UMF IULIU HAȚIEGANU UNIVERSITY OF MEDICINE AND PHARMACY CLUJ-NAPOCA

MAX PLANCK INSTITUTE FOR NEUROLOGICAL RESEARCH COLOGNE

FOUNDATION OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

FACULTY of MEDICINE DEPARTMENT of NEUROSCIENCES

Facultatea de Medicină Cluj

International School of Neurology

RoNEURO RoNeuro Institute for Neurological Research and Diagnostic

Seminar

Non-Invasive Brain Stimulation in Rehabilitation

Department of Neurosciences
University of Medicine and Pharmacy "Iuliu Hatieganu"
Cluj-Napoca | Romania
in cooperation with
Max Planck Institute for Neurological Research
Cologne | Germany

DECEMBER 12TH-14TH, 2014

Imogen Reasearch Institute
43 Victor Babes Street, Cluj-Napoca, Romania

UMF "Iuliu Hatieganu"
Multimedia Room, 8 Victor Babes Street, Cluj-Napoca, Romania

"RoNeuro" Institute for Neurological Research and Diagnostic
37 Mircea Eliade Street, Cluj-Napoca, Romania

Welcome Address

It is a pleasure to welcome you to the 21th edition Seminars of the Neurosciences Department, "Non-Invasive Brain Stimulation in Rehabilitation", December 12th-14th, 2014. The seminars are hosted by the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania and RoNeuro Institute for Neurological Research and Diagnostic.

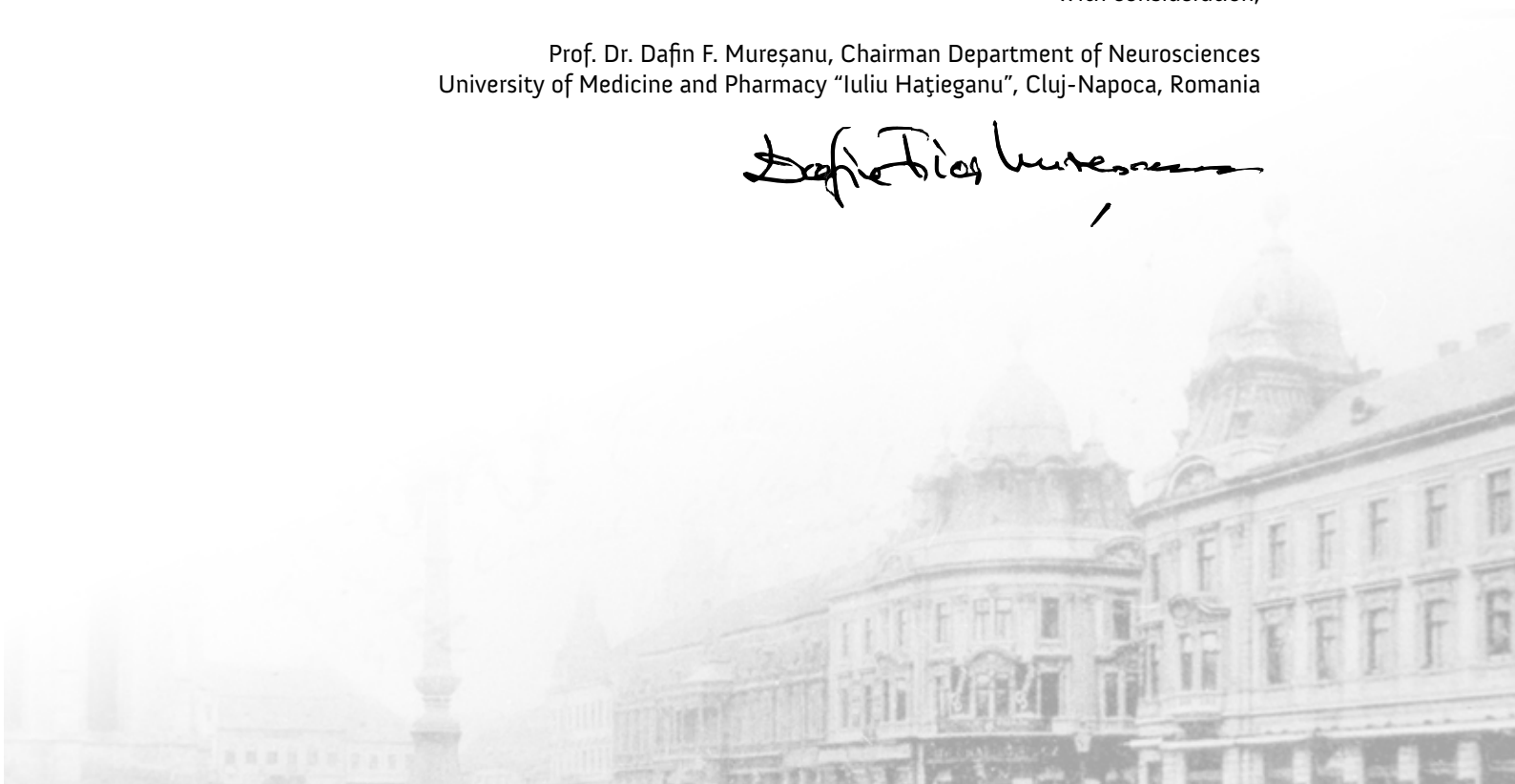
These seminars aim to establish a highly useful framework enabling local specialists to benefit from the expertise of our invited speakers who are part of associated international faculty of our Department of Neurosciences. Our goal is to flourish over years and set up an educational network tool meeting our junior and senior specialists' needs.

In contrast to large international conferences, the intention behind these seminars is to create an informal and intimate setting, which hopefully will stimulate open discussions. As organizers, we would therefore be deeply grateful if you participate and share your time with us.

We are looking forward to your active participation in this educational event!

With consideration,

Prof. Dr. Dafin F. Mureșanu, Chairman Department of Neurosciences
University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania



Organizers

UMF
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University of Medicine and Pharmacy
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NEUROPLASTICITY

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RoNEURO

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Institute for Neurological
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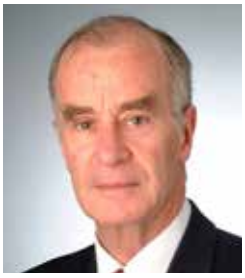
Speakers

Speakers



WOLF-DIETER HEISS /GERMANY

Wolf-Dieter Heiss, born 31.12.1939 in Zell am See, Austria, graduated in medicine from the University of Vienna, Austria, in 1965. He achieved his training in neurology, neurophysiology, psychiatry and nuclear medicine at the University hospital in Vienna and spent research fellowships at the MIT, Cambridge, USA, the Physiological Institute in Stockholm, Sweden, the Department of Physiology of SUNY, Buffalo, NY and the Department of Neurology of the University of Minnesota, Minneapolis, USA. 1976 he was appointed associate professor at the Department of Neurology of the University of Vienna. In 1978 he became director of the Center for Cerebrovascular Research of the Max Planck Institute for Brain Research and of the Department of Neurology of the City Hospital Cologne-Merheim, Germany. 1981 he was appointed as director at the Max Planck Institute for Neurological Research. 1985 – 2005 he was professor of neurology and chairman of the Department of Neurology of the University of Cologne and director of the Department of General Neurology at the MPI in Cologne. He was president of the International Stroke Society 1992-96, was on the board of directors of the Society for Cerebral Blood Flow and Metabolism, deputy editor of the Journal of Cerebral Blood Flow and Metabolism and at present is associate editor of the Journal of Nuclear Medicine and section editor of Stroke. He was chairman of the program committee of the European Federation of Neurological Societies (EFNS) 1998 - 2001 and was president of the EFNS 2001 – 2005. Since 2005 he is Visiting Professor at the Danube University in Krems, Austria, and since 2009 Adjunct Professor at the McGill University in Montreal, Canada. His significant portfolio of scientific articles includes 617 papers indexed on Web of Knowledge-ISI, rating a Hirsch index of 63. In 2013 he became Associated Professor of the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Romania.

Speakers

MATTHIAS
KIENLE
/GERMANY

- January 2011- present
  - MagVenture A/S Farum Denmark, International Application Specialist
  - My duties include user training on device handling and clinical application in Neurology, Psychiatry, Brain Research, Neurorehabilitation
  - Furthermore, I'm responsible in establishing reference sites for Magnetic Stimulation in Diagnostic, Research and Treatment

- August 2007 – December 2010
  - Alpine Biomed GmbH Langenfeld Germany, Product Manager/ Specialist for NeuroDiagnostic
  - I was responsible for user training on device handling and clinical application in Neurology, NeuroSurgery and Neurorehabilitation (EMG, NCV, EP, ERP, IOM, EEG, Sleep)

- September 1998 – August 2007
  - Medtronic GmbH Dusseldorf Germany, Product Manager/ Specialist for NeuroDiagnostic
  - I was responsible for user training on device handling and clinical application in Neurology, NeuroSurgery and Neurorehabilitation (EMG, NCV, EP, ERP, IOM, EEG, Sleep)

- September 1996 – August 1998
  - Schwamedico GmbH Giessen Germany, Product Specialist for Acupuncture, TENS

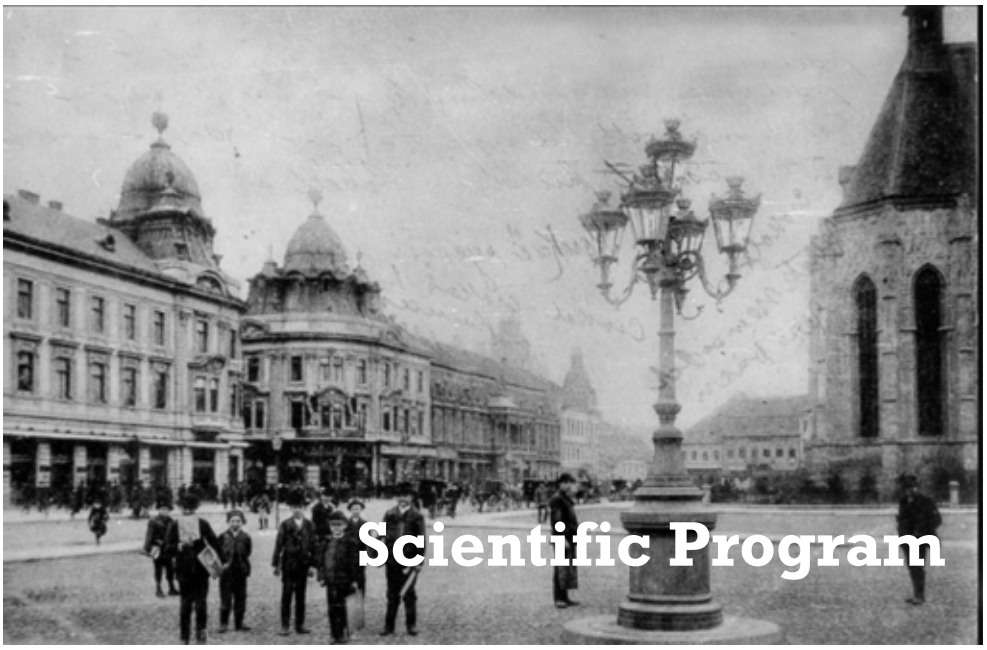
- January 1993 – August 1996
  - ProScience Research Center Linden Germany, Assistant for Neuropharmacological Research

- March 1987 – December 1992
  - University Hospital Giesen, Nurse Neurosurgery Intensive Care Unit Education/ Qualification
  - 2002 - Physiotherapy: Basic Education Munich School of Physioterapy
  - 1993 – Graduation: Diplom – Ingenieur FH Biomedizinische Technik, Fachochschule Giesen-Friedberg

Speakers

TUDOR
LUPESCU
/ROMANIA

Dr. Tudor Lupescu obtained his medical degree from "Carol Davila" University of Medicine in Bucharest, in 1989. After 3 years of training at Colentina Clinical Hospital he became Specialist in Neurology in 1994. Since 2006 he is running the Neurology Department al Agrippa Ionescu Hospital in Bucharest. In 1998, he qualified as Consultant Neurologist. Since his early years of training in Neurology, Tudor Lupescu has shown a special interest in Clinical Neurophysiology. In 2000 he earned a Competence in Clinical Neurophysiology (EEG, EMG, and Evoked Potentials). 1997 he was the first to use Transcranial Magnetic Stimulation in Romania. This was also the subject of his PhD thesis presented in 2005. Since 2008, Tudor Lupescu is President of ASNER – Romanian Society of Electrodiagnostic Neurophysiology. He is also founding member and vice-president of the Romanian Society of Diabetic Neuropathy. Dr. Tudor Lupescu is associate member of the American Academy of Neurology, and associate member of the American Association of Neuromuscular and Electrodiagnostic Medicine. Between 2008 and 2013 he was also member of the Neurophysiology Subcommittee of ENS.



Scientific Program

Scientific Program

Friday, DECEMBER 12th, 2014

Imogen Reasearch Institute
43 Victor Babes Street, Cluj-Napoca, Romania

09.50 - 10.00	Opening Remarks - Dafin Muresanu
10.00 - 11.30	Non-Invasive Brain Stimulation in Rehabilitation after Stroke /Wolf Dieter Heiss
11.30 - 12.15	PET Studies for the Evaluation of Dynamics in Stroke Pathophysiology /Wolf Dieter Heiss
12.15 – 13.00	Break/ Transfer to W.D. Heiss Doctor Honoris Causa Ceremony

UMF "Iuliu Hatieganu", Multimedia Room
8 Victor Babes Street, Cluj-Napoca, Romania

13:00 – 14:30	Doctor Honoris Causa Ceremony - Wolf Dieter Heiss
14.30 - 15.00	Break/ Transfer to RoNeuro Institute

RoNeuro Institute for Neurological Research and Diagnostic
37 Mircea Eliade Street, Cluj-Napoca, Romania

15.00 - 15.20	Course timeline/RoNeuro Institute
15.20 - 16.00	Introductory data (principles, technical data, device, coils) /Matthias Kienle
16.00 - 17.00	Single pulse TMS - technique, parameters, clinical applications /Tudor Lupescu
17.00 - 17.30	Coffee Break
17.30 - 18.30	rTMS - principles, technical data, stimulation parameters, including TBS /Matthias Kienle
18.30 - 19.00	Safety issues /Tudor Lupescu
19.00 - 20.00	Practical demonstration + Day 1 Conclusions

Scientific Program

Saturday, DECEMBER 13th, 2014

RoNeuro Institute for Neurological Research and Diagnostic
37 Mircea Eliade Street, Cluj-Napoca, Romania

9.00- 11.00	rTMS - Diseases, Protocols Stroke, Psychiatry, Pain /Matthias Kienle
11.00-11.30	Coffee break
11.30-12.30	Practical demonstration
12.30 - 13.00	PAS /Matthias Kienle
13.00-14.30	Lunch
14.30 - 15.30	Neurorehabilitation /Matthias Kienle
15.30-16.00	Other Indications for rTMS /Tudor Lupescu
16.00- 17.00	A summary of recent data on rTMS /Tudor Lupescu
17.00-17.30	Coffee break
17.30- 18.30	Practical demonstration
18.30-19.00	Day 2 Conclusions

Scientific Program

Sunday, DECEMBER 14th, 2014

RoNeuro Institute for Neurological Research and Diagnostic
37 Mircea Eliade Street, Cluj-Napoca, Romania

9.00 - 10.00	Current and future clinical studies discussions/ideas
10.00 - 11.00	Perspectives, Q&A, conclusions

Abstracts

W. D. HEISS/ GERMANY

NON-INVASIVE BRAIN STIMULATION IN REHABILITATION AFTER STROKE

The functional deficit after a focal brain lesion is determined by the localization and the extent of the tissue damage. Since destroyed tissue usually cannot be replaced in the adult human brain, improvement or recovery of neurological deficits can be achieved only by reactivation of functionally disturbed but morphologically preserved areas or by recruitment of alternative pathways within the functional network. The visualization of disturbed interaction in functional networks and of their reorganization in the recovery after focal brain damage is the domain of functional imaging modalities such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Longitudinal assessments at rest and during activation tasks during the early and later periods following a stroke can demonstrate recruitment and compensatory mechanisms in the functional network responsible for complete or partial recovery of disturbed functions. Imaging studies have shown that improvements after focal cortical injury are represented over larger cortical territories, an effect which appears to be dependent on the intensity of rehabilitative training. It has also been shown that the unaffected hemisphere in some instances actually inhibits the recovery of ipsilateral functional networks and this effect of transcallosal inhibition can be reduced by non-invasive brain stimulation.

Non-invasive brain stimulation (NIBS) can modulate the excitability and activity of targeted cortical regions and thereby alter the interaction within pathologically affected functional networks; this kind of intervention might promote the adaptive cortical reorganization of functional networks after stroke. Non-invasive brain stimulation (NIBS) uses direct current (DCS: excitation under the anode, inhibition under the cathode) or repetitive transcranial magnetic stimulation (rTMS: excitatory at high frequency, inhibitory at low frequency). Since recovery from poststroke deficits seems to be more effective in patients who recover function in the ipsilateral perilesional area, NIBS trials aimed to activate this region: this effect can be achieved by excitatory NIBS (high frequency repetitive transcranial magnetic stimulation, rTMS; intermittent theta burst stimulation, iTBS; anodal transcranial direct current stimulation, tDCS) to reactivate the perilesional area or by inhibitory NIBS (low frequency rTMS or cathodal tDCS) to reduce increased activities in the contralesional homologous areas.

DCS as well as rTMS were applied in combination with rehabilitative measures in order to improve various symptoms after stroke, especially motor deficits and aphasia. In both applications recovery was improved with combined treatment in comparison to standard therapy without NIBS. All types of NIBS were used in rehabilitation of motor deficits after stroke and positive effects on recovery were observed. Among the different modalities low-frequency inhibitory stimulation of the motor cortex in the contralateral non-affected hemisphere seems to be the most prominent approach, but large controlled trials are still missing.

In poststroke aphasia several studies attempted to restore perilesional neuronal activity in the injured left inferior frontal gyrus by applying excitatory high frequency rTMS or iTBS or anodal tDCS to small series of patients in the chronic stage: They showed favorable effects in speech performance for several weeks to a few months. Only one study coupled ipsilesional anodal tDCS to language therapy in chronic nonfluent aphasia and observed improved speech / language performance for 1 week to 2 months. Most NIBS studies in poststroke aphasia employed inhibitory low frequency rTMS for stimulation of the contralesional pars triangularis of the right inferior frontal gyrus (BA 45) in order to reduce right hemisphere hyperactivity and transcallosal inhibition on the left Broca's area. Most studies reported single cases or small case series with chronic poststroke aphasia without any control condition and beneficial effects on speech performance lasting for several months. Only a few controlled studies including sham stimulation were performed in chronic stage after stroke. A controlled trial with inhibitory cathodal tDCS stimulation of the non-dominant right Wernicke area in patients with subacute global aphasia resulted in some improvement of comprehension in the treatment group. In one controlled randomized study changes in PET activation pattern in the subacute course were related to the clinical improvement. The shift of the activation pattern to the dominant hemisphere induced by inhibitory rTMS over the right inferior frontal gyrus could be demonstrated in the PET activation studies and correlated to improved performance in aphasia tests. NIBS might be a treatment strategy which could improve the effect of other rehabilitative efforts.

W. D. HEISS/ GERMANY

PET STUDIES FOR THE EVALUATION OF DYNAMICS IN STROKE PATHOPHYSIOLOGY

The concepts of pathophysiology of ischemic brain damage as the basis for therapeutic strategies are derived from results of experiments in animal models. For their transfer into clinical application methods are required which permit repeated noninvasive quantitative determination of regional cerebral blood flow, oxygen consumption and energy metabolism in patients after acute ischemic stroke. The method of choice for this purpose is still positron emission tomography (PET) which can be applied for high resolution quantitative imaging of various parameters – cerebral blood flow, oxygen consumption, glucose metabolism, but also of molecular events and of functional states – in humans as well as small animals. In this review some examples of PET applications for translational research in stroke are described.

One successful application of PET was regarding the transfer of the concept of the penumbra into the clinical management of acute ischemic stroke. Experiments in baboons and cats in the 70s and 80s defined blood flow values for functional disturbance and irreversible morphological damage, which could also be established by PET in patients with acute stroke. The progression of irreversible damage, the core of ischemia, into the functionally impaired area, the penumbra, could be followed in experimental models. Also the potential for recovery of these areas with reperfusion within the time window was demonstrated in these models, a result which formed the basis for thrombolysis and other reperfusion therapies. In animal models tracer for neuronal integrity were tested which are useful for early detection of irreversible tissue damage.

The second example is the prediction of malignant course after occlusion of large arteries. In experimental MCA occlusion in cats a malignant course was indicated by severe ischemia in 55 – 75 % of the hemisphere at the end of 3 hours occlusion. Hyperperfusion after reopening of the MCA turned into hypoperfusion and finally led to severe global ischemia with transtentorial herniation. In patients with MCA occlusion PET measurements within 24 hours after stroke showed larger volumes of ischemic core (mean, 144.5 versus 62.2 cm3) and larger volumes of irreversible neuronal damage (157.9 versus 47.0 cm3) in patients with malignant course (ie, edema formation with midline shift) than in patients with benign course. Corresponding to the experimental results, PET allowed prediction of malignant MCA infarction within the time window suggested for hemicraniectomy.

Another example is the assessment of subacute and chronic pathophysiological changes after stroke: Results from animal experiments indicated the importance of neuroinflammation, which can be visualized as microglia activation, for progression of damage into areas primarily not affected by ischemia and for prognosis of functional deficits. These inflammatory changes might also play an important role for increased amyloid deposition and might therefore be involved in the development of poststroke dementia.

These few examples underline the role PET has played for translational research in stroke in the last 30 years. Its impact might even be increased by the advent of combined MR / PET equipment and the introduction of more sophisticated molecular tracers into clinical application.

TUDOR LUPESCU / ROMANIA

SINGLE PULSE TMS - TECHNIQUE, PARAMETERS, CLINICAL APPLICATIONS; SAFETY ISSUES; OTHER INDICATIONS FOR rTMS; A SUMMARY OF RECENT DATA ON rTMS

Transcranial magnetic stimulation (TMS) is a neurostimulation and neuromodulation technique, based on the principle of electromagnetic induction of an electric field in the brain. This field can be of sufficient magnitude and density to depolarize neurons, and when TMS pulses are applied repetitively they can modulate cortical excitability, decreasing or increasing it, depending on the parameters of stimulation, even beyond the duration of the train of stimulation. This has behavioral consequences and therapeutic potential.

The use of TMS has grown in the past decade, new protocols of TMS have been developed, changes in the devices have been implemented, TMS is being increasingly combined with other brain imaging and neurophysiologic techniques including fMRI and EEG, and a growing number of subjects and patients are being studied with expanding numbers of longer stimulation sessions.

TMS delivered to different levels of the motor system (neuraxis) can provide information about the excitability of the motor cortex, the functional integrity of intracortical neuronal structures, the conduction along corticospinal, corticonuclear, and callosal fibres, as well as the function of nerve roots and peripheral motor pathway to the muscles. The patterns of findings in these studies can help to localise the level of a lesion within the nervous system, distinguish between a predominantly demyelinating or axonal lesion in the motor tracts, or predict the functional motor outcome after an injury. The abnormalities revealed by TMS are not disease-specific and the results should be interpreted in the context of other clinical data. Some TMS findings can be quite useful for an early diagnosis (eg, multiple sclerosis, Bell's palsy, psychogenic paresis, plexus neuropathy) and prognostic prediction (eg, multiple sclerosis, stroke, cervical spondylosis etc).

Therapeutic utility of TMS has been claimed in the literature for psychiatric disorders (such as depression, acute mania, bipolar disorders, panic, hallucinations, obsessions/compulsions, schizophrenia, catatonia, post-traumatic stress disorder, or drug craving), neurologic diseases (such as Parkinson's disease, dystonia, tics, stuttering, tinnitus, spasticity, or epilepsy), rehabilitation of aphasia or of hand function after stroke, pain syndromes (such as neuropathic pain, visceral pain or migraine).

Also, a special attention will be given to the safety issues and side effects of TMS, contraindications and precautions, and a screening standard questionnaire for rTMS candidates

MATTHIAS KIENLE / GERMANY

INTRODUCTORY DATA (PRINCIPLES, TECHNICAL DATA, DEVICE, COILS); rTMS - PRINCIPLES, TECHNICAL DATA, STIMULATION PARAMETERS, INCLUDING TBS; DISEASES PROTOCOLS STROKE, PSYCHIATRY, PAIN; PAS; NEUROREHABILITATION

Magnetic stimulation is a non-invasive, pain free technique used to excite and depolarize neurons in the brain and peripheral nervous system using induced currents. The excitation is caused by weak electric currents induced in the tissue by rapidly changing magnetic fields. The discovery is based on the principle of electromagnetic induction – discovered in 1831 by British scientist Michael Faraday.

When used to stimulate the brain it is normally referred to as Transcranial Magnetic Stimulation (TMS). TMS can be either single or paired pulse TMS or repetitive Transcranial Magnetic Stimulation (rTMS). Single/paired pulse TMS is mainly used for physiological research and diagnostic purposes. When the magnetic stimulation is delivered at regular intervals, it is termed rTMS. When stimulating the brain rTMS can produce lasting effects on cerebral functions, such as improvement of mood in depression

During the seminars it will be discussed the basic principles of TMS regarding both single pulse TMS and repetitive TMS (rTMS): technical data, device, coils, stimulation parameters (including TBS), rTMS protocols used for neurorehabilitation purposes or for clinical research purposes ("virtual lesion", speech area, cognition, visual area, memory etc.).

Repetitive Transcranial Magnetic Stimulation (rTMS) is approved for the treatment of Major Depressive Disorder. The use of rTMS for any other purpose is considered investigational. A vast amount of research using rTMS, for other indications than depression, is ongoing. Areas of research include anxiety, bulimia, migraine, pain, rehabilitation of aphasia and motor disability after stroke, tinnitus, Parkinson's disease, and schizophrenia.

The triple stimulation technique (TST) combines single pulse TMS with peripheral electric stimulation in order to provide a reliable method of measuring cortical recruitment of the motor fibers. During the seminar, there will be a general presentation on TST along with hands-on sessions.

Paired associative stimulation (PAS) refers to a paradigm consisting peripheral auditory, sensory or motor stimulation combined with transcranial magnetic stimulation (TMS) over the specific areas in order to induce long term potentiation and long term depression. During the seminar will be presented a brief overview of this technique, with applicability in clinical studies.

Notes

Notes

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