BRAIN SCIENCE PODCAST

With Ginger Campbell, MD

Episode #32

A Brief Introduction to Brain Anatomy Based on the Book, *Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain*, by David Bainbridge

Aired March 7, 2008

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INTRODUCTION

This is the *Brain Science Podcast* – the podcast for everyone who has a brain – and I'm your host, Dr. Ginger Campbell. On the *Brain Science Podcast* we explore how recent discoveries in neuroscience are unraveling the mysteries of how our brains make us who we are. For more information including Show Notes, links to previous episodes, and information about how to subscribe please go to the website brainsciencepodcast.com. We also have a Discussion Forum at brainscienceforum.com, and you can send me email at docartemis@gmail.com.

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Welcome back to the *Brain Science Podcast*. This is Episode 32. Today I am going to be talking about the book, *Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain*, by David Bainbridge.

But first I need to make one brief announcement. I started a new website called sciencepodcasters.org which can be found at sciencepodcasters.org. This site gives science podcasters a place where they can share announcements, show notes, and links to their podcasts.

My goal is to create a place where science podcasters can help each other promote their podcasts. So, if you have a favorite science podcast I hope you'll let me know what it is. If it's somebody you know, tell them to write to me. Otherwise I would love to hear your suggestions. You can post these on the Forum or send me email.

So, let's get into today's episode.

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DISCUSSION

When I gave my summary for the first year of the podcast I said that I was avoiding the subject of anatomy. I thought that the subject did not lend itself very well to the audio format. However, I found this wonderful book, *Beyond the Zonules of Zinn*, and I realized that with the help of this book I thought I could give you something that would make sense in podcast form.

Also, I am happy to announce that the author, David Bainbridge—who is a clinical veterinary anatomist at the University of Cambridge in the U.K.—has given me permission to use the images from his book. I'm going to post those up in the Show Notes so that hopefully by the time you get ready to listen to this—maybe not the first time, but if you go back and listen to it a second time—maybe you'll be able to find these images on the website. I'm going to make an effort to make it so that you don't need the images to understand what I'm talking about, but I'm going to give you references where I know that the images will help make it make more sense.

Beyond the Zonules of Zinn was just published in January of 2008. The unusual title that it has refers to the Zonules of Zinn, which are the tiny fibers that connect the lens of the eye to the muscle ring, or iris. This is just one of the many weirdly named parts of the brain. One of the points that Bainbridge makes is that the gross anatomy of the brain was mapped out before we knew much about what the structures actually did. And in his book he gives a lot of great stories behind the names.

Now, I'm not going to be giving these stories. You're going to have to read the book for that. This is a lot of material to squash into a podcast. But, his deeper purpose is to share how understanding the structure of the brain helps us to understand how it works. And this is also what we want to do on the *Brain Science Podcast*.

What we're going to do is, we're going to start at the spinal cord [Figure 6][1] and work our way up. Now, before we get more into the brain itself, there is one other thing that he says early in the book that I think is worth noting; and that is, he makes an observation about one of the key differences between brains and computers. Those of you who are regular listeners know that this is one of my sort of favorite themes.

He points out something that I hadn't really thought much about, and that is the fact that computers are very vulnerable to damage. You know, if you have one bad chip in your computer the whole thing quits working. In contrast, the brain is designed to withstand damage. You hit your head, you drink alcohol, you get infections, and then there's the degeneration of aging. On page 37 he says, "In short, the brain is meant to be in a constant state of coping with failure. Although it may seem sad, this is one of its greatest achievements."

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[1] Figures have been added to the end of this Transcript. They come from *Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain* (2008) by David Bainbridge, with the author's permission. The numbers correspond to those in his book.

One of the best chapters in this book is the chapter about brain development—which is called 'A River Runs Through It'—because understanding how the brain develops in the embryo helps us to understand why it looks the way it does. I'm going to give you a very brief overview of this. One thing I'm planning to leave out is most of the discussion of the cerebrospinal fluid and the ventricles, which are the spaces in the brain where the fluid flows.

At about 15 days after fertilization the embryo is a three-layered disk. [see Fig 1][2] We share this structure with most other animals. The layers are called the endoderm, mesoderm, and ectoderm. The brain, and the spinal cord, and the skin come from the top layer—the ectoderm. There is also a cord running through the mesoderm which is called the notochord. This is important because it divides our body into symmetrical halves. It ends up forming the jelly-like disks that we have between our vertebrae.

This flat disk starts curling toward the endoderm—I'll try to put a figure of this up in the Show Notes [see Figure 1]—and as it is curling toward the endoderm there is a groove forming down the top in the ectoderm. So, the belly closes up in the front while the groove in the back eventually closes over to form the neural tube. So, basically the curling up of the endoderm is going to make the GI tract, and this tube on the back, which is the neural tube, is what becomes the brain and the spinal cord.

The brain is basically an outgrowth of the spinal cord, and it starts out as a series of bulges in the neural tube. These bulges eventually will form all the main structures of the brain, but understanding how it forms makes the structures make sense. And it also helps us to understand how much we have in common with other animals—especially mammals.

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The simplest way of looking at the brain is to consider the three main bulges [Figure 2], starting with the one nearest the spinal cord, which is called the hindbrain. This contains the pons and the medulla. Then there is the midbrain, and finally the forebrain. The hind and midbrain make up what is known as the brainstem. The forebrain will include the cerebral hemispheres.

Now, one of the things that happens during brain development is that some of the regions are going to grow faster than others, and this leads to a 90 degree kink in the midbrain. This is so that everything can kind of fit inside the head—this is, again, shown in the diagram I'll put in the Notes—and the parts of the hindbrain also have to kink up to fit. The endbrain grows out laterally from the forebrain and wraps itself around the rest of the brain.

The bulge that later becomes the cerebellum arises a little bit later, but because it grows so rapidly it ends up being much more densely packed with neurons. In the mature human brain the endbrain, which grew out of the forebrain and the cerebellum, are the dominant structures. The basic developmental steps are the same in all vertebrates, but while in most mammals most of the kinks straighten out, in our brain these kinks remain. And this helps everything fit in our head, but it also seems to be related to our erect posture.

I have just barely touched on his excellent description of this. And while he has given me permission to use the diagrams, I really want to refer you back to his book if you want to know the details of this. But this should at least give us a starting point so that we can take sort of a tail-to-head look at the basic anatomy of our nervous system.

[music]

OK, so now I'm going to talk a little bit about the spinal cord. Our spinal cord does less than it does in most other animals, but it has about the same basic structure. One thing that's interesting is that in the spinal cord the gray matter, which is the neurons, is on the inside, and the white matter, or the axons, are on the outside. But if you look at a cross-section of the spinal cord [Figure 6][3] what you'll see is this gray butterfly-shaped thing which is where the neurons are. In the middle of that there will be a canal, which is the spinal canal where the cerebrospinal fluid goes.

There will be two horns on the front which contain motor roots and two horns on the back which contain sensory roots. And at every level spinal nerves are coming off that contain both sensory and motor nerves to a certain body segment. He points out that this arrangement of sensory in the back and motor in the front is a theme that continues through most of the brain.

Now, the spinal cord is not just a passive conduit for information going up to and from the brain. There are spinal cord reflexes that are hard-wired. One, for example, is the crossed extensor reflex. This is what happens when you step on something painful. You automatically pull up your foot and the other leg automatically reflexively straightens so that you don't fall over. These kinds of reflexes always involve exciting certain muscle groups and relaxing the opposing muscle groups. These reflexes are also more important in other animals than they are in humans.

OK, so that's the spinal cord. Now we're getting to the brain itself. His approach is to first talk about the sensory organ that is coming in to a particular brain area—to talk about it and to talk about that area of the brain. For the very lowest part of the brain, or the hindbrain, an important sensory input at this level is what comes from the ear. So, I'm going to start out by talking a little bit about the origins of the ear.

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This is interesting because in considering the ear Bainbridge introduces us to some of what is known about vertebrate brain evolution. And he remarks that this is an area where there is going to be an unavoidable uncertainty, since brains don't leave fossils. However, what's different about the ear is that since it contains bones it is possible to trace the fossil evidence for its development. Remember that the ear actually has two functions. And I'm not talking about the part that sticks out from your head, I'm talking about the organs inside—the inner ear, so to speak.

Besides hearing, we have functions related to the position of the head. We commonly call this balance. Most vertebrates have three semicircular canals that are arranged at right angles. And he talks a little bit in the book about how these are arranged, and how they work, and how they've changed in evolutionary history. Part of detecting head motion involves detecting acceleration. There are little stones in the fluid of the canals, and then the hair-like neurons are stimulated when the stones move around.

The area where the hair-like sensing neurons are is called the macula. And at some point in evolution this area also began to detect pressure waves of low-frequency sound. This is probably the method that fish use for hearing. However, sound waves don't transfer very well from air into the liquid-filled inner ear, so this means it's probable that the first land animals were deaf.

There is evidence that the ability to hear seems to have evolved at least five times: in frogs; turtles; lizards; mammals; dinosaurs; and birds, which came from dinosaurs. The basic solution is to develop an acoustic coupling that converts the sound waves in air to the sound waves in the inner ear fluid. The middle ear—which is the one that causes so much trouble in small children with ear infections—is thought to be a remnant of the fish's first gill; which might explain why it connects to the throat via the eustachian tube.

But the middle ear is not the key structure. What matters is the stapes, which is a stirrup-shaped bone that conducts vibrations from the eardrum through the fluid in the inner ear, or the labyrinths of the cochlea. Now, he goes into a lot of detail about how hearing evolved, including the cochlea. The cochlea is important to hearing music, and it also is very important to other unique aspects of mammalian hearing.

But why should I even talk about hearing? Well, he thinks that the hearing drove the evolution of the lowest part of the brain—the hindbrain, which is the part closest to the spinal cord—and that it is important to understanding the structure of the brain. Where does the information from the ear go? He gives us a sort of simple way of looking at it. He is going to take the three special senses and talk about how they send their inputs into the three bulges. So, we have hearing going to the hindbrain, vision going to the midbrain, and smell going to the forebrain. Now, this is really an oversimplification, but it gives you a useful tool for getting a grasp of the basic structure of the brain.

As the spinal cord is merging into the hindbrain the basic structure remains about the same. The bottom part of the hindbrain is called the medulla [Fig 11][4], and at this level many of the so-called cranial nerves start to come in: cranial nerves VII through XII. This includes the nerves that go to and from the tongue and the face; cranial nerve VIII, the vestibulocochlear nerve, which includes hearing and balance; and cranial nerve X, which is the vagus nerve, which is important because it carries signals to and from most of the internal organs including the heart.

As we start to move up the hindbrain the gray matter becomes more scattered into so-called nuclei. The cochlear and vestibular nuclei are actually large enough to be seen as swellings. They connect up to another set of nuclei called the olives,

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which in turn connect to many other parts of the brain. The vestibular nuclei are wired to all the major motor areas of the brain and they have direct connections back to the limb muscles via the spinal cord. And this is because they are so important for balance.

Processing sound occurs in a string of nuclei that extend up the brain stem, and this includes encoding information into spatial and tonal maps. There are also taste nuclei in the hindbrain. Much of the structure of the hindbrain is still not very well understood, but we do know that there is a nucleus for inducing vomiting and another one that detects acidity and makes you breathe faster in order to get rid of the excess acid.

Much of the hindbrain is white matter, which is made up of the large tracts that are carrying information to and from the higher parts of the brain. In the front we have the pyramids, which contain the major motor tracts. These are really big in people, which is thought to be related to the dexterity of humans. And in the back there are the posterior columns which carry sensory information.

One sort of strange thing that happens at the level of the medulla is that the fibers from these tracts start to cross over, or switch sides. This is called the decussation. Thus at the level of the cerebral hemispheres the left hemisphere senses and moves the right side of the body, and the right senses and moves the left. This crossing over at the decussation I think is mainly motor, because most of the sensory fibers actually cross over down in the spinal cord shortly after they enter the spinal cord.[5] That's the reason why you can have an injury that causes a

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[5] According to neurologist Dr. Gregory Dardas "This is true when considering sensory fibers carrying pain and temperature information, and it usually takes one or two levels to cross over. Position and vibratory information ascend ipsilaterally up to the level of the medulla. There they too decussate after synapsing at the nucleus gracilis (leg) and nucleus cuneatus (arm).

This point is of value in terms of localization of spinal cord injuries, particularly incomplete ones, when the patient may have ipsilateral loss of position and vibratory sense at the level of the lesion, and contralateral loss of pain and temperature loss, a spinal level or two below the level of the lesion."

deficit where you have a sensory deficit on one side and a motor deficit on the opposite side.

The hindbrain is relatively small. It contains the medulla and the pons. But it does a lot of important stuff. There are the cranial nerves, which we already talked about. And it has an essential role in controlling breathing. So, if you get much damage to this area you basically are dead. If you have an injury involving paralysis it depends on whether it's above or below the decussation as to how much paralysis you will have.

[music]

We're ready to move up to the next area, which is known as the midbrain. The midbrain receives inputs from cranial nerves that are involved with the muscles of the eye and the second cranial nerve, which is the optic nerve. So, before we talk about the midbrain we're going to talk a little bit about the origins of the eye. Obviously the eye didn't leave any fossil record, but we know a lot about how it forms in the embryo.

Bainbridge describes the eye as, "… a product of the brain." The eyes begin to form very early on in the embryo. As soon as the future brain has sealed into a tube, bulges start to protrude from each side. These eye stalks literally are part of the brain, and when this stalk gets near the surface of the embryo it induces the formation of the eye plaque, which is what will eventually become the lens. Now, this eye plaque is different from the plaques that form all the other sense organs because it doesn't form any actual sensory cells. It becomes the lens, which was the last part of the vertebrate eye to evolve.

The book contains some wonderful drawings that show how the folding of the eye stalk around the eye plaque incorporates the future lens into the eye. The retina is the part of the eye that contains the light-sensitive rods and cones. It develops from the eye stalk, which folds around the lens. So, it is literally true to say that the retina is part of the brain; which is what I tell patients when I'm looking in their eyes with an ophthalmoscope. I'll tell them, 'I'm looking at the only part of the brain that we can see from the outside.'

Now, there's lots of neat stuff about the brain in this chapter, including a discussion about the way our eyes are different from those of other animals. Bainbridge observes that animals seem to fall into three main groups with respect to vision. About a third are totally blind—that is they can detect no light at all. Another third have light-sensitive cells that can detect diffuse light coming in. And the final third can focus an image on a sheet of light-sensitive cells.

Those who study brain evolution suspect that our ancestors detected light before they were able to focus. Again, I'll refer you back to the book for details. But there are a few highlights I want to mention. One is that light detection is surprisingly similar across species. It involves a molecule imbedded in the detector that contains a smaller vitamin A-like light-sensitive molecule. The big molecule is called opsin and the small molecule—the light-sensitive molecule—is called a chromophore.

Bainbridge observes that this system is found in everything from single-celled organisms to the giant blue whale. Humans can make their own opsins, but we can't make chromophores, which is why we need vitamin A. Humans have four different opsins, and three of these are related to detecting different colors. The current evidence is that the photoreceptor evolved only once, but there are at least three different ways of arranging photoreceptors.

But even when eyes appear to be very similar they may actually be very different. An example he gives in the book is the difference between humans and octopi. In the octopus the receptors point toward the light, but in humans they actually face the back of the eye. This is one reason why biologists think that eye evolution occurred over 100 times in different realms of the animal kingdom.

And that's pretty remarkable when you consider that the creationists and intelligent design types are still using the complexity of the eye as an argument against evolution. The argument that intermediate structures would not be useful fails in the face of actual examination. For example, clearly some light detection is better than none at all, and a lens that focuses imperfectly still offers an advantage over no focus at all.

So, in contrast to the creationist position, Bainbridge observes, "Making eyes turns out to be the easiest, most natural thing in the world. In fact it is now difficult to see why so many species with photoreceptors don't bother to evolve eyes." The same photoreceptor is seen from the single-cell organism up into the whale, but not everything has an eye.

Many eyeless animals have the genetic code to form eyes, but it's not turned on. And this might have to do with the high energy demands of photoreceptors. You would have to have a very strong need for vision in order for these to be worth the energy that they use. And that wouldn't be true, for example, if you lived in a place where it's totally dark—being able to see would be a total waste of energy.

I've left out a lot of the interesting and weird properties about eyes which he talks about, including how the retina seems to be built totally backwards. As he observes, this is something that no intelligent designer would countenance. He says that this is, "…perfect evidence to show that the imperfect, illogical bodies that we have today are the results of millions and millions of years of blind historical accident." [Be sure to look a Figure 13 and Figure 14][6]

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As I mentioned, the inputs from the eye come into the brain at the level of the midbrain, which is the top part of the brainstem. This is where we begin to observe a major principle about what the brain does with most of the sensory information it receives—it throws it away. And you might be surprised to learn that this process actually begins in the eye itself. Only the information from the center of the retina—the fovea—leaves the eye in its original form.

Some fibers that are leaving the retina actually contain information accumulated from hundreds of photo receptors. Why? It's not just to avoid information overload. It's so that the optic tracts can be a reasonable size. He says that if every photoreceptor had its own axon the optic tract would be over an inch thick. It might make for an interesting alien.

You may have heard that information from the right eye goes to the left side of the brain and visa versa. In all vertebrates some of the optic fibers cross over to the opposite side before they enter the brain. In non-mammals this is a complete process. In mammals it's more complicated. In animals that have eyes on the sides of their heads all the fibers cross, but in mammals whose eyes face forward—like humans—only half the fibers cross. The fibers from the outside of the retina don't cross. Again, I will refer you to the diagram which I will put into the Show Notes. [Figure 15]

Now, I didn't mention that the image on the retina is reversed. So, when this is combined with the crossing over it means that the visual information from the right side of the body goes to the left side of the brain, and the images from the left side of the body go to the right side of the brain. So, the key idea here is that it's not about which eye the information is coming from, but which side of the body it's coming from.

In mammals a lot of visual information heads for the forebrain, but there is still a significant input at the level of the midbrain. I will refer you again to his excellent description of what the midbrain does, but there are a few things I will briefly touch on. One is that the midbrain controls whether our pupils constrict. It also has a very primitive visual map that controls our ability to gaze at objects, and it controls the saccades, which are those little rapid eye movements that allow us to focus everything that we see onto the fovea so that the whole world looks sharp.

The midbrain also controls our automatic responses to potential danger such as turning our heads toward things in our peripheral vision, and ducking and closing our eyes when something comes at our head. There are actually dedicated fibers that go to the muscles of the neck.

In this area of the midbrain there is the hillocks [Figure 12][7], which is part of the midbrain, which also maps sensory information including sound, and touch, and probably integrates them to some extent. This upper hillocks part of the midbrain has been implicated in blind sight, which is when people show evidence of having some ability to see even when they are consciously blind.

This brings us back to a theme we have considered before—the surprising importance of what happens at the unconscious level in our brain. We don't have any conscious access to the maps and functions of the midbrain, but it is absolutely essential to things we take for granted in our lives. Can you imagine if you had to figure out how to look at something?

Now, the division between the conscious and unconscious visual pathways is not clear-cut. There seem to be interconnections. And we're learning more and more about how widespread visual processing is. For example, we know that the amygdala—which we'll discuss shortly—is essential for visual recognition of emotions; especially fear.

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The lowest part of the midbrain, which is called the tegmentum, seems to be largely devoted to motor function. This is where there are the cranial nerves such as III and IV that control eye movements, and also cranial nerve II that carries the visual information from the retina. Another important structure in the midbrain is the reticular formation, which is important to arousal.

Bainbridge includes in his discussion of the midbrain a nucleus known as the substantia nigra, which is important in Parkinson's disease. It contains dopaminergic neurons, and when we have Parkinson's disease we lose our smooth coordinated motor activity. Usually I have read of the substantia nigra as being part of the basal ganglia, which is one of the deepest structures of the forebrain. I think that just demonstrates the fact that the division of the parts is somewhat arbitrary, especially at this level as they are gradually transitioning from one to the next.

[music]

Now we are about ready to talk about the forebrain, and this brings us to our third special sense which is smell. Smell is unique because it is the only sense that plugs directly into the forebrain. And even though our sense of smell is weak compared to most other animals, the fact that it still connects directly to the forebrain explains why smells can have such a powerful effect on our emotions and our behavior.

Bainbridge talks a little bit about how smell probably evolved. We know that 5% of the genes in mammals are devoted to smell receptors. We have the same number of genes for this as mice, but about 60% of our genes are either degenerate or inactive. Vertebrates all seem to have the same basic smell plan, but invertebrates are different. Unlike vision, there doesn't seem to be a universal system for smell detection. This suggests that smell happened after vertebrates broke off from invertebrates, which makes it a more recent acquisition.

Just a little bit more about smell. We know that our smell receptors can adapt to ambient smells so well that we can no longer smell them. The discovery of how smell works is actually fairly recent. The 2004 Nobel Prize in Medicine and Physiology went to Linda Buck and Richard Axel for their discovery of odorant receptor proteins and the organization of the olfactory system.

We have about 10 million smell cells, and each one of these has about 1000 different receptors. And other species may have even more receptors than we do, and more smell cells. So, it starts to make sense that some of us are genetically unable to smell certain things, because we just aren't coding for the receptors.

Smell goes to many different places in the brain. In fact, he observes, "Smell pervades our brain in a way the other senses do not." I'm actually working on doing an episode about smell later, so we'll get to talk about this in more detail on a future podcast.

Now we're going to talk about the forebrain [Figure 17][8]. First we have to consider how the transition into the forebrain occurs. We have this canal that contains the cerebrospinal fluid that goes all the way down into the spinal cord. When we get to this level it starts to open up and form what's called the third ventricle. And the walls of the third ventricle form what he calls the interbrain, which is the transition between the brainstem and the forebrain.

The walls of the third ventricle contain two important structures: the thalamus and the hypothalamus. We tend to refer to these organs as if they were single

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structures, but there is actually one on each side. So, there are actually two thalami and two hypothalami.

This is at the level where things are starting to become, as he calls it, "...more brainy and less spinal." 'Hypo' just means under, so that tells us that the thalamus lies above the hypothalamus. And then on the roof of this third ventricle—or the epithalamus—there is the infamous pineal gland and several other poorly understood functions.

You may remember that the pineal gland was what Descartes thought was the place where the non-physical mind would be communicating with the brain. And this turns out to be extremely wrong because in people the pineal gland gets only a very tiny bit of visual information—basically light sensation. And it makes melatonin at night, which is important for sleep. But that's about all it seems to do in people.

In this same area there is something called the habenula, which is part of the reward system of the brain and gets a lot smell inputs. And the habenula connects to something a little bit lower down, called the interpeduncular nucleus of Gudden, via the fasciculus retroflexus. I only mention this bunch of gobbledegook because the fasciculus retroflexus has been observed to be degenerated in some cases of addiction. And you know that this whole idea of addiction and its involvement with the reward system of the brain is a very hot area of research right now.

The thalami are the major structure in the inner brain. They are a very important component of the sensory system. Everything except for smell is relayed to the cortex via the thalamus. Traditionally it was thought the thalamus was just a relay system, but we now know it does much more than that. A lot of sensory processing and interpretation is actually going on at the level of the thalamus.

This has been best studied for vision because the lateral geniculate nuclei—LGN—has been greatly studied. That's the main input place where the optic nerve comes in to the lateral geniculate nucleus and then it sends its information to the primary visual cortex. It has been traditionally thought that there were two major pathways that were parallel—a what and a where—but this is kind of becoming a little bit controversial about whether other information might actually be separated out, such as color information or time information.

Exactly how much of this is really being separated out at the level of the thalamus is still a subject of debate. But, again, remember that the smell information has gone straight to the cortex; so it skipped the thalamus, even though smell information is going to come back down to the thalamus.

Below that there is the hypothalamus, which is sometimes thought of as the body's thermostat because it's the master controller of most of our visceral functions like body temperature, appetite, aggression, and sex. When somebody talks about their body weight's set point or something like that they're referring to functions attributed to the hypothalamus.

It is a very primal structure. It may be one of the oldest parts of the brain, because every vertebrate has one. It gets inputs from almost every other part of the brain and the body. And it sends out signals in two ways. One is by sending signals to other parts of the nervous system, such as telling us that we need to get out of the cold, for example. But it also sends out hormones. It does this via the pituitary gland, which is something that also all vertebrates have.

The pituitary gland kind of hangs down from the brain. It has two parts—a kind of brainy part and a glandular part. The back part, called the posterior pituitary, is really essentially part of the brain. It releases ADH, which controls water metabolism, and oxytocin, which is involved in birth contractions, milk secretion, and orgasm, and recently has been discovered to have some other important roles, too.

ADH and oxytocin are actually being synthesized in the hypothalamus, but they are released by the pituitary. In contrast, the other hormones that come from the glandular part of the pituitary are actually made in the pituitary. And these are the hormones that control the thyroid, the adrenal glands, metabolism and growth, and sex hormones. This includes things like thyroid stimulating hormone, growth hormone, prolactin, and follicle stimulating hormone.

So, here's an example of how it works. The hypothalamus will release thyroid releasing hormone and it sends this to the pituitary gland to tell it to release thyroid stimulating hormone, which in turn tells the thyroid to make and release thyroid hormone. When you read a description about hormones, usually the releasing hormones are the ones that are coming from the hypothalamus, the stimulating hormones are coming from the pituitary, and the actual hormone is coming from the endocrine glands such as the adrenal, the thyroid, or the sex organs.

[music]

We're almost ready to get up to the real forebrain, which he also calls the endbrain, because basically you have two endbrains that are growing out of the side of the forebrain that then wrap around the rest of the brain in the end. So, what about the cerebral hemispheres makes them different from the rest of the nervous system?

Now we find that the gray matter—or the cell bodies—is on the outside, and we have a cortex that's basically a thin continuous sheet of gray matter. This is in contrast to the lower parts of the brain where we have the scattered nuclei; and then, of course, in the spinal cord where all the gray matter is on the inside.

We've gone from gray matter on the inside, to gray matter scattered, to gray matter spread around the outside. There is also a unique columnar organization for the cerebral cortex; but he doesn't really talk about that in this book.

He has a good brief description comparing the evolution of the forebrain among the different land vertebrates—reptiles, birds, and mammals. And while the cerebral cortex is unique to mammals, the reptiles and birds have brain structures that seem to share similar functions in that they get diverse inputs from throughout the nervous system. In reptiles this is called the dorsal ventricular ridge, and in birds it's called the avian wulst. And especially in birds we're learning that at least some kinds of birds can be a lot more intelligent than was once thought. [Figure 20]

He points out that there is nothing inherently modern about our mammalian cortex. So, calling it the neocortex is a little bit of a misnomer. The supposedly mammalian tendency to concentrate higher processing in the forebrain is actually a general vertebrate trait. All living vertebrates use their forebrain to varying extents to integrate sensation and action. Now, this tendency might be limited in most vertebrates, whereas in mammals it becomes quite prominent. The forebrain houses both the smell and higher centers, but in humans the processes of the cortex that aren't related to smell tend to overshadow the smell function.

Looking at the features of the mammalian cortex, one thing is that there are six layers in the cortex. And that is unique. The dendrites and the axons are short and stubby because they're communicating mostly with each other or nearby neurons. And they are called pyramidal because of the shape of the cell body. This might be a feature that helps them to be better at collating inputs.

Why is the surface so wrinkly? It seems that this is a way of increasing surface area. Think about scrunching up a piece of paper to get it to take up less space. The basic structure of the cerebral hemispheres is very similar from person to person. [Figure 18][9] We have the gyri and sulci—the bumps and the grooves. The big groove that everyone has is called the fissure of Rolando, and that is roughly separating the sensory parts of the brain, which are in the back, with the motor parts that are in the front.

The primary motor area and the primary sensory area are found right on either side of this groove. However, we now know that this is very much an oversimplification, since many parts of the brain are turning out to have a mixture of motor and sensory neurons. And, of course, we usually divide each hemisphere into four lobes—the occipital lobe in the back, the temporal lobe on the side, the parietal lobe on the top, and the frontal lobe in the front.

I have to mention a few other structures at this end of the brain. There's the cerebellum, kind of on the back and bottom of the brain, and it is very important in coordinating motor activities. It's even more wrinkly than the cerebral hemispheres and has a very dense concentration—the densest concentration—of neurons in the brain.

And then, buried very deep in the forebrain is, as I mentioned before, the basal ganglia [Figure 21][10]. This includes the substantia nigra, the subthalamic nucleus, the striatum, the putamen, the caudate, and the nucleus accumbens. Now, there is a lot of debate about whether or not these really should all be lumped together. What they seem to have in common is that they are areas of gray matter located in the white matter of the cerebral hemisphere. These are the parts that have a structure more like the lower parts of the brain instead of the six-layer structure of the cortex proper.

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[9] Figures have been added to the end of this Transcript. They come from *Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain* (2008) by David Bainbridge, with the author's permission. The numbers correspond to those in his book.

[10] Figures have been added to the end of this Transcript. They come from *Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain* (2008) by David Bainbridge, with the author's permission. The numbers correspond to those in his book.

I guess I should mention how the two cerebral hemispheres communicate with each other, because they are actually remarkably separate for the most part. But there is a large connection that you can see with your naked eye called the corpus callosum, which actually only placental mammals have. And then there are several different smaller connections that are called commissures.

Finally, before we conclude this very brief whirlwind tour of the brain, there are a few more parts of the cerebral hemispheres that we need to talk about that are a little bit different from the cortex proper. These are parts that are shared by all vertebrates, and that is why they are sometimes called the old cortex. But they don't have that six-layer structure.

Recent research indicates that the emphasis shouldn't be on which structure is the oldest, because all the vertebrates seem to share the same basic forebrain structure, with different regions being emphasized in different groups. And what I'm talking about here is which ones are emphasized in these structures that are deep down in the inner surfaces of the hemispheres. They have varying importance in different animals.

It's not that they are particularly old, it's just that they are easy to find in many different types of vertebrates. And so, there is a lot of debate about what to call this area. The 'medial temporal lobe' might be the most accurate anatomical description, although you usually hear it referred to as the limbic system; which is misleading mostly because it tends to lump things together that don't necessarily belong together. There is a nice diagram in the book that shows how these parts of the brain got to have the shape that they have now, which is kind of loopy looking.

From the top of the brain down on the inside of the temporal lobe we have the cingulate gyrus, the amygdala, and the hippocampus. Some of this is what we were traditionally told was the limbic system, and we were traditionally told that this was our emotional brain. But we now know that it is a little bit more complicated than that.

Even so, we do know that the amygdala is a very important area for processing emotional information—especially fear. A lot of times when you read about the limbic system in the older literature they may actually be describing amygdala function, although it's not that easy to isolate out what the amygdala does by itself, because injury to the amygdala is very rare.

However, the amygdala is clearly different from the hippocampus which is, as we've talked about several times in the past, very important for forming long-term memory and also for our spatial awareness. We have talked about memory quite a bit, and I refer you back to Episode 3 and Episode 12 if you're new to the *Brain Science Podcast*.

Now, with regard to the cingulate gyrus, it's a little bit unclear when he talks about this in the book whether he's talking about a specific surface of the cortex or whether he's talking about the anterior cingulate cortex, which we now know contains mirror neurons. I would think at this point it is fair to say that our understanding of this area is fairly limited.

And then another thing he doesn't mention at all is the insula, which communicates with some of these structures. The insula is actually located on the medial, or inside surface of the parietal lobe. Recent research has indicated that it is involved in the reward system and in addiction.

So, this has been a pretty long episode to describe the parts of the brain. I talked a little bit about the origins of hearing, sight, and smell. It is kind of surprising to find out that there is only one kind of photoreceptor but that eyes appear to have evolved quite a number of times. Hearing seems to—although it has arisen several times—be based on a pretty similar pattern from animal to animal. And smell seems in some ways to be the newest of the senses in that it is different between vertebrates and invertebrates.

The basic pattern that we can remember is that if we start at the spinal cord, at the level of the spinal cord the neurons are on the inside and the axons are on the outside. As we move up into the brainstem the neurons begin to be clustered into nuclei scattered among the white matter of axons. And at the level of the brainstem most of the cranial nerves come in.

As we move up into what we normally think of as the actual brain, the structure gradually changes again. We have at the lower parts of the brain still scattered nuclei that communicate with each other; until finally we reach the level of the cortex where now all the gray matter is on the outside, with the neurons in a sheet on the surface of the brain, with a six-layer structure and a columnar organization that seems to be organized to promote the special extreme interconnection that occurs at the level of the cortex compared to the rest of the brain.

I am going to try to get the pictures into the Show Notes sometime in the next few days. Right now it's looking like I will probably post this episode before I have a chance to do that. So, if you come to the website and the diagrams are not yet available, please check back again in a few days and I'll have those up there. And I definitely want to thank David Bainbridge for giving me permission to use the diagrams from his book, because I think you'll find those helpful.

Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain, by David Bainbridge is a book that I can recommend to listeners of all backgrounds. If you've ever studied anatomy this is a great review. And if you have never looked at the brain at all, this will be a wonderful introduction.

[music]

As always, you can give me feedback by email at docartemis@gmail.com. But the best way to leave feedback is to participate in the Discussion Forum which is at brainscienceforum.com. Our next episode is going to be an interview with Dr. John Ratey of Harvard, and we're going to talk about exercise and the brain. That episode should be up in a couple of weeks.

I want to take a moment to thank everyone who has been sending me emails and posting comments. And I want to remind you that the Forum is a great way to meet other people that enjoy the podcast, but another place where you can share in the community is at the Flickr Group that I set up for the *Brain Science Podcast*. This is at flickr.com/groups/brainscience.

Flickr pictures from the Group actually appear on the front page of the website. It does it in the order that pictures have been posted, so if you put a picture in that group, your picture will go up onto the front page until the next time someone does. What I've really been trying to do is get people to post their pictures from all the different places where they live, because I love seeing pictures from all around the world.

Another thank you I need to make is to those of you who have donated to help support the *Brain Science Podcast*. That means an awful lot to me. And I wanted to address a couple of issues with regard to this that have come up in response to a couple of emails I got in the last week or so.

First of all, one person wrote to me and said that they had been meaning to give something for six months. And I think they might have been being a little hard on themselves, because I don't think that I've had the PayPal donation stuff set up on the website for that long. At any rate, I appreciate the fact that they told me that they didn't mind being reminded.

More importantly, I got an email asking me about how much is PayPal taking out of donations. I don't want to go into that in any kind of detail right now, but I do want to mention one thing. You don't have to have a PayPal account to make a donation. But if you make a donation with a credit card instead of a straight PayPal account, then it does have a fee deducted that is slightly larger if you're from a non-U.S. location.

I have posted the details of this up on the Discussion Forum if you want to know exactly how much it is. I hope it won't discourage you from contributing, because it's pretty much standard for something to be taken out of any kind of credit card payment, so PayPal is not doing anything different. They're just making it affordable for me, because I couldn't afford to do regular credit card payments.

I'm sure there's something I'm forgetting to remind you about, because I always do that. I hope you will check out my other podcast *Books and Ideas* at booksandideas.com. And don't forget to check out the new website at sciencepodcasters.org. And please refer your favorite science podcast to me. I'm trying to get as many science podcasters on there as possible.

I want to thank everyone for listening and for supporting the podcast, and I'll talk to you again real soon.

[music]

[music]

Transcribed by Lori Wolfson
All errors or omissions responsibility of the transcriber

Important Note:

The following pages contain figures from [*Beyond the Zonules of Zinn: A Fantastic Journey Through Your Brain*](#) (2008) by David Bainbridge.

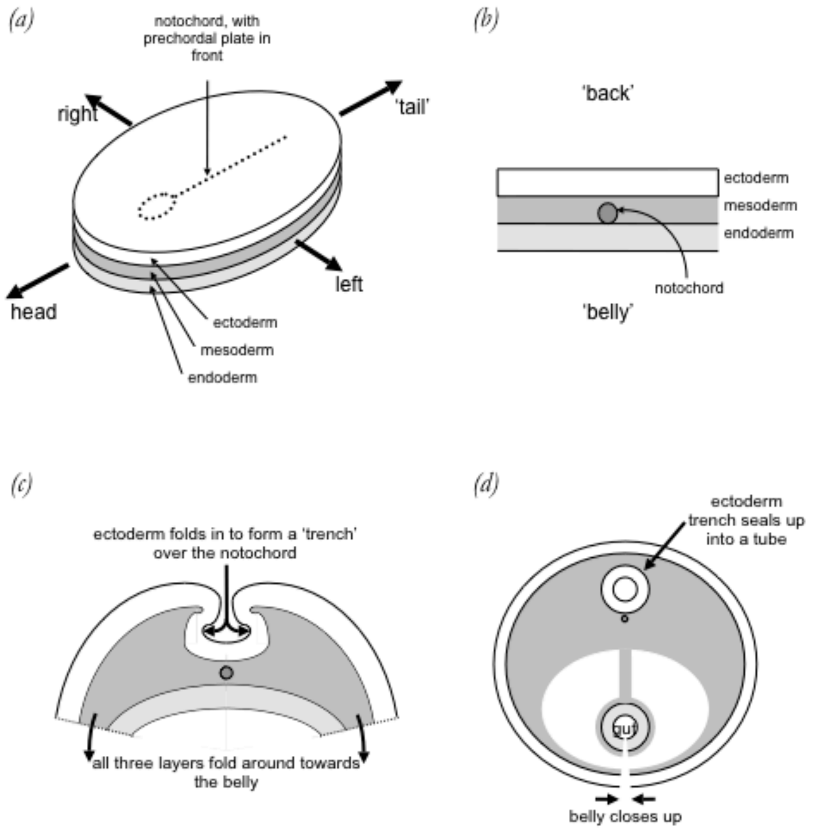
Figure 1. The developing human embryo.

(a) The three-layered human disc-embryo from above. It already has a front-back and left-right orientation, mainly apparent at this stage from the notochord and prechordal plate lying deep in the mesoderm layer. The ectoderm layer will form most of the brain and spinal cord.

(b) A cross section through this three-layered embryo showing the ectoderm, mesoderm and endoderm layers, as well as the notochord which lies along the head-to-tail body axis.

(c) A cross section of the embryonic disc as its edges start to curl downwards and inwards. At the top of the embryo a trench has formed above the notochord – this will become the central nervous system.

(d) A later cross section. The downwards and inwards folding continues until the belly closes up.The trench at the top of the embryo has now sealed over leaving an buried ectoderm tube – the central nervous system.



These figures are used here with the author's permission, but should not be copied or reproduced without contacting him at mail@davidbainbridge.org.

Figure 1

Figure 2. The developing human brain.

(a), (b) Viewed from the front, the brain is seen to divide into three and then five swellings, each containing their own fluid-filled ventricle . (c), (d) Viewed from the left side (as if the embryo is facing to the left of the page), the same bulges may be seen, along with the kinks which form in the midbrain and hindbrain regions.

(e), (f) Later, the end-brains and cerebellum start to form and come to dominate the brain. The other regions are just visible below the end-brains and are collectively known as the brainstem. The end-brains, especially, are starting to outgrow the other regions and their hind-most parts have bent around to create a 'boxing-glove' shape.

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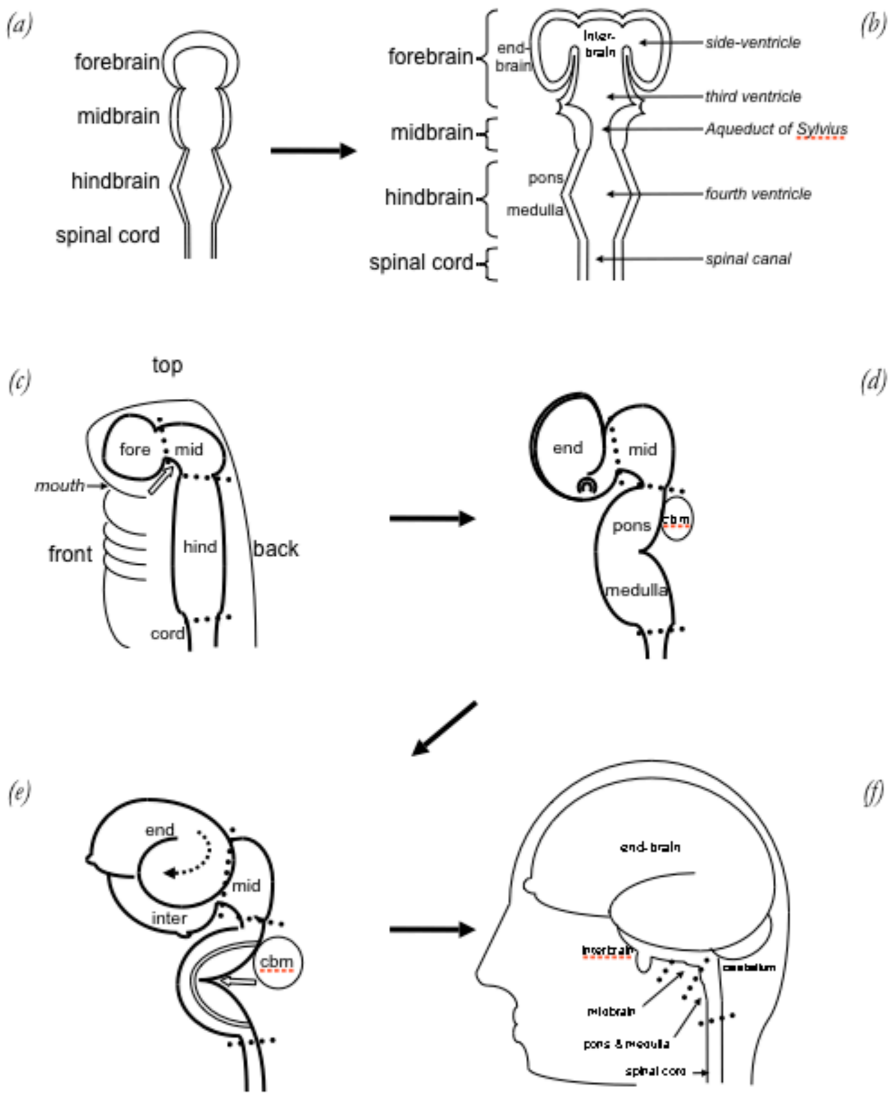

Figure 2

Figure 6. The arrangement of the spinal cord.

(a) In cross-section, an outer layer of white matter may be seen enclosing an inner, butterfly shaped core of grey matter, divided into front and back horns on each side.

(b) This arrangement persists throughout the cord. In this figure, four segments of the spinal cord are viewed from the back. In each segment, a back and a front nerve root emerge on each side. These then unite into a short common trunk which then divides into branches.

The back roots bring back sensory information to the cord and the front roots convey motor information from the cord.

The main part of the motor nerve cells is in the cord itself, but the main part of the sensory nerves is in a little bulge on the back roots – the back root ganglion.

Sensory information can pass up the cord to the brain, just as motor commands can pass down the cord from the brain. However, sensory inputs to the cord can also directly effect movements without any involvement of the brain – reflexes.

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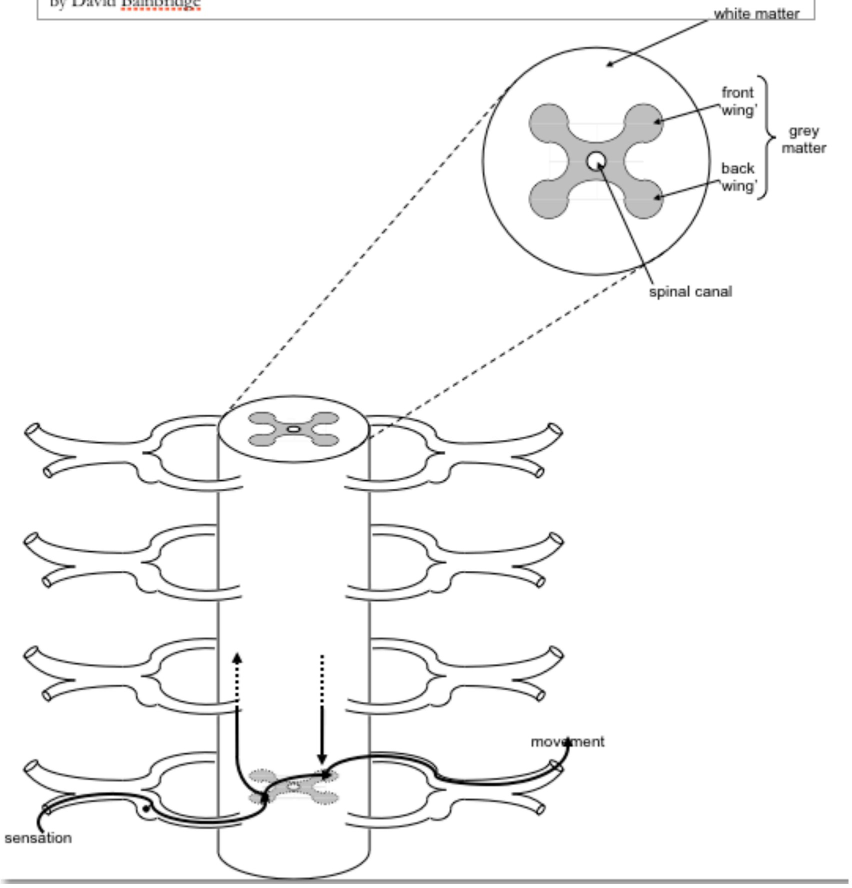

Figure 6

Figure 11. A series of schematic cross-sections showing how the spinal cord merges into the hindbrain.

(a) As the cord approaches the skull, its central canal lies further and further back until only a thin membrane separates it from the outside (middle picture). The continuation of the canal into the medulla of the brain becomes broader and flatter – the fourth ventricle. As the fluid space in the centre of the cord shifts, the motor and sensory cells shift with it. The motor cells at the front of the cord end up near the middle of the medulla, whereas the sensory cells at the back of the cord end up nearer the outside of the medulla.

(b) The ancestral upper hindbrain was probably similar in structure to the lower hindbrain – a flat slab of nervous tissue, with the fourth ventricle behind it, covered by a thin membrane. In vertebrates, the cerebellum grows out of the side and front 'lips' around the fourth ventricle. It is a large, globular structure that sits 'atop' the hindbrain on stalks, or 'peduncles'. Nerve fibres pass to and from the cerebellum via these peduncles. In mammals, many of the connections of the cerebellum are with the cortex, and they need to cross from one side to the other. To allow this, a bridge or 'pons' evolved which transfers fibres from the peduncles to the opposite side.

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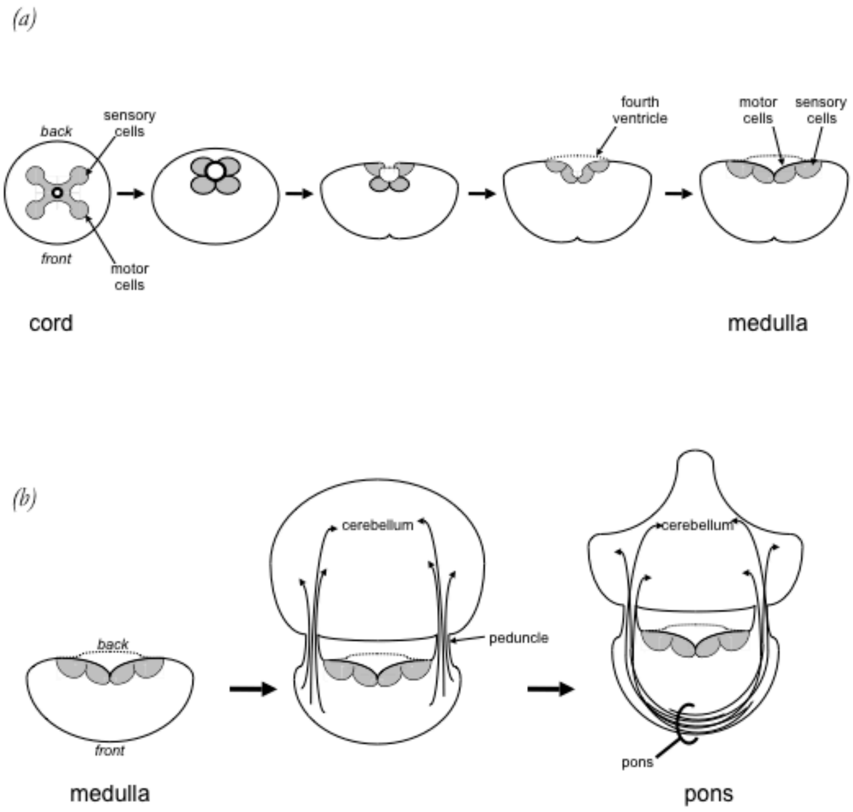

(numbers

correspond to those in Bainbridge, 2008)

Figure 11

Figure 12. A series of cross-sections of the brain stem, from cord to midbrain.

For each cross-section, the front of the brainstem is at the bottom of the diagram.

Inset is a profile (by Leonardo da Vinci) overlain by an outline of the brain. The bold lines are the approximate levels of the six sections in the main diagram.

The canal of the spinal cord opens up into a flat, diamond-shaped lake in the medulla and pons, which then connects to the narrow aqueduct of Sylvius through the midbrain.

The cerebellum has been omitted for clarity – it would be a large globular structure atop the brainstem around the level of the pons, and connected to it on each side by its 'peduncles'.

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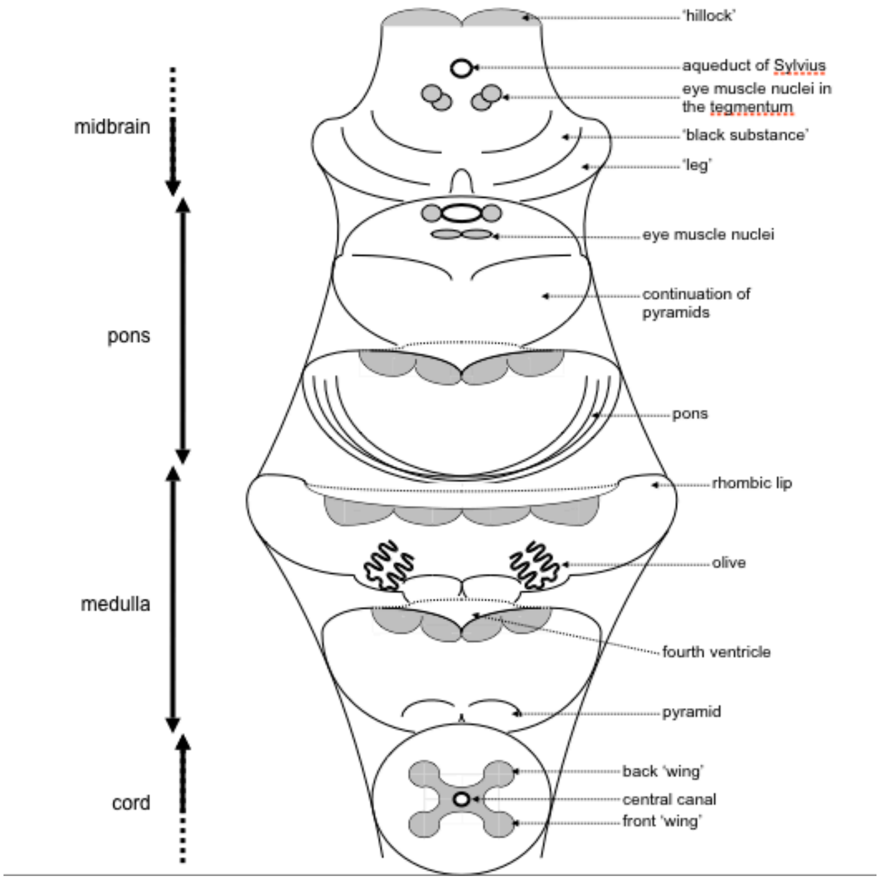

Figure 12

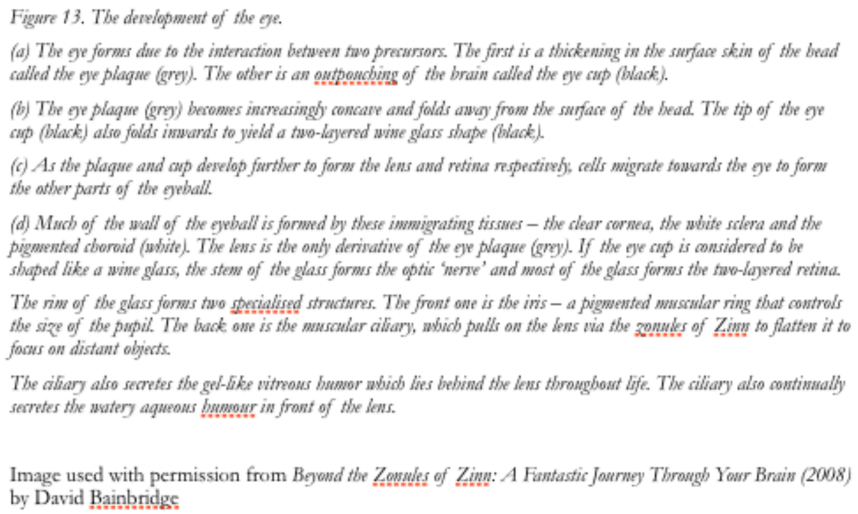

Figure 13. The development of the eye.

(a) The eye forms due to the interaction between two precursors. The first is a thickening in the surface skin of the head called the eye plaque (grey). The other is an outpouching of the brain called the eye cup (black).

(b) The eye plaque (grey) becomes increasingly concave and folds away from the surface of the head. The tip of the eye cup (black) also folds inwards to yield a two-layered wine glass shape (black).

(c) As the plaque and cup develop further to form the lens and retina respectively, cells migrate towards the eye to form the other parts of the eyeball.

(d) Much of the wall of the eyeball is formed by these immigrating tissues – the clear cornea, the white sclera and the pigmented choroid (white). The lens is the only derivative of the eye plaque (grey). If the eye cup is considered to be shaped like a wine glass, the stem of the glass forms the optic 'nerve' and most of the glass forms the two-layered retina.

The rim of the glass forms two specialised structures. The front one is the iris – a pigmented muscular ring that controls the size of the pupil. The back one is the muscular ciliary, which pulls on the lens via the zonules of Zinn to flatten it to focus on distant objects.

The ciliary also secretes the gel-like vitreous humor which lies behind the lens throughout life. The ciliary also continually secretes the watery aqueous humour in front of the lens.

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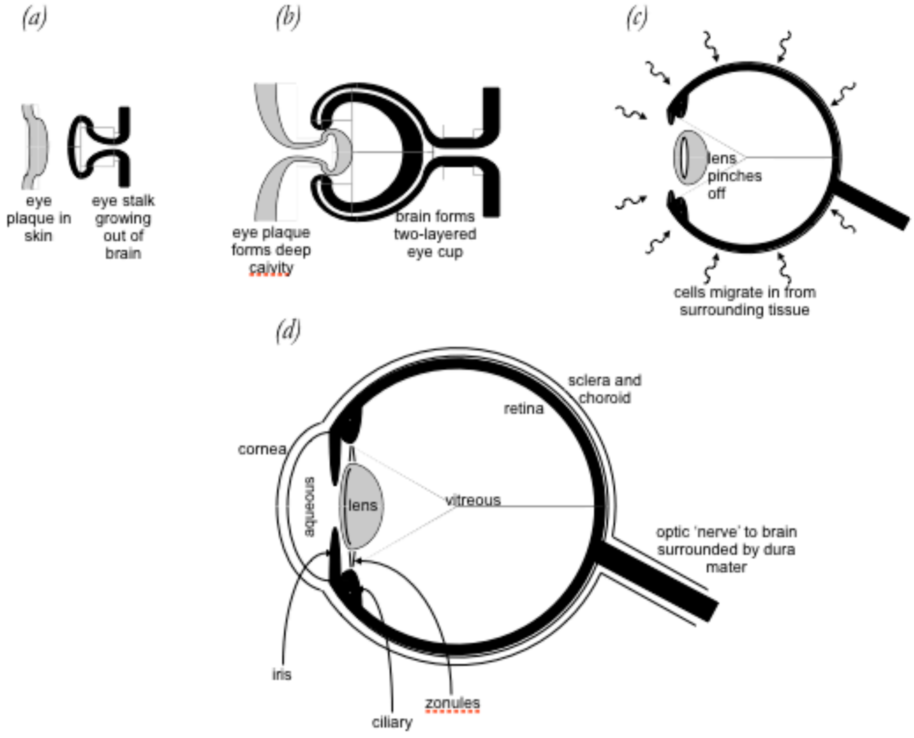

Figure 13

Figure 14. The human retina is arranged 'inside-out', and how it got that way.

(a) Light is detected by a sheet of specialised ciliated cells called photoreceptors. Once these are activated, they induce activity in an orderly array of neurons which eventually convey the visual information back to the brain. The photoreceptors are the furthest part of the retina from the incoming light, and so all light must pass through, and presumably be distorted by, all the other layers of retinal cells before it reaches the actual site of light detection.

(b) Four proposed stages in the evolution of our 'wrong-way-round' retina. Each is a cross section of the head of one of our distant ancestors. The the vertebrate nervous system started off as a flat slab of tissue on the surface of our ancestors' backs, just as it does in developing human babies. Two patches of light-sensitive cells then formed on this patch, just as the progenitor of the eye wine glasses is detectable at the equivalent stage in an embryo. These eye spots formed near the surface of the nervous system slab, so that they could better catch the light. When the nervous system folded inwards to create the sealed tubular nervous system we have today, the eye spots ended up on the internal surface of the brain. To get over this problem, the eye spots were pushed back out towards the surface of the head on little stalks, which eventually became the optic nerves. However, the eye spots were still deeper inside the head than the brain tissue and so to this day, the photoreceptor cells remain buried below a layer of brain.

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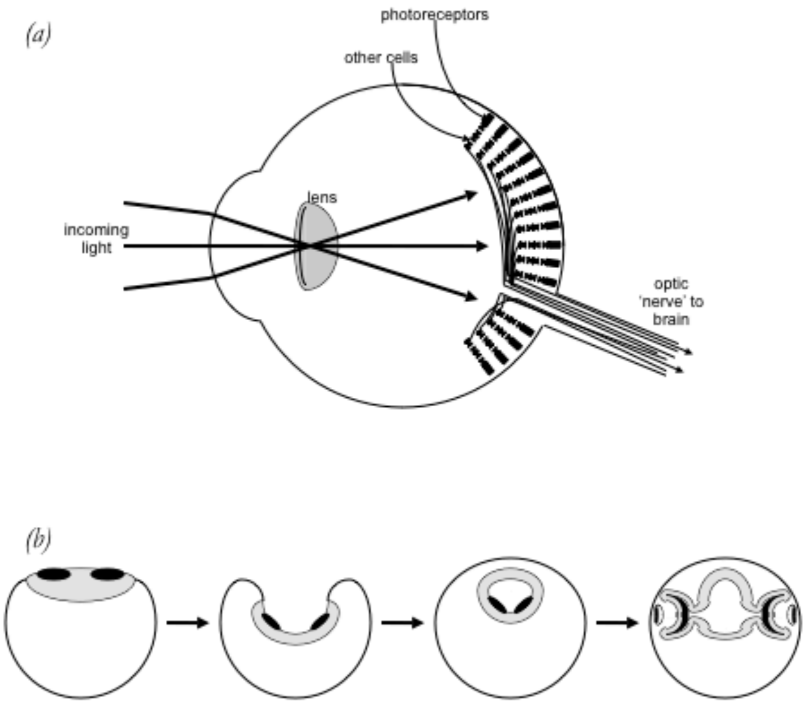

Figure 14

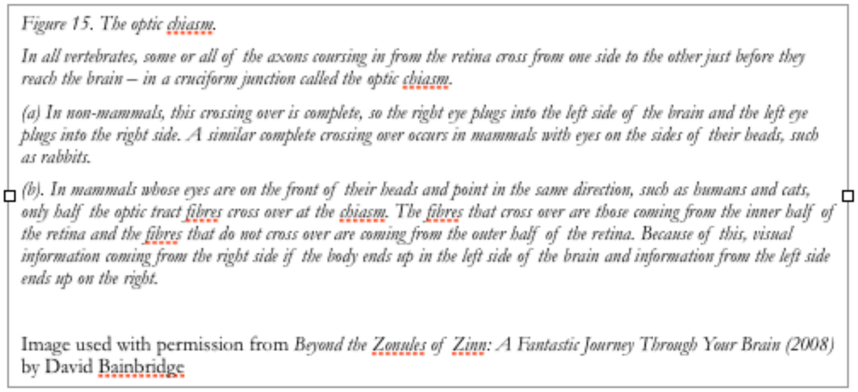

Figure 15. The optic chiasm.

In all vertebrates, some or all of the axons coursing in from the retina cross from one side to the other just before they reach the brain – in a cruciform junction called the optic chiasm.

(a) In non-mammals, this crossing over is complete, so the right eye plugs into the left side of the brain and the left eye plugs into the right side. A similar complete crossing over occurs in mammals with eyes on the sides of their heads, such as rabbits.

(b). In mammals whose eyes are on the front of their heads and point in the same direction, such as humans and cats, only half the optic tract fibres cross over at the chiasm. The fibres that cross over are those coming from the inner half of the retina and the fibres that do not cross over are coming from the outer half of the retina. Because of this, visual information coming from the right side if the body ends up in the left side of the brain and information from the left side ends up on the right.

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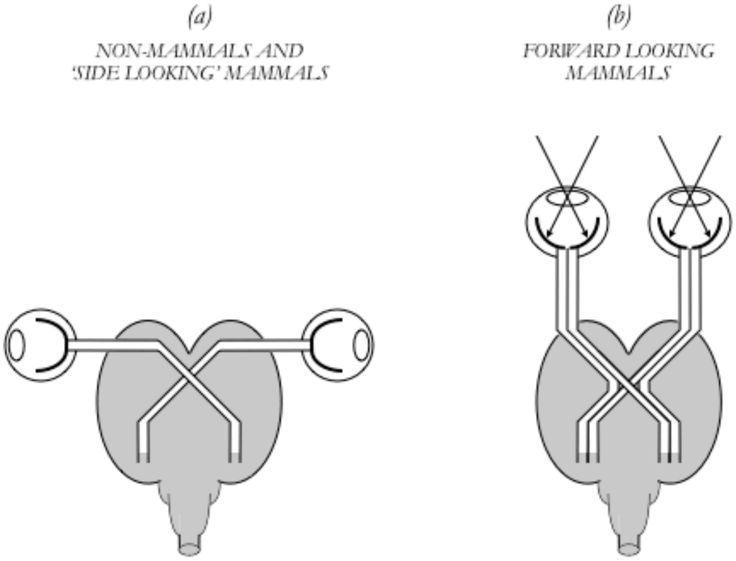

Figure 15

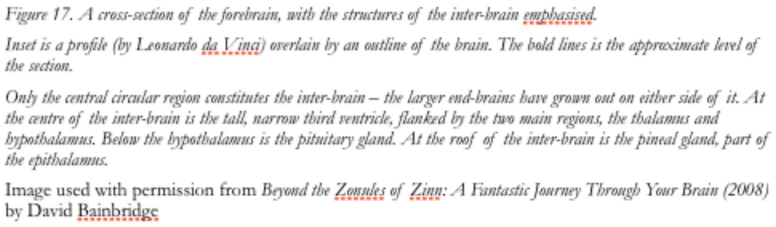

Figure 17. A cross-section of the forebrain, with the structures of the inter-brain emphasised.

Inset is a profile (by Leonardo da Vinci) overlain by an outline of the brain. The bold lines is the approximate level of the section.

Only the central circular region constitutes the inter-brain – the larger end-brains have grown out on either side of it. At the centre of the inter-brain is the tall, narrow third ventricle, flanked by the two main regions, the thalamus and hypothalamus. Below the hypothalamus is the pituitary gland. At the roof of the inter-brain is the pineal gland, part of the epithalamus.

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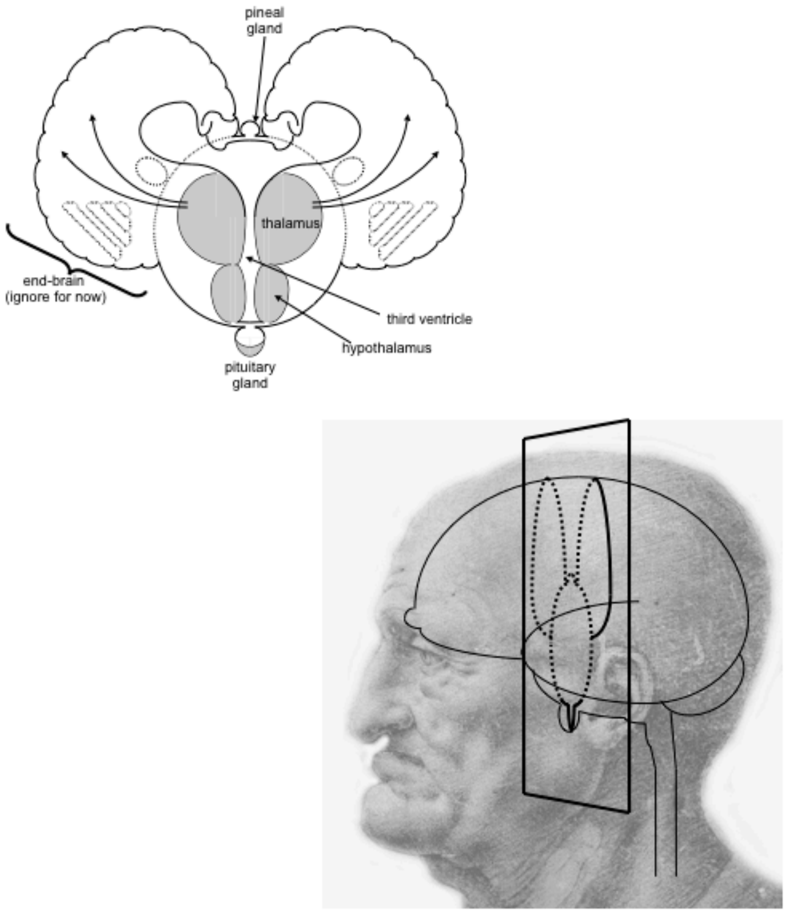

Figure 17

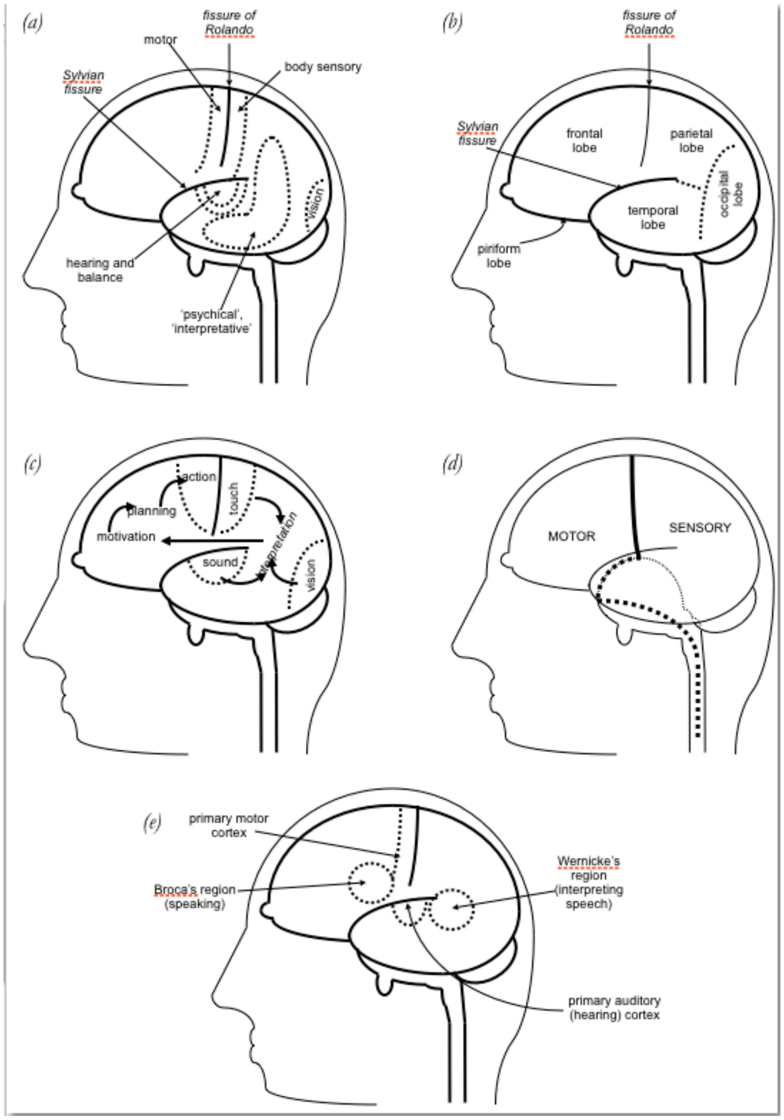

Figure 18. Some different ways of looking at the cerebral hemispheres

(a) A simplified version of Wilder Penfield's maps of the brain, derived from information from operations in which he electrically stimulated the cortex of conscious humans.

(b) The lobes of the human cerebral cortex. Some lobes are separated by obvious fissures or clefts – such as the fissure of Roalndo which separates frontal from parietal and the Sylvian fissure, separating temporal from frontal. The boundaries between others are more arbitrary.

(c) A simplified view of how the cerebral cortex works. The primary sensory regions, where sensation first reaches the cortex, are in the back half of the hemispheres. From these regions, the different sensory strands are transmitted to new areas where they are processed and analysed further, first in isolation from each other, and then all together to yield a combined, contextualised view of the world. From here, this view of the world is sent forward to the frontal lobes where it is used to generate motivations, plans and eventually actions by activation of the primary motor cortex.

(d) An even more over-simplified view of the arrangement of the brain in which the arrangement of cells in the spinal cord – sensory at the back and motor at the front – is continued all the way up to the cortex.

(e) Some cortical regions involved in language. Wernicke's region is involved in the interpretation of speech and lies conveniently close to the primary hearing cortex. Broca's region coordinates speaking and is next to the primary motor cortex for the mouth region.

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Figure 18

Figure 19. Wilder Penfield's functional maps of the strips of cortex on either side of the fissure of Rolando.
(left): the regions of the body in which tinglings are felt when different parts of the strip behind the fissure are stimulated.
(right): the regions of the body which tremble when different parts of the strip in front of the fissure are stimulated.

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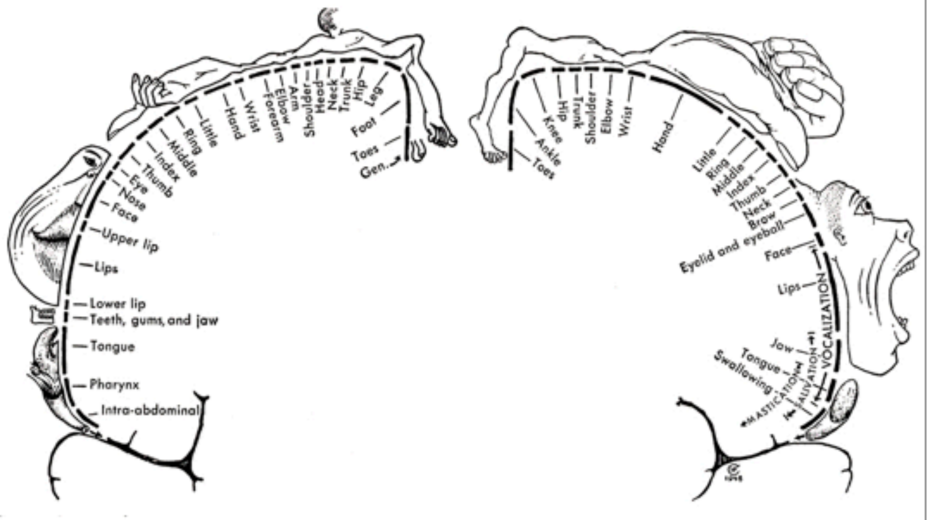

Figure 19

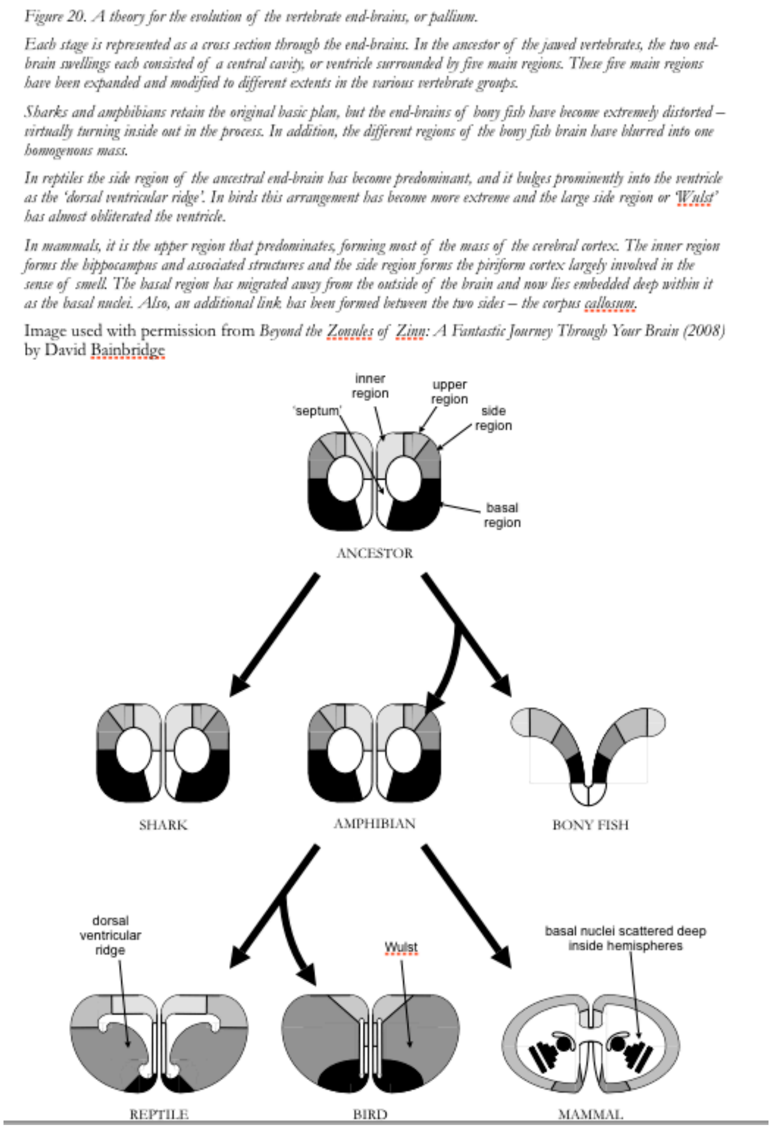

Figure 20. A theory for the evolution of the vertebrate end-brains, or pallium.

Each stage is represented as a cross section through the end-brains. In the ancestor of the jawed vertebrates, the two end-brain swellings each consisted of a central cavity, or ventricle surrounded by five main regions. These five main regions have been expanded and modified to different extents in the various vertebrate groups.

Sharks and amphibians retain the original basic plan, but the end-brains of bony fish have become extremely distorted – virtually turning inside out in the process. In addition, the different regions of the bony fish brain have blurred into one homogenous mass.

In reptiles the side region of the ancestral end-brain has become predominant, and it bulges prominently into the ventricle as the 'dorsal ventricular ridge'. In birds this arrangement has become more extreme and the large side region or 'Wulst' has almost obliterated the ventricle.

In mammals, it is the upper region that predominates, forming most of the mass of the cerebral cortex. The inner region forms the hippocampus and associated structures and the side region forms the piriform cortex largely involved in the sense of smell. The basal region has migrated away from the outside of the brain and now lies embedded deep within it as the basal nuclei. Also, an additional link has been formed between the two sides – the corpus callosum.

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Figure 20

Figure 21. A cross-section of the forebrain with the structures of the cerebral hemispheres emphasised.

Inset is a profile (by Leonardo da Vinci) overlain by an outline of the brain. The bold lines is the approximate level of the section.The central circular region is the inter-brain out of which the cerebral hemispheres have grown out on either side. At the centre of the inter-brain is the tall, narrow third ventricle, which communicates with the lateral ventricles of each hemisphere.

Deep in each hemisphere lie the basal nuclei, and between these runs the internal capsule carrying long axons to and from the cerebral cortex. In mammals, there is an additional link between the two hemispheres at the top, the corpus callosum.

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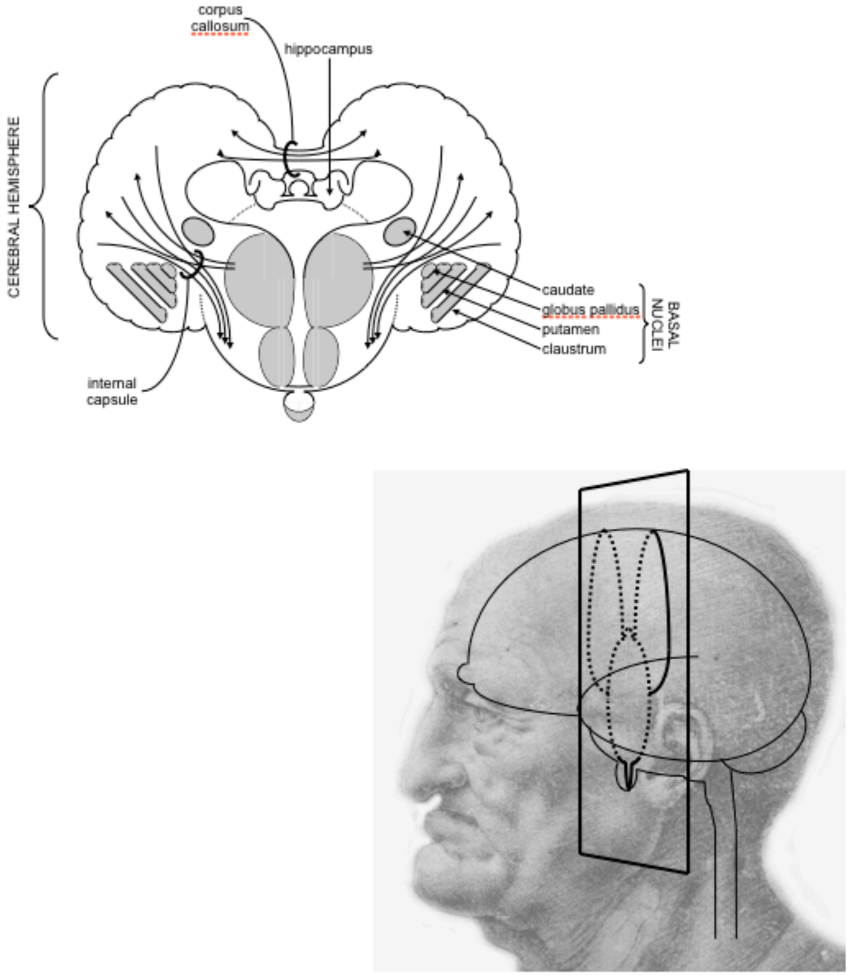

Figure 21