6 ms or longer and is mediated to a large extent through transcallosal excitatory connections that terminate on inhibitory interneurons (Gerloff et al., 1998).

Interhemispheric facilitation (IHF) between primary motor areas could be induced in a small window (3-5 ms) of slightly suprathreshold (up to 105% AMT) conditioning intensities and only in the pre-activated target muscle with an anterior–posterior-directed current flow over the test pulse hemisphere (Hanajima et al., 2001).

IHF is subtle and highly variable, whereas IHI is a consistent phenomena that can readily be produced at intensities above individual RMT both at rest and during contraction.

(Ferbert et al., 1992).
RMS.jpg

Repetitive transcranial magnetic stimulation

High (10-20 Hz) and low frequency rTMS (1-5 Hz).
• Note different definition! High (>1 Hz) and low (≤ 1 Hz) frequency rTMS.

• Theta Burst Stimulation (TBS) consists of repeating bursts of stimuli. Each burst consists of three stimuli repeating at 50 Hz; bursts are repeating at 5 Hz. The intensity of stimulation is set at 80% of the active motor threshold (AMT). In normal individuals a continuous train of 100 bursts (300 stimuli) (Talelli et al., 2007).
Afferent inhibition

- D2 stimulation elicited a three-phase response of modest MEP facilitation followed by inhibition and further facilitation.
- Inhibition is augmented by descending rather than segmental input to spinal motor neurons.

Clouston et al., 1995

Effect of digital nerve stimulation on responses to TMS at different intensity, FDI

Tokimura et al., 2000

Kofler et al., 2001
TMS compatible EEG

- TMS induces a pronounced negativity in EEG (N100).
- N100 appears to represent an inhibitory response following TMS.
- This is in agreement with intracellular recordings in animals and paired-pulse TMS studies.

*Nikulin et al., 2003*
Possible combinations of stimuli:
- Single pulse TMS over different cortex areas.
- Peripheral stimulation + single pulse TMS (afferent inhibition).
- Paired pulse TMS (ICI and ICF, IHI and IHF).
Navigated brain stimulation

Typical layout of NBS systems (Nexstim Ltd)

Recommended room size:
- Length 5.0 m (16.4 ft.)
- Width 3.0 m (9.8 ft.)
- Height 2.8 m (9.2 ft.)
The Robotized TMS Coil Positioning System (Advanced Neuro Technology (ANT))

- Allows planning of a complete stimulation session ahead by defining stimulation sites based on anatomical MRI information and functional information like fMRI, PET or EEG/MEG.

- During the execution of the TMS stimulation sequence, the system places the coil at the predefined target positions and keeps the coil in place even if the head of the patient/subject moves.

http://www.youtube.com/watch?v=iigQM0I_WRU
TMS and fMRI

• In contrast to EEG mapping of cortical neuronal activity, fMRI can provide a measure of regional synaptic activity in the entire brain, including deep brain structures.

• Neuronal stimulation by TMS is followed by an inhibitive phase in fMRI that compensates for the effect of an initial neuronal activation. It is further concluded that the signal increases during motor cortex fit a sensory feedback from the moving body parts (Kemna, Gembris, 2003).

• In stroke patients with increased BOLD signal, percent amplitude ICI decreased (Hamzei et al., 2006).

Bestmann et al., 2004

Fig. 2. BOLD MRI responses to suprathreshold rTMS of left premotor cortex (group analysis, n = 9, P < 0.01, corrected). (a) Sagittal (x = −40), coronal (y = −11), and transverse (z = 55) view of activity in the left PMd. (b) Six transverse sections showing activity changes in the cingulate gyrus, PMv, auditory cortex, caudate nucleus, left posterior temporal lobe, medial geniculate nucleus, and cerebellum with coordinates indicated. Activation maps are projected onto a template brain (Montreal Neurological Institute, MNI). L: left, R: right. Bestmann et al., 2005
Triple stimulation technique (TST) - accurately detects cortico-spinal impairment. TMS (130% RMT) followed by two supraliminal electrical stimuli, the first one applied to the ulnar nerve at the wrist, and the second to the brachial plexus at Erb’s point, with appropriate intervals.

Amplitude of MEP is a less sensitive variable than SP because there is a considerable variability due to desynchronization of descending volleys. TMS by triple stimulation technique permits resynchronization of the MEP, making it a more sensitive method (Magistris et al., 1999).
The threshold tracking strategy is developed on the basis of preliminary observations that the stimulus–response relationship was exponential (Awiszus et al., 1999; Fisher et al., 2002).

**Application:**
- In the conventional PP technique, the conditioning and test stimuli are kept at constant intensities, and changes in the MEP amplitude are measured.
- Using TTT the output (MEP response) was fixed and changes in the test stimulus intensity required to generate this target response, when preceded by either sub- or suprathreshold conditioning stimuli, were measured.

*Vucic et al., 2006*
TMS for cognitive studies

- TMS can be used to transiently disrupt the function of a given cortical target, thus creating a temporary functional lesion, without complications from compensatory mechanism.
- Localisation of sensory function and language studies.
- rTMS and short-term working memory.
- Lateralization of self-representation


Transcranial magnetic stimulation as a tool for cognitive studies

CHRISTOPHER J. BAILEY,1 JARI KARHU1 and RISTO J. ILMONIEMI1,2

1 BioMag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital, Finland
2 Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, Finland
In PD: reduced MT and/or enhanced MEP size at rest (Lou et al., 2003), but increased MT and/or reduced MEP facilitation during contraction (Tremblay and Tremblay, 2002); ICF is significantly reduced (Bares et al., 2003; Lefaucheur et al., 2004); SP duration is shortened (Lefaucheur et al., 2005); abnormal ipsilateral SP - a marker of transcallosal interactions (Wolters et al., 2004); SICI is reduced (Lewis and Byblow, 2002). Patterns of cortical excitability in PD seem predominantly affected by an abnormal output from the basal ganglia to the cortex rather than by the involvement of the cortico-spinal projections (Kuhn et al., 2004).

In multiple system atrophy of Parkinsonian type, progressive supranuclear palsy and idiopathic PD patients RMT and SP duration did not differ between any of the patients groups and the ICI at ISI 3 ms was significantly lower in all the patients than in the control subjects (Eusebio et al., 2007).

In Huntington’s disease a lengthening of the SP duration without significant change in the MT (see Chistyakov et al., 2001).

Multiple sclerosis: abnormal ipsilateral SP (Boroojerdi et al., 1998; Schmierer et al., 2002) and loss of IHI inhibition related to corpus callosum atrophy (Manson et al., 2006). MEP absent, reduced in amplitude, or more dispersed (Hess et al., 1987).

In focal hand dystonia: abnormal ipsilateral SP (Niehaus et al., 2001).
Inamyotrophic lateral sclerosis (ALS): SP duration is shorter early in the disease, MT is normal or decreased (cortical motor neuron hyperexcitability induced by glutamate) in the early stages of the disease, and raises as the disease progresses (Mills and Nithi, 1997; Mills, 2003). The early part of the SP reflects spinal cord inhibition whereas the later part originates from the cortical mechanism (Inghilleri et al., 1993) implicating GABAergic system (Priori et al., 1994). The abnormalities of cortical excitability mirror the parameters of cortico-spinal conduction since they are, at least partly, due to changes in the intrinsic properties of the cortico-spinal projections.

In the lower motor neuron disease (LMND) (e.g. pure motor neuropathy): no abnormality of SP (Attarian et al., 2005).

In stroke patients: delayed MEPs and reduced amplitudes, increased ICI and decreased ICF (Hamzei et al., 2006); a deeper premovement IHI with paretic than non-paretic hand movements (Duque et al., 2005); elevated MT in affected hemisphere and decreased in unaffected hemisphere (see Curra et al., 2002).

In epilepsy: increased MEP amplitude (Hufnagel et al., 1990); decreased MT (George et al., 1999); less prominent ICI and ICF in both hemispheres (see Curra et al., 2002) and decreased IHI (Hanajima et al., 2001).

In schizophrenia: abnormal ipsilateral SP (Bajbouj et al. 2004; Boroojerdi et al. 1999); decreased IHI (Daskalakis et al., 2002).
Fundamental studies of pathogenesis

**Chronic pain** (fibromyalgia): increased RMT, normal MEP amplitude, shortened SP, and reduced ICF and ICI (for long ISIs and suprathreshold paired pulses) (*Salerno et al.*, 2000).

**Regional pain syndrome**: normal RMT, MEP amplitude, and ICF, but reduced ICI in the both hemispheres (*Schwenkreis et al.*, 2003) or only in the hemisphere corresponding to the side of pain (*Eisenberg et al.*, 2005).
**Testing of corticospinal tract and peripheral nerve conductivity**

**In multiple system atrophy** of Parkinsonian type and **progressive supranuclear palsy**: the TST pattern was abnormal but not in **idiopathic PD** patients or controls (Eusebio et al., 2007).

**In amyotrophic lateral sclerosis, multiple sclerosis and stroke**: central motor conduction time (CMCT) is prolonged and TST is changed.

**ALS**: in early stage where there are no upper motor neuron signs, slowing of central motor conduction can provide valuable evidence of an additional pyramidal lesion.

**In cervical myelopathy**: where there is doubt from imaging studies of the level of compression, TMS with recording from a sequence of upper limb muscles can provide evidence of the level of functional impairment.

The TST is a quite quick and easy technique that does not require any particular cooperation on the part of the patient. In addition, it is highly reproducible (Humm et al., 2004) and does not depend on preactivation, which can be tricky to control in rigid and/or tremulous PD (Eusebio et al., 2007). TST is preferable method for upper limb muscles (less invasive, distance is short for CMCT).

CMCT can be measured to a wide range of muscles and normal values are available for muscles in which the peripheral component of conduction is difficult to estimate.
Presurgical functional mapping

The accuracy of a 3-dimensional magnetic resonance imaging-navigated TMS system (nTMS) with the gold standard of direct cortical stimulation (DCS) was compared. Navigated TMS is a reliable tool for preoperative mapping of motor function (Picht et al., 2011)
Pre- and intraoperative monitoring of corticospinal function

3D model: Middle-aged woman with right fronto-parietal AVM (blue). fMRI (red), TMS (green) and intraoperative cortical mapping (purple) showed diffuse distribution of motor cortex.

Treatment

In some cases, the severity of clinical impairment correlated with the magnitude of IHI abnormality (Murase et al., 2004; Schmierer et al., 2002).

These findings led to the hypothesis that correction of IHI abnormalities may result in clinical gains. Pal et al. (2005) describe a possible strategy to manipulate IHI. Downregulation of activity in one motor cortex using 1 Hz rTMS (Chen et al., 1997) results in decreased IHI over the opposite motor cortex that outlasts the period of stimulation.

The possible therapeutic effects of premotor rTMS may therefore involve indirect effects of PMd on SICI and RI, which this study has shown can be normalised by cTBS (Huang et al., 2010).
Treatment: neurodegenerative disorders

- **PD**: low-frequency rTMS over motor cortex improves motor functions (*Filipović et al., 2010*). Intermittent theta-burst stimulation (TBS) of the motor and prefrontal cortices appears safe and improves mood, but failed to improve motor performance and functional status in PD (*Hamada et al., 2008*).

- **Dementia**: high frequency rTMS over DLPFC (*Coteli et al., 2008*)

- **Alzheimer disease**: high frequency rTMS over DLPFC (*Coteli et al., 2011*)

- **Huntington disease**: (*Medina, Tunez, 2010*).
Treatment: neurological disorders

- **Dystonia patients**: premotor cortex TBS \((Huang \text{ et al.}, 2010)\).

- **Stroke** rehabilitation:
  based on a model of interhemispheric rivalry between
  the motor areas of the stroke and intact hemisphere.

  Low-frequency rTMS or cathodal Transcranial Direct Current Stimulation (TDCS)
  have been used in single-session designs to suppress excitability in intact
  hemisphere (benefit of 10–20%). Excitatory stimulation of the stroke hemisphere
  has mainly been tested in the form of anodal TDCS and seems to be equally
  effective in improving motor function in chronic stroke patients \((Talelli \text{ et al.}, 2007)\).

- **Migrain and chronic pain**: high-frequency rTMS \((Mazzoni \text{ et al.}, 2007)\).
  Pain syndrome treatment (over motor cortex).
  Migraines treatment (over Oz).

- **Epilepsy**: low-frequency rTMS \((Kimiskidis, 2010)\) (over vertex, or dysfunctional
  cortex).
TMS and mood

• In healthy volunteers, the reversed direction of the mood changes seen after high-frequency rTMS to the left and right DLPFC (Pascual-Leone et al., 1996) suggests that both the left and right hemisphere are involved in mood regulation.

• The mechanism by which rTMS may alter neuropsychiatric functioning is unknown. Some studies, however, suggest that rTMS may downregulate beta adrenoreceptors (Fujiki, Steward, 1997) and increase dopamine and serotonin levels in the striatum, frontal cortex, and hippocampus (Ben-Shachar et al., 1997).
Treatment: affective disorders

• **Major depression:** 10 single pulse TMS over the frontal area of both sides (total of 20 stimuli in a session) for 5 days as an add-on therapy. SPECT showed that the regional cerebral blood flow of the bilateral frontal region had increased after treatment *(Fujita and Koga, 2005)*.

rTMS may in the future prove to be an effective treatment for mood disorders.

- rTMS has fewer cognitive side effects and is medically safer than electroconvulsive therapy *(ECT)*.
- ECT is currently more effective for treating depression than is rTMS.

• **Mania and bipolar disorders:** rTMS over prefrontal cortex *(Harel et al., 2011)*.
Treatment: anxiety disorders, schizophrenia

rTMS

- **Obsessive compulsive disorder** (Greenberg et al., 2008),
- **Post-traumatic stress disorder** (Cohen et al., 2004)
  (over prefrontal cortex).

- **Schizophrenia** (Tranulia et al., 2008)
  and tinnitus treatment (Iyer et al., 2003)
  (over tempoparietal cortex)

*Agid et al., 2007*
Several issues and problems extend across all psychiatric TMS studies:

- optimal method for a sham control,
- appropriate coil location,
- best device parameters (intensity, frequency, dosage, and dosing schedule)
- refining what subjects should be doing during treatment (activating pathologic circuits or not).
Monitoring the effects of neurotrophic drugs on cortical activity

Changes in ICI and ICF tested with PP TMS after 3,4-diaminopyridine (black) and placebo (white) intake in 12 patients with multiple sclerosis.
Useful review publications

**Transcranial magnetic stimulation techniques in clinical investigation**

A. Curra, MD; N. Modugno, MD; M. Inghilleri, MD; M. Manfredi, MD; M. Hallett, MD; and A. Bernardelli, MD

Abstract—Transcranial magnetic stimulation (TMS) is a technique that can activate cortical motor areas and the corticospinal tract without causing the subject discomfort. Since TMS was introduced, numerous applications of the techniques have been developed for the evaluation of neurologic diseases. Standard TMS applications (central motor conduction time, threshold and amplitude of motor evoked potentials) allow the evaluation of motor conduction in the CNS. Conduction studies provide specific information in neurologic conditions characterized by clinical and subclinical upper motor neuron involvement. In addition, they have proved useful in monitoring motor abnormalities and the recovery of motor function. TMS also gives information on the pathophysiology of the processes underlying the various clinical conditions. More complex TMS applications (paired-pulse stimulation, silent period, ipsilateral silent period, input-output curve, and evaluation of central fatigue) allow investigation into the mechanisms of diseases causing changes in the excitability of cortical motor areas. These techniques are also useful in monitoring the effects of neurotrophic drugs on cortical activity. TMS applications have an important place among the investigative tools to study patients with motor disorders.

**Medicina (Kaunas) 2005; 41(10) 813**

**APŽVALGINIS STRAIPSNIS**

**Transcranial magnetic stimulation in clinical practice**

Miglė Ališauskienė, Andre Truffert¹, Nerija Vaičienė, Michel R. Magistris¹

Clinic of Neurology, Kaunas University of Medicine, Lithuania
¹Clinic of Neurology, Geneva University, Switzerland
