Non-therapeutic and investigational uses of non-invasive brain stimulation

Robert Chen, MA, MBBChir, MSc, FRCP C
Catherine Manson Chair in Movement Disorders
Professor of Medicine (Neurology), University of Toronto
Senior Scientist, Toronto Western Research Institute
Director, the Eliot Phillipson Clinician Scientist Training Program
Acting Associate Dean, Physician Scientist Training, University of Toronto
Use of Transcranial Magnetic Stimulation (TMS)

- Clinical Diagnosis
- Presurgical mapping
- Research Utility: Investigations of normal brain functions, pathophysiology of neurological and psychiatric disorders

Other panelists will discuss
- Cognitive enhancement
- Over the counter or consumer initiated use
- Adult vs. children
Invited review

The clinical diagnostic utility of transcranial magnetic stimulation: Report of an IFCN committee

Robert Chen a,*, Didier Cros b, Antonio Curra c, Vincenzo Di Lazzaro d, Jean-Pascal Lefaucheur e, Michel R. Magistris f, Kerry Mills g, Kai M. Rösler h, William J. Triggs i, Yoshikazu Ugawa j, Ulf Ziemann k

a Division of Neurology, Toronto Western Research Institute, University of Toronto, 7MC411, Toronto Western Hospital, 399 Bathurst Street, Toronto, Ont., Canada M5T 2S8
b Department of Neurology, Massachusetts General Hospital, Boston, USA
c Department of Neurological Sciences, Ospedale A. Fiorini Terracina, LT, University of Rome La Sapienza Polo Pontino, Italy
d Istituto di Neurologia, Università Cattolica, Rome, Italy
e Service de Physiologie – Explorations Fonctionnelles, Hopital Henri Mondor, Creteil, France
f Department of Clinical Neuroscience, University Hospital of Geneva, Geneva, Switzerland
g Department of Clinical Neurophysiology, Kings College Hospital, London, United Kingdom
h Department of Neurology, University Hospital of Berne, Berne, Switzerland
i Department of Neurology, University of Florida, Gainesville, FL, USA
j Department of Neurology, The University of Tokyo, Tokyo, Japan
k Department of Neurology, Johann Wolfgang Goethe University of Frankfurt, Frankfurt, Germany

Accepted 18 October 2007
Available online 11 December 2007
A practical guide to diagnostic transcranial magnetic stimulation: Report of an IFCN committee


Department of Neurology, Christian Albrechts University, Kiel, Germany
Hospital Nacional de Parapléjicos, Toledo, Spain
Department of Neurology, The University of British Columbia, Vancouver, Canada
Department of Neuroscience, Psychiatry and Anesthesiology, University of Messina, Messina, Italy
Human Cortical Physiology and Stroke Neurorehabilitation Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA
Department of Neuropediatrics and Muscle Disorders, University of Freiburg, Freiburg, Germany
Department of Neurology, Inselspital, University of Bern, Bern, Switzerland
Human Brain Research Center, University Graduate School of Medicine, Kyoto, Japan
Dipartimento di Neuroscienze, Sezione Neurologia e Neuropsicologia Clinica, Università di Siena, Policlinico Le Scotte, Siena, Italy
Centre for Neuromuscular and Neurological Disorders, M518, University of Western Australia, Nedlands, Australia
Institute of Neurology, Catholic University, Pol Gemelli; IRCCS S. Raffaele-Psana and Casa di Cura S. Raffaele-Cassino, Roma, Italy
Department of Neurology, Goethe-University Frankfurt, Frankfurt am Main, Germany
Unitat d’EMG, Servei de Neurologia, Hospital Clinic, Universitat de Barcelona, Spain
Danish Research Center for Magnetic Resonance, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
TMS Techniques

- Single and paired TMS
  - Central conduction time
  - Measurement of brain excitability
Central motor conduction time (CMCT)

- Cortical interneuron
- Spinal motoneuron
- Muscle

Transcranial Magnetic Stimulation (TMS)

Peripheral stimulation

Corticospinal tract neuron in motor cortex
Central motor conduction time (CMCT)

- Obtain MEP latency for TMS for active target muscle
- Obtain peripheral conduction time by F-wave, electrical or magnetic stimulation over the cervical or lumbar spines
- CMCT = MEP latency – peripheral conduction time
Central motor conduction time (CMCT)

- Prolonged in neonates and children (maturation)
- Correlates with height for CMCT to the lower limbs (Udupa & Chen 2013, Handb Clin Neurol)
Measures of cortical inhibition/excitation using TMS

TEST STIMULUS

SHORT-INTERVAL INTRACORTICAL INHIBITION (SICI)

LONG-INTERVAL INTRACORTICAL INHIBITION (LICI)
Short latency afferent inhibition (SAI)

TMS-pulse

median nerve stimulation (MNS)
Diagnostic use of TMS
## Demonstrated Utility

<table>
<thead>
<tr>
<th>Condition/disease</th>
<th>Test</th>
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<tbody>
<tr>
<td>Myelopathy</td>
<td>CMCT/TST</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>Combination of CMCT/TST, MT, SP, SICI, MEP</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>CMCT/TST</td>
</tr>
<tr>
<td>Presurgical Mapping</td>
<td>Navigated TMS – motor: single pulse, language: TMS train</td>
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## Potential Utility

<table>
<thead>
<tr>
<th>Condition/disease</th>
<th>Test</th>
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<tr>
<td>Cerebellar diseases</td>
<td>Cerebellar stimulation, CMCT</td>
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<tr>
<td><strong>Dementia</strong></td>
<td><strong>SAI</strong></td>
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<tr>
<td>Facial nerve palsy</td>
<td>TMS of facial nerve and motor cortex</td>
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<tr>
<td>Multiple sclerosis</td>
<td>IHI/iSP</td>
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<td>Movement disorders</td>
<td>SICI, CMCT/IHI/iSP (parkinsonian syndromes)</td>
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<tr>
<td>Stroke</td>
<td>Bilateral ipsi- and contralateral MEP recordings, SICI, IHI</td>
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<td>Migraine</td>
<td>Phosphene threshold measurement</td>
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<tr>
<td>Epilepsy</td>
<td>Cortical excitability studies</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>Cortical excitability studies</td>
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</tbody>
</table>
Amyotrophic lateral sclerosis (ALS)

- MEP amplitude expressed at % of CMAP increased in ALS but not in mimic disorders

Vucic et al. JNNP, 2013
Amyotrophic lateral sclerosis (ALS)

- SICI decreased and distinguish from mimic disorders
- Suggestive of cortical hyperexcitability

Other measures to improve sensitivity & specificity: CMCT to orofacial muscles, trapezius (specificity)

Triple Stimulation Technique correlates with corticospinal tract integrity measured by diffusion tensor MRI (Gapperon et al. Muscle & Nerve 2014)
70% of Alzheimer’s Disease patients had abnormal short latency afferent inhibition (SAI)

Abnormal SAI, together with large increase in SAI after single dose of rivastigamine treatment associated with favorable long-term response

May be used to predict long-term response?
Alzheimer’s disease – reduced SAI

Di Lazzaro,
JNNP, 2005
Improvement in SAI after single dose of rivastigamine correlated with no. of neuropsychological tests improved or stable after 1 year

Di Lazzaro, JNNP, 2005
Mild Cognitive Impairment

- Decreased SAI in Parkinson’s disease with mild cognitive impairment
- Possible biomarker for development of dementia

Yarnall et al., 2013, Mov Disord
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- Research Utility: Investigations of normal brain functions, pathophysiology of neurological and psychiatric disorders

Other panelists will discuss
- Cognitive enhancement
- Over the counter or consumer initiated use
- Adult vs. children
Navigated TMS: Presurgical Evaluation of eloquent motor areas

- Location of the motor cortex
- 155 patients – used TMS preoperatively to evaluate the corticospinal tract. Reliably predicted the response to transcranial electrical stimulation performed intraoperatively (Galloway et al. J Clin Nerophysiol 2013)
- May also be used in recurrent glioma (Krieg et al. Clin Neurophysiol 2013)
Navigated TMS: Presurgical Evaluation of speech areas

- Bursts of repetitive TMS to disrupt speech during a naming task
- Correlated well with the results of direct intraoperative electrical cortical stimulation in 20 patients (Pichet et al. Neurosurgery 2013)
Navigated TMS: Presurgical Evaluation of speech areas

- TMS and MEG imaging in 12 subjects with brain tumors in cortical language area
- TMS correlated better with direct cortical stimulation than MEG

Tarapore et al, Neuroimage 2013
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Online TMS to examine (disrupt) functions of cortical areas

- 3 TMS pulses delivered 100 ms apart between target signal and go signal to three different posterior parietal cortex areas

Use of Transcranial Magnetic Stimulation (TMS)

- Clinical Diagnosis
- Presurgical mapping
- Research Utility: Investigations of normal brain functions, *pathophysiology of neurological and psychiatric disorders*

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Motor cortex plasticity in PD

- Levodopa induced dyskinesia occurred in 40% of patients after 4-6 years of levodopa therapy
- Abnormal synaptic plasticity in the cortico-striatal pathway have been found in animal models of dyskinesia
- Aim: test the hypothesis that dyskinesia is associated with aberrant plasticity in the motor cortex
Paired associative stimulation – Long term potentiation (LTP) plasticity

I Session: “Off”
3 days

II Session: “On”

Baseline

21.5 msec
0.01 Hz
180 pairs

RMT MEP

RMT MEP

RMT MEP

RMT MEP

T0

T30

T60

Morgante et al. Brain 2006
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Paired associative stimulation in PD

Controls

Non Dyskinetic PD

Dyskinetic PD

Morgante et al. Brain 2006
PAS – Off medications

Ratio of baseline MEP

- Control
- Dyskinetic PD
- Non Dyskinetic PD

Morgante et al. Brain 2006
PAS – On medications

Morgante et al. Brain 2006
Effects of STN DBS on long term potentiation (LTP) plasticity

Kim et al. submitted
Cortical plasticity in PD

- LTP-like plasticity is deficient in chronically treated PD patients off medications and was restored by levodopa in non-dyskinetic but not in dyskinetic patients.
- Abnormal synaptic plasticity in the motor cortex may play a role in the development of levodopa-induced dyskinesias.
- STN DBS with medications restored LTP-like plasticity in dyskinetic PD patients.
Transcranial direct current stimulation (tDCS)

- Investigation of normal cortical functions
- Pathophysiology of neurological and psychiatric disorders
Summary: Non-therapeutic and investigational uses of NIBS

- Clinical Diagnosis
- Presurgical mapping
- Research Utility: Investigations of normal brain functions, pathophysiology of neurological and psychiatric disorders