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

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U of T NEUROLOGY

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

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

Review on diagnostic utility of TMS

ELSEVIER

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Invited review

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

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Guide on how to perform diagnostic TMS studies (2012)

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A practical guide to diagnostic transcranial magnetic stimulation: Report of an IFCN committee

S. Groppa [a], A. Oliviero [b], A. Eisen [c], A. Quartarone [d], L.G. Cohen [e], V. Mall [f], A. Kaelin-Lang [g], T. Mima [h], S. Rossi [i], G.W. Thickbroom [j], P.M. Rossini [k], U. Ziemann [l], J. Valls-Solé [m], H.R. Siebner [n,*]

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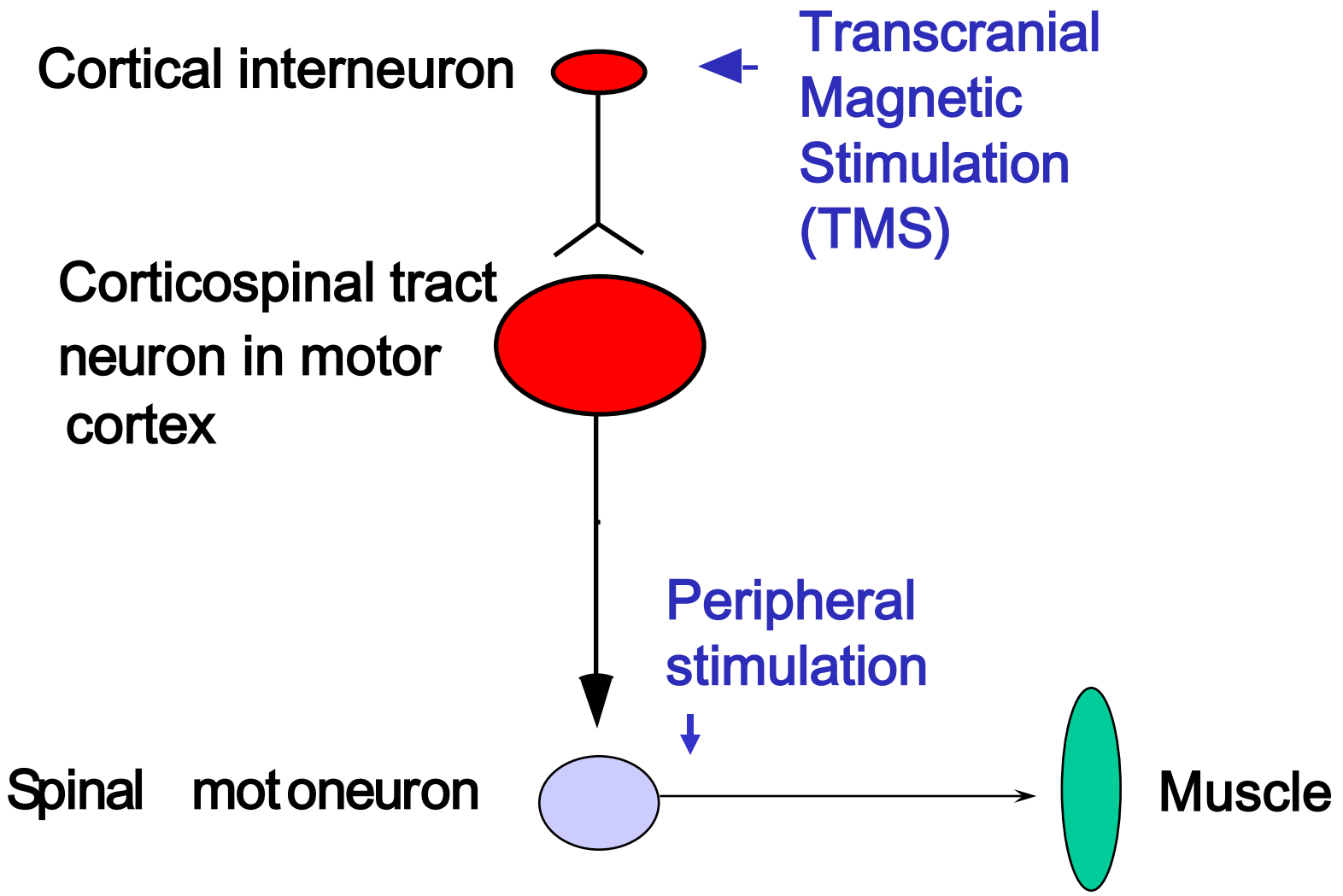
TMS Techniques

- Single and paired TMS
  - **Central conduction time**
  - **Measurement of brain excitability**

Central motor conduction time (CMCT)



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)

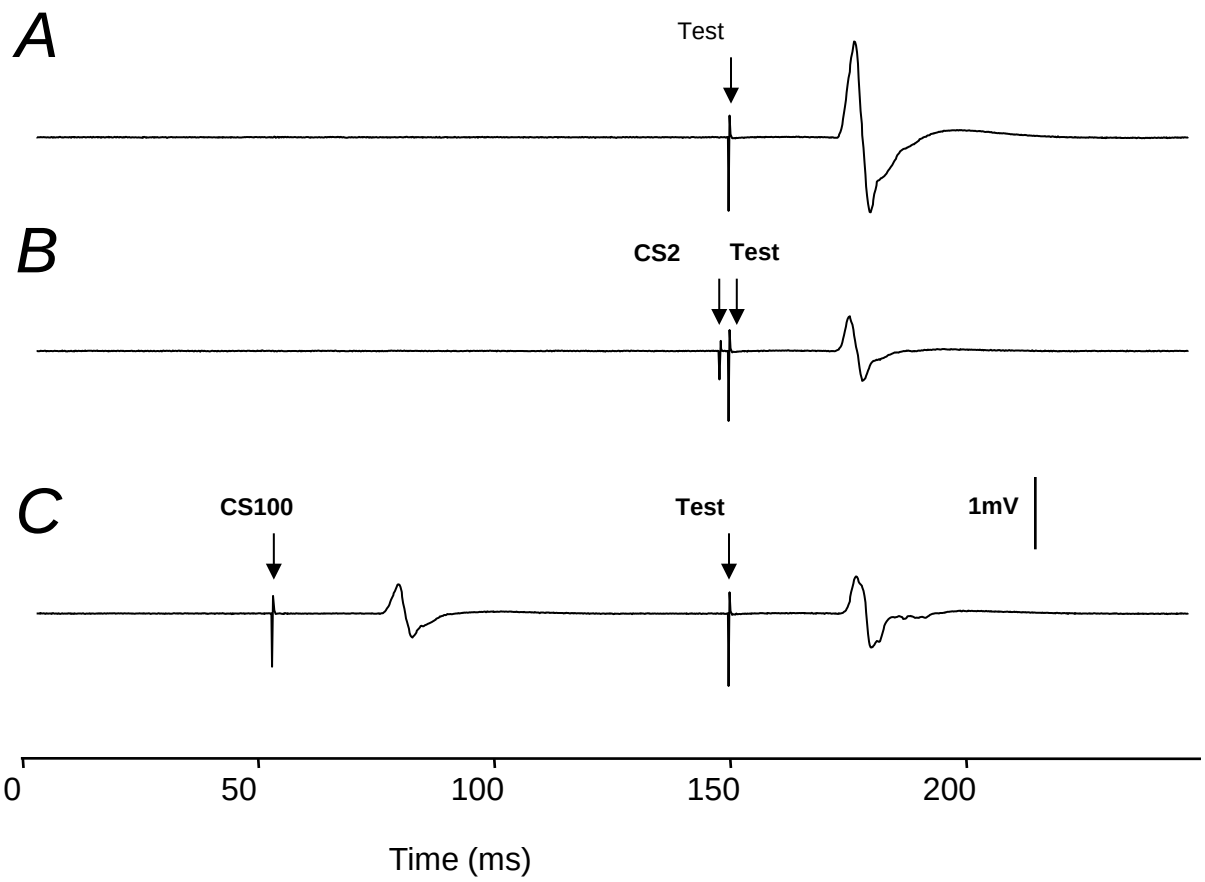
- Prolonged in neonates and children (maturation)
- Correlates with height for CMCT to the lower limbs (Udupa & Chen 2013, Handb Clin Neurol)

Measures of cortical inhibiton/excitation using TMS

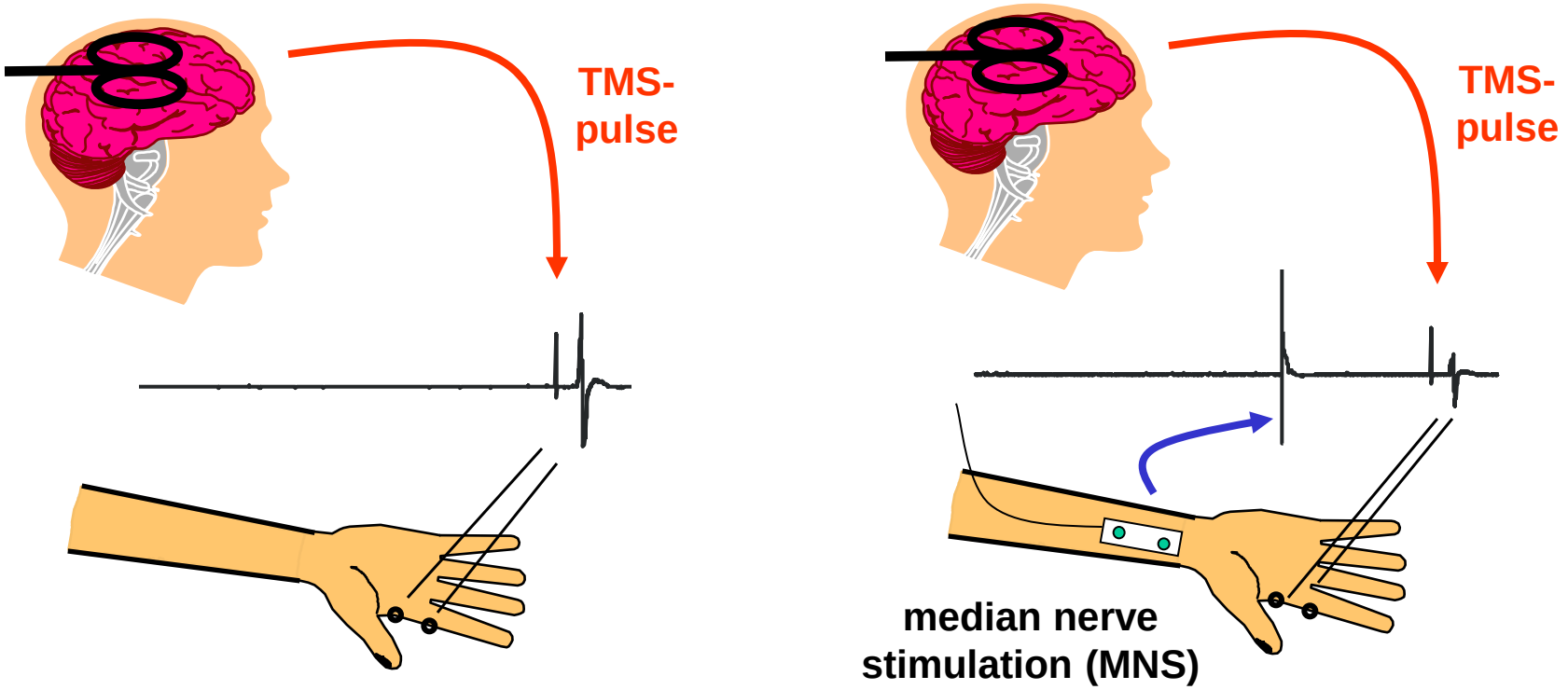
TEST STIMULUS

SHORT-INTERVAL INTRACORTICAL INHIBITION (SICI)

LONG-INTERVAL INTRACORTICAL INHIBITION (LICI)



Short latency afferent inhibition (SAI)



Diagnostic use of TMS

Demonstrated Utility

Condition/disease	Test
Myelopathy	CMCT/TST
Amyotrophic lateral sclerosis	Combination of CMCT/TST, MT, SP, SICI,MEP
Multiple sclerosis	CMCT/TST
Presurgical Mapping	Navigated TMS – motor: single pulse, language: TMS train

Potential Utility

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

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

Vucic et al. Clin Neurophysiol, 2011

Amyotrophic lateral sclerosis (ALS)

- Other measures to improve sensitivity & specificity: CMCT to orofacial muscles, trapezieus (specificity)
- Triple Stimulation Technique correlates with corticospinal tract integrity measured by diffusion tensor MRI (Gapperon et al. Muscle & Nerve 2014)

Dementia

- 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

Alzheimer's disease

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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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 parietial cortex areas

Michael Vesia et al. J. Neurosci. 2010;30:13053-13065

Michael Vesia et al. J. Neurosci. 2010;30:13053-13065

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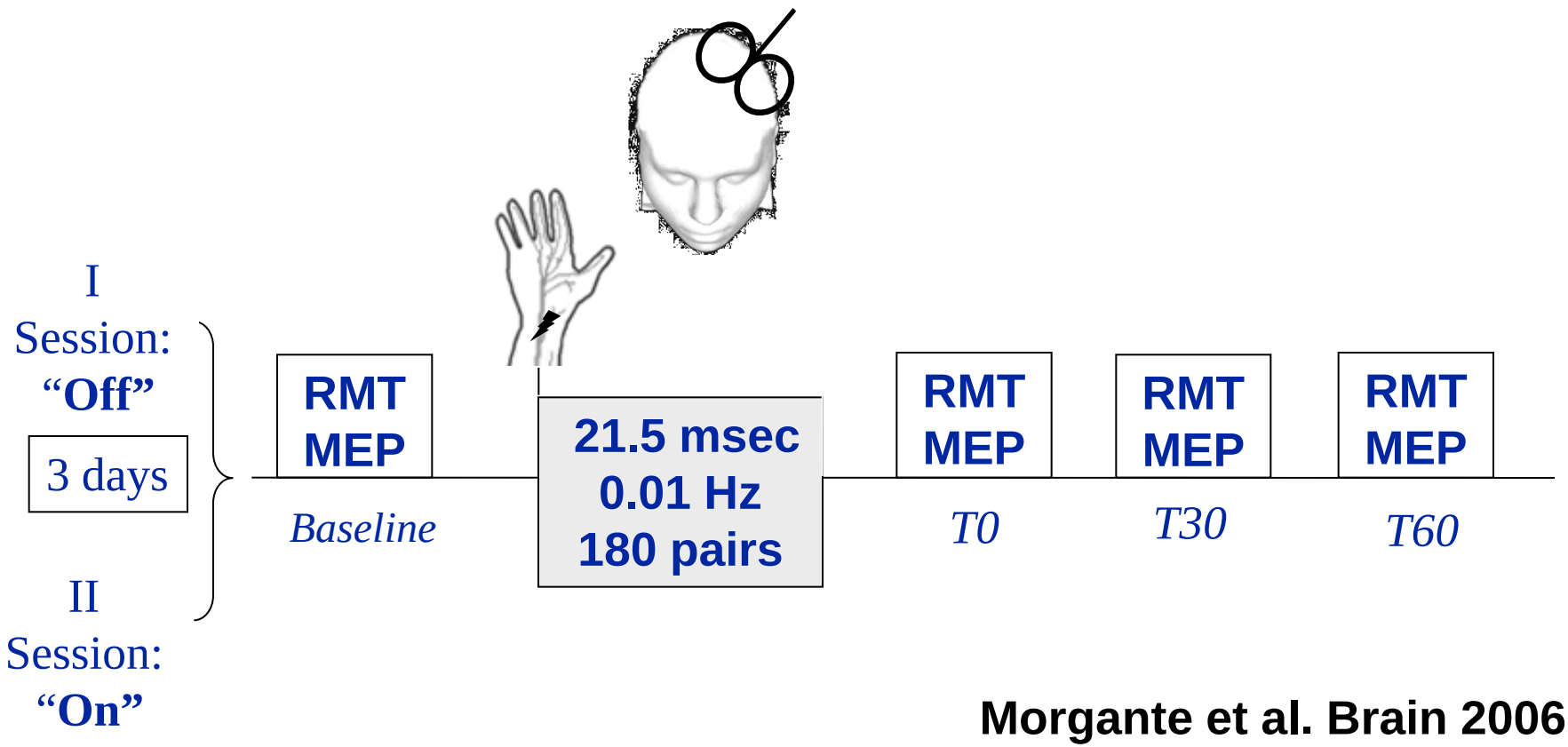
Motor cortex plasticity in PD

- 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



Morgante et al. Brain 2006

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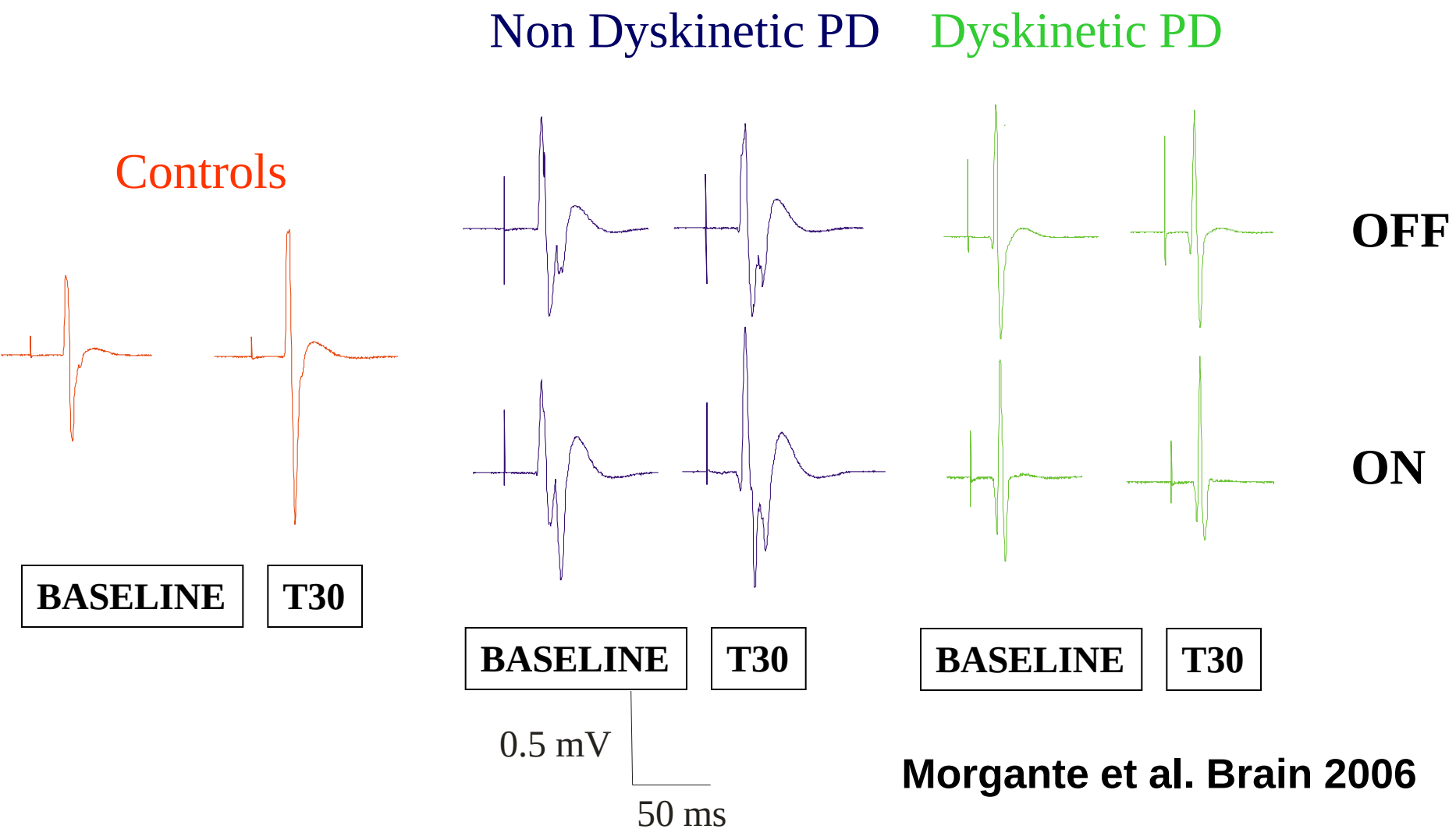
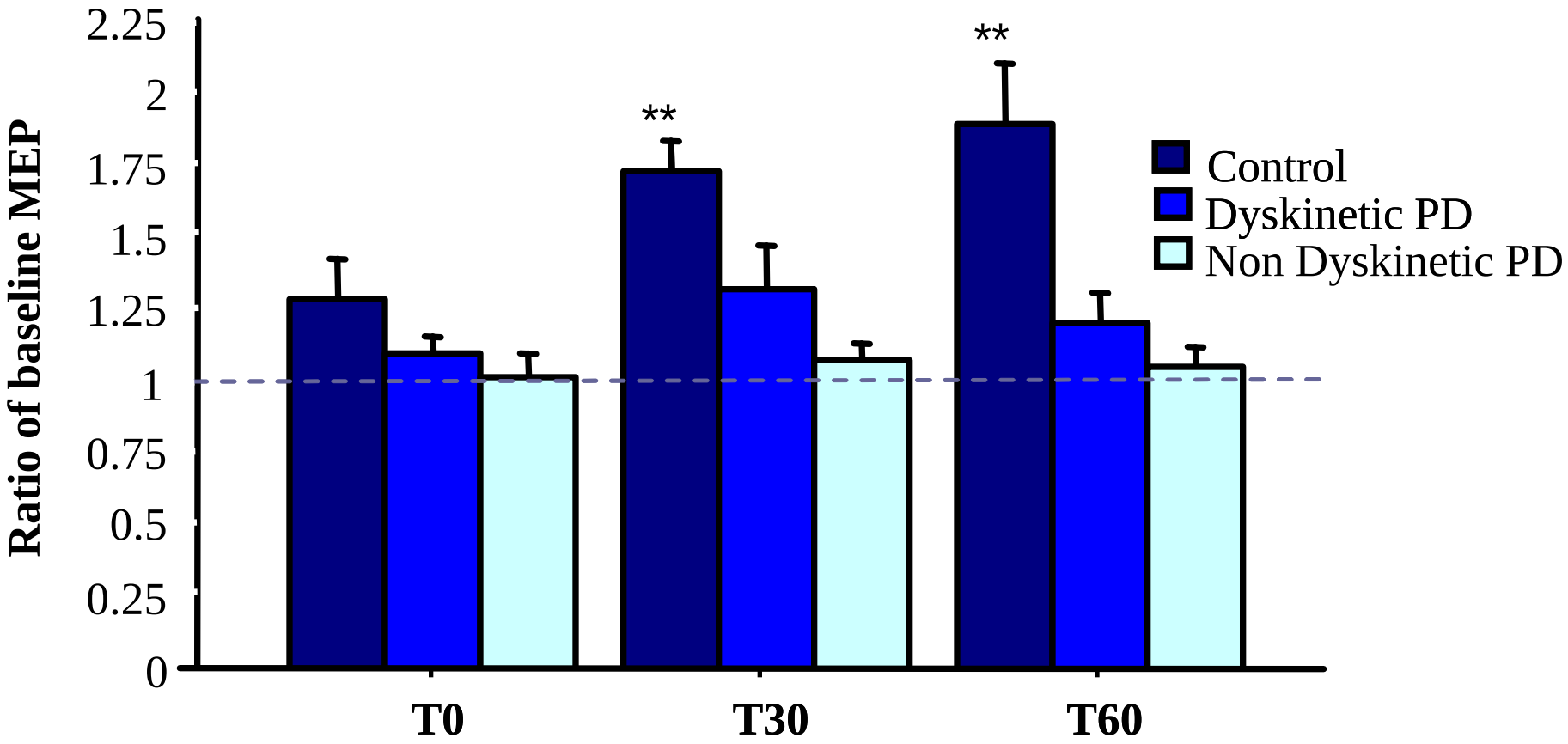
Paired associative stimulation in PD



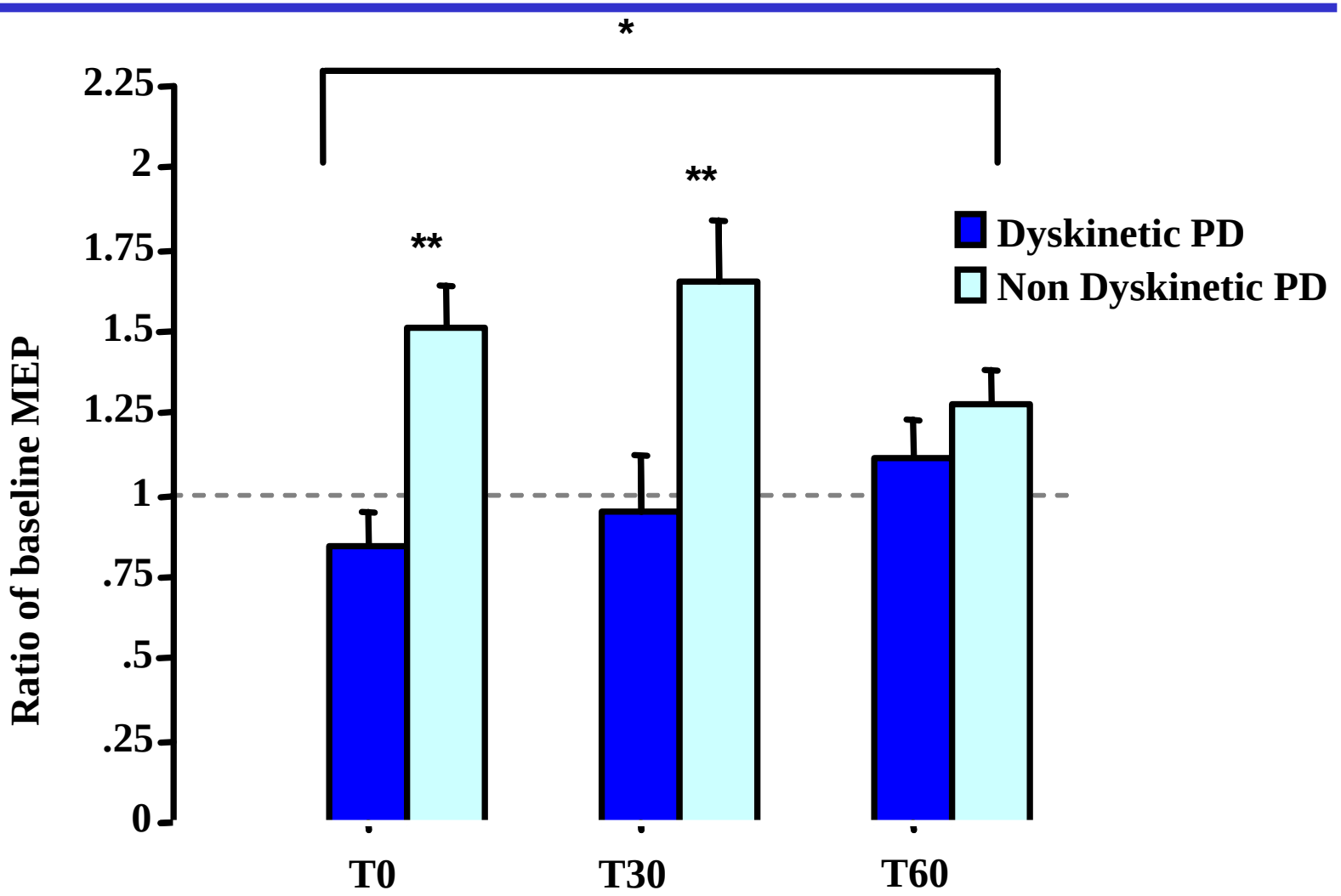
Morgante et al. Brain 2006

PAS – Off medications



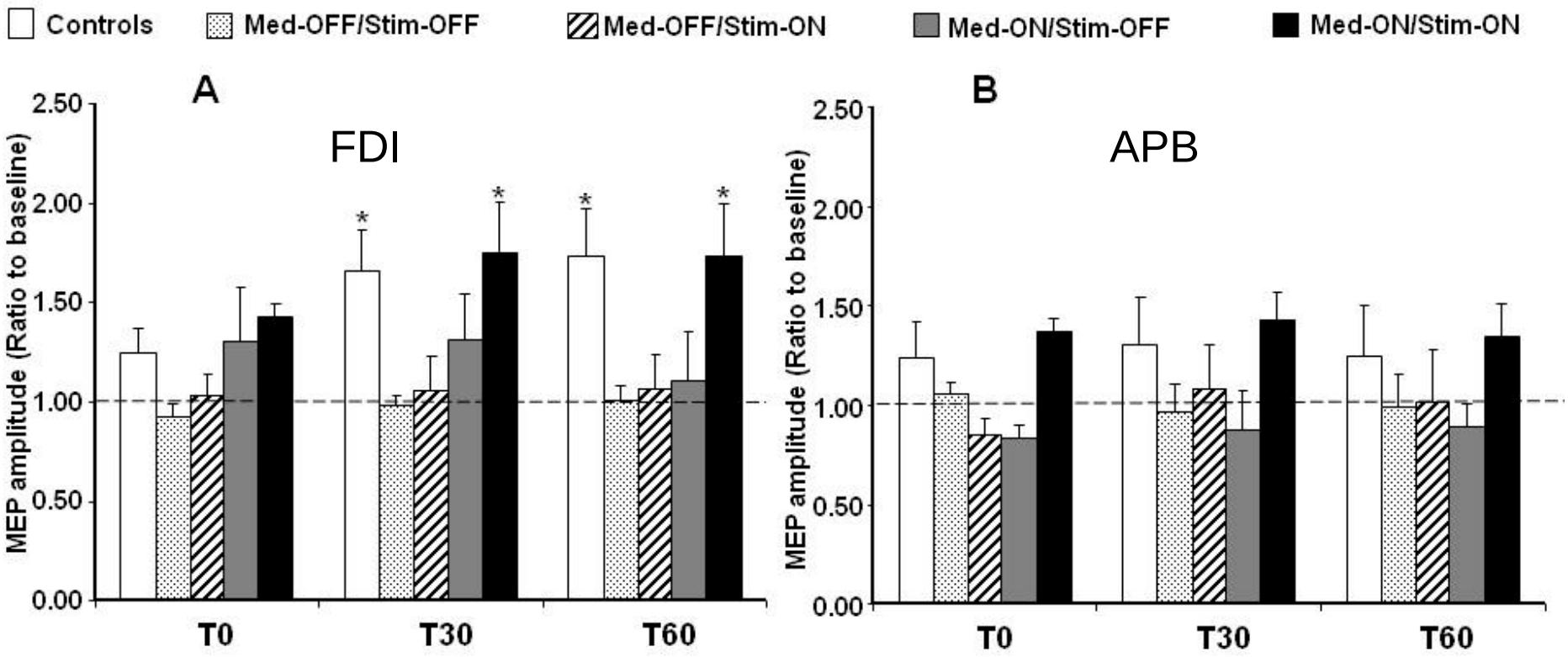
Morgante et al. Brain 2006

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