‘The story of the most complex object in the universe has never been told with greater clarity, insight and wit. Charting the route to future discoveries, this is a masterpiece.’ Adam Rutherford, author of *The Book of Humans*

‘Not only is this a work of phenomenal erudition, but it has the rare distinction among books on the brain of promoting no premature “explanation” of how this astonishingly complicated organ does its job. Instead, Cobb offers an honest appraisal both of what we know and what is still a mystery. There is no better primer to one of the most profound questions facing science today: how matter creates thought and consciousness.’ Philip Ball, author of *How to Grow a Human*

‘Thoughtful and thought-provoking, this is a book I wish I could have written, and one that I will be thinking about for a long time. It is a down payment for future brain research.’ Marina Picciotto, editor-in-chief, *Journal of Neuroscience*

‘Humanity’s quest to understand the brain has led us to some of our most important ideas, but as Matthew Cobb shows in his riveting, eye-opening book, that isn’t all it gave us. In fact, the road to our hi-tech present was strewn with brutes, eccentrics – and victims. Highly entertaining and deeply authoritative. Read it.’ Paul Mason, author of *Clear Bright Future*

‘*The Idea of the Brain* is a superb book describing the surprising history of research on how the Universe’s most complex object produces memories, consciousness and volition.’ Jerry Coyne, author of *Why Evolution is True*

‘This exquisitely researched and thrilling book charts an epic quest to understand our deepest selves. Its scale and scope is phenomenal, and it leaves us with a profound sense of wonder about science and humanity, as well as the brain itself. Altogether a feast.’ Daniel M. Davis, author of *The Beautiful Cure*

‘A scholarly and wonderfully entertaining guide to the advances that have driven our knowledge of the brain, and the extraordinary people who have made them.’ Chris Frith, author of *Making Up the Mind*

‘A masterful examination of the vast history of humans trying to figure out how the brain does its tricks. The scope, sweep and insight are

First published in Great Britain in 2020 by
PROFILE BOOKS LTD
29 Cloth Fair
London EC1A 7JQ

www.profilebooks.com

Cover design: Samantha Johnson
Cover image: iStock

A CIP catalogue record for this book is available from the British Library.

ISBN 9781781255896
eISBN 9781782832256

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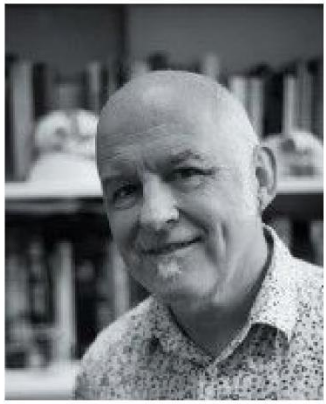

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Life's Greatest Secret: The Race to Crack the Genetic Code

The Egg and Sperm Race: The 17th-Century Scientists Who Unravelled the Secrets of Sex, Life and Growth

Smell: A Very Short Introduction

The Resistance: The French Fight Against the Nazis

Eleven Days in August: The Liberation of Paris in 1944

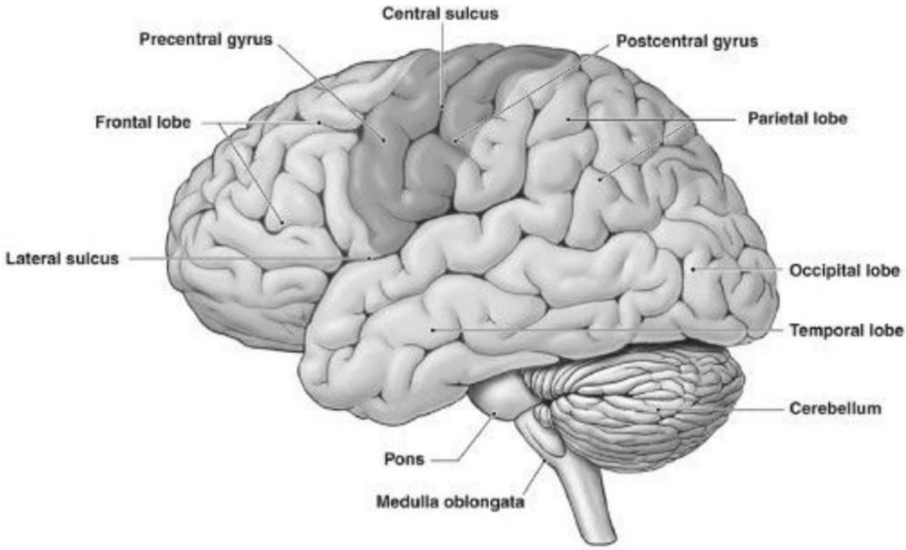
In memory of Kevin Connolly (1937–2015),
Professor of Psychology at the University of Sheffield,
who set me on the road to here.

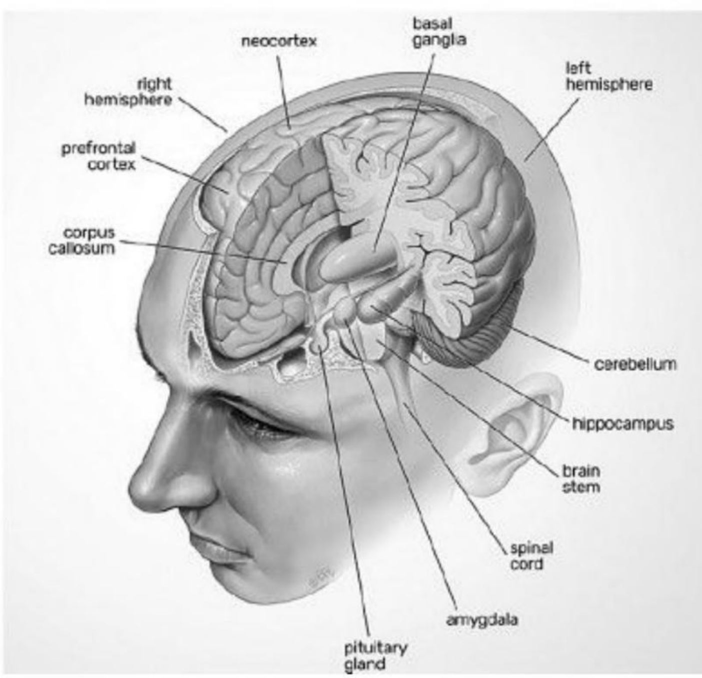
THE IDEA OF THE BRAIN

A HISTORY

Matthew Cobb

PROFILE BOOKS





Key areas of the human brain.

The brain being indeed a machine, we must not hope to find its artifice through other ways than those which are used to find the artifice of the other machines. It thus remains to do what we would do for any other machine; I mean to dismantle it piece by piece and to consider what these can do separately and together.

Nicolaus Steno, *On the Brain*, 1669

INTRODUCTION

In 1665 the Danish anatomist Nicolaus Steno addressed a small group of thinkers gathered together at Issy, on the southern outskirts of Paris. This informal meeting was one of the origins of the French Académie des Sciences; it was also the moment that the modern approach to understanding the brain was set out. In his lecture, Steno boldly argued that if we want to understand what the brain does and how it does it, rather than simply describing its component parts, we should view it as a machine and take it apart to see how it works.

This was a revolutionary idea, and for over 350 years we have been following Steno's suggestion – peering inside dead brains, removing bits from living ones, recording the electrical activity of nerve cells (neurons) and, most recently, altering neuronal function with the most astonishing consequences. Although most neuroscientists have never heard of Steno, his vision has dominated centuries of brain science and lies at the root of our remarkable progress in understanding this most extraordinary organ.

We can now make a mouse remember something about a smell it has never encountered, turn a bad mouse memory into a good one and even use a surge of electricity to change how people perceive faces. We are drawing up increasingly detailed and complex functional maps of the brain, human and otherwise. In some species we can change the brain's very structure at will, altering the animal's behaviour as a result. Some of the most profound consequences of our growing mastery can be seen in our ability to enable a paralysed person to control a robotic arm with the power of their mind.

We cannot do everything: at least for the moment, we cannot artificially create a precise sensory experience in a human brain (hallucinogenic drugs do this in an uncontrolled way), although it appears that we have the exquisite degree of control required to perform such an experiment in a mouse. Two groups of scientists recently trained mice to lick at a water bottle when the animals saw a set of stripes, while machines recorded how a small number of cells in the visual centres of the mice's brains responded to the image. The scientists then used complex optogenetic technology to artificially recreate that pattern of neuronal activity in the relevant brain cells. When this occurred, the animal responded as though it had seen the stripes, even though it was in complete darkness. One explanation is that, for the mouse, the pattern of neuronal activity was the same thing as seeing. More clever experimentation is needed to resolve this, but we stand on the brink of understanding how patterns of activity in networks of neurons create perception.

This book tells the story of centuries of discovery, showing how brilliant minds, some of them now forgotten, first identified that the brain is the organ that produces thought and then began to show what it might be doing. It describes the extraordinary discoveries that have been made as we have attempted to understand what the brain does, and delights in the ingenious experiments that have produced these insights.

But there is a significant flaw in this tale of astonishing progress, one that is rarely acknowledged in the many books that claim to explain how the brain works. Despite a solid bedrock of understanding, we have no clear comprehension about how billions, or millions, or thousands, or even tens of neurons work together to produce the brain's activity.

We know in general terms what is going on – brains interact with the world, and with the rest of our bodies, representing stimuli using both innate and acquired neural networks. Brains predict how those stimuli might change in order to be ready to respond, and as part of the body they organise its action. This is all achieved by neurons and their complex interconnections, including the many chemical signals in which they bathe. No matter how much it might go against your deepest feelings, there is no disembodied person floating in your head looking at this activity – it is all just neurons, their connectivity and the chemicals that swill about those networks.

However, when it comes to really understanding what happens in a brain at the level of neuronal networks and their component cells, or to being able to predict what will happen when the activity of a particular network is altered, we are still at the very beginning. We might be able to artificially induce visual perception in the brain of a mouse by copying a very precise pattern of neuronal activity, but we do not fully understand how and why visual perception produces that pattern of activity in the first place.

A key clue to explaining how we have made such amazing progress and yet have still barely scratched the surface of the astonishing organ in our heads is to be found in Steno's suggestion that we should treat the brain as a machine. 'Machine' has meant very different things over the centuries, and each of those meanings has had consequences for how we view the brain. In Steno's time the only kinds of machine that existed were based on either hydraulic power or clockwork. The insights these mahcines could provide about the structure and function of the brain soon proved limited, and no one now looks at the brain this way. With the discovery that nerves respond to electrical stimulation, in the nineteenth century the brain was seen first as some kind of telegraph network and then, following the identification of neurons and synapses, as a telephone exchange, allowing for flexible organisation and output (this metaphor is still occasionally used in research articles).

Since the 1950s our ideas have been dominated by concepts that surged into biology from computing – feedback loops, information, codes and computation. But although many of the functions we have identified in the brain generally involve some kind of computation, there are only a few fully understood examples, and some of the most brilliant and influential theoretical intuitions about how nervous systems might 'compute' have turned out to be wrong. Above all, as the mid-twentieth-century scientists who first drew the parallel between brain and computer soon realised, the brain is not digital. Even the simplest animal brain is not a computer like anything we have built, nor one we can yet envisage. The brain is not a computer, but it is more like a computer than it is like a clock, and by thinking about the parallels between a computer and a brain we can gain insight into what is going on inside both our heads and those of animals.

Exploring these ideas about the brain – the kinds of machine we have imagined brains to be – makes it clear that, although we are still far from fully understanding the brain, the ways in which we think about it are much richer than in the past, not simply because of the amazing facts we have discovered, but above all because of how we interpret them.

These changes have an important implication. Over the centuries, each layer of technological metaphor has added something to our understanding, enabling us to carry out new experiments and reinterpret old findings. But by holding tightly to metaphors, we end up limiting what and how we can think. A number of scientists are now realising that, by viewing the brain as a computer that passively responds to inputs and processes data, we forget that it is an active organ, part of a body that is intervening in the world and which has an evolutionary past that has shaped its structure and function. We are missing out key parts of its activity. In other words, metaphors shape our ideas in ways that are not always helpful.

The tantalising implication of the link between technology and brain science is that tomorrow our ideas will be altered yet again by the appearance of new and as yet unforeseen technological developments. As that new insight emerges, we will reinterpret our current certainties, discard some mistaken assumptions and develop new theories and ways of understanding. When scientists realise that how they think – including the questions they can ask and the experiments they can imagine – is partly framed and limited by technological metaphors, they often get excited at the prospect of the future and want to know what the Next Big Thing will be and how they can apply it to their research. If I had the slightest idea, I would be very rich.

*

This book is not a history of neuroscience, nor a history of brain anatomy and physiology, nor a history of the study of consciousness, nor a history of psychology. It contains some of these things, but the history I tell is rather different, for two reasons. First, I want to explore the rich variety of ways in which we have thought about what brains do and how they do it, focusing on experimental evidence – this is rather different from telling the story of an academic discipline. It also means that the book does not deal solely with how we have thought about the human brain – other brains in other animals, not all of them mammals, have shed light on what is happening in our heads.

The history of how we have understood the brain contains recurring themes and arguments, some of which still provoke intense debate today. One example is the perpetual dispute over the extent to which functions are localised in specific areas of the brain. That idea goes back thousands of years, and there have been repeated claims up to today that bits of the brain appear to be responsible for a specific thing, such as the feeling in your hand, or your ability to understand syntax or to exert self-control. These kinds of claims have often soon been nuanced by the revelation that other parts of the brain may influence or supplement this activity, and that the brain region in question is also involved in other processes. Repeatedly, localisation has not exactly been overturned, but it has become far fuzzier than originally thought. The reason is simple. Brains, unlike any machine, have not been designed. They are organs that have evolved for over five hundred million years, so there is little or no reason to expect they truly function like the machines we create. This implies that although Steno's starting point – treating the brain as a machine – has been incredibly productive, it will never produce a satisfying and full description of how brains work.

The interaction between brain science and technology – the thread that runs through this book – highlights the fact that science is embedded in culture. So an element of this story reveals how these ideas have reverberated through the works of Shakespeare, Mary Shelley, Philip K. Dick and others. Intriguingly, cultural history shows that metaphors can flow both ways – in the nineteenth century, just as the brain and the nervous system were thought of as a telegraph network, so too the flow of Morse Code messages down the telegraph wires and the responses they evoked in their human readers were seen in terms of nervous activity. Similarly, at its birth the computer was seen as a brain – biological discoveries were used to justify John von Neumann's plans to build the first digital computer, rather than the other way around.

The second reason why this is not simply a history can be seen from the contents page – the book is divided into three parts: Past, Present and Future. The conclusion of the 'Present' section, which deals with how our understanding of the brain has developed over the last seventy years or so under the computational metaphor, is that some researchers sense we are approaching an impasse in how we understand the brain.

This might seem paradoxical – we are accumulating vast amounts of data about structure and function in a huge array of brains, from the tiniest to our own. Tens of thousands of researchers are devoting massive amounts of time and energy to thinking about what brains do, and astonishing new technology is enabling us to both describe and manipulate that activity. Every day we hear about new discoveries that shed light on how brains work, along with the promise – or threat – of new technology that will enable us to do such far-fetched things as read minds, or detect criminals, or even be uploaded into a computer.

In contrast to all this exuberance, there is a feeling among some neuroscientists, as shown by think-pieces in academic journals and books over the last decade or so, that our future path is not clear. It is hard to see where we should be going, apart from simply collecting more data or counting on the latest exciting experimental approach. That does not mean that everyone is pessimistic – some confidently claim that the application of new mathematical methods will enable us to understand the myriad interconnections in the human brain. Others favour studying animals at the other end of the scale, focusing our attention on the tiny brains of worms or maggots and employing the well-established approach of seeking to understand how a simple system works, and then applying those lessons to more complex cases. Many neuroscientists, if they think about the problem at all, simply consider that progress will inevitably be piecemeal and slow, because there is no Grand Unified Theory of the brain lurking around the corner.

The problem is twofold. Firstly, the brain is mind-bogglingly complicated. A brain – any brain, not just the human brain, which has been the focus of much of the intellectual endeavour described here – is the most complex object in the known universe. The astronomer Lord Rees has pointed out that an insect is more complex than a star, while for Darwin the brain of an ant, which is so tiny but which can produce such diverse behaviour, was 'one of the most marvellous atoms of matter in the world, perhaps more so than the brain of a man'. That is the scale of the challenge before us.

Which leads to the second aspect. Despite the tsunami of brain-related data being produced by laboratories around the world, we are in a crisis of ideas about what to do with all that data, about what it all means. I think that this reveals that the computer metaphor, which has served us so well for over half a century, may be reaching its limits, just as the idea of a brain as a telegraph system eventually exhausted its power in the nineteenth century. Some scientists are now explicitly challenging the usefulness of some of our most basic metaphors about the brain and nervous systems, such as the idea that neuronal networks represent the outside world, through a neuronal code. This suggests that scientific understanding may be chafing at the framework imposed by our most deeply held metaphors about how the brain works.

It may prove to be that even in the absence of new technology, developments in computing, in particular relating to artificial intelligence and neural networks – which are partly inspired by how brains do things – will feed back into our views of the brain, giving the computational metaphor a new lease of life. Perhaps. But, as you will see, leading researchers in deep learning – the most fashionable and astonishing part of modern computer science – cheerfully admit that they do not know how their programs do what they do. I am not sure that computing will provide enlightenment as to how the brain works.

One of the most tragic indicators of our underlying uncertainty about the brain is the very real crisis in our understanding of mental health. From the 1950s, science and medicine embraced chemical approaches to treating mental illness. Billions of dollars have been spent developing drugs, but it is still not clear how, nor even if, many of these widely prescribed treatments work. As to future pharmaceutical approaches to major mental health problems, there is nothing on the horizon – most of the large drug companies have abandoned the search for new drugs to treat conditions such as depression or anxiety, considering that both the costs and the risks are far too great. This situation is not surprising – if we do not yet properly understand the functioning of even the simplest animal brains, there does not seem much prospect of responding effectively when things apparently go awry in our own heads.

A great deal of energy and resources are being devoted to describing the myriad connections between neurons in brains, to create what are called connectomes, or more crudely and metaphorically, wiring diagrams. There is currently no prospect of creating a cell-level connectome of a mammalian brain – they are far too complex – but lower-definition maps are being established. Such efforts are essential – we need to understand how bits of the brain are connected – but on their own they will not produce a model of what the brain does. Nor should we underestimate how long this might take. Researchers are currently drawing up a functional connectome that includes all 10,000 cells in a maggot brain, but I would be amazed if, in fifty years' time, we fully understand what those cells and their interconnections are doing. From this point of view, properly understanding the human brain, with its tens of billions of cells and its incredible and eerie ability to produce the mind, may seem an unattainable dream. But science is the only method that can reach this goal, and it will reach it, eventually.

There have been many similar moments in the past, when brain researchers became uncertain about how to proceed. In the 1870s, with the waning of the telegraph metaphor, doubt rippled through brain science and many researchers concluded it might never be possible to explain the nature of consciousness. One hundred and fifty years later we still do not understand how consciousness emerges, but scientists are more confident that it will one day be possible to know, even if the challenges are enormous.

Understanding how past thinkers have struggled to understand brain function is part of framing what we need to be doing now, in order to reach that goal. Our current ignorance should not be viewed as a sign of defeat but as a challenge, a way of focusing attention and resources on what needs to be discovered and on how to develop a programme of research for finding the answers. That is the subject of the final, speculative part of this book, which deals with the future. Some readers will find this section provocative, but that is my intention – to provoke reflection about what the brain is, what it does and how it does it, and above all to encourage thinking about how we can take the next step, even in the absence of new technological metaphors. It is one of the reasons this book is more than a history, and it highlights why the four most important words in science are ‘We do not know’.

Manchester, December 2019

PAST

THE HISTORY OF SCIENCE is rather different from other kinds of history, because science is generally progressive – each stage builds upon previous insights, integrating, rejecting or transforming them. This produces what appears to be an increasingly accurate understanding of the world, although that knowledge is never complete, and future discoveries can overthrow what was once seen as the truth. This underlying progressive aspect leads many scientists to portray the history of their subject as a procession of great men (and it generally has been men), each of whom is given approval if they are seen as having been right, or criticised – or ignored – if they were wrong. In reality, the history of science is not a progression of brilliant theories and discoveries: it is full of chance events, mistakes and confusion.

To properly understand the past, to provide a full background to today's theories and frameworks, and even to imagine what tomorrow may hold, we must remember that past ideas were not seen as steps on the road to our current understanding. They were fully fledged views in their own right, in all their complexity and lack of clarity. Every idea, no matter how outdated, was once modern, exciting and new. We can be amused at strange ideas from the past, but condescension is not allowed – what seems obvious to us is only that way because past errors, which were generally difficult to detect, were eventually overcome through a great deal of hard work and harder thinking.

Where people in the past accepted mistaken or what now appear to be unbelievable ideas, the challenge is to understand why. Often, what now might be taken as ambiguity or lack of clarity in an approach or set of ideas in fact explains why those ideas were accepted. Such imprecise theories may allow scientists with different views to accept a common framework, pending the arrival of decisive experimental evidence.

We should never dismiss past ideas – or people – as stupid. We will be the past one day, and our ideas will no doubt seem surprising and amusing to our descendants. We are simply doing the best we can, just as our forebears did. And, like previous generations, our scientific ideas are influenced not only by the internal world of scientific evidence, but also by the general social and technological context in which we develop those ideas. Where our theories and interpretations are wrong or inadequate, they will be proved so by future experimental evidence and we will all move on. That is the power of science.

– ONE –

HEART

PREHISTORY TO 17TH CENTURY

The scientific consensus is that, in ways we do not understand, thought is produced by the activity of billions of cells in the most complex structure in the known universe – the human brain. Surprising as it may be, this focus on the brain seems to be a relatively recent development. Virtually all we know from prehistory and history suggests that for most of our past we have viewed the heart, not the brain, as the fundamental organ of thought and feeling. The power of these old, pre-scientific views can be seen in our everyday language – words and phrases like 'learn by heart', 'heartbroken', 'heartfelt', and so on (similar examples can be found in many other languages). These phrases still carry the emotional charge of the old world-view that we have supposedly discarded – try replacing the word 'heart' by 'brain' and see how it feels.

Our earliest written artefacts show the importance of this idea to past cultures. In the *Epic of Gilgamesh*, a 4,000-year-old story written in what is now Iraq, emotions and feelings were clearly based in the heart, while in the Indian Rigveda, a collection of Vedic Sanskrit hymns written around 3,200 years ago, the heart is the site of thought.[1] The Shabaka Stone, a shiny grey slab of basalt from ancient Egypt, now in the British Museum, is covered in hieroglyphs that describe a 3,000-year-old Egyptian myth focused on the importance of the heart in thinking.[2] The Old Testament reveals that at around the same time as the Shabaka Stone was carved, the Jews considered the heart to be the origin of thought in both humans and God.[3]

Heart-centred views also existed in the Americas, where the great empires of Central America – the Maya (250–900 CE) and the Aztecs (1400–1500 CE) – both focused on the heart as the source of emotions and thought. We also have some insight into the beliefs of those peoples from North and Central America who did not develop extensive urban cultures. In the early years of the twentieth century, US ethnographers worked with indigenous peoples, documenting their traditions and beliefs. Although we cannot be certain that the recorded views were typical of the cultures that existed before the arrival of Europeans, most of the peoples who contributed to these studies considered that something like a 'life-soul', or an emotional consciousness, was linked to the heart and to breath. This view was widespread, from Greenland to Nicaragua, and was held by peoples with ecologies as diverse as the Eskimo, the Coast Salish of the Pacific north-west, and the Hopi of Arizona.[4]

These views are remarkably congruent with the account of the Swiss psychoanalyst Carl Jung, who in the early decades of the twentieth century travelled to New Mexico. On the roof of one of the white adobe buildings built by the Pueblo people on the high Taos plateau, Jung talked with Ochwiay Biano of the Taos Pueblo. Biano told Jung that he did not understand white people, whom he considered cruel, uneasy and restless – 'We think that they are mad', he said. Intrigued, Jung asked Biano why he thought this:

> 'They say they think with their heads,' he replied.
> 'Why, of course, what do you think with?' I asked him in surprise.
> 'We think here,' he said, indicating his heart.[5]

Not all cultures have shared this widespread focus on the heart. On the other side of the planet, a key aspect of the outlook of the

Aboriginal and Torres Strait Islander peoples in Australia was (and is) their link with the land, which extends to ideas about mind and spirit. Locating the seat of thought within the body appears not to have been part of their world view.[6] Similarly, traditional Chinese approaches to medicine and anatomy were primarily focused on the interactions of a series of forces, rather than localisation of function. However, when Chinese thinkers did seek to identify the roles of particular organs, the heart was the key.[7] The Guanzi, a document originally written by the Chinese philosopher Guan Zhong in the seventh century BCE, argued that the heart was fundamental for all functions of the body, including the senses.

Heart-centred views correspond to our everyday experience – the heart changes its rhythm at the same time as our feelings change, while powerful emotions such as anger, lust or fear seem to be focused on one or more of our internal organs, and to course through our bodies and change our way of thinking as though they are transported in, or simply are, our blood. This is why those old phrases about being 'down at heart' and so on have persisted – they correspond to the way we perceive an important part of our inner life. Just as with the appearance that the sun goes around the earth, everyday experience of being human provided a simple explanation of where we think – our hearts. People believed this idea because it made sense.

*

Even though the heart was widely seen as the centre of our inner life, certain cultures recognised that the brain had some kind of function, even if this could only be detected through injury. For example, in ancient Egypt a number of scribes created a medical document known as the Edwin Smith Papyrus.[8] The manuscript includes a brief description of the convolutions of the brain and the recognition that damage to one side of the head could be accompanied by paralysis on the opposite side of the body, but for these writers, as for all ancient Egyptians, the heart was nevertheless the seat of the soul and mental activity.

The first recorded challenge to our global heart-centred view occurred in ancient Greece. In the space of about three and a half centuries, between 600 and 250 BCE, Greek philosophers shaped the way that the modern world views so many things, including the brain. The early Greeks, like other peoples, considered that the heart was the origin of feelings and thought. This can be seen in the epic oral poems now attributed to Homer, which were created sometime between the twelfth and eighth centuries BCE; similarly, the ideas of the earliest recorded philosophers were focused on the heart.[9] In the fifth century BCE the philosopher Alcmaeon took issue with this view. Alcmaeon lived in Croton, a Greek town in the 'foot' of Italy, and is sometimes presented as a physician and as the father of neuroscience, although everything we know of him and his work is hearsay. None of his writings survive – all that remain are fragments quoted by later thinkers.

Alcmaeon was interested in the senses, and this naturally led him to focus on the head, where the key sense organs are grouped. According to subsequent writers, Alcmaeon showed that the eyes, and by extension the other sense organs, were connected to the brain by what he called narrow tubes. Aetius, living 300 years after Alcmaeon, is reported as having said that, for Alcmaeon, 'the governing facility of intelligence is the brain'. It is not clear how exactly Alcmaeon arrived at this conclusion – subsequent writers imply that he based his ideas not simply on introspection and philosophical musings, but also on direct investigation, although there is no evidence of this. He may have dissected an eyeball (not necessarily a human one) or he may have witnessed the culinary preparation of an animal's head, or he may simply have used his fingers to see how the eyes, tongue and nose were connected to the inner parts of an animal's skull.[10]

Despite these insights, the earliest unambiguous statements about the centrality of the brain were written several decades after Alcmaeon died; they came from the school of medicine on the island of Kos, whose most famous member was Hippocrates. Many of the works produced by the Kos school of medicine are attributed to Hippocrates, although the actual authors are unknown. One of the most significant of these documents was *On the Sacred Disease*, which was written around 400 BCE for a non-specialist audience and dealt with epilepsy (why epilepsy was considered a sacred or divine disease is unclear[11]). According to the author(s):

> It ought to be generally known that the source of our pleasure merriment, laughter, and amusement, as of our grief, pain, anxiety, and tears, is none other than the brain. It is specially the organ which enables us to think, see, and hear, and to distinguish the ugly and the beautiful, the bad and the good, pleasant and unpleasant ... It is the brain too which is the seat of madness and delirium, of the fears and frights which assail us, often by night, but sometimes even by day, it is there where lies the cause of insomnia and sleep-walking, of thoughts that will not come, forgotten duties, and eccentricities.[12]

The argument in *On the Sacred Disease* was based partly on some pioneering but rudimentary anatomy ('the brain of man, as in all other animals, is double, and a thin membrane divides it through the middle', the author(s) stated), but it also revealed a great deal of confusion. For example, the document claimed that 'when a person draws in air by the mouth and nostrils, the breath goes first to the brain', arguing that the veins transport air around the body. Epilepsy was explained by the idea that a humour or fluid called phlegm entered the veins, preventing the air from getting to the brain and so causing the fit. Some people took the implications of localising epilepsy to the brain very seriously. Aretaeus the Cappadocian, a Greek physician who lived around 150 BCE, treated it by trepanation – drilling holes in the skull – a tradition that lived on in European medical manuals until the eighteenth century.[13]

Aretaeus did not invent this operation – the earliest traces of any medical intervention are holes that were drilled or scraped into people's skulls and which can be found all over the planet, sometimes from over 10,000 years ago.[14] Although it is tempting to view prehistoric trepanation as an early form of psychosurgery (it is often suggested that trepanation was performed to let out 'evil spirits'), the global dominance of heart-centred ideas about the origins of thought suggests this is unlikely. There are more credible justifications for such a dangerous operation, including relief of painful subcranial bleeding or removal of bone fragments following a head injury.

Despite the arguments of Alcmaeon and of the Kos school, in the absence of any evidence to prove that the brain is the site of thought and emotion, there was no reason to prefer this claim to the obvious explanation that the heart plays this role. This led one of the most influential Greek philosophers, Aristotle, to dismiss the idea that the brain played any significant part in thinking or movement. As he wrote in *Parts of Animals*:

> And of course, the brain is not responsible for any of the sensations at all. The correct view [is] that the seat and source of sensation is the region of the heart ... the motions of pleasure and pain, and generally all sensation plainly have their source in the heart.

Aristotle's argument for the centrality of the heart was based on apparently self-evident principles, such as the link between movement, heat and thought. Aristotle noted that the heart clearly changed its activity at the same time as emotions were felt, whereas the brain apparently did nothing; he also affirmed that the heart was the source of blood, which is necessary for sensation, while the brain contained no blood of its own. Furthermore, all large animals have a heart, whereas – he claimed – only the higher animals have a brain. His final argument was that the heart is warm and shows movement, both of which were seen as essential features of life; in contrast, the brain is immobile and cold.[15] Given there was no actual proof of any link between thought and the brain, Aristotle's logical arguments were just as valid as those to be found in the writings of the Kos school. There was no way to choose between them. Elsewhere around the planet, things continued as before: for the vast majority of people, the heart was what counted.

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After Aristotle's death, insight into the role of the brain emerged from Alexandria, at the western edge of the Nile Delta, in Greek-ruled Egypt. With a grid system of streets, underground plumbing and a multicultural population, Alexandria was one of the most significant centres of the Graeco-Roman world. Among those who benefited from this fertile intellectual atmosphere were the two leading Greek anatomists of the period, Herophilus of Chalcedon and Erasistratus of Ceos, both of whom worked in Alexandria.[16]

None of the writings of Herophilus and Erasistratus have survived, but subsequent writers claimed that they made important discoveries in the structure of the brain. The reason these breakthroughs came about in Alexandria was that, for a brief period, and apparently for the first time in history, the dissection of human bodies was permitted. It is even said that criminals who were condemned to death were vivisected under what must have been appalling circumstances. Exactly why dissection was allowed in Alexandria but not elsewhere is unclear, but whatever the case, physicians in the city made substantial anatomical advances relating to the liver, the eye and the circulatory system. They even described the heart as a pump.

The direct study of human anatomy enabled Herophilus and Erasistratus to make significant discoveries with regard to the brain and the nervous system. Herophilus supposedly described the anatomy of two key parts of the human brain – the cortex (the two large lobes of the brain), and the cerebellum, at the back of the brain, which he considered to be the seat of intelligence – as well as showing the origin of the spinal cord and how the nerves branch. He is said to have distinguished between nerves that were linked to the sense organs and the motor nerves that guide behaviour, developing a theory of sensation in which the optic nerve was hollow and some kind of air moved through this space.[17] Erasistratus apparently took a different approach, comparing the human brain with the brains of stags and hares, concluding that the greater complexity of the human brain, as shown by its convolutions, was responsible for our greater intelligence.

Despite the accuracy of their descriptions, the work of Herophilus and Erasistratus did not settle the issue of whether the heart or the brain is the site of thought and feeling. They merely showed that the brain was complicated. Aristotle's heart-centred view remained enormously influential, partly because of his immense prestige, but above all because it corresponded to everyday experience.

It was another 400 years before decisive evidence about the role of the brain was obtained, through the work of one of the most influential thinkers in the history of Western civilisation: Galen. A Roman citizen, Galen was born in 129 CE to a wealthy family in the city of Pergamon in what is now western Turkey.[18] Although today Galen is principally known as a writer on medical matters – his ideas shaped Western medicine and culture for 1,500 years – he was in fact one of the major thinkers of the late Roman world, producing millions of words of philosophy, poetry and prose.[19]

Galen travelled and studied throughout the eastern Mediterranean, including Alexandria, but the key years of his life were spent in Rome. He arrived there in 162 CE, aged thirty-two, following a four-year stint as physician to the gladiators in Pergamon, during which time he learned much about the human body by treating the fighters' wounds. He soon became a fashionable Roman physician, attending some of the leading figures in the city, including Emperor Marcus Aurelius, and gaining a reputation as a brilliant anatomist who had a taste for polemical argument. To demonstrate his discoveries Galen used 'lecture-commentaries' in which he simultaneously described his new knowledge and showed it in an animal. In these lectures the audience was invited to witness Galen's performance, and thereby to validate his claims – this was part of Galen's emphasis on the importance of experience in understanding. (The following explanation of how Galen came to some of his conclusions is rather grisly. If you are squeamish, you might prefer to skip the next three paragraphs.)

One of the key issues that interested Galen was the role of the brain and the location of thought and the soul – he was convinced that the brain was fundamental to behaviour and thought, and that he could prove it by experimentation on animals. All this at a time where there were no anaesthetics. Galen was not immune to the horror that he was inflicting – he counselled against using monkeys as their facial expressions during the experiment were too disturbing. Although Galen disagreed with those who argued that animals lacked part of the soul relating to anger and desire, he said nothing about pain – pain is not to be found in his descriptions of his work.[20]

One of Galen's most decisive experiments focused on the role of the nerves in the production of the voice; this was done on a pig because 'the animal that squeals the loudest is the most convenient for experiments in which the voice is harmed'.[21] With the poor pig strapped down on its back, its muzzle bound tightly shut, Galen cut into the flesh and revealed the recurrent laryngeal nerves that run either side of the carotid artery in the neck. If he tied a thread tightly round the nerves, the muffled squealing of the animal ceased; if he loosened the ligature, the voice would return. Although squealing was clearly produced by the larynx, something appeared to be moving down the nerves from the brain.

This insight was reinforced by one of Galen's most remarkable demonstrations, in which he proved the importance of the brain by directly confronting opponents with the implications of their heart-centred views. Having cut open a living animal, Galen obliged his contradictor to squeeze the beast's heart and prevent it from beating. Even with the heart stopped, the poor animal continued its muted whimpers, showing that the movement of the heart was not necessary for the animal to make sounds. But when Galen opened the skull and made his rival press on the brain, the animal immediately stopped making a noise and became unconscious. When the pressure was released, Galen reported, 'the animal returns to consciousness and can move again'. This must have been quite astonishing for the audience. As the historian Maud Gleason has put it, 'Galen's anatomical performances look less and less like an intellectual debate and more like a magic show.'[22]

On the basis of this evidence – supported by many other anatomical descriptions and surgical interventions, including on patients – Galen became certain that the brain was the centre of thought. He argued that the brain produced a special kind of air or *pneuma* that leaked out if the brain was injured, producing unconsciousness; when enough of this air accumulated, consciousness returned. Movement of the body was a consequence of the air produced by the brain moving down the apparently hollow nerves, Galen said. His anatomical work – most of it done on animals rather than on humans – showed that all nerves came from the brain, not the heart as Aristotle had claimed.

Despite the evidence that Galen presented, the authority of thinkers such as Aristotle and the power of everyday experience prevented brain-centred views from driving out the old ideas, even in Rome. Galen left an immense volume of work – around 400 treatises, of which over 170 survive, covering the whole range of medicine and natural science – but the decline and fall of the Roman Empire led to a collapse of the intellectual environment that could have permitted further discoveries. Simply thinking about where thought came from would never resolve the issue – as Galen's work indicated, it would require anatomical and experimental investigation, which in turn could occur only in a context of intellectual openness and knowledge of past successes and failures through the circulation of ideas. Those conditions would not be repeated for centuries.

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Much of the cultural heritage of Rome and Greece was preserved in the libraries of the eastern Roman Empire, centred on Byzantium (modern-day Istanbul). From the seventh century onwards, the appearance of various caliphates associated with the rise of Islam led to a culture that spread to France in the west, to Bulgaria in the north and to Turkmenistan and Afghanistan in the east. This Islamic society placed a high value on knowledge and technical skills, and to meet the appetites of the new dominant classes and ruling groups, bridges and canals were constructed, horoscopes were cast, paper and glass were made. All this required rediscovering old wisdom or developing new understanding.[23]

First there was a wave of translations of the Greek and Roman texts that could be found in Persian or Byzantine libraries – this trend was centred on Baghdad and was sponsored by the caliphs and rich merchants. The ideas in these documents were soon extended as thinkers developed whole new areas of knowledge such as algebra, astronomy, optics and chemistry. But medicine and anatomy remained firmly anchored in Greek and Roman views, tied to the texts that were translated. In particular, the arguments about the roles of the heart and the brain that had existed since the time of Aristotle and Hippocrates were transmitted down the centuries more or less intact.

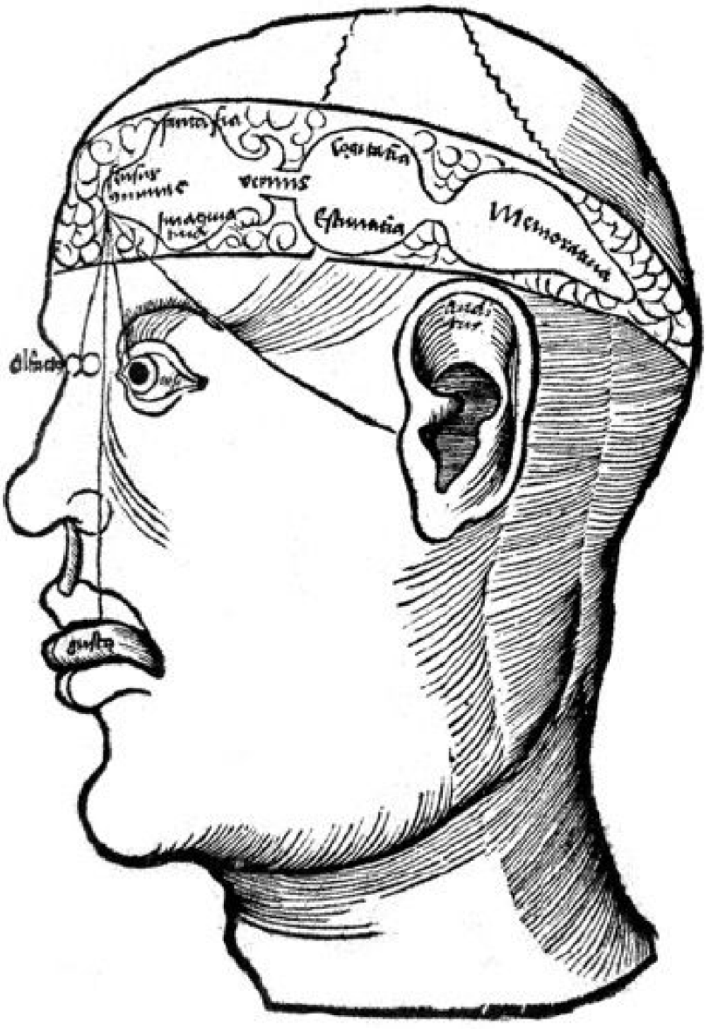
One of the leading physicians and philosophers of this period was Ibn-Sīnā, known in the West as Avicenna. Born in what is now Uzbekistan in 980, Avicenna lived in what is now Iran and wrote hundreds of books. His work combined Greek and Arabic thinking as well as treatments and diagnoses from as far afield as India; translated into Latin in the twelfth century, it exerted a profound influence on Western medicine for 500 years. Avicenna accepted Galen's claim that nerves arise from the brain or the spinal cord, but insisted, like Aristotle, that the primary source of all movement and sensation was nevertheless the heart.[24] This view also fitted with the Qur'an, which often refers to the heart as the source of understanding and, like the Bible, contains no mention of the brain at all.

Another route by which Galen's ideas were transmitted during this period was through the work of the tenth-century physician 'Alī ibn al-'Abbās Mağūsī, known in the West as Haly Abbas – a historian has described him as 'a Persian who took an Arab name and wrote in the language of the Qu'ran, a Zoroastrian who was imbibed with Greek traditions, a thinker from the Islamic world who was adopted by the Western Latin community less than a century after his death'. To emphasise the cosmopolitan mix of this period, his work was subsequently translated into Latin in Italy by a Christian monk who had been a Muslim refugee from North Africa.[25]

Among the writings of Galen that Haly Abbas translated were those covering the structure and the role of the brain: 'The brain is the principal organ of the psychical members. For within the brain is seated memory, reason and intellect, and from the brain is distributed the power, sensation and voluntary motion.'[26]

Haly Abbas also put forward an idea that was not present in Galen – he claimed that the three cavities or ventricles in the brain were full of animal spirits* that were created in the heart and transported in the blood. Each of the ventricles, he said, had a different psychological function: 'Animal spirit in the anterior ventricles creates sensation and imagination, animal spirit in the middle ventricle becomes intellect or reason, and animal spirit transmitted to the posterior ventricle produces motion and memory.'

Despite the lack of evidence for this idea, it was widely held throughout Europe and the Middle East for over a millennium.[27] It had first appeared in the writings of the fourth-century Bishop Nemesius of Emesa in Syria, and a few decades later was briefly mentioned by Saint Augustine, thereby acquiring a patina of religious approval that helped maintain its popularity.[28] For over 1,200 years, ventricular localisation was widely accepted as self-evident – between the fourth and sixteenth centuries, at least twenty-four different versions were put forward.[29] Among those who unquestioningly accepted this theory were some of the greatest thinkers of Europe and the Arab world, including Leonardo da Vinci, Roger Bacon, Thomas Aquinas, Averroes and Avicenna.



The theory of ventricular localisation as portrayed by Gregor Reisch, from 1504. Perception and imagination are located in the front, cognition in the centre and memory at the back.

*

By the beginning of the thirteenth century, Latin translations of Avicenna’s writings, including its uneasy alliance of ventricular localisation and a heart-centred origin for all thought and emotion, became dominant in the new universities of Europe.

Although Haly Abbas's version of Galen's brain-centred views had been spread by the medical school of Salerno, south of Naples, Avicenna's ideas were eventually favoured because they were based on Aristotle's philosophy. Aristotle's ideas came to dominate thinking in Europe partly through the writings of the Dominican monk Thomas Aquinas, who towered over Western intellectual life for centuries. Aquinas sought to render Aristotle's ideas compatible with Christianity, fusing Christian dogma with the contradictory ideas of the ancient pagans. Areas of understanding that should have been the focus of empirical investigation, such as anatomy, became shrouded in a fog of religiosity, with theologians playing a decisive role in transmitting knowledge and in determining what was acceptable.

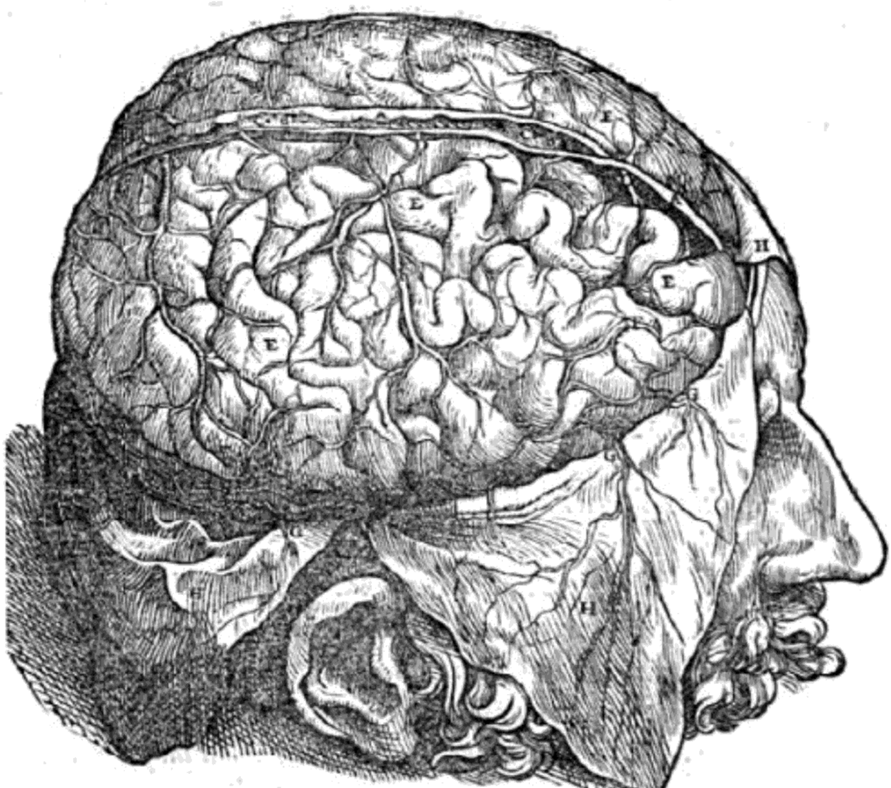
Readers of these newly available texts were well aware of the difference between the heart-centred view of Avicenna and Aristotle, the brain-oriented conceptions of the Salerno school and Galen, and the various attempts to reconcile them. In the thirteenth century, for example, Albertus Magnus squared the circle by simply arguing that Galen was wrong, and that all nerves did indeed have their origin in the heart, as Aristotle said.[30] The modern response to such contradictory claims would be to make direct observations; the solution in the Middle Ages was scholastic and theoretical – thinkers tried to resolve the contrasting views of their revered predecessors by close textual analysis, not by experimentation.

But at the beginning of the fourteenth century, medieval scholasticism's grip on anatomical knowledge was loosened slightly in the Bologna medical school, where Mondino de Luzzi was Professor of Medicine and Anatomy. Mondino wrote a manuscript entitled *Anatomia Mundini* (Mondino's Anatomy), which was based on his experience of dissecting the human body – the first such account since the time of Erasistratus and Herophilus in Alexandria over 1,500 years earlier.

The moral and sociological changes of the early 1300s that allowed Mondino to carry out dissections are not clear. The cadavers he dissected appear to be those of criminals (his instructions begin, matter-of-factly: 'The human corpse, killed through decapitation or hanging, is placed in the supine position.'[31]) There were some precedents – animal dissections were carried out in Salerno in the twelfth century, and post-mortem investigations had taken place in Bologna in the previous decades, apparently in order to determine the cause of death. Mondino's integration of dissection into the training of physicians may therefore have felt more like an obvious development, rather than a daring innovation.[32] It did not mark a break with religious teaching – dissection was not forbidden by either Christian or Islamic theology. Some Arabic texts from the ninth and twelfth centuries refer to dissection, but in general it seems that when scholars discovered and translated the writings of Galen and Aristotle, they were satisfied with the knowledge they contained, and did not seek to compare the views of the ancients with their own observations.[33] That now began to change. And unlike the brief period in Alexandria over 1,500 years earlier, this shift in attitude to dissection became permanent, in western Europe at least.

The decisive point was not that Mondino looked inside a dead body, but that in so doing he revealed the importance of personal investigation. The implication – that claims about the human body could be tested, and that knowledge could be independently acquired and not simply copied from the ancients – would eventually prove revolutionary. However, although Mondino's method was radical, his conclusions were not – he simply reiterated Galen's views with regards to anatomical structures and added an Aristotelian interpretation of their function, according to which the heart was the origin of movement, including the voice.[34]

Mondino's book showed that dissection was a potential tool for are highly selective and posed representations of what can be seen.[38] Nevertheless, the *Fabrica* represented an immense step forward in anatomical knowledge. For example, Vesalius reported that he was unable to observe the *rete mirabile* – the network of blood vessels that Galen claimed enabled the animal spirits to enter the brain. Vesalius audaciously – and accurately – concluded that Galen was wrong and that this structure did not exist in humans.[39] Students, he argued, should attend an autopsy, look closely, 'and in the future have less faith in anatomy books'.[40] Vesalius turned his objection to Galen's claim about this structure into a rallying-cry for a new way of studying the body.



Dissection of the human brain by Vesalius.

Vesalius also grappled with the mystery of what it all might mean, how the body – and in particular the brain – might actually work. And at this point, his scalpel understandably failed him. Careful dissection of the human body could reveal structures, but apart from trivial cases (bones, sinews and nerves), it could not provide any real insight into function. These difficulties of interpretation were at their greatest when it came to understanding the origins of behaviour in humans and of our differences with animals. The problem, Vesalius explained, was that when he looked, he discovered that 'there is no difference at all in the structure of the brain in the parts I have dissected in the sheep, goat, cow, cat, monkey, dog, and birds when compared with the human brain'.[41]

Although the brain was proportionately much larger in humans than in other animals, Vesalius could find no qualitative difference between the structure of a human brain and that of other vertebrates. Whatever produced the evident behavioural and psychological differences between us and animals, Vesalius could not see it. Although his dissections were unable to provide an explanation of how the brain worked, they did suggest that the dominant ventricular theory of psychology might be wrong – the ventricles appeared to be 'nothing more than cavities or passages'. Without a better explanation of how the brain worked, Vesalius concluded by saying that 'nothing should be told about the locations in the brain of the faculties of the supreme spirit', lashing out at the theologians who dared to localise them, describing their ideas as 'lies and monstrous falsehoods'. Strong stuff.

The whole of Vesalius's study of the brain was based on the idea that it, rather than the heart, was the origin of thought and movement. The evidence for this assumption was in fact rather poor – the only experimental proof came from Galen over 1,200 years earlier. Three decades after the death of Vesalius, André du Laurens, Professor at the University of Montpellier and physician to Henri IV of France, could do no more than assert his belief in the role of the brain:

> I say then that the principall seate of the soule is in the braine, because the goodliest powers thereof doe lodge and lye there, and the most worthie actions of the same doe there most plainly appeare. All the instruments of motion, sence, imagination, discourse and memorie are found within the braine, or immediatly depending thereupon.[42]*

As to the role of the ventricles, du Laurens cautiously avoided the question, merely stating that it 'is not fully resolved upon'.

All these hesitant steps towards understanding the role of the brain in generating thought show that there was no single 'brain-centric moment' when thinkers realised that the brain, not the heart, was the key organ. The evident complexity of the brain compared with the heart strongly suggested where thought and emotion might be located, but the weight of tradition and the power of everyday experience meant that contradictory ideas were held by some of the greatest thinkers of the sixteenth and seventeenth centuries. The confusion many people felt was nicely summed up by Shakespeare, in one of the songs from Act 3 of *The Merchant of Venice*:

> Tell me where is fancy bred,
> Or in the heart or in the head?[43]

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* The term 'animal' has the same root as in 'animated', and refers to *animus*, the Latin word for heart and mind.

* Du Laurens described the widespread 'glass delusion' in which patients were convinced they were made of glass and feared they might shatter. Reporting of these symptoms declined in frequency from the early nineteenth century, showing that some mental health symptoms are tightly linked to social context. This is even true for post-traumatic stress disorder in soldiers – very different symptoms are

reported now compared to those in the First World War. Speak, G. (1990), *History of Psychiatry* 1:191–206.

– TWO –

FORCES

17TH TO 18TH CENTURIES

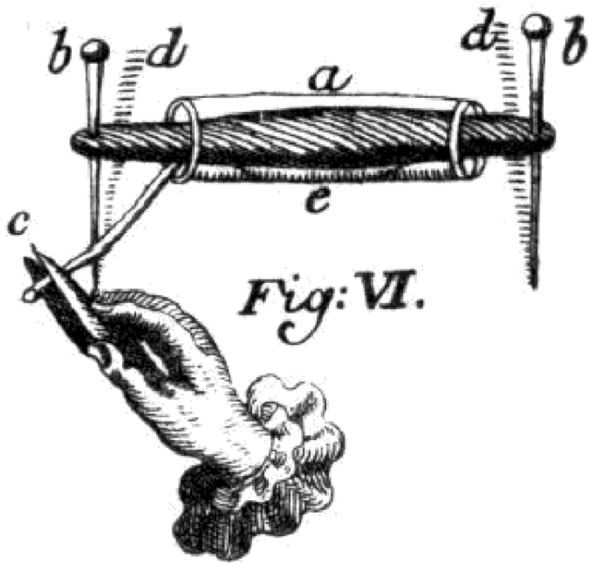
During the seventeenth century, European thinkers became increasingly convinced that the answer to Shakespeare's question was most definitely 'the head' and, more precisely, the brain. The shift in attitude was slow and complex – there was no single experiment or dissection that resolved the question in favour of the brain. Instead there was a gradual accumulation of ideas and knowledge, all of which suggested a role for the brain, although old and new ideas coexisted. For example, in the 1620s William Harvey showed that 'the heart is simply a muscle', as the Danish anatomist Nicolaus Steno put it some decades later.[1] Although Harvey recognised the brain's complexity, calling it 'the organ of sensation' and 'the richest member of the body', he also felt that Aristotle was right, and that the blood carried some mysterious spirit that was generated by the heart. What now appears as a lack of clarity in Harvey's thinking reflected the absence of decisive evidence at the time.

One of the most influential figures to emphasise the significance of the brain was the French thinker René Descartes, who made dissections of the brain in the 1620s and 1630s. Although he decided not to publish his ideas following the condemnation of Galileo by the Catholic Church in 1633, they finally appeared posthumously in 1662.[2] Like many other thinkers, Descartes dismissed the suggestion that the heart was the seat of the fire, because the spirits had moved from the foot, along the nerve, up into the brain and then back down again to the muscles in the leg. All this represented a decisive step forward from previous rather vague explanations of behaviour and nerve function. For thousands of years, thinkers had suggested that the spirits moved like a fluid or the wind – the rapidity and intangibility of these forms of motion made them attractive analogies. The organisation of hydraulic power in automata was a far more compelling metaphor, but despite its significance, there was still widespread disagreement as to what the spirits in nerves were made of, and Galen's confusing ideas about nervous air or *pneuma* were not much help.* Steno outlined the problem in 1665:

> Could they be a special substance separated from ... glands? Might not serous substances be their source? There are some who compare them to spirit of wine, and it is suspected that they are in fact of a substance similar to light. In short, our standard dissections cannot clarify any of these difficulties concerning animal spirit.[8]

Steno's confident dismissal of all existing descriptions of nerve function was based partly on work using the latest technology – the microscope. His friend the Dutch microscopist Jan Swammerdam and the Italian anatomist Marcello Malpighi had both studied the contents of nerves, and agreed that there was neither fluid nor air within them – Swammerdam described such ideas as idle and absurd.[9] Experimental evidence against Descartes's hydraulic view of nerve function came when Swammerdam showed that if he stroked the outside of a dissected frog nerve with a pair of scissors, the attached muscle would contract, a result that he claimed 'applied to all the motions of the muscles in Men and Brutes'. Whatever was happening in nerves to produce behaviour, it was nothing like the moving water in Descartes's hydraulic automata – the same thing happened even if the end of the nerve was cut, thereby allowing any liquid or gaseous spirit to escape. As Swammerdam explained: ‘a simple and natural motion or irritation of the nerve alone is necessary to produce muscular motion, whether it has its origin in the brain, or in the marrow, or elsewhere’.

Although Swammerdam was convinced that the true explanation of nerve function lay ‘buried in impenetrable darkness’, he was prepared to speculate, using a new metaphor for how nerves work:



Swammerdam’s experiment showing that touching a frog nerve (c) with metal scissors causes the muscle (a) to contract, pulling the pins (b) to position (d).

> it cannot be demonstrated by any experiments, that any matter of sensible or comprehensible bulk flows through the nerves into the muscles. Nor does any thing else pass through the nerves to the muscles: all is a very quick kind of motion, which is indeed so rapid, that it may be properly called instantaneous. Therefore the spirit, as it is called, or that subtle matter, which flies in an instant through the nerves into the muscles, may with the greatest propriety be compared to that most swift motion, which, when one extremity of a long beam or board is struck with the finger, runs with such velocity along the wood, that it is perceived almost at

the same instant at the other end.

Swammerdam's experiments showed that neither the pneumatic nor the hydraulic models of nerve function were correct; instead, it seemed that some kind of intangible motion was involved – irritation of the nerve produced an almost instantaneous response in the muscle, like a vibration. Swammerdam was groping for appropriate metaphors, but the key point was that he had shown that previous explanations were wrong, and that it was possible to produce movement artificially, by physically stimulating the nerve.

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At the same time as the basis of nerve function was being explored, new studies of the brain were undertaken as anatomists responded to Descartes's ideas. Probably the most significant contribution came from Thomas Willis, a well-connected physician from Oxford. His gossipy contemporary John Aubrey sketched him in half a sentence – 'middle stature: darke brindle haire (like a red pig) stammered much'.[10] Influenced by Robert Boyle, the intellectual leader of the newly founded Royal Society of London, in the early 1660s Willis began to sketch out materialist explanations of mental health problems, which he saw as having their origins in the brain.[11]

In 1664 Willis published a book in Latin describing the anatomy of the brain, which was beautifully illustrated by his friend Christopher Wren. Over the following two decades the book went through eight editions and was published in Amsterdam and Geneva as well as London. The English translation, which appeared in 1684, is hard to understand, partly because of the archaic language but also because, according to the curmudgeonly historian of comparative anatomy F. J. Cole, Willis's Latin was 'elegant but involved'. For Cole, Willis lacked 'the gift of clear and material mind:

> I would ask those, that say the Brain has neither sense, reason, nor self-motion, and therefore no Perception; but that all proceeds from an Immaterial Principle, and an Incorporeal Spirit, distinct from the body, which moveth and actuates corporeal matter; I would fain ask them, I say, where their Immaterial Ideas reside, in what part or place of the Body?[22]

Princess Elizabeth of Bohemia had similarly expressed her incomprehension at Descartes's views in a private letter to the French philosopher, written in 1643: 'I have to say that I would find it easier to concede matter and extension to the soul than to concede that an immaterial thing could move and be moved by a body.'[23]

For the Princess, it was more straightforward to imagine the existence of thinking matter than to accept Descartes's suggestion that an immaterial substance – whatever that was – somehow interacted with the physical world.

A few decades later the radical Dutch philosopher Baruch Spinoza was convinced that 'mind and body are one and the same thing', but he also accepted that, given the knowledge of the time, this identity could not be proved:

> Again, no one knows how or by what means the mind moves the body, nor how many various degrees of motion it can impart to the body, nor how quickly it can move it. Thus, when men say that this or that physical action has its origin in the mind, which latter has dominion over the body, they are using words without meaning, or are confessing in specious phraseology that they are ignorant of the cause of the said action, and do not wonder at it.[24]

Many philosophical heavyweights were opposed to materialist explanations of mind. In one of his last writings, in 1712, Gottfried Leibniz expressed the commonly held view that there was no such thing as thinking matter, because it was impossible to imagine how

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