

9 500 Million Years of Evolution

What does evolution tell us about the organization of the brain when we consider all vertebrates groups: mammals, birds, reptiles, amphibians, and fishes? To appreciate what evolution teaches us, we need to keep track of several moving pieces so that we can compare neuroanatomies across taxonomic groups—say, fishes and birds. Although this makes for potentially more challenging reading, we'll learn important lessons as we identify similar structures (such as the striatum) and connectional systems (such as the one involving the basal ganglia) across the vertebrates. Unsurprisingly, there are many important differences, too, even involving structures that neuroscientists like to refer as “conserved” (like the amygdala). Together, chapters 9 through 11 make up a unit that puts the different parts of the brain together into an interconnected whole, starting from an evolutionary perspective that helps discern a broader picture of brain organization.

When we think of a brain, most of us conjure images of the human cerebral cortex—the outer surface with its protrusions and grooves. But how does it vary across animals? The brain of a human weighs more than 1,000 grams, that of a rhesus monkey around 100 grams, and that of a marmoset less than 10 grams. Despite spanning two orders of magnitude in weight, they are quite similar. But how about the brain of a dolphin or an elephant (a large African elephant's brain weighs over 5,000 grams)? If the similarity of the first three species (they are all from the primate order) wasn't curious enough, the resemblance of all five will be a surprise if you haven't seen open specimens in a science fair or a zoo. The species discussed thus far are all mammals. But how about the brain of a salmon, a common frog, an alligator, or a crow?

We are now talking about vertebrates, which together cover a very broad range of body types and life styles, from aquatic to terrestrial to aerial. The evolutionary timescale here is truly mind-bending. The common ancestor to all vertebrates inhabited earth more than 500 million years ago (figure 9.1).

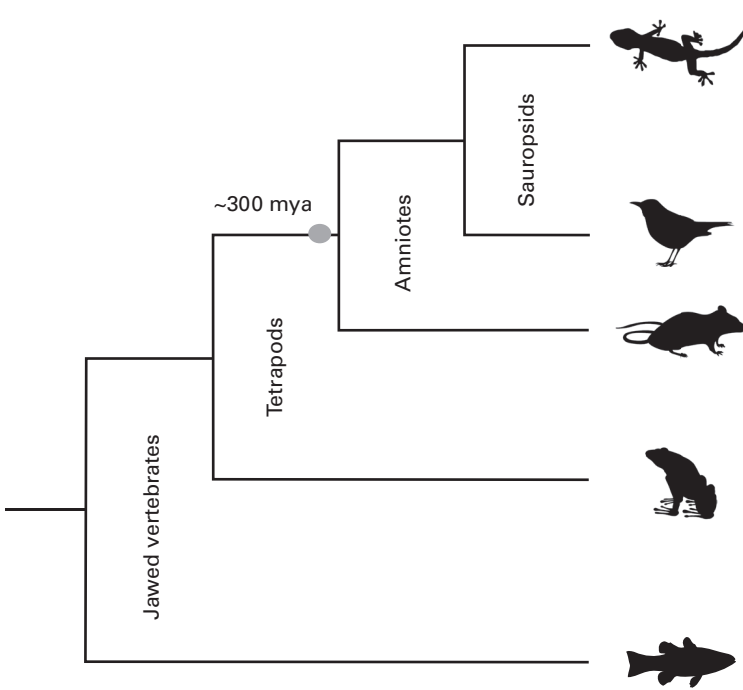


Figure 9.1

Evolutionary tree of living vertebrates. Note that the evolutionary trajectories of mammals and sauropsids (reptiles and birds) diverged over 300 million years ago (mya).

Amniotes are animals that have an amniotic sac that provides nutrition to the embryo; they include reptiles, birds, and mammals. Note that the evolutionary trajectory of mammals diverged from that of reptiles and birds (sauropsids) more than 300 million years ago. This underappreciated fact means that mammals are not descendants of reptiles and, as such, there's no reptilian brain inside the mammalian brain! At first glance, the brain of a fish looks rather different from that of a human (figure 9.2). But what do we find if we dissect it and carefully analyze it? Anatomists started doing just that at the end of the nineteenth century, a time when evolution was establishing itself as a principle at the core of biology.

Unfortunately, evolutionary thinking would be colored with the notion of “progress toward advanced forms” well into the second half of the twentieth century, and descriptions of evolution in terms of an ascending ladder with humans at the top were customary. T. H. Huxley, the academic who

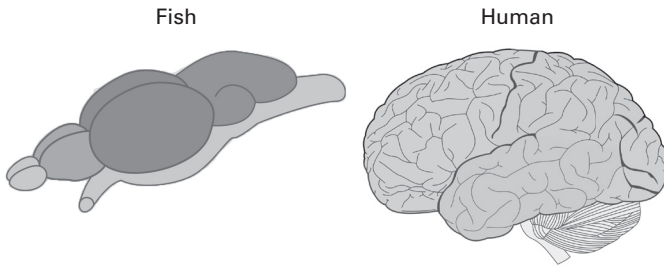


Figure 9.2

Considerable macroscopic differences exist between the fish and human brain.

fought many intellectual battles in defense of Darwin, may have been the first to describe brain evolution as proceeding linearly from fish to human (Striedter 2005). Indeed, Victorian England scientists were prompt to reuse the old Aristotelian concept of the *scala naturae*: elements can be ordered into a series of steps ascending from rocks all the way to the almighty.

Although this view is no longer held by scientists, it is at times hard to break from thinking of evolution in terms of “directed progress,” which places mammals, if not primates or the great apes, at some higher level and everyone else below. But properly understanding the evolutionary history of vertebrates is critical for thinking about the human brain, not least because of the popular view that a “reptilian brain” lies deep inside the primate brain. This notion, repeatedly incessantly by nonbiologist researchers and scholars (and still a few neuroscientists!), is glaringly erroneous and severely distorts what the study of the anatomy across vertebrates—comparative neuroanatomy—has taught us in the past decades.

The Basic Chassis

The evolutionary path of the vertebrates is a story of over half a billion years. The central nervous system of all vertebrates has three major components: the hindbrain, the midbrain, and the forebrain. Recall that the hindbrain includes the lower part of the brainstem; the midbrain includes the upmost part of the brainstem; and the forebrain includes subcortical structures like the thalamus and, in mammals, all of the cortex. Although brains differ considerably in overall shape across classes (mammals, reptiles, and so on), and indeed within a class, they all contain these macroscopic

components. In a nutshell, vertebrate brains have a three-part chassis. But as we will see, the commonalities extend well beyond this coarse level of organization (figure 9.3).

In mammals, the vertebrate forebrain includes the cortex dorsally and the subcortex ventrally. In other vertebrates, the forebrain also has dorsal and ventral parts, but because they are structurally different from that of mammals, anatomists call them “pallium” (meaning cloak in Latin) for the dorsal part and “subpallium” for the ventral part (every time you read these terms, go back to figure 9.3 to remind yourself). So, in this chapter we will use these two terms when talking about the forebrain. In mammals, the pallium contains all of the different types of cortex, from the hippocampus with a basic three-layer organization to the so-called isocortex with six layers. In nonmammals, the pallium isn’t organized in a layered fashion but instead has clusters of cells with different properties and arrangements.¹ By following brain development, neuroanatomists can identify subsectors of the pallium that are common to all vertebrates. They are unimaginatively labeled “dorsal,” “ventral,” “medial,” and “lateral.” Thus, when trying to understand how the brain of, say, a reptile and a mammal map to each other, it is important to keep track of these sectors, as we’ll discuss later.

The mammalian subpallium is comprised of cell masses at the base of the forebrain, including the striatum and parts of the amygdala, both of which are found in all vertebrates. But several other regions are found in common, too, including the hypothalamus and the thalamus. In the roof of the midbrain, we find the optic tectum (called superior colliculus in mammals), which we studied in chapter 3.

We see, therefore, correspondences at three levels at least: that of broad territories, such as the forebrain; that of their subdivisions, such as pallium versus subpallium; and that of areas like the amygdala. Working out such correspondences is one of the central goals of evolutionary neuroscience. The challenge is one of establishing mappings between subparts that can be quite distinct; the brain of a dog is not an enlarged version of the brain of a salmon. The problem is fiendishly complex, as it’s not clear what criteria should be applied. For example, the amygdala of a mammal is not just there for the picking in a bird or a reptile. So, is there one? And if so, how should it be defined? Should we recognize the amygdala in, say, a fish based on its position in the forebrain, cellular composition, gene expression pattern, anatomical pathways, and function? And how should these factors

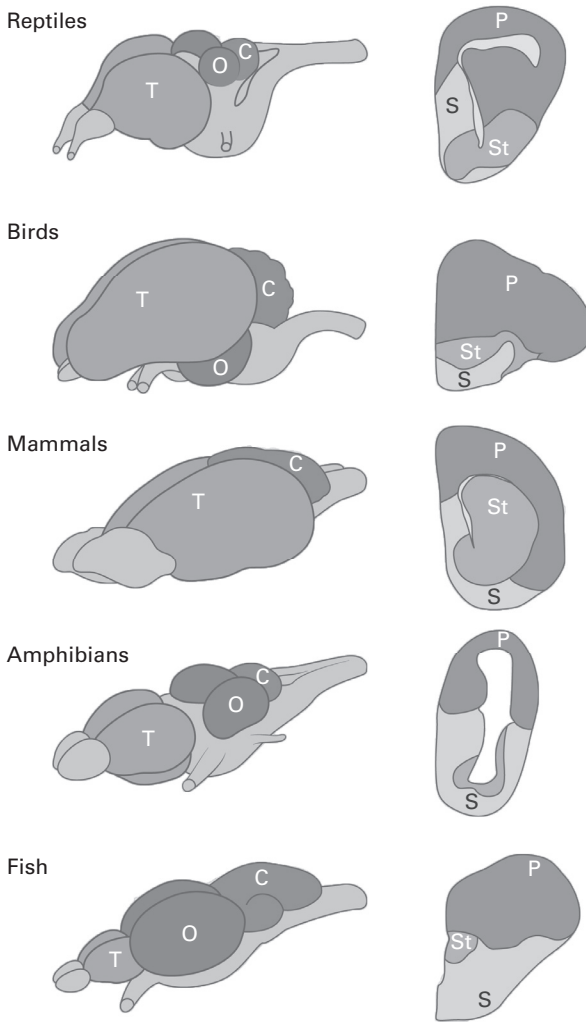


Figure 9.3

Vertebrate brains. All vertebrate brains contain corresponding sectors, including the telencephalon (T), the optic tectum (O), and the cerebellum (C). The optic tectum, which is called superior colliculus in mammals, is not visible from the outside in mammals and lies at the top of the midbrain, next to the periaqueductal gray (see figure 5.1). The leftmost part in all brains is the olfactory lobe. On the right, cuts through the brain are shown at the level of the telencephalon, revealing the pallium (P), subpallium (S), and striatum (St), which are present in all vertebrates.

be weighted? What's more, these variables are not static but change during embryological and developmental stages, from the earliest phases of the central nervous system to the adultlike, completed form. Not surprisingly, comparative neuroanatomy remains a contentious field of research, and arguments can get very heated.

No Rat Was Ever an Ancestor of Any Monkey

Not a single fossil brain has ever been recovered.² Fossilization is possible for hard body parts, such as bones and teeth, and the brain definitely isn't one of these. With roughly the consistency of jello, it needs to be encased in an armored cranium to be kept safe. Absent fossil brains, how can we use evolution to understand changes to the brain? Broadly, the strategy has two main components. First step: Select animals that are descendants of a common evolutionary lineage. If you are interested in the human brain, you could study the brain of *living* monkeys and rodents, or you could extend the timeline and consider all tetrapods (that is, amphibians, reptiles, birds, and mammals). Second step: Assume that the brain of *current*, living animals in question are sufficiently similar to the *ancestral* forms, so that some inferences about the ancestral forms can be drawn.

Take the first step. The extensive fossil record and careful examination of body parts provides a foundation for understanding the evolution of major lineages. Add to that genetic information gathered in the past decades and a good picture emerges. Now to the trickier second step. Here, we must recognize that animals chosen to represent ancestral groups are not the actual ancestors—they are descendants. They are suitable for phylogenetic comparisons because they possess many features that are *primitive*—that is, relatively unchanged from ancestral forms. The primitive feature of a group can often be *inferred* by comparing those of the living members of the group and looking for elements *common to all* (such as four major appendages or limbs in vertebrates). However, the greater the degree of diversity and specialization within a group (such as fins in fish and forelimbs in reptiles), the greater the need for studying more variants. In the case of living animals, the assumption is usually made that the more primitive characteristics a given species has, the more likely it is to resemble the ancestral form. The upshot is that step two will always involve a considerable, though acknowledged, uncertainty. As stated by a prominent researcher of brain evolution, this field of study is not for those averse to uncertainty! Nevertheless, an

evolutionary perspective is absolutely required for a deeper grasp of the structure of the human brain—and, in fact, all brains.

By now the title of this section should be clearer to you. A rat, a living species, cannot be an ancestor to a human, another living species (or vice versa). In fact, 75 million years separate humans and rodents. That is to say, their common ancestor diverged approximately 75 million years ago, a window of time during which the brains of both lineages have evolved.

Consider figure 9.3 once again. The telencephalon is identified in all major vertebrate taxonomic groups. The conclusion drawn is that this brain sector was present in the common ancestor to all vertebrates, which was trekking around 500 million years ago. In one sense, this is a gigantic inferential step. So why is it made? One can gain a handle on the question by considering alternative explanations. The central one is called “convergent evolution,” the process by which the same solution (here, creating a telencephalon) is independently reached and *not* inherited from a common ancestor. In the present case, perhaps the telencephalon was created from scratch for each of the major vertebrate groups. This alternative, though logically possible, is considerably less parsimonious than the one based on common ancestry. But perhaps it could happen, right? No, once we consider the large amount of data about the telencephalon, including what we know about embryology, genetics, cell types, anatomical connectivity, function, and more, the second solution starts looking absurd—the odds of such scenario would be vanishingly small.

Changing Views on Animal Cognition

For most of the twentieth century, scientists had vertebrates other than mammals in low esteem. These were creatures with a narrow stock of stereotypical behaviors, largely stimulus driven (give it an input, and a more or less fixed action ensues), and confined to the here and now.

In recent decades, our view of animals’ behavioral capabilities has witnessed a sea change thanks to striking discoveries from ethologists (who study behavior as it occurs in natural environments) and comparative psychologists (who study behavior across species). Field studies have revealed complex behaviors across phylogenetically distant taxonomic groups in vertebrates (and even invertebrates). New approaches and techniques in the laboratory have been employed to elucidate the mechanisms underlying behaviors in different species. The emerging picture is one in which

behavioral plasticity—the extent to which they can be modified—and flexibility are widespread in the animal kingdom.

Take, for example, spatial cognition: how animals navigate through the world and process positional information. All vertebrates have to move efficiently within their environment and thus need to learn and retrieve the location of different resources or threats. Different species of mammals, birds, reptiles, amphibians, and fishes exhibit parallel spatial abilities, such as those involved in homing behavior, spatial navigation, and spatial learning. Another research area of growing interest is social behavior. The ability to learn from others, discriminate among individuals, and categorize them as offspring, mates, rivals, allies, or neighbors is common to most vertebrate classes.

Perhaps nowhere are sophisticated behaviors more remarkable than in some birds (Emery and Clayton 2004). A person who has wronged a crow in the past is promptly recognized, scolded, and mobbed. Careful lab studies show that corvids (including crows) and parrots solve problems and have complex episodic memory capabilities. The former involves both tool use and manufacture, and the latter includes “mental travel” in time and space, such as retrieving information about the “what, where, and when” of experiences. Indeed, the intelligence of some birds rivals that of the great apes and dolphins, if not actually surpassing it.

Amphibians and reptiles show many traits common to those found in birds and mammals, including elaborate forms of communication, problem solving, parental care, play, and complex sociality.³ Fishes learn spatial tasks and engage in social interactions driven by repeat interactions with the same clients (such as other fish species that they clean). Looming evidence even indicates that fishes engage in problem solving and invent tools; for instance, wrasses use rocks as anvils to crack clam shells. And to think that not long ago, the use of tools was believed to be an exclusively human capability!

It is now abundantly clear that vertebrates other than “advanced” mammals are a far cry from being rudimentary automatons. Unraveling how these behavioral capabilities are enabled by the brain is the challenge now.

Evolving Our View of Brain Evolution

In 1896, the German anatomist Ludwig Edinger published *The Anatomy of the Central Nervous System of Man and Other Vertebrates*. The book, which

established Edinger's reputation as the founder of comparative neuroanatomy, described the evolution of the forebrain as a *sequence of additions*, each of which establishing new brain parts that introduced new functions.

Edinger viewed the forebrain as containing an "old encephalon" found in all vertebrates. On top of the old encephalon, there was the "new encephalon," a sector only more prominent in mammals. In one of the most memorable passages of his treatise, Edinger illustrates his concept by asking the reader to imagine precisely inserting a reptilian brain into that of a marsupial (a "simple" mammal). When he superimposed them, the difference between the two was his new encephalon. He then ventures that, in the brain of the cat, the old encephalon "persists unchanged underneath the very important" new encephalon (Edinger 1908, 446). Put differently, the part that was present before is left unaltered. Based on his coarse analysis of morphological features, Edinger's suggestion was reasonable. But to a substantial degree, his ideas were very much in line with the notion of brain evolution as progress toward the human brain—à la old Aristotle and the *scala naturae*. Given the comprehensive scope of Edinger's analysis across vertebrates, his views had a lasting impact and shaped the course of research for the subsequent decades.

More than a century later, knowledge about the brains of vertebrates has expanded by leaps and bounds. Yet, old thinking dies hard. Antiquated views of brain evolution continue to influence, if only implicitly, neuroscience. As an example, bear in mind that most frameworks of brain organization are heavily centered on the cortex. These descriptions view "newer" cortex as controlling non-cortical regions, which are assumed to be (relatively) unchanged throughout eons of evolution. Modern research on brain anatomy from a comparative viewpoint indicates, in contrast, that brain evolution is better understood in terms of the *reorganization of large-scale connectional systems*. We will develop this idea in the remainder of the chapter having in mind particular parts of the brain. To set the stage, figure 9.4 illustrates the overall organization of connectivity in vertebrates.

Decoupling Sensory Signals from Motor Responses

In chapter 3, we discussed a circuit involved in both defensive and appetitive behaviors centered on the optic tectum/superior colliculus of the mid-brain. This system is extremely important across vertebrates. In rodents,

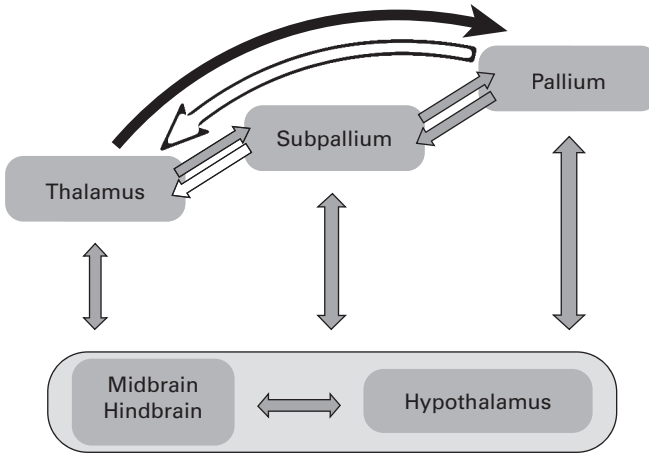


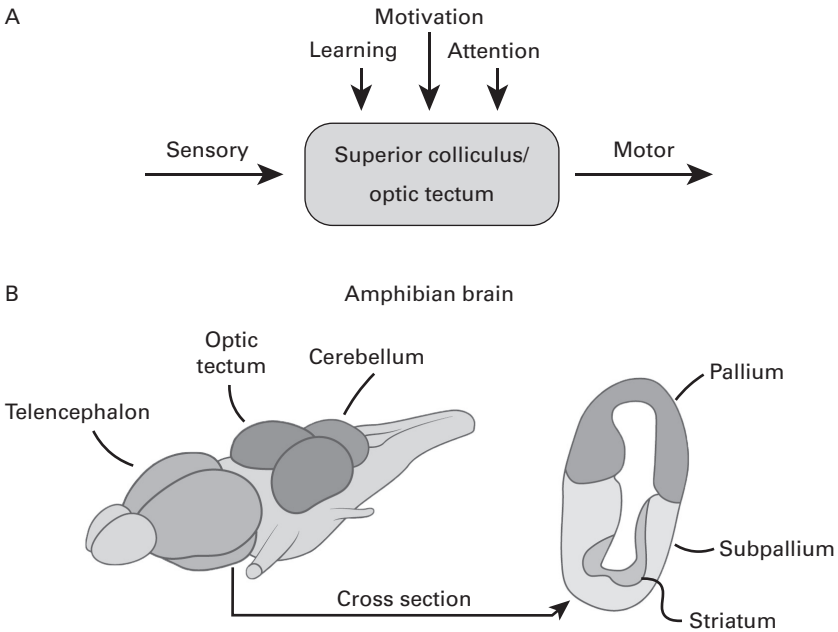
Figure 9.4

Overall anatomical connectivity plan of the vertebrate brain. Pathways shown by white arrows aren't present in fishes or amphibians. The black pathway from the thalamus to the pallium is very weak in fishes, more pronounced in amphibians, and considerably more substantial in reptiles, birds, and mammals.

it helps the animal decide if it should flee when movement is detected overhead or possibly approach and explore further if the movement is in the lower visual field. But the animal's behavior is flexible and not fixed by the input—the context in which it occurs, encompassing both external and internal worlds, is critical.

But how about toads and frogs (the Anuran family), with more limited behavioral repertoires?⁴ The optic tectum allows Anurans to tongue-snap when stimuli are in certain parts of their visual field, like an insect flying overhead, a reaction considered to be rather automatic. In these animals, the optic tectum is described as a sensorimotor interface because it receives retinal projections carrying visual signals and projects to brainstem and medullary motor circuits (see chapter 3), being thus well positioned to eject the tongue when attempting to capture prey.

Both motivational and attentional factors mold these behaviors (figure 9.5). During the mating season, prey-catching is minimal, and other behaviors are favored (not surprisingly, males approaching females). Regarding attention, when an animal is prepared to attack, the presence of prey causes animals to reorient themselves in a way that favors the strike; physiologically,

**Figure 9.5**

Decoupling inputs from outputs. (a) Input stimuli can trigger actions very directly through the superior colliculus/optic tectum. Nevertheless, the animal's motivational and attentional state, as well as past learning, contextualize the responses, bringing them relative flexibility. (b) Amphibian brain highlights some of the parts discussed in the text.

the related sensory cues evoke considerably stronger cell firing in the optic tectum. Prey-catching is also tuned by learning. In one study, toads that were hand-fed on mealworms later responded to the hand alone, demonstrating an association between food and the initially meaningless stimulus (the hand). Together, these examples show how an animal's responses, possibly to the same input, are shaped by diverse variables.

Back in chapter 3, we saw how the optic tectum's participation in multiple circuits allows it to generate context-dependent actions. For one, signals in the hypothalamus reflect several motivational variables, including sex-related ones that fluctuate seasonally. Hypothalamic outputs can influence the optic tectum through projections to its deep layers, which are the ones that have direct connections to motor areas.⁵ Other long-range circuits play a role in the case of learning. The circuit involving the medial pallium is necessary for both learning associations and for using the acquired information later.

Intriguingly, the medial pallium in mammals is the sector of the forebrain that forms into the hippocampus, a simple type of cortex with only three loosely organized cell layers. In chapter 11, we will discuss the hippocampus in more detail, including its roles in memory and spatial navigation.

No doubt, context sensitivity and behavioral flexibility are more limited in amphibians compared to reptiles, birds, and mammals, which produce a broader range of behaviors. So, let's consider the architecture of the optic tectum in other vertebrates, with the anatomical connective systems that interlink disparate brain parts.⁶ In reptiles, the basic connective architecture is noticeably enlarged. The thalamus is more richly connected with other parts of the forebrain and connects to additional sectors of the pallium. In birds and mammals, the connections of the optic tectum with the thalamus and pallium are, in turn, extensively developed compared to those in reptiles. Overall, the number of potential long-range circuits is quite large. In mammals, in particular, the overall connectivity of the superior colliculus is enormous.

Why such a degree of complexity involving long-range circuits that span the midbrain, thalamus, and pallium/cortex (see figure 9.4), even in “simple” animals (if one applies this label to most vertebrates including small mammals)? I suggest that it confers a high degree of behavioral flexibility allowing animals to cope with the multifaceted interactions they engage in involving predators, prey, potential mates, and so on. In species with more malleable behaviors, survival benefits from circuits that can form *combinatorially*—from region A to region B via multiple routes—as the number of conditions related to the internal and external worlds of the animal are exceedingly high. We will return to this idea in chapter 10.

Returning to a principle outlined in chapter 3, another way to think about this type of organization is that it *decouples* sensory and motor elements: Sensory signals do not necessarily trigger motor actions; when an action ensues, the sensorimotor transformation takes into account an array of influences, and sensation and action are part of a continuous loop that can flexibly update itself (that is, acting on the world changes the information that is sensed, leading to revised actions). Multiple variables are entertained that cancel, enhance, or otherwise refine the types of actions undertaken. As we'll see below, this decoupling property is not particular to the optic tectum but is an essential element of the vertebrate brain—from “simple” to “sophisticated” animals.

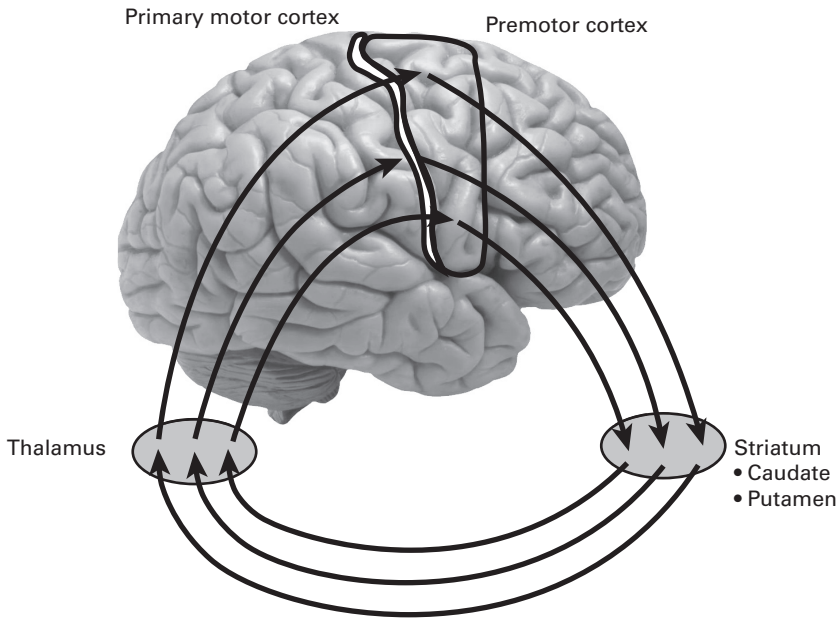
The Great Loops of the Basal Ganglia

The striatum and adjacent regions at the base of the brain are collectively referred to as the basal ganglia (chapter 2). Neurodegenerative diseases that affect this system include Parkinson's disease and Huntington's chorea. Parkinson's is related to cell loss in the dopaminergic regions of the midbrain that project to the striatum and compromises the ability to initiate voluntary movements. Huntington's impacts the major output projection neurons of the basal ganglia and is characterized by uncontrolled movements.

A major discovery in the 1970 and 1980s was that in mammals, the basal ganglia work in close coordination with the cortex through a loop-like circuit. For example, motor and somatosensory cortex project to the striatum, which connects back to the cortex through the thalamus (figure 9.6). Strikingly, the basal ganglia are involved not only in this movement-related circuit, but are part of multiple loops. Whereas sensorimotor cortical areas target dorsal parts of the striatum, other parts of the cortex project to more ventral ones, including the nucleus accumbens.⁷ Again, the circuit loops back to the cortex through the thalamus. Given the participation of the accumbens in motivational processes and its connections with regions such as the amygdala, this circuit is frequently labeled "limbic," but as we saw in chapter 6, this term is next to meaningless.

The pathways interlinking the cortex with the basal ganglia reveal that the two work in a coordinated fashion. Given the prominence of this arrangement in mammals, are there comparable features in other vertebrates? Not only are the subregions that make up the basal ganglia present across vertebrates, but loop-like circuits are found in the tetrapods (amphibians, reptiles, birds, and mammals). This is remarkable as it shows that an elaborate circuit was most likely a property of a common ancestor to all tetrapods. But there are notable differences, too. Amphibians and reptiles only have loops involving the *ventral* parts of the striatum. Birds have circuits coursing through both *ventral* and *dorsal* striatal territories, just like in mammals. Importantly, the connectivity in both birds and mammals is substantially more developed, at once more extensive and with stronger pathways.

What are some of the implications of the basal ganglia template across tetrapods? To answer this question, we need to consider the organization of the pallium in vertebrates and which of its sectors project to the ventral striatum. Ventral striatum circuits have a major influence on the energy and vigor of behavioral responses—the amount of *effort* that is exerted by

**Figure 9.6**

Cortical-subcortical loops. The cortex and subcortex work in close coordination through systems of pathways forming loops. The primary motor cortex is indicated by the thick white stripe.

an animal. Lesions that compromise the ventral striatum impair how much effort is exerted in the pursuit and avoidance of rewarding and punishing stimuli. In particular, the ventral striatum helps *invigorate* the animal to approach a reinforcing stimulus—that is, a stimulus that has the potential to lead to reward.⁸ In nature, prey, mates, and so on are never at arm's length. It's a basic fact of life that performing work and tolerating delays (waiting) are necessary for attaining positive outcomes.

It is only possible to obtain motivationally relevant items by engaging in behavior that brings them closer or makes their occurrence more likely. In fact, because animals are usually separated from reinforcing items by a long distance or by various obstacles, effective behaviors require work, such as foraging for food. Animals must thus allocate considerable resources toward “seeking behaviors,” which vary in terms of speed, persistence, and overall level of “output.” Although the exertion of effort can be relatively brief at times (for example, a predator pouncing on a prey), under

many circumstances it must be sustained over long periods of time. Thus, effort-related capabilities are highly adaptive—they are advantageous for survival—because in nature survival depends on how well animals overcome work- and time-related response costs.

Let's return to basal ganglia loops. Ventral basal ganglia loops connect the pallium with the ventral striatum, which, as discussed, is a major *motivational hub* that helps regulate the amount of vigor and energy expended. We find an interesting property across tetrapods. In amphibians, two major sectors of the pallium have loops with the ventral basal ganglia. In reptiles and birds, this number grows to three, and in mammals four. It stands to reason that the number of pallial sectors that engage in loops with the basal ganglia—as few as two and as many as four—determine the types of signal from the pallium that have a more direct impact on actions. The larger the number of sectors, the more diverse the signals from the pallium that impinge on the striatum, allowing a broader range of variables and their combinations to influence behaviors.

But the possibilities in birds and mammals are enlarged further (figure 9.7). They have an expanded set of basal ganglia loops, as circuits course through the dorsal striatum in addition to the ventral striatum. And, again, these loops involve very diverse parts of the pallium; in both birds and mammals, all four pallial sectors project to the dorsal striatum. The dorsal parts of the basal ganglia process sensory and motor signals, which are distinctly important in the control of finer movements—like reaching out to grasp a ripe fruit. Furthermore, as behaviors develop temporally as one action merges into another, basal ganglia loops allow the continuous adjustment of movement parameters and goals (“move here; now veer to the left some”). That is to say, the basal ganglia support the generation of actions in a dynamic fashion.⁹ As motor behaviors unfold, cortical-basal ganglia loops continuously update motor programs so as to reflect the most recent data.

More so than in other vertebrates, in birds and mammals, processing in the pallium spans a wide range of abstractness and, in many instances, is not closely tied to sensory and motor variables. Thus, loops involving more regions of the pallium with “abstract” properties support complex spatiotemporal behaviors, including exploiting available goods, exploring the environment, and avoiding threats. By bringing the pallium to bear on actions, they provide a scaffold for more flexible and sophisticated behaviors. In a very real sense, the extensive projections from all major sectors of

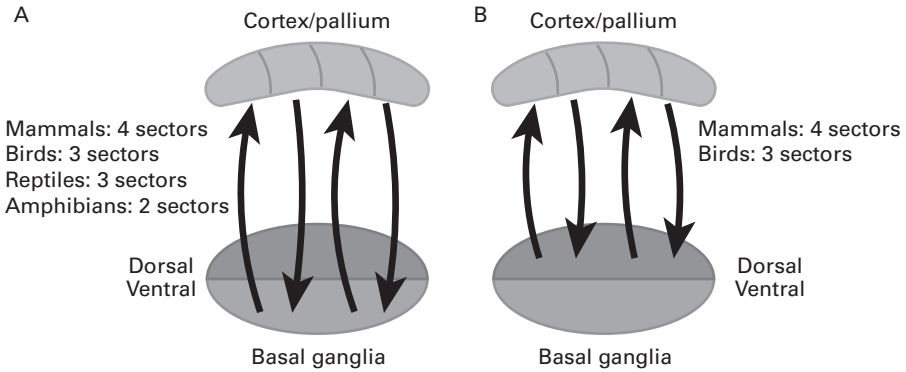


Figure 9.7

Cortex-subcortex loops via the basal ganglia across vertebrates. (a) Ventral loops are present in all vertebrates, except fish, but vary in the number of sectors of the cortex/pallium they involve. (b) Dorsal loops are only observed in mammals and birds.

the pallium to the striatum in birds and mammals bring the multitude of functions of the pallium/cortex into the circuits of the striatum.¹⁰

Thus far, we have not discussed the most numerous and diverse vertebrates on the planet. How are the basal ganglia organized in fishes? As in other vertebrates, the pallium projects to the striatum. But here a rather different type of arrangement is found: The striatum projects directly to the pallium, which is a feature not seen in other vertebrates where the circuit is always indirect and courses back to the pallium by way of the thalamus. What is especially interesting is that the striatum of fishes is a convergence area where pathways from many parts of the brain impinge, including the hypothalamus, midbrain, and hindbrain, in addition to thalamus and pallium. In all likelihood, pallium-striatum circuits communicate and exchange a broad spectrum of signals. As fish don't make the most conducive lab animals, little is known about their neurophysiology. But it would be revealing to investigate diverse species because their telencephalon is quite variable. In some cases, it is rather pronounced, and as mentioned, some fish display sophisticated behaviors, even making simple tools.

Large-Scale Circuits of the Amygdala

It is common for neuroscientists to think of the amygdala as triggering immediate, obligatory emotional responses. We discussed in chapter 5

the two major amygdala sectors: basolateral and central. In mammals, the pallium includes all forms of cortex. Thus, it will be surprising that the basolateral amygdala is part of the pallium: Embryologically, the tissue that eventually forms the pallium produces this sector, too. In contrast, the central amygdala is part of the subpallium. So, these two parts of the amygdala, which interact so strongly, are actually structurally rather distinct creatures, more like distant cousins than siblings. The different origins of the two amygdala components also helps explain their different connectivity profiles, as further discussed below.

Given the reputation of the amygdala as a “primitive” structure, one might imagine that identifying it across vertebrates would be straightforward.¹¹ This is far from true. For one, the amygdala straddles the pallium and subpallium, and their boundary is very challenging to track with confidence. Additionally, the deep evolutionary split between mammals and sauropsids (reptiles and birds), separated as they are by about 300 million years, has thus far prevented comparative neuroanatomists from conclusively determining the correspondence between some regions and even larger parts of their brains. In sauropsids, for example, a rather prominent part of the forebrain (known by the unhelpful name of “dorsal ventricular ridge”) is not easily mapped to mammalian features. As it turns out, the basolateral amygdala is at the center of current scientific debates (and battles!) on how to understand the brain of mammals and sauropsids.

In chapter 5, we considered how, in mammals, the anatomical pathways of the basolateral and central amygdala are strikingly different. The basolateral amygdala is interlinked bidirectionally with most of the cortex, from occipital to frontal. In particular, the basolateral amygdala is a convergence site for all sorts of sensory information, thus in a privileged position to simultaneously take into account the environment and the body, helping the animal segregate the significant from the mundane. The central amygdala, instead, has extensive interconnections with the hypothalamus and brainstem nuclei (including sites in the midbrain, pons, and medulla) involved in behavioral, autonomic, and neuroendocrine responses (there are some pathways between the central amygdala and cortex, too). If we consider that the basolateral amygdala is pallial in origin but the central amygdala originates in the subpallium, it is perhaps a little less mysterious how these two regions of the brain, close enough to be joined together under the same umbrella—“the amygdala”—associate anatomically with such different partners.

In birds, a pallial amygdala-like region has been identified, too, and exhibits extensive interconnectivity with other regions of the telencephalon in a way that strongly resembles the mammalian counterpart. For example, it receives multiple sensory inputs from other pallial areas as well as inputs from “association” areas in the pallium that are not so directly linked to sensory processing. (Neuroscientists call areas of the pallium/cortex “associational” because they combine multiple perceptual attributes.) Because these connections are bidirectional, the pallial amygdala can influence these regions, too. In reptiles, as in birds, a pallial amygdala-like region also has a broad range of telencephalic pathways, likewise interconnecting it with sensory and association areas of the pallium. The pallial amygdala is actually a very prominent association center of the reptilian brain—a region that influences and is influenced by multiple areas of the pallium.

Overall, in amniotes (mammals, birds, and reptiles), the pallial amygdala is a major hub region of the telencephalon. But the interconnectivity doesn't stop there. This sector also projects to the subpallium, including the central amygdala and the hypothalamus. Of particular interest here are the connections of the pallial amygdala with both the dorsal and ventral basal ganglia. In the previous section, we discussed the arrangement of dorsal and ventral basal ganglia loops and their roles in shaping vertebrate behaviors. The pathways from the pallial amygdala to the striatum intertwine the connectivity of the former with the loops of the latter, creating a giant network of connectivity (figure 9.8).¹² Taken together, the pallial amygdala of birds and mammals, in particular, is in a focal position to integrate disparate information and to influence both emotional and motivated behaviors, in addition to cognitive functions. Bearing in mind that the connectivity is more restricted (both weaker and connected to fewer places) in reptiles, the pallial amygdala likely plays a comparable role in these animals, too.

How about the case of fishes and amphibians? A pallial amygdala-like area has been identified in amphibians. In fishes, stronger evidence of a related area has been obtained for teleost fishes. (Teleost fishes comprise up to 96 percent of existing fish species and have modifications of the musculature that allows them to protrude the jaw outward from the mouth; this is behaviorally advantageous because it allows them to grab prey and draw them into the mouth.) In teleost fishes and amphibians, the pathways of the pallial amygdala are reminiscent of the amniote organization, including connectivity with other pallial regions, although these connections are scarcer.

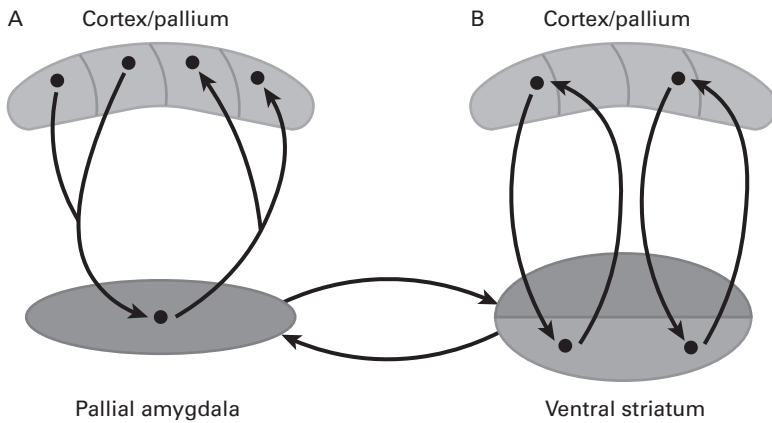


Figure 9.8

Interlinking of circuits. The cortical-subcortical circuits of the pallial amygdala are interconnected with ventral basal ganglia loops.

We started this section saying that neuroscientists like to describe the amygdala as producing basic, obligatory emotional responses, such as generating an alarm call when a predator is spotted by a prey. True, this is an important function of the amygdala—or to be precise, it is an important function of one of the two amygdalas, the central one, which is part of the subpallium. But this grossly oversimplifies—in fact, mischaracterizes—the complexity and scope of the interactions that the pallial amygdala of all vertebrates engages in. In the end, the contributions of the amygdala involve all major dimensions—sensory, motor, emotional, motivational, and cognitive.

Conservation of Structure and Function

The amygdala of primates can be identified in other mammals—that much is easy. Researchers thus invoke the idea of evolutionary *conservation* to stress that the amygdala is present among evolutionary lines stretching tens of millions of years. For example, primates and rodents diverged more than 75 million years ago (before the extinction of the non-avian dinosaurs)—their common ancestor roamed the planet around that time.

On the surface, conservation appears to be a straightforward concept: Identify a feature (cortex, region, or molecule) in an animal line which is

also present in a distantly related line and, voilà, it is established. Yet the situation is far from simple. As can be gathered from the previous section, a brain region doesn't come in exact copies to be found in an amphibian and a mammal, for instance. Is the amygdala in an amphibian conserved if it has only a central and not a basolateral part as in a mammal? How about if both sectors are found but their anatomical connectivity is substantially different? Or they have substantially different cell types? In other words, what should count to establish conservation?

We need here the concept of *homology*. In evolutionary biology, two structures are homologous if they were present in a common ancestor. Thus, the cortex is thought to be homologous across mammals because it is present in the ancestor of all mammals. But homology doesn't depend on *function* at all; the common origin is the one that matters. For example, fins and hands are homologous even though they serve entirely different purposes. Still, conclusive genetic evidence shows that they are derived from genetic regulatory systems present in the common ancestor to the vertebrates.

But if homology is independent of function, what is exactly conserved? Only genetic programs? Indeed, the question is baffling enough that evolutionary biologists have been pondering it for a long time.¹³ At its core, the question confronts the seemingly impossible problem of elucidating what is *new* in biology. If animal species derive from common ancestors by a process of descent with modification—the central tenet of Darwinian thinking—at what point is a feature (also called a character) of the phenotype truly novel? Needless to say, I will not be foolish enough to attempt to answer this question, but I suspect that, like in many other cases, part of the problem lies in phrasing it as a dichotomy in the first place—novel or not?

Armed with the above ideas, let's revisit the evolution of the basal ganglia. The basal ganglia are deeply conserved because essential components are identified across tetrapods. Does this mean that the basal ganglia of a marmoset monkey are roughly the same as that of a toad? We know this can't be true because the amphibian basal ganglia only have loops via the ventral striatum, not the dorsal; the mammalian basal ganglia have loops involving more territories of the pallium than the amphibian one. And, of course, such changes will have functional ramifications. Perhaps signals will be combined in mammals in ways that are not possible in amphibians or, alternatively, be more segregated from one another. That is to say, the new components present in mammals will alter the circuit's computational

capabilities. Thus, brain evolution involves changes to pathways that have the potential to bring about significant functional modifications.

This view is quite different, of course, from seeing evolution as adding new brain parts atop older ones. Let's develop the idea a bit further by thinking about the appearance of the cortex in mammals. As stated, according to older views, "newer" cortex controls subcortical regions, which are assumed as a rule to be relatively unchanged throughout evolution. The enlargement of the forebrain with the addition of multilayered cortex is seen through the lens of hierarchical organization. In contrast, if both the cortex and subcortex change, as proposed here, they may change in a coordinated fashion—in the resulting circuitry, the cortex and subcortex are mutually *embedded*.

The amygdala provides a good example of this type of joint embedding. One study found that parts of the basolateral amygdala are considerably more "developed" in monkeys than in rats (Chareyron et al. 2011). The authors suggested that the differences in the relative subregion size and neuron numbers between the two species are related to the connectivity of this sector. In this manner, the "enhanced" properties of the monkey basolateral amygdala parallel the greater development of the cortical areas with which the basolateral sector is interlinked. Such correlated evolution likely supports higher convergence and integration of information in the basolateral amygdala. Irrespective of the mechanisms behind these evolutionary changes, differences between species are considerable. Studies comparing humans, apes (such as chimpanzees and gorillas), and monkeys discovered that the number of neurons in parts of the basolateral amygdala are 50 greater in humans.¹⁴ Such substantial differences are rarely seen in comparative analyses of human brain evolution. For example, the volume of the human cortex is 24 percent larger than expected for a primate of our brain size, whereas the human frontal lobe, frequently assumed to be enlarged, is approximately the size expected for an ape of human brain size.

Understanding evolutionary conservation is far from a technical issue or armchair musing. The National Institutes of Health in the United States and funding agencies around the world invest billions of dollars in brain research in the hopes of curing, or at least ameliorating, conditions that stem from brain malfunction. Simply put, most of the research cannot be done ethically in humans, and animal models of diseases are, at present, the only way forward. The assumption, of course, is that by studying the mouse or rat brain, for example, we will gain important knowledge that is transferable to

deciphering the human system. But essential components of brain function have to be conserved for this approach to be sound. Our brief incursion into the evolution of the vertebrate brain in this chapter shows that, while studying animal models is certainly informative, we need to proceed with caution. Only by studying a broader range of animals will it be possible to clarify how varying neural architectures support behaviors. In this sense, the heavy emphasis on studying mice and rats is very shortsighted.

To conclude: The human brain, or even more generally the mammalian brain, is not a sophisticated cortical machine built atop old, inflexible brain territories that only support simple, stereotypical behaviors. The anatomical architecture of vertebrates supports signal communication across all major brain territories, including between the pallium and subpallium in the forebrain and between the forebrain, midbrain, and hindbrain. At the same time, pathways vary considerably across taxonomic groups. Whereas long-distance circuits are present in fishes and amphibians, they truly flourish in the amniotes, especially birds and mammals.

This is a section of [doi:10.7551/mitpress/14636.001.0001](https://doi.org/10.7551/mitpress/14636.001.0001)

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DOI: [10.7551/mitpress/14636.001.0001](https://doi.org/10.7551/mitpress/14636.001.0001)

ISBN (electronic): 9780262372107

Publisher: The MIT Press

Published: 2022

The open access edition of this book was made possible by generous funding and support from MIT Press Direct to Open



The MIT Press

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The MIT Press would like to thank the anonymous peer reviewers who provided comments on drafts of this book. The generous work of academic experts is essential for establishing the authority and quality of our publications. We acknowledge with gratitude the contributions of these otherwise uncredited readers.

This book was set in Stone Serif and Stone Sans by Westchester Publishing Services.

Library of Congress Cataloging-in-Publication Data

Names: Pessoa, Luiz, author.

Title: The entangled brain : how perception, cognition, and emotion are woven together / Luiz Pessoa.

Description: Cambridge, Massachusetts : The MIT Press, [2022] | Includes bibliographical references and index.

Identifiers: LCCN 2021061878 (print) | LCCN 2021061879 (ebook) | ISBN 9780262544603 (paperback) | ISBN 9780262372107 (pdf) | ISBN 9780262372114 (epub)

Subjects: LCSH: Perception. | Emotions and cognition. | Brain. | Neuropsychology.

Classification: LCC BF311 .P3767 2022 (print) | LCC BF311 (ebook) |

DDC 153—dc23/eng/20220411

LC record available at <https://lcn.loc.gov/2021061878>

LC ebook record available at <https://lcn.loc.gov/2021061879>