CHAPTER
2

OBJECTIVES

The reader will be able to:

1. Describe the anatomy of the nervous system in relation to aphasia.
2. Describe the blood supply of the brain and how it relates to the signs and symptoms of aphasia.
3. Demonstrate knowledge of the neuronal organization of language.
4. Understand the methods available to study the nervous system.
5. Describe the clinical syndromes of aphasia.
6. Link the clinical manifestations of aphasia syndromes to the localizations of the cortical lesions.

Elements of Neurology Essential for Understanding the Aphasias

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INTRODUCTION

There is still much to be done to understand the nature of aphasia and to elucidate the organization of the brain relative to behavior. Nevertheless, since the time of Paul Broca, who was the first to show, in 1861, that a particular lesion of the cerebral cortex could lead to a disorder of language (Broca, 1861, as cited in Hécaen & Dubois, 1969), our knowledge of cerebral organization related to language has greatly advanced and the clinical repercussions of cerebral lesions have been extensively described. In this chapter, we outline briefly the anatomy, physiology, and pathology of the nervous system, as well as the methods available for its study, and we then sketch the functional organization of the cerebral correlates of language. This brief overview concludes with the description of the clinical characteristics of the various forms of aphasia.

ELEMENTS OF THE NERVOUS SYSTEM

Language is a very complex function involving substantial parts of the central nervous system; indeed, few brain sites could be destroyed without resulting in some language deficit. Speech, which is just one of the language outputs, is an extremely complex act: consider, for example, the production of a single sound like the phoneme /a/. It involves the coordinated activity of several nerves and muscles for the air to be exhaled from the lungs, passing through the larynx, the pharynx, and the articulators (tongue, lips, teeth, cheeks), and multiple other actions such as inspiration, expiration, opening and closing of the vocal

cords, movement of the larynx, pharynx, mouth, and so forth. Moreover, for their successful coordination, these actions need to be monitored, and monitoring requires sensory feedback to the brain from sensory nerves in the vocalization system, attesting to its correct configuration. Moreover, in real-life circumstances, speech sounds rarely, if ever, emerge as context-free productions: the phoneme /a/ in this example would sound different depending on the mood, on the intention, and on the physical condition of the speaker, as well as on the surrounding circumstances affecting the audibility of the sound produced. The speaker is therefore capable of modulating the sound to be produced, and this requires that its mode of production be decided first at a higher level, such as the frontal association cortex, and a signal transmitted to the "execution" part of the brain, the motor cortex. In the meantime, the auditory cortex of the temporal lobes informs the speaker about background sonority to modulate the voice, and the visual cortex informs the speaker about the relative position of his or her conversation partner. It is the purpose of the following section of this chapter to provide an outline of the nervous system, emphasizing those components that are necessary to support the processes of production and perception of speech and language.

Gross Anatomy

The two cerebral hemispheres, brain stem, and cerebellum together with the spinal cord form the central nervous system (CNS). Each hemisphere is divided into lobes: the frontal, the parietal, the temporal, and the occipital (Figure 2-1). On the surface of the brain are elevated convolutions called gyri separated by grooves called sulci. For example, the frontal lobe is divided into three convolutions, the superior, middle, and inferior frontal gyri. The two cerebral hemispheres are interconnected with commissures, the most massive of them being the corpus callosum. Behind and below them are located the brain stem and the spinal cord. The cerebellum consists of a central part, the vermis, and two cerebellar hemispheres. It is attached to the posterior part of the brain stem and resides under the cerebral hemispheres (Figure 2-1). All these structures are protected by three layers of meninges (i.e., dura mater, arachnoid membrane, pia mater) and the bony tube formed by the skull and the vertebrae that are part of the spinal column. These structures are bathing in the cerebrospinal fluid (CSF), which absorbs noxious vibrations. The brain contains the ventricular system (Figure 2-1), also filled with CSF, which communicates with the spinal fluid surrounding the CNS. Two lateral ventricles, one in each hemisphere, with horns corresponding

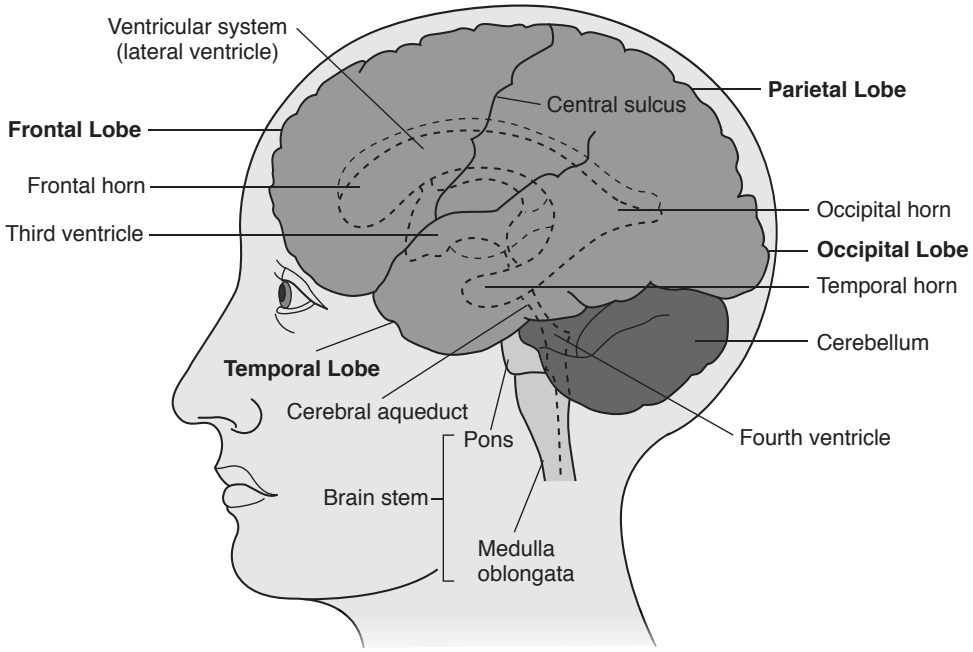

Figure 2-1 Anatomy of the structures of the CNS.

to each lobe (frontal, temporal, and occipital), communicate with a single third ventricle, above the brain stem, which continues through the cerebral aqueduct to the fourth ventricle, located between the back of the brain stem and the anterior surface of the cerebellum. Its extension is the small-diameter central canal that runs through the entire length of the spinal cord. The content of CSF in cells, proteins, sugar, or other substances varies, normally, only slightly. However, in various pathologic conditions its consistency or pressure is altered. For example, an infection and other conditions are characterized by the presence of particular types of leucocytes in the CSF and/or elevations in its pressure. Therefore, we can assess the condition of the CNS by analyzing CSF samples collected through insertion of a needle in the intrameningeal space between the last lumbar vertebrae (where the spinal cord comes to its end, a procedure called lumbar puncture, LP). In neurosurgical settings, it is also possible to monitor the intracranial pressure, which usually increases after traumatic brain injury, by inserting pressure sensors directly in the brain's ventricular system.

The Vascular System of the Brain

The maintenance and the function of brain cells depend on arterial blood supply (see Figure 2-2). Blood arrives to the brain through two systems: the anterior or carotid circulation system and the posterior or vertebrobasilar circulation system. A communication system between the two carotids and the posterior system, the circle of Willis, allows arterial blood to circulate in both directions in case of disturbance of the normal inflow in either of the systems. For example, if one of the carotid arteries is obstructed by a blood clot, the corresponding anterior parts of the brain are supplied from the other carotid or from the posterior system. However, this system does not protect the areas irrigated from arteries beyond the circle of Willis.

Each of the two common carotid arteries divides into an exterior branch (external carotid), irrigating the face and meninges of the brain, and the internal carotid feeding the anterior two-thirds of the brain hemispheres. The first branch (the ophthalmic artery) irrigates the corresponding eye. The anterior cerebral artery emerges next (Figure 2-3b), directed to the front and curving backward, around the corpus callosum, at the internal surface of each hemisphere. It irrigates the anterior part of the frontal lobe, the corpus callosum, the interior part of the frontal and parietal lobes, including the sensorimotor cortex part corresponding to the lower limb. The middle cerebral artery is the final branch of the internal carotid artery (Figure 2-3a), irrigating about two-thirds of the cerebral hemisphere, from the cortical surface to its depths. Specifically, it irrigates the basal ganglia, the posterior

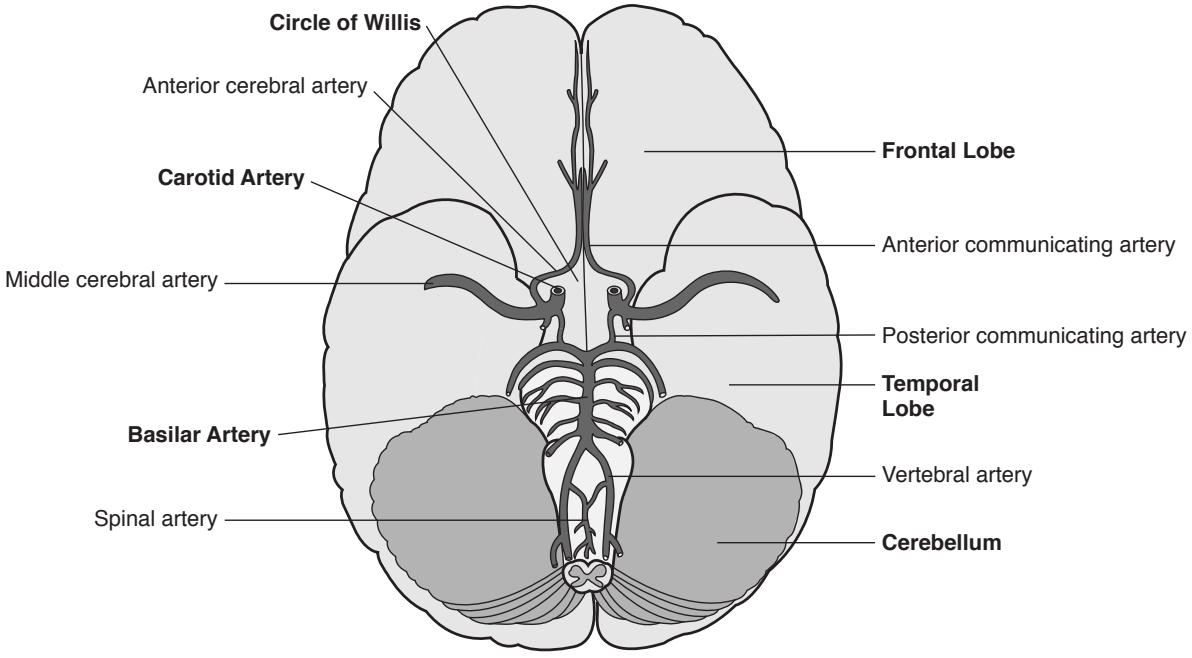

Figure 2-2 The vascular system of the brain and the circle of Willis.

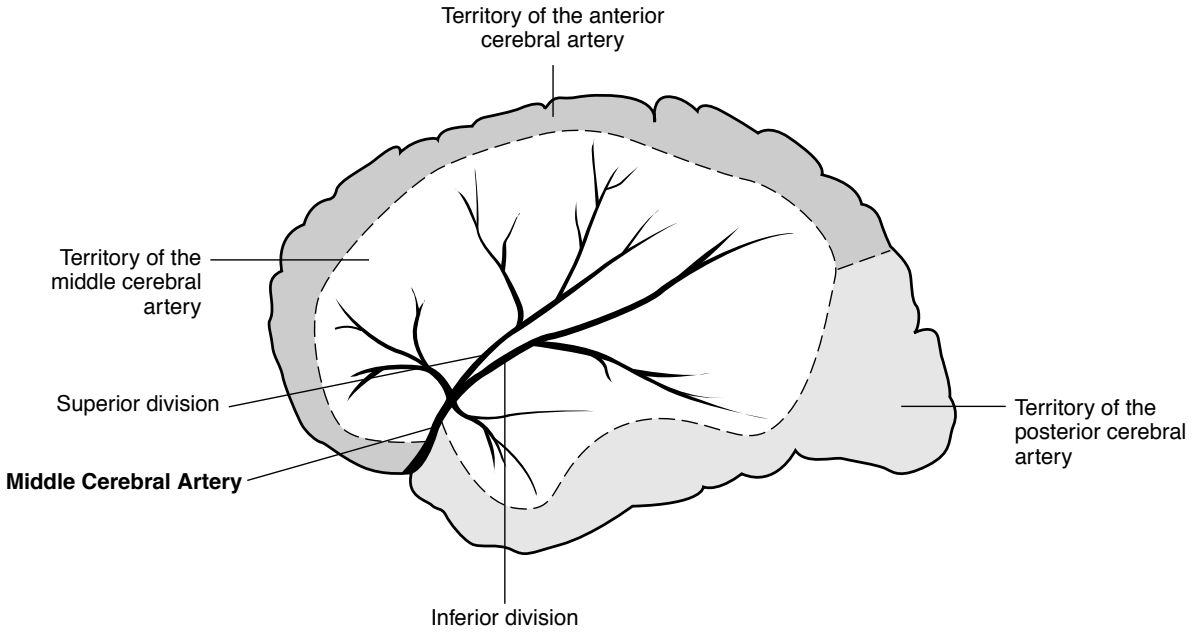

Figure 2-3a Irrigation areas of the brain's arteries. Schematic representation of irrigation territories of the cerebral arteries. External surface of the hemisphere.

lateral part of the frontal lobe, the lateral aspects of the temporal and the parietal lobes, including the sensorimotor strip, except for the region corresponding to the lower limb, which is irrigated by the anterior cerebral artery.

The confluence of the two vertebral arteries forms the basilar artery, which irrigates the brain stem and the cerebellum; it is then divided in the two posterior cerebral arteries (Figure 2-3b), irrigating the corresponding

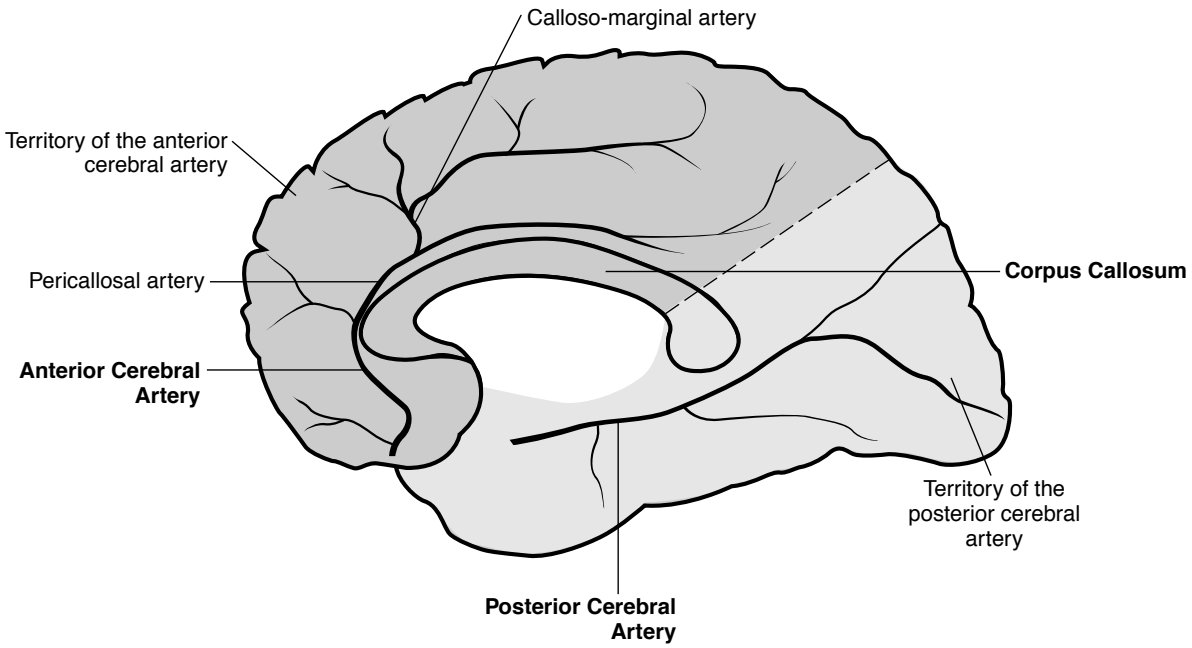

Figure 2-3b Irrigation areas of the brain's arteries. Schematic representation of irrigation territories of the cerebral arteries. Internal surface of the hemisphere.

occipital lobes, the posterior part of the temporal lobes, and some subcortical structures, such as the thalami.

Neurons and Synapses

The brain consists of about 100 billion neural cells, a supporting system of glial cells, and the cerebral vascular system. The neural cell, also called *neuron*, includes a cell body and multiple extensions: one axon and one or more dendrites through which it establishes up to 10,000 connections with other neurons, the synapses. At the level of the synapse, chemical substances are exchanged and electric signals—positive (excitatory), negative (inhibitory)—are transmitted between the neurons. The several trillions of synapses within the brain form an immense network, which is the basis of the integrative function of the CNS, which may be understood through the analogy of the action of high-power computer systems. However, this analogy fails to capture many attributes of the nervous system, most importantly the lifelong capacity of neurons to continuously rearrange their synapses. This is the core element of the brain's capacity for functional reorganization, called *plasticity*. Rehabilitation techniques used for correcting many brain dysfunctions, such as spasticity control, or sensitivity enhancement to ameliorate reduced capacity for movement, are based on the principle of plasticity.

Gray and White Matter

We call *gray matter* the brownish tissue consisting of the bodies of neurons that constitute the cerebral cortex, that is, the surface of the cerebral hemispheres, and the cerebral nuclei, that is, the neural masses deep in the cerebral hemispheres (the basal ganglia, the thalamus, and the hypothalamus; see Figure 2-4), and the nuclei of the cranial nerves in the brain stem. A similar arrangement is found in the cerebellum. The gray matter occupies a central position in the spinal cord, forming the wall of spinal canal. When seen in transverse sections, it has the shape of a capital *H*, with anterior and posterior horns. The bodies of the motor neurons are found in the anterior horns. Motor axons, which exit the spinal cord as the ventral root, and sensory axons, which enter the posterior horns as the dorsal root, together form the peripheral nervous system (PNS; see also the section titled "The Peripheral Nervous System: Peripheral Versus Central Paralysis" later in this chapter).

The white matter fills the rest of the cerebral hemispheres, between cortex and basal ganglia, the brain stem, around the nuclei of cranial nerves, and the periphery of the spinal cord. White is the color of the sheath of myelin around the neural axons, and white matter consists of bundles of axons (fasciculi or tracts) that connect areas of the cortex with one another, the

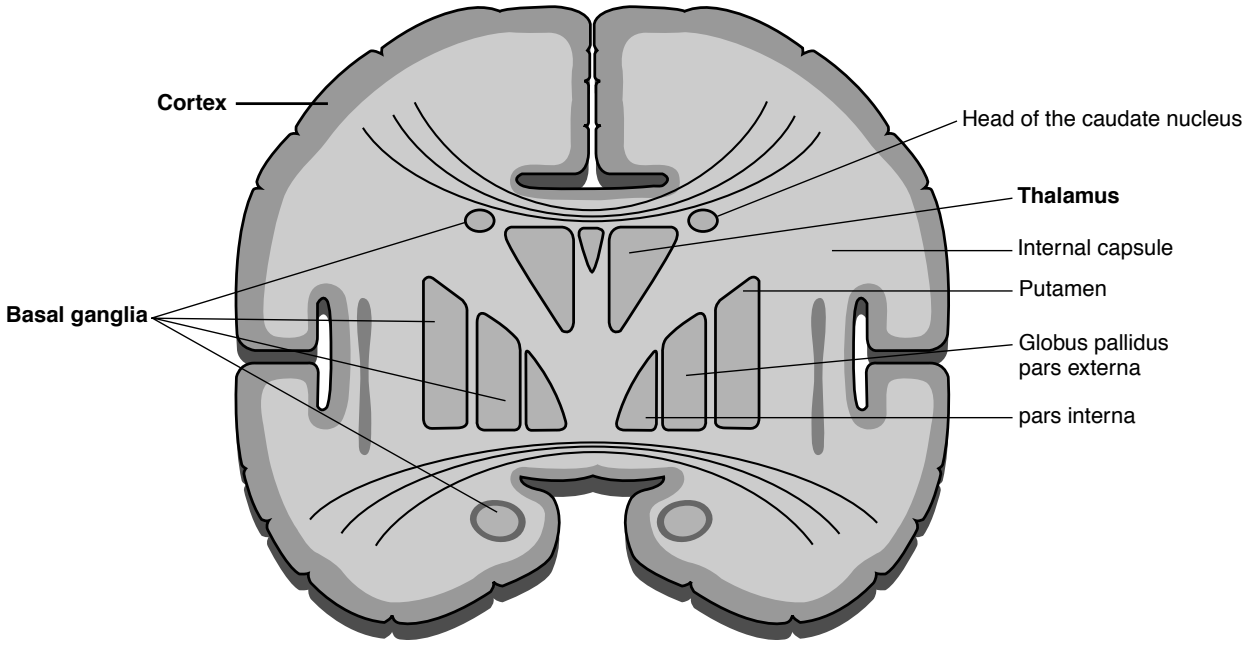

Figure 2-4 Coronal section of the cerebral hemispheres.

cortex with the nuclei in the hemispheres and the brain stem, and also with all levels of the spinal cord.[1]

The corpus callosum and other commissures (also white matter tracts) connect the two hemispheres and allow the communication and reciprocal control of cortical areas on both sides of the brain. Lesions that interrupt connections between areas of the cerebral cortex produce disconnection syndromes. A typical example of such disconnection is the one resulting in pure alexia or alexia without agraphia. It consists of a lesion interrupting communication between visual areas of both occipital lobes with areas for language in the left hemisphere. Another example is the split-brain syndrome, caused by the section of the corpus callosum, which results in various disorders, such as the difficulty of naming objects palpated with the left (but not with the right) hand.

Long bundles of axons (i.e., tracts) connect the cortex, the brain stem, and the spinal cord, forming efferent and afferent tracts: an efferent, descending, motor pathway, the pyramidal tract, consists of the axons of neurons in the motor area of the cortex (first-order motor neuron), terminating in the motor nuclei of the brain stem (corticobulbar tract) and the anterior horns of the spinal cord (corticospinal tract). The pyramidal tract controls the motor cranial nerves exiting the brain stem and the motor neurons of the spinal cord (second-order motor neuron). Sensory axons form the afferent, ascending, or somatosensory tract, connecting sensory receptors all over the body to the somatosensory area of the cortex via the thalamus (one of the subcortical structures that functions as a relay station). Both the efferent and the afferent tracts spread out like a fan under the cortex, forming the corona radiata, which presents a narrow stem in the center of each hemisphere between the masses of gray matter, the internal capsule. The tracts continue beyond this level, along the brain stem and the spinal cord, crossing at midline (from left to right and conversely[2]) at various levels of the brain stem (see Figure 2-5a and b).

These anatomic details are useful to explain how a tiny lesion at the level of the internal capsule, such as a small lacunar infarct, is sufficient to completely interrupt these pathways, producing a hemiplegia with severely impaired motor and sensory function of the opposite half of the body, and also why a very large lesion would be necessary to produce a comparable effect at the level of the corona radiata and of the motor and somatosensory areas of the cortex.

The Extrapyramidal System

The basal ganglia, the thalamus, and the cerebellum form complex circuits, comprising the so-called extrapyramidal system. These circuits are connected to the direct motor pathway described previously,

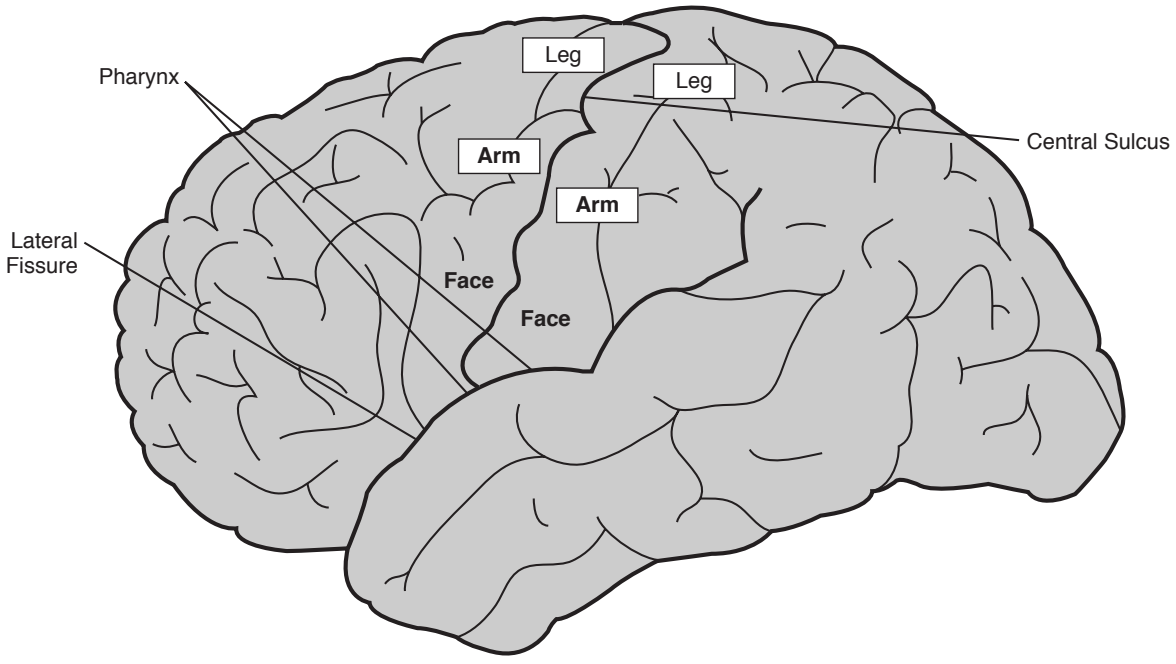

Figure 2-5a Representation of body parts on the motor and somatosensory areas of the cortex.

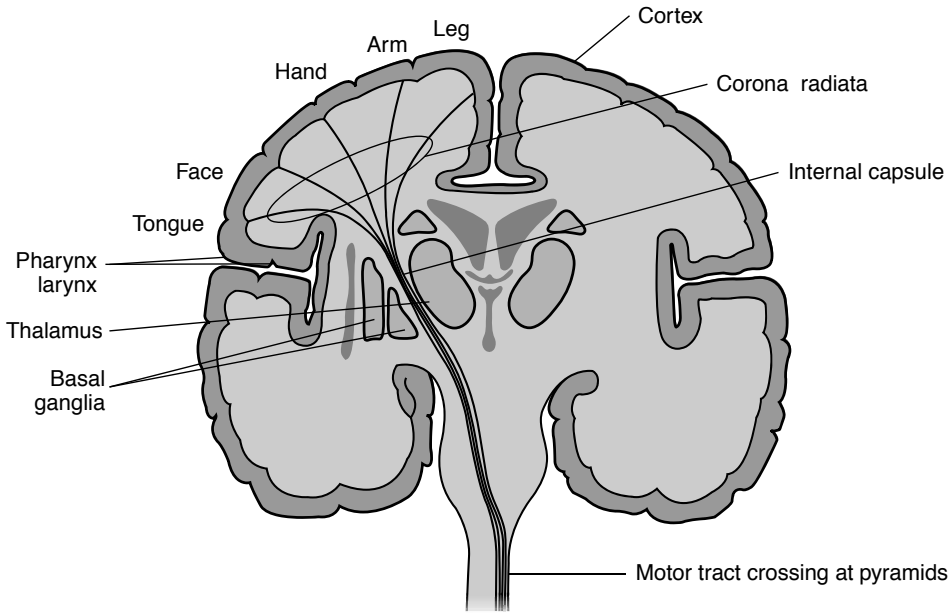

Figure 2-5b Coronal section of the brain showing the descending motor tract, forming the corona radiata, narrowing at the internal capsule between basal ganglia and thalamus, and then crossing at the level of the medullar pyramids.

rendering control and coordination of movement possible. The basal ganglia[3] receive input from almost all regions of the cerebral cortex and send projections to some nuclei of the thalamus, which, in turn, are connected to the executive, premotor, and motor areas of the cortex. This system also involves two other loops, one through the pars compacta of the substantia nigra and another through the subthalamic nucleus of Luys (Figure 2-6). It is believed that this complex circuitry is mainly organized around the pars compacta of the substantia nigra and its production of dopamine.[4]

These circuits control the execution of overlearned and automated movement patterns, leaving control of voluntary activity to the premotor and motor cortex. For example, when we walk we do not have to think about the movements of our feet or the swinging of our arms, though they are indispensable to prevent falls. Also, highly elaborated movement patterns, such as dancing or piano playing, become possible because performers can concentrate on artistic expression, mediated by the cortex, while all the rest, such as maintenance of equilibrium and coordinated contractions of all the muscles involved, is automatically controlled by the basal ganglia.

Extrapyramidal disorders are described as hypokinetic or hyperkinetic syndromes. Hypokinesia is slow and effortful movement, with limited or absent automatic movements and rigidity of limbs and body. Parkinson's disease is the most typical and most common hypokinetic condition, frequently accompanied by a characteristic rest tremor of the limbs. Hyperkinetic syndromes present with a variety of abnormal, involuntary, quick or slow movements.[5] Such syndromes bear such names as *Gilles de la Tourette syndrome*, *idiopathic tremor*, *Huntington's disease*, *generalized dystonia*, and many others.[6] Speech is more or less affected in all these conditions, and characteristic dysarthrias have been described. Parkinsonian or hypokinetic dysarthria consists of hypophonia, fainting of the voice at the end of the word or phrase, blurred articulation, fluctuations between slow and rapid speech, repetitions of syllables or words, and other signs and symptoms.

The cerebellum has rich connections to the brain, the brain stem, and the spinal cord and is responsible for body balance and the coordination of movements of hands and feet, head, eyes, and mouth. It ensures that each isolated movement and muscle contraction does not appear awkward or interrupted, but smooth, with precise start and end points, at intended and definite intervals. Moreover, it monitors the succession of movements necessary to achieve a precise action that consists of multiple movements. For example, clapping of hands that produces exactly the noise we desire, or pointing our index finger to our nose, or walking. Absence of cerebellar control, on the other hand, produces defective

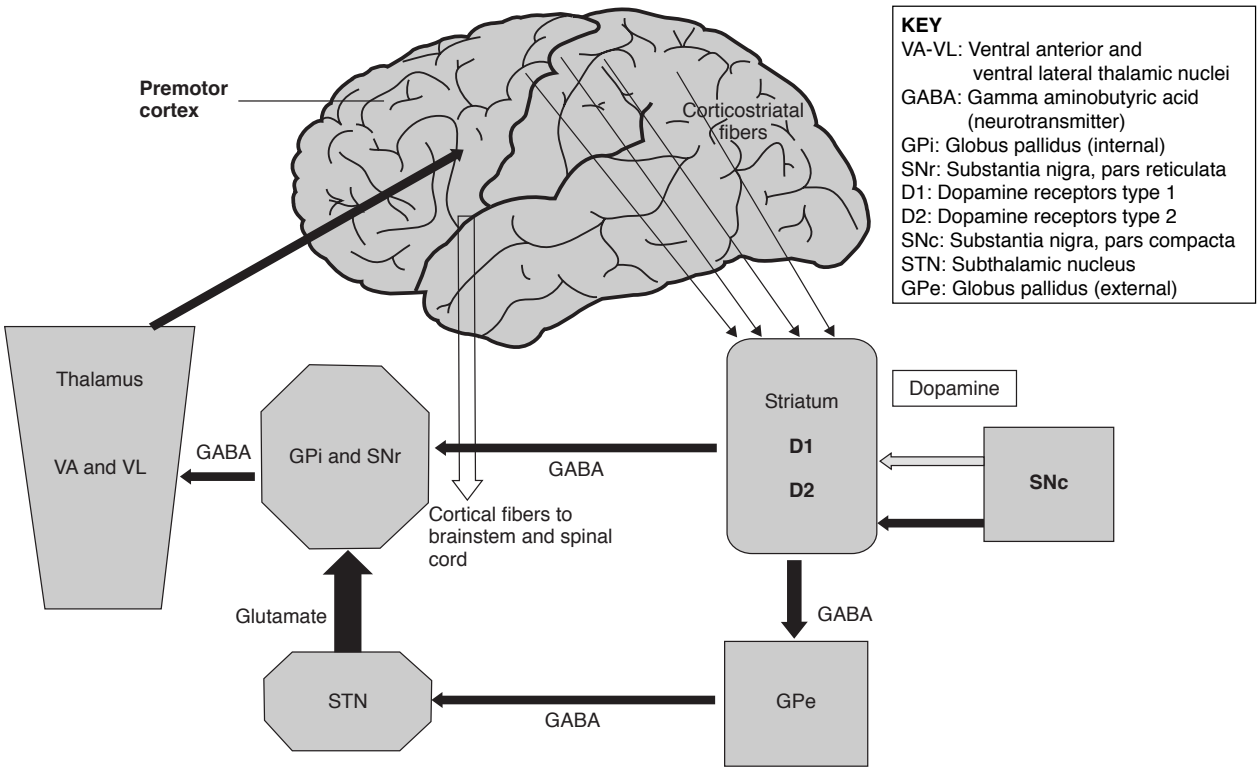

Figure 2-6 Schematic representation of basal ganglia circuits.

movement patterns such as the gait of a drunken person, who walks with his or her legs spread wider to reduce the risk of falling. The cerebellum also monitors speech movements. For a precise sound to be produced, each contraction of the lips, tongue, vocal cords, diaphragm, or intercostal muscles is precisely monitored so as to follow the intended speech production plan. Cerebellar lesions result in cerebellar (ataxic) dysarthria, a condition characterized by a more or less slow, blurred, and hesitating speech, with fluctuating intonation and either mute or explosive phonemes. (See Chapter 20, this volume.)

The Peripheral Nervous System: Peripheral Versus Central Paralysis

The nerves are bundles of axons of the motor and/or the sensory neurons. Sensory axons carry signals from receptors in all tissues and organs of the body to the brain. Those forming the cranial nerves enter the brain stem. The rest enter the posterior aspect of the spinal cord and are called spinal nerves. The information they convey varies according to their diameter. Thin, unmyelinated fibers inform about superficial sensitivity, that is, pain, temperature, and light touch. Thicker, myelinated fibers convey information about joint position, vibration, pressure, and discriminative (conscious) sensations. These kinds of sensation follow different tracts in the spinal cord. Motor nerves carry executive signals from the CNS to the striated muscles of the body, that is, muscles under voluntary control. They emerge from the brain stem (motor cranial nerves), innervating the region of the head and the neck, and from the spinal cord (spinal motor nerves), innervating the striated muscles of the body and limbs.

All spinal nerves are mixed in that they contain sensory and motor axons. Cranial nerves are of different kinds. Some, such as the olfactory and optic nerves (I and II cranial pairs), and the acoustic and vestibular nerves (together forming the VIIIth cranial nerve), are purely sensory, transmitting olfactory, auditory, and

visual information and information regarding the position of the head and body in space. The rest of the cranial nerves are either motor or mixed and innervate the face and the muscles necessary for speech production (articulators).

The trigeminal (Vth cranial nerve), though also controlling mastication movements, is mainly the sensory nerve of the face. The facial (VIIth cranial nerve) is the principal motor nerve of the face (including the lips and the chin). Paralysis of the facial nerve on one side results in asymmetry of the face (peripheral facial paralysis, i.e., Bell's palsy), involving difficulties in speech, drooling, and difficulties in eye closure. Central facial paralysis is a different kind of paralysis caused by lesions in the central nervous system, such as stroke or other types of lesions in the trajectory of the motor tract from the motor cortex to the facial nucleus. It concerns mainly the lower part of the face and the voluntary movements of the face, and it may be part of the clinical picture of hemiplegia.[7]

The glossopharyngeal (IXth), the vagus (Xth), and the hypoglossal (XIIth) cranial nerves innervate the muscles of the pharynx, the larynx, the vocal cords, and the tongue. Their paralysis affects speech and voice in general as described in Chapter 20. Hypophonia, whispering voice resulting from paralysis of one vocal fold caused by a lesion in the vagus nerve, prompted Galen to suggest that voice comes from the brain.

Nerves sustain lesions either in their axons (axonal lesions) or in the sheath of myelin (demyelinating lesions). These lesions have various etiologies and different prognoses. An axonal lesion is more or less definitive, whereas demyelinating processes often involve a continuous alternation of demyelination and remyelination,[8] finally resulting in axonal damage. These lesions produce motor and sensory paralysis, muscular weakness, and sensory deficits. The clinical pictures resulting from such lesions are variable (radiculopathies, plexopathies, or neuropathies), depending on the kind of fibers affected (motor, sensory, mixed, small fibers, etc.) and the location along the length of the nerve (from its root to its most distal point). It also depends on the number and location of the nerves affected (mononeuropathies, asymmetrical multifocal neuropathies, and symmetrical polyneuropathies). For instance, distal, symmetrical numbness and weakness in the feet slowly progressing to the hands is typical of polyneuropathies, one of the most common being diabetic neuropathy.

The Autonomic Nervous System

The smooth muscles of the internal organs, such as the heart, bowels, and bladder, function almost entirely unconsciously through the coordinated action of the sympathetic and parasympathetic divisions of the autonomic nervous system. The balance between these two divisions depends on internal and external conditions, including emotions and other psychological reactions. For instance, a chain reaction is initiated when we are frightened that includes reactions ranging from changes in heart rate to hair standing up and pupils dilating. The brain, mainly through the limbic system (a set of structures including the hypothalamus and the amygdala located in the medial aspect of the temporal lobes), controls and coordinates the autonomic system. The various parts of the nervous system function in close coordination with each other and with the rest of the body. The limbic system's activity may affect the capacities of a person to speak. This is true in the case of a student under the stress of examinations and in the case of an aphasic speaker who performs differently when stressed or relaxed.

A MORE DETAILED VIEW OF THE CEREBRAL CORTEX

Primary Sensory and Motor Areas

The primary motor cortical area lies on the precentral gyrus, on the anterior bank of the central sulcus. Every part of the body that can be voluntarily moved is represented in this area, not proportionally to its size but to the complexity and accuracy of the movements that it can perform. The mouth and the fingers, for example, are represented by a vast area compared to that of the hip or the torso. This point-to-point correspondence is called somatotopy and is reversed in both directions, such that the right half of the body is represented on the left hemisphere and the foot is represented at the top of the motor strip, above the hip, torso, arm, hand, face, and mouth (Figures 2-5a and 2-7).

On the postcentral gyrus, on the posterior bank of the central sulcus, lies the primary somatosensory cortical area. It is also somatotopically organized, receiving sensory information from the different body regions, proportionally not to their size but to their sensitivity. Here again, the lips and the fingers represent an area proportionally more extensive than the hip or the torso.

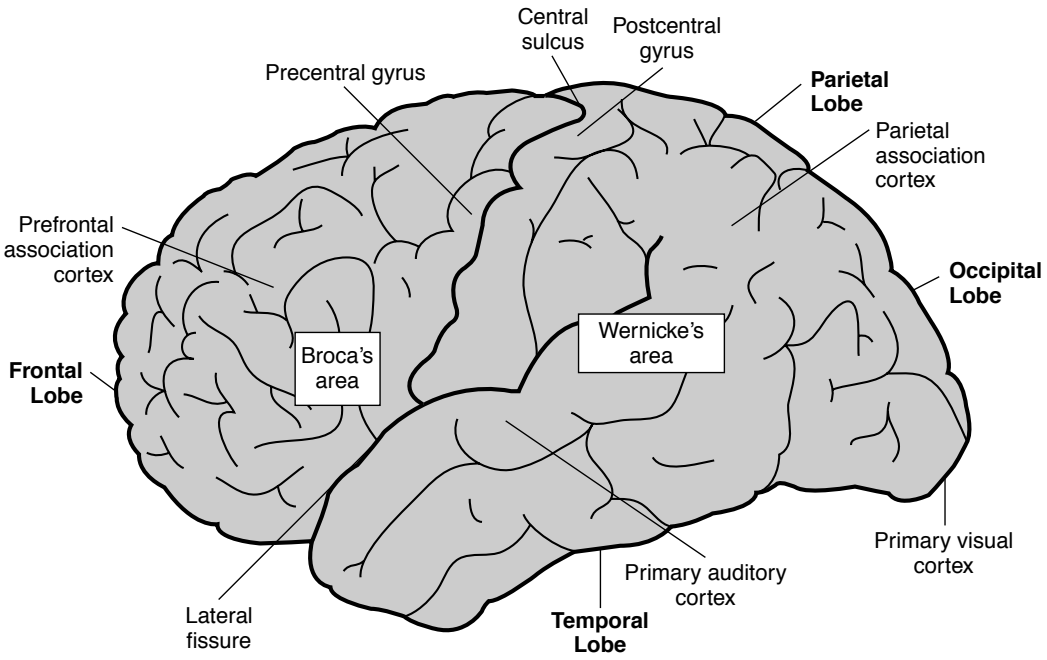

Figure 2-7 External surface of the left cerebral hemisphere.

The motor and somatosensory areas work in close collaboration, and they are together referred to as the sensorimotor area of the cortex.

The temporal lobe, beneath the lateral sulcus (or Sylvian fissure) is divided into three convolutions. The primary auditory cortex is located on the middle portion of the superior temporal convolution (gyrus of Heschl) and is organized in a "tonotopical" way, that is, according to the frequency of sounds. Finally, at the posterior end of the hemispheres lies the primary visual cortex, around the calcarine sulcus (Figure 2-7); the right half of the visual field of *both* eyes is represented at the left visual cortex, and vice versa. A lesion in this area (e.g., a stroke of the posterior cerebral artery) makes the person blind in the contralateral visual field.

Association Areas

The primary cortical areas described previously are surrounded by modality-specific, or unimodal, association cortical areas. Specifically, areas around the primary auditory area process information about sounds coming from the primary auditory area to recognize and identify these sounds. Areas around the primary visual area, in the anterior part of the occipital cortex and extending to (1) the temporal and (2) parietal cortices, process the visual stimuli so as to identify and locate them in space. The identification of the nature of a visual object involves the association cortex toward the inferior posterior temporal cortex (the "what" pathway), whereas the location of the object in space involves regions toward the posterior parietal cortex (the "where" pathway). Finally, parietal regions immediately posterior to the somatosensory cortex process somatosensory stimuli. These unimodal association areas are not connected to each other so as to avoid mixture of sensory information and ensure sensory fidelity. But recognition of an object, as a whole, requires convergence sensory information from multiple sources in the high-order multimodal association areas of the cortex. These areas include the prefrontal cortex, the perisylvian zone, posterior parietal cortex, lateral temporal cortex, and parahippocampal gyrus.

Lesions in the association areas of the cortex may produce selective perceptual deficits (e.g., erroneous perception of shapes, motion, colors) or agnosias, that is, bizarre situations where the patient cannot recognize things that he or she readily recognized before. For example, patients may not recognize very common objects or familiar faces through vision (visual agnosia, prosopagnosia), or pure sounds, words, or music through audition (acoustic or auditory agnosia, auditory verbal agnosia), or familiar objects through palpation; they may not be able to orient themselves or move in familiar surroundings (spatial agnosia).

The anterior multimodal association cortex, the prefrontal cortex, is dedicated to the executive functions, including working memory, planning and organizing of motor sequences, and monitoring and control of various behaviors, either motor or social. People with lesions in the frontal lobes present with dysexecutive syndrome (see Chapter 17, this volume), including awkward social behavior and many behavioral problems, such as apathy and passivity or disinhibition and aggressiveness, depending on which area of the frontal lobe (lateral or medial) is affected. These disorders are frequently encountered in closed traumatic brain injuries, which are unfortunately frequent in younger individuals.

Finally, lesions in various parts of the association cortex may produce conditions known as apraxias, of which there are two basic types: ideomotor apraxias, wherein the patient finds it impossible to perform simple movements such as a military salute or waving goodbye, and ideational apraxias, that is, difficulty in executing a sequence of simple movements necessary to achieve a complex task, such as lighting a fire or addressing and mailing a letter.

Cortical Areas Related to Language

Language obeys the same principles as other cognitive functions, and its deficits (i.e., the *aphasias*) are the result of lesions of relevant multimodal association regions usually of the left perisylvian regions of the cortex.[9] Note that the two hemispheres are not *equipotential* in this regard. That is, they are not responsible for the same functions. In the case of the cerebral organization for language, the left hemisphere is considered dominant in the great majority of people. Although we refer to the "dominant" or "left" hemisphere interchangeably in the following paragraphs, bear in mind that, in some people, there may be a different organization (see also the following section titled "Aphasia in Left-Handed Individuals" later in this chapter). The anterior brain regions are involved in language output, and the posterior brain regions are involved in reception of language. In the left inferior frontal gyrus, anteriorly to the motor area for the mouth and the face, lies Broca's area, and in the left superior temporal gyrus lies Wernicke's area (Figure 2-7).

Cytoarchitectonic Organization of the Cortex

The cortex is obviously "doing" different things within its different regions. These regions have been thoroughly studied and microscopically compared to each other, showing histologic differences. "Cytoarchitectonic maps" of the cortex were introduced in the beginning of the 20th century, the most widely known being those by Brodmann and by Von Economo and Koskinas. Brodmann's 52 areas are more frequently used in scientific communications (See Figure 2-8). For instance, we refer to Broca's area as Brodmann's area (BA) 44 and 45, and Wernicke's area as BA22.

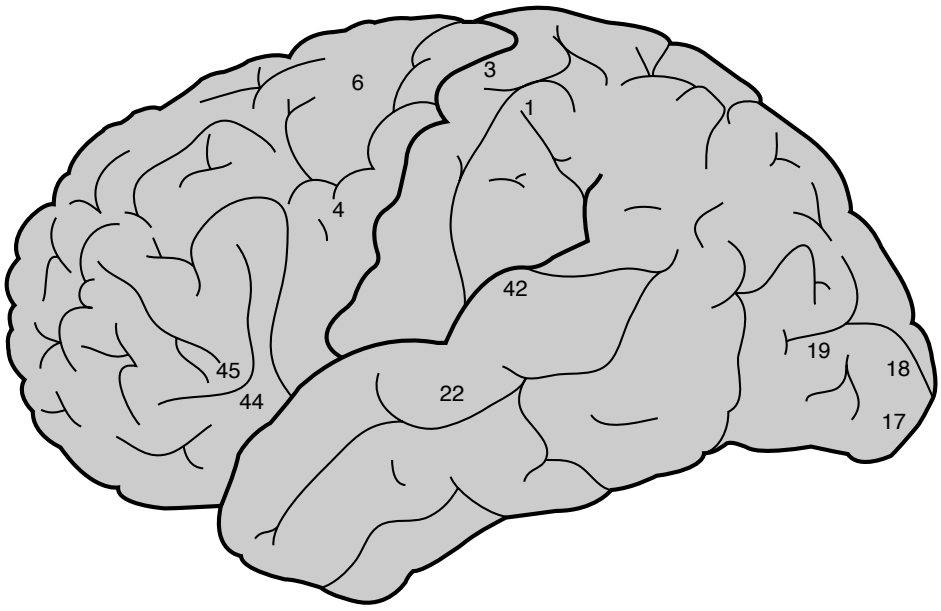

Figure 2-8 Brodmann's areas.

METHODS FOR THE STUDY OF THE NERVOUS SYSTEM AND THE BRAIN

The nervous system and the brain in particular can be studied in their normal condition or in pathologic situations. There are two main categories of methods: imaging methods, either structural or functional, and the clinical method, that is, the study of the effects of lesions on behavior. Lesions may be natural (e.g., resulting from stroke, traumatic brain injury [TBI]) or they may be experimental and reversible (e.g., resulting from the Wada test, transcranial magnetic stimulation [TMS], direct electrical stimulation of the cortex).

The clinical examination method is historically the first and still the most important method for the exploration of the nervous system. It enables us to relate particular areas of the brain to particular cognitive operations. Symptoms and combinations of symptoms (i.e., syndromes) are behavioral and psychological phenomena resulting from lesions in specific parts of the nervous system, and their presence enables us to localize lesions within the nervous system (NS). Moreover, the temporal development of the clinical picture (as, for example, whether the signs and symptoms appear suddenly or progressively or whether they appear one by one or all together) and the necessary knowledge about the person affected (which is obtained through medical history) may guide us to discern the nature of the pathologic cause. For example, symptoms of disordered speech with sudden onset together with a right hemiplegia in an aged right-handed man are most likely caused by a stroke in the left cerebral hemisphere. A similar syndrome, but with progressive onset, also in an aged person might be caused by a growing lesion, such as a tumor or a chronic subdural hematoma. A complete medical history taken from the patient and from significant others (parents or friends) is, therefore, of great importance and forms an integral part of clinical assessment.

In view of the fact that all laboratory exploration furnishes additional elements to this assessment, we may proceed to explore the brain or the NS in two ways: first, through the study of its anatomy and the localization and nature of lesions, and, second, through the study of the electrochemical processes that mediate its various functions and their alterations resulting from pathology. Broca, Wernicke, and the other students of aphasia and neurology in general in the late 19th and the early 20th centuries reported anatomic lesion evidence linked to the syndromes they had observed. This anatomoclinical method provided the first strong argument in favor of an association between clinically observed disorders and their cerebral background. For a long time, physicians, based on the data collected through this method, had to rely on fine clinical semiology, that is, a detailed description of signs and symptoms, to infer what the cause of those signs and symptoms were. A further refinement of this method was the development of objective and quantitative behavioral tests designed to assess particular psychological functions or subsidiary cognitive operations. These tests constitute the core of modern clinical neuropsychology.

Observation and testing were supplemented and, for the purpose of lesion identification, replaced with the advent of imaging, starting with computed tomography (CT) at the end of the 1970s followed by magnetic resonance imaging (MRI) in the beginning of the 1980s. These techniques enabled the procurement of quite precise anatomic images of the brain in vivo. The CT scan (Figure 2-9) is still used as the first step of the diagnostic process in the case of strokes and reveals stroke-induced lesions. However, it is not accurate for small lesions, whether vascular or demyelinating, and it is not sensitive to brain stem lesions. These latter can

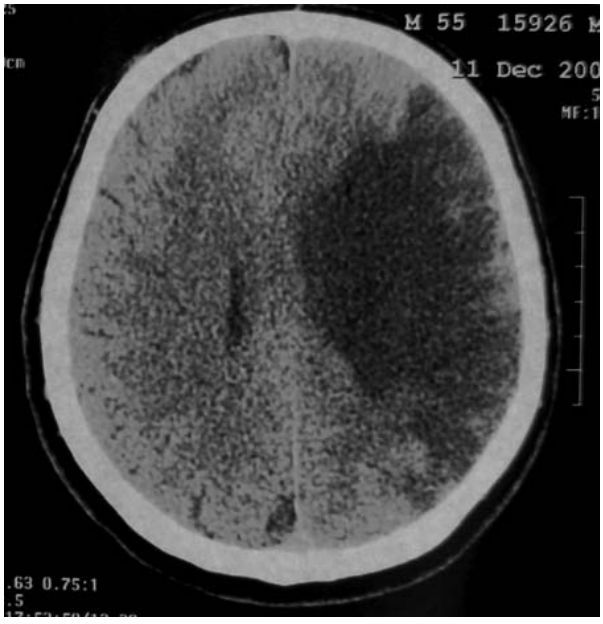

Figure 2-9a Samples of CT-scan.

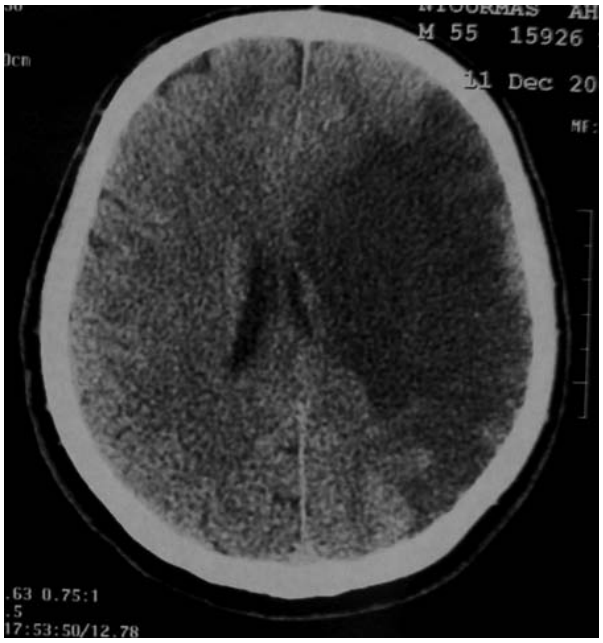

Figure 2-9b Samples of CT-scan.

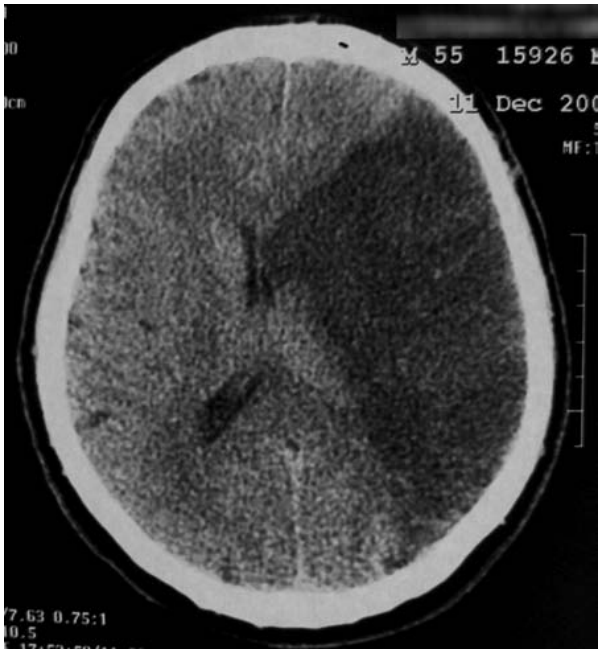

Figure 2-9c Samples of CT-scan.

be detected through MRI (Figure 2-10), which offers a variety of possibilities for identifying various structures and tissues, including the time of onset of a vascular lesion (how old it is). The vascular network of the brain can also be visualized and obstructed arteries or bleeding vascular lesions (such as aneurysms) identified either through magnetic resonance angiography (MRA) or through digital angiography, which requires the injection of a substance directly into the arterial system. All the preceding methods are part of "structural" imaging in the sense that they involve visualization of the structures of the brain, their physical appearance, the existence of lesions, and their location within the brain.

If, however, we are interested in the function—or malfunction—of particular structures rather than in their anatomy, *functional* imaging methods are needed. The oldest of these (since the 1930s), the electroencephalogram (EEG), is the recording of the electrical activity of the brain through the skull via electrodes placed on the scalp. It is always valuable as a method for diagnosing epileptic conditions—not necessarily associated with anatomically visible lesions—and to differentiate the various stages of sleep and wakefulness.

Its counterpart within the peripheral nervous system, electromyography (EMG), and electroneurography are techniques for recording the electrical activity of muscles when contracted and testing the integrity of nerves, or localizing the possible site of their lesions. It is also possible to electrically stimulate nerves (whether motor or sensory) at various points of their trajectory and record their conduction velocity using the time interval between stimulation and responses.

Direct brain stimulation is limited to neurosurgical operations, under local anesthesia. However, transcranial magnetic stimulation (TMS) is a method to stimulate brain regions through electromagnetic induction. It consists of applying very short magnetic pulses to the skull. These induce electrical currents that can depolarize or inhibit neurons of the brain and thus activate or inhibit cortical functions. The application of TMS to the skull above a region of the motor strip results in the movement of the body part corresponding to this region, a response that we can precisely measure. The repetition of this stimulation (rTMS) at different frequencies results in enhancing or inhibiting activity of the brain regions to which it is applied, with seemingly longer-lasting changes. This is the reason rTMS is now experimentally applied for the treatment of various pathologic conditions.

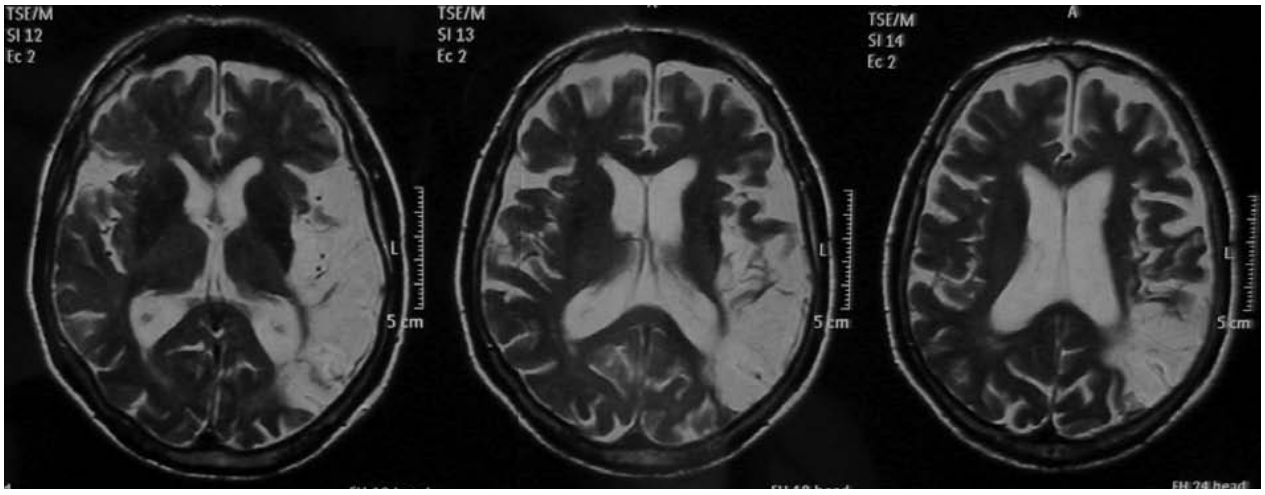

Figure 2-10a Samples of MRI.

Evoked potentials (EPs) and event-related potentials (ERPs) are based on the same principle as the EEG. They are records of the electrical activity of particular regions of the brain, showing the timing and the magnitude of responses of specific cerebral regions—mainly primary sensory areas—to particular stimuli such as, for instance, the response of the primary auditory (temporal) cortex to a sound, or the response of the posterior (occipital) cortex to a light pattern. The latest version of the functional imaging methods is magnetoencephalography (MEG), which, through recording of the magnetic fields created by the electrical activity of the brain, reveals the response of the brain to various stimuli or the activation of cerebral regions during a variety of cognitive, linguistic, and affective tasks. A huge advantage of this method over positron emission tomography or functional magnetic resonance (described subsequently) is its temporal resolution, that is, its capacity for revealing the sequence of activation of brain regions within milliseconds.

Various methods have also been developed to reveal brain function indirectly through indices of metabolism (such as variations of blood flow, glucose or oxygen consumption, or neurotransmitter binding). Functional

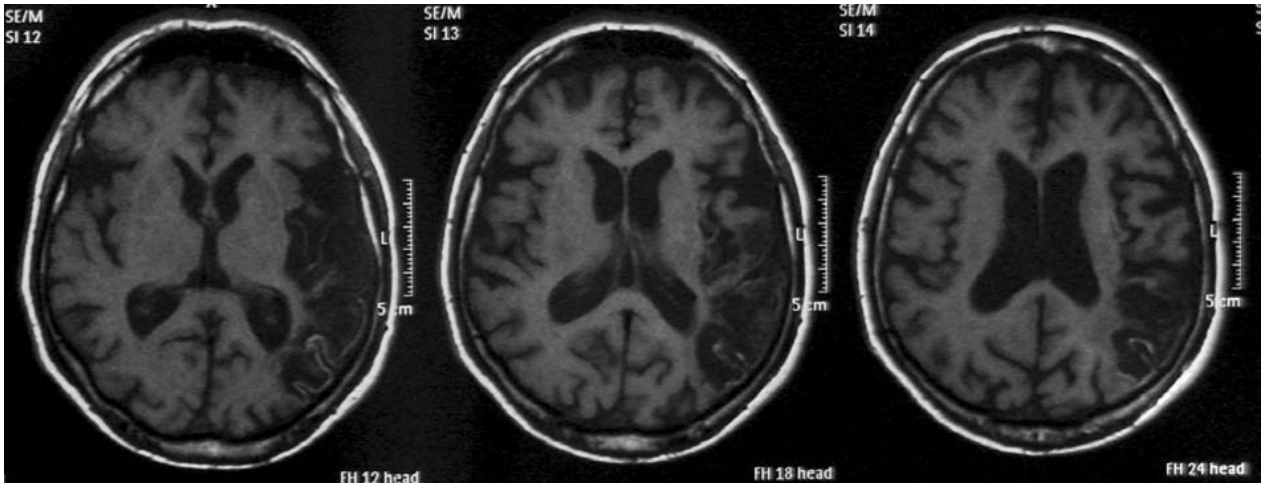

Figure 2-10b Samples of MRI.

magnetic resonance imaging (fMRI) shows the activation of particular brain regions through the rates of blood supply during performance of various tasks. Likewise, positron emission tomography (PET) shows the activation of cerebral structures by visualizing the amount of glucose consumed or oxygen supplied to an area during performance of various tasks.

ELEMENTS OF CLINICAL NEUROLOGY

Overview

The brain is subject to various pathologies, such as infectious, vascular, demyelinating, neoplastic, and degenerative diseases, as well as trauma. Language disorders could be manifestations of any of the preceding pathologies. Consequently, aphasia classification has been highly dependent on studied pathology. Aphasic syndromes can and have been classified differently, on the basis of characteristic symptoms and lesion loci, but also underlying pathology (see, for instance, descriptions of aphasias by the clinicians of the 19th century examining stroke patients compared to descriptions by A. Luria, who studied mainly traumatic brain injuries).

Traumatic brain injuries (TBIs) are a frequent cause of fatalities and serious handicaps in younger individuals, and they have been extensively studied from a neuropsychological point of view because they often result in cognitive and behavioral deficits. TBI lesions, although diffuse, are not random; they affect specific brain areas, such as the orbital and lateral surfaces of the frontal lobes, the inferior surface of the temporal lobes, and portions of the corpus callosum and brain stem. Frontotemporal lesions result in characteristic behavioral disorders, including apathy, fluctuating temper, disinhibition, sometimes aggressiveness, lack of initiative, and, often, severe memory deficits (see Chapter 17, this volume).

Benign tumors developing from the brain's meninges and evolving slowly without evident signs and symptoms and, more frequently, malignant neoplasms originating from glial or other supporting cells and metastatic lesions from lung or breast cancer often interfere with specific cognitive functions. Symptoms of intracranial tumors may be diffuse or focal. Diffuse symptoms result from the pressure exerted by the tumor, brain swelling, or increase in intracranial pressure. Symptoms of impaired mental concentration and slow reaction time progressing into loss of consciousness may appear rapidly, depending on the tumor's position. For example, tumors of the midline (i.e., in the third ventricle) or in the posterior fossa (a small space in the skull containing the brain stem and cerebellum; a tumor growing there can block the flow of spinal fluid) may quickly produce hydrocephaly and increased intracranial pressure, headache, vomiting, papilledema (edema at the fundus of the eye), and the cognitive deficits mentioned earlier. Signs and symptoms generally depend on the tumor's location. Frontal lobe tumors may result in behavioral disorders including apathy, indifference, euphoria, facetiousness, lack of initiative (collectively referred to as the "frontal lobe syndrome"), motor impairments of the opposite part of the body, and often aphasic symptoms if located in the left hemisphere. Temporal lobe tumors may present with auditory and olfactory deficits, aphasic symptoms, memory impairment, and personality and mood changes, or psychotic disorder. Agnosias, apraxias, somatosensory and visuospatial deficits may be associated with neoplasms of the parietal lobe. Visual impairments are the main feature of occipital tumors. Lesions other than neoplastic (abscesses, hematomas, etc.) may cause similar signs and symptoms, caused by either their location or their size.

Degenerative diseases diffusely affecting the cerebral cortex also give rise to neuropsychological symptoms. Cortical degeneration early in Alzheimer's disease affects mainly the medial aspect of the temporal cortex, initially producing episodic memory encoding deficits (see Chapter 18, this volume). Frontotemporal dementias may initially produce frontal lobe syndrome but also poor oral expression and word-finding difficulties. Vascular dementias resulting from multiple infarcts are characterized by sudden onset and escalating severity and give rise to various signs and symptoms depending on the location of the infarcts.

Vascular Pathology of the Brain

Irrigation of the brain, which is about 2% of total body weight, uses about 20% of the total cardiac supply, and the gray matter requires a sixfold quantity of blood compared to that of the white matter.

Eighty percent of all strokes are caused by a reduction or interruption of blood supply to brain areas resulting from a blood clot formed either in situ (thrombosis) or carried by the normal circulation of the blood from elsewhere, where it was initially formed (embolism), leading to ischemia of the cerebral tissue.[10] Bleeding within the brain is called *intracerebral hemorrhage* and

represents 12% of strokes. But blood can also drain into the subarachnoid space, causing acute and intense headache together with neck stiffness, an emergency condition, menacing life: subarachnoid hemorrhages account for 8% of strokes. A very small percentage of strokes are caused by central venous thrombosis.

The risk of stroke depends on various factors: age (older people are mostly affected), gender (men are affected more than women are), race (black and Asian individuals have higher incidence rates), and heredity (those with a family history of stroke are more likely to be affected). There are, however, other factors such as hypertension, smoking, diabetes, heart disease, hyperlipidemia,[11] use of estrogens, use of alcohol, disorders of coagulation, and specific blood diseases, the influence of which may be controlled through preventive measures.

If the obstruction of the vessel persists, the ischemia of a region results in a sequence of modifications, the final consequence being the death or *necrosis* of the cerebral substance. The necrotic area progressively expands, and the surrounding zone, the *penumbra zone*, where cells are still partially functioning, in turn gradually narrows. The swelling (or edema) developing around the lesion compresses small vessels and blocks local circulation, thus worsening the situation. The extent to which the cells in the penumbra zone survive and recover their normal function contributes to the final outcome of the stroke. Together with the resorption of the edema, the survival of these cells partially explains spontaneous recovery that occurs within a few days post stroke.

Strokes have a sudden onset and their clinical picture is established within minutes to hours. However, they may also evolve continuously within days from onset. The stroke is transient if its symptoms last minutes or hours, and reversible if symptoms last up to some days, with subsequent recovery. Transient ischemic attacks (TIAs) are of great importance in that they are, most likely, precursors of another, more severe stroke, with permanent or established symptoms. However, even when established, the symptoms may partially recover over a 3- to 6-month period post stroke. Cerebral plasticity, a process that still remains largely elusive, whether spontaneous or occasioned by rehabilitation, is considered to be the cause of recovery. It is hypothesized that this process includes a number of subsidiary events, such as redistribution of impaired functions to healthy parts of the brain, reorganization of cerebral connections, perhaps even repair of certain injured structures (see Chapter 3, this volume). Thrombolysis, aiming at dissolving the obstructing blood clot, is the ideal emergency treatment of ischemic stroke, but it has to be performed within very few hours following onset and involves potential risks.

Obstruction of the internal carotid may not produce any clinical signs if it progresses slowly enough to allow the collateral circulation to function. If sudden, a variety of symptoms may occur from the territories of the ophthalmic, anterior, and middle cerebral arteries, such as blindness of the corresponding eye, and weakness and hemianesthesia of the opposite half of the body. Usually, however, carotid ischemia is associated with mild, transient symptoms, such as blindness of short duration ("amaurosis fugax") of the corresponding eye, sometimes combined with weakness of an opposite limb. Occlusion of the first branch of the internal carotid, the ophthalmic artery, produces a permanent or temporary blindness of the eye.

The relatively rare syndrome of the anterior cerebral artery obstruction includes paralysis and sensory deficit of the opposite lower limb, urinary disorders, and behavior problems.

Obstruction of the middle cerebral artery—the final branch of the internal carotid artery—results in a severe clinical syndrome, sometimes including confusion or coma, with paralysis and sensory loss in the opposite limbs (hemiplegia and hemianesthesia, respectively), loss of vision in the opposite half of the visual field (hemianopia), and aphasia if the lesion is located in the dominant hemisphere for language (usually the left). If ischemia involves the "minor" hemisphere (usually the right), there may be agnosia of the opposite half of the body, and agnosia or indifference for the left half of the space (hemispatial neglect, a condition different from hemianopia). Frequently, also, the patient may deny, ignore, or be indifferent to his or her own paralysis (anosognosia). If the superior branches of the artery are concerned, there may be central facial paralysis with insensitivity and numbness of the opposite lower half of the face (i.e., a central VII) and of the opposite upper limb, together with Broca's aphasia if the lesion is in the left hemisphere. Ischemia in the territory of the inferior branches leads to contralateral hemianopia or superior quadrantanopia and to Wernicke's aphasia if the hemisphere dominant for language is affected. Ischemia in the territory of the penetrating branches (basal ganglia and part of the internal capsule) is associated with hemiplegia affecting both the contralateral upper and lower limbs and lower face. This capsular hemiplegia may be accompanied by hemianopia, dysarthria, or aphasia.

The vertebral arteries irrigate the inferior part of the brain stem (medulla oblongata), and the obstruction of one of them may remain asymptomatic if the other one is still functioning. Acute occlusion of the vertebral artery usually manifests with cerebellar symptoms (e.g., dysarthria, ataxia) and with lateral medullary ischemia (often resulting in ipsilateral sensory deficits in the face and contralateral sensory deficits in the body). Partial obstruction of the basilar artery may remain asymptomatic if gradual and if the collateral circulation is sufficient. However, it may result in a very severe syndrome involving paralysis of the four limbs (quadriplegia) and profound coma and a multitude of pathologic signs involving eye movements and cranial nerve functions (strabismus, double vision or diplopia, enlargement or mydriasis of the pupil, ptosis of the upper eyelid, hypesthesia—diminished sensation—and peripheral paralysis of one half of the face, dizziness, abnormal movements of the eyes, hoarse or whispering voice, and swallowing disorders), cerebellar symptoms all on the side of the lesion, and motor and sensory deficits involving the opposite side of the body. Many of these symptoms may be caused by obstruction of one of the thin arterial branches irrigating parts of the brain stem.

The *locked-in* syndrome, caused by a lesion in the upper part of the brain stem, is characterized by complete paralysis, including the head, only with the possibility of vertical movement of the eyes and eyelids. The most salient feature of this syndrome is that, whereas consciousness and sensation may be intact, they pass unnoticed by all observers because of the pervasive paucity of all capacity for movement.[12]

Ischemia in the territory of one posterior cerebral artery leads to hemianopia in the opposite visual field, which may be associated with hemiparesis and hypoesthesia or unilateral absence of movement coordination of the limbs (ataxia) resulting from the interruption of cerebellar circuits. Hemianopia may be the only symptom of the obstruction of the surface branches, associated with visual agnosia and/or alexia (loss of reading ability) when the lesion is located in the dominant hemisphere for language.

Sometimes, ischemia occurs *between* the previously mentioned major arterial territories, in their boundary zones and not within them. We then speak about "watershed infarction" and in some cases we suppose that the cause is not arterial occlusion but rather low flow of the blood caused by severe arterial hypotension, for example, in cases of cardiac arrest or cardiac surgery. This may happen either in the posterior boundary zones, between the territories of the middle cerebral artery and the posterior cerebral artery, in the conjunction of the parietal and the occipital cortex, or in the anterior boundary zones, between the territories of the middle cerebral artery and the anterior cerebral artery, in the frontal area close to the summit of the cerebral hemisphere. These infarcts may be unilateral or bilateral, and whenever they affect the dominant hemisphere they cause aphasia.

CEREBRAL REPRESENTATION OF LANGUAGE

This section is not intended to be a historical account of notions regarding aphasia, such as are presented in the first chapter of this volume. We do, however, summarize the basic correlations between lesion location and aphasic deficits that emerged over the years from clinical observation. Paul Broca, a French surgeon, found on the postmortem examination of his "aphemic" patients (including his first patient who uttered almost nothing but the syllable *tan*) a lesion involving "the third frontal convolution" (Broca, 1861, as cited in Hécaen & Dubois, 1969, p. 60), anterior to the motor area responsible for mouth and face movement, and speculated that this damaged region was the "seat of the faculty of articulate speech" (Broca, 1865, as cited in Hécaen & Dubois, 1969, p. 108).[13]

Some years later, Carl Wernicke (1874), a German neurologist, described a woman who spoke fluently, though erroneously, with distorted words, that is, *paraphasias*, but could not understand speech. He thought that the lesion had destroyed the "center for acoustic images of the words" in the superior temporal gyrus. This lesion was, according to Wernicke, the cause of her "sensory aphasia." He considered "Broca's region" as the "center for motor images of the words," and a lesion in it was the cause of a "motor aphasia." Lesions of the association fibers connecting these two "centers" were thought to produce "conduction aphasia" (fluent speech, good comprehension, but impossible repetition, with paraphasias).

Lichtheim (1885, cited in Compston, 2006) conceived an additional, not anatomically defined, "center of concepts." He, in fact, proposed a simple scheme for all aphasia known as the "Lichtheim's house" (see Figure 1-4 in Chapter 1). According to it, speech sounds arrive from the ears and the auditory regions of the brain and are identified as words in the center of acoustic images. Then, they are transmitted to the center of motor word images, both

directly and indirectly, through the concept center. From there, they are transmitted to the nuclei of nerves innervating the speech apparatus. According to this scheme, "transcortical aphasias" (transcortical sensory, motor transcortical, and mixed transcortical aphasia) are caused by lesions in large cortical regions, outside Wernicke's and Broca's areas, and they affect connections between those areas and the concept center.

Clinicians retained in practice Wernicke's and Lichtheim's schemes, using the criteria of fluency of speech, comprehension, and repetition (Table 2-1). Thanks to their simplicity and heuristic value, generations of neurologists (especially before the advent of structural brain imaging such as CT, MRI) were, and still are, able to deduce the existence and gross localization of brain lesions in aphasic patients from the type of aphasic symptoms.

Later, Dejerine (1892) described the case of a patient, a highly cultivated man, who suffered a pure verbal blindness, also called pure alexia or alexia without agraphia, as a consequence of a stroke. This patient spoke readily and correctly, understood well what he was told, but, when asked to read, he gave the impression of an illiterate individual. He could write perfectly well, but he could not read what he had just written! The lesion was located in the visual area (in the left occipital lobe) and included the posterior part of the corpus callosum called *splenium*, consisting of axons coming from the visual area of the opposite hemisphere (Figure 2-11). Thus, no visual information whatsoever, from either hemisphere, could reach the language region in the left hemisphere (Dejerine, 1891/1977, pp. 94, 109). In this way, there would be no need for a specific center for reading besides the primary visual areas and a "language center." This associationist view could apply more generally in neuropsychology, explaining many pathologic situations as "disconnection syndromes." In general, a disconnection syndrome occurs because of rupture of connections between brain centers, which, in theory, are specific for a particular function (for example, Broca's area, the alleged speech center, as a part of the perisylvian language network) (see Figure 1-4, in the first chapter of this volume).

The contemporary "neoassociationist" Wernicke–Geschwind model (Geschwind, 1965) was based on the preceding assumptions. Geschwind (1967) included most of Lichtheim's original formulation and suggested that semantic processing is mediated by a specific brain region, probably the inferior parietal cortex.

Meanwhile, many theorists have questioned the Wernicke–Geschwind model on various grounds, including Freud (who argued against Wernicke's model in his monograph "On Aphasias," in 1891), Pierre Marie,[14] and John Hughlings-Jackson, who maintained that "to locate the damage that destroys speech and to locate speech are two different things" and that "to discuss the functions of the cortex as if they were based on abrupt geographical locations is logically absurd" (Finger, 1994, p. 379).

Hughlings-Jackson and others—including, incidentally, P. Broca[15]—observed some cases of severely aphasic patients with large lesions of the left hemisphere who still uttered "automatic" speech, and they stated that language can be both automatic (swear words, poems, or prayers), supported by the right hemisphere, and "propositional" or "intentional," supported by the left hemisphere (Basso, 2003).[16] Thus, an important detail in studying aphasia is whether a patient can or cannot use language, a dissociation that constitutes evidence that language is not lost but only inaccessible under certain circumstances.[17] This notion is the basis of the stimulation approach in aphasia therapy (Basso, 2003).

Table 2-1 Usual Characteristics of Aphasic Syndromes

Type of Aphasia	Fluency	Comprehension	Repetition	Naming
Global	Nonfluent	-	-	-
Broca	Nonfluent	+	-	-
Motor transcortical	Nonfluent	+	+	-
Mixed transcortical	Nonfluent	-	+	-
Wernicke	Fluent	-	-	-
Sensory transcortical	Fluent	-	+	-
Conduction	Fluent	+	-	-
Anomic aphasia	Fluent	+	+	-

Note: - = mostly impaired; + = mostly preserved.

Source: Adapted from J. R. Hodges, 1998. *Cognitive assessment for clinicians*. Oxford, England: Oxford Medical Publications.

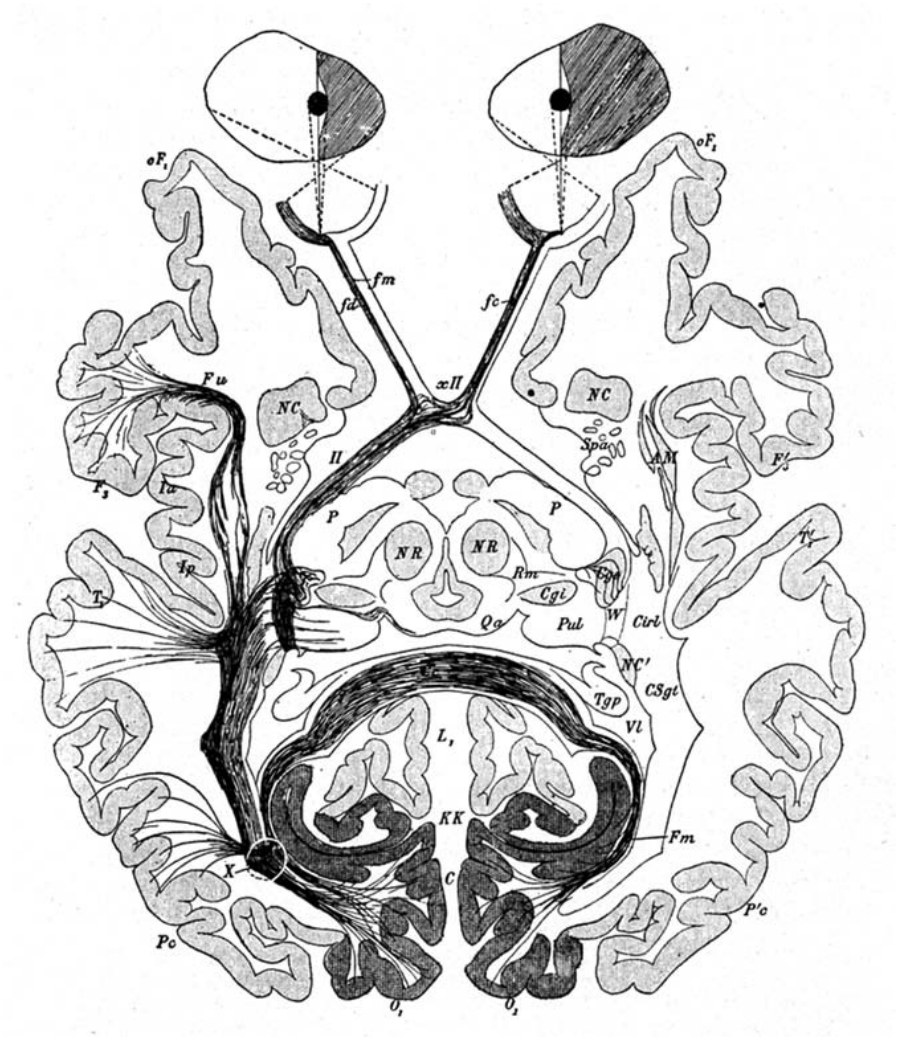

Figure 2-11 Design of Dejerine's lesion.

Source: This image was published in: *Sémiologie des affections du système nerveux, J. Dejerine*. Pure verbal blindness, p. 109, © Elsevier, 1914/1977.

Many clinicians adopting the holistic approach, such as Henry Head, Kurt Goldstein, and others, did not see language as localized in particular centers, but, instead, they conceived the brain working as a whole (Lantéri-Laura, 1987; Riese, 1959) to mediate language.

There are now two supplementary kinds of evidence on which concepts of cerebral organization for language are based: first, some cases reported in the literature, but also some systematic studies of series of cases (e.g., Kreisler et al., 2000; Willmes & Poeck, 1993), have shown that there is no absolute one-to-one correspondence of symptoms or syndromes to localization of lesions. Second, functional studies with PET and fMRI in healthy persons show the participation in language of many regions, varying according to the linguistic task (e.g., Hagoort, 2005; Hickok & Poeppel, 2004; Shalom & Poeppel, 2008); these studies also show the activation of various brain structures along the recovery phases of aphasia after a stroke, in fact, the flexibility and plasticity of the brain (e.g., Breier, Maher, Schmadeke, Hasan, & Papanicolaou, 2007; Saur et al., 2006). Indeed, language processing is not dependent on Wernicke's and Broca's areas alone, but depends on many neural sites linked as systems and working in concert.

Broca's and Wernicke's areas may be "conceptualized as transmodal gateways [coordinating] reciprocal

interactions between the sensory representations of word forms and the arbitrary (second-order or symbolic) associations that give them meaning." They would "constitute the two epicenters of a distributed language network" (Mesulam, 2000, p. 37). "They also provide 'neural bottlenecks' in the sense that they constitute regions of maximum vulnerability for lesion-induced deficits in the pertinent cognitive domain" (Mesulam, 2000, pp. 16–17). In other words, Broca's and Wernicke's areas play the role of epicenters or gateways of a network for language, which includes primary sensory and association cortical areas, as well as motor areas. Language is therefore distributed all over the left hemisphere, including even regions of the right hemisphere.

TYPES OF APHASIA, TYPICAL LESION LOCATIONS, AND TYPICAL SIGNS AND SYMPTOMS

As can be gathered from the preceding description, language disorders have been classified in several different ways, often based on different theoretical frameworks. The most typical classification is the so-called neoassociationist classification, which is based on the anatomic disconnection model (Geschwind, 1967). According to this model, a lesion in a specific brain area results in a more or less well-defined aphasic syndrome. In *Broca's aphasia*, speech is effortful, nonfluent, consisting of short phrases or single words. However, the clinical picture may vary from a complete loss of speech to a mild deficit characterized simply by word-finding difficulties. For example, in the case of telegraphic speech (i.e., agrammatism), all small, function words (e.g., prepositions) are absent and the patient communicates using mainly nouns and verbs. This pattern may also extend to written language. Automated verbal sequences, such as reciting the days of the week or counting, and occasionally cursing or emotional speech, are usually preserved. Comprehension is relatively spared. Nevertheless, thorough examination reveals specific comprehension deficits regarding complex syntactic structures. Repetition of words or sentences, reading aloud, naming, and writing are also affected. Phonemic paraphasias[18] are occasionally observed. Individuals with Broca's aphasia in general also suffer from apraxia of speech (Basso, 2003), ideomotor apraxia (Benson, 1993), and right hemiplegia of various degrees. Broca's aphasia is classically associated with a lesion in the posterior part of the inferior frontal gyrus, the insula, and the frontal operculum (the most posterior portion of the inferior frontal gyrus [i.e., of Broca's area] is part of the operculum). Premotor and prefrontal areas of the cortex, subcortical regions, and parts of the basal ganglia may also be affected.

An almost reverse image, with difficulty in understanding language while the ability of verbal expression remains unaffected, is diagnosed as *Wernicke's aphasia*. The extent of comprehension problems may vary among patients and moderate comprehension deficits are not uncommon (Basso, 2003). Verbal output is fluent, and it is characterized by the presence of phonemic and semantic paraphasias,[19] neologisms,[20] and empty speech,[21] while rich content words are reduced in frequency. When severe, this condition is called *jargon aphasia*. Because the persons with aphasia are unable to monitor their own verbal output because of the comprehension deficit, such patients are often unaware of their language disorder (i.e., anosognosia) and this further affects communication difficulties and often hinders rehabilitation. Repetition, naming, reading aloud, and writing are impaired. Ideomotor apraxia and hemianopia (Basso, 2003) or superior right quadrantanopia (Adams, Victor, & Ropper, 1997) are common in Wernicke's aphasia, while motor disorders are rare. Wernicke's aphasia is usually associated with lesions of the posterior left perisylvian region, localized in particular at the posterior part of the superior temporal region traditionally referred to as Wernicke's area, and occasionally extending to the adjacent parietal and temporal areas.

In *conduction aphasia*, repetition is compromised though speech remains relatively fluent, albeit characterized by phonemic paraphasias and word-finding difficulties. Patients are aware of their verbal paraphasias, and often, while trying to correct themselves, they produce several phonemic variations of the target word, a phenomenon called *conduite d'approche* (Alexander, 2000). Comprehension is generally spared, with some patients having problems understanding complex syntactic structures (Basso, 2003). Deficits in naming and writing are common. Reading aloud is impaired and contains semantic and phonemic paralexias.[22] Ideomotor apraxia and motor and/or sensory deficits may be present (Basso, 2003). The lesion associated with this aphasic syndrome is typically located in the left temporal-parietal junction. However, it has been proposed that conduction aphasia is the result of a more extensive lesion including other structures, such as the insula, the primary auditory cortex, and the supramarginal gyrus (Damasio, 1998).

Global aphasia includes severe deficits in all aspects of language. Speech is nonfluent and often limited to

stereotypic utterances ("ta-to," "to-po"). However, overlearned, automatized sequences (reciting the days of the week, for example) are sometimes preserved. Comprehension, naming, repetition, reading, and writing are severely impaired (Alexander, 2000). Such a condition is the result of a lesion covering a large portion of the perisylvian area, often caused by total occlusion of the left middle cerebral artery, therefore causing severe motor and sensory deficits involving the right half of the body and occasionally visual field defects, as well as oral, ideomotor, and ideational apraxias (Cummings & Mega, 2003).

Anomic aphasia is often referred to as *amnestic*, *amnesic*, or *nominal aphasia*. *Anomia* refers to the patient's inability to find names of people or objects. The patient, although aware of the nature of an object, is unable to name it upon request. Verbal output is fluent, characterized by word-finding difficulties, frequent pauses, and circumlocutions, while phonemic and semantic paraphasias are rare. Repetition, comprehension, and reading aloud are spared. Anomic aphasia may be associated with lesions affecting posterior language areas, including the angular gyrus (in the parietal lobe, near the superior edge of the temporal lobe) or the middle temporal gyrus. However, it is frequently observed as the outcome of many recovered aphasics. Moreover, several brain regions are involved in confrontation naming, depending on the type and modality of the stimulus. Thus, anomic aphasia is considered to have little or no localization value (Basso, 2003).

Transcortical aphasias are characterized by a disproportionately preserved capacity of repetition. They result from a more or less complete isolation of the speech areas (i.e., the perisylvian language zone of the left hemisphere) from the rest of the cortex (Assal et al., 1983) caused by multiple cerebral infarcts or diffuse lesions (due to anoxia) in the border zones of irrigation of the arteries of the brain (i.e., the "watershed" area). Ischemic lesions in such cases may cover a hemicircular area from the convexity of the frontal lobe to the junction between parietal and occipital cortex, through the superior parietal cortex, or portions of this area, or deeper subcortical regions under this area.

Patients suffering from *transcortical motor aphasia* demonstrate nonfluent speech with preserved comprehension and relatively spared naming. Reading aloud and writing are impaired, and phonemic paraphasias are observed in some cases. There is a striking preservation of the repetition capacity that, in some cases, takes the form of passive, "parrot-like" echoing of everything heard (echolalia). Depending on the site and extent of the lesion, accompanying neurologic symptoms, such as mild dysarthria and sensory and motor disorders, may be present (Alexander, 2000). Transcortical motor aphasia may be the sequel of a recovered Broca's aphasia or part of the syndrome resulting from massive frontal lobe lesions, in which case it is accompanied by lack of initiative and akinetic mutism.[23] It corresponds to the "dynamic aphasia" described by A. Luria (Adams et al., 1997; Roch-Lecours & Lhermitte, 1979). Overall, the lesions that cause it have been found in various sites: in the frontal region anterior or superior to Broca's area (Benson, 1993), at the supplementary motor area, or at the cingulate gyrus (Cummings & Mega, 2003). In some cases, the lesion is subcortical, affecting white matter beneath the frontal lobe (Damasio & Geschwind, 1984).

In *transcortical sensory aphasia*, speech is fluent but in many cases meaningless or unintelligible (i.e., jargon), with many paraphasias and neologisms. Comprehension of oral and written language, naming, reading, and writing are severely impaired, while the most prominent characteristic is again the preserved ability of the patient to repeat words and sentences. Echolalia is present in some cases.[24] This type of aphasia is associated with lesions posterior to the perisylvian region, in the parietal-occipital region (Adams et al., 1997).

Mixed transcortical aphasia is a rare syndrome combining signs and symptoms of motor and sensory transcortical aphasias. Speech is nonfluent, and comprehension, naming, writing, and reading are severely impaired. Its salient feature is preserved repetition of words and sentences, often in the form of echolalia (Alexander, 2000). The lesion site is typically the watershed area.

Several other attempts of classification, made at various times in the history of aphasiology, have not been able to dislodge from its position of prominence the associationist classification based on the anatomic disconnection model. This model remains dominant and extensively used despite the fact that on its basis many aphasic patients are labeled "unclassified" and many symptoms are not clearly explained, as for instance, anomia, the comprehension deficits found in many individuals with Broca's and conduction aphasia. On the other hand, the utility of the associationist classification is doubtless the result of its inclusiveness and basic correctness, which facilitate the task of clinicians diagnosing and treating aphasic patients and of researchers studying aphasia in general. As stated by Benson and Ardila (1996), "The syndrome classification originally

developed by the 19th century continental investigators remains basically accurate, replicable, and clinically useful" (pp. 111–112).

In any case, clinicians should follow a deficit-based assessment methodology. A careful and detailed analysis of language deficits is the best way to obtain a detailed patient profile and potentially a more efficient intervention strategy. Aiming to rehabilitate a single symptom and not the syndrome in its entirety would probably result in a better therapeutic outcome.

Subcortical Aphasia

Lesions of the white matter and the subcortical nuclei that do not affect the cortex can also result in various aphasic symptoms (Fasanaro et al., 1987; Hayashi, Ulatowska, & Sasanuma, 1985; Kreisler et al., 2000; Radanovic & Scaff, 2003; Willmes & Poeck, 1993; Yamadori, Ohira, Seriu, & Ogura, 1984). Thus, subcortical aphasia is not a homogeneous entity and clinical manifestations often vary among patients. The syndrome related to lesions confined to the head of the left caudate nucleus and the anterior limb of the internal capsule (containing fibers from the frontal cortex to brain stem and from the thalamus to frontal lobes) includes deficits in comprehension, dysarthria, and motor impairments (Damasio, Damasio, Rizzo, Varney, & Gersh, 1982). Thalamic aphasia is characterized by nonfluent speech and rarely by comprehension deficits, sometimes complete suppression of speech at onset and later by low voice volume, severe reduction of spontaneous speech, mainly restricted to responses to direct questions only, and by semantic paraphasias (Darby & Walsh, 2005).

Aphasia in Left-Handed Individuals

Hécaen and Ajuriaguerra (1963), who examined a population of 309 right-handed and 59 left-handed individuals with either left or right lesions, concluded that aphasic disorders are more frequent but less severe in left-handed individuals because of a hemispheric specialization that remains less strong. Other researchers suggest that aphasia in left-handed persons with left hemisphere dominance for language is clinically different from aphasia in right-handed individuals and has a better prognosis (Gloning et al., 1976; Luria, 1970; Subirana, 1969; all cited in Basso, 2003).

However, Basso, Farabola, Pia Grassi, Laiacona, and Zanobio (1990) state that differences in type of aphasia and recovery between right-handed and non-right-handed individuals have been overemphasized and must be reconsidered. An invasive method used to address these questions, usually before surgical interventions for intractable epilepsies, is the intracarotid injection of sodium amytal, also known as the Wada test (Wada & Rasmussen, 1960). Left or right dominance for language is inferred from the presence of transient aphasic symptoms after injection of a barbiturate, typically sodium amytal, in the left or right internal carotid. If aphasia is present after both injections, language representation is considered to be bilateral. With this method Rasmussen and Milner (1977) found left-hemisphere dominance in 96% of subjects and 4% of right dominance in 140 right-handed subjects; they found also 70% of left dominance, 15% of bilateral representation, and 15% of right dominance in 122 non-right-handed subjects (either left-handed persons or those with mixed manual preference). These numbers are still used as basic reference in the matter, but we have to keep in mind that the patients in this study had epilepsia, and that their repartition in left- and right-handed groups depends on the method used for the evaluation of manual preference (Dellatolas & Potagas, 2009).

Crossed Aphasia

Occasionally, there are cases of right-handed individuals suffering from aphasia after right hemisphere lesions. Since 1975, more than 180 such cases have been described (Mariën, Paghera, De Deyn, & Vignolo, 2004). Apart from these rare cases, patients with right hemisphere lesions will probably perform well in traditional aphasia tests, but they may present deficits in extralinguistic aspects of language, such as prosody and processing nonliteral verbal stimuli (e.g., metaphors, ironic or humorous phrases) and abstract concepts (Darby & Walsh, 2005; see Chapters 15 and 16, this volume).

Sign Language Aphasia

Deaf people who use a sign language can acquire aphasia in that language as a result of lesions in the left hemisphere, much in the same way as oral language users. Reported in the literature are cases of such aphasic patients who could pantomime and understand an action such as "brushing of the teeth," whereas they were unable to produce or understand the sign for *toothbrush*, despite the similarity of the gesture and the sign (MacSweeney, Capek, Campbell, & Woll, 2008, p. 232). Such findings indicate that language is heavily dependent on the left hemisphere, whether the output is verbal (spoken language) or not (sign language).

Study Questions

1. Name the structures of the central nervous system.
2. Which are the important arteries supplying the brain with blood?
3. Which lesions of the cerebral hemispheres are related to aphasic signs and symptoms? In which arterial territories can ischemia cause aphasic symptoms?
4. Which cranial nerves are related to speech impairments?
5. What kind of speech disorders are caused by dysfunctions of the extrapyramidal system? In which way can a cerebellar lesion affect speech?
6. What are the symptoms of the main aphasic syndromes?
7. What deficits may accompany Broca's aphasia, beyond language deficits?
8. What are the fundamental characteristics of Wernicke's aphasia?
9. What is the usual localization of a cerebral lesion causing Broca's aphasia?
10. What is the usual localization of a cerebral lesion causing Wernicke's aphasia?
11. Can a deaf person become aphasic? In what sense is sign language aphasia similar to aphasia of patients with no hearing impairment?
12. What is the common characteristic of the three transcortical aphasic syndromes?

NOTES

1. Indeed, the vast majority of the connections between neurons are made within the brain and only a very small number of the neurons connect with lower parts of the CNS, that is, the brain stem and the spinal cord.
2. The motor, or pyramidal, pathway crosses at the pyramids, at the level of the brain stem's medulla oblongata; the ascending posterior tract of the spinal cord, conveying the proprioceptive sensation, crosses a bit higher, at the interior lemniscus. The ascending fibers conveying superficial sensitivity (pain, temperature, light touch) go directly to the thalamus of the same side (spinothalamic tract) because they have already crossed at the level of their entry in the spinal cord.
3. The cortex is extensively connected to the external part of the basal ganglia, or neostriatum, consisting of the caudate, the putamen, and the pars externa of the globus palidus; these are, in turn, connected to the internal part of the ganglia, or paleostriatum, consisting of the pars interna of the globus palidus and the reticulate portion of the substantia nigra.
4. Dopamine (DA) is one of the neurotransmitters, the chemical substances serving the transmission of messages in the synapses of the nervous system.
5. *Myoclonus*, *tics*, *tremor*, *chorea*, *athetosis*, and *dystonic movements* or *positions* are the terms used to describe forms of involuntary movements seen in hyperkinetic extrapyramidal syndromes.
6. For the interested reader, clinical stories richly and vividly describing—and explaining—these and other conditions can be found in Oliver Sacks's books *The Man Who Mistook His Wife for a Hat and Other Clinical Stories*, *Awakenings*, and *Musicophilia*.
7. Paralysis of half of the body.
8. The same is also true in the frame of the CNS in cases of demyelinating diseases, including multiple sclerosis.
9. Lesion loci in the left perisylvian region are the most common cause of aphasia. However, several cases have been reported in the literature where aphasia was caused by a lesion in the right hemisphere or a lesion in the left hemisphere but outside the perisylvian zone.
10. Thrombus is usually the result of atherosclerosis of big or medium arteries of the brain; thrombi are formed of the atherosclerotic plaques on the artery's wall, thus gradually narrowing and finally obstructing the artery. Emboli of various sizes may be produced in other large arteries (usually in the common or the internal carotid artery) or the heart as a result of atherosclerosis or heart disease, and they migrate, obstructing smaller arteries. Stroke can also be the result of bleeding or hemorrhage caused by a lesion of some vessel.
11. Abnormally elevated levels of any or all lipids in the blood.

12. This condition has been vividly illustrated in the first person by Jean-Dominique Bauby. On December 8, 1995, at the age of 43, Bauby suffered a stroke. When he woke up 20 days later, he was entirely speechless; most of his body was paralyzed, but his mental facilities were intact. He could only blink his left eyelid. Despite this condition—the locked-in syndrome—he wrote the book *The Diving Bell and the Butterfly* by blinking when the correct letter was reached by a person slowly reciting the alphabet over and over again. The book was published in France on March 7, 1997. Bauby died 10 days after the publication of his book.
13. The lesion was in fact much more important as "the frontal lobe of the left hemisphere was softened in the bigger part of its surface," extending to "the ascending fold of the parietal lobe (. . .) the marginal fold of the temporal lobe (. . .) the insula, and the corpus striatum" (P. Broca, 1861, cited in Hécaen & Dubois, 1969; p. 60).
14. Pierre Marie (1906) argued that there is only one true aphasia: Wernicke's aphasia, caused by a lesion in Wernicke's area and characterized by the loss of a specialized *form of intelligence*, a psychological construct referring to an integrated set of notions and procedures learned through instruction. However, in case of additional, coexistent lesions, this "true" aphasia can be accompanied by other symptoms, such as anarthria, which is caused by an anterior extension of the lesion into the deep white matter and the lenticular nucleus.
15. Paul Broca mentions the complex swear of his aphasic patient Tan, the famous "*Sacré Nom de D[ieu]!*" (Broca, 1861, cited in Hécaen & Dubois, 1969; pp. 64, 75, 77).
16. This dissociation between voluntary or propositional versus automatic uses of language had already been described by Baillarger in 1865 as "automatic-voluntary dissociation" (Baillarger, 1890, cited in Hécaen & Dubois, 1969; Roch-Lecours & Lhermitte, 1979).
17. Alajouanine provided another example to illustrate the automatic-voluntary dissociation: he

    *had asked an aphasic patient the name of her daughter, who was sitting beside her. After vainly struggling for her daughter's name, the lady turned toward her daughter and said in a very distressed voice, "*Ma pauvre Jacqueline, voilà que je ne sais plus ton nom!*" ("My poor Jacqueline, I don't even know your name!"). (Alajouanine, 1968, p. 250; cited by Basso, 2003)*

    As Basso (2003) comments: "Answering Alajouanine's question required an intentional search for her daughter's name, but addressing her by her name was automatic" (p. 13).
18. Mispronunciation of a word as a result of deletion, substitution, transposition, or addition of one or several phonemes.
19. Substitution of a whole word with another one, usually semantically related.
20. Severe disturbance of the phonemic integrity of a word resulting in a new, sometimes meaningless, word.
21. The patient speaks fluently, but the verbal output is of poor content.
22. The equivalent of paraphasia, when referring to reading aloud.
23. The patient does not initiate speaking or moving.
24. For example, during the aphasia assessment, the patient automatically repeats what the examiner says.

ACKNOWLEDGMENTS

The authors are grateful to Sotiris Filippakopoulos for his drawings and Professor Andrew Papanicolaou for revising the text.

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