

## Cognition: An Overview of Neuroimaging Techniques

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### Anatomical Techniques

Anatomical techniques are used in a variety of ways in the service of the study of cognition, for example, to localize neuropathies in patients with cognitive disabilities or to compare the size of specific brain structures between groups of subjects through volumetric analysis. Additionally, anatomical techniques are used in conjunction with functional techniques in order to localize brain activity.

The earliest technique for imaging brain structure was computed tomography (CT). Today, it has been largely replaced by the much more powerful technique of magnetic resonance imaging (MRI). MRI provides excellent detailed structural information and enables the naked eye to distinguish gray matter (neuronal cell bodies) from white matter (myelinated tracts). New anatomical techniques, such as diffusion tensor imaging, have been developed to specifically visualize myelinated tracts. These methods can be used to track the normal and abnormal development of neural pathways in childhood.

### Functional Techniques

Functional techniques have been the dominant force in cognitive neuroscience because they enable us to determine when and where neural activity in the brain is associated with the ability to perform a particular cognitive task. These techniques allow us to examine the workings of the human brain throughout the life span, in sickness and in health.

It is common to design several task variants that differ slightly in terms of task requirements. On the basis of this approach, differences in brain activation between the task variants enable us to isolate brain structures that are implicated in hypothesized cognitive processes. For example, if one wanted to identify brain regions involved in actively maintaining information in mind (referred to as working memory), one might parametrically vary the number of items (or the load) that subjects needed to maintain and then identify brain regions in which the level of activation varied according to working memory load. Although parametric variation is arguably the most powerful functional brain imaging manipulation, a more

standard approach is to compare two task variants that differ only in that task 1 but not task 2 is hypothesized to engage a specific cognitive process. This approach relies on the assumption of 'pure insertion'; that is, the assumption that the insertion of the new task requirement affects only the cognitive process of interest.

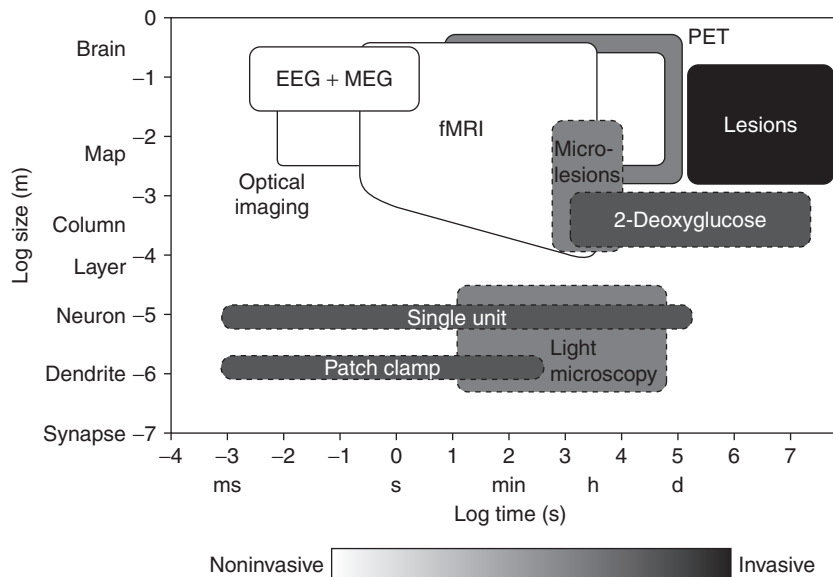
### Classes of Functional Neuroimaging Techniques

A variety of noninvasive functional neuroimaging techniques are available for use in humans ([Figure 1](#)); these techniques are categorized into two main classes. The first consists of methods for directly measuring electrical activity associated with neuronal firing, such as electroencephalography (EEG) and magnetoencephalography (MEG). The second main class consists of methods for indirectly measuring neuronal activity, which operate under the principle that neural activity is supported by increased local blood flow and metabolic activity. These methods include positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and near-infrared spectroscopy (NIRS). More information on each of these methods is provided in the following sections.

#### Direct measures of neural activity: EEG and MEG

EEG is the oldest functional brain imaging technique, dating back to Berger's discovery in 1929 that brain electrical activity could be recorded from electrodes placed on the scalp. This technique is still widely used today because of its ability to provide real-time measurements of brain activity. EEG records transient electrical dipoles generated by the net flow of electrical current across the cellular membrane during neuronal depolarization associated with postsynaptic potentials. Global EEG is used to measure neural activity during different brain states, such as sleeping and waking. A more powerful tool for cognitive neuroscience than global EEG measurements consists of event-related potentials, which refer to EEG activity averaged over a series of instances (or trials) triggered by the same event (e.g., the presentation of a visual stimulus).

Whereas EEG records the electrical activity associated with neuronal depolarization, the newer technique of MEG records the magnetic field produced by this electrical activity. The signal measured by both techniques results primarily from the activity of pyramidal neurons, which constitute roughly 70% of cells in the neocortex and are oriented perpendicular to the cortical sheath. EEG records electrical activity oriented perpendicular to the surface of the brain,



**Figure 1** Relative spatial and temporal sensitivities of different functional brain imaging techniques. The level of invasiveness of each technique is indicated by a grayscale; more highly invasive techniques are shown in darker gray. Techniques used in animals only are outlined with a dashed line. Adapted from Cohen MS and Bookheimer SY (1994) Localization of brain function using magnetic resonance imaging. *Trends in Neuroscience* 17(7): 268–277.

whereas MEG records activity oriented parallel to the surface of the brain. Thus, EEG measures the activity of pyramidal cells in cortical gyri and the depths of the sulci, whereas MEG is sensitive primarily to the activity of pyramidal cells in the superficial parts of the sulci, and it is therefore more limited in its scope.

The major challenge with both EEG and MEG is referred to as the ‘inverse problem,’ which is the challenge of identifying the source of the underlying signal. This source can be a great distance from the point on the scalp at which it is measured, and it is affected by factors such as head shape and dipole location and orientation. Thus, it is necessary to build source localization algorithms to determine the likely source of a signal. One advantage of MEG over EEG is that the signal is less sensitive to factors such as head shape. Thus, the two techniques are complementary in that EEG samples from more neurons, but MEG is less sensitive to signal distortion. As such, some researchers take the approach of measuring EEG and MEG simultaneously to take advantage of what each technique has to offer.

**Indirect measures of neural activity: PET** Roy and Sherrington first showed in 1890 that brain stimulation led to a local increase in blood flow to active populations of neurons. Landau and others subsequently used radioactive tracers to measure regional cerebral blood flow (rCBF) in animals (1955), and in 1963 this technique was first applied to humans. The most widely used radioactive tracer is  $^{15}\text{O}_2$ , an oxygen molecule in which one electron has been removed

from the atom to give an unstable form that will emit one positron to revert to the stable form  $^{16}\text{O}_2$ . In a PET scan, a small amount of radioactive tracer is injected into a vein. The tracer enters the brain after approximately 30 s, and in the following 30 s radiation in the brain rises to its maximal value; a picture of the rCBF is taken during this time frame.

The greatest advantage of PET over the more recent method of fMRI is the choice of radioactive tracer. Researchers can synthesize radiopharmaceutical compounds that bind to dopamine or serotonin receptors (C-11 or F-18 *N*-methylspiperone), opiate receptors (C-11 carfentanil), etc. PET is likely to continue to be important for understanding the role of various neurotransmitters in cognition. However, there are several disadvantages of PET that have led to its being surpassed by fMRI as the most widely used indirect measure of brain activity. The first of these is cost; PET facilities require not only a PET camera but also a cyclotron, which is used to produce the radioactive tracers. The second disadvantage is the poor temporal resolution – on the order of 1 min compared to 6–8 s for fMRI. Finally, PET is more invasive than fMRI, requiring the injection of a radioactive tracer (albeit one with a half-life of a few minutes), and thus it is not suitable for use in children or other special populations.

**Indirect measures of neural activity: fMRI** fMRI is currently the most widely used brain imaging technique for a number of reasons, including (1) widespread availability of MRI scanners and technology,

(2) relatively low cost per scan, (3) the lack of recognized risks for properly screened subjects, (4) good spatial resolution, and (5) better temporal resolution than other indirect neuroimaging methods.

In addition to observing that brain activity was associated with local changes in blood flow, Roy and Sherrington noted that the increase in total oxygenated blood delivered far exceeded the demand. It is this surplus of oxygen that is detected with fMRI, with what is known as the blood oxygen-level dependent (BOLD) contrast. Oxygenated hemoglobin, or oxyhemoglobin, has magnetic properties different from those of deoxyhemoglobin. Thus, the deployment of a strong magnetic field (typically 1.5–4 tesla when used in humans) enables one to measure changes in the ratio of oxy- to deoxyhemoglobin in local draining venules and veins. An increase in blood flow in response to a specific stimulus (be it brain stimulation or the presentation of a visual or auditory stimulus) is referred to as a hemodynamic response. This response is sluggish with respect to the underlying neural activity; for example, the hemodynamic response in visual cortex to a brief (e.g., 30 ms) visual stimulus peaks roughly 4–6 s after the onset of the stimulus.

## Related Techniques

Perfusion fMRI enables direct measurement of the hemodynamic response, unlike BOLD fMRI, which relies on the comparison of hemodynamic responses under different conditions. This technique is less widely used than BOLD fMRI because of its much lower sensitivity. Magnetic resonance spectroscopy is used to measure the relative concentration and distribution of specific ions or compounds, such as hydrogen, phosphorus, or carbon.

## Optical Brain Imaging

NIRS operates according to the same principle as optical brain imaging techniques that have been used in animals. Both techniques capitalize on the fact that changes in hemoglobin concentration in cortical tissue affect the absorption of infrared light by the tissue. However, NIRS is noninvasive, whereas optical imaging in animals is accomplished by exposing the surface of the brain. Because the cortical surface is not exposed in NIRS, light scattering by the skull leads to reduced spatial resolution.

During the past few years, Gratton, Fabiani, and colleagues have developed a new analytic approach to the analysis of optical data, known as the event-related optical signal (EROS). The EROS signal is based on measures of the optical properties of cortical tissue, which change when the tissue is active. The

changes in these optical properties are likely to be due to changes in light scattering as a function of neuronal activity. Because this type of optical signal is directly linked to neural activity, rather than blood flow, it provides a much higher temporal resolution than the signal typically analyzed in NIRS studies. Additionally, the EROS signal has a high degree of spatial resolution, in that it can be localized to an area of less than 1 cm<sup>3</sup>.

A drawback of all three optical imaging techniques noted previously is that they can only be used to measure activity on or near the surface of the brain (within 3–5 cm of the surface). However, these techniques are advantageous in that they are relatively inexpensive and completely noninvasive. Furthermore, because these techniques are not as sensitive to head movement as fMRI, they hold much promise for the study of clinical populations and children.

## Trade-Offs between Temporal and Spatial Resolution

Direct measures of neural activity, such as EEG and MEG, have exquisite temporal resolution. They are sensitive to changes in neural activity on a millisecond resolution. However, these methods have poor spatial resolution in that it is difficult to pinpoint the precise origin of the signal. In contrast, indirect measures of neural activity have better spatial resolution than EEG or MEG but poor temporal resolution. The spatial and temporal characteristics of these various methods are shown in [Figure 1](#). Thus, there is currently a trade-off between high temporal precision and high spatial precision. One solution to this problem is to use fMRI data to limit the possible sources of neural activity in EEG and MEG data; another – and even more challenging – solution is multimodal imaging, for example, the concurrent acquisition of fMRI and EEG data.

## Advantages and Limitations of Neuroimaging Techniques

To date, much of what we know about the functions of different brain regions comes from neuropsychological studies in humans and lesion studies in animals. A distinct drawback of neuroimaging techniques is that, unlike neuropsychological and lesion techniques, they cannot demonstrate the necessity of a brain region for a specific cognitive process. However, neuroimaging techniques can demonstrate that humans without neurologic damage routinely recruit this region to perform the task. Moreover, it is possible to compare levels of activation across individuals and to state that greater activation of this region is

associated with better performance on a task. Better yet, it is possible to compare activation between trials within an individual and to state that on trials in which the subject made an error, activation was lower in this region than on trials in which the subject performed correctly. Thus, functional brain imaging techniques can be used to characterize a region's contribution to specific cognitive processes. Moreover, brain imaging techniques can be paired with techniques for temporarily disrupting neural activity in a temporally and spatially precise manner (transcranial magnetic stimulation).

There are several important advantages of neuroimaging techniques over neuropsychological ones. First, neuropsychological studies necessarily rely on the output of behavior as the critical dependent measure, whereas neuroimaging studies can focus on cognitive processes that take place prior to – or are not associated with – a behavioral response. For example, it is impossible to determine whether lesions that result in a long-term memory impairment are associated with a deficit at encoding and/or retrieval. With brain imaging, however, one can identify brain regions associated with the effective encoding of memories separately from brain regions associated with effective retrieval.

Second, neuroimaging techniques enable us to identify the entire neural circuit underlying a cognitive process. Lesion studies in animals can accomplish this only piecemeal by lesioning each area in turn. Neuropsychological studies in humans would be hard-pressed to accomplish this at all, given the limited availability of patients with specific brain lesions. This point is an important one because with lesion studies it is possible to completely overlook – or instead to overestimate – the contributions of a specific region to cognitive function. For example, the hippocampus has long been thought to be the primary structure contributing to the encoding and retrieval of memories. However, brain imaging has demonstrated that in the healthy brain, prefrontal cortex routinely contributes to memory encoding and retrieval.

The third point is also related to the limited availability of neuropsychological patients: neuroimaging techniques enable one to examine the role of a given human brain region in cognition even if one does not have access to specific patient groups. Moreover, it can be very difficult (or next to impossible, depending on the brain region) to find a patient with a lesion limited to the region in which one is interested because most brain lesions are rather coarse. Furthermore, cortical reorganization can lead to recovery of function over time, which could lead one to assume mistakenly that a lesioned brain region is not normally involved in a specific cognitive process.

Finally, neuroimaging techniques with high temporal resolution, such as EEG and MEG, provide us with important clues about brain mechanisms. It is helpful to say that brain regions X and Y are involved in memory retrieval, but if we can say that brain region X is active a short time after region Y, we can begin to gain insight into the cascade of events leading to memory retrieval.

A common criticism of neuroimaging studies is that they can be highly unconstrained and atheoretical. Like any scientific tool, however, brain imaging can be used wisely or foolishly. Certainly, many exploratory brain imaging studies have been conducted, particularly in the initial phase of brain imaging, when it was important to validate the new techniques. However, the second generation of imaging studies, starting in the late 1990s, has been much more focused. On the whole, cognitive neuroscientists carefully devise experimental manipulations designed to test psychological theories or specific predictions about brain function. Brain imaging techniques are likely to be an important force in cognitive neuroscience for the foreseeable future.

### **Contributions to the Study of Cognition**

Neuroimaging research has been used to enrich our understanding of the neural basis of a wide variety of cognitive abilities, including attention, language, and memory. In addition, neuroimaging techniques have been used to gain insight into the etiology of neurobehavioral disorders, for surgical planning, and to assess functional recovery after brain damage.

One area in which neuroimaging studies are making important contributions is that of memory. For example, studies of long-term semantic memory have begun to uncover the ways in which stored information is organized in the brain. These studies show that different attributes of an object are stored in a distributed manner across several brain regions, with visual form information stored in a region that processes form, and functional information stored near a region that processes motion. Furthermore, studies of memory encoding have been able to pinpoint the precise regions for which level of activation during stimulus processing predicts subsequent memory for that stimulus. Additionally, studies of memory retrieval are being used to adjudicate between models of episodic memory positing that recollection (i.e., distinct remembrance of an item and the context in which it was previously encountered) and familiarity (a vague sense that the item has previously been encountered) are either distinct processes or merely

on a continuum of memory retrieval. These examples show how brain imaging studies can be used to test or adjudicate between psychological models.

Perhaps the most important contribution of neuroimaging to the field of cognition will be in the study of higher cognitive functions, which are not highly developed in nonhuman species and are therefore best studied in humans. Carefully designed brain imaging experiments have begun to fractionate the cognitive processes that underlie language, reasoning, problem solving, and other high-level mental functions, but further investigation is necessary.

*See also:* Cognitive Neuroscience: An Overview; Cognitive Control and Development; Electroencephalography (EEG); Event-Related Potentials (ERPs) and Cognitive Processing; Executive Function and Higher-Order Cognition: Neuroimaging; fMRI: BOLD Contrast; Magnetic Resonance Spectroscopy; Neuroimaging; Perfusion MRI; Single Photon Emission Computed Tomography (SPECT): Technique; Voxel Based Morphometry.

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