

Physiological Basis, Technique, and Applications

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The technique's origin, albeit in a very specific and restricted field of neuroscience, is worth discussing in detail, as it highlights important aspects of the motivation for combining the two modalities.

EEG-fMRI emerged from the field of epilepsy imaging, soon after the development of fMRI, when John Ives and colleagues wheeled their EEG machine into the scanner room at the Beth Israel Hospital in Boston, USA. This action was doubtless driven by the desire to map epileptic brain activity. The reason is simple: the need for noninvasive imaging of the epileptic focus. Even today, EEG source estimation during seizures remains a formidable challenge, and while in some cases structural imaging reveals abnormal brain regions, which for all practical purposes correspond to the focus, this is not the rule—even with current MRI. The same could be said for "functional" imaging techniques such as PET and SPECT. Epilepsy is a condition defined by perturbed brain activity. Techniques that can record changes in brain activity between two states-normal and epileptic for examplethus have an immediate appeal. The time scale of these perturbations ranges from 10 ms to minutes or even hours (the bandwidth extending into the tens of Hz), hence the crucial role of EEG, with its exquisite temporal resolution, in the study of epilepsy. The most common EEG abnormality observed in patients with epilepsy is the interictal epileptiform discharge, commonly called "epileptic spike", which has a duration of 100 ms; their relative abundance and often close relationship between their generator and the focus makes them scientifically and clinically attractive. Although a great deal of effort has been dedicated to estimating the generators of spikes, electrical source imaging suffers from the well-known intractability of the EEG inverse problem. What about imaging spikes? Spikes occur without any external manifestation, in contrast to seizures, and are considered a purely EEG phenomenon. Furthermore, they occur spontaneously, which means that producing images of the "spike state" requires the recording of EEG. The temporal resolution of fMRI, which is somewhere between that of EEG and that of PET/SPECT, makes it uniquely suitable for the study of the haemodynamic correlates of individual spikes noninvasively and

throughout the brain. In epilepsy, we therefore have an ideal application of this multimodal approach: the "EEG" in "EEG–fMRI applied to epilepsy" is simply a necessity if one is interested in mapping the haemodynamic correlates of spikes. The same can be said of the study of spontaneous (paradigm-free) brain activity, such as natural variations in EEG background (alpha rhythm), wakefulness, or activity in the default mode network.

Apart from the study of EEG and fMRI correlation in the resting state, what can EEG– fMRI bring to the neuroscience table? Another way of expressing the conditions under which simultaneous multimodal acquisitions are necessary is the need to eliminate potential intersession bias. In the case of interictal epileptic activity and the study of spontaneous variations in brain rhythms, for example, there is no way of guaranteeing matched datasets without simultaneous EEG. In the field of cognitive neuroscience, and the study of evoked responses in particular, simultaneous acquisitions are also a means of eliminating the potential effects of habituation, learning, attention, fatigue, anxiety, etc., across sessions.

Once this has been achieved, and the resulting data can be guaranteed to relate to the same brain activity, one has the possibility of studying the variance that is left once the experimental, deterministic factors have been taken into account, since averaged effects can be studied offline (in the absence of systematic intersession bias). For example, we will see how EEG–fMRI can been used to study the relationship between response latency and BOLD signal change and the the relationship between spontaneous variations in local field potential and the BOLD signal, leading to improved understanding of the electrophysiological substrate of the BOLD signal.

Therefore, simultaneous EEG–fMRI is the technique of choice to guarantee matched EEG and fMRI datasets, and is necessary for the study of the unpredictable parts of the signals.

An unfortunate aspect of the way EEG–fMRI is perceived is the often-stated claim that it combines the advantages of EEG (high temporal resolution) with those of fMRI (better spatial coverage), while of course the experimentalist soon realises that it also suffers from the limitations of both (EEG's spatial sensitivity bias and fMRI's sluggish relationship to neuronal events).

In cognitive neuroscience, research has been performed for decades using EEG and ERP to describe the neural basis of cognitive processes. ERPs such as the P300 potential, the N100 or the ERN have been used successfully to better understand brain function involved in target detection, selective attention or error processing. In addition, specific oscillation patterns have been identified as being associated with cognition (e.g. theta or gamma oscillations). However, for most of these potentials or oscillation patterns, discussions concerning their generation have continued and several lines of information have been used to get the desired knowledge (intracranial recordings, studies in patients with lesions, animal studies, EEG source localisation). All of these strategies have their limitations, and therefore imaging techniques such as fMRI represent an attractive alternative to get reliable information on neuroanatomical structures related to cognitive processes.

EEG-fMRI therefore may be a strategy that can make use of the high temporal resolution of EEG to achieve goals such as "mental chronometry" (describing the timeline of brain activity in relation to cognitive processing) and to specify the role of distinct oscillation patterns in combination with reliable information about the neuroanatomical structures involved. While this can be seen as the ultimate goal of EEG-fMRI in cognitive neuroscience, there are a number of pitfalls in terms of basic physiology, study design, artefacts and analysis techniques that have to be taken into account to avoid misguided data acquisition strategies or oversimplified interpretations of EEG-fMRI findings.

As the reader new to the field will soon discover, EEG–fMRI has mainly been used as an imaging technique: a special form of fMRI. In most applications, EEG is used as either an epoch (image) categorisation device or as a supplier of potential explanatory variables for the BOLD model. This bias or asymmetry in its use and interpretation is probably a reflection of the intrinsic visual instinct of humans, the associated need for explanations for numerous EEG observations made over the last 80 years, and also the perceived weakness of EEG-derived localisation. We believe that this represents a form of underachievement and a challenge. Success will doubtless come from discoveries on the nature of the relationship between electrical and MR signals, and it is our hope that this book will provide some of the required motivation.

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Louis Lemieux and Christoph Mulert