The Strange Anatomy of the Brain*

By David Bainbridge

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Human curiosity about the workings of the brain dates back at least 46 centuries. The first appearance of the word "brain" is on the Edwin Smith Surgical Papyrus, an Egyptian manuscript dating from around 1600 BC but thought to have been copied from the writings of Imhotep, an engineer, architect and physician who lived 1000 years earlier. The papyrus is the earliest known work on trauma medicine, and among other things it describes head injuries.

We do not know whether those injuries were suffered during the carnage of war or in the chaos of an ancient building site, but they make sobering reading: men who are paralysed, men who can only crouch and mumble, and men whose skulls are split open to reveal the "skull offal" inside, convoluted like "the corrugations . . . in molten copper". The author marvels at the opportunity to study this most mysterious of organs, and describes how his patients start to shudder when he thrusts his fingers into their wounds.

Today we know so much about the brain it is easy to forget that for much of human history its workings were entirely hidden from view. For centuries it was the preserve of anatomists who catalogued and mapped its internal structure in exquisite detail even though they had little idea what any of the structures actually did. Only now, as we finally gain access to the brain's inner workings, have those brain maps from the past started to make real sense.

Two millennia after Imhotep, the ancient Greeks were less enamoured of skull offal. Aristotle placed the control centre of the body at the heart, not the brain, presumably because it is demonstrably physically active, diligently pulsing throughout life. He found the brain to be still, and erroneously described it as "bloodless, devoid of veins, and naturally cold to the touch". This coldness, as well as its corrugated surface, led Aristotle to suggest that the brain was merely a radiator, dissipating the heat generated by the heart.

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It was Galen, a second-century Greek physician, who finally established the crucial role of the brain in controlling the body. Much of his evidence came from detailed anatomical study of animal brains. Galen was impressed by the brain's complexity—its anatomy is far more complicated than that of any other organ—which suggested to him that it must be doing something important. He thought its purpose was to interact with the sense organs in the head.

Galen was a practical man, and he confirmed his ideas about brain function with public experiments on live animals. He describes with great relish how, having tracked the nerves from a pig's brain to its voice box, he could expose them in the neck of a living, squealing animal, only to silence it with a cut. These ghoulish experiments showed that the brain controls the body, and Galen went on to argue that the brain and its nerves are also responsible for sensation, perception, emotion, planning and action.

Galen's work on brain function remained the state of the art right up to the 20th century. In the absence of new experimental techniques there was little more that could be done to study its inner workings. Yet the brain remained of great interest to anatomists, and over the course of the intervening 17 centuries they methodically mapped and catalogued its structure in ever finer detail. The impressive complexity of all those parts must have screamed out the idea that the brain was doing something very complicated, but what exactly? There was no way to find out.

This mapping and cataloguing of the brain's many structures has left a legacy of wonderfully descriptive and evocative names—almonds, sea horses, hillocks, girdles, breasts and "black stuff"—all the more so for being expressed in Latin and Greek. There are mysterious regions bearing the names of their otherwise-forgotten discoverers, such as the tract of Goll, the fields of Forel, Monro's holes and the radiations of Zuckerkandl. Others seem inexplicable (brain sand), starkly functional (the bridge) or ludicrously florid (nucleus motorius dissipatus formationis reticularis, which translates as "the dispersed motor nucleus of the net-like formation"). Some are just plain defeatist (substantia innominata or "unnamed stuff").

Fanciful as many of these names are, once they had been chosen they tended to stick, and many have survived into the exacting world of modern neuroscience. Memory researchers now probe the molecular machinery of the sea horse (hippocampus); scientists studying emotion scan the almonds (amygdalae) for flickers of fear. The modern geography of the brain has a deliciously antiquated feel to it—rather like a medieval map with the known world encircled by terra incognita where monsters roam.

ANTIQUATED FEEL

The old names bear little relation to our understanding of brain function, so navigating around the brain can be an arcane pursuit. Yet the quaintly outdated nomenclature has scarcely held science back, and in some respects this detailed mapping of the brain has helped clinicians, evolutionary biologists, philosophers and others make sense of it. The structure of the brain has always formed the core of what we know about the mind—after all, its anatomy remains the only thing about it that we do know for sure.

Take evolutionary biology: the structure of the brain is excellent evidence for evolution, and of our unexceptional place in the scheme of things. Before Darwin, it must have seemed inexplicable that humans, the divinely chosen overseers of the Earth, should have brains almost indistinguishable from those of dumb beasts. No one had been able to find an obvious structural difference in the human brain which explained our intelligence, language, wisdom and culture. But that did not stop anatomists searching for it. In 1858, a year before *On the Origin of Species*, a small protrusion into one of the brain's inner cavities—called either the hippocampus minor (little sea horse) or calcar avis (cockerel's spur)—was hailed as the definitive distinguishing feature of the human brain. Yet almost immediately supporters of the theory of evolution demonstrated that this little structure is also present in many other primates, and the uniqueness of the human brain vanished once more.

As it turns out, all parts of the human brain are also present in other primates, and we share the general plan of our brain with all backboned animals. A trout's brain is made up of the same three major regions as a human brain, and many of its parts have similar functions to their human equivalents. These structural similarities are reassuring to evolutionary biologists because they imply that the human brain evolved by the same processes that generated all other animals' brains. Yet confusingly, they leave us with no obvious location for the abilities we think of as distinctively human.

Vertebrates probably share a common brain architecture for two reasons. First, once an ancient ancestral vertebrate had a brain, it seems unlikely that evolution would have any reason to dismantle it and start afresh. Little surprise, therefore, that human brains conform to a standard vertebrate plan. The other reason is that, despite our different environments and ways of life, all animals have to process the same types of information. No matter how bizarre a vertebrate is, it receives only three types of incoming sensory data: chemical (smell and taste), electromagnetic (light, and electric and magnetic fields) and movement (touch and sound). This restricted sensory palette may have been what gave rise to the three-part vertebrate brain, with the front part processing smell information, the middle dealing with vision and the back interpreting sound. The laws of physics have never changed, so no new senses ever appeared and no new segments were added to our brains.

This still leaves us with the problem of how humans can be so intelligent when their brain has the same arrangement as a trout's. At this point all those centuries of anatomical cataloguing come in handy, because they tell us how heavy different animals' brains are. We like to think that human brains, at 1300 grams, are unusually large; indeed, comparison with the 500-gram chimp brain bears this out. However, bottlenose dolphin brains weigh in at around 1600 grams, while sperm whales are cerebral giants at 8000 grams, so sheer size is not the only thing that matters. However, in most mammals there is a strong mathematical relationship between body size and brain size: the weight of an animal's brain can usually be predicted with a high degree of accuracy from the weight of its body. This is why whales, for example, have such big brains. But not so with humans: our brains are at least three times as large as would be expected from the calculations, suggesting that we have evolved tremendous cerebral overcapacity.

This huge expansion of the human brain, most of which occurred within the last 10 million years, suggests that the differences between the mental abilities of humans and those of other animals are down to brain size: quantity, not quality. Perhaps we have passed a "critical mass" at which language, abstraction and all our other cognitive abilities can start to develop.

An additional trend in human brain evolution has been the way in which many functions have been shunted to novel locations. For example, sensory processing and control of movement have been squashed ever higher into the upper regions of our brain—the cerebral cortex. The huge human cortex may look like a larger version of any other animal's, but it is stuffed full of so many different functions that it may have come to work in a fundamentally different way.

ANATOMY RETURNS

Somewhat ironically, the one discipline where brain anatomy has not always held centre stage is brain science itself. Once the anatomists had completed their work in the early 20th century, neuroscientists promptly turned their backs on it as function superseded structure at the cutting edge of research. In the past few years, however, we have come to the realisation that to understand the function of the brain we must also understand its complex structure. Brain anatomy is in the ascendant again, and here are two reasons why.

The first is a practical, clinical one. Medical and veterinary students of my generation were often perplexed by the amount of time we spent studying brain anatomy, especially stained cross sections cut from the brains of dead people and animals. After all, the brain is invisible on radiographs and for most clinical purposes it was treated as a black box hiding inside the impenetrable skull. What use could all that anatomy possibly have?

However, an invention that has come along since I finished my clinical training has changed all that. Magnetic resonance imaging (MRI) scanners detect the radio pulses released by spinning protons as they realign in a magnetic field after they are knocked about by a pulse of radio waves. This phenomenon can be used to map the anatomy of the living brain, giving access to its workings for the first time. The information yielded by MRI comes in the form of computer-generated cross sections through the brain: suddenly, the old brain slices have taken on a new importance as part of the everyday process of diagnosing and treating disease.

The other reason why brain anatomy is important once again is a more philosophical one. Looking back over a century of studying brain function, one lesson is clear: we cannot truly understand a mental process until we know where it occurs. We now understand many complex brain processes—something that would have seemed incredible a few decades ago—and in every case that understanding followed our discovery of where the activity takes place. Memories are manipulated in the sea horse, fear in the almonds, vision is processed near the cockerel's spur, and hearing in the hillocks (colliculi). Once neuroscientists know where a process occurs, they can start to pick it apart and find out how it occurs.

The importance of place is also illustrated by a counter-example—consciousness. We are pretty sure that consciousness takes place in the brain and that it must have evolved by the same mechanisms as every other cerebral process. Beyond that we are stumped. There are many theories of the nature of consciousness, but they are often difficult to test. A major reason for this is that we do not know where consciousness happens, so we cannot study the brain regions which generate it. Of course, there may be no single area of the brain that produces consciousness—it may be widely distributed across many regions—but again we do not know what those regions are. Until we do, consciousness will remain stubbornly resistant to our investigations.

Brain anatomy is in vogue again. For much of the time humans have pondered the nature of the brain, its anatomy was all we knew. In the 20th century it looked as if function had overtaken structure as the best way to understand the brain, but we can now see that the two are inextricably linked. More than anywhere else in the body, in the brain a sense of geography is crucial. There are many fantastic journeys ahead.

Brainbox[*]

A History and Geography of the Brain

The Economist, December 23, 2006

The reason that people have brains is that they are worms. This is not a value judgment but a biological observation. Some animals, such as jellyfish and sea urchins, are radially symmetrical. Others are bilaterally symmetrical, which means they are long, thin and have heads.

Headless animals have no need for brains. But in those with a head the nerve cells responsible for it—and thus for sensing and feeding—tend to boss the others around. That still happens even when a long, thin, animal evolves limbs and a skeleton. Bilateralism equals braininess.

A healthy human brain contains about 100 billion nerve cells. What makes nerve cells special is that they have long filamentary projections called axons and dendrites which carry information around in the form of electrical pulses. Dendrites carry signals into the cell. Axons carry signals to other cells. The junction between an axon and a dendrite is called a synapse.

Information is carried across synapses not by electrical pulses but by chemical messengers called neurotransmitters. One way of classifying nerve cells is by the neurotransmitters they employ. Workaday nerve cells use molecules called glutamic acid and gamma aminobutyric acid. More specialised cells use dopamine, serotonin, acetylcholine and a variety of other molecules. Dopamine cells, for example, are involved in the brain's reward systems, generating feelings of pleasure.

Many brain drugs, both therapeutic and recreational, work either by mimicking neurotransmitters or altering their activity. Heroin mimics a group of molecules called endogenous opioids. Nicotine mimics acetylcholine. Prozac promotes the activity of serotonin. And cocaine boosts the effect of dopamine, which is one reason why it is so addictive.

Apart from specialised nerve cells, there is a lot of anatomical specialisation in the brain itself. Three large structures stand out: the cerebrum, the cerebellum and

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the brain stem. In addition, there is a cluster of smaller structures in the middle. These are loosely grouped into the limbic system and the basal ganglia, although not everyone agrees what is what.

Most brain structures, reflecting the bilateral nature of brainy organisms, are paired. In particular, the cerebrum is divided into hemispheres whose only direct connection is through three bundles of nerves, the most important of which is called the corpus callosum. (Many parts of the brain have obscure Latin names.)

This anatomical division of the brain reflects its evolutionary history. The brains of reptiles correspond more or less to the structures known in mammals as the brain stem and cerebellum. In mammals the brain stem is specialised for keeping the hearts and lungs working. The cerebellum is for movement, posture and learning processes associated with these two things. It is the limbic system, basal ganglia and cerebrum that do the interesting stuff that distinguishes mammalian brains from those of their reptilian ancestors.

The limbic system is itself divided. Some of the main parts are the hippocampus, the amygdala, the thalamus and the hypothalamus. The largest of the basal ganglia is the caudate. The pineal gland, which lies behind the limbic system, is the only brain structure that does not come in pairs. The 17th-century French philosopher René Descartes thought it was the seat of the human soul.

Descartes, however, was wrong. It is in fact the cerebrum's outer layer, the cerebral cortex that is man's true distinguishing feature. The cerebral cortex forms 80% of the mass of a human brain, compared with 30% of a rat's. It is divided into lobes, four on each side. The rearmost one, called the occipital, handles vision. Then come the parietal and temporal lobes, which deal with the other senses and with movement. At the front, as you would expect, is the frontal lobe.

This is humanity's "killer app", containing many of the cognitve functions associated with human-ness (although that most characteristic human function, language, is located in the temporal and parietal lobes, and only on one side, usually the left). Man's huge frontal lobes are the reason for the species' peculiarly shaped head. No wonder that in English-speaking countries the brainiest of the species are known as "highbrow".

In Our Messy, Reptilian Brains*

By Sharon Begley

Newsweek, April 9, 2007

Let others rhapsodize about the elegant design and astounding complexity of the human brain—the most complicated, most sophisticated entity in the known universe, as they say. David Linden, a professor of neuroscience at Johns Hopkins University, doesn't see it that way. To him, the brain is a "cobbled-together mess." Impressive in function, sure. But in its design the brain is "quirky, inefficient and bizarre . . . a weird agglomeration of ad hoc solutions that have accumulated throughout millions of years of evolutionary history," he argues in his new book, "The Accidental Mind," from Harvard University Press. More than another salvo in the battle over whether biological structures are the products of supernatural design or biological evolution (though Linden has no doubt it's the latter), research on our brain's primitive foundation is cracking such puzzles as why we cannot tickle ourselves, why we are driven to spin narratives even in our dreams and why reptilian traits persist in our gray matter.

Just as the mouse brain is a lizard brain "with some extra stuff thrown on top," Linden writes, the human brain is essentially a mouse brain with extra toppings. That's how we wound up with two vision systems. In amphibians, signals from the eye are processed in a region called the mid-brain, which, for instance, guides a frog's tongue to insects in midair and enables us to duck as an errant fastball bears down on us. Our kludgy brain retains this primitive visual structure even though most signals from the eye are processed in the visual cortex, a newer addition. If the latter is damaged, patients typically say they cannot see a thing. Yet if asked to reach for an object, many of them can grab it on the first try. And if asked to judge the emotional expression on a face, they get it right more often than chance would predict—especially if that expression is anger.

They're not lying about being unable to see. In such "blindsight," people who have lost what most of us think of as vision are seeing with the amphibian visual

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system. But because the midbrain is not connected to higher cognitive regions, they have no conscious awareness of an object's location or a face's expression. Consciously, the world looks inky black. But unconsciously, signals from the midbrain are merrily zipping along to the amygdala (which assesses emotion) and the motor cortex (which makes the arm reach out).

Primitive brains control movement with the cerebellum. Tucked in the back of the brain, this structure also predicts what a movement will feel like, and sends inhibitory signals to the somatosensory cortex, which processes the sense of touch, telling it not to pay attention to expected sensations (such as the feeling of clothes against your skin or the earth beneath your soles). This is why you can't tickle yourself—the reptilian cerebellum has kept the sensation from registering in the feeling part of the brain. Failing to register feelings caused by your own movements claims another victim: your sense of how hard you are hitting someone. Hence, "but Mom, he hit me harder!"

Neurons have hardly changed from those of prehistoric jellyfish. "Slow, leaky, unreliable," as Linden calls them, they tend to drop the ball: at connections between neurons, signals have a 70 percent chance of sputtering out. To make sure enough signals do get through, the brain needs to be massively interconnected, its 100 billion neurons forming an estimated 500 trillion synapses. This interconnectedness is far too great for our paltry 23,000 or so genes to specify. The developing brain therefore finishes its wiring out in the world (if they didn't, a baby's head wouldn't fit through the birth canal). Sensory feedback and experiences choreograph the dance of neurons during our long childhood, which is just another name for the period when the brain matures.

With modern parts atop old ones, the brain is like an iPod built around an eight-track cassette player. One reptilian legacy is that as our eyes sweep across the field of view, they make tiny jumps. At the points between where the eyes alight, what reaches the brain is blurry, so the visual cortex sees the neural equivalent of jump cuts. The brain nevertheless creates a coherent perception out of them, filling in the gaps of the jerky feed. What you see is continuous, smooth. But as often happens with kludges, the old components make their presence felt in newer systems, in this case taking a system that worked well in vision and enlisting it [in] higher-order cognition. Determined to construct a seamless story from jumpy input, for instance, patients with amnesia will, when asked what they did yesterday, construct a story out of memory scraps.

It isn't only amnesiacs whose brains confabulate. There is no good reason why dreams, which consolidate memories, should take a narrative form. If they're filing away memories, we should just experience memory fragments as each is processed. The cortex's narrative drive, however, doesn't turn off during sleep. Like an iPod turning on that cassette player, the fill-in-the-gaps that works so well for jumpy eye movements takes the raw material of memory and weaves it into a coherent, if bizarre, story. The reptilian brain lives on.