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Functional magnetic resonance imaging (fMRI)

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Functional magnetic resonance imaging is a noninvasive technique for measuring and mapping neural activity in the brain. In a typical fMRI experiment, volunteers lie inside an MRI scanner and perform a cognitive task. During the task, a series of three-dimensional images are taken of the participant's brain. Typically, these images have a spatial resolution of 3–4 mm and a temporal resolution of 1–4 s.

The images are designed to utilize the blood oxygen level–dependent (BOLD) effect, whereby the intensity of the MR signal in each portion of the image is affected by the amount of neural activity in that region. The BOLD effect is based on the fact that an increase in local neural activity produces an increase in local cerebral blood flow. This increase produces an increase in the local ratio of oxygenated relative to deoxygenated hemoglobin. Oxygenated and deoxygenated hemoglobin have different magnetic properties (deoxygenated hemoglobin is paramagnetic) such that the magnetic susceptibility of blood varies linearly with oxygenation over a broad range. The result is that an increase in local neural activity produces an increase in the local MR signal.

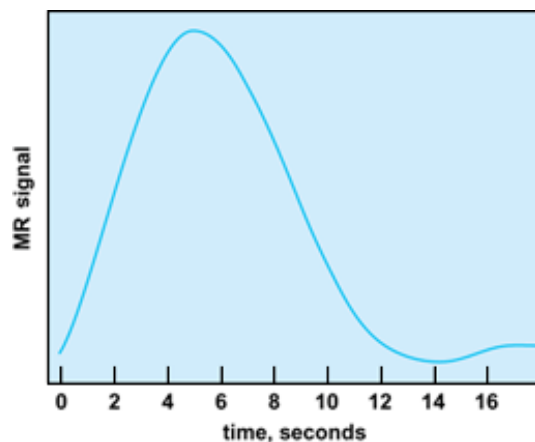
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This increase in MR signal (often referred to as the hemodynamic response) is thought to be an approximately linear transformation of the underlying neural activity. However, the BOLD hemodynamic response to neural activity is both delayed and protracted over time, resembling the effect of a low-pass filter. For example, the hemodynamic response to a brief burst of neural activity rises to a peak approximately 6 s after the neural activity and does not return to baseline levels until 12–20 s following the neural activity (Fig. 1). It should be noted also that there is no inherent baseline for the MR signal. The absence of an absolute baseline (a specific MR signal value corresponding to zero neural activity) means that fMRI must be used as a contrastive or subtractive technique. That is, neural activity associated with one task condition or in response to one type of stimulus must always be assessed in contrast to the activity associated with a different task or in response to a different type of stimulus.

Fig. 1 Hemodynamic response time following neural activity. The response time is delayed and protracted.



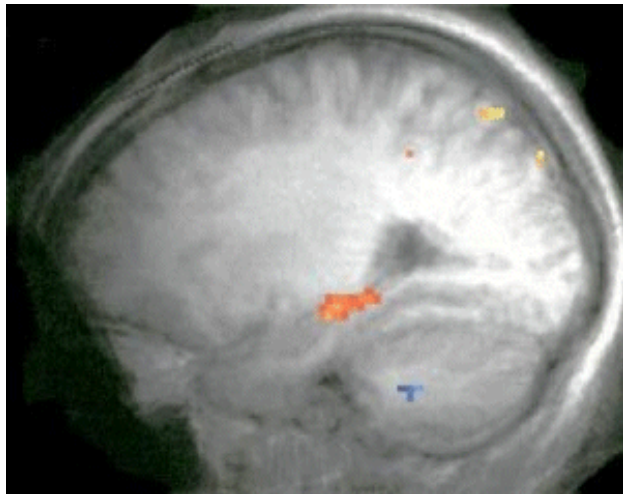
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Experimental design

The delayed and protracted nature of the MR response to underlying neural activity complicates the design and analysis of fMRI experiments, as the responses to multiple closely spaced trials will overlap in typical cognitive experiments. In so-called blocked fMRI experimental designs, two task conditions or two types of stimuli (for example, familiar and unfamiliar stimuli) are presented in alternating blocks, each typically 20–40 s in duration. The hemodynamic responses to the trials within each block, when added together, provide a percent MR signal change that is greater than the MR signal change produced in a single trial. Typically, the fMRI data from each voxel (a three-dimensional unit in the image measuring perhaps 3 mm³) are analyzed by correlating the MR signal in that voxel with a reference function based on the alternation between task conditions or stimulus types and adjusted for typical values of the hemodynamic response. Voxels with activity significantly correlated with the alternation in the blocked design are identified and typically color-coded according to the strength of the correlation and then overlaid on high-resolution structural MRI images (Fig.

2).

Fig. 2 Structural MRI image overlaid with fMRI-determined voxels of neural activity.



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Two types of event-related fMRI designs can also be used. In spaced or nonoverlapping designs, stimuli are presented at sufficiently long intervals (typically at a rate of one stimulus per 16–20 s) such that the hemodynamic response to individual events does not overlap. The MR signal in response to different task conditions or stimulus types is then calculated by simple event-locked selective averaging of the fMRI data. In rapid or overlapping designs, stimuli are presented at the same rates as are used in typical cognitive experiments in the laboratory (for example, one stimulus every 2 s). The analysis of rapid event-related designs relies on the observation that the hemodynamic response to multiple events sum together in an approximately linear fashion so that the response to different types of trials can be reconstructed with selective averaging or general linear modeling of the fMRI data.

Experimental findings

Since its initial development in 1992, fMRI has become a widely used tool in cognitive neuroscience (the study of cognition and the brain). It has been applied in areas ranging from visual perception to executive function and consciousness. For example, fMRI data have been used not only to identify occipito-parietal and occipito-temporal regions of the brain responsible for visual perception, but also to identify the different roles played by these regions. fMRI has also been used to demonstrate that attention, driven by a frontal-parietal network, has a modulatory effect on activity even in primary sensory regions (cortical areas that receive sensory input).

For the study of higher-level cognition, fMRI has been particularly useful for the study of the neural basis of learning and memory. Memory is considered to consist of three phases: learning (or encoding), storage, and retrieval. The learning phase refers to the initial acquisition and internal representation of the information that will constitute a memory. The storage phase refers to the period of time between learning and retrieval, during which the memory may become reorganized, weakened through forgetting, or strengthened through rehearsal. The retrieval phase refers to the subsequent accessing of memory (or some part of the memory) to guide thought or action.

Neuropsychological studies of the effects of brain lesions in both humans and experimental animals have provided the cornerstone for the present understanding of the neural basis of learning and memory. These studies have identified a system of structures within the medial portions of the temporal lobes (MTL) that are essential for the formation of long-term memory. Damage to these structures impairs the ability to learn new facts and events (also known as declarative memory). The advent of fMRI promises to greatly expand understanding of the mnemonic role of the MTL (that is, its role in learning, storage, and retrieval) and its anatomical components. In the few years that fMRI has been successfully used to study the neural basis of memory, it has been discovered not only that activity in the medial temporal lobe increases during the learning of new information, but also that this activity is lateralized based on the type of information being learned. During the learning of words, only the left MTL is engaged. During the learning of pictures of namable objects, both the left and the right MTL are engaged. During the learning of nonverbalizable visual objects (for example, nonsense objects), only the right MTL is engaged. Further, the amount of activity in the MTL during the learning of new information can predict how well that information will later be remembered.

The MTL has also been observed to demonstrate increased fMRI activity during the retrieval phase of memory. In addition, this activity has been found to correlate with whether or not individuals can successfully remember having learned the information. That is, fMRI activity in the MTL appears to correlate more with retrieval success than with retrieval effort. Further, because of the relatively high resolution available in fMRI, these activities can be localized to individual structures within the MTL, providing information to inform and constrain theories of MTL function. For example, recent studies have found activity within the hippocampus related to recollective success during simple recognition memory tasks. The hippocampus is at the top of the anatomical hierarchy within the MTL and receives input from other structures within the system.

It is also of interest that the frontal lobes are typically quite active during learning and during retrieval, as well as when information is being held in mind for short periods of time (a process called working memory). Frontal lobe activity appears to be more related to retrieval effort than to retrieval success.

Although fMRI studies have been informative and compelling, the impact of fMRI on the study of cognition and the brain will be even greater in the coming years. In less than a decade since its discovery, fMRI has become a major tool in cognitive neuroscience. As the MRI hardware, pulse sequences, and data analysis techniques continue to develop and as more researchers apply fMRI to investigations of the brain, the promise and potential of fMRI will continue to grow. As with any new technique, the full promise of fMRI lies not in what it may reveal in isolation, but in the possibility of using information from fMRI in conjunction with other techniques in both humans and experimental animals.

See also: [Brain](#); [Cognition](#); [Electroencephalography](#); [Hemispheric laterality](#); [Information processing \(psychology\)](#); [Learning mechanisms](#); [Medical imaging](#); [Memory](#); [Perception](#)

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