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Single-trial EEG–fMRI reveals the dynamics of cognitive function

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Two major non-invasive techniques in cognitive neuroscience, electroencephalography (EEG) and functional magnetic resonance imaging (fMRI), have complementary advantages with regard to their spatial and temporal resolution. Recent hardware and software developments have made it feasible to acquire EEG and fMRI data simultaneously. We emphasize the potential of simultaneous EEG and fMRI recordings to pursue new strategies in cognitive neuroimaging. Specifically, we propose that, by exploiting the combined spatiotemporal resolution of the methods, the integration of EEG and fMRI recordings on a single-trial level enables the rich temporal dynamics of information processing to be characterized within spatially well-defined neural networks.

Introduction

Electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) recordings provide complementary advantages with regard to the temporal and spatial resolution of brain activity. fMRI enables brain regions engaged during cognitive processes to be localized with high spatial precision; however, the blood-oxygenation-level-dependent (BOLD) response is too slow to capture fully the rich temporal dynamics that underlie cognitive processes. By contrast, the EEG signal is directly coupled to neuronal electrical activity and has millisecond precision; however, EEG picks up a blurred spatial mixture of the underlying cortical activity and therefore provides only limited spatial resolution. Accordingly, great hope lies in the integration of EEG and fMRI to achieve both high temporal and high spatial resolution of human brain function [1–5]. Here, we propose that simultaneous EEG and fMRI recordings provide a major improvement that will advance considerably our understanding of how cognitive functions are implemented by the brain. Importantly, simultaneous EEG–fMRI recordings enable the investigation of trial-by-trial fluctuations of brain activity, which reveals important insights into the dynamics of cognitive function.

The fundamental assumption behind any integration approach is that the signals recorded in both modalities are at least partly produced by the same neural generators. However, a positive correlation between EEG features and the BOLD signal cannot necessarily be expected [6]. In fact, the major methodological differences of EEG and fMRI are in principle consistent with positive, negative or no correlations. When combining fMRI and EEG, it is therefore crucial to provide strong evidence that both measures refer to the same underlying substrate. After providing an overview of previously available procedures for EEG–fMRI integration, we introduce a recently established method of combining simultaneously recorded event-related EEG and fMRI on a single-trial level (Box 1). This new approach enables the study of dynamic properties of cognitive processing beyond the common focus on evoked brain responses.

fMRI-informed ERP-source modeling

Commonly, only the averaged response in the EEG signal, the event-related potential (ERP), is considered informative. Constraining the possible source locations of ERPs using neuroimaging results has a relatively long tradition [2]. In this approach, equivalent current dipoles supposed to account for the measured ERP are 'seeded' into those brain regions that are identified using neuroimaging methods such as positron emission tomography (PET) and fMRI [7–11]. Compared with the regional BOLD response, the resulting ERP-source waveforms produce more accurate information about the temporal evolution of activity in a network of cortical areas. However, this approach rests on the implicit assumption that the activity of the ERP generators leads to local hemodynamic changes that can be identified using fMRI. Cortical regions identified by fMRI do not always provide a good starting point for ERP-source modeling [3,4,12]. Each method can be blind to the activity detected by the other method under certain circumstances [13], and ERP and fMRI can differ in their sensitivity to experimental manipulations. Therefore, the corresponding neural generators might lack substantial overlap.

Parametric design and EEG–fMRI covariation

An alternative approach for integrating ERP and fMRI is based on parametric task manipulations. A range of parametrically graded experimental conditions are employed to identify cortical regions for which the BOLD response shows the same modulation across conditions as a specific

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Box 1. Trial-by-trial EEG–fMRI analysis

Recent advances in EEG hardware development have made it feasible to record multi-channel EEG data and an fMRI signal simultaneously, even at 3 T (Figure Ia of this box). EEG signals recorded inside the scanner are contaminated with two serious artifacts (Figure Ib). Gradient artifacts are due to the switching of magnetic resonance (MR) gradients necessary to collect MRI data. They are relatively invariant, so gradient artifacts can be removed by subtraction procedures. The ballistocardiogram (BCG) artifact is related to the pulsatile movement of blood and the pulsatile movement of electrodes adjacent to large blood vessels. Powerful multivariate BCG-correction procedures now enable the major properties of the EEG signal to be reconstructed [20,22] (Figure Ib). However, similar to EEG recordings outside the scanner, the inside-scanner EEG signal corrected for MR-gradient and BCG artifacts still represents a mixture of overlapping brain and non-brain activities, such as eye blinks, spontaneous oscillations or transient, event-related responses. To isolate these signals, blind-source separation algorithms, such as independent component analysis (ICA), have been used successfully [22,32,33] (Figure Ic). ICA linearly decomposes EEG data corrected from MR-gradient and BCG artifacts into several components. The components can be characterized by their maximally temporally independent time courses, their condition effects and their spatial properties [35]. One or several independent components that reflect task-related EEG activity can be used to obtain single-trial EEG amplitudes. Alternatively, components that represent artifacts can be discarded and the artifact-corrected signal can be used (Figure Ic). Several studies suggest that single-trial amplitudes from selected independent components not only reflect evoked condition-related effects but also preserve event-related trial-by-trial fluctuations within each condition (Figure Id). Convolution of these single-trial amplitudes with the hemodynamic response function (HRF) takes into account the temporal evolution of the fMRI BOLD response (Figure Ie). The result is one or several parametric regressors that can be used to predict the BOLD response that have been acquired concurrently from the same subject (Figure If). Recent work suggests that EEG-informed fMRI analysis, as described here, can help to identify brain areas that are involved in cognitive processing with more functional (and therefore spatial) specificity than the conventional analysis of fMRI alone [32,33]. EEG-informed fMRI analysis seems capable of localizing the neural generators of EEG measures, and provides a powerful way to study the functional role of dynamic trial-by-trial fluctuations of brain activity.

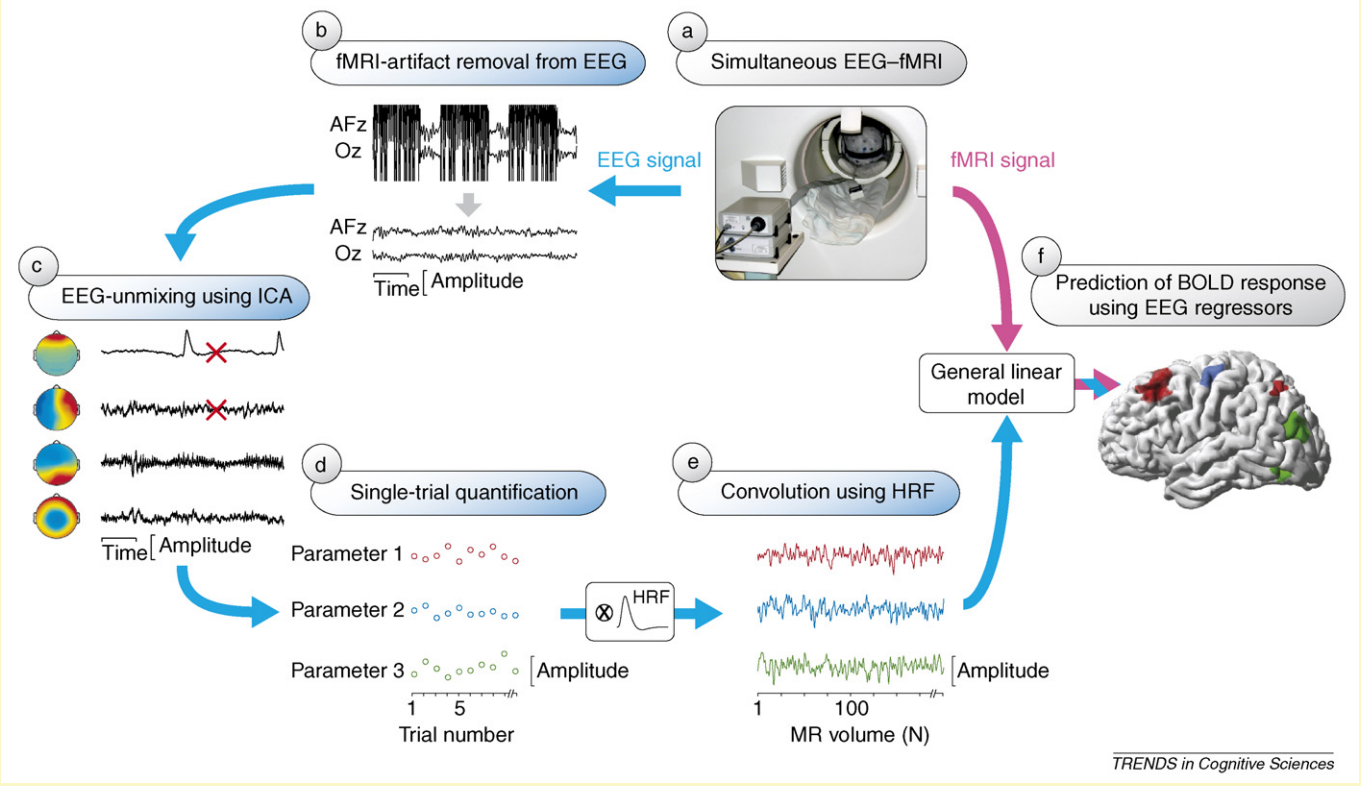

Figure I. EEG-informed fMRI analysis. EEG (blue arrows) and fMRI (pink arrow) can be recorded simultaneously **(a)** and, subsequently, EEG signals are corrected for fMRI artifacts. This is illustrated for two (AFz and Oz) out of a larger number of EEG channels **(b)**. ICA applied to the continuous EEG signal returns artifact-related and brain-related component activations and maps; typical artifact-related components are marked with red crosses **(c)**. Selected components reflecting brain activity of interest can be used to obtain a measure for each recorded trial **(d)**. After convolution (⊗) with the hemodynamic response function (HRF), the single-trial amplitudes yield EEG regressors **(e)** that parametrically predict the BOLD response **(f)**.

ERP component. Several groups have applied this method successfully to separately recorded EEG and fMRI signals and have reported systematic covariations of ERP amplitudes with regional BOLD responses [9,14–16]. The parametric-design approach helps to localize indirectly a cognitive process that is temporally defined using an ERP amplitude, without the need for simultaneous measurements of EEG and fMRI. Similar to fMRI-informed ERP-source modeling, this strategy builds on the assumption that the neural generators of BOLD and ERP responses overlap. However, the evidence of covariation across conditions provided in support of this assumption is limited. A brain region might depict the same parametric BOLD modulation as an ERP component, even though this region might not be the generator of the respective component and might exhibit a different temporal activation profile. In addition, not every experimental manipulation can be meaningfully implemented in a parametric design. Owing