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Monkey Brain, Human Brain

Around the time Baddeley and Hitch proposed their tripartite model of working memory, some researchers were beginning what would later become an explosion of articles on the functions of the monkey prefrontal cortex. These advances were largely based on single-neuron electrical recording with microelectrodes (also known as single-unit recording). This marked the beginning of a period devoted to mapping the electrical activity of individual neurons in different parts of the central nervous system. Single-unit recording was a revolutionary technique that allowed for the first time to record the electrical responses of neurons, elicited by sensory stimuli and associated with behavioral patterns. The first studies, with notable exceptions, focused on vision and provided a fundamental conceptual framework for the development of cognitive neuroscience. Some key notions that emerged from this research were then applied to other sensory systems, particularly auditory and language processing. Consequently, it is important to give an overview of these early findings in order to provide the neurobiological bases on which the study of language has been built.

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The Visual Paradigm

In the late 1950s, titanic researchers consolidated the single-unit recording technique in neuroscience. This was science at its best, starting with the studies by John Eccles on motor neurons of the spinal cord, for which he was honored with the Nobel Prize in 1963 (Eccles 1967). Another crucial advance was made by Steven Kuffler and Horace Barlow, who recorded electrical activity from retinal cells in response to light stimuli (Spillman 2014). After them, the team led by Jerome Lettvin, in which Humberto Maturana was a key author, made a substantial discovery analyzing the visual responses of single neurons in the frog retina and optic tectum, a midbrain structure that is the main visual processing component of lower vertebrates. Lettvin and collaborators had been motivated by Roger Sperry's earlier studies on the development of the frog visual system, in which he sectioned the optic nerve, detaching the eye, and then allowing the visual fibers to regenerate their severed projections into the optic nerve (see Chapter 4). Maturana, Lettwin and coworkers began studying the visual responses of frog retinal cells, following Kuffler's method of directly illuminating the eye and recording neuronal electrical activity. In an earlier study, Maturana and coworkers sectioned the frog optic nerve as Sperry had done before and physiologically confirmed Sperry's behavioral findings that regenerated fibers grew into their original positions even after having rotated the eye (Maturana et al. 1959). But the group's most important finding came soon after this. As Maturana told the story, one day he was alone in the lab with a frog with an implanted electrode while his co-workers were at lunch when he made perhaps one of the most serendipitous discoveries in the history of neuroscience. He accidentally moved his hand in front of the frog's eye and observed a strong electrical response from the retinal neuron that was being recorded. Maturana's finding was that not only light, but also a moving shadow could provoke a visual response. The team began searching for specific kinds of stimuli that could trigger visual responses in the retina, and observed that the frog eye has only four separate visual operations: detection of sharp boundaries, detection of convex borders ("bug perceivers", presumably involved in catching prey), moving edge detection (as with Maturana's hand), and light dimming detection (Maturana et al. 1960). These cell types had different electrophysiological properties and their axons differed in terms of myelination. Furthermore, they projected to distinct layers in the optic tectum, where the presence of these same response types was confirmed. Lettvin, Maturana and collaborators published an influential paper titled *What the frog's eye tells the frog's brain*, in which they argued for the existence of "feature detectors" that extract behaviorally relevant cues according to basic perceptual configurations (Lettvin et al. 1968; Spillman 2014). With that the search began for operations that detect stimulus regularities to construct the visual world. This perspective had strong impact on the field of computer science, with efforts to construct image-processing devices. Maturana and Lettvin were nominated for the Nobel Prize for their findings, but the prize went in the end to the aforementioned David Hubel and Torsten Wiesel, who went more deeply into these findings in the monkey, and extended their studies on neuronal development in cats. Subsequently, Maturana took up epistemological issues regarding the nature of reality in terms of the operation of the nervous system. He refuted the paradigm he had contributed to constructing, and concluded that it makes no sense to speak of detecting features or information processing in the nervous system, as it is a dynamic system and its internal operations are much more relevant than its external interactions. This notion came together with an overarching conceptualization of the organization of living forms, defined by Maturana as "autopoietic", that is, self-producing machines. Although influential in the social sciences, Maturana's views have had limited acceptance in biology and neuroscience.

At about the same time as Maturana and Lettvin, Hubel and Wiesel began a series of studies to analyze neuronal response to specific configurations of stimuli (Hubel and Wiesel 1977; Hubel 1988). They characterized neurons according to their response selectivity when different kinds of stimuli were presented. For example, neurons in the retina or the lateral geniculate nucleus of the thalamus (the main relay nucleus to the cerebral cortex) respond to very simple stimuli, such as spots of light. In the mid-layers of the primary visual area (also called V1), neurons are more responsive to a light bar in a specific angular orientation (they called these “simple cells”), while in more superficial cortical layers, “complex cells” are more sensitive to attributes like the direction of movement (say left or right), and respond to a wider range of stimuli than do simple cells. Even more cryptic than these are the “hypercomplex cells”, usually located in secondary visual areas and very difficult to describe in terms of their stimulus-response properties. The simplest hypothesis for these findings is that several aligned spot-detecting thalamic cells converge to form a simple cell, which would explain the preference for linear stimuli in a specific orientation. Subsequently, several simple cells converge to form a complex cell in the superficial layers of the visual cortex, and several of these converge to form hypercomplex cells in other areas. Extending this idea implies that recognition of complex patterns, such as faces, depends on the progressive convergence of many simple attributes of the visual stimuli that are sequentially integrated to construct a specific perceptual scene, which is perceived by one or more neurons located somewhere in the brain. This notion led to Jerry Lettvin’s ironic concept of the “grandmother cell”, a neuron that specifically recognizes one’s own grandmother. Among the main objections to this interpretation was that this architecture is not compatible with the system’s plasticity, and that too many of these grandmother-like cells would be needed to account for all the things we are able to perceive, let alone the complex percepts we learn in our lives. Alternative models were proposed based on lateral interactions between neighboring cells and the establishment of distributed large-scale networks involving different areas, but to date none of these hypotheses has been unequivocally supported by the evidence. Perhaps the most likely situation is that there is a bit of both, that is, a hierarchical processing network that is strongly modulated by preexisting activity in neighboring and distant regions. Some years ago, Rodrigo Quian Quiroga and collaborators reported a subset of hippocampal neurons in human subjects, selectively firing in response to specific images of known faces (like Jennifer Aniston, Halle Berry or Luke Skywalker), places, objects or animals (Quiroga et al. 2005). From then on, the “grandmother cell” rejuvenated into the “Jennifer Aniston neuron”, with much more glamor. However, there is not just one neuron in the brain preferring Jennifer Aniston, but rather about a million (about one in every thousand hippocampal neurons). Furthermore, some of these neurons also fire in response to related faces, such as co-stars in the same series. The result is that there are overlapping neuronal networks involved in the responses to specific semantic stimuli, rather than a single hierarchically positioned neuron involved in complex recognition. Furthermore, Quiroga doubts that these cells are specifically involved in individual recognition. Rather he postulates that these neuronal ensembles participate in generating associative networks with preexisting memories that permit consolidating memory and recall of contextual information about a perception (Quiroga et al. 2008; Quiroga 2012).

Subsequent studies depicted a mixed organization of the visual system, where together with hierarchical organization, parallel streams are involved in processing different attributes of the visual scene. The work on the visual system was fundamental for recognizing the dorsal and ventral pathways for speech and language, and I will succinctly review it here (Zeki 1993). The visual pathway begins in the retina, the ganglion neurons of which send axons to the lateral geniculate nucleus of the thalamus, which then projects to the primary visual cortex or V1. There are two main kinds of ganglion neurons in the retina. The first are parvocellular neurons, selective for chromatic or color stimuli and visual details (the “P” pathway); and the other are magnocellular neurons, selective for movement and gross shapes (the “M” pathway). The two neuronal types project to different layers in the lateral geniculate nucleus (P and M layers, respectively), and neurons in these layers project to different subdivisions of the mid-layers in the primary visual cortex, such that the laminar segregation acquired in the thalamus is maintained in the visual cortex (Fig. 7.1). Information from visual detail from the P-receiving sublayer projects to superficial layers of V1; and the chromatic-responding neurons cluster in these layers in small cellular aggregates called “blobs” (Hubel 1988; Zeki 1993).

There are a series of stripes in the secondary visual area (V2) that cover all layers and run the length of the area in a sort of zebra stripe pattern. The stripes can be distinguished by the activity of a mitochondrial enzyme, cytochrome oxidase. There are three types of stripes, thick, thin and what are termed inter-stripes. From the P pathway, the color-processing blobs of V1 project to the thin stripes of V2, and the

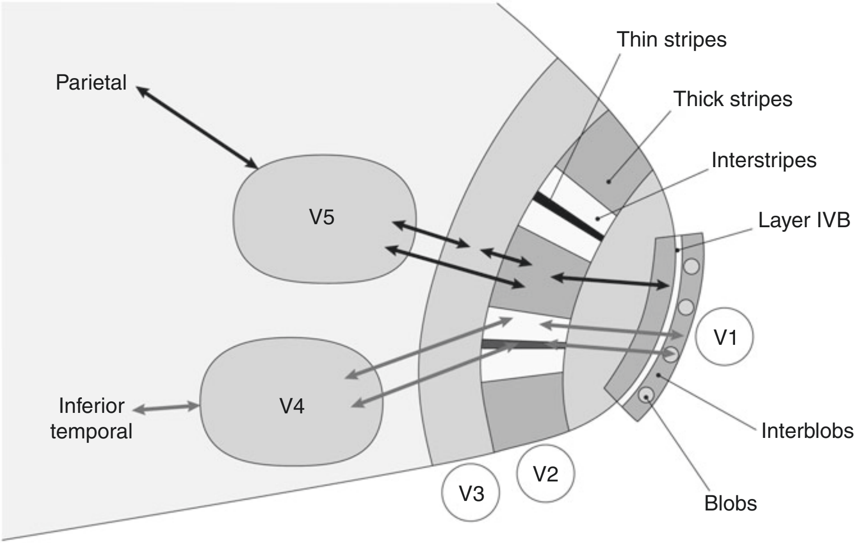

Fig. 7.1 Connections between visual areas. In gray arrows, the ventral pathway, processing object information and details. In black arrows, the dorsal pathway, processing spatial and movement information. Area V1 is separated in its laminar components, while area V2 is composed of tangential "stripes". Different laminar and stripe elements convey distinct kinds of visual information

superficial layers of V1 connect with the inter-stripe band. Neurons from the M-receiving sublayer of V1 project directly into the thick stripes of V2. Thus, the laminar segregation of inputs in V2 is transformed into micro-areal segregation, where different stripes convey different attributes of the visual stimulus. At higher levels of the visual processing network, V2 micro-areal segregation becomes large scale areal separation into two main processing pathways (Hubel 1988; Zeki 1993).

Area V2 projects to third-order visual areas called V3, V4 and V5, which receive different types of inputs from the former. For example, area V4, located in the inferior temporal lobe, receives color (thin stripes) and detailed visual (inter-stripes) information from V2. V4 is essential for the subjective perception of color. Lesions in this area produce a condition called achromatopsia in which patients become partly color-blind in the visual field contralateral to the site of the lesion. Notably, color perception is not exactly the same as the ability to discriminate wavelengths. The studies by Semir Zeki and others have provided substantial evidence that the perception of color is a subjective phenomenon, and depends on contextual variables (Zeki 1993). To understand this, we first have to realize that objects do not have color by themselves, as the light they reflect depends on the light by which they are illuminated. Thus, a red object could be made to reflect more green than red light, if illuminated with intense green light and faint red light. The brain compensates for this effect in a phenomenon called color constancy, where despite different lighting conditions, the object remains the same color, within some limits of course. What the brain actually does is to calculate how much red light and how much green light the object is emitting compared to ambient light. Thus, regardless of how much red and green light the object reflects at any instant, it will reflect more red and less green light compared to its immediate surroundings if the ambient is illuminated with the same light, and surrounding objects have a balanced chromatic composition. Thus, the object is labeled as "red" because it reflects more red light than its surroundings, and is not "green", even if it reflects more green than red light. This object-surroundings computation occurs in visual area V4, as chromatic cells in the retina and V1 are strictly responsive to light wavelength. That is, the hypothetical red object illuminated with mostly green light would be labeled in V1 as "green". There are ways to fool the system by altering the chromatic properties of the surroundings, which produces what is called color shadows, in which one sees colors that are not present (Zeki 1993). A good example of this is a dress that recently circulated in the Internet that appeared blue or white depending on the observer and contextual conditions. I have taken this small detour because I will make a similar argument in Chapter 10, but in the area of speech perception.

Area V4 connects extensively with many areas in the inferior temporal lobe, containing neurons selective to distinct objects such as faces (recall Quiroga's Jennifer Aniston neurons), hands and inanimate objects or places. Bilateral lesions of the inferior temporal lobe produce visual agnosia, which is the incapacity to recognize objects, of which the most dramatic is prosopagnosia, referred to as the inability to recognize the faces of familiar persons. This condition is usually caused by severe brain injury, although there are examples of developmental prosopagnosia in absence of evident neurological lesions. Some celebrities like Brad Pitt have claimed to be prosopagnosic, possibly a good excuse for ignoring many of the people that approach them. It would in any event be interesting to find out what happened with his Jennifer Aniston neurons. Visual areas from the inferior temporal lobe are highly connected to the anterior tip of the temporal lobe (the temporal pole), which serves as an interface between these sensory areas and limbic regions involved in emotional processing and memory. On the other hand, the dorsal visual pathway runs in the parietal lobe, in which area V3 receives projections from the M pathway (thick bands of V2 and the M-receiving sublayers of V1), and projects to V5 (also called MT). These areas are selective for gross shapes and movement, and lesions in V5 sometimes lead to a rare condition called akinetopsia, in which subjects are unable to perceive movement. They have difficulty crossing streets, as they cannot tell the velocity of vehicles or filling a teacup because they cannot tell how full it is. These patients report not being able to sense continuous movement but instead visualize a series of static photographs that keep changing. V5 and other areas from the inferior and posterior parietal lobe connect with higher order parietal areas that in turn project into frontal areas for motor action (Zeki 1993).

Thus, two main streams were recognized in visual processing, a ventral one running via the inferior temporal lobe, associated with object recognition (the P pathway), and the other running dorsally to the parietal lobe (the M pathway), associated with spatial information and movement or space-time processing. These two pathways are usually dubbed as the “what” (or “who”) and the “where” pathways, respectively, although more recent interpretations prefer to nickname the dorsal stream as the “how” pathway, as it links visuospatial processing with motor commands in the frontal cortex via the parietal lobe. The ventral pathway is involved in recognition, emotional and semantic processing, while the dorsal pathway codes for context-dependent behavioral patterns. However, this is not to say that these two streams are totally independent; there are well known connections between the two that may serve to maintain an integrated perception of say, a bouncing colorful beach ball. The general problem of perceptual integration has intrigued neuroscientists for some time, and has been referred to as the binding problem. Synchronic oscillatory activity was proposed by Wolf Singer, Francisco Varela and others as the main mechanism by which distributed areas of the brain involved in different processing domains might integrate their activities contributing to a unified perceptual image (Singer 1999; Varela et al. 2001). In this context, Jason Yeatman and collaborators recently used tractographic imagery to analyze the human vertical occipital fasciculus, which connects the dorsolateral and ventrolateral visual cortices (see Chapter 2) (Yeatman et al. 2014). This tract was originally described by Wernicke in non-human primates, and may serve as a main channel to integrate the ventral and dorsal visual pathways.

Mapping Memory

In the 1970s, electrophysiologists began studying the activity of neurons in higher-level cortical areas of the monkey to understand the mechanisms underlying higher cognitive processes like memory and attention. These studies were largely inspired by the groundbreaking work in the 1930s of Carlyle Jacobsen, who pioneered a controversial operation, the lobotomy (Jacobsen 1938). Jacobsen showed that monkeys with bilateral prefrontal lesions (more precisely, in the dorsolateral prefrontal cortex) had no problem solving complex puzzles if the required information was available on sight, but the moment there was an interruption of even a few seconds the monkeys could no longer continue the task. This mirrored the observations by earlier neurologists like John Hughlings Jackson of human patients with prefrontal lesions, and reflected a significant deficit in short-term memory, which many researchers later likened to Baddeley's visuospatial working memory (York and Steinberg 2011). Jacobsen even advanced the concept that short-term memory must be maintained by some sort of sustained activity in the absence of stimuli, or by recall of past events. Other researchers like Karl Pribram and Mortimer Mishkin also made important contributions to understanding the role of the prefrontal cortex in behavior, with studies indicating distractibility, inflexibility and perseverative behavior following lesions in this region (Pribram and Mishkin 1956; Mishkin and Pribram 1955, 1956).

Two scientists were key in providing insights into the neurobiological underpinnings of working memory. One was Joaquín Fuster, who trained monkeys in the delayed match-to-sample task (Fuster and Alexander 1971; Fuster 1995, 2003), which consists of briefly presenting stimuli on a screen (the sample), followed by a short delay of a few seconds in which stimuli are erased, after which a second set of stimuli is presented. The animal then has to select stimuli from the second set that fit properties from the first sample. For example, the sample could be a colored dot, and the monkey has to remember the color during the delay and match it to the same color in the new set of stimuli. In 1971, Fuster and Garrett Alexander, in one paper and Kisou Kubota and Hiroaki Niki in another described sustained firing of prefrontal and thalamic neurons during the performance of a delayed response task (Fuster and Alexander 1971; Kubota and Niki 1971). The two papers reported a variety of neuronal responses during the task, some of which activated with the presentation of the sample, others activated just before the response, and still others activated precisely during the delay when no stimulus was present. These cells were selective for the sample and were not considered to reflect a general attentional state. Rather, their activity was interpreted as encoding or "keeping in mind" the information that was required for a near-future task. In the previous chapter, I mentioned Mark D'Esposito's critique of this assumption (D'Esposito and Postle 2015). In subsequent studies, Fuster, and others observed a variety of "memory cells", some firing more intensely at the beginning of the delay and then decaying, others with the reverse pattern of firing more at the end, and others still that showed a truly sustained pattern of activity during the delay (Fuster 1995, 2003). Nonetheless, Fuster is reluctant to use the term "working memory" and uses the term "active memory", making reference to a more general process in which information not only from the environment but also stored in long-term memory is activated by sustained firing. Fuster envisions active memory as a broad associative network formed by interactions between different brain systems that are maintained as a memory fragment in the context of a behavioral outcome in the short term. In this way, Fuster gets closer to the non-localizationist tradition that views the brain as resulting from the operation of large-scale and pervasive networks that encode multimodal information. Moreover, he views the brain as a hierarchically organized system with distributed executive processes in the frontal lobe, connecting with perceptual memories in the posterior brain (parietal, temporal and occipital lobes). Lower-level representations from sensory and motor networks are nested in these large-scale networks in an organization that reflects the different levels at which memory operates, from contextual to sensorimotor. One of his well-known dictums is that there is no system in the brain for memory, but rather there is the memory of different systems. He views memory as a property of the distinct sensorimotor networks involved in behavior, rather than as a separate cognitive system involved in the storage of different kinds of information. Finally, Fuster claims that from birth, memories are formed by associative interactions that depend on experience, and build over phylogenetically established frameworks that connect sensory and motor domains, a point that I will discuss further in the next chapter.

The other main contributor to the neurobiology of working memory was Patricia Goldman (later, Patricia Goldman-Rakic), who followed Jacobsen's studies and attempted to define the region of the frontal cortex that is critically involved in short-term spatial memory (Goldman and Rosvold 1970). She found that animals with lesions in the dorsolateral prefrontal cortex, located dorsally to the ventrolateral prefrontal cortex where Broca's region is located, had short-term spatial memory impairments. However, the animals were able to do spatial tasks that did not require memory. Goldman then worked with the renowned neuroanatomist Walle Nauta in visualizing the connectivity of these areas with tract tracing methods and found columnar organization of inputs in the dorsolateral prefrontal cortex, reminiscent of what David Hubel and Torsten Wiesel had described earlier in the visual system (Goldman and Nauta 1977). Together with Carmen Cavada and other researchers, Goldman-Rakic found that the principal sulcus of the prefrontal lobe, involved in spatial working memory, is closely connected to the parietal association cortex, particularly in the intraparietal sulcus and neighboring areas (more technically, areas 7a and 7lip) (Cavada and Goldman-Rakic 1989a, b). Moreover, these two regions are intensely connected to other frontal, temporal and parietal areas involved in different aspects of perception and behavior, as well as with many subcortical nuclei (Fig. 7.2).

After becoming acquainted with Fuster's and Kubota's works, Goldman-Rakic started working with Shintaro Funahashi using a delayed match-to-sample task in which the animal did not have to push buttons as in previous experiments, but was only required to move its eyes to a location (Funahashi et al. 1989, 1991). Eye movements were precisely monitored by an eye-tracking device, an apparatus that is now commonplace in cognitive neuroscience laboratories. Goldman-Rakic used spatially located samples as cues, instead of object properties like color or shape, and identified spatial-specific delay cells that fire continuously with the location of an object that is maintained in memory, and suppress firing when other locations are remembered. Notably, small lesions in the cell′s

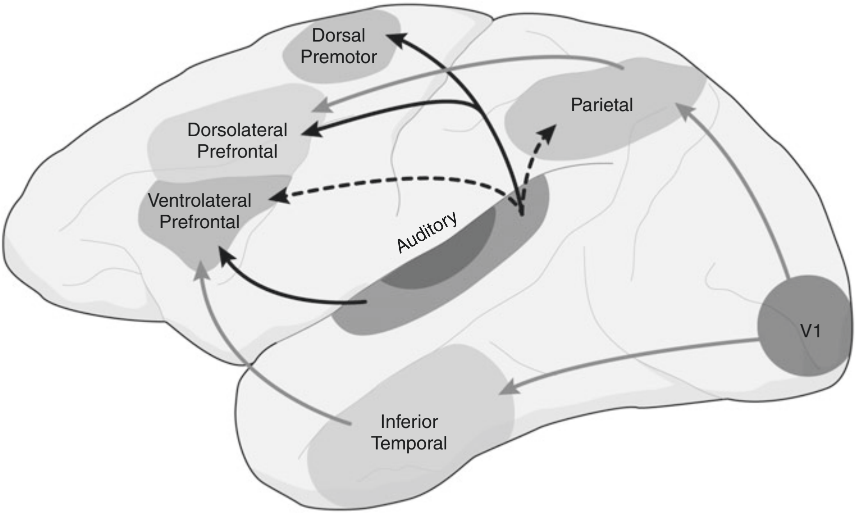

Fig. 7.2 Dorsal and ventral pathways for vision and audition. The diagram depicts the arrangement of the visual- prefrontal (gray arrows) and auditory-prefrontal (black arrows) projections in the macaque, each depicting ventral and dorsal components. Segmented arrows indicate projections that are less developed in the monkey than in humans

surroundings produced impairment in the memory but not in the perception of the precise location. This finding apparently challenges Michael D'Esposito notion that memory is strictly represented in sensory areas (Chapter 6) (D'Esposito and Postle 2015), but these higher order areas may work by stabilizing neural activity in sensory regions by top-down mechanisms that contribute to maintaining the memory trace. In additional experiments, Goldman-Rakic and her collaborators separated prefrontal neurons selective for locations in more dorsal regions of the prefrontal cortex from neurons encoding stimulus features such as color, shape and even faces in more ventral prefrontal positions. Together with Amy Arnsten, Goldman-Rakic identified the neuronal types involved in sustained firing, located mainly in cortical layer 3 and displaying extensive axonal arborization to neighboring neurons with similar perceptual properties (Arnsten et al. 1994). These connections engage in relatively extended circuits that maintain activity during the delay period due to recurrent excitation. Recurrent excitation during working memory tasks is modulated by inhibitory interneurons, and more notably by the neurotransmitter dopamine. Dopamine has a bell-shaped dose-response relationship in which an intermediate doses provides optimal results while doses that are too low or too high result in functional impairment associated with distractibility or anxiety, respectively. Goldman-Rakic then focused on the study of prefrontal function in schizophrenia, providing important insights before her unexpected death in 2003 (Arnsten 2013).

Goldman-Rakic and Fuster agreed that these neurons are the cellular basis of mental representations, but Goldman-Rakic's interpretations were more on the localizationist side than Fuster's. Following the scaffolding provided by research on the visual system, Goldman-Rakic distinguished two separate circuits involved in visual working memory (Fig. 7.2) (Goldman-Rakic 1990, 1995; Goldman-Rakic et al. 1999). The first is a dorsal stream selective for spatial cues that involves the primary visual area, posterior parietal cortices, and dorsal regions of the dorsal prefrontal cortex. The second circuit is a ventral stream that conveys object and facial information, involving the primary visual area, the inferior temporal lobe and more ventral regions of the lateral prefrontal cortex. Note that these two circuits together fit Louis Foville's longitudinal subdivision of the brain described in Chapter 2, while Foville's Sylvian convolution corresponds to the dorsal and ventral auditory pathways to be described below. Anatomically, connectivity between superior parietal areas and dorsal prefrontal areas that subserve visuospatial working memory is provided by the superior longitudinal fasciculus, the massive tract of fibers that connects the parietal and frontal lobes. On the other hand, the inferior longitudinal fasciculus, running along the temporal lobe, contributes to the object and face-related ventral stream. There are several tracts from the anterior temporal lobe that may connect the ventral stream with the ventro-lateral prefrontal cortex, like the capsula externa, the capsula extrema and the uncinate fasciculus. Goldman's Rakic's depiction of a dorsal visuospatial pathway, and a ventral object/face pathway for working memory made a strong impact on the neuroscientific community, and contributed significantly to the exponential increase in publications involving working memory and the prefrontal cortex.

These experiments intrigued John Jonides and collaborators, who developed a design to distinguish object and spatial working memory in humans (Jonides et al. 1993). Subjects had to retain either the spatial location or the shape of three objects for three seconds. While the spatial task induced strong right hemisphere activation (occipital, parietal and prefrontal areas), the object task activated left hemisphere regions, particularly inferotemporal and parietal areas. This confirmed the dissociation between a dorsal spatial-related network, and an object-related ventral network, also revealing differences in hemispheric specialization. Further studies showed that lateralization for object working memory depends on the nature of the stimulus, with the left hemisphere dominant with abstract shapes and the right dominant for faces. These were seminal studies for understanding the neural substrates of visual working memory. However, little information was available in the seventies and eighties about the neuroscience of auditory working memory, which could be a lot more interesting for people working on language.

The Search for Homology

As a biology undergraduate in the seventies, and then a graduate student in neuroscience in the eighties, I was deeply intrigued by the Geschwind/ Wernicke neuronal model of language, which at the time was depicted as a circumscribed circuit with no counterpart in non-human primates. The evolutionary origin of this circuit was a complete mystery that practically no one at that point had tried to solve. My undergraduate mentors Humberto Maturana and Francisco Varela were reluctant to recognize the existence of localized systems in the brain and adhered to the concept of dynamic large-scale networks in which the anatomical delineation of neural systems was less relevant than their functional dynamics. However, when I moved to the United States in the late 1980s, first to the lab of Al Galaburda, and then to the labs of Eran Zaidel and Arne Scheibel, the perspective was more localizationist, and the notion of a brain subdivided into distinct modules specialized for different functions was well accepted. As I said earlier in this book, the systemic or holistic paradigm provides a wealth of theoretical perspectives, but the localizationist approach has nourished us with substantial empirical evidence and has allowed us to chart the first maps of brain function. The combination of the two views of the brain may actually represent the optimal approximation of brain function, working with a trial and error strategy. Moreover, the module-based approach in a way simplifies the issue of tracking the phylogenetic ancestry of a function or organ, as it is easier to search for similar components in other species. In this line, the studies at the time by Fuster, Goldman-Rakic and their colleagues seemed to me a promising framework to understand the origin and evolution of language circuits. I could not help but imagine similarity between the large-scale networks for visuospatial working memory depicted by Patricia Goldman-Rakic, and the Wernicke-Geschwind model of the language circuit via the arcuate fasciculus. The ventral pathway for language was not yet fully recognized.

The existence of a circuit comparable to the language network in the monkey would strongly imply evolutionary continuity between non-human primates and us. The first step in this line was to determine elements in other species homologous to Broca's region, Wernicke's region and their connections (Aboitiz 1988). But homology does not mean identical. Richard Owen, whom we met in the Chapter 1, defined homology in the mid-1800s as the "same" organ in different species, regardless of differences in form or function (Owen 1837; Rupke 1994). This means that homologous organs can display a variety of shapes and functions, like the fins of fish and the limbs of mammals. With Darwin, the concept of homology acquired a completely new historical dimension as it implied a structure present in the common ancestor of two species that diverged into different forms but is still recognizable in terms of development, inner structure or relative position. Unfortunately, there is no clear-cut criterion to determine homology, which has sometimes led to agitated controversies, as I will discuss in Chapter 9.

Fortunately, finding areas homologous to those assigned to the classical language circuits was not that difficult. In the early 1980s, Al Galaburda, working with Friedrich Sanides and Deepak Pandya, parcellated the human and macaque auditory cortices in detail, subdividing it into a mosaic of interconnected areas organized around the primary auditory regions (Brodmann's areas 41 and 42; see Chapter 2) (Galaburda and Sanides 1980; Galaburda and Pandya 1983). One of the most posterior of these areas was Tpt in the planum temporale, which we have referred to before in relation to its asymmetry in the human, and its possible correspondence to Wernicke's region. Subsequent studies by Todd Preuss and Goldman-Rakic identified area Tpt in the galago, a basal primate, indicating that this area has a long evolutionary history and predates the origin of speech (Preuss and Goldman-Rakic 1991a). What happened with area Tpt in human evolution, did it acquire a new function, associated with speech processing? Things like this may happen. An example is the visual word form area in humans, described by Stanislaas Dehaene, which decodes the visual structure of letters translating them into phonological representations (see Chapter 2) (Cohen et al. 2002). This area exists in illiterate people, but obviously does not play this function, and probably participates in a bimodal or multimodal integration network. Furthermore, the capacity for orthographic processing is present even in pigeons, showing that this ability can develop from general perceptual abilities (Scarf et al. 2016). Likewise, area Tpt is probably part of a multimodal interface in primates, and may have acquired its function in human evolution through its engagement in a novel auditory-vocal interface. Area Tpt has been described as a multisensory “hub” in which visual, auditory and somatosensory inputs from the occipital, parietal and temporal lobes converge, respectively. In this sense, it is well placed to participate in the sensorimotor transformation of vocal sounds, and to associate these sounds with other sensory modalities. As I have said, elucidating the relationship between this area and area Spt described in the previous chapter may be worth pursuing. The identification of a homologue to Broca’s region was also relatively straightforward. As I described in Chapter 2, Broca’s area consists at its core, but not exclusively, of cytoarchitectonic areas 44 and 45 in the ventrolateral cortex of the human brain. Preuss and Goldman Rakic identified area 45 (corresponding to anterior Broca’s region, pars triangularis), but not area 44, in the macaque (Preuss and Goldman Rakic 1991b). For many researchers, areas 44, corresponding to posterior Broca’s region in the human, emerged in humans as an outgrowth from the ventral premotor region that represented orofacial movements.

However, the connectivity between the presumed homologues of Broca’s and Wernicke’s regions provided some surprising findings. By the 1980s and 1990s there were studies on the frontal connectivity of the macaque inspired largely by the earlier work by Goldman-Rakic. The most important at that time were a series of papers published by Todd Preuss and Goldman-Rakic, and Michael Petrides and Deepak Pandya (Preuss and Goldman-Rakic 1991c; Petrides and Pandya 1984, 1988). This evidence indicated that the main input to what corresponds to Broca’s area in the monkey originated in the inferior parietal lobe, traveling via the superior longitudinal fasciculus. On the other hand, the main output of the posterior auditory areas was directed to dorsal premotor regions involved in eye movement control, instead of running via the arcuate fasciculus into the ventrolateral prefrontal cortex as was supposed in humans. No strong evidence had been found of a direct connection between the homologues of Broca’s and Wernicke’s areas via an arcuate fasciculus. There was only one study, by Terrence Deacon indicating direct connectivity between a region lateral to area Tpt and ventral premotor areas in the monkey, which overlaps with terminations from inferior parietal regions (Deacon 1992).

In 1995, I wrote an article in a low-profile journal proposing that the language areas and their connections arose through the establishment of a robust temporoparietal-prefrontal auditory-vocal network that served as a basic working memory system for names and primitive vocal utterances (Aboitiz 1995). I speculated that the capacity to keep vocal signals in mind for some time was critical for tasks such as recalling the name of an object that was not present. Thus, an amplification of vocal working memory capacity was the basis of the origin of the language-related circuits and speech. Subsequently, Ricardo García and I proposed a more detailed scheme for the homologies and evolution of the language regions (Fig. 7.3) (Aboitiz and Garcia 1997). We depicted a three-way input to Broca's area and its corresponding region in the monkey. The evidence at that time indicated that the main projection to Broca's homologue in the monkey is not from auditory areas but from the inferior parietal lobe, particularly areas 40 and 39, together corresponding to the human supramarginal and angular gyri. We speculated that auditory projections reach the inferior parietal lobe via a projection from the superior temporal lobe. This makes an indirect projection between Wernicke and Broca's areas via the inferior parietal lobe, which we argued is also present in the human. A second input to the homologue of Broca's area consists of a direct projection from auditory regions via the arcuate fasciculus as specified by the Wernicke-Geschwind model. However, this tract was considered rudimentary in the monkey, if present at all. Finally, we proposed a third input to Broca's area or its homologue from the anterior temporal lobe, carrying complex visual information to be associated with auditory projections. This projection fits the ventral visual pathway described above, which, as we will see below, partly merges with the ventral auditory pathway.

Adding and subtracting a few elements, the network for language we proposed is essentially the same as the one that is accepted today and was depicted in Chapter 2. We hypothesized that the vocal repertoire of early humans expanded concomitant with the amplification of the arcuate fasciculus and other projections from premotor regions to the brainstem

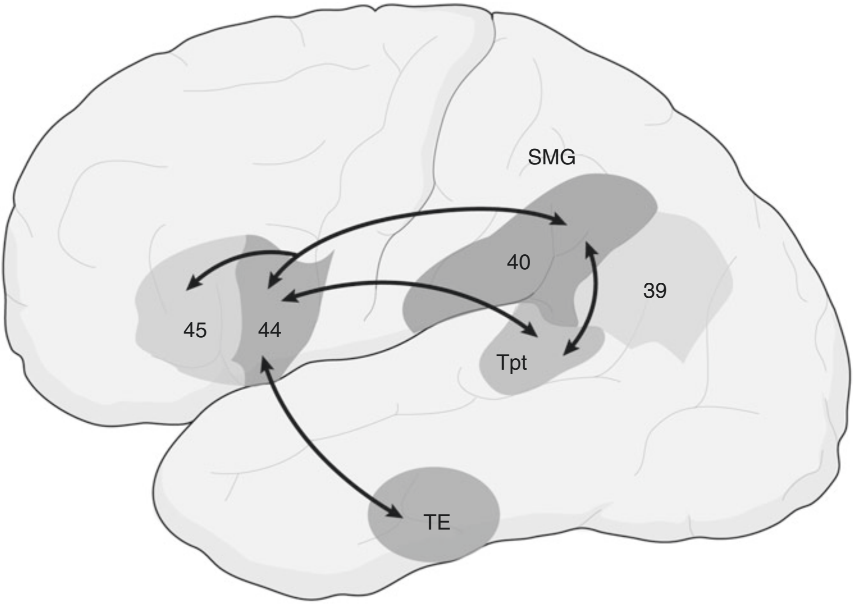

Fig. 7.3 Our original model of language connectivity. We proposed that connections between area Tpt and area 40, and between area Tpt and Broca's area (areas 44, 45) became amplified in the human lineage. Note however that area 44 had not yet been described in the monkey (Aboitiz 1997). Connections between Broca's area and the dorsolateral prefrontal cortex were also depicted in the original model (not shown). Overall, the diagram contains many of the elements shown in Fig. 2.3. AF, arcuate fasciculus; SMG, supramarginal gyrus, TE, area TE; Tpt, area Tpt

controlling vocal musculature. Together with this expansion, an increase in auditory working memory capacity was provided by the growing arcuate fasciculus and inferior parietal projections, generating an incipient phonological loop for learning increasingly complex vocal utterances. In subsequent articles, my students and I emphasized the anatomically more conservative arrangement of the ventral auditory pathway, which in monkeys may be the main circuit for auditory-vocal coordination. On the other hand, the dorsal pathway (especially the arcuate fasciculus) has undergone the greatest degree of expansion in human evolution (Aboitiz et al. 2006, 2010; Aboitiz and García 2009; Aboitiz 2012).

The Paths of Sound

A couple years after our proposal, two independent groups, one led by Liz Romanski in collaboration with Goldman-Rakic and Josef Rauschecker, and the other involving Troy Hackett and Jon Kaas, confirmed that the dorsal auditory stream in the monkey directs to dorsal prefrontal areas instead of the homologue of Broca's area. In addition, they described a robust ventral stream of auditory-prefrontal projections originating in the anterior temporal lobe, which ends principally in the anterior ventrolateral prefrontal cortex and adjacent areas (Fig. 7.2) (Romanski et al. 1999a, b, 2000; Romanski 2007; Kaas and Hackett 1999). These studies showed that the dorsal auditory pathway is associated with spatial and motion auditory processing, while the ventral pathway is more involved in identifying sounds including vocalizations and speech. Ricardo Gil-da-Costa and collaborators also showed that species-specific calls induce activation of visual and limbic areas of the inferior temporal lobe of the macaque (Gil-da-Costa et al. 2004). These notable findings were widely confirmed by a subsequent series of studies indicating a similar organization of visual and auditory projections, both subdivided in dorsal and ventral pathways.

Romanski and Goldman-Rakic also described an auditory domain in the ventrolateral prefrontal cortex (areas 12 and 45) of the monkey, with auditory neurons sensitive to conspecific vocalizations, intermingled with visual neurons sensitive to faces (Romanski and Goldman-Rakic 2002). This indicates that the ventral auditory and visual pathways converge in this region, integrating vocalizations and orofacial gestures. More recently, Romanski and collaborators showed that a population of neurons in the monkey ventrolateral prefrontal cortex responds to videos of conspecific faces, auditory vocalizations or a combination of these (Romanski and Diehl 2011; Romanski 2012; Sugihara et al. 2006). In addition, the activity of some neurons is suppressed when incongruous face-vocalization pairs are presented, which may be relevant for determining the caller's identity (Diehl and Romanski 2014). Likewise, Steffen Hage and Andreas Nieder analyzed single neurons in the macaque ventrolateral prefrontal cortex, the discharge rate of which is modulated by both vocalizations and the perception of species-specific calls (Hage and Nieder 2015). Altogether, this evidence provides an excellent starting point for the development of Broca's area in human evolution, notably receiving its main projection from the ventral auditory and visual pathways. Nonetheless, face-voice associations may not be as developed in monkeys as they are in humans. Julia Sliwa, Sylvia Wirth and collaborators recently described dissociation between facial and vocal responses in hippocampal and inferotemporal cortex neurons of monkeys, in which facial information correlated with individual recognition while voice information did not (Sliwa et al. 2016). This finding contrasts with the reports by Quian Quiroga and collaborators that hippocampal neurons in humans can multimodally represent familiar conspecifics (Quiroga 2012). Thus, associations between faces and voices in the ventral pathway may have been strengthened over the course of human evolution (Viskontas et al. 2009).

Subsequent findings in the ventrolateral prefrontal cortex of the macaque further refined the homologies with Broca's area. Michael Petrides and collaborators were the first to identify area 44 in the macaque brain, providing a complete homology between human and macaque areas 44 and 45, the core of Broca's region (Petrides et al. 2005, Frey et al. 2014). Stimulation of area 44 triggered orofacial movement and rarely hand movements, but not ocular movements, indicating that it is mainly involved in the control of vocal behavior. Eye and hand movements were elicited with stimulation in other dorsal premotor areas. Therefore, the rudiment of Broca's region in the monkey contains two components, an anterior sensory one (area 45) that receives auditory and visual input, and a posterior motor one (area 44) that controls orofacial movement. The ventral auditory and visual pathways feed into the anterior component, while the posterior component receives projections from the dorsal pathway.

Petrides and collaborators subsequently analyzed the dorsal pathway to Broca's area in the human and its homologue in the macaque (Petrides 2014). The authors depicted a nested hierarchy of connections between ventrolateral prefrontal and inferior parietal areas in which lower-order sensory and motor areas close to each other are heavily interconnected, while slightly more distant middle-order parietal and frontal areas are also interconnected. The even more distant higher order parietal and prefrontal areas also have strong connectivity between them (see Fig. 2.3 of Chapter 2). In addition, Petrides and collaborators proposed that the temporal lobe feeds multimodal input (including auditory signals) to the inferior parietal lobe, which provides a route connecting the auditory cortex, the inferior parietal lobe and Broca's area or its homologue (Petrides 2014, Yeterian et al. 2012, Petrides et al 2012). Petrides and his group also described an arcuate fasciculus in the monkey, directly connecting area Tpt and area 45, but it seems less developed than in humans. Finally, the superior temporal lobe connects with anterior Broca's area (area 45) via the ventral pathway (Frey et al. 2008; Petrides and Pandya 2009; Margulies and Petrides 2016). Although here I tried to make a simplified scheme of inferior parietal-prefrontal connections, there are still some discrepancies among authors in the details of this network, which will probably be resolved by further work and the development of more sophisticated imaging techniques (see next Chapter). In a very similar vein, Marco Catani, Dominic ffychte and Valentina Bambini depicted a quite conserved pattern of connectivity between the language-related networks and their homologue regions in the monkey brain (the SCALED model; see Chapter 2) (Catani et al. 2005; Catani and Bambini 2014; Tremblay and Dick 2016). In both species, there are profuse longitudinal tracts along the ventral pathway, but the direct connections between Wernicke's and Broca's regions via the arcuate fasciculus, and between Wernicke's area and the inferior parietal lobe are poorly developed in the monkey, as was proposed in our original scheme (Fig. 7.3).

The above model is widely accepted today as the basic network for language processing (see Chapter 2), and is consistent with our original proposal of a phylogenetically conserved tripartite input into Broca's region or its monkey homologue. In humans, the dorsal pathway processes phonological and articulatory information, and complex syntactic processes, while the ventral pathway has more to do with identification of sounds and speech, and with associating these inputs with other stimuli and long-term memories in a semantic network. Accordingly, while the more posterior part of Broca's area (area 44), which is connected to the dorsal pathway, has a role in phonological fluency and grammatical processing, the anterior Broca's region (area 45), which is more connected to the ventral pathway, is more related to associative processes and memory retrieval.

From Ape to Human

A potential weakness of the aforementioned studies is that none of them has directly compared the auditory pathways in humans and non-human primates in a single study. James Rilling and collaborators made such pioneering comparative studies using tractographic information from monkey, chimpanzee and human brains (Rilling et al. 2008). In a groundbreaking study, they reported that the arcuate fasciculus is present in monkeys, chimpanzees and humans. Nonetheless, Rilling and colleagues found a progressive expansion of the arcuate fasciculus from the macaque to chimpanzee, with maximum development in humans. Conversely, the ventral pathway has remained relatively unchanged in primates, and therefore becoming relatively smaller than the dorsal pathway as brains have increased in size. Note that the dorsal pathway visualized by Rilling and colleagues includes fibers from both inferior parietal and superior temporal areas, possibly including elements from the superior longitudinal fasciculus. As I said in Chapter 2, these fiber tracts are most likely not discrete entities but made up of a continuous plexus of longitudinal fibers covering the white matter below the posterior temporal, parietal and frontal lobes. Very recently, the group led by Kristina Simonyan found robust connectivity in humans between the area in the motor cortex representing the larynx (aptly termed the laryngeal motor cortex) and somatosensory and inferior parietal regions, much stronger than that observed in the macaque, which further highlights the relevance of inferior parietal components in controlling speech processing (Kumar et al. 2016).

Rilling and his team also found that the arcuate fasciculus proper emerges in humans both from the superior temporal sulcus and middle temporal gyrus, while in the chimp these fibers originate only in the superior temporal gyrus (Rilling et al. 2012; Rilling 2014). This implies a broader connectivity in the former, and supports the concept of a role of the dorsal pathway (including inferior parietal projections) in human language. Nonetheless, the arcuate fasciculus of the chimpanzee is larger than that of the monkey. Furthermore, in the chimpanzee the authors found asymmetry in this tract similar to that in the human, consistent with earlier reports of an asymmetric planum temporale in both species (see Chapter 4). One possibility is that the gradual amplification of the dorsal auditory pathway, compared to the conservation of the ventral pathway, is explained by the allometry of cortical expansion. In other words, there is disproportionate expansion of the posterior ventrolateral prefrontal regions and the inferior parietal lobe or posterior temporal areas (making up the dorsal pathway) compared to the more conservative growth of anterior ventrolateral prefrontal regions connected to the anterior temporal lobe. From this perspective, the arcuate fasciculus can be considered an extension of the ventral aspect of the superior longitudinal fasciculus, as there is no clear-cut separation between the two tracts. As I discussed in Chapter 3, the evidence for selective enlargement of the entire frontal lobe in primates and humans is controversial. However, the group led by Marcello Rosa (Chaplin et al. 2013) tackled this question by quantifying the differential volumetric expansion of specific cortical regions using surface models of the cortex of New World monkeys and macaques, and identified homologous regions as points of reference. They further compared these patterns with published data on the cortical expansion of the human brain. Their results show selective expansion across species of the temporoparietal junction, the ventrolateral prefrontal cortex and the dorsal cingulate cortex. Moreover, the above authors argue that these regions are among the latest to mature in the cerebral cortex, which agrees with Georg Striedter and Barbara Finlay's assertion that late developing brain components have undergone the greatest expansion during brain growth (Chapter 3). More recent reports have reached similar conclusions (Margulies et al. 2016).

Another issue is that although anatomical evidence has shown robust connectivity between the inferior parietal lobe and Broca's region or its surroundings, the function of this projection in verbal processing and working memory remains enigmatic, partly after Buchsbaum and D'Esposito's critique of these areas as representing the phonological storage of Baddeley's phonological loop (Buchsbaum and D'Esposito 2008). In the last chapter, I proposed that the inferior parietal lobe supports working memory in different ways, but at this point it may be of interest to discuss the role of these areas in the non-human primate in order to visualize an evolutionary transition to their role in human speech. In this line, Jon Kaas and collaborators have emphasized the general development of parietal-frontal connections in mammalian and primate evolution, very likely concomitant with increasing brain size, ant their role in the selection of complex ethologically relevant behavioral patterns among competing motor programs (Kaas and Stepniewska 2016). Specifically, the inferior parietal lobe represents a converging site of different sensory modalities and participates in the execution of several complex motor behaviors, including grasping behavior and object manipulation, but it also drives facial motor patterns and communicative gestures, which may have been of relevance for early human communication. Dietricht Stout and Tierry Chaminade associated these areas with tool use, particularly in the right hemisphere (see Chapter 4) (Stout and Chaminade 2012). On the other hand, Josef Rauschecker has offered an interpretation more related to vocal-auditory circuitry. He proposes that the dorsal pathway conveys a backward "efference copy" (that is, a template of ongoing motor activity) from prefrontal and motor cortices into the inferior parietal lobe to reach auditory areas in order to generate an "optimal state estimation" of vocalizations and refine the output. That is, the dorsal pathway not only works forwardly, but is also bidirectional, like most cortical pathways (Rauschecker 2012). This is complementary to Angela Friederici's proposal that the arcuate fasciculus in humans conveys a top-down influence on early speech processing areas, which originates in Broca's region (Chapter 2) (Skeide and Friederici 2016). Thus, the co-option of the inferior parietal areas to support an incipient phonological loop could have originated from a top-down control system to optimize vocalizations, which may have been increasingly relevant as our human ancestors learned to vocalize, as opposed to the stereotypical calls of other primates.

Function and Behavior

Concomitant with tract-tracing analyses, a series of comparative functional imaging studies have yielded important evidence of the activation patterns of the macaque brain in relation to heard or produced vocalizations. Most of these studies have shown striking resemblance between the areas involved in language processing in humans and those supporting conspecific vocalization processing in non-human primates. For example, some years ago Ricardo Gil-da-Costa and collaborators published a PET study with macaques in which they observed activations in the ventral premotor area, auditory area Tpt and the posterior parietal cortex after exposure to species-specific vocalizations (Gil-da-Costa et al. 2006). Notably, the activations were either bilateral or had no consistent left or right asymmetry (see Chapter 4). More recently, the group led by Christopher Petkov showed that learning a simple artificial grammar involves perisylvian regions highly similar to the language networks in both humans and monkeys (Wilson et al. 2013). They used a simple sequential pattern that had specific variants, and assessed the brain activity of consistent sequences, contrasted with violations of these sequences. The authors observed activations in monkeys associated with this contrast in brain areas comparable to those seen in relation to language tasks, particularly involving syntactic processing (perisylvian, frontal temporal and parietal areas). In a subsequent study, Petkov and colleagues examined the brain activity of monkeys during a non-word sequencing task and found activation in the ventrolateral prefrontal cortex similar to that in humans performing syntactic tasks (Wilson et al. 2015). They concluded that syntactic capacity evolved in humans from a domain general system involved in sequential processing. This evidence and that reviewed in the previous sections indicate that human speech networks can be traced to a basic circuitry involved in processing species-specific vocalizations in other primates. But the innovation in the human brain that allowed our ancestors to make the leap to speech and language is that we humans are endowed with a new functional circuit, the phonological loop, which produced a big bang in our communicative and cognitive capacities.

In addition to neuroanatomical evidence, there is functional and behavioral data supporting the emergence of the phonological loop in humans. Franz-Xaver Neubert and collaborators used a combined tractography and resting-state functional connectivity analysis of some 20 human brains and 20 macaque brains to unveil the relationships between the ventrolateral prefrontal cortex and other cortical areas (Neubert et al. 2014). They found an overall species similarity of network organization, although they described fundamental differences in the connectivity of posterior auditory areas (associated with the dorsal pathway) with prefrontal regions. In humans, there was a conspicuous interaction between posterior auditory areas and several areas in the ventrolateral prefrontal cortex, not only those traditionally involved in language, while in macaques these projections are minimal. Anterior auditory areas (the ventral pathway) evidenced similar frontal connectivity in the two species. These functional differences imply distinct behavioral capacities. Another recent report analyzed intracortical connectivity in macaques and humans, again concluding that the arcuate fasciculus enables the emergence of verbal working memory, a key capacity for language learning (Schomers et al. 2017).

Finally, Brian Scott, Mortimer Mishkin and Pingbo Yin provided behavioral support for a selective amplification of auditory working memory in our species. These authors presented an auditory delayed-match-to-sample task to macaques, and found that their working memory was seriously impaired when interfering stimuli were placed during the maintenance period, which indicates a strong instability of the short-term auditory memory trace (Scott et al. 2012). This contrasts with their performance in visual working memory, which is much more robust in these animals. In a more recent review, Scott and Mishkin presented evidence that short-term auditory memory in monkeys relies on passive sensory retention of the stimulus, while human working memory is based on phonological mechanisms activated by long-term memories (Scott and Mishkin 2016). Likewise, Amy Poremba and collaborators analyzed the response patterns of monkey neurons in the auditory cortex during a delayed match-to-sample task and observed little sustained activity during the retention interval. Most of the neurons changed activity either at the beginning or end of the interval (Bigelow et al. 2014). Furthermore, they also recorded similar short-term auditory memory cells in the anterior temporal lobe and found that this information is carried predominantly by the ventral auditory pathway.

A Key Innovation

In several articles we have proposed that the recruitment of the dorsal pathway to support both phonological articulation and working memory was a radical event in human evolution, astronomically propelling the vocal repertoire of our species (Aboitiz 1995, 2012; Aboitiz and García 1997, 2009; Aboitiz et al. 2006, 2010,). This process may have begun as early as Australopithecines, first with the transition from primitive fixed forms of vocal communication to more flexible, learned patterns that became strongly adaptive in social behavior. Learned vocal utterances may have been involved in mother-child relations, the establishment of individual alliances, facilitating group cohesion and other social functions, providing advantages for those groups with more elaborate vocal repertoires. Initially, vocal learning capacity was acquired by a series of peripheral adaptations including modifications of orofacial musculature and the oral cavity, and more refined neural control of the vocalization system based on the development of a descending cortical projection to brainstem nuclei controlling vocalizations (see Chapter 10). Suzana Herculano-Houzel has suggested that increasing cortical control of both the hand and orofacial motor systems is just a parallel consequence of increasing cortical size relative to subcortical systems, which concomitantly increased the density of descending cortical projections into the brainstem or spinal nuclei (see Chapter 3) (Herculano-Houzel et al. 2016). Thus, greater vocal plasticity could have been partly a consequence of increase in brain size, facilitating more complex vocal communication that in turn generated selective pressure for increasing brain size, and so on.

In addition, the eventual development of an incipient phonological loop that increased verbal working memory capacity was key to learning progressively complex vocal repertoires in the context of bidirectional, conversational interactions with others, establishing a rudimentary form of speech. Larger brain size in early humans provided the basic scaffolding for the development of a direct auditory-vocal interface in the cerebral cortex, producing the first impetus for the amplification of the dorsal auditory pathway. Specifically, the arcuate fasciculus and related tracts may have provided benefits for the development of an auditory-vocal sensorimotor interface, facilitating and amplifying learned oral communication. In addition, the indirect dorsal pathway, connecting the posterior temporal lobe with the inferior parietal lobe, and then with the ventrolateral prefrontal cortex (prospective Broca's area) and motor cortices, may have been recruited for vocal behavior by contributing to select appropriate motor commands to execute the learned utterances, and by providing a top-down control that served to refine output during learning. Recent evidence suggests that this articulatory system is to some extent bilateral, notwithstanding the possibility of hemispheric segregation of functions, as with speech perception (Cogan et al. 2014; see Chapter 4).

As vocalization behavior became crucial for social interactions in early humans, a selective tendency arose favoring genetic and epigenetic modifications that strengthened the functional connectivity of the incipient auditory-vocal circuits and their descending projection to vocal motor nuclei in the brainstem, inducing further lateralization of these functions. The developmental mechanisms involved in the refinement of these projections may not be particularly complex, including the modulation of connectivity by generating new connections or eliminating others, again by modifying the labels that axons use to establish synaptic contacts with their presumed targets. Additionally to this, and possibly more importantly, is the initial exuberance and the subsequent dramatic reduction of connectivity that occurs in early cortical development, where the majority of connections established in utero are lost by the first or second year of life (see Chapters 3 and 5). This process occurs in all cortical areas and subcortical connections, and has been associated to critical periods of language acquisition (see Chapters 1 and 10). Some of these early transient projections can be maintained by experimental means, avoiding their retraction and allowing them to form functional circuits in targets that otherwise would not receive such projections. As discussed in Chapter 3, the studies by Migranka Sur and Sarah Pallas have shown that experimental manipulations can stabilize the transient exuberant ectopic connections in the developing brain, generating novel functional circuits (Sur et al. 1990). This provides a mechanism by which neuronal connectivity can rapidly change in evolution, using minimal genetic modifications. In this line, many authors such as Dale Purves, have proposed that the process of axonal retraction during development can be viewed as a reservoir of connections that can be used for brain plasticity after early lesions. More relevant to this discussion, this transient axonal exuberance can also provide a supply for rapid evolutionary change in connectivity, where the balance of retraction of axons can be modulated to generate new circuits and eliminate old ones (Purves 1988).

In the next chapter, I will discuss other functions of the expanding parietal system and dorsal pathway that contributed to the development of human communication as a multimodal process involving not only vocalizations but also facial, hand and body gestures. This network provides a unifying context in which toolmaking, manual dexterity and gestuality contributed to shaping vocal language. As I have repeatedly said, human communication is an opportunistic phenomenon that takes advantage of any possible behavioral means to convey emotional or descriptive contents. It is in this context that human speech arose, where there was probably strong pressure for flexibility in communication, perhaps associated with more complex social life, including a rudimentary culture and the benefit of developing increasing emotional bonds among individuals.

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