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TMS field modelling-status and next steps

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IS 3. TMS field modelling-status and next steps—A. Thielscher (Copenhagen University Hospital Hvidovre, Danish Research Center for Magnetic Resonance, Copenhagen, Denmark, Technical University of Denmark, Kgs. Lyngby, Denmark, Max-Planck-Institute for Biological Cybernetics, Tübingen, Germany)

In the recent years, an increasing number of studies used geometrically accurate head models and finite element (FEM) or finite difference methods (FDM) to estimate the electric field induced by non-invasive neurostimulation techniques such as transcranial magnetic stimulation (TMS) or transcranial weak current stimulation (tCS; e.g., Datta et al., 2010; Thielscher et al., 2011). A general outcome was that the field estimates based on these more realistic models differ substantially from the results obtained with simpler head models. This suggests that the former models are indeed needed to realistically capture the field distribution in the brain. However, it is unclear how accurate even these more advanced models are and, in particular, to which extent they allow predicting the physiological outcome of stimulation. An experimental validation of the novel methods for field calculation is thus necessary.

Focusing on motor cortex stimulation by TMS, our goal is to explore to which extent the field estimates based on advanced models correlate with the physiological stimulation effects. For example, we aim at testing whether interindividual differences in the field estimates are also reflected in differences in the MEP responses. This would indicate that the field calculations accurately capture the impact of individual macroanatomical features of the head and brain on the induced field distribution, in turn strongly supporting their plausibility.

Our approach is based on the SimNIBS software pipeline (www.simnibs.de) that allows for the automatic creation of accurate head models from structural and diffusion-weighted magnetic resonance images (MRI) (Windhoff et al., 2011). This enables us to perform field calculations for multiple subjects, as required in neuroscientific studies. We substantially improved the software in order to improve its usability in a group analysis. At the moment, we are performing field calculations and are acquiring motor mapping data in a group of subjects for a systematic comparison of both data sets.

I will give an overview on the status of the SimNIBS project. I will start by summarizing the key findings on how the individual brain anatomy shapes the electric field induced by TMS (Thielscher et al., 2011; Opitz, 2011). The putative link between the modeling results and basic physiological TMS effects is highlighted. I will then introduce the novel features of SimNIBS that include the import of coil positions from neuronavigation systems, improved support for diffusion-weighted MRI and transformation of the estimated fields into MNI space for group analysis. Preliminary results on the comparison between field estimates and motor mapping data will be presented.

To summarize, field estimates based on accurate head models have already proven highly useful for a better understanding of the biophysics of non-invasive brain stimulation. The improved software tools now allow for systematic tests of the links between the estimated fields and the physiological effects in multi-subject studies. This will give the knowledge needed, e.g., for a more accurate spatial targeting of specific brain areas by TMS.

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IS 4. Modelling TBS—Y.-Z. Huang (Chang Gung University, Taipei, Taiwan)

Theta burst stimulation, a form of repetitive transcranial magnetic stimulation, can induce lasting changes in corticospinal excitability through plasticity-like mechanisms on cortical synapses. Interestingly, the direction of the effect on synaptic efficiency depends on whether the bursts are delivered continuously (cTBS, producing long-term depression (LTD)-like effects) or intermittently (iTBS, producing long-term potentiation (LTP)-like effects). We firstly built a simple phenomenological model based on knowledge of calcium-dependent mechanisms of post-synaptic plasticity to successfully explain this by postulating (1) that burst stimulation induces a mixture of excitatory and inhibitory effects, (2) those effects may cascade to produce long-lasting effects and (3) the final effect of TBS (potentiation or depression) depends on the summation of these two effects.

Furthermore, we went onto extend the model by including spike timing dependent plasticity with detailed calcium dynamics based on kinetic equations that mimic protein kinase interactions at the cellular and molecular levels. However, the post-synaptic calcium dependent plasticity model alone was not sufficient for describing diverse plasticity effects aroused by different rTMS protocols. We then further recruited the pre-synaptic mechanism for the extended model, because we noticed that shot-term pre-synaptic depression due to vesicle depletion could play a critical key in the regulation of long-term plasticity in post-synaptic neurons. In results, the new improved synaptic model has successfully simulated not only the results of TBS but also those of conventional rTMS protocols.

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IS 5. Clinical efficacy of non-invasive transorbital alternating current stimulation in optic neuropathy: A double-blind, randomized, sham-controlled multi-center study—C. Gall[a], A. Federov[a,b], A. Antal[c], M. Schittkowski[d], S. Kropf[e], A. Mante[f], S. Schmidt[f], B. Sabel[a] ([a] University of Magdeburg, Medical Faculty, Institute of Medical Psychology, Magdeburg, Germany, [b] EBS Technologies GmbH, Kleinmachnow, Germany, [c] Georg-August University Göttingen, Department of Clinical Neurophysiology, Göttingen, Germany, [d] Georg-August University Göttingen, Department of Ophthalmology, Göttingen, Germany, [e] University of Magdeburg, Medical Faculty, Institute of Biometry and Medical Informatics, Magdeburg, Germany, [f] Universitätsmedizin Charité, Department of Neurology, Berlin, Germany)

Question: Non-invasive brain current stimulation enhances neuronal plasticity in the visual system both in normal subjects and in patients with visual field loss (Antal et al., 2012; Sabel et al., 2011). In order to improve visual functions in patients with optic nerve damage we have now validated the efficacy of repetitive transorbital alternating current stimulation (rtACS) for the treatment of optic nerve damage in a randomized, multi-center clinical trial.

Methods: A total of 98 patients were randomized in rtACS and sham group using stratified block randomisation considering the study center (3 levels) and the defect depth of visual fields at baseline (2 levels) as a potential prognostic factor. Patients were stimulated with 4 stimulation electrodes positioned near the closed eyes on 2×5 consecutive weekdays for 25–40 min daily with square