TC-probe: aims and software overview

The combination of transcranial magnetic stimulation (TMS) and high-density electroencephalography (HD-EEG) allows to directly stimulate a subset of cortical neurons and measure, with good spatial-temporal resolution, the effects produced by this perturbation in the rest of the brain. In principle, this perturb-and-measure approach has important advantages compared to current electrophysiological and neuroimaging techniques. First, TMS/HD-EEG by-passes sensory pathways, subcortical structures and probes directly the cerebral cortex. Thus, at difference with peripherally-evoked potentials and event-related metabolic activations, it does not depend on the integrity of sensory and motor systems and can access any subject (de-afferentated, paralyzed, unconscious) and any cortical area (primary and associative). Second, with TMS/HD-EEG it is possible to perturb the cerebral cortex with a wide range of intensities, beyond the limited bandwidth of peripheral receptor and nerves. In this way it is possible to obtain a full excitability profile, from threshold to saturation, of the stimulated cortical area. Third, TMS/HD-EEG, by recording the effects of the activation of the stimulated neurons on distant cortical areas, can provide an unambiguous measure of cortical effective connectivity, an important parameter for recovery of function, consciousness and cognition.

Given its unique characteristics, TMS/HD-EEG may represent a powerful tool to probe thalamocortical circuits in the lab and at the patient's bedside. However, while using this technique we can probe human thalamocortical circuits with an unprecedented degree of freedom, we also face the challenge of dealing with a black box. At difference with peripheral nerve stimulation, when we apply TMS to perturb directly one of the many accessible cortical sites at one of the many possible intensities, we have very little a priori knowledge about whether, where and when we should expect relevant activations. The only assumptions that can possibly apply to any TMS perturbation are i) that TMS can activate, locally, the axons and the neurons underlying the coil ii) that this local activation can be transmitted to connected cortical sites iii) that TMS can trigger and/or induce thalamocortical oscillations. These notions clearly imply that the EEG output recorded after a TMS pulse contains several relevant information about the state of the underlying thalamocortical circuit, on the other hand, they are too general to implement a hypothesis-driven analysis.

With the TC-probe software package, we offer a data-driven procedure to extract from TMS/HD-EEG data maximum information using minimal a priory knowledge. All routines are accessible from a common user interface that allow easy data access and streamlined analysis. After artefact rejection and basic processing at the sensors level, source modelling of TMS-evoked potentials is performed on a single-trial basis. After source modelling, a non-parametric permutation test is applied to single-trial cortical currents in order to detect the timing and the location of significant cortical activations with an entirely data-driven approach. Significant current time series are also analyzed in the frequency domain using Hilbert transform to obtain a global phase locking factor and using wavelets to calculate event-related spectral perturbation and inter-trial coherence. Finally, an automatic classification of the individual's cortical surface, based on anatomical (lobules) or cytoarcitectonical atlases (Broadmann areas), offers the option of reducing the data in space. In this case, the significant currents detected in each region are cumulated before further analysis. Thus, significant currents, phase locking and power modulation, can be extracted at different spatial and temporal resolutions to obtain both synthetic and analytical indexes; from the whole brain level during the entire post-stimulus period, in order to obtain indexes of global reactivity, to the regional level (sources, lobules and areas) during selected periods, in order to obtain indexes of local excitability and connectivity. Overall, the analysis procedure is designed to harmonize four general principles:

1. Minimal computational load,
2. Minimal intervention by the user
3. Maximum information extraction vi) maximum data reduction.

The TC-probe package can be generally applied to the perturbation of any cortical site (and peripheral nerve), is fully automatic and relays on minimal assumptions. The output of the procedure consists of synthetic and statistically solid indexes of global reactivity, local excitability and local connectivity patterns in the human cerebral cortex for research and clinical use.