Navigated Transcranial Magnetic Stimulation in Neurosurgery

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Editor

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Foreword

With the goal to achieve optimal precision and safety in the operating theater, a neurosurgeon must investigate not only the structure and vasculature of the brain but also its neural functions. The human central nervous system (CNS) is the single most complex organ in the known universe, and its functional networks are not yet perfectly understood. In this setting, in order to preserve the quality of life of patients who will undergo brain surgery, it is crucial to study the organization of neural circuits before removal of a part of the CNS affected by a cerebral disease, e.g., epilepsy or tumor. Due to a major interindividual anatomo-functional variability, especially in case of brain lesions, which can induce mechanisms of neuroplasticity, mapping techniques are very helpful to understand the distribution of cortical and subcortical pathways underlying motor, language, cognitive, and emotional functions at the individual level. To this end, intraoperative direct electrical stimulation (DES) in awake patients remains the gold standard to optimize the extent of resection (EOR) while minimizing neurological morbidity. However, even though this method allows real-time anatomo-functional correlations throughout the surgical procedure, in order to detect and to preserve the structures crucial for brain functions, it is also important to benefit from complementary techniques that permit a noninvasive preoperative mapping. Functional neuroimaging has been extensively used in the past decade, but its main limitation is the impossibility to differentiate critical areas which should not be removed during surgery, to avoid permanent deficit, versus regions involved in a neural network but which can be compensated—and thus surgically resected.

In this state of mind, navigated transcranial magnetic stimulation (nTMS) represents an original tool opening new avenues in the exploration of the CNS, especially in brain-damaged patients. Indeed, as intraoperative DES, nTMS offers the unique opportunity to create a transient virtual disruption of neural networks, with the aim to identify the cortical areas crucial for brain functions. However, contrary to DES, nTMS is a noninvasive technique that can be used before surgery to map the eloquent cortex and to plan the resection accordingly. This is the reason why a textbook on nTMS in neurosurgery was desperately needed. Led by the editor, Sandro M. Krieg, this collective body of work will serve as a comprehensive textbook for all physicians with an individualized personal approach of brain surgery. What makes this book so unusual is that it contains all required information to use nTMS in a department of neurosurgery and outlines pros and cons to other techniques. The approach the authors have taken in defining this new technology and its implication for neurosurgical management are quite unique and innovative, to say the least.

The book is organized in a very logical and informative fashion, starting off with critically important chapters covering the basic principles of nTMS. The clinical aspects are further evoked in chapters on preoperative motor and language mapping. To this end, Dr. Krieg is a master at explaining and detailing how to use nTMS for surgical planning and how to combine this method with other techniques, as fiber tracking. I particularly like the way in which further brain functions can be mapped by nTMS and in which this methodology may be used in children—knowing that it is very difficult to achieve awake surgery in pediatric population, especially under 10 years. Interestingly, the fact that nTMS is also able to modulate neural networks for neurosurgical applications, as previously done in neuropsychiatry for depression, is depicted in a series of detailed chapters on these subjects. For example, nTMS can be helpful to treat chronic pain. In the future, this technique could also be considered to induce and canalize neuroplasticity, allowing an increase of the EOR or even an improvement of the neurological status—for example, by combining it with specific programs of rehabilitation in patients with neurological deficits. Finally, in the field of cognitive neurosciences, nTMS may represent a unique tool to investigate CNS processing in humans. Indeed, thanks to recent advances in the new science of connectomics, which aims to comprehensively map neural connections at both structural and functional levels, coordination of cognitive and behavioral domains is now attributed to parallel and intersecting large-scale neural circuits that contain interconnected cortical and subcortical components. In this context, a technique based on the concept of transitory disruption of neural circuits will undoubtedly provide new insights into the organization of such a networking brain. Yet, it is worth noting that nTMS can achieve only a mapping of the cortex, but it is not able to map the white matter tracts that nonetheless constitute a crucial part of the connectome. From a clinical point of view, preservation of subcortical pathways is essential during brain surgery, because the white matter connectivity is a well-known limitation of neuroplasticity. In other words, currently, nTMS should still be combined with other mapping techniques, especially intraoperative DES, in order to be more extensively validated and to compensate its inability to investigate directly the function of the fibers.

It is crucial for modern clinical neuroscience, and especially for neurosurgery, to incorporate advances in this complex field of brain mapping in as timely a fashion as possible, so that patient care becomes guided by the latest increments of relevant technology and knowledge with regard to CNS processing. I have no doubt that this comprehensive volume edited by Dr. Krieg and his colleagues will serve this purpose with considerable distinction. All in all, this text is a major contribution that will be significant in the history of neurosurgery and cerebral mapping. If you only have one reference source on nTMS in brain surgery, this must be it!

Montpellier, France Hugues Duffau, M.D., Ph.D.

A Word from the Editor

Seven years ago, our neurosurgical department started implementing nTMS. First, we performed preoperative motor mappings, and then we tried to establish language mapping protocols (using ourselves as volunteers). Finally, we used language mapping to analyze our brain tumor patients. Recently, we began applying nTMS to map other brain functions and using it for therapeutic applications.

At the same time, we have optimized the way that we actually integrate the functional nTMS data into our neurosurgical routine. We started with surgeons, as they had to get used to these data, and then integrated nTMS data in our interdisciplinary tumor board discussions.

By making the data easily available to every physician via integration into our hospital's electronic infrastructure, everyone in the department quickly became used to dealing with nTMS data.

Along with these developments, we engaged in seminal international collaborations that led to highly valuable clinical data and—more importantly—many new friends.

This book is thus the result of our interaction with the international neurosurgical nTMS community. In this way, it serves as a signal to all of us that, in neurosurgery, nTMS research means cooperation with an international community.

In this spirit, each year, our group at TUM has served as a host for numerous guests from all over the world, providing them with training and insights into nTMS research and its clinical uses. In doing so, we have gained many collaborators and friends, as well as unlimited options for scientific exchange.

In the future, we want to welcome even more visitors and to continue establishing a researcher exchange program, which we have already started with some of our closest collaborators.

This book was created through the efforts of a team that is composed of experienced, well-known international experts, making this book an exclusive composition of information about the use of nTMS in neurosurgery, which has not previously been available in any other form. By containing different approaches of various international experts, I did not try to create a consensus for the described stimulation protocols, analysis software, or used nTMS devices. Contrariwise, I welcomed the description of differing approaches by the individual authors in order to make this book a collection of feasible approaches rather than a document of my personal opinion.

Therefore, I want to encourage every reader to provide the team, and me in particular, with criticisms, suggestions, and personal wishes regarding how to further improve this unique collection of information for all those who work in this evolving field.

Sandro M. Krieg, M.D., M.B.A.

Contents

Introduction

Mapping and monitoring of brain function is far from being new. It has always been in the focus of neurosurgeons, i.e., already in the days of Wilder Penfield using awake surgery to map motor and sensory function (Penfield and Boldrey 1937). The reason for this being quite obvious is to completely remove tumors or epileptogenic tissue without hurting the patient. To achieve this ideal goal has stimulated many neurosurgeons ever since, among them myself. In the early stages of my career in the late 1980s, I developed an interest in clinical neurophysiology, focusing on the rather new technique of motor evoked potentials (MEP) (Meyer and Zentner 1992; Barker et al. 1985). This technique triggered a development of monitoring and mapping of motor function in the asleep (anesthetized) patient. Several innovative groups paved the road for the integration of this technique into clinical routine, while simultaneously, awake craniotomy for language mapping and monitoring saw a renaissance (Penfield and Boldrey 1937; Taniguchi et al. 1993; Cedzich et al. 1996; Deletis 1993). Thus, it became part of the neurosurgeons' armamentarium even before studies showed that intraoperative MEP mapping and intraoperative monitoring (IOM) can actually prevent neurological damage (Sanai and Berger 2010; Duffau et al. 2005; De Witt Hamer et al. 2012). Today, IOM and intraoperative MEP mapping via DES are well-established techniques, which according to me are mandatory for the resection of highly eloquent tumors.

More than ever, it has become clear that the aim of surgery of low- as well as of high-grade gliomas and metastases has to be gross total resection (GTR) to achieve the most favorable oncological and functional outcome (Laws et al. 1984; Polin et al. 2005; Stummer et al. 2006). Thus, neurosurgeons were seeking for a proper method, which would preoperatively allow outlining functionally relevant areas for estimating surgical risk and planning appropriate and safe approaches, in short, for being prepared before going to the operating room with our patients.

Preoperative mapping in a noninvasive fashion was for a long time reduced to functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) (Sobottka et al. 2002; Tarapore et al. 2013; Leclercq et al. 2010). While MEG requires substantial infrastructure and thus never reached broad acceptance, fMRI was considered the standard for noninvasive mapping of neurosurgical patients for about two decades (FitzGerald et al. 1997). Yet, blood-oxygen-level-dependent (BOLD) contrast as measured by fMRI does not have the required spatial resolution and accuracy especially close to intracerebral tumors because these tumors severely impair oxygenation and therefore BOLD contrast. As a result, fMRI mapping and intraoperative DES mapping do not correlate sufficiently in the vicinity of brain tumors (Lehericy et al. 2000; Bizzi et al. 2008; Roessler et al. 2005; Giussani et al. 2010). Consequently, there was still no proper methodology available, which reliably provided accurate preoperative noninvasive functional mapping in patients harboring brain gliomas or metastases. The gold standard being invasive mapping was also only available in dedicated centers (i.e., with an epilepsy program) and required substantial logistics (Kral et al. 2006).

Only recently, nTMS was introduced as a new modality for preoperative mapping in neurosurgery. The combination of the “old” accurate method to map motor function via transcranial magnetic stimulation (TMS) (Barker et al. 1985) and neuronavigation has been advanced over the years, resulting in real-time localization of the intracranially induced electric field and its field strength allowing for highly precise noninvasive mapping today (Ruohonen and Ilmoniemi 1999; Ilmoniemi et al. 1999; Picht et al. 2009; Krieg et al. 2012). For the first time, we neurosurgeons now have a tool, which allows us to outline eloquent and noneloquent cortex before surgery with a comparable accuracy to intraoperative DES. By providing such exact data, it changes our clinical practice by allowing functional data to influence patient consultations, surgical approaches, and oncological considerations. While preoperative mapping of motor and language function has already been established, the possibilities of neuropsychological or cognitive mapping are currently further investigated. Their potential, e.g., by guiding intraoperative awake mapping, is rather high.

Additionally to pure functional mapping, navigated repetitive TMS (nrTMS) is also able to modulate function. Besides other therapeutic applications for depression or chronic pain, nrTMS also showed a positive effect on the improvement of aphasia as well as motor recovery in chronic stroke patients in randomized multicenter studies by inducing functional reorganization (Huang et al. 2004; Kim et al. 2006; Takeuchi et al. 2009; Takeuchi and Izumi 2012; Abo et al. 2014; Naeser et al. 2011; Du et al. 2016). Thus, rather than waiting for tumor-induced functional reorganization, the potential of nrTMS-induced spatial functional reorganization in order to move eloquent brain functions away from the planned resection cavity requires further investigation. Its impact, though, would be enormous. However, usually progress in clinical science comes in small steps. It is clear now already that nTMS is one of those small but distinct steps to enhance our performance and bring us somewhat closer to the ideal goal.

The following book therefore represents the first comprehensive guide, which aims to introduce this new modality to neurosurgeons, describing the currently available data, its clinical application, and future potential of this new technique.

Munich, Germany Bernhard Meyer, M.D.

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Abbreviations

2D	Two-dimensional
3D	Three-dimensional
ADC	Apparent diffusion coefficient
ADM	Abductor digiti minimi
AH	Abductor hallucis muscle
aMT	Active motor threshold
APB	Abductor pollicis brevis muscle
ARAT	Action Research Arm Test
aSTG	Anterior superior temporal gyrus
AVM	Arteriovenous malformations
BA	Brodmann area
BEM	Boundary element method
BIC	Biceps muscle
BMRC	British Medical Research Council
BOLD	Blood-oxygen-level-dependent
CCD	Coil-to-cortex distance
CI	Confidence interval
CNS	Central nervous system
COG	Center of gravity
CPS	Cortical parcellation system
CRS-R	Coma Recovery Scale-Revised
CSE	Corticospinal excitability
CSP	Cortical silent period
CST	Corticospinal tract
CT	Computerized tomography
cTBS	Contralesional theta-burst stimulation
DBS	Deep brain stimulation
DEC	Directionally encoded colors
DES	Direct electrical stimulation
dHb	Deoxyhemoglobin
DICOM	Digital imaging and communications in medicine
DLPFC	Dorsolateral prefrontal cortex
DOC	Disorder of consciousness
DT	Display time

DTI	Diffusion tensor imaging
DTI FT	Diffusion tensor imaging fiber tracking
DWI	Diffusion-weighted imaging
ECD	Equivalent current dipole
ECMS	Previous MCS
ECoG	Electrocorticography
ECR	Extensor carpi radialis muscle
EEG	Electroencephalography
e-field	Electric field
EMG	Electromyography
En-TMS	Electric field-navigated TMS
EOR	Extent of resection
EPSP	Excitatory postsynaptic potential
ER	Error rates
ERP	Event-related potentials
F1	Superior frontal gyrus (=SFG)
F2	Middle frontal gyrus (=MFG)
F3	Inferior frontal gyrus (=IFG)
FA	Fractional anisotropy
FACT	Fiber assignment by continuous tracking
FAT	Fractional anisotropy threshold
FCD	Focal cortical dysplasia
FCR	Flexor carpi radialis muscle
FDA	US Food and Drug Administration
FDI	First dorsal interosseus muscle
FEM	Finite element method
fMRI	Functional magnetic resonance imaging
FT	Fiber tracking
fT	Femtotesla
GC	Gastrocnemius muscle
GCP	Good clinical practice
GTR	Gross total resection
HDR	Hemispheric dominance ratio
HF	High frequency
HGG	High-grade glioma
HIS	Hospital information system
IAP	Intracarotid amobarbital procedure (=Wada test)
IC	Internal capsule
ICMS	Intracortical microstimulation
IEEE	Institute of Electrical and Electronics Engineers
IFC	Inferior frontal cortex
IFCN	International Federation of Clinical Neurophysiology
IFG	Inferior frontal gyrus
iFS	Inferior frontal sulcus
IOM	Intraoperative monitoring

IPI	Interpicture interval
IPSP	Inhibitory postsynaptic potential
ISI	Interstimulus interval
iTBS	Ipsilesional theta-burst stimulation
LF	Low frequency
LGG	Low-grade glioma
LIS	Locked-in syndrome
Ln-TMS	Line-navigated TMS
LTD	Long-term depression
LTP	Long-term potentiation
M1	Primary motor cortex
M2	Secondary motor cortex
MCS	Minimally conscious state
MEG	Magnetoencephalography
MEN	Mentalis muscle
MEP	Motor evoked potential
MFG	Middle frontal gyrus
MFL	Minimum fiber length
MPR	Multiplanar reconstruction
MRI	Magnetic resonance imaging
NBS	Navigated brain stimulation
NIBS	Noninvasive brain stimulation
NPV	Negative predictive value
NREM	Non-rapid eye movement
nrTMS	Navigated repetitive transcranial magnetic stimulation
nTMS	Navigated transcranial magnetic stimulation
OrO	Orbicularis oris muscle
OT	Occupational therapy
PACS	Picture archiving and communication system
PAS	Paired associative stimulation
PCI	Perturbational complexity index
PD	Parkinson’s disease
PET	Positron-emission tomography
PMC	Premotor cortex
PMd	Dorsal premotor cortex
PNS	Peripheral nerve stimulation
PPC	Posterior parietal cortex
PPFM	*Pli de passage fronto-pariétal moyen*
PPV	Positive predictive value
PT	Phosphene threshold
PTI	Picture-to-trigger interval
RC	Recruitment curve
REM	Rapid eye movement
RMS	Root-mean-square
rMT	Resting motor threshold

ROI	Region of interest
rTMS	Repetitive transcranial magnetic stimulation (non-navigated)
S1	Primary somatosensory cortex
SAM	Synthetic aperture magnetometry
SD	Standard deviation
SEM	Standard error of mean
SFG	Superior frontal gyrus
sFS	Superior frontal sulcus
SMA	Supplementary motor areas
SMG	Supramarginal gyrus
SPECT	Single photon emission computed tomography
SQUID	Superconducting quantum interference device
STDP	Spike-timing-dependent plasticity
STG	Superior temporal gyrus
STR	Subtotal resection
TA	Tibialis anterior muscle
tACS	Transcranial alternating current stimulation
TBS	Theta-burst stimulation
TCI	Transcallosal inhibition
tDCS	Transcranial direct cortical stimulation
TES	Transcranial electrical stimulation
TMS	Transcranial magnetic stimulation (non-navigated)
TPJ	Temporoparietal junction
VAS	Visual analog scale
VNS	Vagus nerve stimulator
vPrG	Ventral precentral gyrus
VS	Vegetative state