EEG signals and fMRI activation overlap to some extent. It is the scientific question that determines which method will be appropriate.

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Letters Response

Towards single-trial analysis in cognitive brain research

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Bledowski and coworkers advocate functional magnetic resonance imaging (fMRI)-constrained source analysis of event-related potentials (ERPs), that is, trial-averaged electroencephalogram (EEG) responses, over the single-trial based EEG–fMRI integration technique we recently proposed [1]. The authors focus on three arguments.

First, they argue that our EEG-informed fMRI analysis approach might misidentify cortical generators of EEG activity by not taking into account physically plausible locations of ERP sources. We agree that if the goal is to identify the neural sources of ERPs, spatial constraints are valuable and should be used in the analysis. Independent component analysis (ICA) does not explicitly include this information, but it is readily gleaned by a comparison of the location(s) identified by fMRI with the dipole source analysis of the independent component(s). Indeed, we have previously shown a close correspondence between the dipole source location of the selected independent component and the single-trial EEG–fMRI integration result [1]. Therefore, although the ICA-based trial-by-trial approach can easily incorporate ERP source analysis, the reverse is not feasible. We consider it an advantage of our analysis that it is, in principle, not limited to the identification of common generators of EEG and fMRI. By contrast, the method can deliberately be used to identify functionally defined neural networks that are correlated with temporally well-localized EEG features, using the spatial resolution of fMRI [2].

Second, Bledowski and colleagues argue that the EEG-informed fMRI analysis approach assumes a linear correlation between fMRI and EEG features. Although a linear model is a natural starting point for this analysis scheme, the proposed method is, in fact, not limited to a linear correlation. The method can be generalized to any non-linear relationship simply by constructing corresponding non-linear fMRI regressors from the single-trial EEG features of interest [3].

Third, Bledowski *et al.* argue that the trial-by-trial approach suffers from the assumptions inherent in ICA. In particular, they state that current ICA algorithms require knowledge about the number of sources contributing to the mixed data. The infomax ICA algorithm we use is among the most widely applied algorithms [4] and does not in practice require this knowledge. However, the authors might be referring to the underlying problem, which is the selection of those independent components that can be reliably identified. We have successfully used different strategies to tackle this issue [5,6] and, consistent with others, have found ICA to be of great value – in particular for the direct integration of EEG and fMRI [1,2,7,8]. By contrast, the 'number of sources' problem applies to the fMRI-constrained ERP analysis approach because fMRI does not unambiguously identify the number of possible ERP dipole sources. It is worth recapitulating that fMRI could be blind to some EEG phenomena and vice versa. Hence, none of the currently available EEG–fMRI integration approaches unambiguously tells how many sources are relevant.

To advance EEG–fMRI integration, we need to further our understanding of how these signals relate to each other. However, the fMRI-constrained ERP source-analysis approach does not have much potential in addressing the fundamental question of EEG–fMRI coupling. The sole consideration of trial-averaged data in each modality neglects the amount of information that can be extracted from fluctuations across trials. By contrast, the trial-by-trial approach can help to identify which fractions of EEG

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and fMRI signals are related to each other and which are not. Importantly, single-trial EEG [1] and fMRI signals [9,10] have predictive power with regard to trial-by-trial fluctuations of behaviour. In fact, a rapidly growing body of evidence shows that temporal fluctuations of neuronal activity are not merely noise, but instead are functionally relevant signals [11]. Thus, the analysis of simultaneous EEG–fMRI signals on a trial-by-trial level is likely to provide key information for a deeper understanding of the brain–behaviour relationship.

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