2

Pandora's Box

It may seem obvious to many of us that our capacities for reason and language are the product of the activity of interconnected neurons in the brain. However, coming to this interpretation is the result of a long history, starting from early conceptions that interpreted brain matter as little more than a cushion to protect the spirits inside the brain from harm. Furthermore, identifying the brain regions related to speech and language processing became possible only after the postmortem study of language-impaired individuals, a discipline that progressed quite slowly during the late nineteenth and twentieth centuries. Only with the advent of brain imaging techniques in the late twentieth century have we gained more detailed insight into the organization and structure of language-related networks. This chapter provides a historical account of the discovery of the brain as the organ for thought and language, and the different interpretations and controversies that shaped the history of neurolinguistics, many of which are causing sparks to this day.

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White Matter, Gray Matter

Modern neuroanatomy probably began with the work of Thomas Willis in Oxford in the mid seventeenth century (Zimmer 2004). Willis was the first to emphasize the difference between gray and white matter, and to pay attention to the cerebral convolutions of the brain. His interest in the minute anatomy of the brain led him to make fundamental contributions to what is now modern neurology (in fact, he and his colleagues coined the term "neurology"). He made elegant descriptions of the cranial nerves, the corpus callosum (then called the mesolobe, and noted that it was composed of fine parallel lines), the corpus striatum (a deep nucleus inside the cerebral hemisphere, so named because of the mixture of gray matter and fiber tracts), the thalamus and other regions, including the circle of Willis, a circle of arteries surrounding the hypothalamus, obviously named after him. Besides these empirical contributions, Willis also came to the conclusion that it is in gray matter that our feelings and thoughts are located. He conceived white matter as a series of channels that convey perceptions and thoughts into the gray matter of the cerebral cortex, which stores them as enduring memories. Willis drew attention to the distinct brain folds and convolutions in different animals, which he believed served to store sensory impressions, and noted that these were less complex in quadrupeds than in apes and humans. Furthermore, he believed that "storms" of atoms in the brain caused mental phenomena, and that mental disorders might be effectively treated with pharmaceutical products.

After Willis, another important step in advancing neurology was the development of phrenology in the early nineteenth century by the German anatomist Franz Joseph Gall. Instead of observing cerebral tissue itself, Gall dedicated himself to analyzing the variability of skull shapes, which according to him represented the development of different parts of the brain in individuals, resulting in outward pressure on the cranium during growth. Thus, he developed an elegant but seriously erroneous map of different mental faculties located in specific parts of the brain, represented by distinct "bumps" on the surface of the skull (Corsi et al. 1991; Steinberg 2009). This discipline is often dismissed as a classic example of pseudoscience, as there was no empirical support for the proposed localizations. This was solidly demonstrated by Pierre Flourens when he sectioned brain regions of animals and observed their behavioral effects. However, the influence of Gall on the subsequent development of neurology was tremendous. Jerry Fodor proposed that Gall set the path for the concept of cerebral localization in which different functions are circumscribed to specific brain regions. Perhaps more fundamentally, he argued for what is called "faculty psychology", that is, the psychological processes like attention, memory, and language are functionally different faculties (Fodor 1983). Furthermore, his notion that the growth of "bumps" on the skull (and the underlying brain) corresponds to the development of different capacities presaged the modern concept of experience-dependent plasticity. We all take these notions for granted now, but Gall's implicit influence on these basic ideas is substantial.

Gall considered that language is localized in the region of the frontal lobes above the eye orbits, which is now called the orbitofrontal cortex. This notion received support in the early nineteenth century from Jean Baptiste Bouillaud, who presented postmortem evidence from lesioned patients that indicated frontal localization of speech functions (Corsi et al. 1991). Bouillaud's work was highly criticized by many, but the point was made that at least one of the frontal lobes was found to be damaged in the autopsied brains of individuals that had lost the capacity for speech, while there were no cases of loss of speech in individuals with intact frontal lobes. Bouillaud distinguished the capacity to produce mental symbols and ideas that are preserved in memory (inner speech, controlled by the frontal lobe gray matter), from the actual articulation of these ideas in concrete words (external speech, controlled by frontal lobe white matter).

The Power of the Microscope

Unlike Gall, Paul Broca (whom we met in Chapter 1) was interested in brain anatomy and the structure of brain convolutions, which were notably conserved in distinct species. By that time, the comparative study of brain gyri was well on its way after the work of Luigi Rolando in the early nineteenth century, who divided the brain into posterior and anterior components, separated by Rolando's fissure (now called the central fissure). Sometime before in the seventeenth century, Franciscus Sylvius described the other main sulcus of the human brain, called the Sylvian or lateral fissure (Zimmer 2004; Schiller 1992). Broca had studied with Jules Baillarguer, who discovered the microscopic six-layered structure of the cerebral cortex, which is conserved across the different gyri but with subtle differences in the thickness of these laminae, as, for example, the bands of Baillarguer, two horizontal stripes of myelinated fibers that are especially prominent in the visual cortex. These findings were precursors to the field of cytoarchitectonics, which consisted of the systematic analysis of the laminar composition of the cerebral cortex across brain regions. Researchers like Theodor Meynert found that the thickness and appearance of the different laminae are not uniform across the cerebral cortex, which could be parcellated into several areas, each being relatively homogeneous in its laminar composition. This provided support to the concept of the cerebral cortex as a mosaic of specialized areas rather than a uniform, homogeneous mantle covering the encephalon (Schiller 1992; Corsi et al. 1991).

Cytoarchitecture received substantial support from the emerging studies of the cellular composition of the nervous system, led by Camillo Golgi and Santiago Ramón y Cajal. Both scientists took advantage of Golgi's discovery of a silver staining method to analyze the fine structure of individual neurons, which permitted observing the immense variety of neuronal types in different regions of the nervous system. Particularly, two main neuronal morphologies were observed in the cerebral cortex, first pyramidal cells with vertically oriented apical dendrites that are organized in columns perpendicular to the cortical laminae, and second smaller granular cells, with star-like dendritic arborizations (so-called stellate cells), of which there are two kinds: spiny (displaying small dendritic "spines" on the surface), and smooth stellate cells. The characteristic laminar distribution of these cell types represented important evidence for the field of cytoarchitectonics. It later turned out that spiny cells and pyramidal neurons are excitatory, while smooth stellate cells are inhibitory. The evidence of a vertical organization of neurons in the cerebral cortex, mainly provided by Cajal, complemented the horizontal laminarity concept of Baillarguer, both of which form the basic scaffolding for the modern conception of cortical anatomy (see Fig. 2.1) (Corsi et al. 1991).

Perhaps the most important exponent of cytoarchitectonics was Korbinian Brodmann, who in 1909 published a comprehensive account of the cerebral cortical areas in different mammals including humans and described more than 50 areas in the human brain (Fig. 2.2) (Brodmann 1909). This map is the most commonly used by contemporary researchers, as several of these areas were found to correspond to different sensory and motor regions in the brain. Subsequent students of cytoarchitectonics that deserve mention are Constantin Von Economo and Georg Koskinas, who made an exhaustive study in 1925 of laminar differentiation of the cerebral cortex (Von Economo and Koskinas 1925). They observed that cytoarchitectonic characteristics did not change abruptly; rather there is a gradient of differentiation along the cerebral cortex. Thus, regions involved in sensory processing display densely packed small (granular) neurons, especially in the middle layer, while motor and limbic areas show large pyramidal neurons, especially in the deep layers. Between these regions, there are extensive areas where granularity decreases with distance from sensory areas and the pyramidal component increases with proximity to motor regions. Another characteristic of these intermediate regions is the enlarged thickness of the superficial layers, considered to be the site for associative connectivity. Von Economo and Koskinas' approach also represented a slight departure from a more phrenologically oriented view of the brain, consisting of discrete areas or modules, to a gradual pattern of functional differentiation along the cerebral cortex (Corsi et al. 1991). Combined approaches including high-resolution cytoarchitectonics, gene and receptor distribution, and new imaging techniques have been used recently to produce high-resolution atlases of the human cerebral cortex (Ding et al. 2016b; Glasser et al. 2016). Although these are promising achievements, their consistency and reliability still needs to be improved.

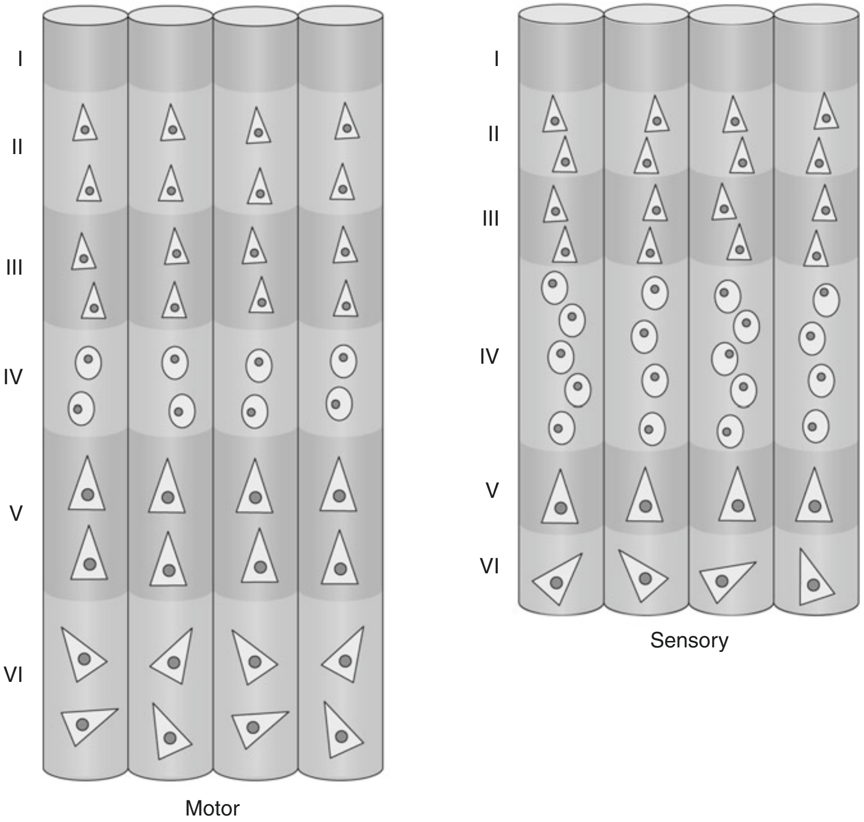

Fig. 2.1 Cellular organization of the cerebral cortex. The cerebral cortex is organized in horizontal laminae (layers I–VI) and vertical columns crossing each of the laminae. Cytoarchitectonics refers to the parcellation of the cerebral cortex in different areas, based on the relative development of the layers in different regions. As an example, a motor area, with a robust layer V (output layer), is contrasted to a sensory area displaying a thick layer IV (input layer). Morphologically, excitatory cells are of two kinds: pyramidal (triangles), and spiny granular cells (circles), the latter concentrated on layer IV. Inhibitory interneurons (also called smooth granular cells; not shown) are distributed in all layers

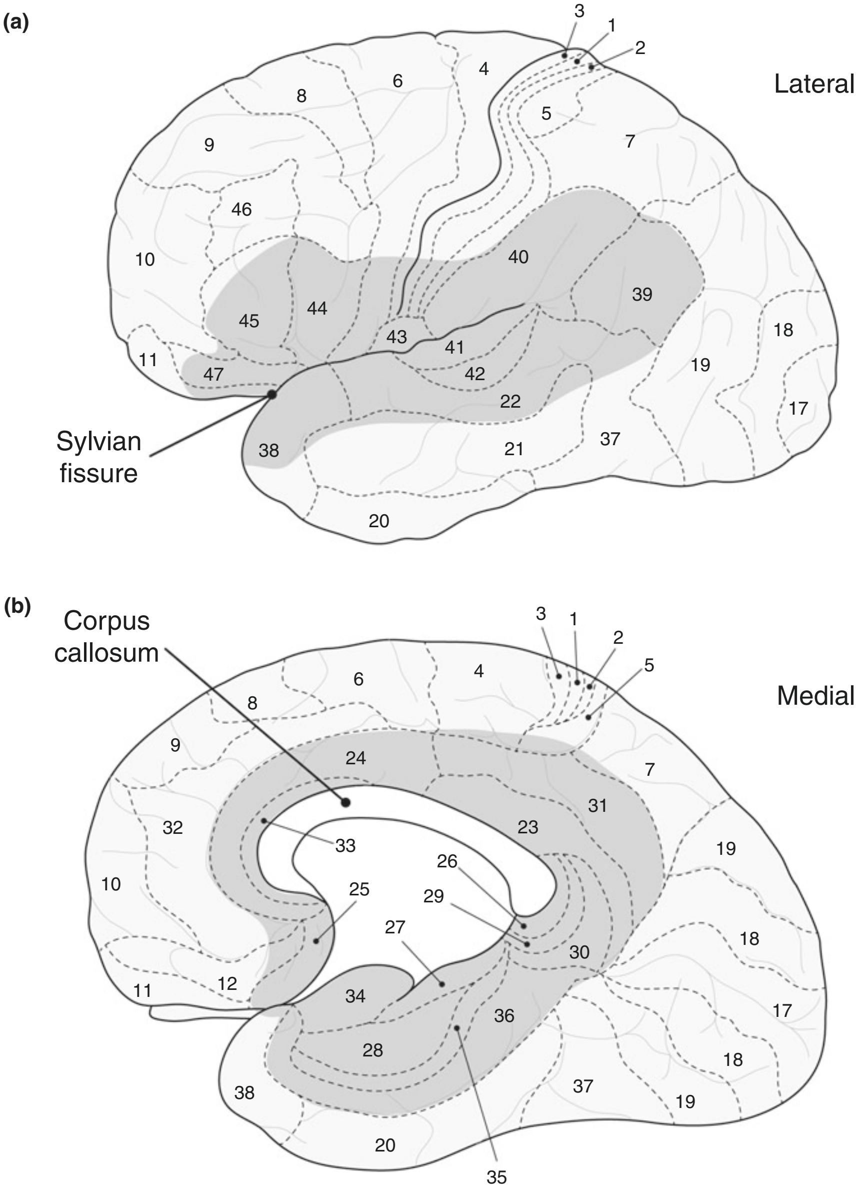

Fig. 2.2 Lateral and medial aspects of the human cerebral hemispheres. Figures depict Brodmann's cortical areas in numbers, and the longitudinal

Broca's Brains

To Broca the evidence above strongly indicated that convolutions supported distinct mental functions. In the following, I will mainly refer to Francis Schiller's lucid biography of Broca, which is probably the main modern reference to his work (Schiller 1992). On April 18, 1861, Broca reported in the *Societé D'Anthropologie* the postmortem brain of his patient Leborgne, who had a lesion of the left third frontal convolution of the left hemisphere. This region is now referred to as the inferior frontal gyrus, or ventrolateral prefrontal cortex (which is to be distinguished from the ventral premotor cortex, located just posteriorly, which codifies complex motor patterns executed by the ventral motor cortex). From now on, I will use the term "ventrolateral prefrontal cortex" to specify the location of Broca's region. Leborgne had a specific impairment to articulate speech (he could only pronounce the word "tan"), while speech comprehension was intact. A few months later, Broca found Lelong, another patient with a similar lesion, whose speech was also impaired, being able to utter only six French words: *oui* (yes), *non* (no), *tois* (*trois*, which meant not only three but any number), *tojours* (always), and *Lelo* (Lelong). Like Leborgne, this patient showed a reasonable capacity to understand what was said to him. Leborgne had a long-lasting, presumably progressive

Fig.2.2 (Continued)
subdivisions specified by Foville in gray. (**a**) In the lateral aspect, Foville's *circonvolution d'enceinte*, or the Sylvian convolution surrounds the Sylvian fissure. This includes the inferior parietal lobe (areas 39 and 40, angular and supramarginal gyri), the ventrolateral prefrontal cortex (areas 44-pars opercularis, 45-pars triangularis, and 47), and the ventral premotor (area 6), motor (area 4), somatosensory (areas 3, 1, 2) and insular (area 43) regions. In the temporal lobe, areas 22, 41 and 42 make up the superior temporal gyrus, which is separated from the middle and inferior temporal gyri (areas 20, 21 and 37) by the superior temporal sulcus (not shown). The temporal pole corresponds to area 38. (**b**) The medial aspect of the hemisphere depicts Foville's and Broca's limbic lobe (in gray). The anterior cingulate cortex corresponds to area 24, and areas 23, 26, 29, 30 and 31 behind the corpus callosum make up the posterior cingulate cortex or retrosplenial region. The default mode network involves areas 10 and 32 in the frontal lobe, and the posterior cingulate cortex

condition, as his brain had softened in regions spanning the white matter, the basal ganglia, and nearby cortical regions. Lelong acquired this condition suddenly, likely due to a localized brain hemorrhage in the same left third frontal convolution (the ventrolateral prefrontal cortex). Finally, localization of brain functions was confirmed. Broca called this condition aphemia, and postulated that it was due to the loss of a special kind of memory involved in the procedure used for articulating words (Broca 1865). He was, however, clear in saying that not all cerebral faculties were as circumscribed as this one. It is less known that the neurologist Marc Dax, at Sommières (a small town close to Montpellier), had made similar observations some 25 years before Broca, but instead of specifying the brain region, he emphasized the left hemisphere as the site where lesions produced language disturbances. Dax was largely ignored in his time, presumably due to his early death 1 year after his findings. After Broca's presentation, Dax's son published these observations again, but was unsuccessful in vindicating his father. Broca was late in recognizing the leftward asymmetry of the observed lesions, initially attributing them to chance, but eventually he concluded that there was in fact a clear tendency shown by evidence (Schiller 1992).

Broca was not without his detractors, among them the anti-localizationist Pierre Flourens, who viewed these interpretations as a new form of phrenology. In addition, the eminent Jean Martin Charcot presented a case with undeniable aphemia with a lesion on the upper border of the Sylvian fissure (in modern terms, the gyrus supramarginalis in the inferior parietal lobe). Responding to this, Broca claimed that a single case did not make a tendency, but perhaps more importantly for our purposes, he relied on Louis Foville's anatomical descriptions of brain convolutions, which contrary to Rolando's depiction, subdivided the brain into three major longitudinal lobes (Fig. 2.2). The most medial of these was the convolution of the hem, which includes the cingulate gyrus and the medial temporal lobe. Secondly, there was a large lobe encompassing dorsal frontal, superior parietal, occipital, and inferior temporal areas, and finally there was the convolution around the Sylvian fissure or *circonvolution d'enceinte*, involving all areas surrounding the Sylvian fissure. In modern terms, these are Broca's region, the adjacent premotor and motor cortices and the inferior parietal lobe on the upper side of the

Sylvian fissure, and on the lower side, the superior temporal gyrus where auditory areas and Wernicke's region are located. Broca initially argued that the speech organ was the entire Sylvian convolution, and that there are differences in its organization among individuals, but he later insisted on the third frontal convolution (the ventrolateral prefrontal cortex) as the site of speech (Schiller 1992).

Although little recognized today, Foville's subdivision fits the current notions about the arrangement of major longitudinal tracts of the brain. Broca renamed the hem convolution as the limbic lobe. He published a massive work on the "great limbic lobe" of mammals, surrounding the medial borders of the cerebral hemispheres. Broca also made a thorough analysis of the brains of several mammals, and concluded that the primate brain was divided into regions comparable to the brains of other animals, indicating a conservatism in structure that was not generally agreed on at that time (Broca 2015). The limbic convolution is connected through a tract called the cingulum bundle and other tracts, making up a circuit that was described in the twentieth century by James Papez, and termed the Papez circuit. Foville's large convolution in the middle is the arrangement of the visual system, with one pathway following through the superior parietal and dorsal frontal cortices (as we will see, this is involved in visuomotor coordination), and the other pathway running along the middle and inferior temporal lobe (involved in visual recognition). Finally, all the areas included in the Sylvian convolution have been directly or indirectly associated with language processing. We will come back to this anatomical partition in Chapter 7.

Another antagonist of Broca was Armand Trousseau, who analyzed a large series of brains of speech-impaired individuals. Although he found a clear prevalence of left hemisphere lesions, when looking for the exact location of the lesion in a subset of the subjects he studied he found no strong evidence for Broca's hypothesis. Ironically, Trousseau coined the word "aphasia", which eventually replaced Broca's term aphemia. But perhaps Broca's hardest critics were the neurologists John Hughlings Jackson in England and Pierre Marie in France. Jackson considered language a very complicated faculty and was highly skeptical of the localizationist perspective. He emphasized subcortical regions involved in language, particularly the corpus striatum, which could have been damaged in aphasic patients. In addition, he claimed that damage to one part of the brain could produce effects in distant regions, affecting functions not necessarily located in the damaged site. Jackson also highlighted the case of a patient who had severe difficulties in speaking normally, but was able to swear with complete precision and vigor (York and Steinberg 2011). Pierre Marie had a similar interpretation to Jackson's, arguing that language is one and indivisible, and that Broca's cases only involved the lower motor systems involved in speech production rather than an intellectual impairment. Notably, Marie argued that aphemia or aphasia could be produced not only through lesions of the left third frontal convolution, but also with deeper lesions involving the insula (a portion of the cortex that is buried deep within the Sylvian fissure), or the basal ganglia. The dispute between holists and localizationists went on for over a century, the former providing important theoretical insights, while the latter contributed increasingly detailed anatomical evidence in their support (Schiller 1992; Steinberg 2014).

Comprehending Speech

Broca's observations fell short on the capacity to perceive speech and language. In 1874, at the age of 26, Karl Wernicke proposed the existence of a brain center involved in the storage of speech sounds, located in the posterior superior temporal gyrus (Wernicke 1874). This is now called Wernicke's area, corresponding to the posterior part of Brodmann's area 22, a region now associated with high level auditory processing. This region is dedicated to storing acoustic images of words that are then transferred to Broca's area, controlling speech. Supporting this notion, Wernicke described patients that could hear but had difficulty understanding speech. He distinguished this "word deafness" or sensory aphasia, as opposed to Broca's motor aphasia, from semantic deficits. Thus, he believed that this sensory speech region was responsible for transforming orthographic signals into phonological patterns, and making the generation of inner speech possible (Corsi, 1991; Schiller 1992; Petrides, 2014; Weiller et al. 2011).

Wernicke was greatly influenced by the work of Theodore Meynert, who beside his contribution to cytoarchitectonics, was also the first to propose a systematic subdivision of the fiber tracts in the human brain, with ascending or descending projection fibers, commissural fibers connecting the cerebral hemispheres via the corpus callosum, and association fibers connecting different regions of the cerebral cortex within each hemisphere. Following Meynert, Wernicke postulated a connection between Wernicke's and Broca's areas that made the association of sensory inputs with motor commands possible. In contrast to the localizationist view, Wernicke emphasized the associative nature of these projections, presaging modern concepts of brain connectivity. Lesions in the connectivity between the sensory (Wernicke's) and motor (Broca's) regions resulted in a disconnection syndrome called conduction aphasia, which included paraphasia. This consisted of the generation of erroneous syllables, words or even phrases during speech. Another symptom was impaired writing, although speech was fluent and comprehension preserved. Wernicke attributed the production of paraphasias to the suppression of mental reverberation of acoustic images while speaking, which serves to monitor motor images. However, a cardinal symptom of conduction aphasia was eventually specified as the difficulty to repeat sentences or utterances presented to the patient, something that Wernicke did not originally describe (Corsi et al. 1991; Schiller 1992; Petrides 2014).

It is widely believed that Wernicke's model considered that conduction aphasia was due to disruption of the arcuate fasciculus, a tract of fibers that runs around the Sylvian fissure, deep to the inferior parietal lobe, and connects the posterior superior temporal lobe (Wernicke's area) with Broca's region (Fig. 2.3). However, Cornelius Weiller has recently argued that although Wernicke may have been aware of the existence of this tract, his original diagrams point to a much shorter pathway via the mid-or anterior temporal lobe, which he considered traveled deep to the insula, a buried cortical area located between Wernicke's and Broca's regions

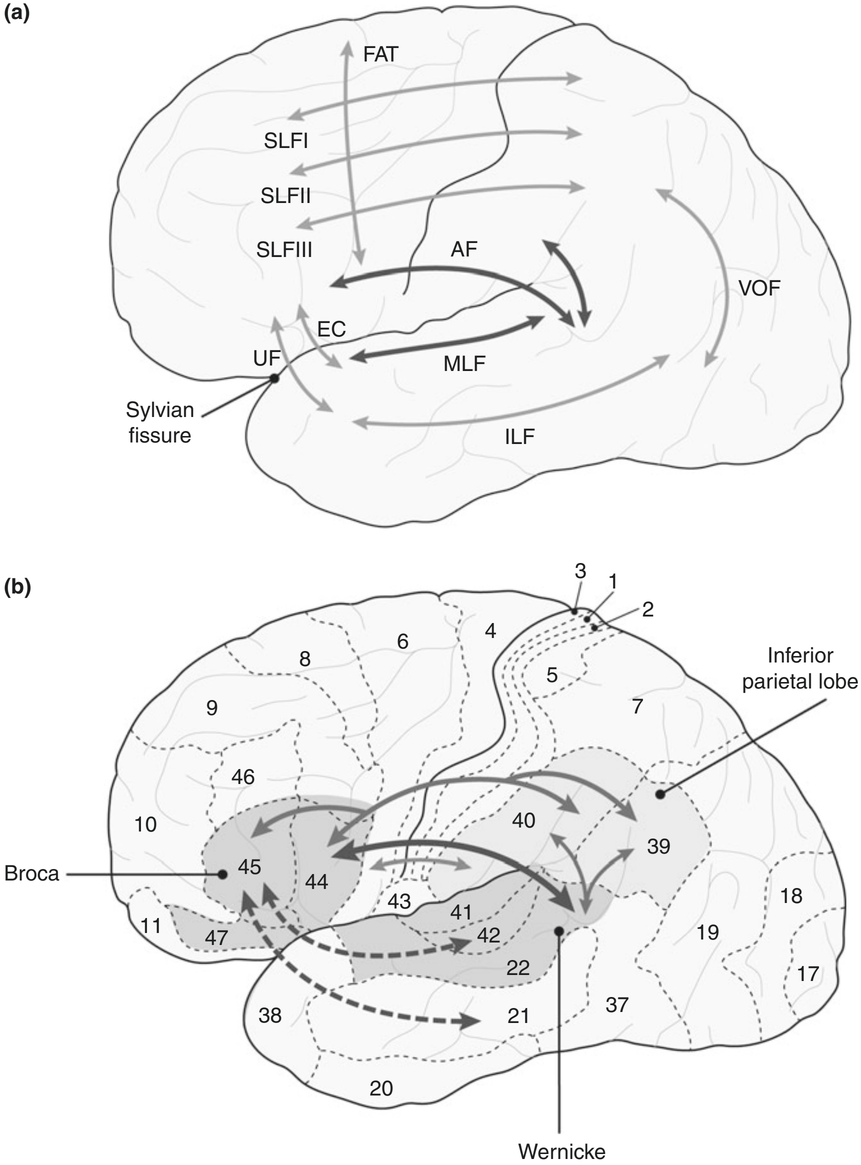

Fig. 2.3 The main cortico-cortical tracts discussed in this book. (**a**) This schematic is not intended to be anatomically accurate but to reflect the topographical arrangement of these tracts. In addition, these tracts are not

(Weiller et al. 2011). The arcuate fasciculus, named after Karl Burdach, was first described at the beginning of the eighteenth century by Johan Cristian Reil as a bundle of fibers running around the superior border of the Sylvian fissure, encompassing the superior temporal, inferior parietal and inferior frontal areas, beneath Foville's upper Sylvian convolution (see above). Constantin von Monakow first postulated that this tract plays a role in aphasia, and it was only later that Wernicke accepted that it is a main tract in language pathways, whose disruption produces conduction aphasia (nonetheless, more recent findings have evidenced gray matter involvement in many cases of conduction aphasia). From then on, Wernicke's original model of a short language pathway underlying the insula fell into oblivion, as attention shifted to the arcuate fasciculus as the main connection between Broca and Wernicke's areas (Schiller 1992; Catani and Mesulam 2008a; Weiller et al. 2011).

Fig.2.3 (Continued)
discrete bundles but rather overlap in a continuous plexus below the cortical surface. AF, Arcuate fasciculus; EC, Extreme capsule; FAT, Frontal aslant tract; ILF, Inferior longitudinal fasciculus; MLF, middle longitudinal fasciculus; SLF I, II, III, dorsal, middle and ventral components of the superior longitudinal fasciculus, respectively; UF, Uncinate fasciculus; VOF, Vertical occipital fasciculus. The curved arrow at the posterior end of the Sylvian fissure connects superior temporal and inferior parietal areas, and has been termed the posterior segment of either the arcuate fasciculus or the middle longitudinal fasciculus, depending on the nomenclature. (**b**) Functional subdivisions and connectivity of the language-related circuit. In the superior temporal gyrus, areas 41 and 42 make up the auditory cortex, while Wernicke's area roughly corresponds to posterior area 22. Broca's area, in a restricted sense, has been defined as area 44-pars opercularis, and area 45-pars triangularis. The dorsal language pathway has two components, one connecting Wernicke's area mainly with area 44 and neighboring regions via the arcuate fasciculus (black arrow), and the other connecting Wernicke's area with the inferior parietal lobe, and then projecting to areas 44 and 45 via the superior longitudinal fasciculus (dark gray arrows). There are additional connections between motor, premotor and somatosensory areas (light gray arrow). The ventral pathway (segmented arrows) is a polysynaptic tract that connects the anterior temporal gyrus (auditory component), and the middle and inferior temporal gyri (visual component) with areas 45 and 47

Nonetheless, recent investigations have confirmed the existence of two parallel pathways connecting Wernicke and Broca's region (Fig. 2.3). One is the dorsal pathway, running through the arcuate fasciculus, whose interruption (or of the gray matter above it) leads to conduction aphasia. The second is the so-called ventral pathway, connecting the anterior temporal lobe and the inferior frontal gyrus along the extreme capsule, which has been proposed to participate in auditory recognition. The ventral pathway has been proposed as a better fit to Wernicke's original notion of a short connection to Broca's region beneath the insula (Saur et al. 2008; Weiller et al. 2011; Fridriksson et al. 2016). Again, Foville's Sylvian convolution fits these two pathways, the dorsal pathway/arcuate fasciculus running through the inferior parietal lobe, and the ventral pathway/extreme capsule running through the temporal lobe and below the insula to reach Broca's area. Furthermore, Reil's original depiction of the arcuate fasciculus as a curved tract running the length of the upper Sylvian convolution is also consistent with this notion. Possibly due to the neglect of the ventral pathway during most of the last century, the arcuate fasciculus came to be viewed only as the dorsal component linking Broca's and Wernicke's areas.

The Disconnection Syndrome

Since Wernicke's findings, an influential associationist tradition emerged in the late nineteenth and early twentieth centuries, in which disconnection syndromes were described in other brain areas beyond the language regions (Mesulam 2015). Wernicke's student Heinrich Lissauer described a patient with intact visual capacity but incapable of recognizing familiar objects by sight, a condition called visual agnosia that is due to interruption of the connectivity between visual areas and higher order association areas. Another student, Hugo Liepmann, described the apraxias resulting from disconnection of the motor centers from sensory regions and characterized by the incapacity to imitate meaningless movements or manipulating imaginary objects (Weiller 2011). Finally, Jules Déjérine coined the term pure alexia, meaning the acquired inability to read (while the capacity to write remains spared) due to a disconnection between visual areas and Wernicke's area. In 1881, Déjérine described a patient with a lesion in the fusiform gyrus (part of the inferior temporal lobe), who was unable to read but could write and otherwise had intact visual and language skills. Déjérine slightly departed from the pure associationist school by proposing a specific brain center dedicated to processing word images (Corsi et al. 1991). More recent research, notably by Stanislaas Dehaene, has identified a region called the visual word form area in the inferior temporal lobe, which is specifically involved in recognizing the shapes of words and letters, and projects to Wernicke's area where these visual percepts associate with auditory phonological representations (Cohen et al. 2002). The visual word form area does not activate with reading, and cannot do so, in illiterate people, and is the result of enculturation among the literate. Subsequent studies suggest the existence of a nearby visual number form area, and an area involved in graphemic motor control (called Exner's area), above Broca's region (Roux et al. 2009). As I mentioned in the Chapter 1, culture can make enormous changes in the structure and functional organization of our brains. Is language an example of enculturation, as the neural substrate is for reading?

The associationist school became firmly consolidated much later in 1965, with Norman Geschwind's monumental work *The disconnection syndromes in animals and man* (Geschwind 1965). Geschwind made an extensive account of acquired neurological symptoms that could be explained by the disconnection between different brain centers. He proposed a series of pathways connecting visual, auditory and somatosensory areas with each other, but also with motor and limbic areas whose specific damage yielded a particular neurological symptomatology. A key element in these networks was the inferior parietal lobe (the supramarginal and angular gyri, part of the Sylvian convolution), where auditory, visual, and somatosensory projections converged. Marco Catani and collaborators recently summarized these ideas in a diagram highlighting the inferior parietal lobe as a critical node for cortico-cortical connectivity, and appropriately called it "Geschwind's area" (Catani and ffytche 2005; Catani and Mesulam 2008b). Concerning the language circuits, Geschwind emphasized the case of conduction aphasia and the role of the arcuate fasciculus in conveying sensory information from Broca's to Wernicke's areas. Furthermore, he consolidated the now classical model of language areas that prevailed through the second half of last century, consisting of a posterior, perceptive Wernicke's region, connected via the arcuate fasciculus with Broca's anterior motor region.

In 1964, Geschwind published a little known article, called *The development of the brain and the evolution of language*, where he proposed that the capacity to establish direct cortico-cortical associations, especially between different sensory modalities (but also within a sensory modality), was particularly well developed in humans as opposed to other primates (Geschwind 1964). This allows us to name objects in the world and acquire symbolic representations. On the other hand, non-human primates are much slower in learning cross-modal associations, and require an intact limbic system to perform such associations. Humans, with their big brains, have freed themselves of the limbic connection by emphasizing direct cross-modal, cortico-cortical associations. This is not to say that in humans there are no limbic associations, but that much faster cortico-cortical associations can be readily made that allow us to rapidly associate words with objects. Again, an essential part of Geschwind's proposal was that the temporo-parietal junction serves as a node in which sensory information converges from the visual, tactile, and auditory modalities, and is connected to Wernicke's area in the superior temporal lobe. Later evidence that apes are able to learn a relatively extensive vocabulary using sign language has challenged this hypothesis. However, apes learn words through a long and painstaking training procedure, while children acquire their vocabulary rapidly and effortlessly.

In the twentieth century, human neuroanatomy made some discrete progress, particularly in the study of cytoarchitectonics and brain-behavior correlations, a field termed by Geschwind as "behavioral neurology" (Catani and Mesulam 2008a,b). Broca's area became circumscribed to two specific regions of the ventrolateral prefrontal cortex. One is the posterior part of Broca's area or pars opercularis, comprising Brodmann's area 44, more related to phonological and vocal articulatory processes, and the other is the anterior part or pars triangularis, which includes Brodmann's areas 45 and 47, and is related to lexical and semantic processing.

Nonetheless, there is a noticeable individual variability in the symptoms of classical Broca's aphasia. This condition now includes a wide spectrum of acquired speech dysfunctions, including more subtle speech articulation and fluency deficits, difficulties to find words, and some comprehension problems, particularly of complex grammatical sequences. Moreover, studies in the late twentieth century, notably by Nina Dronkers, Marco Catani and others, have found that Broca's aphasia can be produced by lesions in several regions surrounding areas 44 and 45, including neighboring cortical areas, the insula, the underlying white matter and the basal ganglia, which is in agreement with Pierre Marie's descriptions (see above) (Thiebaut de Schotten et al. 2015). Thus, instead of being a strictly localized brain region, Broca's area encompasses a wide network in the left ventrolateral prefrontal cortex. Moreover, damage restricted to areas 44 and 45 is now thought to produce only transient speech deficits, while long-lasting impairments may include lesions in white matter tracts that connect Broca's region with other areas, or in more extensive cortical regions. In this line, Alfredo Ardila proposes the term "Broca's complex" to account for Broca's aphasia symptomatology, which includes prefrontal areas 44, 45, 46, 47 and part of the ventral premotor cortex (area 6) (Ardila et al. 2016).

Dronkers and collaborators analyzed in detail the brains of Leborgne and Lelong, confirming Broca's original descriptions, but localizing Leborgne's lesion in the middle of the inferior frontal gyrus (Dronkers and Sanides 2007). The posterior part of this gyrus, where modern researchers have located Broca's region, is altered but is not the most damaged area. In Lelong's brain, there are signs of atrophy consistent with chronic dementia, but there is also evidence of a stroke located in the pars opercularis, sparing the pars triangularis. Further analyses using magnetic resonance imaging techniques show extensive damage in Leborgne's brain, restricted to the left hemisphere, including regions like the insula, superior temporal lobe and inferior parietal lobe, while in Lelong's brain resonance imaging confirms the lesion localized in the pars opercularis. This supports the idea that Broca's aphasia does not result from damage in a strictly localized brain region, but may require more extensive cortical, subcortical or white matter lesions. Nonetheless, anatomical studies have by necessity been restricted to a handful of areas, particularly areas 44 and 45, although sometimes including neighboring regions. Although this may only be part of a larger network for language production, science accumulates information step by step, from the particular to the general in order to keep the required simplicity for executing highly demanding technical procedures. Below, I will refer to some recent studies that use the more restricted definition of Broca's area, involving only areas 44 and 45 (and sometimes 47), a notion that, while criticized for reasons outlined above, has been extremely useful to trace the neural connectivity that makes up language and speech networks.

On the other hand, Wernicke's area remains ill defined, corresponding to a wide region including Brodmann's posterior area 22 and surrounding areas. This covers the posterior superior temporal gyrus and a triangular region within the lower bank of the Sylvian fissure called planum temporale. In front of the planum temporale are the gyri of Heschl, containing the primary and secondary auditory areas. Cytoarchitectonic studies in the 1960s by Friedrich Sanides, Deepak Pandya and their then student Albert Galaburda subdivided the auditory areas into three concentric rings, a "core" region containing primary and secondary auditory areas, which are successively surrounded by an intermediate auditory "belt" and an outer "parabelt". In the posterior parabelt, Galaburda and Pandya described a region called Tpt, which is thought to occupy a large part of the planum temporale, and has been ascribed (but not exclusively) to Wernicke's area (Galaburda and Sanides 1980, Galaburda and Pandya 1983). Notably, all the regions composing Broca and Wernicke's regions exist in monkeys and apes, indicating that they are highly conserved in evolution. How did these areas acquire a linguistic function? This is a major question I intend to address in this book, and will discuss in more detail in Chapter 7.

The Imaging Revolution

For most of the twentieth century, the study of the human brain was limited to postmortem, gross anatomical, and microscopic cytoarchitectonic studies. There were few possibilities of studying the brain in action (one exception being electroencephalography) or brain connectivity, as was being done with animals for most of that time. Anatomical and electrophysiological studies were yielding much information about animal brains, but to what extent these findings could be extrapolated to the human brain was in many cases a matter of question. At least since the 1980s, neuronal connections can be visualized in high detail in animals by injecting chemical tracers that are absorbed by the respective axons or neurons in one brain region, and then observing the distribution of the tracer in the rest of the brain in the postmortem tissue. Apart from some details, this technique continues to be used to trace connections in most animal brains. However, this cannot be done with humans, and until recently the only way to analyze connectivity was in postmortem specimens that had suffered brain stroke in life. When neurons die due to injury, their axonal projections undergo a degenerative process called Wallerian degeneration, which leaves traces in the neural tissue that can be observed after death. However, this method depends on the site and size of the lesion, and has very low resolution compared to animal tract-tracing procedures.

A different strategy emerged in the 1950s and 1960s, when neurosurgeons Wilder Penfield and Lamar Roberts made groundbreaking studies with patients undergoing brain surgery by electrically stimulating their brains and observing the behavioral reactions (Penfield and Roberts 1959). Since neurosurgery has to be done with the patient awake and using only local anesthesia, patients were conscious and able to respond to the stimulation procedure. Penfield and colleagues depicted the famous body homunculus in the sensory and motor cortices; and also identified areas whose stimulation elicited vocalizations, notably in the ventral precentral and supplementary motor regions of both hemispheres (areas 6 and 4, ventral). They further found that stimulating the ventrolateral prefrontal cortex (Broca's area), the motor and premotor cortices, and some regions around the Sylvian fissure, all in the left hemisphere, could lead to interference with or the arrest of speech.

But revolutionary discoveries were about to change the study of language for good. Since the 1960s, new brain imaging techniques were developed that made it possible for the first time to study local brain activity in living humans, even if they evidenced processes only indirectly associated with neuronal activity. The first of these techniques were SPECT (single photon emission computed tomography) and PET (positron emission tomography), which detect emissions from a radioactive tracer in the bloodstream, sensed by an array of detectors that anatomically localize the source of the emission in the brain. These techniques measure differences in blood flow, but also glucose consumption and even the binding of radioactive ligands to their receptors. An underlying assumption is that local differences in blood flow or glucose metabolism reflect changes in neuronal activity in the corresponding brain regions. However, the most influential neuroimaging technique has been magnetic resonance imaging (MRI), first developed by Paul Lauterbur, and optimized by Peter Mansfield (both received the Nobel Prize for their contribution), a totally non-invasive technique that measures the magnetic field orientation of water molecules in different tissues (Pearson 2003). MRI made it possible to generate high-resolution three-dimensional images of the brain for detailed quantitative analyses of brain morphology in living subjects. Moreover, two techniques derived from MRI have been the most relevant for the development of cognitive neuroscience and particularly for understanding the language neural networks. One is functional MRI (fMRI), which takes advantage of the magnetic properties of the oxygen-carrier protein hemoglobin, depending on whether or not it is oxygen-binding. Counterintuitively, brain regions show a larger oxygen supply when they are more, rather than less active, presumably because the overall increase in blood flow overcomes the higher oxygen consumption by active neurons. Compared to SPECT and PET, fMRI has higher neuroanatomical precision and, as noted, is totally non-invasive, as it does not require radioactive tracers, which also makes it more affordable. However, one drawback for language studies is that speech produces image distortions due to jaw movements, so subjects' responses are restricted to button pressing. As well, the machine is quite noisy, which complicates the delivery of auditory stimuli.

Another technical difficulty with imaging techniques is that the brain is never quiet, and blood flow is evident throughout the brain. One way to overcome this is a subtraction procedure, where the difference in activity between two related conditions is determined. In most instances, subjects have to perform two quite similar tasks, but differing only in one parameter. For example, imagine the N-back task, a procedure to assess short-term memory, where subjects are exposed to a semi-random string of numbers (avoiding the chance of repeated numbers), and at some point the sequence stops. Subjects are then asked to immediately recall the last number of the sequence. This is the 0-back condition, which requires attention from the subject, but on the other hand it puts little demand on short-term memory capacity. If the subject is then asked to recall the next-to-last number (1-back condition), the demand on memory is higher, and still more demanding if the subject has to recall the second-to-last number (2-back condition) (Gaspar et al. 2011). Thus, brain activation in the first 0-back task evidences networks involved primarily with attention, but that have less to do with memory, while activation patterns in the 1-back and 2-back tasks increasingly activate networks involved in memory and executive processes, but also activate attentional networks. If we subtract the activation pattern of the 0-back from that of the 1-back, we minimize activation due to attentional mechanisms and emphasize memory-related networks. By subtracting the 1-back and the 2-back conditions, we may obtain understanding of higher-level executive processes. The usual results are that a small group of areas are highlighted by the subtraction procedure.

However, the technique has its drawbacks, as it downplays connectivity and the participation of brain regions that may be highly relevant for the specific function but also participate in the control task. Furthermore, the specific areas that “light up” in a subtraction procedure may depend on the statistical method and criterion used to identify significant differences. Furthermore, results are usually (but not always) reported as grand averages of several trials with each subject, and then averaged among the subjects that compose the sample. Under these conditions, the observed activity locus is usually attributed to specific cytoarchitectonic areas. However, in practice, this is impossible to verify because of inter-individual differences in brain activity profiles and the neuroanatomy of cortical areas, where fissurization patterns are highly variable, and presumably so is the arrangement of cytoarchitectonic areas. The best we can get is an approximation of the cortical areas involved. Furthermore, Eklund et al. (2016) and collaborators recently performed a comprehensive study, finding an astonishing 70% of false-positives when analyzing imaging data with standard fMRI softwares, which calls into question the results of some 40,000 previous studies. There have been recent technical developments such as single-trial fMRI approaches, but these are still not widespread and have not yet produced important results. Most of the studies presented in this book rely on averaged samples of subjects.

Resting Brains

One alternative to rescue network thinking has come from a technique called functional connectivity, which is basically the statistical analysis of covariance in activity between different brain regions. That is, the activity level of a brain region is not constant but changes over time, either as a result of sensory stimulation, or by endogenous mechanisms. If we analyze different brain regions and find areas where activity changes more or less synchronically, we can say that these areas are functionally connected. This is not exactly the same as anatomical connectivity, as functional connectivity results from a statistical study of correlated variability between two areas. Thus, we can observe which area becomes preferentially activated in a given task, and then analyze the constellation of brain areas that are functionally connected to it to unveil the distributed brain network to which it belongs. One notable example of this was provided by the groundbreaking experiments by Marcus Raichle and his collaborators, who criticized the standard imaging protocols for always using a control task that requires an executive function, and then contrasting this with the experimental task. Raichle wondered what happens when the brain does not have to perform any task at all, as opposed to executing some sort of cognitive task. Thus, he asked participants to lie quietly on the fMRI machine with their eyes open while he recorded their brain activity. Then, he and colleagues compared the observed pattern with the average activations found for a series of cognitive tasks. His findings have become among the most relevant in the history of cognitive neuroscience, although not without controversy, as every respectable innovation should be (Raichle et al. 2001; Raichle 2015).

Raichle determined that in the resting condition, also called the default mode condition, there was a typical activity pattern in which some brain areas increase their activity. Notably, these are the dorsomedial prefrontal cortex and posterior cingulate cortex in the dorsal midline of the hemisphere (see Fig. 2.2), and a few other areas in the lateral aspect of the hemisphere. On the other hand, these same areas significantly decrease their activity when the brain engages in an executive task. In the latter condition, there is a different set of areas that increase their activity, including premotor areas that are involved in short-term memory processes, in eye movement control and others. When studying the functional connectivity in these networks, it was found that their activity was strongly oscillatory, with a notable within-network positive synchrony. That is, within the resting networks all areas activate and decrease their activities more or less at the same time; and conversely, within the executive network all areas also show a highly positive activity correlation. However, between networks there is strict anti-synchrony, that is, when the resting state network is active, the executive network goes down, and conversely, when the executive network engages, the resting state network disengages (Fox et al. 2005, 2007). As I said, this is an oscillatory process, in which we normally alternate in periods of one or more minutes from activating the executive networks and deactivating the resting network, and then activating the resting network and deactivating the executive network. Thus, we do not fully concentrate even when we are engaged in serious tasks, but from time to time disengage and make an update of our internal state and contextual situation, to again re-enter the task after a brief while. This fits quite well with our own personal experiences at work, when writing, as I am now, or in any other task. Thus, our cognitive or behavioral efficiency may relate better with the appropriate alternation between these two tasks than with keeping to the executive network at the expense of the resting network.

I used these long words to describe the resting state and default network because they are related to two mental processes that are highly relevant to language and to language origins: one is social behavior, as the default network has been associated with empathy and mentalization, the capacity to understand the other's mental states;

and the second is introspection and particularly daydreaming, which are related to the development of inner speech, a capacity that I will argue marked an inflection point in the evolution of speech and language. Importantly, the language network does not strictly belong to either the executive or the resting state networks, but rather is recruited by one or the other in different circumstances, say when daydreaming (activating the resting state network, as noted above), or for example when teaching a class or opening conference (activating the executive network). The speech circuits may actually contribute information stored in both networks and supply a way of transferring memories between them (See Chapter 4).

The Language Network Updated

The second derivation of MRI is tractographic diffusion tensor imaging (DTI), which measures the asymmetry of water diffusion in nerve fiber tracts. Inside a tract, water tends not to diffuse symmetrically in all directions, but diffuses in the same direction as the fibers. By measuring the direction of water flow in nerve tracts, it is possible to follow their trajectory in the living human brain and represent them in three dimensions. Using a combination of fMRI and DTI, we can find for example the areas that activate under a given experimental task, and then use these areas as "seeds" to trace their anatomical connections to the rest of the brain, thus visualizing the "hard" network to which each area belongs. Although DTI does not have the resolution to determine which fibers are afferents (incoming) or efferents (outgoing) to the respective area, practically all cortico-cortical fiber tracts are bidirectional, containing both kinds of axons. MRI and DTI do not yet have the same resolution as animal postmortem techniques, but they have provided invaluable information that was totally inaccessible some 50 years ago. As I said above, these findings have provided substantial evidence that the language circuit contains dorsal and ventral components that run in the dorsal and ventral aspects of the Sylvian convolution, respectively.

Early tractographic studies of the language regions, first by Marco Catani and later by several groups, including those led by James Rilling, Cornelius Weiller, Michael Petrides and Angela Friederici, confirmed the existence of an arcuate fasciculus connecting Wernicke's and Broca's regions, running deep to the inferior parietal lobe and the ventral somatosensory and motor cortices, which was larger on the left than on the right hemisphere (Catani et al. 2005b; Glasser and Rilling 2008, Saur et al. 2008, Frey et al. 2008, Friederici 2009, Brauer et al. 2013, Tremblay and Dick 2016; Fridriksson et al. 2016). In addition, Catani and Dominic ffytche noted an important connection from the inferior parietal lobe into Broca's region (Catani and ffytche 2005; Catani et al. 2005). The name of the tract containing these fibers differs among authors, and I will refer to it as being part of the superior longitudinal fasciculus. Furthermore, there is another tract that connects Wernicke's region with the inferior parietal lobe, therefore closing the circuit between the auditory cortex, the inferior parietal cortex and Broca's area. Again, this tract has received distinct names from different authors, and I will refer to it as the posterior middle longitudinal fasciculus (Petrides 2014; Catani and Bambini 2014). Adding to these projections that make up the dorsal stream, the above studies also described the so-called ventral pathway for language. This encompasses fibers along the superior temporal lobe, recruiting fibers from the anterior auditory regions, connecting them with the anterior temporal lobe, and reaching the anterior part of Broca's area and its vicinities (areas 47 and 45). The auditory and neighboring areas in the anterior temporal lobe play a role in semantic processing and identifying the speaker, as in some cases lesions in this region lead to anomia, that is, the inability to generate the names of categories of objects or perceptions like colors. The pathway connecting these areas includes two longitudinal tracts, the inferior longitudinal fasciculus, and the inferior fronto-occipital fasciculus. From now on, I will refer to it as the "ventral pathway" for speech or language (for a summary diagram, see Fig. 2.3).

Recently, Catani and Valentina Bambini summarized the language-related projections in the social communication and language evolution and development (SCALED) model, which separates the different tracts according to their distinct functions (Catani and Bambini

2014, Tremblay and Dick 2016). According to this model, (i) the arcuate fasciculus is involved in syntactic analysis; (ii) the inferior parietal projection to the posterior part of Broca’s area participates in recognition and production of motor patterns. (iii) Wernicke’s area and the inferior parietal lobe are connected via a tract (the posterior middle longitudinal fasciculus) involved in pragmatic aspects of speech. (iv) the ventral pathway, involving two longitudinal fascicles along the temporal lobe (middle and inferior longitudinal fascicles), and their connection to the anterior part of Broca’s region via the uncinate fasciculus and the extreme capsule, is involved in lexical and semantic processing. I have to note that some 20 years ago, Ricardo García and I proposed a connectivity diagram for the language circuit containing essentially the same elements as this model (see Chapter 7) (Aboitiz and García 1997).

Based on these and other findings, Gregory Hickok and David Poeppel provided a functional-anatomical model of language processing, with an early stage of speech perception that takes place in the superior temporal lobe (auditory cortex, Wernicke’s area) of both hemispheres, involving the analysis of auditory signals and early phonological processing (see Chapter 4) (Hickok and Poeppel 2004, 2007). From there, there is a pathway that runs along the temporal lobe (predominantly in the left hemisphere) and involves lexical representations, and a left-hemisphere dorsal pathway that controls articulatory processes. Following earlier authors like Ludwig Lichtheim and Antonio Damasio, Hickok and Poeppel proposed a diffuse “conceptual network” that interacts with these two pathways in an as yet unspecified manner. Interestingly, the right hemisphere auditory pathways participate in prosodic processing. Daniela Sammler, Pascal Belin and other coauthors made a thorough imaging study of the neural basis of prosody, evidencing that it takes dual routes in the ventral and dorsal auditory pathways of the right hemisphere, with a similar organization to that of left-hemisphere language networks (Sammler et al. 2015).

The separation of dorsal and ventral pathways prompted to a redefinition of the role of Broca’s region in language processing. Angela Friederici and collaborators parcellated this region into three components, areas 45 (pars triangularis), area 44 (pars opercularis), and a region called the deep frontal operculum that borders the deep insular cortex (Friederici et al. 2006; Anwander et al. 2007). The dorsal pathway is associated with area 44 and participates in recursive syntactic processing, and verbal working memory. On the other hand, area 45 and its connections via the ventral pathway are linked to simple (non-recursive) grammatical forms, and semantic and lexical analyses. More recently, Friederici and collaborators have proposed a model for Broca's region in which area 45 receives auditory information from the ventral pathway and then areas 45 and 44 convert the phonological and lexical inputs into a vocal articulatory pattern that is conveyed to the premotor cortex to codify speech utterances (Skeide and Friederici 2016). Thus, Broca's area may not be directly involved in the production of speech, but rather coordinates the transformation from phonological representations into neuromuscular articulatory processes. This is consistent with the recent finding by Nina Dronkers and collaborators, who found that while Broca's area activates during word presentation in a vocal repetition task, at the time of the speech response there is activation of the ventral motor cortex, but not of Broca's region. Nonetheless, Broca's region activated when novel articulatory sequences had to be executed when presenting non-word stimuli, that is, phonetically correct but meaningless phonological sequences, like "dago", which requires conscious control of vocalization (Flinker et al. 2015).

Finally, Catani, Marsel Mesulam and other collaborators have discovered an additional tract, called the frontal aslant. This is a vertical fiber bundle that connects the supplementary and pre-supplementary motor areas in the superior frontal gyrus (dorsal prefrontal cortex) with the inferior frontal gyrus where Broca's area is located (Catani et al. 2013). Catani and his group found that the aslant tract was affected in a subgroup of patients with primary progressive aphasia (a neurodegenerative condition that results in progressive loss of speech), which is characterized by lack of fluency in speech or in its more serious condition, complete mutism. The aslant tract is also present in monkeys, and may be part of a secondary but ancestral vocalization system that includes the medial frontal cortex and its descending projections to the brainstem, which we will discuss in more detail in Chapter 10 (Ackermann et al. 2014).

Connecting It All

Perhaps surprisingly to some, the language areas are not different from other cortical areas in their intrinsic architecture. Angela Friederici, Wolf Singer and several others have emphasized that the synaptic organization of different cortical regions is essentially the same, based on a "canonical microcircuit" that repeats serially throughout the cortex (Friederici and Singer 2015). The idea of a modular organization of the cerebral cortex was introduced by Vernon Mountcastle in the 1950s, based on the vertical organization of neuronal clusters in the cerebral cortex, in arrays termed columns (Edelman and Mountcastle 1978; Mountcastle 1997). Mountcastle proposed that cortical columns have a conserved synaptic organization across the entire cortical mantle. There are minor differences between cortical areas arising from the relative development of distinct laminar components, for example, large pyramidal neurons in motor areas and abundant granular neurons in sensory areas. Mountcastle also asserted that each cortical region should be defined by the unique pattern of connectivity of each area with the rest of the brain, rather than by its cytoarchitectonic features. In this context, the specificity of functions of each given area depends more on the particular embedding of this area in a larger scale neural network rather than on its internal organization. Thus, localization emerges more as a consequence of the network configuration than as an intrinsic property of each brain region. Furthermore, recent evidence has revealed significant individual variability in the organization of these networks. Emily Finn and her collaborators have described an individual fingerprint in the connectome, which allows for distinguishing one subject from others. This indeed provides each of us with a specific signature, characterized by the organization of large-scale neural connections in our brains (Finn et al. 2015).

Network thinking has led to the connectome project, which is an ambitious computational endeavor that aims to account for all connections of the human brain. The connectome was independently proposed in 2005 by Olaf Sporns and Patric Hagmann, in analogy to the human genome project, and has been developed by the U.S. National Institute of Health as a major endeavor to describe the connectivity of the entire nervous system in humans and animals (Hagmann et al. 2008). Connectome models emphasize complex and distributed networks encompassing widespread brain areas, in which there are critical nodes where many connections converge and are therefore key regulators of the overall network. Stefan Fuertinger, Kristina Simonyan and collaborators proposed a speech-specific connectome model that includes the classical language networks, the dorsal and the ventral pathways described here, and other regions like the insula, anterior cingulate gyrus and other regions (Fuertinger et al. 2015). Notably, a critical node in this network is the posterior motor cortex, which can be considered a connector through which motor output is directed to brainstem centers. Pascale Tremblay and colleagues have proposed a complex network subserving language systems, emphasizing a descending cortical "motor stream" that includes Catani's frontal aslant tract, which anchors the distributed language network in a specific motor pathway (Dick et al. 2014). These findings are relevant for the origin of speech, as it has been commonly argued that the direct control of the descending cortical over laryngeal musculature was the key process that allowed the voluntary control of vocalizations and hence the appearance of speech as the main communicative modality.

These extended networks support the notion of a widespread region associated with Broca's aphasia. In this line, Evelina Fedorenko has subdivided the language-related networks into a functionally specialized "core" of coactive areas during speech and language processing (Broca and Wernicke's areas in the restricted sense), and a "periphery" that includes areas like the insular cortex, inferior parietal areas and other regions (Fedorenko 2014; Fedorenko and Thompson-Schill 2014; Chai et al. 2016). These areas contribute domain-general mechanisms like attention, short-term memory, motivation and motor control to linguistic processes, but may also provide cognitive control over other tasks. Furthermore, cortico-cortical connections are usually reciprocal, so that information can be transferred in both directions, from sensory-related to motor-related areas (bottom-up), and vice versa, from motor-related to sensory-related areas (top-down). A statistical methodology called dynamic causal modeling, developed in the 2000s by Karl Friston and collaborators, analyzes the effect that changes in activity in one region can have on activity in another connected region (Friston et al. 2003). Using this technique, Dirk-Bart den Ouden and collaborators determined a significant top-down effect of Broca's area and the adjacent premotor cortex into Wernicke's area, via the dorsal pathway, particularly for mechanisms of sentence processing (den Ouden et al. 2012). Other authors like Angela Friederici and Josef Rauschecker have also proposed a top-down regulation of Wernicke's area from Broca's area (Rauschecker 2012; Skeide and Friederici 2016). More specifically, the arcuate fasciculus and the adjacent tract stemming from the premotor cortex probably play an important role in modulating early stages of speech processing in function of current motor programs (see Chapter 7).

Thus, there is a much more intricate cortical network for language than was envisioned in the early models of Wernicke and Geschwind. This becomes even more complicated when we consider that these areas are not isolated from the rest of the brain and that they are highly interconnected with other neuronal systems. For example, the production of speech, writing or sign language requires the execution of complex motor patterns that are controlled by the cerebellum and the basal ganglia (Jeon et al. 2014; Ackermann et al. 2014; Leisman et al. 2014; Moberget and Ivry 2016; Krishnan et al. 2016). The basal ganglia are extensively connected with the cerebral cortex, and Broca's and Wernicke's areas, as well as the motor cortex controlling the vocal tract. People with lesions in these subcortical nuclei usually display speech deficits like dysarthria or apraxia (the incapacity to form and articulate speech sounds, although patients seem to know what they want to say). Furthermore, stuttering is also caused by basal ganglia dysfunction, and pharmacological blockage of dopamine (a neurotransmitter critical for basal ganglia function) can ameliorate these speech deficits. In addition, the basal ganglia are believed to participate in the execution of automatic speech patterns acquired over many years, like producing the past tense in regular verbs in English. In Parkinson’s disease, a condition that primarily affects the basal ganglia, there is in fact difficulty in applying this rule to newly learned verbs. Another subcortical structure that is relevant for speech and language is the thalamus, a potato-shaped complex of nuclei at the base of the cerebral hemispheres that is highly and reciprocally connected to the cerebral cortex, to which some of its nuclei convey auditory, visual and somatosensory stimuli (Jeon et al. 2014; Klostermann et al. 2013; Bohsali et al. 2015). Lesions in the thalamus have been linked to aphasia, but the relationship with language or speech production is still difficult to understand and separate from cortical damage. A common effect of thalamic effects on language is dysnomia, which is thought to be due to insufficient arousal caused by damage to the thalamic reticular nucleus. The study of subcortical components in speech and language is only in its beginnings, and probably the coming years will witness exciting discoveries in this area. Finally, a recent study revealed that the hippocampus, a limbic structure of the temporal lobe involved in memory processing (see Chapter 6), participates in language processing by linking incoming words with stored semantic representations, possibly associated to the ventral language pathway (Piai et al. 2016).

Brain Waves

Another recent source of evidence on language processing has come from more direct measurements of neuronal activity, such as electroencephalography (EEG, the analysis of electrical fields on the surface of the skull) and the much more recent magnetoencephalography (MEG), which measures the magnetic fields associated with electrical fields. Compared with imaging methods, whose time resolution analysis is on the order of minutes, EEG and MEG record electromagnetic activity every millisecond, which reveals the microdynamics of the brain in real time. However, they lack the anatomical resolution of imaging methods, as they are recorded directly from the skull, after tremendous distortions of the electromagnetic field as it crosses the braincase. The electrical activity of the brain surface was first analyzed in the 1870s by the American neurologist Richard Caton, and was subsequently measured by several other researchers (Caton 1875). However, it was the German psychiatrist Hans Berger who, in 1924, recorded the first human EEG on the skull surface (Berger 1929). Berger had studied mathematics before enrolling in medicine, and had an interest in the physics of the brain, but more than that, he was motivated by his belief in telepathy, and was trying to find physical evidence for this. His electrical recordings unveiled a complex oscillating electrical signal that was, however, much too weak to travel any significant distance away from the skull. He discovered the alpha rhythm of the EEG (an oscillatory activity of some 8–13 cycles per second), which is evident in occipital regions when subjects close their eyes, but is substituted by the faster beta rhythm (between 12 and 30 cycles per second) when subjects open their eyes. His findings revealed that the brain is actually an active network at all times, working as a highly complex oscillatory machine with electrical activity with cycles at many different frequencies at the same time. Brain oscillations come in different flavors, and the EEG signal is in fact a composite of many oscillatory activities that occur at frequencies from one tenth of a cycle per second or less, up to some 80 cycles per second or more. These frequencies can be separated, much the way white light can be broken down into its different frequencies or colors through a prism, by a mathematical method called Fourier analysis, or other more modern methods such as wavelet analysis. Thus, brain activity occurs at different timescales that, interestingly, fit spatial requirements so that high frequencies seem to be related to local processing, and are nested in wider networks operating at higher frequencies that serve as associative links between different regions.

Work in this century by György Buzsáki, Nikos Logothetis, Wolf Singer and many others have determined that neuronal oscillations are ubiquitous across species and brain regions, and have been found to be critical for brain activity, including cognitive processes (Buzsáki et al. 2013). Ongoing oscillatory activity is fundamental for controlling and synchronizing the “spiking” activity of neurons, that is, the generation of very strong but extremely brief all-or-none electrical signals called action potentials that make up the basis of neuronal signaling. In a seminal article, Eugenio Rodríguez, working with Francisco Varela and others, showed that high-frequency synchronization of neuronal oscillations across brain regions is associated with feature perception in human subjects (Rodríguez et al. 1999; Varela et al. 2001). Furthermore, my former student Conrado Bosman, working with Pascal Fries and me (in two separate papers) has recently proposed that the canonical cortical circuit discussed above is essentially an oscillatory device, highly conserved not only across cortical areas but also across many species (including birds, reptiles and perhaps some invertebrates) (Bosman and Aboitiz 2015, Lewis et al. 2015). This circuit serves basic computational processes inherent to a variety of sensory, motor and cognitive functions (see Chapter 9). As Angela Friederici and Wolf Singer have emphasized, the neuronal networks for language are no exception to this phenomenology (Friederici and Singer 2015). David Poeppel has advanced the hypothesis that brain rhythms are essential for language processing and that their nested organization partly reflects the hierarchical structure of language by packaging information at different temporal levels. Poeppel specifies three main levels of processing that fit distinct neuronal frequencies, namely phonemes are processed at very high frequencies (some 25–35 cycles per second or more, called the high beta or low gamma ranges), the syllabic rate occurs at around 4–7 cycles per second (the so-called theta frequency); and lexical and phrasal units are processed at slower frequencies, say 1–2 cycles per second (delta frequency). Additional studies have found that differences in the amplitude of gamma oscillations in auditory regions are also associated with differences in semantic contents, while the theta rhythm is related to short-term verbal memory, a capacity that is critical for language acquisition (Chapters 6 and 7) (Poeppel et al. 2012; Poeppel 2014; Giraud and Poeppel 2012; Ghitza et al. 2013; Chait et al. 2015, Hickok and Poeppel 2015). Noteworthy, a recent study mentioned above, indicating involvement of the hippocampus in language processing, revealed that modulation of theta oscillations in this region are associated with semantic expectations during speech perception (Piai et al. 2016).

Thus, speech and speech processing take place in an oscillatory domain where interrelated frequency ranges must be tightly coordinated for appropriate execution and perception. Provided that the speech rhythm is maintained, the nested organization of these activities is able to provide contextual cues (provided by low frequencies) to local processing (occurring at high frequencies). Under these conditions, it may be possible to solve perceptual ambiguities and facilitate comprehension. In the auditory cortex, ongoing oscillations in superficial layers, especially in the theta and gamma ranges, synchronize with the acoustically imposed rhythmic activity provided by the speech signal, which hits the middle layers of the cortex, and is projected to higher order cortical areas. On the motor side, speech itself is a highly rhythmic activity involving lip, tongue and vocal fold movements that also take place semi-periodically (just like many other motor activities). Furthermore, the tight coordination between the different organs involved in speech (lips, tongue, and vocal folds) requires fine coordination of the motor pacemakers located in the brainstem, which are controlled by brain oscillatory activity. In this same line, Nai Ding, Lucia Melloni, Poeppel and colleagues recently analyzed spectral activity at different timescales in subjects listening to fluent speech, observing that cortical activity accurately tracked the time course of words, phrases and sentences, while purely acoustic cues or the predictability of incoming words did not correlate with the recorded activity (Ding et al. 2016a). This suggests that grammatical constructions reflect a timescale hierarchy of neural processing, a point I will return to in Chapter 6. Some very recent studies have used intracranial recordings during surgery of epileptic patients. For example, the group led by Stanislaas Dehaene found that oscillatory activity in the left hemisphere increases as words are being read in a sentence (possibly reflecting working memory load), but this activity decreases in the moment the phrase is formed, which may relate to the syntactic function Merge (see Chapter 1) (Nelson et al. 2017).

Finally, another way of analyzing human brain electromagnetic activity has been the study of event-related potentials (ERPs), a technique developed in the 1930s by Pauline and Hallowell Davis (Davis et al. 1939). It consists of averaging EEG signals after many trials that are time-locked to the presentation of a stimulus in a sensory modality (visual, auditory or tactile). Since the recordings are time-locked, trial averaging eliminates all non-coherent variation in activity, unveiling a smooth signal that shows voltage or magnetic deflections at specific times after the presentation of a stimulus. These deflections are the ERPs, which are classified as early potentials (occurring around 100–200 milliseconds after the stimulus), which reflect activation of specific sensory cortices; and late potentials (300 milliseconds or later), reflecting multimodal cognitive operations. Although a relatively old technique, the study of ERPs has been revived in the last 30 years due to their usefulness in the study of attentional processes. As we will see in Chapter 5, there has been a steadily increasing number of ERP studies in language processing, partly triggered by the seminal reports of Marta Kutas and Steve Hillyard on semantic-related activity (Kutas and Hillyard 1980).

The time resolution of the ERP signal has allowed for establishing a sequence of events in speech processing that was elegantly summarized in a recent model proposed by Michael Skeide and Angela Friederici. According to them, speech information is first processed in the auditory cortex, and some 20–50 milliseconds after presentation, the phonological representation of words is recognized in the superior temporal sulcus. Then, two parallel streams run along the temporal lobe, one involved in morphosyntactic categorization (assigning syntactical categories to words) (40–90 milliseconds) and analysis of basic phrase structure (120–150 milliseconds in the anterior temporal lobe). The other stream is lexical-semantic processing in which, for example, words are distinguished from non-words (50–80 milliseconds), followed by lexical retrieval processes in which word meanings are fully recognized (110–170 milliseconds in the left anterior temporal lobe). These are bottom-up processes that are conveyed mainly by the ventral acoustic stream. Top-down mechanisms then ensue via a projection from the anterior temporal lobe to Broca's area. First (between 200 and 400 milliseconds), lexical information reaches areas 45 and 47 in the left hemisphere via the ventral pathway, where semantic analysis is performed. In addition (between 300 and 500 milliseconds), morphosyntactic input is conveyed to area 44, where higher-level syntax is processed. After this, both semantic and syntactic information are transmitted back from Broca's region to Wernicke's area, where syntactic and semantic information converge to generate a unified conceptual representation of the speech string. On the other hand, prosodic processing has a longer onset time, beginning at 200 milliseconds in the right auditory cortex, while activity related to prosodic information begins in the right ventrolateral prefrontal cortex at some 300 milliseconds post-stimulus (Skeide and Friederici 2016).

No doubt we have come a long way since Broca's time. Researchers have been able to identify a sophisticated network involved in speech processing, and accessory networks supplying basic cognitive processes to support the demands of linguistic behavior. Still, the evolutionary questions of how did these networks originate, and whether they emerged from some ancestral system present in the non-human primate brain remains unanswered. First, we need to explore other features of the human brain that are intimately related to our communicative capacity: the large size of our brain, hemispheric dominance and interhemispheric communication, and our memory system. After discussing these, I will begin to track the ancestry of our speech-related brain networks and behavior by looking for similar phenomena in non-human primates, other mammals and even non-mammals like birds.

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