Multimodal Applications of Non-Invasive Brain Stimulation (NIBS)

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Overview

The use of NIBS has surged in popularity, with increasing numbers of exploratory studies and randomized controlled trials making use of NIBS. However, the possibilities of multimodal NIBS applications are often overlooked due to their complexity. Recent developments have significantly increased the feasibility of multimodal NIBS which provides unique opportunities in multiple areas of brain research. The desired learning objectives are: The working mechanism of the invididual multimodal NIBS applications; Potential pitfalls in the application of multimodal NIBS; An example of the use of multimodal NIBS in a clinical study and future perspectives.

Lecture 1: *Dynamic effects of tDCS on fMRI functional connectivity*
Deborah Klooster Presenter

Debby Klooster will shed light on the dynamic effects of transcranial direct current stimulation (tDCS) on fMRI functional connectivity. Resting-state fMRI (rs-fMRI) data was collected before and during 20-minutes active and sham tDCS in 40 healthy female subjects. The anode was placed over the left dorsolateral prefrontal cortex and the cathode over the right orbitofrontal cortex and the stimulation intensity was 1.5 mA. Electric field simulations were used to derive a seed region for the functional connectivity analysis. The dynamic functional connectivity toolbox was used to compute the functional connectivity between the seed region and all gray matter voxels as a function of time. During the symposium, Debby will show that active tDCS has different effects on functional connectivity compared to sham tDCS, especially in the networks that are engaged in the tDCS stimulation (i.e., the default mode network and the frontoparietal network, and to a lesser extend the ventral attention and limbic networks).

Lecture 2: *Concurrent application of TMS and optical imaging (FOS/EROS)*
Chun-Yu Tse Presenter

The combination of TMS and optical imaging, especially the fast optical signal (FOS) or the event-related optical signal (EROS), to investigate the causal connections of brain network will be introduced. The FOS/EROS is associated with the neuronal responses. It can temporally and spatially localize the brain responses in the millisecond and sub-centimeter range to unfold the spatiotemporal dynamics and activation sequences of brain regions. Due to the optical nature, FOS/EROS can be recorded with TMS without interference. Previous studies (Tse et al., 2018, Xiao et al., 2020, Lui et al., 2021) demonstrated the causal connection of the frontotemporal cortical network in pre-attentive change detection based on the predictive coding framework. The development of this combination of TMS and optical imaging will be discussed.

Lecture 3: *Concurrent TMS-fMRI of the dorsolateral prefrontal cortex*
Sebastiaan Neggers Presenter

Major depressive disorder (MDD) is a severe mental disorder associated with high morbidity and mortality rates, which remains difficult to treat, as both resistance and recurrence rates are high. Repetitive transcranial magnetic stimulation (TMS) of the left dorsolateral prefrontal cortex (DLPFC) provides a safe and effective treatment for selected patients with treatment-resistant MDD. Little is known about the mechanisms of action of TMS provided to the left DLPFC in MDD and we can currently not predict who will respond to this type of treatment, precluding effective patient selection. In order to shed some light on the mechanism of action, we applied single pulse TMS to the left DLPFC in 10 healthy participants using a unique concurrent TMS-fMRI set-up, in which we could record the direct effects of TMS on whole brain activity. Stimulation of the DLPFC triggered activity in a number of connected brain regions, including the subgenual anterior cingulate cortex (sgACC) in four out of nine participants. The sgACC is of particular interest, because normalization of activity in this region has been associated with relief of depressive symptoms in MDD patients. This is the first direct evidence that TMS pulses delivered to the DLPFC can propagate to the sgACC, which may be an accurate biomarker for efficacy of rTMS treatment for depression.

Lecture 4: *Mapping reorganization of the motor cortex after stroke with nTMS-EMG*
Jord JT Vink Presenter

Many stroke patients suffer from long-term impairment of upper limb function with variable levels of spontaneous recovery. Motor recovery has been associated with reorganization of the primary motor cortex, which can be measured with navigated transcranial magneticstimulation (nTMS) and electromyography (EMG). Continuous theta burst stimulation (cTBS) is a promising tool for the promotion of upper limb motor recovery in stroke patients but is remains unclear whether NIBS affects cortical reorganization. We randomly assigned 60 stroke patients to ten sessions of cTBS, or sham cTBS. Functional recovery of the upper limb was assessed from the Fugl-Meyer (FM) arm score. The resting motor threshold (RMT) of the ipsi- and contralesional primary motor cortex (M1) was used as a measure of corticospinal excitability of the motor cortex. And motor mapping with nTMS-EMG was performed to identify changes in the cortical organization of upper limb muscles. Active cTBS significantly improved the FM arm score (β=9.1; 95%CI=1.1–17.1; p=0.026) and treatment significantly reduced the ipsilesional RMT on the 10th treatment day (β=-10.6; 95%CI=-18.5–-2.7; p=0.009). Motor mapping results are pending and will be discussed during the presentation.