Symbiosis of fMRI and Transcranial Electrical Stimulation: Methodology, Implications and Challenges

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Symposium

Recent work shows that transcranial electrical stimulation (tES) produces widespread changes in human brain activity at the site of stimulation and also in remote regions. The effects of stimulation are influenced by network state at the time of stimulation and the structure of the network. Robust effects on network activity are seen with relatively short durations of stimulation, providing a way to casually investigate the relationship between brain stimulation and network activity. Individualized head models of current distribution along with fMRI might provide an additional level of state/trait-based predictability for neural response to tES. There is a large variability in tES-fMRI study designs and parameters, such as site, intensity and frequency. These provide great flexibility in experimental design but also challenge for optimizing the parameters of stimulation. In this symposium, we will explore the challenges of designing combined tES and fMRI studies, the potential questions that might be addressed and the conclusions that can be drawn from the studies conducted to date. The speakers invited are drawn from labs across the world that have contributed to this methodological development and innovative study designs.

Objective

Identify the applications and use of fMRI for tES
Evaluate methodological concerns in a sample experiment design and hardware when combing tES and fMRI
Design a sample study to answer predictive or mechanistic questions about tES via fMRI

Target Audience

This symposium targets wide range of human brain mapping (HBM) audience who are interested to know more about potential applications that brain stimulation technologies could provide to the field of HBM.

Presentations

Mechanistic Biomarkers for tES: How fMRI Can Inform Us about tES Effects

Transcranial electrical stimulation approaches, including direct current stimulation (tDCS) and alternating current stimulation (tACS) are showing increasing promise as potential adjunct therapies in a range of neurological and psychiatric conditions. However, recent studies are increasingly highlighting the variability of responses, and questioning the assumptions about neural effects. I will discuss a number of recent studies that use fMRI combined with both tDCS and tACS to understand the effects of stimulation on both neural activity and connectivity within the functional motor network. tDCS has been used to modulate local neural activity in a number of studies investigating behavior and functional network connectivity. Here, I will discuss our recent work using tDCS in combination with fMRI and MR Spectroscopy, demonstrating a link between local inhibitory processing, cortical organization and functional network connectivity. tACS offers the additional ability to study the role of activity within specific frequency-bands. Our recent study demonstrated that tACS applied to the primary motor cortex (M1) in the beta frequency range (20Hz) leads to frequency-specific, complex effects on the connectivity of M1. We then went on to use 20Hz tACS in combination with MR Spectroscopy to study the neurochemical basis of this neural effect, showing a relationship between the frequency difference between endogenous beta activity and the 20Hz tACS, and local GABA levels. I will conclude by discussing what we can learn from these studies, what their limitations might be, and how novel technical advances may allow us to overcome these, at least in part.

Presenter

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Understanding the effects of transcranial electrical stimulation on cognitive control through simultaneous functional MRI and measurement of brain network structure.

Despite its widespread use in cognitive studies, there is still a limited understanding of whether and how transcranial electrical stimulation (tES) modulates brain network function. I will discuss our recent work showing how functional magnetic resonance imaging (fMRI) simultaneously recorded during tES stimulation can be used to directly study its physiological effects. We investigated the effects of transcranial direct current stimulation (tDCS) by stimulating the Salience Network (SN) and simultaneously recording fMRI during performance of range of tasks with differing cognitive loads. I will discuss the methodological challenges of this approach, including how to optimise fMRI acquisition during concurrent tES and the complexities of data analysis. Widespread modulation of cognitive control networks was seen with tDCS of relatively brief durations (seconds) applied to the right inferior frontal gyrus (rIFG). These physiological effects were dependent on brain state at the time of stimulation, i.e. the cognitive task that was being performed, as well as the polarity of tDCS stimulation. The effects of tDCS were also dependent on the structure of a stimulated brain network. We have previously shown that structural connectivity within the SN, specifically the fronto-insular part of the Aslant Tract (FIAT), is particularly important for cognitive control. Damage to this tract produced by traumatic brain injury (TBI) is associated with abnormal functional connectivity and impaired response inhibition. Our new results show that rIFG stimulation can improve response inhibition in healthy subjects, supporting a causal influence role for the SN in cognitive control and confirming it as a target for produce cognitive enhancement using tES. Importantly the behavioural and physiological effects of this stimulation was influenced by individual differences in the structure of the FIAT. Participants with high fractional anisotropy in this white matter tract showed improved response inhibition and increased activation of the SN with anodal TDCS, whilst those with low fractional anisotropy did not. Our findings show the value of simultaneously studying the physiological effects of tES with concurrent fMRI. They also

demonstrate the importance of incorporating information about network connectivity into the analysis and interpretation of the behavioural and physiological effects of tES. The work has particularly important implications for planning and interpreting clinical studies in populations where patients have altered structural connectivity. I will discuss this issue in relation to a clinical study that has used the same stimulation approach in TBI patients with impairments of executive function and white matter damage produced by axonal injury. This shows that the effects of stimulation on behaviour and physiology are dependent on network structure and confirms that tES therapy needs to be tailored to the individual depending on specific patterns of brain network damage.

Presenter

David Sharp, Imperial College London, AK
United Kingdom

FMRI and Head Modeling: Addressing State and Trait Predictors in Response to tES

This talk describes the various strategies to combine functional imaging (fMRI, EEG, fNIRS) with anatomical-image derived current flow models. Functional imagining can be used before tES to identify anatomical ROIs that are they targeted by current flow models. Functional imaging before and after tES can be used to measure outcomes of tES. Individual functional imaging before tES can be correlated with current flow models to test hypothesis about the interaction of activity and current flow in ROIs with outcomes. Thus, combining functional imaging and current flow models can increase the rigor of tES trials as well as support optimization of intervention including individuals' assessments. However, combing tES and functional imaging requires nuances understand of the features and limitations of both modulation and measurement techniques, with potential for artifactual outcomes. Specific topics includes: 1) using imaging to validate current flow models; 2) techniques and considerations for online tES and imaging; 3) unexpected interactions when combining and imaging study design techniques that are suitable in isolation; 4) leveraging functional targeting, when individual brain state determines the outcomes of stimulation; 5) state-of-the-art consideration for reliable image-derived current flow models vs tools for automated high-throughout modeling.

Presenter

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Methodological Parameter Space in Combining tES and fMRI: From Mechanism to Prediction

Combination between non-invasive brain stimulation techniques and neuroimaging methods have enabled researchers to go beyond the correlational associations between brain activity and behavior. Functional (f)MRI in combination with transcranial electrical stimulation (tES), have helped researchers to understand the effects of tES beyond the stimulated area and the mechanisms by which tES produces changes across different levels of the nervous system. To explore variability in the tES-fMRI methodological parameter space (MPS), I will report a systematic review on tES-fMRI studies and their MPS along with our experiences in running tES-fMRI studies. Based on the role of fMRI, tES-fMRI studies are classified to mechanistic, predictive, and electrode positioning. I will present potential explanations on how tES modulates activation and connectivity beyond the stimulated areas especially with prefrontal stimulation. However, in our systematic review, there were no two studies with same

MPS to replicate their results. Potentials and challenges for consensus guidelines to harmonize MPS in future studies will be discussed.

Presenter

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