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Event-related functional imaging and episodic memory

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Abstract

Electrical and haemodynamic measures of neural activity can be time-locked to an event-of-interest, such as the presentation of a stimulus or a behavioural response. Both of these measures can be employed in studies where the aim is to elucidate the relationship between neural activity and cognitive processes. This review highlights a number of considerations that arise when these techniques are employed in pursuit of this goal, with a particular emphasis on functional imaging studies of retrieval from episodic memory. The review includes: a discussion of some limitations that each technique imposes at the stage of experimental design, consideration of the relative strengths and weaknesses of each technique, a commentary on assumptions that are common to both, and a brief review of the ways in which these techniques can be extended in order to index two distinct classes of cognitive operations that have correspondingly distinct neural signatures. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

There are a number of techniques that permit the neural activity supporting mental events to be recorded. For human participants, the techniques of choice are, for obvious reasons, those in which the recording instrument or instruments reside outside the skull. Techniques that meet this criterion include positron emission tomography (PET), functional magnetic resonance imaging (fMRI), electroencephalography (EEG) and magneto-encephalography (MEG). These four techniques do not record neural activity in the same way, and this has important consequences for the ways in which each can be employed in order to elucidate the relationship between neural and mental events.

PET and fMRI measure neural activity indirectly by tracking changes in regional cerebral blood flow (rCBF). These haemodynamic techniques can be used as an index of the neural activity that supports mental events since rCBF is correlated in space and time with neuronal activity. The techniques do not, however, provide a temporally accurate measure of neural activity. This is because the rCBF modulation that is associated with a change in neuronal activity is somewhat smeared in time [21,48]. More specifically, the haemodynamic response that is set in train by a single event lags approximately 2 s behind the event and does not return to baseline for a further 10–12 s [38,48] (for comments on longer-lasting changes, see Refs. [10,22,23]; for comments on the variability of the haemodynamic response across brain regions, see Refs. [8,34,60]).

The ways in which PET and fMRI track the haemodynamic response differ greatly. The former involves injection of a radioactive isotope into the bloodstream of participants. Measurement of the haemodynamic response is accomplished by detecting annihilation events that occur during the process of radioactive decay. For fMRI, measurement of the haemodynamic response is accomplished by detecting radio-frequency signals that are emitted as a result of applying magnetic field gradients to a participant who is located in a strong magnetic field (for a more detailed characterisation of both methods, see Ref. [66]). An important advance for the fMRI recording technique was the demonstration that changes in blood oxygenation give rise to detectable MR signal change [33,43,44,68]. Analysis of the blood oxygen-level dependent (BOLD) response is now the most widely used approach in fMRI studies of neural and cognitive function.

The fact that this approach does not rely on an exogenous tracer means that it is hard to justify the use of PET for studies of normal cognitive function. This ethical concern notwithstanding, the routine selection of fMRI over PET for studies of this kind would doubtless have come about for other reasons, most notably because fMRI imposes fewer constraints on the kinds of cognitive paradigms that can be

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employed, a point which will be elaborated upon in subsequent sections. This advantage is conferred primarily by virtue of the greater sensitivity of fMRI to blood-flow responses that accompany the neuronal activity that is evoked by single events.

In contrast to PET and fMRI, EEG and MEG provide real-time measures of neural activity. The EEG indexes changes in electrical field potentials that are generated intra-cranially, while MEG indexes changes in the magnetic field that occur in parallel with changes in the electrical field (for a more detailed comparison of the two, see Refs. [32,53]). The most widely used measures of electrical activity in studies of cognitive function are event-related potentials (ERPs). Their magnetic counterparts are referred to as ERFs. Both provide a measure of the neural activity that either precedes or is set in train by the stimulus event to which the activity is time-locked.

ERPs and ERFs provide only a selective measure of neural activity. That is, there are regions of neural tissue that, by virtue of their cellular configuration, as well as the orientation and temporal firing properties of the cells, do not generate a signal that can be recorded by detectors that are located outside the skull [73]. In this regard, ERFs are constrained more tightly than are ERPs, as they are sensitive only to activity that is generated in neuronal populations where the cells are oriented tangentially to the scalp. Using electrical measures it is possible to detect activity from populations where cells are oriented either radially or tangentially. For both techniques the signals that propagate to the scalp are biased towards those generated in tissue that is proximal to the detectors, since the strength of the electrical and magnetic fields decays rapidly with distance from the source. The rate of decay is greater for MEG than for its electrical counterpart.

As a result of these factors the proportion of neural tissue from which activity can be monitored is greater for the electrical than for the magnetic measure. Set against this advantage, however, is the fact that magnetic fields pass through the skull undistorted, whereas electrical fields do not. This means that the electrical signal that is detected at the scalp is somewhat smeared, with the degree of smearing varying across individuals and scalp locations because of local variations in skull thickness. Consequently, MEG data acquisition may be preferred if the goal is to infer intracranial generators on the basis of activity recorded over the surface of the scalp, although the preceding comments point to the fact that the limited sensitivity of the magnetic signal will always restrict the application of the technique in this regard.

It should also be emphasised that for both techniques any inferences about the likely generators of scalp-recorded activity are necessarily tentative. This is because the problem of how to determine the actual brain regions responsible for a pattern of activity recorded on the outside of the skull is mathematically ill-posed. That is, the number of combinations of internal generators that could give rise to any one scalp pattern is not finite [41]. In general, the accuracy of computed estimates of the location, strength and timing of generators of scalp-recorded activity is best determined by assessing the correspondence between these estimates and the neuro-anatomical information that can be garnered from a combination of sources including (but not limited to) PET and fMRI studies, lesion studies in non-human primates and studies of patients with selective brain damage.

The utility of the ERP and ERF recording techniques does not, however, stand or fall on their ability to contribute to an understanding of the mapping between particular neural structures and particular mental operations. Their principal strength lies in the fact that they index neural correlates of cognitive operations in real-time, and this feature has been exploited in order to provide support for (as well as to disconfirm and suggest extensions to) models of cognitive processes in domains including language, memory and attention (for a series of examples, see Ref. [55]). In studies of this kind ERPs have been used more widely than ERFs. There are two reasons for this, the first of which is historical: the technology for recording electrical activity at the scalp was available prior to the technology for recording magnetic activity. The second reason is financial: EEG acquisition systems are considerably cheaper than their MEG counterparts.

The purpose of the foregoing brief and selective review of methods for recording neural activity in vivo was to identify EEG and fMRI as the two functional imaging techniques that are used (and are likely to continue to be used) most widely in studies where the intention is to advance understanding of the relationship between neural and mental events. The remainder of this article comprises a discussion of the ways in which these approaches can be used in pursuit of this goal. The discussion will be concerned primarily with event-related potentials (ERPs) and event-related fMRI (efMRI). The focus in this review is not so much on technical aspects of data acquisition. Rather, it is on the relative strengths and weaknesses of the two techniques, as well as on key assumptions that are common to both. Examples that are employed to illustrate these observations are drawn primarily from studies of human episodic memory, although a number of the general issues raised are also relevant to other cognitive domains.

2. fMRI data acquisition in blocked designs

Were this article to have been written 5 years ago, then the fact that ERPs can be separated on a trial-by-trial basis according to criteria such as experimental condition and/or behavioural responses would have been highlighted as one of the critical advantages that the electrical measure had over both PET and fMRI. Recent advances in MRI technology have, however, enabled the measurement of the BOLD response that is evoked in response to individual events,