INTRODUCTION

In this appendix we provide some estimates of the spatial and temporal resolution, as well as of the invasiveness, of the most frequently used neuroimaging techniques. Before illustrating these estimates, it is important to remember that neuroimaging techniques may be subdivided into two broad categories according to their different aims: imaging of brain anatomy (structural imaging), or of brain function (functional imaging). Structural imaging is used to examine the static outlines of brain structures in both physiological and pathological situations. Functional imaging, on the other hand, is used to gain knowledge on (1) which structures are activated during a specific cognitive task, at sensory and/or cognitive levels, (2) the interactions between the structures that are activated, and (3) the way the functional activation of the brain is reorganized in individuals affected by neurological diseases, strokes, or head injuries.

Generally speaking, the structural category of neuroimaging techniques includes two well-known neuroradiological techniques: computerized axial tomography (CAT) and magnetic resonance imaging (MRI). As far as brain imaging capacity is concerned, both are far superior to their forebear, the X-ray technique.

Functional imaging includes a wide range of techniques, which are listed here in increasing order of spatial and temporal resolution: (1) 2-deoxyglucose cerebral blood flow (2-deoxyglucose CBF), a forerunner of hemodynamic techniques rarely used nowadays; (2) single-photon emission computed tomography (SPECT); (3) positron emission tomography (PET); (4) functional magnetic resonance imaging (fMRI); (4) electroencephalography and event-related potentials (EEG–ERP); (5) magnetoencephalography (MEG); and last, but not the least, (6) microelectrode single-unit recording, which involves recording electrophysiological signals from inside or outside the membrane of a single neuron body by means of microelectrodes.

Although the categorization of neuroimaging techniques into the two aforementioned approaches is generally sound, it should be mentioned that all these techniques have some limitations and attempts are being made to overcome these. Some very recently devised techniques combine both structural and functional imaging information and cannot be classified into either category. A rather interesting example of these combined techniques is the so-called CAT–PET.
SPATIAL AND TEMPORAL RESOLUTION

The accuracy with which the imaging techniques are able to provide definite images of the anatomy of the centers of the central nervous system (CNS), and/or the activation of these centers, in order to be able to localize them reliably, is defined as spatial resolution. Conversely, the speed with which the techniques can keep on scanning the CNS anatomy and physiology, taking into account all intrinsic limitations, i.e., the minimum time that must necessarily pass between the collection of a measure of one CNS activation and the successive one, is described as temporal resolution.

Figure 1 is a graphical representation of an estimate of the normal spatial and temporal resolution for each of the imaging techniques mentioned above. The spatial resolution, expressed in millimeters, is reported on the ordinate axis; the temporal resolution—here indicated in seconds on a logarithmic scale—is depicted on the abscissa. The height and width of the forms with which the different techniques are represented in the figure indicate the known range of spatial and temporal resolutions, respectively, for each of the techniques. The increasing saturation of the gray hue of the different shapes represents the increasing degree of invasiveness of the techniques.

Structural techniques currently have the most accurate spatial resolution or, in other words, localization capacity. Both CAT and PET techniques have a spatial resolution that is vastly superior to that of previous techniques. Indeed, their spatial resolution has become so good that it is now in the order of millimeters.

FIGURE 1 Invasiveness, spatial resolution, and temporal resolution of the main imaging techniques used in humans to investigate function and structure of the brain. The different sizes of the shapes representing the different techniques vary as a function of the level of both spatial resolution (in millimeters) and temporal resolution (in seconds). Note that the increasing level of saturation of the gray color represents the increasing levels of invasiveness of the techniques.
In PET, for example, the activated parts of the brain selectively take up a radioactive tracer previously administered intravenously to a patient or healthy volunteer. The gamma rays deriving from the emission of positrons by these activated structures allow a functional map of cerebral activation to be built; as illustrated in Fig. 1, such a map has a precision ranging between about 2 and 5 mm. fMRI, on the other hand, can reflect structural variations caused by increased local blood flow and dilatation of cerebral tissues with a mean precision of 3 mm, although the range is from 2 to 4 mm.

Notwithstanding their high spatial resolution, none of the functional imaging techniques, with the exception of MEG, can provide functional images that are also accurate in temporal terms. In fact, the temporal resolution with which they can provide accurate images of ongoing functional activation of the brain is rather poor. This resolution can reach the order of a tenth of second (~100–150 msec) with the most technologically advanced type of fMRI—that is, 3 or 4 tesla echo-planar fMRI (or event-related fMRI)—but still remains in the order of seconds with less powerful equipment. The temporal resolution of PET is tens of seconds or even minutes. The significance of this technical limitation to research can readily be appreciated by considering that an action potential originating in the pyramidal motor neurones of the premotor cortex propagating along the efferent pathways takes about 150 msec to reach the muscle bundles of the forearm, causing flexion of the terminal phalanx of the index finger, in order, for example, to press a button for measuring reaction times. Or consider that we can identify an object that enters our visual field within a few hundreds of milliseconds (~180–220 msec). It is clear that the velocity with which the above-mentioned neural processes occur means that their subprocesses escape measurement techniques because of the interval between successive sampling.

Given that the final aim of research on the mind and brain should be to construct a model of functional relations between the pathways and centers of the brain from which mental life comes, besides simple localization of these to particular areas of the brain, it is important to have a temporal resolution of milliseconds for the processes involved. The only imaging techniques that have such a good temporal resolution are the techniques used systematically or on single cells that measure the electromagnetic activity of the brain directly. As illustrated by Fig. 1, the maximal temporal resolution, as well as spatial resolution, is provided by single-unit recordings. Thanks to these it is possible to carry out neurofunctional investigations with a temporal resolution below the order of milliseconds (<10^{-3}), and with a spatial resolution under 1 mm. It is, however, unthinkable to use this technique for functional imaging of the human brain because of its invasiveness; it would require neurosurgery to implant the microelectrodes.

Unlike single-unit recordings, scalp recordings of voltages (EEGs and ERPs) that mirror the intracranial currents originating from neuronal sources in the brain cortex, and spreading by volume conduction throughout the brain and the scalp, can be used as tools for human research. Indeed, while having the advantage of 1-msec temporal resolution, or quite close to this level, the recording method is completely noninvasive. However, because of its irregularities, the skull is not a homogeneous conductor. The volume currents that come in contact with the electrodes over the scalp are distorted by irregularities such that the technique does not have sufficient spatial resolution to be able to locate the real intracranial sources of the currents.

This difficulty translates into a spatial resolution that cannot be relied on for localization purposes. In the best cases, localization of the electric dipole ranges between a minimum of 6 mm and a maxi-
mum of 11 mm or even beyond, depending on a whole series of recording conditions and modeling parameters (see Fig. 1). Even then, there are some extreme cases, such as the so-called far-field potentials, in which the scalp site at which the largest signal is measured is actually far away from the source area; for example, sensory-evoked responses of the auditory cortex to unilateral stimuli, despite originating on the dorsolateral side of the contralateral brain hemisphere close to the ear, produce their largest amplitudes at the top of the scalp.

Although having the same temporal resolution as the EEG, magnetoencephalography is only minimally influenced by the nonuniform conductivity of the brain, skull, and scalp, and if the head is modeled using spherical geometry the recorded magnetic field can be considered completely independent of the conductivity of the head. Referring once again to Fig. 1 it can be seen that only MEG has high levels of both spatial and temporal resolution. In detail, the spatial resolution of this technique ranges from a minimum of 1.5 mm to a maximum of 4 mm for the cortical areas of the brain. Unfortunately, this resolution decreases dramatically to some centimeters for subcortical regions. This technique could, therefore, be the technique of choice for localizing activity in the superficial areas of the brain, i.e., the cerebral cortex, which is responsible for mental processes in general. Unfortunately, this technique is still too expensive to become as widely used as the ERPs.

In order to overcome the various limitations of each of the techniques presented here, strategies are being developed to use combined methods; for example, the images obtained by MRI, fMRI, or PET can be combined with those from microelectrodes, or those from MEG and ERPs. Combination methods can be based on a direct or an indirect approach. The former uses hemodynamic images to obtain a real structural basis of the estimates of functional activation acquired separately, whereas the latter involves parallel recording of these parameters in a single experimental paradigm. Although it is certainly true that the different approaches are very useful individually, only integration of the techniques with different spatial and temporal resolutions can provide truly valuable information on the neurofunctional mechanisms of mental processes, and on their temporal course of activation.

### INVASIVENESS

Techniques to investigate the function and structure of the nervous system can be classified as invasive, semiinvasive, and noninvasive. The difference between the invasive and semiinvasive techniques is that the former implies a surgical lesion (mechanical) and the latter involves a physicochemical stress (with radioopaque or radioactive substances).

Techniques that can be defined as noninvasive are MEG and EEG, both of which involve simple recordings of electrical potentials or natural magnetic fields produced by brain activity without experimentally introduced chemicostructural perturbations of the cerebral regions.

Semiinvasive techniques provide a means to observe dynamic and structural properties through images that are reconstructed on the basis of a principle of both active and passive detectability. In the first case, the products of rapidly metabolized compounds or radioactive substances with a short half-life are detected. The compounds are injected intravenously and, being distributed preferentially to certain regions of the brain, show in the various areas of the brain a differential distribution that is proportional to the state of activation of the area (PET, SPECT, and, when tracers are used, also fMRI and MRI). In the case of passive detection (e.g., CAT), the X radiations are delivered by the machine and hit the cerebral tissues ab externo (with the usual radiographic
principle). Even MRI and fMRI, without injection of markers, induce changes in cerebral or spinal structures. In fact, applying a magnetic field causes a change, albeit transitory, in the characteristics of the spatiotemporal molecular organization, with realignment of the electromagnetic dipoles of charged molecules.

Mechanically invasive techniques belong to the realm of functional neurosurgery; this involves extra- or intradural recordings, or even recordings from deep structures (in the case of therapeutic placement of stimulatory electrodes). These techniques obviously involve surgery on specific nervous tissue and perforation or opening of the skull.

Mechanical or physicochemical invasiveness implies a different degree of danger for the patient. Naturally this creates a boundary; the economic costs and benefits of the results of the diagnostic or surgical intervention must be compared to not carrying out the procedure. On average, given precise conditions and the noninstrumental diagnosis, the indication for an invasive intervention is highly controlled and justifiable.

Suggested Reading

**Single-Unit Recordings**


**Hemodynamic Functional Imaging**


**Electromagnetic Imaging**


Psychology Press, Taylor & Francis Group, Hove East Sussex, UK.


Combining Techniques


