
1

Introduction to brain research

For the last twenty years considerable interest has been directed towards brain research. One of the main reasons for this is the concentration by medical researchers on particular organs with the aims of understanding the total functioning of such organs and of investigating the possibility of their replacement by younger and more efficient units. Kidney and heart transplantation are now practised widely and there has been some success in overcoming initial difficulties caused by organ rejection. One problem is whether the experience gained with these organs could be applied to the central organ, the brain. Let us first consider the technical aspects. The multiple nervous connections that carry sensory input to the brain and outgoing commands to the periphery, the cranial nerves, mean that neural reconnection is biologically and technically impossible (for reasons discussed later). A second problem would be the rejoining of blood vessels. Microsurgery would make this technically feasible, but the brain's continuous need for oxygen would hardly allow sufficient time for transplantation, even if the replacement brain were cooled. But the real problem lies elsewhere. The brain represents the signature of a genetically unique person: the individual fate and memories of that particular person, his or her character. In short, the existence of individual life history makes the idea of a cerebral replacement a foolish and worthless concept.

The idea of brain transplants apart, research on brain structure and function has made great leaps forward since the development of methods for analysing morphological and functional aspects of the brain. Comparative biology and evolutionary principles soon showed that the human brain shared common features with the brains of all vertebrates. Ludwig Edinger (1904), C. U. Ariens-Kappers, G. C. Huber and Elisabeth Crosby (1936) explored and analysed these common neurological features and it became clear that while the human brain had a larger cerebral cortex, it contained no specifically human features. The macroscopic constructional principles of the

vertebrate brain, especially those of primates, have a common organisational layout and differ only in the relative proportions of certain regions. The microscopic features – the wiring up of the components – appear to obey the same rules of microcircuitry in all vertebrates. The similarity in basic connections and in ultrastructure, especially among the primates, allows the full transfer and application of comparative morphological, neurophysiological and neurobiochemical studies to the human brain. This comparative approach is endorsed by evolutionary principles, which show common vertebrate features repeated in individual embryogenesis. With these advances, human neurological diseases have become better understood, and neurosurgery has gained new tools and insight, using extensively the microtechniques of animal experimentation. Psychiatry in particular has benefited from advances in neurobiochemistry and neuropharmacology.

Psychiatry needed these advances most, having been tied down for centuries by religious and philosophical concepts. A prime mover in this field was Paul Flechsig (1847–1929), best known for his studies on myelogenesis in the brain (Flechsig, 1927) and the first medical man appointed to the Chair in Psychiatry at the University of Leipzig. His predecessor, Heinrich, was a philosopher by training and maintained that mental events were independent of bodily processes, being a manifestation of the soul! Flechsig, however, was trained by the eminent physiologist Ludwig, whose pupils included the Russian experimental physiologist Pavlov. Flechsig was determined to break away from his contemporaries' belief in the mystical cause of mental diseases, and concentrated his researches on the maturation of the brain tracts and on neuropathological aspects. He was working during a period of vigorous morphological research, when the Spanish school of neurohistology of Ramón y Cajal and the Italian Golgi were both making rapid advances in the structural analysis of the nervous system. In Germany, scientists such as Edinger, Held,

Weigert, Nissl and Vogt devoted their whole lives to unravelling some of the basic components of the nervous system, some workers using the comparative approach, others the clinical. In England, in a similar endeavour, physiological and clinical methods were used by Ferrier, Sherrington and Horsley, and were later refined and developed by Adrian. The era which started around 1870 with Fritsch, Hitzig and Ferrier and ended in the 1950s with Adrian and Penfield can now be seen as the classical period of brain research. Its results and techniques have been summarised by

Glees (1961a,b,c). After this period, methodology advanced rapidly, with the application of highly refined neurophysiological methods such as micro-electrode recordings and tracer studies of brain metabolism using radioactively labelled substances such as glucose. The scope of morphology gained considerably from electron microscopy and studies of the transport of labelled substances or compounds of low molecular weight along the axon, towards the periphery (downstream) or towards the cell body (upstream).

2

Evolution of the nervous system

Vertebrate evolution

General considerations

Organic evolution on Earth began in the border zone between the Earth's crust and its atmosphere. The interaction of solar energy with the Earth's surface, largely covered by the oceanic basins, resulted in mainly salt solutions. These would become an essential component of life and, eventually, of nervous systems. If we accept the view that the oceans and their rocky surroundings became the fertile grounds for organic evolution, then rock formations and marine sediments become important witnesses for evolution. The remains of early life in rocks and sediments had been known for a long time but it was only in the second half of the nineteenth century that their significance was recognised by science as documentary evidence of the evolution of life on Earth. Up to that time it was the teaching of the Church that the Earth and its inhabitants were created by a single act of God about 4000 years ago. This view was also accepted by scientists, although later modified by the French anatomist Cuvier (1769–1832) who assumed several creative acts in order to explain the different fossil findings in different geological periods. By the fifteenth century the study of mineralogy had attracted Bauer, a German doctor, who studied closely excavations made for the mining industry and who laid the foundation for a close relation between evolution and geology. Berry (1968) has given an excellent account of the interrelation between the exploration of the Earth's crust and the understanding of evolution. Figure 2.1 shows the evolution of animal groups in relation to the geological history of the Earth. It shows that the beginning of vertebrate life was in the Cambrian period. Little evidence of life in the Precambrian period is available.

Considering evolution in general, it can be said that animal life started in a simple form and that early animals and plants shared common features. Animals and plants are constructed for survival and propagation. The need for adaptation to survive in varying

environmental conditions shows the advantage of simple construction. A high degree of specialisation, which can arise from refinements of simple forms, may be disadvantageous in that such specialised organisms are less capable of adaptation to changing environmental conditions; this might explain the extinction of some highly specialised animal species.

The diversity of animal and plant life demands an explanation, which appears to be supplied by the concept of evolution. The variety of life as we see it today is not the product of one act of Creation but is the outcome of continuous change of modifiable species. This continuous remodelling of life, happening slowly or intermittently during geological periods, is generally accepted, but the factors which cause these evolutionary processes are still debated. Since Darwin proposed his theories, two factors appear to be the major ones:

1. Natural selection: survival of the fittest and the propagation of certain advantages – anatomical, physiological or biochemical – in the offspring.
2. Genetic mutations affecting germ cells, caused by exposure to cosmic radiation or other high-energy particles.

These genetic effects were shown to be present by Müller (see Butler, 1954) in his experiments with the fruit fly (*Drosophila*), using X-rays to affect the germ cells. The significance of germ mutation for evolution has been put forward convincingly by the Swiss zoologist Portmann, and his book *Introduction into Comparative Morphology of Vertebrates* should be consulted.

The concept of the origin of life from non-living matter and its development to more and more complicated forms was perceived by the Ancient Greeks. The term evolution usually includes a successive constructional improvement; this is in itself a justifiable assumption but does not need to be the case.

During the eighteenth and nineteenth centuries the study of fossil remains recovered from different

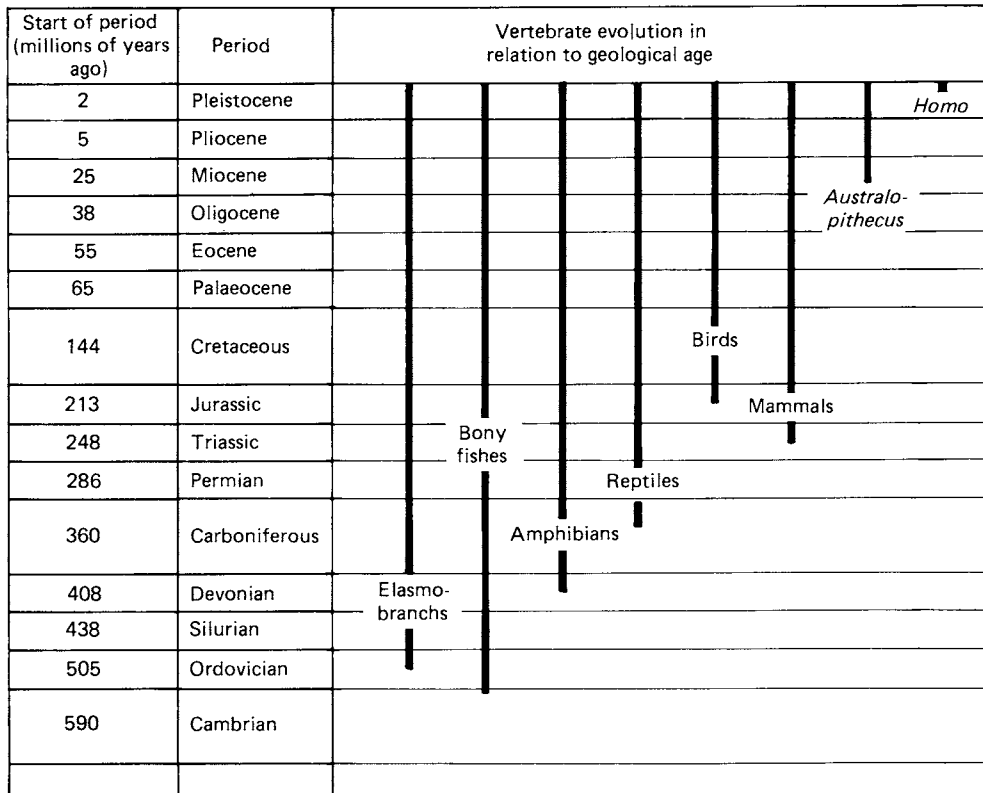
sedimentation layers of the Earth's crust became popular. These studies led to the concept of evolution in the animal world. This was, however, rejected by Baron Cuvier (1769–1832), who postulated a series of creative acts. A comprehensive view of evolution, in particular by selective pressure, is due to Darwin (1809–1882) (Darwin, 1859), Huxley (1825–1895) and Haeckel (1834–1919) (Haeckel, 1874). Darwin's work and writings are well known, have been amply illustrated by excellent television series, and need only a brief comment here. Darwinian evolution is a slow modelling process of animals and plants and is closely related to geological history. The interconnection of great land masses favours an exchange of life forms, while separation from land masses, on islands such as Australia and the Galapagos Islands (Darwin, 1836), leads to survival of species and specialised forms not seen on the larger land masses. The fossil record and the survival of such 'primitive' forms as marsupials are important evidence for evolution.

The concept of evolution is not without its

critics, however. Among them was the late Arthur Koestler, who found the principle of natural selection and survival of the fittest unsatisfactory and believed that Lamarck's view on the inheritance of acquired characteristics still had some justification. Koestler stressed most emphatically his conviction that evolution does not act blindly but follows definite biological and constructive principles. Koestler's (1967) book, *The Ghost in the Machine*, should be consulted for its stimulating and thoughtful approach to evolution and Man's creativity. Koestler's arguments against Darwin's views are, however, often the products of philosophical humanitarian motives rather than critical scientific reasoning.

An important introduction to the history of evolutionary thinking can be found in the biographies of Darwin and Huxley by Irvine (1955) and *Early Man* by Clark Howell (1966). A comprehensive review of evolution, based on an extensive bibliography, was published by Julian Huxley in 1964.

Fig. 2.1. Evolution of the vertebrates related to the geological history of the earth (from Glees, 1971).



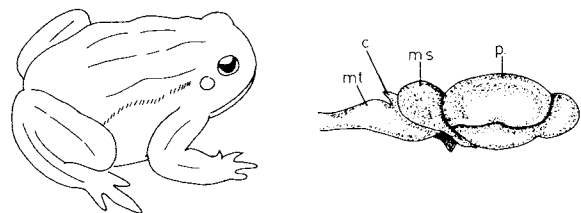
Brief overview

A biological model of primitive vertebrates is the lamprey *Petromyzon* (see Fig. 2.2). These cyclostomes appeared 400 million years ago. They and the hagfish are the sole survivors of Palaeozoic agnathans (jawless fish) and are important witnesses for vertebrate evolution. Hardisty (1979) and Brodal & Fänge (1963) produced extensive reviews of the biology of lampreys, which live in rivers or in the sea and which may follow parasitic or free-living modes of life. Related to the cyclostomes are the jawed fishes (gnathostomes), bearing paired fins. In the Palaeozoic era, a bifurcation into cartilaginous and bony fishes occurred. Cartilaginous fishes still exist (e.g. sharks and rays), while the bony fishes (teleosts) are the dominant fishes today in both fresh and sea water. From the early types of bony fishes, lungfishes developed; usually found in the estuaries of rivers, they breathe air, rising to the surface of the water to gulp, and are capable of survival in dry periods by burrowing in the mud. It is reasonable to assume that a similar fish, capable of breathing on land, might have used its fins to crawl about and might have led to the evolution of new forms of vertebrates, the amphibians (eventually frogs, newts and others; Fig. 2.3), capable of living on land but needing to return to the water

Fig. 2.2. The lamprey (a jawless fish) is an ancient vertebrate (from Glees, 1971). Transverse and sagittal sections through the brain of this animal may be found in Fig. 2.15.



Fig. 2.3. The toad and its brain (from Glees, 1971). c = cerebellum; ms. = mesencephalon; mt. = metencephalon; p. = prosencephalon.

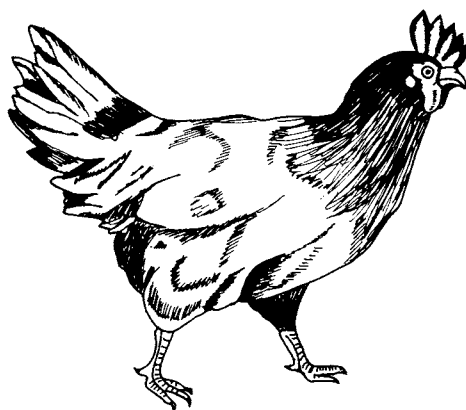


to breed. Reptiles evolved at the end of the Carboniferous period. It seems certain that the main groups of vertebrates – fishes and tetrapods – reached a high degree of specialisation very early in the Earth's history and that only minor modifications occurred later. Thus, it appears that evolutionary progress happened at a faster rate in the past than at present.

Important for progress in the evolution of reptiles was the relatively enormous size of their eggs, providing sufficient nourishment for the development of an animal capable, on hatching, of coping with the environmental factors of life on land. One basic deficiency in present-day reptiles is the lack of the ability to control body temperature in response to climatic changes or seasonal variations. When cooled, reptiles are forced to a reduction in metabolism; they are slowed down and become defenceless. Warm-blooded animals are able to live in the temperate or cold zones of the Earth, while the reptiles are today restricted to hot climates. Two animal groups became independent of temperature variations in the Mesozoic era: the birds, which developed from flying reptiles; and reptiles possessing some mammalian features. The latter group would finally give rise to the mammals.

Birds (Figs 2.4 and 2.5) are highly specialised animals which, apart from being able to regulate body temperature, are further independent of the prevailing climate, since most can fly and thus migrate to suitable geographical regions. This enables birds to escape harsh climates by choosing the most suitable surroundings and to occupy areas of rich feeding

Fig. 2.4. The chicken is an example of a flying land animal whose prosencephalon, devoid of sulci, is a specialised form of the telencephalon and is thus distinguished from the brain of mammals (from Glees, 1971).



grounds. Birds and mammals have one inherent disadvantage in common. When invading new territories, they are both forced to spend much of their time in feeding their young, despite the fact that birds have a relatively short breeding time. These periods of lengthy or intensive caring for offspring impose a limit on the rate of population expansion.

The first mammals to evolve were small, mole-like creatures (Fig. 2.6) similar to present-day insectivores, which lived in burrows. The development of

a placenta inside the uterus provided nourishment in a safe environment for the foetal stages. Thus, a smaller percentage of offspring died in the early stages. When compared with the highly specialised birds, however, mammals are relatively primitive animals. Mammals, with their simple limbs, cannot be compared favourably with the long-distance air travellers such as the albatross (Fig. 2.5). The bird's high body temperature (40–43 °C) is the sign of a fast metabolism, but forces them to search for food most of

Fig. 2.5. The albatross (*Diomedea*), largest of seabirds covering vast areas of the Pacific and Southern Oceans, has a great opportunity for choosing the most suitable habitat.

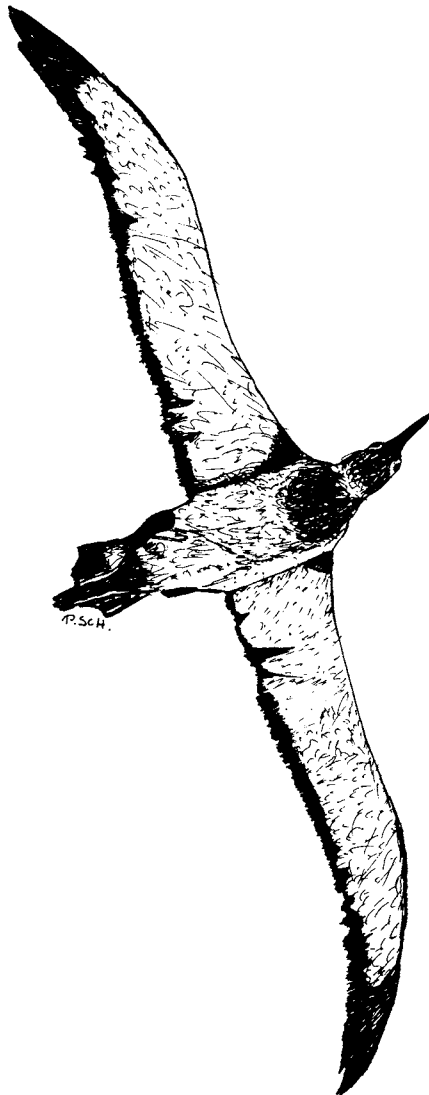
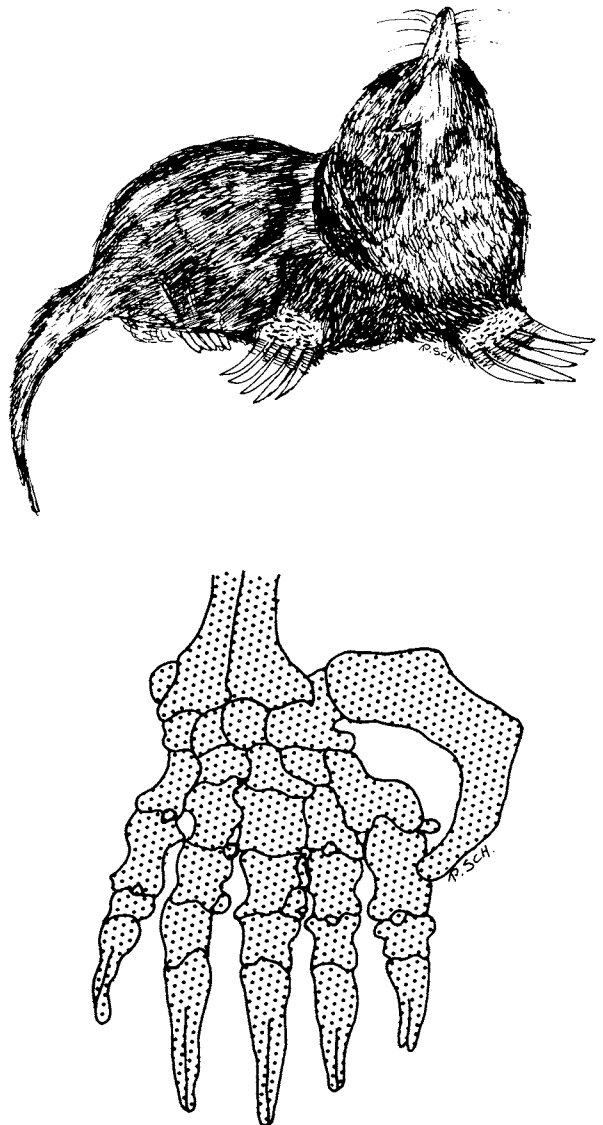


Fig. 2.6. The mole (*Talpa europaea*) is a simple mammal but has its forefeet specialised for digging (forefoot skeleton below).

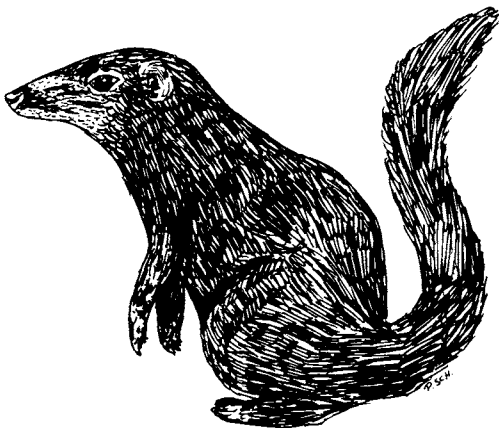


the time. Birds usually do not carry stored energy such as fat deposits, as this would hinder their flight capability (birds kept in captivity and 'fattened up' lose their ability to fly). The lack of fat for emergency nourishment has a further disadvantage: when the sudden onset of a cold period prevents access to food, birds die of starvation while mammals can utilise their fat stores. The highly effective and specialised enzymes of the bird's liver are vulnerable to the toxic insecticides used in agriculture; the less specialised small mammals survive better in a toxic environment.

The essence of mammalian basic construction is the provision for high adaptability in changing environmental conditions (Figs 2.7 and 2.8). This adaptation is shown especially in the shape of the limbs. In the mole (Fig. 2.6), short legs and large feet allow the animal to burrow deep into the ground to make tunnels. Limbs may be extremely long, even different lengths at the front and rear, as in the rabbit and kangaroo, to make for a quick getaway by jumping. The limbs need only slight changes to be suitable for swimming or for climbing and arboreal life.

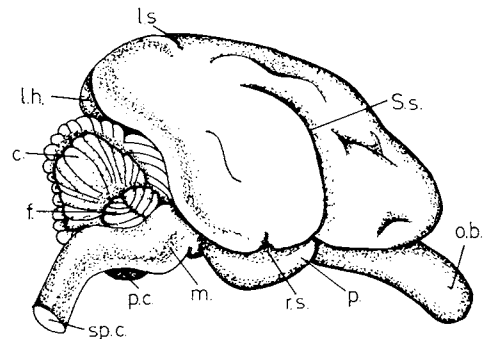
The mammalian brain is similarly suited for adaptation, in contrast to the bird's nervous system. The bird is preprogrammed by genetics much more than is the mammal. The bird behaves after hatching in an automatic pattern in response to a particular trigger situation such as hunger or sex drive. We know from the works of Lorenz (1963, 1965) and Tinbergen (1951) and their pupils how greatly the bird's behaviour pattern is ritualised, predictable and stereotyped

Fig. 2.7. The common tree shrew (*Tupaia glis*). A primitive mammal from southeast Asia, as regards brain development it occupies a position between the Insectivora and the prosimian primates (from Glees, 1971).



(see Chapter 15). The difference between bird and mammal is also clearly demonstrated by the fact that the bird can hardly change its basic pattern of behaviour by experience. Mammals, however (especially

Fig. 2.8. The thick-tailed bushbaby (*Galago crassicaudatus*) and its brain, viewed from the right side. The encephalon is relatively devoid of sulci, showing only the principal sulci of the primate brain (from Glees, 1971). c. = cerebellum; f. = flocculus of the cerebellum; l.h. = left hemisphere; l.s. = lunar sulcus; m. = mesencephalon; o.b. = olfactory bulb; p. = pons; p.c. = palaeocortex; r.s. = rhinoid sulcus (palaeoneo-cortical sulcus); sp.c. = spinal cord; S.s. = Sylvian sulcus.



the 'higher' mammals), have the ability to use individual experience for modifying instinctive behaviour. We see that a bird, when caught in a cage, will press its head against the wires to get out, driven by the panic urge to free itself. A monkey (Figs 2.9–2.11),

however, can be seen to reflect, planning its escape, or to wait for the cage door to be opened. Brain organisation in the primate allows for an intelligent assessment of the situation and the monkey is not harassed by urges and instinct like the bird. In the further chapters of this book, it will be our task to trace what factors of brain evolution and neural construction enabled mammals, and in particular Man, to achieve dominance in the animal kingdom (Figs 2.12 and 2.13). Man has conquered the Earth and pushed his close

Fig. 2.9. The baboon (*Papio*) and its brain. Baboons are intelligent and live in social groups dominated by older males. The brain of the baboon has a larger frontal lobe than that of the macaque monkey (*Macaca mulatta*) and the central sulcus takes a tortuous course (Glees, 1971). c.s. = central sulcus; f.p. = frontal pole; o.p. = occipital pole; S.s. = Sylvian sulcus; t.p. = temporal pole. The numbers refer to results of stimulation experiments and show vector points (Glees *et al.*, 1950). 1 = retraction of tongue ipsilaterally; 2 = retraction of tongue contralaterally; 3 = transitional area from tongue to face; 4 = movements involving nose and tongue; 5 = lip movements; 6 = nose and tongue movements; 7 = supination and extension of thumb and digits 2 and 3; 8 = supination and extension of wrist joint; 9 = extension of wrist; 10 = shoulder movements; 11 = extension of whole arm and hand pushed forward; 12 = extension first, then retraction of arm; 13 = arm movements combined with finger movements; 14 = extension of fingers; 15 = anterior border of hand movements and forearm extension movements.

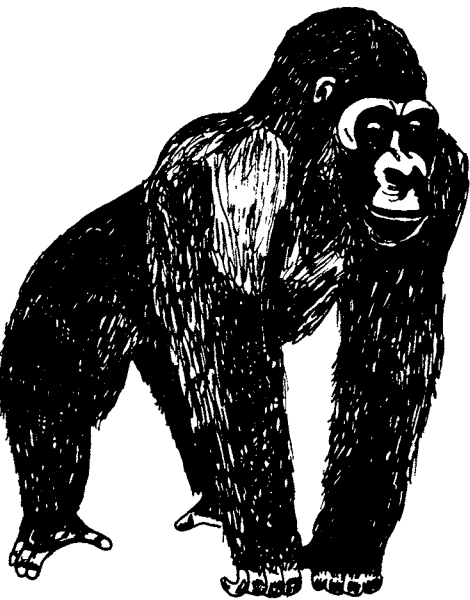
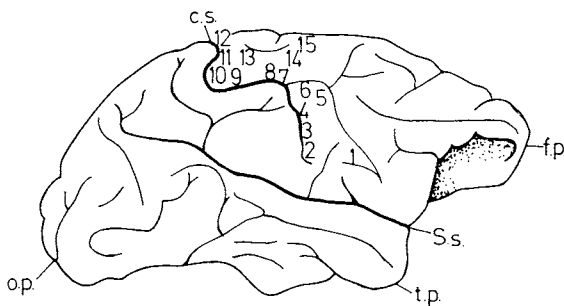
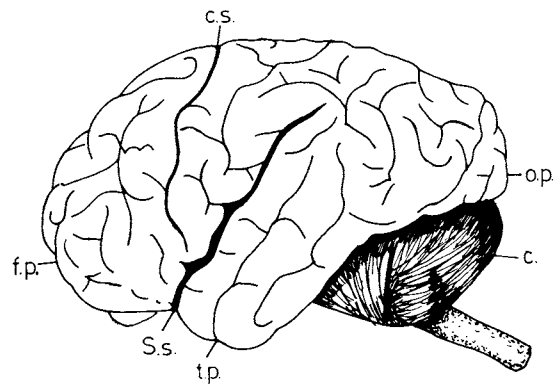


Fig. 2.10. The gorilla and its brain. This example of a higher primate brain shows the similarity to the human brain (from Glees, 1971). c. = cerebellum; c.s. = central sulcus; f.p. = frontal pole; o.p. = occipital pole; S.s. = Sylvian sulcus (fissure); t.p. = temporal pole.

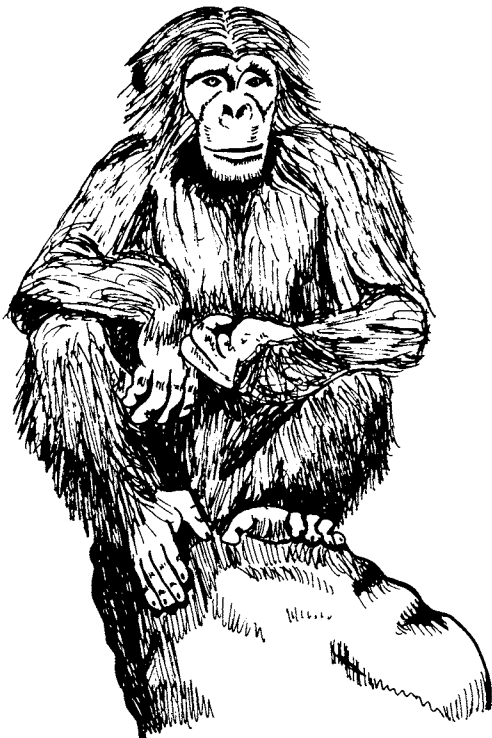


relatives among the primates into the remnants of the primeval forests. It is obvious that the greater brain volume and the brain organisation of Man must give an answer to his superiority. It appears then that a 'primitive' body construction, including a versatile digestive system, and the enormous enlargement of the forebrain were the pillars of human superiority. As we have seen, the forebrain enlargement offered a neural organisation for 'liberating' mammals, in particular primates, from the lower centres of reflex activity and instinctive behaviour. It is the elaboration of the cerebral cortex (see Figs 2.26 and 2.27) – the grey matter – which makes Man the tool-maker and inventor. (For a wide-ranging and detailed overview of the vertebrate brain and intelligence, consult Macphail (1982).)

Nervous system evolution

The primary task of a sense organ is to detect and pass on environmental information. When the

Fig. 2.11. The chimpanzee (*Pan*) is a representative of the higher apes and is found in most zoos. The body hair varies from reddish brown to black. Because of their cooperative intelligence they have been popular circus animals in the past (from Glees, 1971).



sensory information signals danger, an *escape* is initiated; should the signal indicate food, an *approach* results. In each case, innervation of appropriate muscle reaction occurs. It is a fundamental neural arrangement that sensory signals lead to well-ordered muscle contractions. The neural switchboard, the speed of sensory data processing, has been studied in great detail by classical neurophysiology and the principles of reflex action have been established. If we follow the evolutionary history of the nervous system, we find full support for the concepts of reflex actions. An animal seemingly controlled by reflex action alone is the lancelet, *Amphioxus* – a knife-blade-like silvery creature, usually buried in the sand (see Figs 2.14 and 2.15). It can be considered solely as a spinal cord creature, which either has 'given up' as useless a brain during its evolution or may never have developed one.

It is the norm in evolution, however, that the anterior end of the spinal cord enlarges to form primary brain vesicles (Fig. 2.16), which can be best studied in a vertebrate embryo. To start with, we can distinguish three vesicles. Each of these vesicles contains the neural building material for well-defined functional tasks. These vesicles, named from the anterior end of the spinal cord, are the hindbrain, midbrain and forebrain (Fig. 2.17).

These primary brain vesicles (Figs 2.18–2.20) reach different sizes in different animal species and one of the vesicles may be much larger than the two others. Casts of very early fossil skulls of seacows and elephants show these very brain divisions, as demonstrated in 1950 by Tilly Edinger (the daughter of the famous pioneer of brain research, Ludwig Edinger) (see Glees, 1952a,b). The three-vesicle brain pattern is valid for the human brain as well, as it applies in all vertebrates, but in mammals this developmental stage is surpassed early on by five vesicles. The general functional significance of these brain divisions will be discussed below. These divisions contain the imprints of the genetic programmes which emerge in birds after hatching.

Nervous system development

Phylogenetically, the nervous system develops from the outer germ layer, the ectoderm. This mode of development is also present in the ontogeny of the individual (see Fig. 2.21). The ectoderm, being the outer embryonic layer, is in contact with the surroundings. It seems common sense that this layer is destined for contact information and for the elaboration of the external stimuli. To protect the more refined nervous constructions, the data-processing part is moved

Fig. 2.12. The evolution of primates over the last 35 million years (after De Beer, 1964).

