S25. TMS and depression

Chairs: E. Klein (IL), T.G. Bolwig (DK)

S25.1

Treating psychiatric symptom with TMS

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There is an assumption in some clinical research studies, particularly those using neuro-imaging, that a disturbance in discrete cortical regions is associated with distinct psychiatric symptoms or syndromes which may go across ICD-defined mental disorders. Such a hypothesis may be testable by TMS. The presentation will examine likely candidates for such testing in affective and psychotic disorders and produce a number of experimental paradigms that can be employed. Methodological issues, such as exact localization of the stimulation area and operational definition of syndromes, will be discussed. New data on the treatment of sixteen chronic hallucinators with 1Hz superior temporal stimulation will be presented as an example of such an approach.

S25.2

Magnetic seizure induction for the treatment of major depression

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Despite advances in psychopharmacological treatment, major depression remains a significant public health problem and a substantial proportion of patients fail to respond to conventional treatments. Electroconvulsive therapy (ECT) plays an important role in the treatment of the severely depressed, and especially those who do not respond to antidepressant medications, but its use is limited by cognitive side effects. Magnetic Seizure Therapy (MST) refers to the use of repetitive transcranial magnetic stimulation (rTMS) to perform controlled seizure induction under anesthesia. MST has the potential to limit the cognitive side effects of convulsive therapy by focusing seizure induction in specific cortical regions and avoiding current spread to areas implicated in amnestic side effects. MST will be explained and technological as well as clinical needs will be addressed. First results of this putative therapy in major depression will be reported and the general necessity for stimulating at higher amplitudes will be discussed.

S25.3

Transcranial magnetic stimulation as a therapeutic tool in psychiatry: what do we know about the neurobiological mechanisms?

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Potential therapeutic properties of repetitive transcranial magnetic stimulation (rTMS) have been suggested in several psychiatric disorders such as depression, mania, obsessive–compulsive disorder, posttraumatic stress disorder and schizophrenia. By inducing electric currents in brain tissue *via* a time-varying strong magnetic field, rTMS has the potential to either directly or trans-synaptically modulate neuronal circuits thought to be dysfunctional in these psychiatric disorders. To use rTMS optimally, it is most important to know how it is acting in brain tissue, i.e. knowledge concerning the putative neurobiological changes underlying the observed clinical effects. However, the limitations of human research necessitate preclinical studies in suitable animal models and basic studies at the cellular and molecular level to better understand how the induced intracerebral current density is regulated and which regulatory elements might serve as potential treatment targets. rTMS currently still awaits clinical routine administration although there is compelling evidence that it causes changes in neuronal circuits as reflected by behavioural changes and decreases in the activity of the hypothalamic-pituitary-adrenocortical system. Such alterations suggest regional changes in neurotransmitter/neuromodulator release, transsynaptic efficiency, signaling pathways and in gene transcription. Indeed, specific changes in the dynamic release patterns of biogenic amines, amino acids and the neuropeptide vasopressin in response to rTMS could be demonstrated by use of the in vivo microdialysis technique. Moreover, neuroprotective effects of rTMS and an increase in brain-derived neurotrophic factor (BDNF) gene expression were shown. Together, these changes are, in part, reminiscent of those accompanying antidepressant drugs. The data further suggest that a common molecular mechanism may underlie different antidepressant treatment strategies.

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S25.4

Slow rTMS in major depression and schizophrenia. Review of studies and implications for future research

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Recent studies have suggested that repetitive transcranial magnetic stimulation (rTMS) of the dorso-lateral prefrontal cortex (DLPFC) might be effective as a treatment for major depression (MD). One line of studies has reported the efficacy of high frequency rTMS (10–20HZ) to the left DLPFC, using focal stimulation. Our work has focused on the evaluation of low frequency (1HZ) non-fecal (round coil) rTMS to the right DLPFC. Using this approach, rTMS has been shown to be significantly more effective than sham stimulation in a double blind controlled study in 70 subjects with MD. At the end of 10 daily rTMS sessions Hamilton depression ratings (HDRS) were significantly lower in the rTMS group. Also, a significantly larger portion of patients had HDRS ratings <10 and did not need ECT. In a more recent study 28 subjects with MD were randomized to receive 1) right prefrontal rTMS with placebo medication (N=11) or 2) left prefrontal rTMS with placebo medication (N=10) or 3) active medication with sham rTMS (N=7). Ten daily treatments were administered over 2 weeks at 3HZ, 110% of motor threshold using a 80mm round coil (Magstim Rapid). Five patients (50%) in the left rTMS group but only one in each of the other groups, improved by more than 50% on their depression scores after 2 weeks of treatment. In this study left prefrontal rTMS at a frequency of 3HZ was superior to the other treatments and resulted in significant improvement in 5/10 patients. In contrast we failed to show therapeutic efficacy of rTMS in 31 schizophrenic patients using the same treatment protocol. In another study 46 normal volunteers were assessed for neuropsychological effects of one session of low frequency rTMS applied to the right or left DLPFC as compared to sham rTMS. In this double blind study, rTMS did not appear to have any adverse cognitive effects as assessed by several neuropsychological tests. Taken together all these suggest that low frequency (<5HZ) prefrontal rTMS may be selectively

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