CHAPTER 4

Methods in Neuropsychology

We turn now to a consideration of the most important methods in neuropsychology, many of which we have already touched on in our earlier discussions. The data generated by these diverse methods are the soil out of which fruitful hypotheses, illuminating experiments, and novel theories are generated. It is therefore very important to understand the methods that are the basis for the inferences that experiments generate. Like the evil genie in the fairy tale who grants only the precise wish requesters ask for and not the wish they think they are making, nature answers precisely and only the question defined by the methodology of a particular experiment. This is not always the question we think we are asking.

In what follows we will consider (a) methods used to explore the nervous system's structures and its pathways of interconnection; (b) methods that measure functional aspects of the nervous system, such as level of glucose utilization or electrical activity; (c) lesion methods; (d) the study of patients who have undergone split-brain surgery; (e) the sodium amobarbital test; (f) the study of behavioral and cognitive abnormalities in people without detectable brain lesions; and (g) the study of normal human subjects.

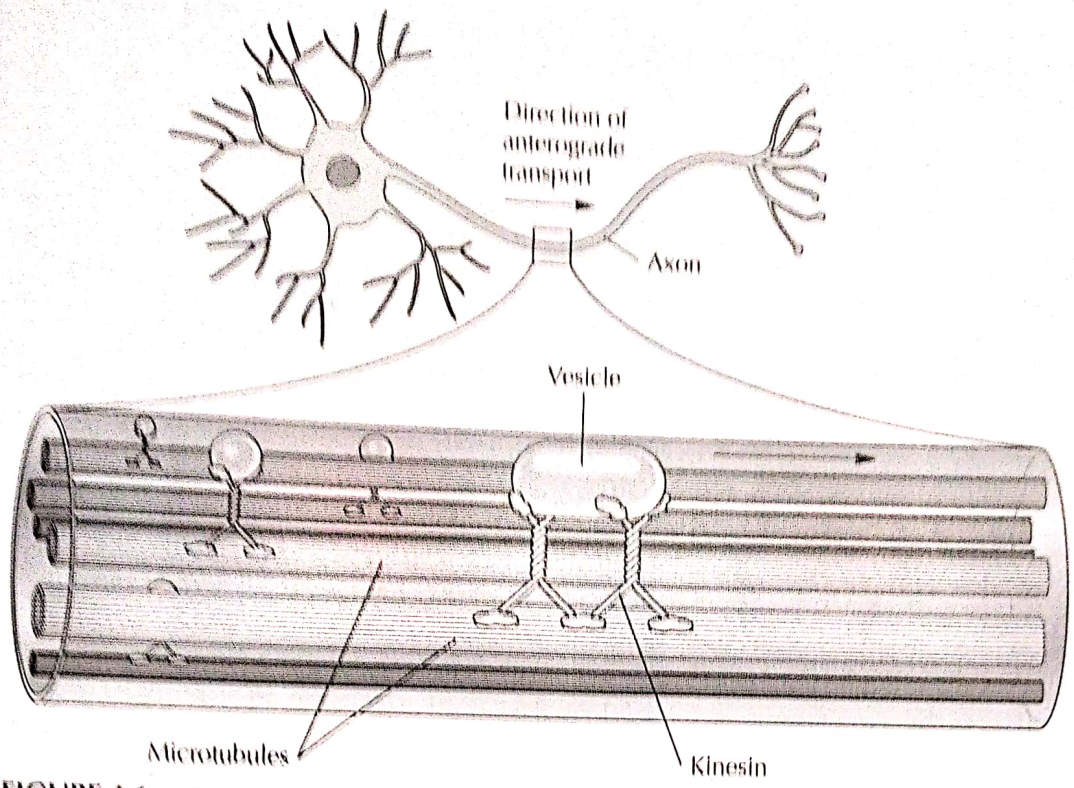


FIGURE 4.1 Molecules, such as proteins, are enclosed in vesicles and transported from their site of synthesis in the soma (cell body) to the axon terminal. The protein kinesin "walks" the vesicle down the microtubules. *(Adapted from Bear, Connors, & Paradiso, 1996, p. 38)*

ANATOMICAL METHODS

Identifying Anatomical Connections

We can identify structures within the nervous system in terms of their gross appearance. But in attempting to understand how the brain works, it is obviously useful to know as much as possible about the interconnections between different structures. Where a particular structure sends its efferents (output) and from where it receives its afferents (input) provide illuminating hints regarding the processes that it is mediating. In subsequent chapters we will see how useful information about anatomical connections can be in our attempts to understand brain-behavior relationships.

One way of determining the connections between structures is to trace the path of large **fiber tracts,** bundles of neurons stretching from one area of the nervous system to another. There are, however, obvious limitations to this method; small fiber tracts will be undetected, and the precise origin and destination of those tracts that are visible will not be known. Fortunately there are some highly revealing methods that get around these problems.

TECHNIQUES USING AXOPLASMIC TRANSPORT

Axoplasmic transport is an active process whereby substances within a neuron are moved across its length. There are two types of axoplasmic transport. **Anterograde transport** conveys materials that are synthesized only in the cell body of the neuron, such as proteins, to the **axon terminal** (the transmitting end of the neuron). This process involves the storage of these materials in membrane-bound spherical spaces called **vesicles,** which then move down the length of the axon along **microtubules** (Figure 4.1). When a radioactive amino acid, such as proline, is injected into a particular region of the brain, it is taken up by the cell bodies of neurons in that region and then transported

to the axon terminals of those neurons. The animal is then sacrificed, and sections of the brain are placed next to a photographic plate so that the radioactivity within them exposes the film. This technique, known as autoradiography, detects the brain regions or regions to which the injected region projects. There are two types of anterograde transport, slow (1–10 mm/day) and fast (up to 1,000 mm/day).

The second type of axoplasmic transport is called **retrograde transport**, and, as its name suggests, it moves substances in the opposite direction from that of anterograde transport, from the axon terminal to the cell body. The function of this direction of transport is not completely understood, but it is thought to provide a mechanism whereby information about the state of the axon terminal is communicated to the cell body, a kind of nervous system within the neuron, if you will. It so happens that there is an enzyme with the unlikely name of horseradish peroxidase (HRP) that is selectively taken up by axon terminals. It is then carried to the cell body by retrograde transport and can be visualized there. The horseradish peroxidase method thus complements methods utilizing anterograde transport by revealing the region or regions projecting to the injected area.

BIOCHEMICAL MICROARCHITECTURE In our discussion of cortical visual areas in chapter 5 we will see that subregions within these areas can be defined in terms of their affinity for particular stains, cytochrome oxidase being one. Cytochrome oxidase is an enzyme that selectively binds to regions of relatively high metabolic activity; it therefore can serve to identify these regions. As we will see in chapter 5, regions defined by such a biochemical method can have distinctive physiological and anatomical characteristics, and the identification of these areas can therefore contribute to our understanding of the functional organization of the brain.

It is also possible, using sophisticated techniques, to stain tissue for the presence of particular neurotransmitters, the molecules released by axon terminals that activate neighboring neurons (see chapter 3). These techniques yield a description of major neurotransmitter pathways and systems within the brain.

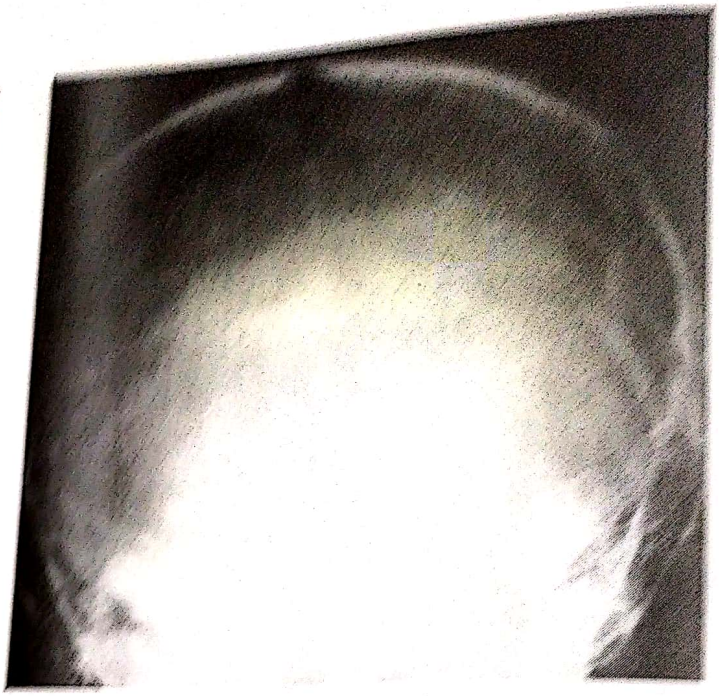
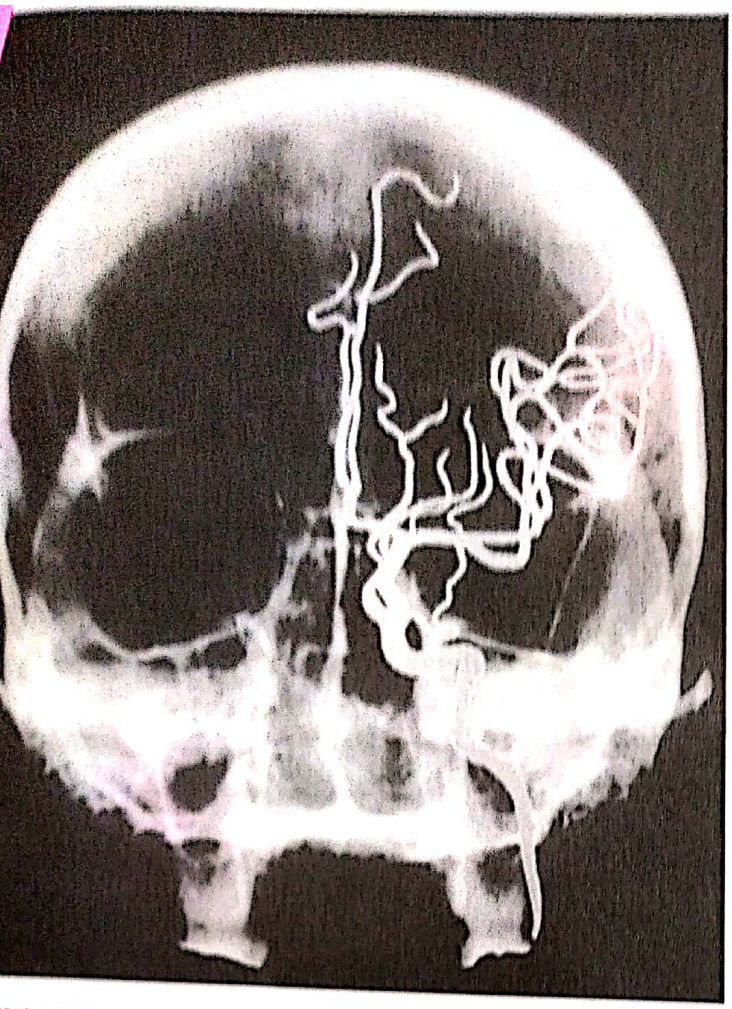


FIGURE 4.2 *A radiograph of the skull. Because X rays are absorbed by bones and other tissues that absorb calcium, all structures appear light, and the differentiation of gray and white matter is not possible. (From Kandel et al., 1995, p. 73)*

Structural Imaging Methods

There are a number of imaging techniques that can provide information about the structure of cerebral tissue. In addition, some imaging techniques provide a measure of the metabolic activity in different regions of the living brain; these techniques will be discussed in the next section. This is a rapidly developing area and one that has generated a great deal of excitement in recent years. Let us begin, however, with some of the more conventional techniques.

SKULL X RAY The first radiological investigation of the brain consisted of simply x-raying the head (Figure 4.2). Although this reveals a good deal about the integrity of the skull (e.g., presence of fractures, etc.), it reveals little about the status of the brain tissue within. This is because the density of brain tissue does not vary greatly, so different parts of the brain absorb about the same quantity of X rays. This situation is analogous to shining a flashlight through a glass of water; no shadows emerge to hint at its inner



IGURE 4.3 An angiogram in frontal view. The radio-aque dye injected into the internal carotid artery reveals he anterior and middle cerebral arteries. *(From Kandel et al., 995, p. 73)*

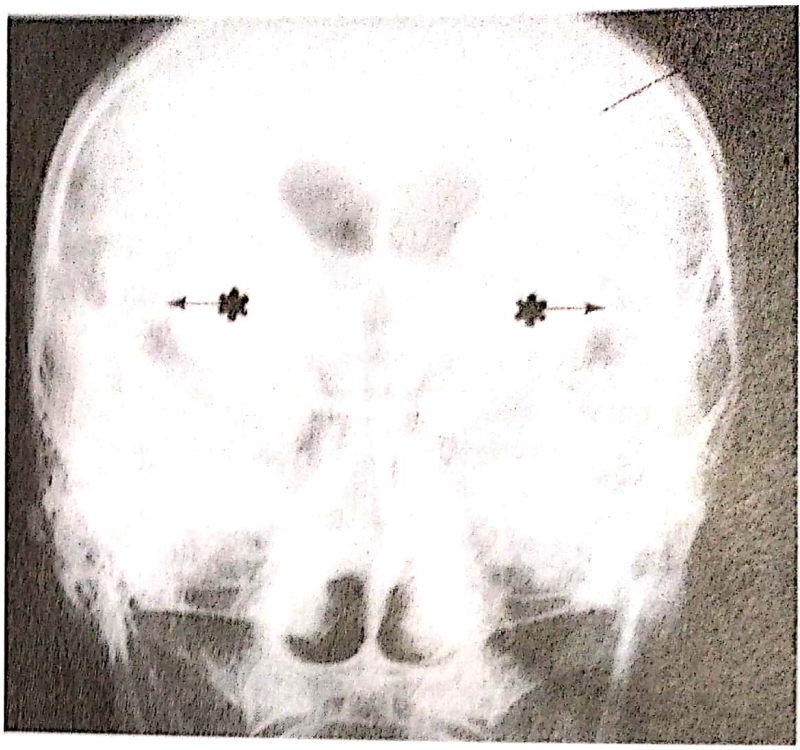


FIGURE 4.4 A pneumoencephalogram. The arrows with asterisks indicate air in the Sylvian fissure. *(From Kandel et al., 1995, p. 73)*

of the vasculature. The pneumoencephalogram, on the other hand, attempts to circumvent the virtually homogeneous density of the brain by draining the cerebral ventricles of cerebrospinal fluid and replacing it with air (Figure 4.4). This makes the ventricles less dense than the surrounding tissue, permitting detec-

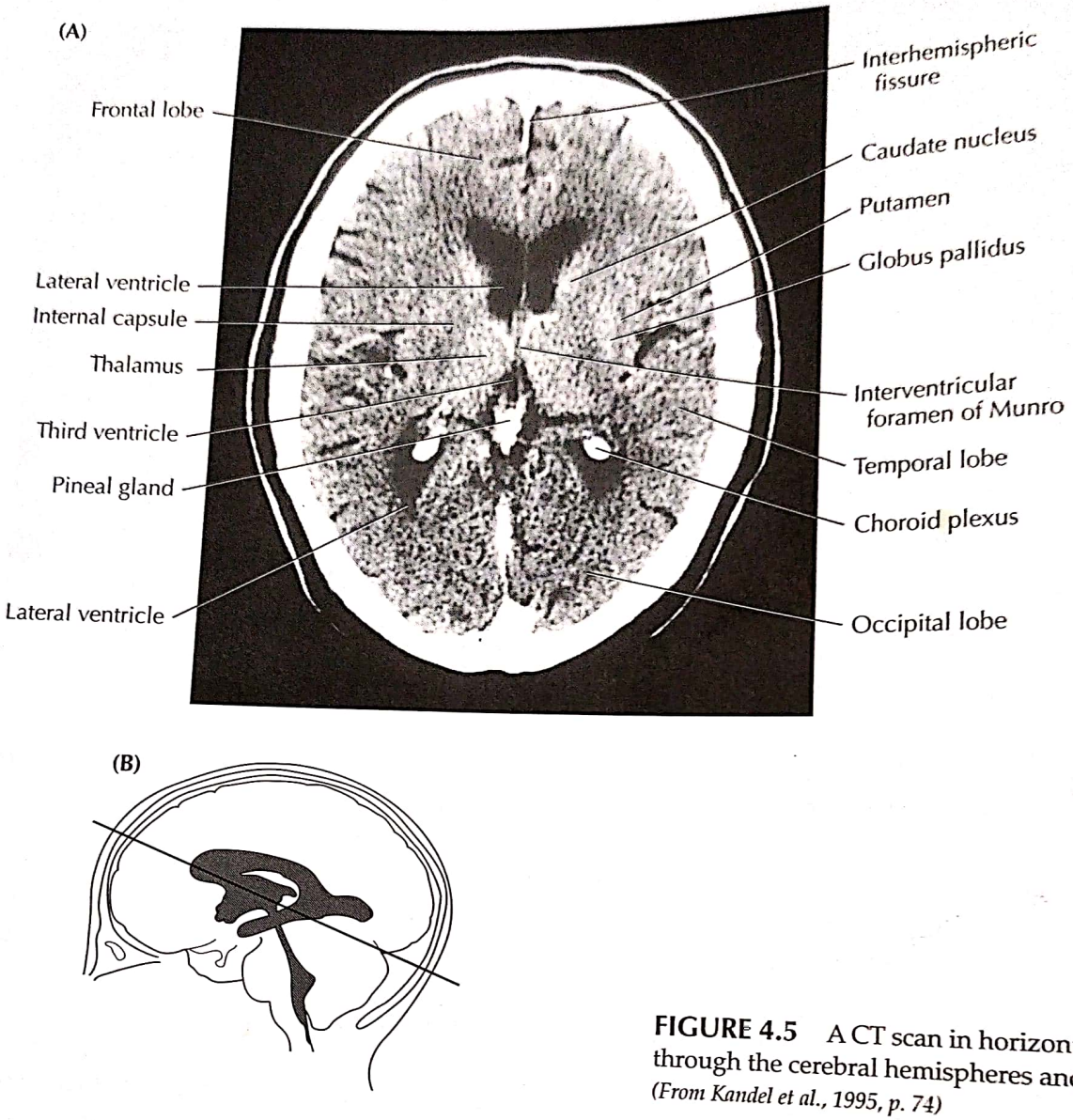


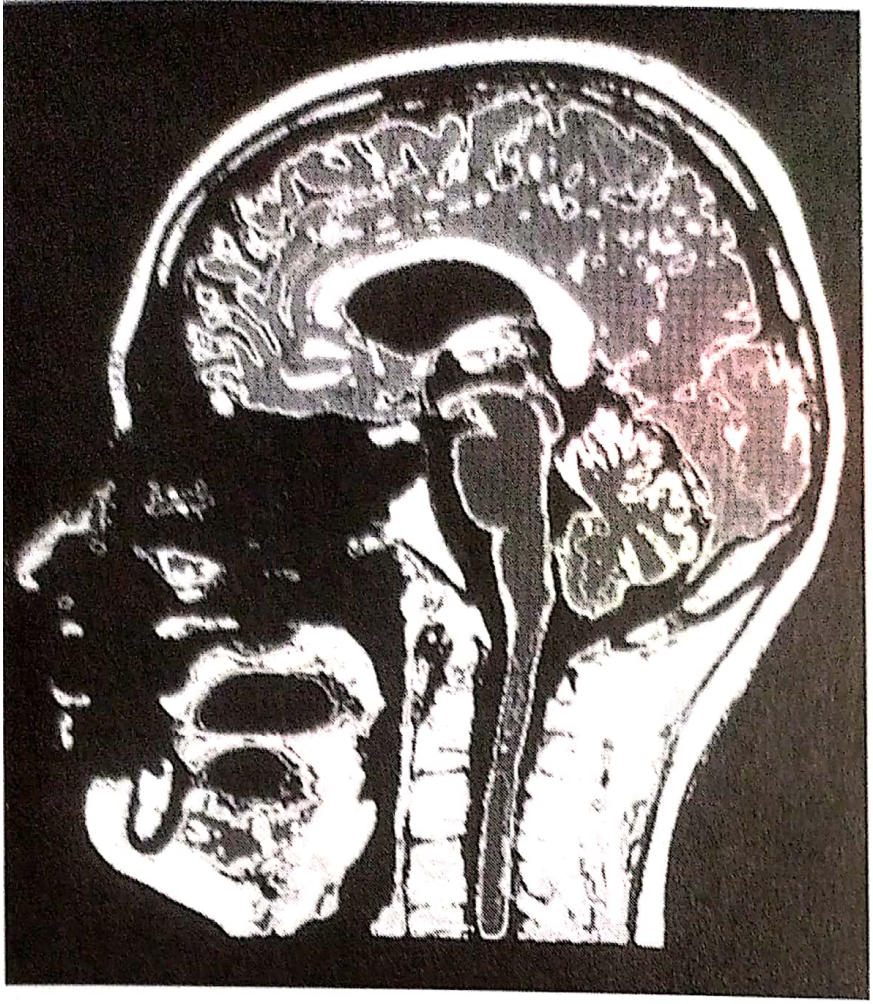
FIGURE 4.5 A CT scan in horizontal section passing through the cerebral hemispheres and diencephalon. *(From Kandel et al., 1995, p. 74)*

ized neuroradiology when it was introduced in the early 1970s.

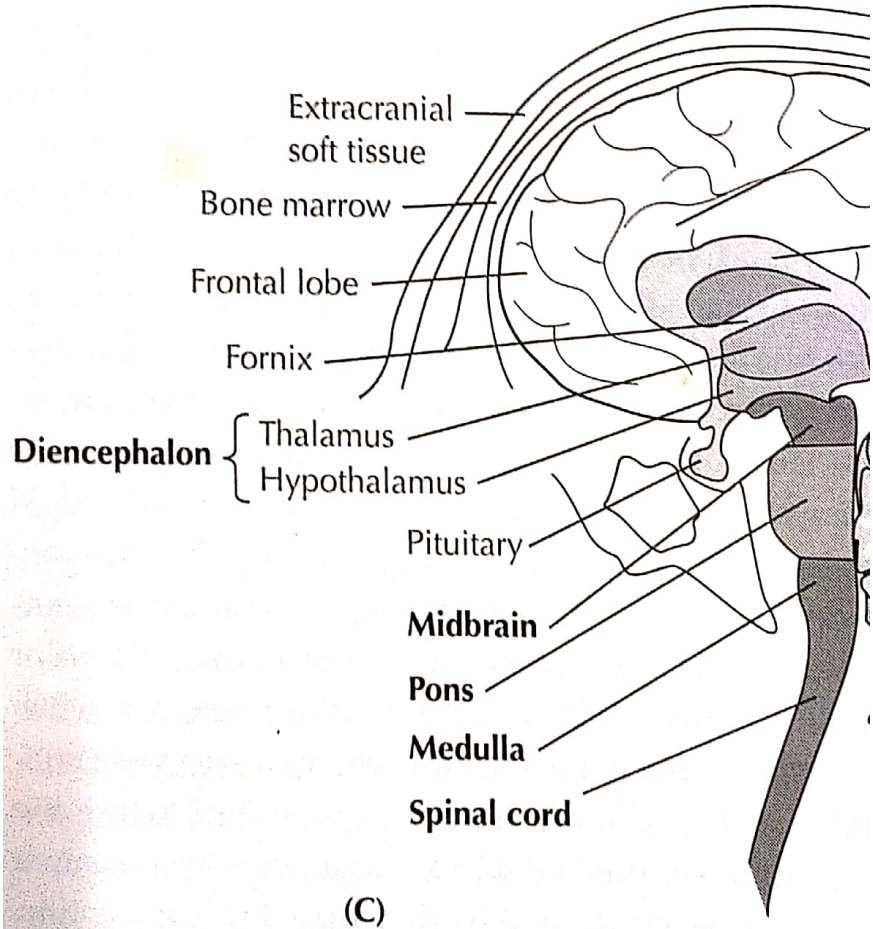
MAGNETIC RESONANCE IMAGING (MRI) This most recent development in imaging, **magnetic resonance imaging (MRI),** takes advantage of certain physical properties of hydrogen atoms. In particular, hydrogen atoms behave like spinning bar magnets in a magnetic field, and, in a high-magnitude magnetic field, they will line up in parallel. If radio waves are then bounced across these atoms, the waves will assume a characteristic pattern that is a function of the number of atoms present, which, in turn, is a function of the density of the tissue. We have then a measure of tissue density that makes possible the formation of images that are far more sensitive to variations in tissue density than CT. The resolution of MRI is also significantly higher than that of CT (Figure 4.6).

METHODS MEASURING FUNCTION

The imaging techniques discussed so far reveal the structure of the brain. In this section we review methods that measure the brain's metabolic activity (functional imaging methods) or its electrical activity (neurophysiological methods).



(A)



(C)

FIGURE 4.6 *(A)* An MRI scan of a midsagittal section th hemispheres, corpus callosum, brain stem, and spinal cord the detail visible in the MRI scan. *(From Kandel et al., 1995, p. 8(*

Functional Imaging Methods

REGIONAL CEREBRAL BLOOD FLOW (rCBF) The first reliable imaging method to measure cerebral functional activity was **regional cerebral blood flow (rCBF).** In this method a radioactive isotope is inhaled or injected into the blood, and its distribution is then measured using a bank of sensors arranged systematically near the surface of the skull. The radioactive label thus is a marker for blood flow, which in turn is a correlate of brain metabolic activity. Using this method, it is in principle possible to visualize those brain areas that are most metabolically active during a particular activity. For example, when a subject is exposed to a visual stimulus, the occipital lobes in the posterior cortex (site of visual processing) show increased blood flow. Analogously, increased blood flow is seen in the motor cortex during movement and in the auditory cortex when a subject is exposed to sound. A subject who is speaking shows increased blood flow in Broca's area, and a subject attending to the meaning of words shows increased blood flow in Wernicke's area.

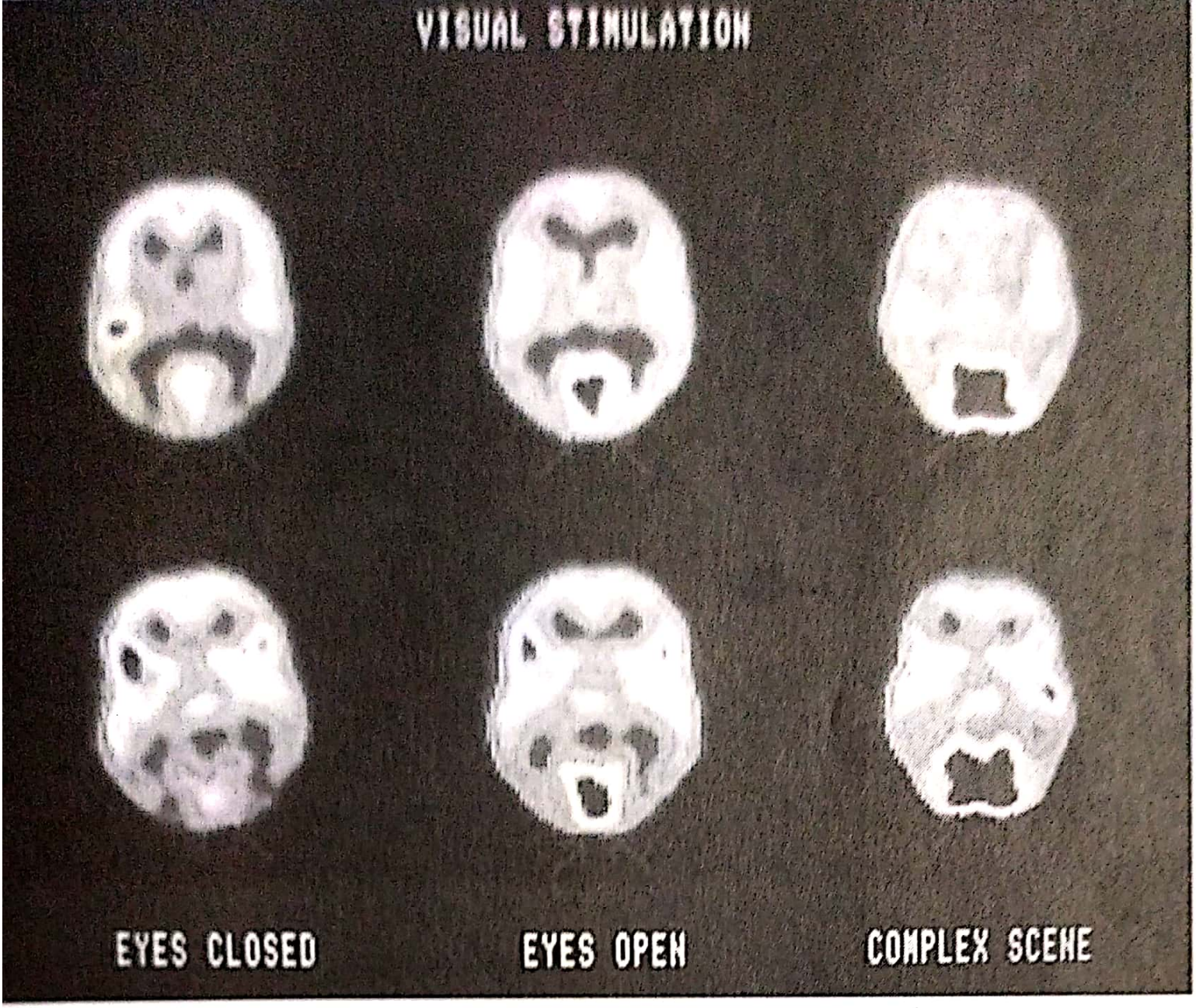
POSITRON EMISSION TOMOGRAPHY (PET) Relative metabolic activity in the living animal or human can be measured by **positron emission tomography (PET).** For this reason PET has been called *in vivo* functional autoradiography. One of its advantages is that it affords great versatility with regard to the atom or molecule being labeled.

The technology involved in PET is rather complicated, but, briefly stated, an unstable radioactive atom such as ^{15}O is injected into the subject. Within the brain this atom emits a positron, the antimatter equivalent of an electron. The positron travels a few millimeters before it loses kinetic energy and comes to rest. When this happens, the positron is attracted to a neighboring electron and, as they come together, they annihilate each other, releasing intense energy and two annihilation photons. These two photons move the site of their creation in opposite directions at the speed of light. A ring of detectors surrounds the patient's head. These detectors are electronically coupled so that they record a radioactive event only when two detectors are struck simultaneously. This arrangement makes possible the precise measurement of the relative concentration of the labeled marker in different areas of the brain.

Using this technique, it can be shown that the primary sensory areas exhibit more metabolic activity during periods of stimulation. For example, when the eyes are open, the posterior occipital cortex shows a higher level of metabolic activity than when they are closed. In addition, a complex visual scene causes a different pattern of stimulation than either simple white light or the eyes-closed condition (Figure 4.7). Suppose, however, that we want to determine the pattern of brain activity associated with a complex cognitive process such as generating a verb that conveys the function of a heard noun (e.g., "cook" when the word "pot" is heard). This situation is complicated by the fact that many regions of the brain may be active during this task that are not directly related to word generation per se. These might include the auditory cortex, Wernicke's area, and Broca's area, among others.

Efforts to surmount this problem have centered on the **subtraction method,** a method developed by F. C. Donders in the 19th century and used extensively by Wilhelm Wundt and other structuralist psychologists, mostly in reaction-time experiments, during the early years of experimental psychology. When applied to PET studies, this method attempts to find a control task that is identical to the task under study except for one critical component. The record obtained during the control task is then subtracted from that obtained during the experimental task. We will see many examples of the use of the subtraction method in later discussions. For example, in chapter 5 we consider a PET study that attempts to identify in humans the area in the occipital cortex specialized for color vision. In this study the activity levels obtained when a subject viewed a black-and-white pattern were subtracted from the activity levels obtained while the same subject viewed a color pattern with the same spatial configuration. In that case the subtraction method yielded a rather precise localization of an area presumed to be specialized for color vision.

SINGLE PHOTON EMISSION COMPUTERIZED TOMOGRAPHY (SPECT) Another tech... photon emission ...



nakes use of the fact that certain commercially avail-
ble tracers emit photons; this permits measurement
f relative metabolic activity in a manner roughly
nalogous to PET. The advantage of this method is
hat these tracers are far less expensive than the iso-
opes used in PET, which, with extremely short half-
ives, must be created in an on-site cyclotron. The
egative characteristic of SPECT is that it has less
patial resolution than PET.

UNCTIONAL MAGNETIC RESONANCE IMAG-

by fMRI. This techniq
quiring injection of a
risk to the patient and
In addition, because a
the same time as the
racy of correlation be
afforded by this meth
fMRI has higher resol

PROBLEMS IN INT
IMAGING STUDIES

the subtraction method as an experimental paradigm in psychology, despite its prolific use by structural psychologists for several decades following its introduction by Donders.

To illustrate this problem, consider the study, which we discussed earlier in the section on PET, that attempted to identify the area specialized for color perception in human subjects. Underlying the use of the subtraction method in that experiment is the assumption that viewing the color pattern results in the same brain activity as that involved in the processing of form in the black-and-white pattern plus activity specific to color perception. It can be appreciated that this may in fact not be the case; the processing of form in the presence of color may involve brain structures and brain activity very different from the processing of form in the black-and-white condition.

A second problem in the interpretation of functional imaging studies arises from the fact that the time course of events that these methods directly measure is slow (on the order of minutes), whereas the neural events inferred from these direct measures take place over milliseconds. The low time resolution of these procedures raises the question of the extent to which these measures are assessing relatively long-term brain states rather than the specific correlates of distinct psychological processes.

Third, despite the clear correlation between sensory stimulation in a given modality and the activity level of cortical areas initially processing that information, an increase in the activity of an area during a *complex* task does not necessarily mean that that area is critical for the function in question. The change in activity may be an indirect effect of change in some other area or areas. This is a particularly important consideration when assessing the metabolic correlates of a relatively long-term state such as a psychiatric disorder. Abnormal metabolism in a given region does not necessarily indicate that the abnormality in that region is the cause of the disorder. The observed abnormality may instead be an epiphenomenon, a correlate of the effects of a primary abnormality in an entirely different area. Thus, although PET studies have provided promising insights into the cerebral metabolic correlates of psychological processes (and are likely to be even more useful in the future, as the methodology is refined), one must interpret findings using this method with particular caution.

Neurophysiological Methods

In contrast to functional imaging methods, neurophysiological methods, which measure brain electrical activity, have the advantage of measuring neural events more directly and with a much higher time resolution. We consider several such methods in this section.

SINGLE-CELL RECORDING **Single-cell recording** involves inserting an exceedingly small diameter electrode into a single neuron and then measuring changes in the cell's electrical potential. This results in a record of the cell's activity, its frequency of firing. As we will discuss in more detail in later chapters, when this activity is in response to sensory stimulation, we define a given cell's **receptive field** as that stimulus which causes the cell to fire maximally or minimally. Single-cell recording thus measures the activity of an individual cell at a particular time and within a particular environmental and/or behavioral context.

Although this approach has the disadvantage of assessing only a small proportion of cells in any given area of the brain, data derived from this method have been enormously illuminating. To take just one example, it is this method that revealed the presence of specialization and localization of sensory/perceptual processing within what had traditionally been known as association cortex, cortical areas in which such specialization and localization were thought to be completely absent. This discovery has caused some radical revisions in our views of cortical processing, which we discuss at greater length in chapter 5.

ELECTROENCEPHALOGRAPHY (EEG) The **electroencephalogram (EEG),** invented by Hans Berger in the 1920s, is a measure of brain electrical activity derived from a bank of electrodes positioned on the scalp. Since the electrodes have the skull and other tissues between them and the brain, the signal is weak and represents the collective activity of a diffuse collection of neurons. Thus, EEG is a bit like putting a stethoscope up to the outer wall of a gymnasium and listening to the fluctuations of volume

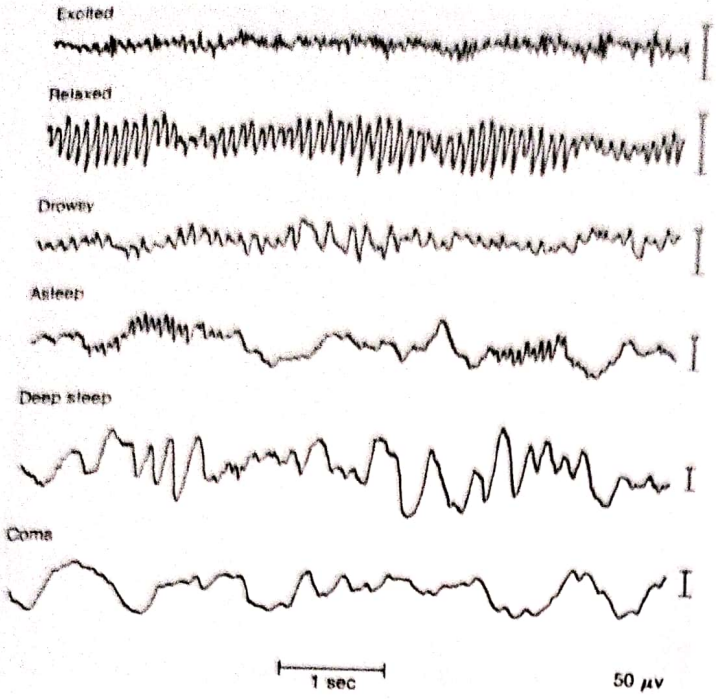


FIGURE 4.8 EEG patterns during various behavioral states in humans. *(From Penfield & Jaspers, 1954 [in Kolb & Whishaw, 1996, p. 78])*

from the crowd within. This technique is useful for the detection and localization of seizure activity in the brain, and it has also been used to study such phenomena as sleep and the effect of drugs on brain activity. Some patterns of EEG activity characteristic of specific sleep stages and levels of consciousness are shown in Figure 4.8. Recently, there has been growing interest in using computerized methods to analyze EEG activity. These promising methods might make it possible to better quantify and localize EEG activity and may contribute to the further understanding of brain-behavior relationships.

EVENT-RELATED POTENTIALS (ERPs) **Event-related potentials (ERPs)** are measurements of the brief change in EEG activity that occurs in a particular area of cortex after a specific event, such as the pattern of activity in the auditory cortex after the presentation of a tone. Investigators have also attempted to detect ERPs associated with more complex and differentiated stimuli, such as words and faces. Because the effect of such stimuli is difficult to detect, due to background neural activity, investigators using ERPs expose their subjects to repeated stimulus presentations and then compute the average response.

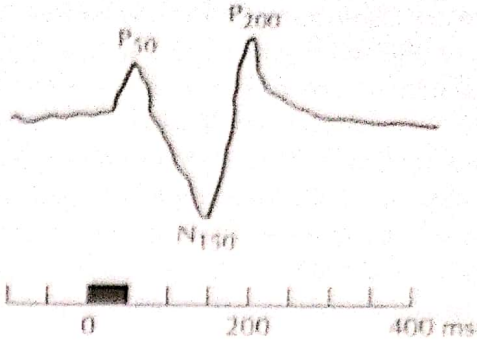


FIGURE 4.9 An ERP in the auditory cortex in response to auditory stimulation (blackened area). Note the two positive waves and the single negative wave, designated with their latency in milliseconds (ms).

Typically, an ERP takes the form of a series of positive and negative waves that are designated P and N, respectively. Different positive and negative waves are often identified with the time in milliseconds between the onset of the stimulus and the peak's appearance (Figure 4.9). For example, a particular wave might be designated P_{150} or N_{300}. This technique is used clinically to assess the integrity of areas of the brain involved in a particular sensory modality, such as vision. For example, the response of brain areas involved in vision to a flashing light might be assessed. When used in this way, this method is sometimes referred to as **evoked potential.**

ELECTROCORTICOGRAPHY (ECo) **Electrocorticography (ECo)** involves stimulating the exposed cortex of a patient during surgery with a low-voltage electrode. This is essentially a refinement of the procedure utilized by Fritsch and Hitzig in their discovery of the motor cortex in dogs in 1870. The American surgeon R. Bartholow first reported its use with humans in 1874, but the earliest systematic use of this procedure as a method for understanding brain-behavior relationships was the work of Wilder Penfield and his colleagues at the Montreal Neurological Institute. They used the procedure to identify specific areas of the cortex by assessing the functional effect of stimulation. This was necessary to allow Penfield to carry out a specially developed neurosurgical

procedure for the relief of seizures. We must digress briefly to explain the procedure.

Most patients with cerebral seizures have reasonably good control when they use an appropriate anticonvulsant medication; this is one of the success stories of modern clinical pharmacology. Unfortunately, however, about 20% of patients are unable to achieve good control of their seizures even after many years of trials on all available medications. These patients may have 30 or more seizures each day, severely compromising the quality of their life and perhaps even being life-threatening.

Of those patients who cannot achieve significant help from available medications, about half benefit from the surgical procedure developed by Penfield. These are patients whose seizure focus (area from which the seizures originate) is in an area of cortex that can be surgically removed without producing an impairment worse than the seizure disorder. (Removing tissue from one of the language areas would, for example, produce such an impairment.) The 50% or so of patients with pharmacologically intractable epilepsy who do not benefit from this procedure are those with a seizure focus in one of the functionally critical cortical areas or those with seizures that originate in the brain stem. Using a range of refined assessment techniques (including electroencephalography, various radiological and other imaging methods, and neuropsychological assessment), it is possible to determine whether a particular patient has a cortical seizure focus and, if so, where in the cortex it is located.

Once it is determined that a candidate for this procedure has seizures that originate from a cortical focus and once the location of that focus is identified, the patient is brought to surgery to remove the epileptogenic (seizure-causing) area. When the cortex is exposed, however, the surgeon does not see the neat and tidy pattern of sulci and gyri typically depicted in neuroanatomy textbooks. Instead, what appears is a rich vasculature and membrane that overlie the cortex, rendering its pattern unrecognizable to even the most experienced neurosurgeon. It is at this point that cortical stimulation becomes indispensable. By it, the surgeon can identify sensory, motor, and language areas based on the patient's response to stimulation. The patient must be awake to participate

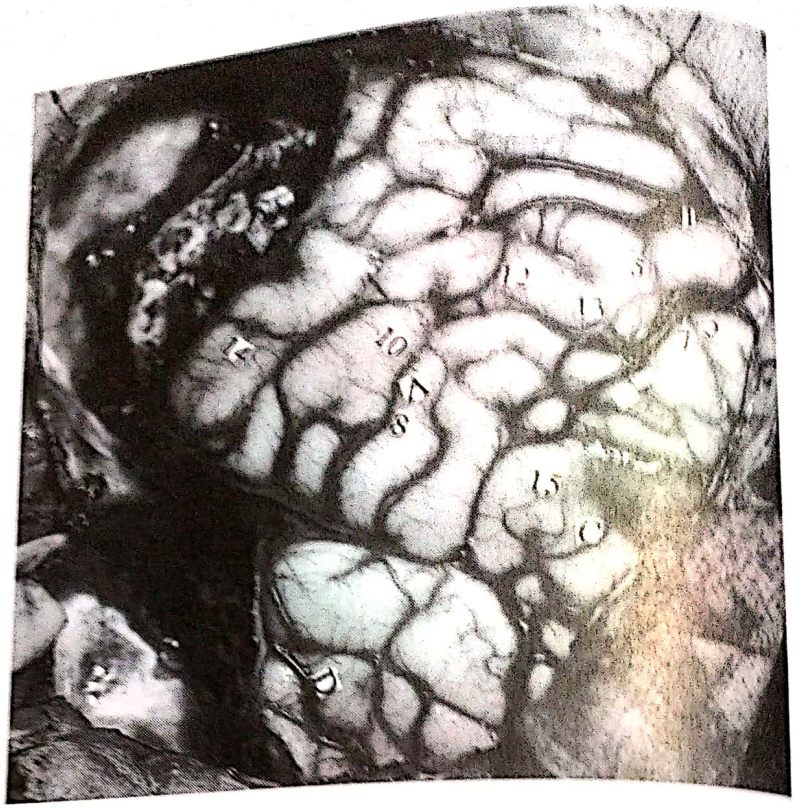


FIGURE 4.10 Photograph of a left frontal and temporal lobectomy at the time of surgery. The numbers indicate responses to electrical stimulation: for example, *14*, saying the months of the year interrupted; *15*, mistake in saying the days of the week forward, corrected after withdrawal of electrode. *(From Rasmussen & Milner, 1975, p. 241)*

in this procedure; the procedure is therefore performed under local anesthetic. Thus, if the surgeon's stimulating electrode elicits feeling in the arm, it may be inferred that the sensory cortex is being stimulated. Similarly, if a patient responds with a twitch of the hand, this identifies the motor cortex as the area of stimulation. Language areas can also be mapped out because stimulation to either will interrupt speech that is in progress (Figure 4.10).

Using this technique, the surgeon can identify major landmarks on the cortical surface and thereby find his or her bearings so that the previously identified epileptogenic area of cortex can be removed. As we will see, much can be learned about the brain from this technique, including the topographical organization (mapping of the body surface) of the motor and somatosensory cortices and the extent of the language areas. Perhaps the best-known result of this work is Penfield's report that the stimulation of [illegible] cortical areas produced [illegible]

will have more to say about this and other work using this technique in subsequent chapters.

MAGNETOENCEPHALOGRAPHY (MEG) A new technique, **magnetoencephalography (MEG)**, also called magnetic source imaging, measures the small magnetic fields generated by the electrical currents of neurons. This technique appears to be promising.

In closing this section, we should note that advances in our understanding are most likely to be achieved through a combination of structural methods and functional methods. For example, those investigators using functional imaging methods (e.g., rCBF, PET, fMRI) are keenly aware of the need to more precisely localize areas of modified activity. This can be achieved by using concurrent measures of structure, such as MRI. In addition, these same investigators, aware of the problems inherent in the slow time course of their functional imaging techniques, are attempting to surmount this problem by using concurrent electrophysiological measures that have relatively rapid time resolution, such as EEG and MEG.

LESION METHODS

We have already seen how illuminating the study of the behavioral and cognitive effects of brain lesions—damage to the brain from whatever cause—can be for an understanding of how the brain works. The basic strategy in lesion studies with humans and with other animals is the same: the investigation of the effect of damage to a particular area. In lesion studies with lower animals, however, investigators can study the effects of precisely localized lesions. This allows for the explicit testing of hypotheses. In contrast, lesion studies in humans necessarily concern themselves with the effect of lesions that have already occurred through disease or trauma.

Despite this disadvantage, studies of lesions in humans have the advantage of allowing the assessment of functions that are specifically human or at least more developed in humans, such as language, problem solving, and planning. In addition, the effects of lesions in humans are sometimes more discernible because patients may be able to provide a phenomenological account of their altered experience. This is poignantly seen in a case study described by Oliver Sacks[1] of a painter with achromatopsia, color blindness due to cortical lesion. Sacks's patient complained despairingly about his achromatic world. Interestingly, because wavelength discrimination is retained in achromatopsia, the condition would be difficult to detect in other animals. Unless some specific experimental manipulations are employed, animals could perform discrimination learning tasks using their intact wavelength discrimination capacity. They would be unable to tell us about catastrophic change in their experience of color.

Dissociation of Function

There are two fundamental (and related) ways in which lesion methods (and other neuropsychological methods, for that matter) further our knowledge: by advancing analysis of the components of cognition and by providing evidence of localization of function. To explain, we must elaborate on a concept we have already mentioned: **dissociation of function.** This concept has at least two meanings. On the behavioral/cognitive level (knowing nothing about the particular lesion involved) dissociation of function denotes the finding that performance on one task is impaired while performance on a second is not. It is in this sense that functions or processes are said to be dissociable, or separable. This dissociation of function may be reciprocal: In some individuals function A is found to be impaired and B is not, whereas in other cases function B is impaired and A is not. On the other hand, it may not be reciprocal: In some instances function A is found to be impaired and B is not, but in no cases is impairment in function B seen

1. Oliver Sacks is a neurologist who has become widely known for his well-written case studies of patients with striking neurological and neuropsychological symptoms. He writes in a powerfully descriptive style that poignantly conveys a vivid impression of the disorders he studies. In addition, he possesses a broadly humanistic perspective from which he attempts to address all facets of neuropsychological impairment and to draw implications from these disorders for an understanding of the human condition in general.

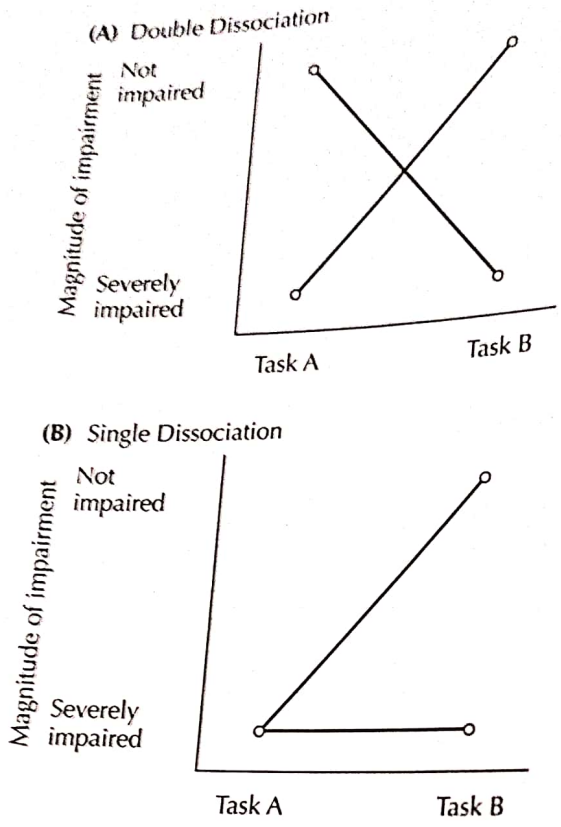


FIGURE 4.11 Patterns of impairment in *(A)* double dissociation and *(B)* single dissociation. Each line depicts the pattern of performance of one individual or group of individuals. *(From McCarthy & Warrington, 1990, p. 19)*

without impairment in function A. The first instance is referred to as **double dissociation,** and the second as **single dissociation** (Figure 4.11).

To take a simple example, deafness and blindness are doubly dissociable. Looking at a number of different cases, we find instances of one impairment in the absence of the other (although there are, of course, also cases in which they both are found). Similarly, Broca's aphasia and Wernicke's aphasia are doubly dissociable. In contrast, the inability to read visual material and blindness are singly dissociable. The inability to read may be seen in the presence of normal vision, but the ability to read visually presented words is not found together with blindness. To take another example, impaired ability to coordinate the fluent production of speech in Broca's aphasia and paralysis of the vocal musculature are singly dissociable. Impairment in fluent speech productio may be seen in the absence of impairment in mov ment of the vocal musculature (Broca's aphasia), b preservation of fluent speech production is not se when the vocal musculature is paralyzed.

Interpretation of Single and Double Dissociation

If we consider the inferences that can be drawn fr these two types of dissociation, we find that dou dissociation provides evidence that two functions relatively separate or independent (e.g., audition vision; fluent speech and language comprehensio Single dissociation, on the other hand, indicates the two functions are separate to some degree that one of them is necessary for the other. This s gests a kind of hierarchical relationship between two (e.g., the capacity to see words is necessary reading visual material; the capacity to move vocal musculature is necessary for fluent speech).

Of course, in the world of data, all is not so cl cut. The person with impaired visual acuity wh not totally blind can nevertheless read, though rapidly. The person with partial paralysis of the v musculature still produces comprehensible spe though slow and slurred. But this too is informa it tells us that although the first function may prerequisite for the second, that second functi nevertheless relatively separate. This may be firmed as we assess the second function by byp ing the impaired first function. Thus we find people with acquired blindness are able to raised letters that are sensed by the fingers and t with completely paralyzed speech musculatur able to express themselves linguistically by wri

Associated Impairments

Just as dissociation of function indicates that the tions in question are to some degree separate an dependent, so the consistent finding of associ (consistent co-occurrence of two or more impairm suggests that the behavioral or cognitive in question are a

and fluent but disrupted verbal output ("word salad") occur together in Wernicke's aphasia. This fact suggests that the disruption of a single underlying process is responsible for both impairments.

Dissociations as a Window on the Structure of Cognition and on Localization of Function

So far we have been talking as if we knew nothing about the lesions producing the impairments we are studying. This is often in fact the case, as, for example, in the study of children with dyslexia. It can be seen that if dissociations are found, we are in a position to understand something new about the nature of cognition, whether or not we know anything new about localization of function. In this way these methods contribute to an understanding of cognition, without necessarily revealing the regions of the brain mediating these processes. If we do have knowledge of the area in the brain that, when damaged, produces the impairment in question, this adds an additional dimension to our inquiry. Not only do we have the basis for making inferences about the structure of cognition, we also are in a position to say something about what parts of the brain are necessary for the mediation of certain functions. Dissociation that is informative in the context of localization of function takes one of two general forms. In single dissociation, a lesion in region X produces an impairment on task A but not task B, whereas a lesion in region Y does not produce an impairment in either task. In double dissociation, a lesion in region X produces impairment in task A but not impairment in task B, and a lesion in region Y produces impairment in task B but not task A.[2] Figure 4.12 illustrates these two forms of dissociation.

The finding of a single or a double dissociation is highly informative. It tells us that a particular observed impairment resulting from a specific lesion is not due to generalized, nonspecific brain dysfunction because the second lesion in another locatio does not produce the impairment. It also tells us th the lesion in question does not produce impairme in all tasks because relatively good performance seen in the second task. Taken together, such findin provide important information about the relatio ship between particular brain regions and speci functions. It should be noted that a dissociation do not require completely normal performance on ce tain tasks. What is central to this method is the pa tern of relative preservation and relative impairme

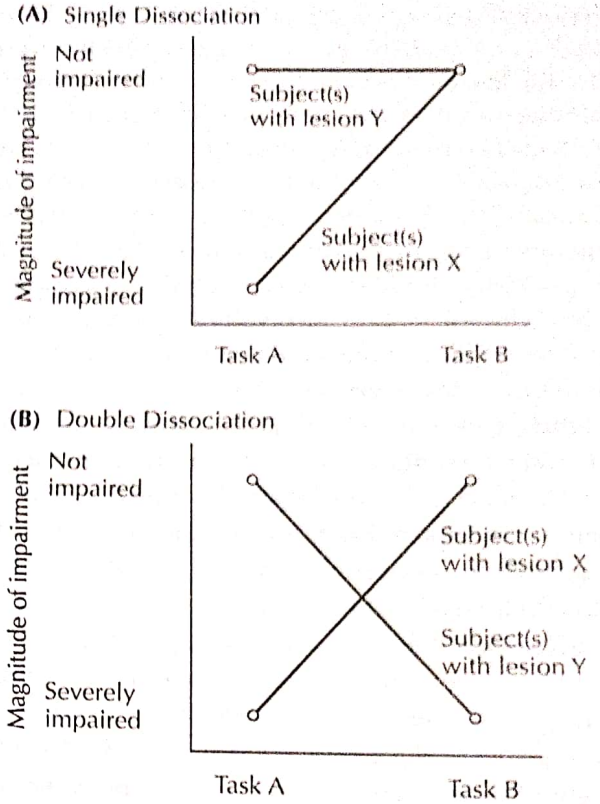


FIGURE 4.12 *(A)* Single dissociation and *(B)* double dissociation used to infer which cerebral areas are involve in the mediation of particular functions. *(From McCarthy & Warrington, 1990, p. 19)*

Limits on the Interpretation of Dissociations

As with all scientific methodology, however, t process of making inferences from lesion data m be conducted with extreme care. The presence o

2. An example of double dissociation is the finding that right parietal-lobe lesions produce impairment in spatial processing but not nonverbal memory, whereas right temporal-lobe lesions produce impairment in nonverbal memory but not spatial processing.

dissociation does not tell us that the impaired function is localized in the area of the lesion. It tells us only that the lesioned area is necessary for the function in question and that the other lesioned area, which did not produce the impairment, is not. Thus, other regions outside the area of either lesion, perhaps the entire rest of the brain, may also be involved in the normal processing of the function under consideration. In this sense the lesion method tells us something about which areas are involved in a particular function and which areas are not involved, but it does not tell us where in the brain the function is localized.

Adding to this conceptual limitation in determining localization of function is the technical problem of identifying the site of a lesion. Despite the development of the remarkable modern techniques for visualizing the brain discussed earlier, it is rarely possible to designate precisely the exact location of a lesion in the living brain. In addition, a lesion may exert temporary disruptive effects on neighboring tissue. This effect, termed **diaschisis**, may be due to swelling, bleeding, or other short-term pathological processes. Moreover, through the destruction of connections between neurons, a lesion may cause long-term disruptive effects in distant regions of the brain.

Further Thoughts on the Logic of Dissociation and Association

A few additional thoughts about the localizing implications of double dissociation and association may be useful at this point. In double dissociation each lesion-impairment pair serves as a control for the other. In this sense double dissociation is highly efficient: In the case of each of the two lesions we learn both that the region it has damaged is involved in a particular function and also that the region is not involved in some other function. There is another sense in which double dissociation is useful, however. Single dissociation leaves open the possibility that the critical lesion produced its effect, not because the area it disrupted is specifically involved in the particular function in question, but because that region of the brain is simply more important in some general sense. To draw on a social analogy, imagine that we shut down a town's power station and see that school classes are disrupted; then in a "control" town we shut down a small gas station and see no associated disruption in the schools. It would clearly be an error to conclude on the basis of these data that power stations are specifically involved in education. They simply have a pervasive and general importance, whereas the single gas station does not.

The demonstration of a double dissociation reduces the likelihood that findings are due to such a nonspecific effect because each lesion has been shown to produce a specific and proportionately significant effect. To modify our metaphor, suppose we shut down the power plant in one town and all gas stations in the other town. Both will disrupt school, so school disruption is now understood to be a nonspecific effect. The double dissociation would be loss of electric power and loss of mobility of automobiles. These are both significant disruptions, and they are both specific. So we are on firmer grounds for inferring localization of function.

Finally, let us consider associated impairments further. We said earlier that failure to demonstrate dissociation between two functions suggests that they have one underlying mechanism. As you might expect, from the point of view of localization of function, the demonstration of association suggests that a single region is necessary for the different functions under consideration. On the other hand, when impairment in two functions usually but not always occurs, this demonstrates that the functions are in fact separable but that brain areas necessary for their mediation are in close proximity. We shall find that Wernicke's aphasia and apraxia, the impaired performance of learned movements in the absence of elementary motor impairment, are an example of two such frequently co-occurring but sometimes dissociable disorders. This has led to the hypothesis that cortical area adjacent to Wernicke's area is critical the execution of learned actions (see chapter 9).

COMMISSUROTOMY

Commissurotomy, or as it is sometimes called, **brain surgery,** involves the cutting of the corpus losum, the band of fibers connecting the two spheres of the brain. As with the antiseizure

described earlier, the purpose is to control seizures, although in this case the rationale is different. Instead of removing the seizure focus, commissurotomy cuts the major fiber tracts between the two cerebral hemispheres in an attempt to limit the spread of seizures between the hemispheres and thereby reduce their severity.

This surgery, which began to be regularly conducted in the 1960s (although a number of patients had received a similar procedure in the 1930s), afforded the opportunity to study the effects of functionally separating the two hemispheres. Actually, "functional separation" is an overstatement because there are significant fiber tracts in addition to the corpus callosum that transmit certain types of information between the two hemispheres. Nevertheless, this procedure radically reduces the neural connections between the hemispheres and thereby affords the opportunity to investigate what each hemisphere is able to do in relative isolation.

Roger Sperry and his colleagues pioneered this work in the 1960s, and since then many investigators have conducted similar work. In the 1950s Sperry and Myers had conducted extensive work along these lines with other animals. By cutting the corpus callosum and the optic chiasm (not cut in human patients) in cats, Sperry and Myers showed that each hemisphere functioned independently on certain tasks. In the intact animal, input to one eye would be projected to both hemispheres because some of the fibers in the optic nerve would cross over to the contralateral hemisphere at the optic chiasm while others continued on to the ipsilateral hemisphere. Cutting the optic chiasm, the point where some of the fibers in the optic nerve cross over to the other side of the brain, confined input to one eye to the ipsilateral hemisphere. If such an animal also has a corpus callosum section, the functioning of each hemisphere can be tested by confining input to one eye.

Using this paradigm, Sperry and Myers were able to assess the independent functioning of the two hemispheres. For example, if one eye is covered, an animal with a section of the corpus callosum is able to learn a visual discrimination (e.g., the peanut is under the card with horizontal stripes). Then, if the covered eye is uncovered and the eye that had been exposed to the visual discrimination learning task is covered, the investigators showed that the animal demonstrated no learning and could actually be taught the opposite visual discrimination. Thus, the two hemispheres could be shown to have learned opposite discriminations and to retain these independently. These and other findings showed that after sectioning of the corpus callosum, learning and other cognitive processes could be confined to one cerebral hemisphere.

The potential usefulness of this method as a source of information about hemispheric specialization in humans would seem to be obvious. Research with humans presented certain technical difficulties, however. In particular, as has been mentioned, in humans the optic chiasm was not sectioned. Because of the way the eye and the brain are hooked up, a topic that we will consider in some detail in chapter 5, input from each eye projects to both hemispheres. Therefore, confining input to one hemisphere is not as simple as covering one eye. What is required is confining input to one visual field, because each visual field (left or right) projects to the contralateral hemisphere. In free vision such restriction is impossible because the movement of the head and eye ensures that a visual stimulus in a specific location in space will, in a brief period of time, appear in both the left and right visual fields.

These and other difficulties in confining sensory input to one hemisphere probably account for the fact that an earlier investigation of a series of patients who had undergone commissurotomy, carried out by the neurosurgeon Akelaitis in the 1930s, failed to yield evidence of behavioral deficits. This prompted some to suggest, not without a dash of humor, that this massive fiber bundle comprising 100 million axons merely served the structural function of mechanically keeping the two hemispheres from falling apart.

However, when commissurotomy again began to be used for therapeutic purposes in the 1960s, the prior work of Sperry and Myers with animals made it clear that some effects should be detectable. Based on this earlier work, Sperry and his colleagues were able to use techniques that would make these patients a highly fruitful source of insight into hemispheric specialization. For example, to restrict visual stimuli to one hemisphere, patients were exposed to

tachistoscopically (rapidly) presented stimuli, each presented for 100 milliseconds or less, to one visual field only. Presentation time was thus too brief for subjects to move their heads or eyes and thereby place the stimulus in the opposite visual field. Using this and other ingenious techniques, Sperry showed, for example, that whereas a word flashed to the right visual field (i.e., left hemisphere) of a commissurotomy patient could be read aloud, words flashed to the left visual field (i.e., right hemisphere) could not.

Something analogous happens for stimuli presented through touch. An object that is out of sight and palpated by the right hand of a split-brain patient can be readily named. In contrast, an object palpated by the left hand cannot, although the left hand (right hemisphere) can be shown to have recognized the object if recognition is assessed by means that do not require verbal processing. For example, the left hand can pick out an object that it previously examined from a collection of objects. As one would expect, transfer between the hands is not possible in split-brain patients because the information from the somatosensory cortex of one hemisphere cannot be communicated across the corpus callosum to the somatosensory cortex of the other hemisphere.

In the case of audition the situation is more complicated because the connections from each ear to the cortex are both ipsilateral and contralateral. In other words, each ear projects to both hemispheres. Based on this anatomical fact, one would not expect effects analogous to those we have just discussed in vision and touch to apply to audition. In fact, if we simply present information to one or the other ear, no such effect is seen. For example, a split-brain patient can repeat words presented (through an earphone) to the left ear alone or the right ear alone. If, however, a commissurotomy patient is presented different verbal stimuli simultaneously to the two ears (a technique termed **dichotic listening**), an effect is found. Thus, when different words or numbers are presented to the two ears simultaneously, those presented to the right ear (contralateral to the left hemisphere) are reported, whereas those presented to the left ear are very seldom reported (Figure 4.13). This phenomenon is called **suppression**; it is as if the right-ear input inhibits the recognition of simultaneous left-ear input. Suppression demonstrates that although the anatomy of the auditory system does not exhibit the manifest contralaterality seen in the visual and somatosensory systems, it nevertheless turns out that the contralateral connections are the most important in audition as well. We shall see shortly that a right-ear effect for verbal material is also seen in normal subjects, although the effect is much weaker than that seen in commissurotomy patients.

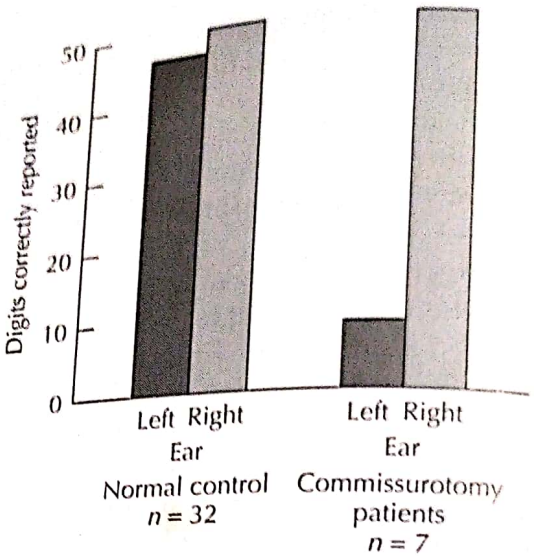


FIGURE 4.13 Number of digits reported by commissurotomy patients and normal control subjects in a dichotic listening task. *(From Milner, Taylor, & Sperry, 1968)*

We will have much more to say about commissurotomy as we discuss particular abnormalities. Before we leave this discussion, however, let's consider the impact of commissurotomy on overall behavior. It might be expected that the two disconnected hemispheres would be in some kind of competition. There have been some silly dramatic plots written on this theme. In one of them a man found, to his distress, that his right hand wanted to murder his girlfriend but his left hand loved her. The story had an unhappy ending: His left hand was unsuccessful in using an ax to chop off his right hand and thus save his beloved, and the right h[illegible] foiled plan was

From Milner, Branch, & Rasmussen, 1964 (in McCarthy & Warrington, 1990, p. 8)

It turns out that commissurotomy patients do briefly experience something like this, although, thankfully, generally with less melodrama. A patient may find herself in a state of indecision as to what to wear as she selects one dress with her left hand and a different one with her right. Interestingly, this competition or incongruity is of brief duration, disappearing shortly after surgery. It is unclear how this happens. It may be that other interhemispheric connections mediate a high level of emotional and motivational coordination between the two hemispheres. In addition, to the extent that they remain independent, the two hemispheres must be like two individuals in an intimate relationship who, though separate, yet are highly sensitive to one another and modify their behavior accordingly.

THE SODIUM AMOBARBITAL TEST

The **sodium amobarbital test,** which has emerged out of the surgery for the relief of seizures that we have already discussed in some detail, creates a transient and reversible inactivation of one cerebral hemisphere. To explain its use, a brief digression is necessary. Up to this point we have been talking as if all persons had speech represented in the left hemisphere and spatial and other nonverbal functions in the right hemisphere. We already alluded to the fact that this is an oversimplification, and our consideration of the sodium amobarbital test provides a useful context to explain this further.

From McCarthy & Warrington, 1990, p. 6

Hemispheric Specialization and Handedness

For right-handed individuals the assumption we have made is true in about 98% of cases. For left-handers the situation is different. About 70% of them have speech in the left hemisphere, as do the vast majority of right-handers. However, 15% have speech in the right hemisphere, and 15% have speech represented in both hemispheres (Table 4.1). These findings could be (and have been) inferred from the study of the relationship between side of cerebral lesion and onset of aphasia in right- and left-handers (Table 4.2). However, the sodium amobarbital test provides a more direct method of assessing this relationship, one that can be used to make this determination in people who are not aphasic.

Use of the Sodium Amobarbital Test in the Neurosurgical Management of Focal Seizures

Surgery for the relief of seizures involves the removal of an area of cortex that has been judged to be the origin of the seizures in a particular patient. It is critical that the surgeon not inflict an aphasia, a more debilitating disorder than the seizure disorder. The surgeon must know with the highest degree of certainty possible whether the area to be removed lies within the language hemisphere. If it does, then extreme care must be taken to avoid damage to the language areas. In contrast, if it is known that the area to be removed lies in the nonlanguage hemisphere, the surgeon can be less conservative in the removal