

AN ANATOMY OF THOUGHT

*The Origin and Machinery
of the Mind*

Ian Glynn

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11 A Cook's Tour of the Brain

When Thomas Cook started his grand circular tours, they were designed so that a traveller, without too much expenditure of time or effort, could get a general idea of the area to be toured, hurry through the dull parts, linger in those that were more interesting, and emerge knowing a little of the history and features of the area and much better equipped to make more detailed visits later. That is, roughly speaking, the sort of tour of the human brain that I want to conduct in this chapter.

AN OVERALL VIEW

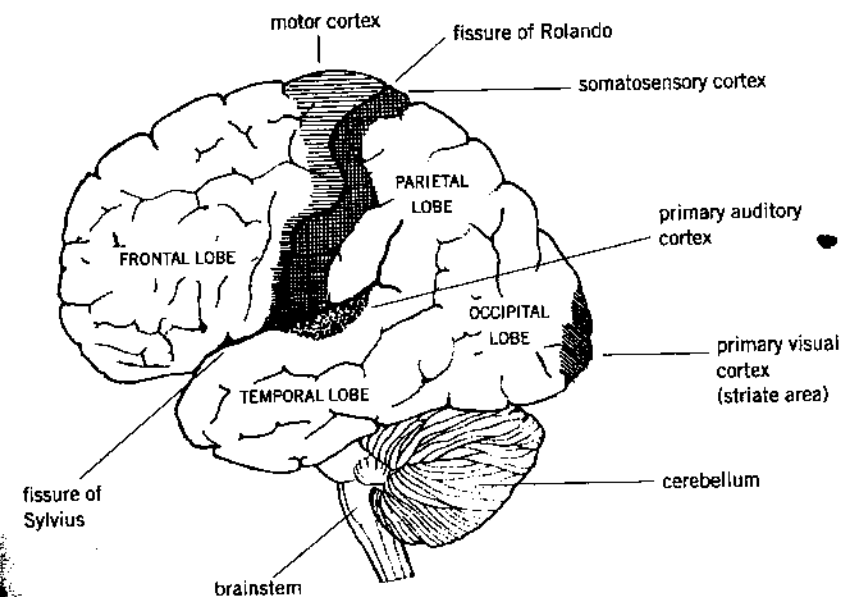
The easiest way to make sense of the structure and organization of the human brain is to look at the way the brain develops in the embryo, and at its evolutionary history. In vertebrates, including ourselves, the nervous system starts as a midline groove in the surface layer of cells on the back of the embryo. This groove becomes deeper, and soon forms a thick-walled tube which separates from the surface, and is destined to form the brain and spinal cord. As the embryo develops, the front end of the tube, which is closed, swells into three connected vesicles which will form the *forebrain*, the *midbrain* and the *hindbrain*, respectively. Later the forebrain divides into an expanded *endbrain*, and a *between-brain* that lies between the endbrain and the midbrain. The way these different regions develop, and the functions they have is different in the different classes of vertebrate but there is a common overall pattern.

You can get some idea of the evolution of the brain – from fish, through amphibia and reptiles, to mammals – by comparing the brains of animals living today. The striking thing in this evolutionary series is the progressive enlargement of the endbrain. In all four classes it develops to form two cerebral hemispheres, but these are small and fused in the fish, larger in amphibia and reptiles, and very large in mammals, particularly in primates. In humans, the cerebral hemispheres are so large that they fill most of the space in the skull. This great increase in size is accompanied by the takeover of roles that in lower vertebrates are performed by other parts of the brain, and by the appearance of behaviour of a complexity not seen in lower vertebrates.

The human forebrain

Figure 11.1 shows the entire human brain viewed from the left side. The very large cerebral hemisphere dwarfs the rest of the brain, parts of which can be seen peeping out below. The surface of the cerebral hemisphere is a crumpled sheet of neurons and supporting cells from 2 to 5 mm thick. This sheet is the *cerebral cortex*, and the many folds and fissures increase the effective area nearly threefold. Underlying the cortex are masses of axons, which, being mainly myelinated (p. 115), look white in contrast to the 'grey matter' of the cortex. A very large bundle of axons – the *corpus callosum* – crosses from one hemisphere to the other, and provides the main pathway for the transfer of information between the two hemispheres. Deep within the white matter of each hemisphere are three further collections of neurons and supporting cells, the *basal ganglia*, the *hippocampus* (from a fanciful resemblance of its shape, in cross-section, to a 'sea horse' – *hippokampos* in Greek) and the almond-shaped *amygdala* (from the Greek word for almond). The basal ganglia are largely involved in the control of movement – it is their malfunctioning that causes the rigidity and tremor in Parkinson's disease. The hippocampus and amygdala, together with other structures play a vital part in memory and emotion.

FIGURE 11.1 The brain from the left side, showing the lobes of the left cerebral hemisphere and the primary motor and sensory areas of the cortex.



The total surface area of the cortex is about a quarter of a square metre – a little larger than a large pocket handkerchief – and it contains something like 100 billion neurons. It is almost certainly to this extraordinary structure, more than to any other part of the brain, that we as a species, owe our remarkable intellectual abilities.

The between-brain shows nothing like the same expansion in the course of evolution. In all vertebrates, during the embryological development of the between-brain, an outgrowth on each side develops into the retina of the eye and the optic nerve. A conspicuous feature of the mammalian between-brain is the presence, in each side wall, of a large mass of neurons called the *thalamus* – the Latin form of a Greek word meaning ‘inner room’. A consequence of the takeover of functions by the cerebral cortex is that, in mammals, information about all sensations has to be carried to the cortex. Some information about smell passes directly from the olfactory organs to a part of the cortex, but information from all the other sense organs (and also information from other parts of the brain) reaches the cortex almost exclusively via one or other thalamus. Each thalamus therefore acts as a great relay station, but this cannot be its sole function as there are even more nerve fibres carrying information from the cortex to the thalamus than there are carrying information from the thalamus to the cortex. The role of these back connections is not known, but a fashionable hypothesis is that they make it possible for the cortex to use representations of information it has just received, to select signals from the thalamus that are most likely to be useful for subsequent cortical processing.¹

In the floor of the between-brain are several collections of neurons that together forms the *hypothalamus* – *hypo* being Greek for below. The hypothalamus is tiny but by controlling the pituitary gland, which secretes hormones that influence other hormone-secreting glands, it dominates the entire hormonal system in the body, and has important effects on metabolism, growth and various processes involved in reproduction. It also acts through the *autonomic nervous system* – a discrete part of the nervous system that, as its name suggests, controls events in the body that occur more or less automatically, though not necessarily unconsciously. Of this part of the nervous system, one division (the *parasympathetic nervous system*) is concerned with ‘housekeeping’ functions such as appetite, thirst, salt and water balance, body temperature, the movements of the gut and the emptying of the bladder. The other division (the *sympathetic nervous system*) is continuously concerned with the control of blood pressure, but it is particularly active when the body has to be prepared for vigorous action. As generations of medical students have been taught, it is the system for ‘fright, flight and fight’. Yet another role of the hypothalamus is to act with other parts of the brain in controlling sleep and wakefulness, and in producing some of the physical changes in the body that are normally associated with emotions such as fear, anger or pleasure.

During embryological development, an outgrowth from the roof of the between-brain forms the pineal gland – Descartes’ ‘seat of the soul’. The evolutionary origin of this gland seems almost as unlikely as Descartes’ hypothesis, but it is believed to represent the vestige of a third eye (situated at the top of the head), an eye that is found in the fossils of certain extinct fish, amphibia and reptiles, and that still exists in one living reptile – the tuatara, a spiny, lizard-like creature found on some offshore islands in New Zealand. In those mammals in which the onset of the breeding season is controlled by the duration of daylight, there is evidence that secretion of a hormone by the pineal is involved. In humans, it is not clear that the pineal has any normal role, though because it secretes a substance (melatonin) during the dark hours but not much during the day, a role in maintaining daily rhythms has been suggested. There have even been attempts to use melatonin to control jetlag. A particular kind of pineal tumour is associated with (among other disorders) extraordinary sexual precocity that can lead to a child of three or four having external genital organs of nearly adult size.

The midbrain

In all vertebrates except mammals, the roof of the midbrain swells into a pair of domes, one on each side. In fish, amphibia and reptiles, these are the main sites for handling visual information and are therefore called optic lobes. In mammals the roof of the midbrain swells into four domes. One pair correspond to the optic lobes in lower vertebrates, but (the handling of visual information having been largely taken over by the cerebral hemispheres) they are mainly concerned with eye movements. The other pair are concerned with handling auditory information on its way to the cerebral hemispheres, and their development is thought to be associated with the evolution of the *cochlea*. They are particularly large in the bat, where they play an important part in the echo-location system. The midbrain also contains collections of nerve cells that, together with nerve cells in the forebrain above and in the hind brain below, are concerned with movement, sleep and arousal.

The hind brain

The hind brain is a tapering tube linking the midbrain and the spinal cord. The roof adjacent to the midbrain is expanded into a large highly folded structure, the cerebellum, which is concerned with balance and posture, with the fine control of movement, and in particular with the learning of complex patterns of movement. The flautist who completes a fast and intricate passage without a thought of the fingering is believed to have stored the necessary instructions in her cerebellum. In all vertebrates the hind brain is concerned with the control of the circulation and of respiration. In lower vertebrates, it is also concerned with

vibration sense (or hearing) and taste, and with the initiation of voluntary movements, but in mammals these functions have largely been taken over by the cerebral cortex.

That completes the rapid part of our itinerary, and I want to spend the rest of this chapter looking in a more leisurely way at the cerebral cortex.

THE CEREBRAL CORTEX: WHAT HAPPENS WHERE

The convolutions

The strikingly convoluted appearance of the surface of the human cerebral cortex was noted in an Egyptian papyrus of about 1700 BC, which compared it with the film and corrugations seen on the surface of molten copper as it cools.² Few of us nowadays are familiar with the appearance of cooling molten copper, but the comparison is, anyway, misleading for it suggests that the convolutions are arbitrary and inconstant. In fact they are sufficiently similar in different brains to be used as landmarks; and in exploring the working of the cortex we need landmarks.

In Figure 11.1 the left cerebral hemisphere is seen from the side. Two striking fissures – the fissure of Rolando, running downwards and forwards from just behind the highest part of the brain, and the fissure of Sylvius, running backwards and slightly upwards from the notch near the front of the brain – divide the hemisphere into frontal, parietal and temporal lobes. (The names of the fissures celebrate Italian and Dutch anatomists of the 18th and 17th centuries; the names of the lobes come from the different bones of the skull with which they are in contact.) A fourth lobe, the occipital lobe at the back end of the brain, is not clearly demarcated from the parietal and temporal lobes on the outward-facing surface of the hemisphere, but has a clear boundary on the surface (not visible in the Figure) that faces the opposite hemisphere. The surface of each lobe is subdivided by numerous smaller fissures into convoluted flattened areas called *gyri* (singular *gyrus*, Latin for circuit).

The idea that different parts of the cerebral hemispheres have different functions is now so familiar that it seems obvious, but it has had a long and chequered history. Hippocrates warned against making incisions in the brain because of the danger of causing convulsions on the *opposite* side of the body. By the 18th century it was well known that injury to one side of the brain often caused paralysis of limbs on the opposite side, and in 1778 Nicolas Sucerotte, an army surgeon, described extremely unpleasant experiments in which he damaged selected areas of the cerebral cortex of dogs by trephining through the skull; he showed that, depending on where he placed the trephine, he could cause paralysis of the opposite forelimb or of the opposite hindlimb. In the early 19th century many attempts were made to identify the functions of different parts of

the brain by destroying them, or by stimulating them mechanically, chemically or electrically, but the results were confused and difficult to interpret.³ The main problem was that, without anaesthetics or precautions against infection, the surgical procedures were so traumatic that the animals tended not to survive long enough to recover fully from the shock of the operation. Even if they did, it was unsafe to argue that, because damage to an area caused loss of a particular function, performance of that function was the normal role of the area; the effect might be an indirect one. Conversely, a genuine loss of function might be concealed by compensatory effects of other parts of the brain. When electrical stimulation was used, the results were complicated by the spread of current to surrounding structures. And the whole question was complicated by the enormous and unsavoury red herring of phrenology.

The bumps

At the end of the 18th century, Franz Josef Gall, a physician practising in Vienna, had developed a new system of psychology. As a boy, he had noticed, or thought he had noticed, that people with particularly good memories had prominent eyes. Regarding the brain as the organ of the mind, he therefore wondered whether a variety of mental characteristics might not be reflected in physical features of the brain, and hence of the skull. His system was based on a number of crucial assumptions.⁴ He assumed that human mental powers can be analysed into a definite number (initially twenty-seven) of independent 'faculties'; that each of these faculties has its seat in a definite region of the surface of the brain; that the size of each region in an individual reflects the strength of the corresponding faculty; and that, because the skull fits the brain like a glove, it is possible to judge the sizes of the different regions by measuring the bumps on the surface of the head. If all Gall's assumptions had been justified, and if his allocation of faculties to regions had been correct, he would have invented a marvelously objective way of assessing character; and in this lay the enormous popular appeal of his system – an appeal that was increased when, in 1802, the Austrian government, influenced by the ecclesiastical authorities, interdicted his lectures as being dangerous to religion. In 1807 he settled in Paris where he made many converts and a great deal of money. His pupil and colleague, J. C. Spurzheim, was so successful in lecturing on phrenology in Great Britain and America that, by 1832, there were twenty-nine phrenological societies in Great Britain, and several English-language phrenological journals.

Phrenology was, almost from the start, both fashionable and a subject of ridicule. The trouble with it was, in the first place, that not all the basic assumptions were justified, and secondly, that, although the allocation of faculties to regions was supposed to be based on empirical evidence from the study of subjects with known character (Gall had been particularly conscientious in

visiting gaols and lunatic asylums), it was largely the product of guesswork. Gradually the influence of phrenology declined, though it lingered on into this century. Francis Crick recalls being taken to a phrenologist by his mother when he was a boy;⁵ the last British phrenological society was disbanded only in 1967; and porcelain heads with the classical faculties marked on them can still be found in British antique shops. What is curious amid all the quackery is that Gall was a highly competent anatomist who did important work sorting out the pathways of the motor nerve fibres that carry information from the cerebral cortex to the spinal cord; and his emphasis on the role of the grey matter of the cerebral cortex in intellectual processes was, of course, correct.*

A prediction confirmed

Gall had associated speech with the frontal lobes of the brain. As always, the evidence was flimsy, but Gall's view was accepted by Jean Baptiste Bouillaud, later Professor of Medicine at the Charité hospital in Paris, whose clinical studies on patients with loss of speech appeared to support it.⁶ Despite successive attempts to persuade them, the members of the Académie de Médecine remained unconvinced, however, and in a debate in the stormy political climate of 1848 the exasperated Bouillaud made an offer: he would pay 500 francs to anyone who would provide him with an example of a deep lesion of the frontal lobes of the brain without a lesion of speech. He also made a prediction: 'At this very moment', he said, 'there is a patient at [the Hospital] Bicêtre who has all the freedom of his intelligence and his movements . . . but he cannot speak . . . I am not afraid to affirm that this man carries a deep lesion in the anterior lobules of his brain.' Thirteen years later, at a meeting of the Société d'Anthropologie, Paul Broca, a surgeon at Bicêtre, presented the brain of a patient who had died the previous day.⁷ The patient was a Monsieur Leborgne, a maker of cobbler's lasts by trade. Epileptic since his youth, he had been admitted to the hospital twenty-one years earlier, at the age of thirty, when he had become unable to speak though still able to use his tongue and lips normally in every other way. During his long stay in the hospital, he was able to understand speech, and to make himself understood by

*Jerry Fodor has argued that Gall also deserves credit for the way in which, in slicing the cognitive powers of the mind into its component faculties, he rejected the usual 'horizontal' divisions into memory, imagination, attention, sensibility, perception, and so on – faculties that are independent of the subject matter and whose operations cross 'content domains' – and instead chose 'vertical' divisions into faculties that are distinguished by reference to their subject matter – amatory propensity, love of children, friendliness, combativeness, acquisitiveness, cautiousness, vanity, benevolence, religious sentiment, wit, and so on. (The words in quotes are those used by Fodor.) See Fodor, J. A. (1983) *The Modularity of Mind*, MIT Press, Cambridge, Mass. Whether Fodor is right in claiming that 'the notion of a vertical faculty is among the great historical contributions to the development of theoretical psychology' seems to me doubtful.

gestures, but his only answer to any question was 'tan tan', or, when he became angry, 'Sacré nom de Dieu'. It is not clear whether this unfortunate man was the man Bouillaud had been referring to thirteen years earlier, but it seems likely. In any event, the frontal lobe of his left cerebral hemisphere showed a fluid-filled cavity about the size of a hen's egg.

Inability to speak 'in individuals who are neither paralysed nor idiots' seemed to Broca to deserve a special name, and eventually it became known as *aphasia* (from the Greek *aphatos* meaning speechless).

Within two years of Leborgne's death, Broca had collected eight cases of aphasia associated with a lesion in the same part of the frontal cortex; and because in many of them the lesion was much more circumscribed, Broca could argue convincingly that the critical area was the posterior part of what is now known as the inferior frontal gyrus (see Figure 16.1, p. 262). In all these cases the lesion was on the left side, but the nearly perfect bilateral symmetry of the brain's anatomy made Broca, and others, reluctant to accept that this was anything more than coincidence. Three events changed this view. The first was the steady accumulation of cases in all of which the lesion was on the left; by March 1864 Broca had collected twenty cases. The second was a demonstration to the Société Anatomique of a case in which a lesion of the inferior frontal gyrus *on the right side* was *not* associated with any speech disorder. The third was the acquisition and publication by the Académie de Médecine of a memoir by a general practitioner from Montpellier called Marc Dax. Dax had died twenty-six years earlier, but in the last year of his life he had given a paper to a congress of physicians in southern France describing forty cases of patients who had lost the power of speech; in all of them, though there were no post-mortem findings, there was evidence (usually from the sidedness of the associated paralysis) that the lesion was on the left side of the brain. By 1864, Broca was convinced: 'Nous parlons avec l'hémisphère gauche'.

At about the same time as Broca, in Paris, was demonstrating a connection of speech with a specific area of the cortex, John Hughlings Jackson, at the Hospital for the Paralysed and Epileptic in Queen Square, London, was beginning the famous series of clinical observations that led him to suggest that particular areas of cortex could cause movements of particular parts of the body.⁸ He was especially interested in those less common epileptic fits – still called 'Jacksonian' – in which the convulsions begin unilaterally; and he demonstrated that, in different patients, the jerking would begin in the thumb or the big toe, or the angle of the mouth, and would then spread in a reproducible manner. Believing that the cause of epilepsy was the 'occasional sudden, excessive, rapid and local discharge of the grey matter' he suggested that the site of the initial jerking was determined by the site of the initial nervous activity, and that the spread of the seizure reflected the spread of this activity over regions of the brain in which movements of parts of the body were represented. The reproducibility of the spread of the seizure suggested that there was an orderly representation of the parts of the body.

Frau Hitzig's dressing table

Within a decade, there was strong support for Hughlings Jackson's hypothesis from the experiments of Gustav Fritsch and Eduard Hitzig in Berlin.⁹ There is a story that, while dressing a wound of the brain during the Prussian–Danish war, Fritsch had noticed that irritation of the surface of the brain on one side caused twitching of the body on the opposite side. In any event, he and Hitzig determined to investigate the effect of stimulating the surface of the brains of anaesthetized dogs, using weak electric currents. At that time there were no facilities at the Physiological Institute in Berlin for working on warm-blooded animals so the first experiments were done in Hitzig's home, and indeed on Frau Hitzig's dressing table. Using a pair of platinum wires stuck through a cork, and currents just strong enough to be felt on the tongue, Fritsch and Hitzig explored the surface of the cerebral hemispheres, and found that stimulation of certain areas in the front half of the brain caused contractions of groups of muscles, producing discrete movements of one or other limb on the opposite side of the body. In later experiments Hitzig defined the limits of these 'motor areas' in both the dog and the monkey.

At about the same time, David Ferrier, physiologist and physician at King's College, London, but working in a laboratory attached to the West Riding Lunatic Asylum in Yorkshire, made a detailed map of the motor areas in the monkey.¹⁰ By electrical stimulation using very weak currents and electrodes only a millimetre apart, he could produce tiny normal-looking movements – the flick of an eyelid, the twitch of an ear. In this way he was able to identify particular areas of cortex with particular parts of the body, and he then showed that removal of an identified area led to paralysis of the corresponding part. Even before Ferrier's work (but following the publication of Fritsch and Hitzig's paper in 1870), Jean Martin Charcot, at the Salpêtrière Hospital* in Paris, had made careful comparisons of clinical observations and of post-mortem examinations of his patients' brains, and had concluded that damage to the gyrus just in front of the fissure of Rolando (Figure 11.1) led to disturbances of movement. Whether these disturbances affected the arm or leg or head depended on which part of the gyrus was damaged.

A second speech centre

All these examples of localization of function in the cerebral cortex have been concerned with motor activity. What about sensory activity? In 1874, thirteen years after Broca had demonstrated the fluid-filled cavity in the brain of

*Built as an arsenal by Louis XIII, its name comes from the saltpetre which had once been manufactured there. In Charcot's time it had about 5000 inhabitants.

Monsieur Leborgne, Carl Wernicke, a twenty-six-year-old physician in Breslau, published a short monograph drawing attention to cases of aphasia that differed in several ways from those described by Broca.¹¹ First, the patients, unlike those of Broca, did have difficulty in understanding speech. Secondly, their difficulty in speaking was not in finding words, but in using them correctly. Instead of the sparse, telegram-like style characteristic of Broca's aphasia, these patients tended to be fluent, sometimes very fluent; but the words were not always the right words or even real words, and the fluent sentences did not always convey much meaning, so that the physician could easily misdiagnose the patient as confused. And thirdly, the brain lesion was not in Broca's area but in the left temporal lobe adjacent to the fissure of Sylvius (see Figure 16.1, p. 262). Modern American examples of the speech of patients with Broca's aphasia and Wernicke's aphasia are given in Chapter 16 (pp. 262–3).

Wernicke attempted to make sense of these differences.¹² In Broca's aphasia, the lesion was in the area which, when stimulated by Hitzig in monkeys, had caused movement of the mouth and tongue. Broca's area, Wernicke argued, was therefore probably the centre for representation of movements made in speaking, and damage to it would cause loss of the ability to speak, without any loss of comprehension. In contrast, the lesion in what was to become known as Wernicke's area was close to part of the cortex that was thought to be concerned with hearing. Wernicke's area was, then, presumably the centre for representation of sound patterns, and damage to it would cause some loss of the ability to understand, or even simply repeat, the spoken word. The predictions that followed from this picture of the organization of speech in the brain, and their dramatic confirmation in some patients, is an interesting story that we will come back to when discussing language (Chapter 16). What is significant in the present context is that, in the 1870s, the division of aphasias into primarily motor (Broca's aphasia) and primarily sensory (Wernicke's aphasia) suggested that particular areas or 'centres' in the cerebral cortex were concerned with particular motor or particular sensory activities. And, judging from the two 'speech centres' it seemed that the levels of activity that were controlled by the 'centres' were intermediate between simple movements or sensations and the highly complex activities – veneration, filial love and so on – that were envisaged by the phrenologists.

Maps in the brain

An even more striking example of the way in which individual areas of the cortex have individual roles came from the work of Salomon Henschen, the Professor of Medicine at Upsala.¹³ In 1888 he published the first of many articles in which he correlated loss of vision in parts of the visual field with damage to parts of the so-called striate cortex in the hindermost part of the occipital lobe. (The name 'striate' comes from a stripe which is found in this part of the cortex when it is

cut across.) Henschen found, first, that loss of the striate cortex on one side was always associated with blindness in the opposite half of the visual field in both eyes.* (The explanation, he showed later, is that all the fibres in the optic nerve that come from the left half of *both* retinas connect with the striate cortex in the left occipital lobe, and all those from the right half of *both* retinas connect with the striate cortex in the right occipital lobe (see Figure 11.2). Since we use the left halves of our retinas to see objects to the right of the mid line, and vice versa, loss of the striate cortex on one side leads to blindness in the opposite half field.) This was impressive, but even more remarkable results came from looking at the effects of small lesions in this part of the cortex. Damage to a small area in, say, the left striate cortex gave rise to a small area of blindness – a *scotoma* – at a *corresponding point* in the right half-fields of both eyes.** This correlation led Henschen to conclude that damage to adjacent areas of the striate cortex caused scotomas in adjacent areas of the visual field; in other words, for an observer whose eyes are still, the visual world seemed to be mapped point by point onto the striate cortex, just as the real world is mapped onto the pages in our atlases. This was localization with a vengeance. And because what we see depends on what is in the images on our retinas, it implied that the fibres in the optic nerves must connect particular points in the retina to corresponding points in the striate cortex. It is worth noting, though, that this does not mean that equal areas of retina are handled by equal areas of striate cortex. In fact, as you might suspect, the areas of striate cortex that are involved in handling information from the small central areas of the retina concerned with detailed vision are much more extensive than those concerned with information from the peripheral parts of the retina.

Shocking the brain

Speech and vision are rather specialized operations so it was, perhaps, not surprising to find areas of the cortex devoted to them. What about more mundane tasks such as the handling of information from touch receptors in the skin or from stretch receptors in the muscles and joints? Answering this question required different approaches depending on whether the owner of the cortex was human or animal. In humans the most successful approach was to stimulate different areas of the cortex, using weak electric shocks, and to ask the patient to report any sensation that followed. This kind of procedure requires, of course,

*A similar effect had been found by Herman Munk, eleven years earlier, following removal of one of the occipital lobes in a monkey.

**The patient is not usually aware of such scotomas, any more than the normal subject is aware of the normal 'blind spot' (the part of the visual field corresponding to the insensitive area of the retina where the optic nerve enters), but they can be detected by asking the patient to fixate on a particular point and then seeing whether a small spot of light is noticed when it is placed at different points in the field of view.

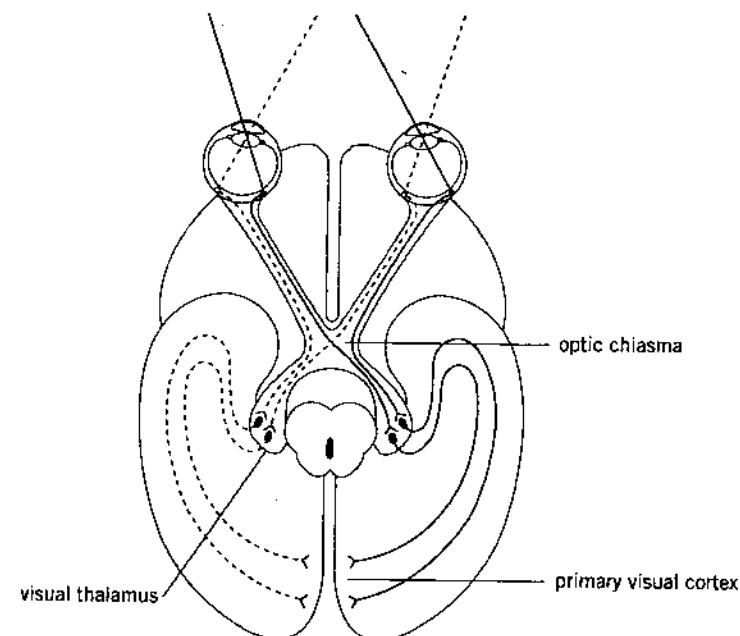


FIGURE 11.2 The optic pathways. Because optic nerve fibres from the nasal half of each retina cross at the optic chiasma, all information about the *left* half of the visual field ends up in the *right* primary visual cortex (black route), and all information about the *right* half of the visual field ends up in the *left* primary visual cortex (dashed route). The two cortical areas are connected by fibres in the corpus callosum (not shown).

that the cortex be accessible and the patient be conscious. There also needs to be a strong medical justification for exposing the patient to a procedure that inevitably carries some risk.

In the first recorded case in which the human cortex was stimulated, this third condition was not satisfied and the outcome was catastrophic. In 1874, Roberts Bartholow, professor of materia medica at the Medical College of Ohio, in Cincinnati, had as a patient a thirty-year-old housemaid, Mary Rafferty, the top of whose skull had been eroded over an area about two inches in diameter by a malignant ulcer.¹⁴ The pulsating brain was visible, covered only by a thin membranous sheet. As the brain had already been deeply penetrated by incisions made for the escape of pus, Bartholow argued that fine needles could be inserted into it without risk of material injury. He showed that such insertion caused no pain. A succession of brief electric shocks to the left side of the brain caused muscles to contract in both the right arm and right leg, and this was accompanied by 'strong and unpleasant tingling' in both these limbs. There was also slight

contraction of the muscle in the left eyelid and widening of both pupils. Similar stimulation on the right side of the brain caused corresponding results. With the needle still in the right side, Bartholow increased the strength of the shocks, but the patient became very distressed, lost consciousness and was violently convulsed for five minutes. Twenty minutes after the beginning of the attack she regained consciousness and complained of some weakness and vertigo. Two days later the unfortunate patient was found to be extremely ill and partially paralysed on the right side. While being questioned she became unconscious, and the following day she had a convulsion and lapsed into a coma from which she did not recover. A post-mortem examination of the brain suggested that the cause of death was thrombosis in the main vessel draining venous blood from the brain, the course of this vessel lying right in the centre of the ulcer. Bartholow's paper caused a storm of criticism, which he seems to have weathered. His name appears as one of the founder members of the American Neurological Association, which had its first meeting the following year.¹⁵

As surgical techniques improved, electrical stimulation of the exposed cortex was to become a useful tool in operating on patients with brain tumours or with epileptic foci that were causing intolerable seizures. Before cutting into the cortex in the neighbourhood of a tumour it was only sensible to try to identify the function of that part of the cortex by looking at the response to weak electrical stimulation. In patients with focal epilepsy, stimulation might reveal the site of the focus by causing the premonitory signs of an attack.

In the 1880s and 1890s there were half a dozen reports of the effects of cortical stimulation, which confirmed that very small electric shocks in the region of the Rolandic fissure caused movements on the opposite side of the body. Sometimes, too, there were tingling sensations, but it was not until 1908 that Harvey Cushing succeeded in producing sensation without movement.¹⁶ This was in the course of investigating two patients, both suffering from distressing epileptic attacks, inaugurated in each instance by strange feelings in the right hand. In each case the cortex was exposed under anaesthesia, but the stimulation was done with the patient fully conscious so that the surgeon might be guided by any sensations that were produced. (The previous year, in an operation to excise a cortical tumour, Cushing had shown that, when the patient had recovered consciousness after the first part of the operation, cutting the cortex and removing the tumour 'not only occasioned no discomfort, but was attended on the part of the patient by a lively and helpful interest in the performance'.) Stimulation of the gyrus just behind the fissure of Rolando caused no movements but definite sensory impressions in the opposite hand and arm – in one patient a sensation of numbness, particularly in the little finger, in the other a sensation 'as though someone had touched or stroked the index finger' or, when the point of stimulation was lower down on the gyrus, as though the back of the hand had been stroked.

The most extensive studies of the effects of stimulating the cortex of conscious

patients were made by Wilder Penfield,¹⁷ and his colleagues at Montreal, in a huge series of cases extending from the 1930s to the 1950s. The justification for operating was usually that the patients had tumours needing removal, or epileptic foci causing intolerable seizures. These studies confirmed that stimulation of the gyrus just in front of the fissure of Rolando generally caused movement, and stimulation of the gyrus just behind generally caused sensations. The former gyrus therefore became known as the *motor cortex*, and the latter as the *somatosensory cortex* (*soma* is the Greek for body).*

The studies also showed that the different parts of the body were represented in an orderly fashion on the surfaces of the two gyri. Figure 11.3 summarizes the patterns of representation – in other words, the system of mapping – and it shows several striking features. First, the arrangement is similar in both gyri so the motor cortex and the sensory cortex dealing with each part of the body are close together across the Rolandic fissure. Secondly, the area of cortex devoted to each part of the body is wildly disproportionate to the size of that part; it relates more to the part's sensitivity and discriminatory ability or the complexity of its behaviour. The areas devoted to the trunk, hips and legs are small, and those devoted to the fingers, thumb, lips and tongue comparatively huge. Penfield's artist has illustrated this by draping two 'homunculi' over the surfaces of the cerebral hemispheres sliced in the plane of the fissure of Rolando. One of these homunculi is sensory, the other motor. Both are upside down, and both show not only gross distortion from the normal human proportions, but also curious discontinuities – the face area, for example, is unconnected with the head or neck and appears (the right way up) below the hands. There are other subtleties, too. Both for movement and sensation, combined activity of the hand and fingers seems to be represented separately from activity of the fingers alone.

Unlike humans, animals cannot describe their sensations, so cortical stimulation followed by interrogation cannot be used to identify the areas of cortex that are concerned with sensation. One way of identifying these areas is to remove bits of cortex and to see whether the response to stimulation of sense organs in different regions of the body is affected. Another way is to take advantage of the electrical activity – the so-called 'evoked potentials' – that can be detected in an area of sensory cortex when sense receptors in the part of the body represented in that area are stimulated. Both methods have been used extensively and show an organization not basically different from that found in humans so long as one allows for the different relative importance of different activities. In rats, for example, there is a relatively enormous area of cortex devoted to the whiskers, in pigs to the snout, and in raccoons (which show great manual dexterity) to the fingers.

*Aldous Huxley's *soma*, which gave such pleasure in his *Brave New World*, is presumably derived from the identical (though unrelated) word in Sanskrit, which refers to an intoxicating drink used in Vedic rituals.

It is interesting that the *movements* caused by stimulation of the human or animal motor cortex – opening or closing of the hand, flexion or extension of the leg, masticatory movements, swallowing – involve the coordinated actions of several muscles, but they are never complex learned movements. They are, as Penfield pointed out, the sort of movements that a baby is able to do at birth or shortly afterwards. The *sensations* caused by stimulating the human somatosensory cortex tend to be tingling or numbness. Even the feeling of being touched or stroked described by one of Cushing's patients is unusual. Clearly, whether motor or sensory, the activities represented in the gyri bordering the fissure of Rolando seem to be rather elementary. This is not true for all areas.

Some of the most startling effects of cortical stimulation were reported by Penfield in operations in which he stimulated the temporal cortex in patients who habitually suffered from severe epileptic seizures of a peculiar kind. The peculiarity lay not in the convulsions themselves – they might even be absent – but in the initial stages of the attacks, which always involved a change in psychological state. The patient entered either a dream-like or hallucinatory state, or a state of altered perception of the environment with perhaps a sense of *déjà vu* or detachment or remoteness or unreality; things might seem to grow larger or smaller, or sounds to be abnormally loud or totally stilled. (The curious 'turns' of the governess in Henry James's *The Turn of the Screw* – the 'intense hush', the 'seeing with a stranger sharpness', the sense of dread – are an example of attacks of this kind that never proceeded beyond the initial stage.)*

In 1938 Penfield operated on a fourteen-year-old girl who had had a single convulsion followed by coma and transient paralysis in infancy, and then periodic seizures from the age of eleven.¹⁸

Her attacks were characterized by sudden fright and screaming. She then held on to people about her for protection. This was followed by falling and occasionally by a major convulsion. On careful questioning it was learned that during the preliminary period of fright she invariably saw herself in a scene that she remembered to have occurred at the age of 7 years.

The scene is as follows: A little girl was walking through a field where the grass was high. It was a lovely day and her brothers were walking ahead of her. A man came up behind her and said: 'How would you like to get into this bag with the snakes?' She was very frightened and screamed to her brothers, and they all ran home, where she told her mother about the event. The mother remembers the fright and the story, and the brothers still recall the occasion and remember seeing the man.

*In a fascinating discussion of the governess as a case of temporal lobe epilepsy, J. Purdon Martin (*British Medical Journal*, 22 Dec 1973, 717–721) points out that Henry James's friend and London publisher, Frederick Macmillan, knew Hughlings Jackson and published the journal *Brain*, of which Hughlings Jackson was an editor and which included accounts of temporal lobe epilepsy.

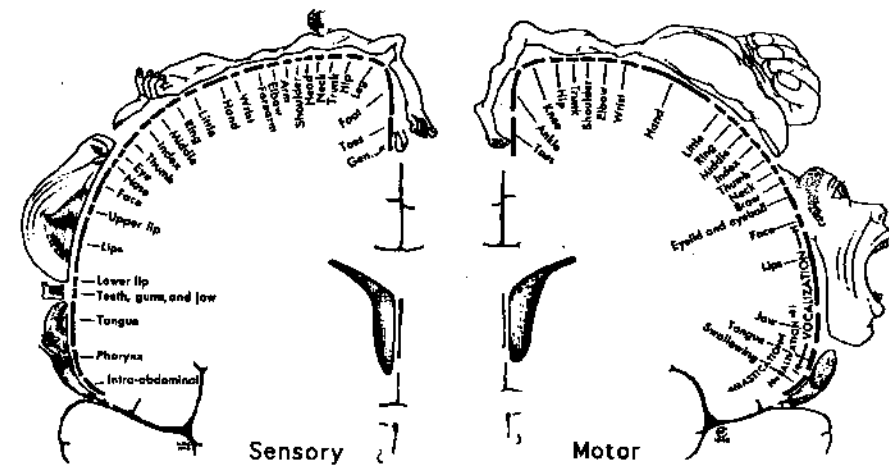


FIGURE 11.3 Penfield's homunculi. Representation of the different parts of the body in the somatosensory cortex and the motor cortex. (From W. Penfield and T. Rasmussen.)

After that, she occasionally had nightmares during her sleep and in the dream the scene was re-enacted. Three or four years later . . . it was recognized that she had attacks by day in which she habitually complained that she saw the scene of her fright. There was a little girl, whom she identified with herself, in the now familiar surroundings. During the attack she was conscious of the actual environment and called those present by name; yet she also saw herself as a little girl with such distinctness that she was filled with terror lest she should be struck or smothered from behind. She seemed to be thinking with two minds.

When Penfield examined the brain he found evidence of an old haemorrhage which, he thought, probably explained the convulsions in infancy. Stimulation far back in the right occipital lobe caused the patient to see coloured stars in the left half of the visual field, presumably because the electrode was in the striate area. But the significant result occurred when he stimulated the outward-facing surface of the right temporal lobe. Depending on the placing of the electrode, he found he could produce in the patient different portions of her 'dream'.

Penfield's interpretation of his observations, and the history, is that the bleeding at the surface of the brain in infancy caused some damage; the serious fright at the age of seven caused periodic nightmares in which the pattern of nervous activity that recorded the frightening events was repeatedly reproduced in proper sequence; that at the age of eleven (as a late consequence of the early damage) the patient began to get seizures; that the point of origin of the epileptic discharge was in the right hemisphere near the junction of the temporal and occipital lobes; and that 'the discharge followed the well-worn synaptic pattern that was capable

of waking the childhood memory'. He points out that the temporal cortex must be the repository of many other patterns but supposes that conduction along the neuronal links associated with the childhood memory had been facilitated first by the repeated nightmares and later by the repeated epileptic attacks. The results of electrical stimulation suggested that the neuronal pattern could be activated from different points, initiating different stages of the dream. If the electrode was held in place, the hallucination progressed like a story unfolding, and it included not just the visual and auditory components but also the terror. In Penfield's words, 'She could hear what the man said . . . she could sense the fright that possessed her, feel her body running.'

Although the attacks did not always proceed to convulsions, they were so wrecking the girl's life that Penfield decided to excise a large part of the right temporal cortex. (Because it was the right cortex there was no risk of causing aphasia.) After the operation the girl 'no longer had hallucinations. But when she was asked about the experience, she could still remember it – the meadow, the man, and her fright'. This implies that the memory was also stored somewhere else in the brain, possibly, Penfield suggested, in the opposite temporal cortex.¹⁹

The 'black reaction' and after

A completely different approach to understanding the cerebral cortex is to look at its microscopic structure. In the course of the 19th century there were great advances in the design of microscopes and in the methods of preparing tissues for microscopy. There were new methods for preserving the tissues, for staining them, and for embedding them in materials (tallow, soap, paraffin wax, celliodin) so that slices could be cut thin enough to be examined by shining light through them. By the end of the 1860s the structure of most tissues was fairly well known, but the structure of nervous tissues, and particularly of the grey matter of the brain, remained puzzling. The reason was straightforward. In most tissues the cells had simple shapes and in suitably stained sections of the tissue their arrangement was not too difficult to decipher. Nerve cells had very complicated shapes with long highly branched processes, and in grey matter they were packed tightly together. They were also, apart from their nuclei, very difficult to stain. It was not even clear that the grey matter was made up of individual cells. Around 1867, Joseph von Gerlach had looked at teased preparations of cortex stained with gold salts, and had concluded that the fine nerve processes in the grey matter joined together to form a continuous network. Gerlach's *reticular theory* – *reticulum* is Latin for net – was to be a matter of contention for the next forty years.

What was needed to sort out the tangle was a method of staining that would pick out an individual cell in its entirety without staining the adjacent cells. In 1873, Camillo Golgi, then aged thirty, was working as resident physician at the Pia

Casa degli Incurabili in the little Lombardy town of Abbiategrasso. Here, in a rudimentary laboratory set up in his kitchen, and working mostly at night, he developed a method – the *reazione nera* (black reaction) – which did just this. Fragments of brain that had been hardened for several days in a solution of potassium dichromate, were soaked for several more days in a dilute solution of silver nitrate. The method was temperamental but when it worked properly the results were astonishing. Under the microscope, thin sections of tissue looked mostly yellow (from the dichromate), but the occasional cell down to its finest ramifications would be jet black 'with the sharpness and brilliance of an indian ink drawing on a pale yellow background'²⁰ – see Figure 11.4. The black material was silver chromate, but why it appeared in only a small fraction of the nerve cells was (and, more than a century later, still is) a puzzle.

Golgi's method revolutionized knowledge of the fine structure of the nervous system. Golgi himself was the first to differentiate between nerve cells and supporting cells (neuroglia), and he was able to distinguish two important classes of nerve cells in the cortex: pyramidal cells, whose axons left the cortex to enter the white matter, and large star-shaped cells whose axons ramified locally in the cortex. In the hippocampus he found an elegant and regular architecture of nerve cells of different types. On the general question of whether nerve cells were separate entities or formed a network, Golgi was less successful. Despite having invented the method that was to solve the problem, he got the wrong answer. He persuaded himself that the fine terminal branches of axons did fuse with the branches of other axons to form a network. (The dendrites he thought were not involved, and he assumed, again wrongly, that they were merely nutritive in function, without any role in conduction.)

What was needed to resolve the problem was a clear demonstration of the way axon terminals did in fact end in the brain. This demonstration was to be provided by Santiago Ramón y Cajal.

Cajal's life has been splendidly described in the autobiography he wrote in his last years.²¹ Born in 1852, the son of a poor surgeon in a tiny village in Navarre, he survived being kicked unconscious by a horse at the age of four, and at seven he coped with his father's letters about patients while his father was away. His parents saw a brilliant future for him, but at school he was a disaster – shy, loathing Latin, Greek and mathematics, and forever being punished. He was keen on games, fighting, bird-nesting and the countryside, and skilled at drawing, which his father thought a waste of time. After brief apprenticeships to a barber and a shoemaker and a further attempt at schooling, he was taken in hand by his father, who decided to teach him about human anatomy, starting with bones he acquired at night from the local cemetery. (This was not *quite* grave robbing. In his memoirs, Cajal describes skeletal remains piled in a hollow 'derived . . . from those wholesale exhumations . . . which the living impose upon the dead . . . under pretext of scarcity of space'.) Interested at last, Cajal seems to have been trans-

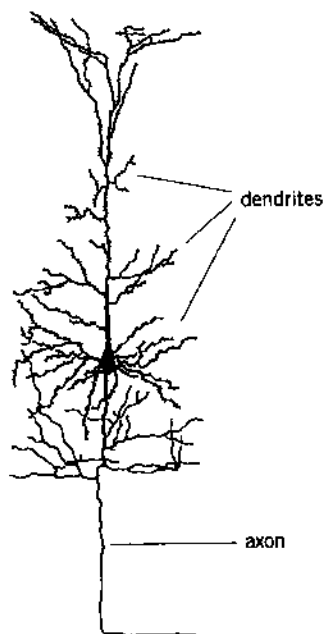


FIGURE 11.4 A nerve cell from the cortex of a mouse, stained (using the Golgi method) and drawn by Ramón y Cajal.

formed. He impressed his father with his anatomical drawings; he studied physics, chemistry, and natural history, and began a course of medical studies at Zaragoza, where his father now had an appointment. When he was twenty-one he qualified as a doctor and, being conscripted into the army, joined the Army Medical Service and was sent to Cuba. Here he learnt about corruption and military incompetence, and nearly died of malaria and tuberculosis. Invalided out of the army, he returned to Spain, gradually regained his health, read Helmholtz's *Physiological Optics*, together with the works of Lamarck, Darwin and Spencer, and just before his twenty-fifth birthday was appointed to a temporary assistantship in anatomy at Zaragoza. From then on his career was a succession of successes, culminating in the award of a Nobel prize for Medicine and Physiology in 1906.

At the age of thirty-two, while visiting Madrid, Cajal was introduced by a colleague to Golgi's *reazione nera*, and was amazed at its power and its capriciousness. After much labour he managed to make it less capricious, but his success in demolishing the reticular theory, by showing that the terminal branches of axons did not fuse with parts of other nerve cells, depended less on improvements in method than on his choice of material to be examined. Finding the grey matter of the adult mammalian brain an impenetrable thicket, he decided to look at embryonic brains. He discovered that by choosing a stage of development before the myelin sheaths were formed, and when the nerve cells

were still relatively small, he could obtain clear pictures of the terminal branches of axons, and they were perfectly free.

This work, and work that followed from it, not only demolished the reticular theory but also established that the contacts between axon terminals and parts of adjacent nerve cells were far from random and sometimes followed a tightly controlled pattern. Ironically, Ramón y Cajal was never able to convince Golgi that the reticular theory was wrong, and in 1906, when they were jointly awarded the Nobel Prize for Physiology and Medicine, Golgi embarrassed everyone by using his lecture to attack Ramón y Cajal and defend the theory.

Another crucial problem tackled by Cajal was the direction of conduction within nerve cells. The many contacts between axon terminals and the dendrites of adjacent nerve cells made Golgi's notion that the dendrites were purely nutritive seem very unlikely. But if dendrites were involved in the interactions between nerve cells, in which direction did they conduct? Cajal solved this problem elegantly by looking at the detailed anatomy of the retina. Knowing that the light stimulus acts on the rods and cones, and that the message concerning the stimulus is eventually carried by the optic nerve to the brain, he was able to conclude from the arrangements in the intervening layers of the retina that the direction of conduction within each neuron must be from dendrites to cell body to axon. He drew the same conclusion from his studies of the olfactory bulb.

During the 1890s, Cajal and others studied the fine structure of the cerebral cortex, work that led on to the very detailed studies of Korbinian Brodmann and Oscar Vogt in Germany during the first decade of the 20th century. On the basis of these studies, Brodmann divided the human cerebral cortex into fifty-two discrete areas. Some of these areas correlated well with areas of known function – Brodmann's area 4, for example, fitted well with the motor area, Brodmann's areas 1, 2 and 3 with the somatosensory area, Brodmann's areas 41 and 42 with the auditory area. Despite the time that has elapsed since Brodmann's work, and despite the idiosyncratic numbering system he used – he seems to have allotted numbers according to the order in which he studied the different areas²² – his fifty-two areas remain a standard for reference, and one of Brodmann's diagrams (Figure 11.5) still tends to appear in current textbooks of physiology.

Although Brodmann's fifty-two areas look different, their structures are all variations on the same basic six-layered pattern. Roughly speaking, the cells in one of the middle layers receive most of the sensory information coming into the cortex; the cells in the inner layers send information to distant regions of the cortex or to other parts of the brain; the cells in the outer layers mainly make local connections with cells in adjacent cortex.

The persistence of Brodmann's diagram in current textbooks does not mean that there have been no advances since 1910. In particular, ingenious methods have been developed to follow the course of individual nerve fibres within the brain. If radioactive amino-acids or sugars are injected in a region containing the

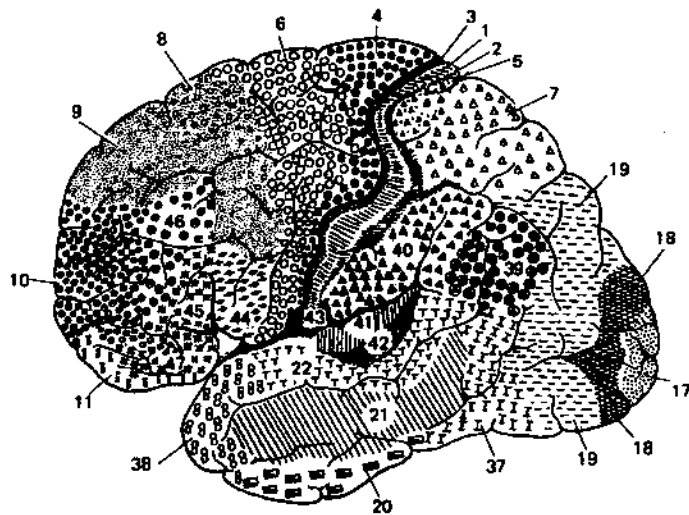


FIGURE 11.5 Brodmann's map of the human cerebral cortex based on its fine structure. What was significant about Brodmann's work was that areas defined by their microscopic appearance often correlated with areas defined by their function. (The numbers have no significance and are merely for reference.)

cell bodies of nerve cells, they are taken up by the cells, incorporated into proteins or glycoproteins and transported to the nerve terminals. If very thin slices of the brain tissue are placed against photographic film, the presence of the radioactive material shows up as a blackened area of film. Conversely, the location of cell bodies belonging to particular nerve terminals can be identified by exploiting the ability of nerve terminals to take up radioactively labelled proteins or small particles in the neighbourhood of the terminal and to transport them back to the cell body. Even more ingeniously, viruses that can cross synapses have been used to trace chains of functionally connected nerve cells.

The 'association areas'

We have seen that the effects of electrical stimulation of different areas of cortex, or the effects of disease or damage in particular areas, led to the identification of the motor cortex, the somatosensory cortex, and the visual cortex. There are also well defined areas of cortex concerned with hearing and with smell. For a long time, what the remaining areas of the cortex did was not clear, and because electrical stimulation caused little in the way of motor or sensory responses they were called 'silent areas'.

A striking difference between these silent areas and the areas with well-defined

functions, was pointed out by Paul Emil Flechsig, the professor of psychiatry in Leipzig, as the result of a long series of investigations beginning in the 1890s. By examining the brains of premature, full-term and early post-natal infants he could divide the cerebral cortex into areas in which the myelin sheaths were laid down before birth and those in which they were laid down later. He found that the areas in which myelination occurred before birth corresponded to the motor cortex, and the various sensory cortices. The areas in which myelination was delayed until after birth corresponded to the intervening silent areas. As myelination is necessary for proper functioning, the delayed myelination of these intervening areas suggested that they only started functioning as the organism began to acquire experience. Flechsig called them *association areas* and he supposed that they not only brought together the information from the different sensory areas, but were also responsible for the higher intellectual functions that develop after birth.

In recent years, the distinction between the sensory areas and the association areas has become blurred, with the realization that fibres bringing sensory information from the thalamus reach all portions of the cortex. And the area of 'association cortex' has shrunk, as more careful investigation has revealed that some areas previously labelled association areas are, in fact, secondary areas for processing motor or sensory information of a particular kind. For example, next to the primary visual area (striate area) there are areas concerned specifically with colour or with movement. But even after the shrinkage, in humans, about half of the total area of cortex remains association cortex (see Figure 11.6).

The proportion of the cortex that is occupied by the association areas is much greater in humans than in other primates, and much greater in primates than in non-primate mammals. This is compatible with Flechsig's view that this part of the cortex is responsible for higher mental functions. If that view is right, it is important to know just what goes on in these areas. Unfortunately, their 'silence' means that the most straightforward method of investigating function – seeing the effects of electrical stimulation – is useless; and attempts to elicit electrical activity in areas of association cortex by applying normal stimuli to the skin or the sense organs have proved unrewarding. Until the development of modern scanning methods – which we shall look at later – elucidation of the functions of different parts of the association cortex therefore depended on the study of the effects of local damage caused by disease, accident or surgical interference.

Studies of this kind led to vigorous controversy about whether there was any localization of function within the association cortex.²³ Obviously, areas concerned with the integration of information of different kinds could not be isolated from each other, but did that imply that the association cortex worked as a single unit? And if it did, did different parts of it have different functions, or did they all act in the same way? This latter alternative was strongly advocated by the American neurophysiologist Karl S. Lashley, who supported his case with

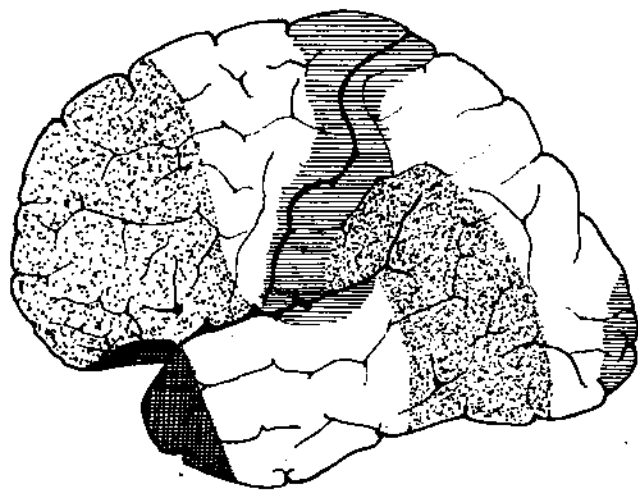


FIGURE 11.6 The association areas in the human cerebral cortex. The three association areas are shown either stippled or cross-hatched. Primary motor or sensory areas are shaded with horizontal lines. The white portion of the frontal lobe is a secondary motor area; the white portions of the other lobes include secondary or higher-order sensory areas.

some surprising observations on rats.²⁴ He found that the effect of damage to the association areas on a rat's ability to learn mazes, (or to cope with mazes learnt before the damage was inflicted) *depended solely on the volume of cortex damaged, and not at all on its location.* Lashley's findings are puzzling and have never been satisfactorily explained, but one possibility is that the tasks he set his rats involved so many different areas that damage to most areas caused a falling off in performance. In any event, Lashley's view eventually had to be abandoned because of overwhelming clinical evidence.

By the middle of the century it was clear that the effects of disease, trauma, or surgical interference on the various areas of the association cortex were very different depending on which area was damaged. Here I only want to give the briefest summary of the pattern that is suggested by those differences. Roughly speaking, the part of the association cortex that lies wholly in the frontal lobe (see Figure 11.6) appears to be concerned with planning, especially the planning of complex patterns of movements, including those involved in speech – in the left hemisphere it includes Broca's area. The part that straddles the parietal, occipital and temporal lobes is concerned with bringing together somatosensory, visual and auditory information, to promote the creation and use of complex perceptions, including shapes and words – in the left hemisphere it includes Wernicke's area. The part that is divided between the lower part of the frontal

lobe and the front part of the temporal lobe contains areas which, when damaged, cause abnormalities in emotion and memory.

... LA VISITE EST TERMINÉE

That completes our tour, and it also completes this section of the book. We have seen what sort of message nerves carry and how they are able to carry them. We have seen in some detail how nerve cells interact with one another, and in the sketchiest outline how networks of such interacting cells might form the basis of control systems capable of deciding, of remembering, and of learning. We have seen how sense organs are able to detect changes in their environment and to code the information they acquire in a form suitable for transmission along nerves to the brain. And we have looked at the overall organization of the human brain and had a glimpse of its evolutionary history. At each stage of the story I have tried to say something about the observations, experiments and arguments that have led to current views, so that those views do not seem like the towers of Toledo at sunrise – ravishing but insubstantial, and resting on nothing but the mist over the Tagus.