# 1 Background to psychobiology

Before we can begin to discuss the various types of hormones, how they are formed, how they are secreted, how they act upon the body, and then how they can possibly influence behaviour, it is first necessary to provide a brief background to some basic psychobiological concepts. In this chapter I will describe the general layout of the nervous system, and explain how cells within the body (and especially within the central nervous system) communicate with one another.

Neuroanatomical directions

Neuroanatomists have devised a three-dimensional system of directional coordinates in order to navigate around the complex machinery of the brain. Instead of terms like 'front' and 'back' or 'top' and 'bottom', which are all relative, they instead employ the following terms that are always taken from the orientation of the spinal cord. There are three main axes: anterior–posterior, dorsal–ventral and medial–lateral. Thus, in most vertebrates that walk on four legs, the front (towards the nose) is called the 'anterior' while the back (towards the tail) is called the 'posterior', though when referring to the brain the terms 'rostral' (towards the front) and 'caudal' (towards the tail) are often used. Towards the surface of the back is referred to as 'dorsal' (think of a shark's dorsal fin) while the aspect towards the chest/stomach is referred to as 'ventral'. Towards the sides is 'lateral' while towards the middle is 'medial'. In addition, something lying above another part is called 'superior', while something lying below another part is called 'inferior'. 'Ipsilateral' refers to structures on the same side of the body or brain, while 'contralateral' refers to structures on the opposite side of the brain or body. This is slightly complicated in humans because we walk on two legs and so the position of our head and brain is altered relative to our spinal cord (Pinel, 2006).

Organisation of the nervous system

The nervous system is divided into two broad components: the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS consists of the brain and the spinal cord, while the PNS consists of

1
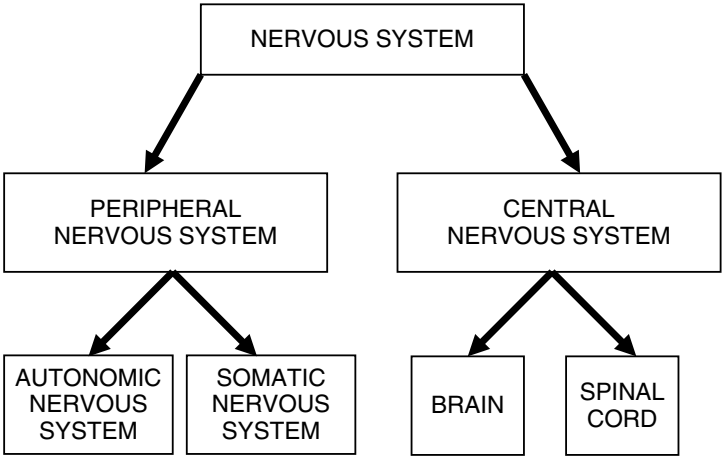
1.1 *Organisation of the nervous system*

the cranial nerves, the spinal nerves, and the peripheral ganglia (ganglion refers to a cluster of nerve cells). A basic way to differentiate these two separate but closely interlocking systems is to think of the CNS as being encased in bone (the skull and the spinal vertebrae), while the elements of the PNS are not. The PNS is further subdivided into the autonomic nervous system (ANS) and the somatic nervous system (SNS) – see diagram 1.1. The ANS acts as the regulator for the internal environment of the body, serving to relay sensory and motor information between the CNS and the internal organs. Thus, neurons (nerve cells) conduct sensory information from the internal organs to the CNS, and transmit motor commands from the CNS back to the internal organs. The SNS serves as the interface between the PNS and the outside world: its nerve cells conduct sensory information from the periphery (the skin, the joints and muscles, the senses, etc.) back into the CNS, while other neurons perform the opposite function by transmitting motor information from the CNS to the skeletal muscles.

Organisation of the brain

At first glance the human brain appears rather uniform in appearance, a globular lump of grey/white tissue overlaid with blood vessels and formed into a series of bumps and troughs. In fact the brain possesses clear divisions derived from the development of the early neural tube from which the brain forms during gestation (Cowan, 1979). Initially the tissue that will develop into the brain consists of a fluid-filled tube out of which three swellings become prominent; these swellings develop into the forebrain, the midbrain and the hindbrain. Later on in development the forebrain and hindbrain further divide into two parts, and thus the fully formed brain is
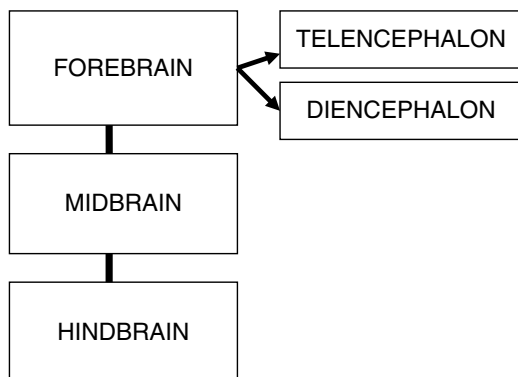
1.2 *Organisation of the brain*

recognised as having five major divisions: telencephalon[1] and diencephalon (which together constitute the forebrain), the midbrain (or mesencephalon) and the hindbrain, see diagram 1.2.

The forebrain

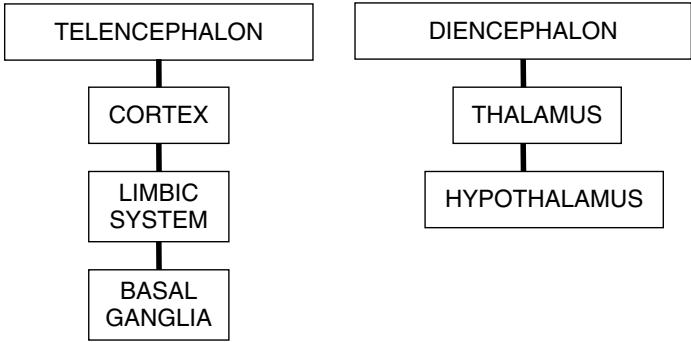The telencephalon and diencephalon are subdivided further – see diagram 1.3.

The telencephalon

The telencephalon comprises three key elements.

Cerebral cortex

The most notable features of the telencephalon are the two large and roughly symmetrical hemispheres which are in fact separate functional systems interconnected by major fibre pathways called the cerebral commissures. The principal commissure is the corpus callosum (which literally means 'hard body') and this wrist-thick bundle of fibres connects the corresponding regions of cortex, so that for example a specific area of temporal cortex in the left hemisphere is connected to the corresponding region in the right hemisphere. Both hemispheres are covered by a thin layer of tissue called cortex (in Latin this translates as 'bark of a tree'), which is not smooth but deeply convoluted, thus allowing for greatly increased material without an increase in overall brain volume. A deep cleft in the cortex is referred to as a fissure, and a shallow one is called a sulcus (the plural being sulci); each ridge is called a gyrus (plural being gyri). Some two thirds of the

---

[1] The suffix -encephalon is derived from the Greek and means 'in the head'.

```
┌─────────────────────┐        ┌─────────────────────┐
│    TELENCEPHALON    │        │    DIENCEPHALON     │
└─────────────────────┘        └─────────────────────┘
         │                              │
    ┌──────────┐                  ┌──────────┐
    │  CORTEX  │                  │ THALAMUS │
    └──────────┘                  └──────────┘
         │                              │
    ┌──────────┐                ┌──────────────┐
    │  LIMBIC  │                │ HYPOTHALAMUS │
    │  SYSTEM  │                └──────────────┘
    └──────────┘
         │
    ┌──────────┐
    │  BASAL   │
    │ GANGLIA  │
    └──────────┘
```

1.3 *Subdivisions of the telencephalon and diencephalon*

surface of the cortex is hidden in these grooves, making the total surface area of an average brain around 2360 cm^2, with the thickness of the cortex being about 3 mm (Carlson, 2004). Because neurons predominate in the cortex, the cortex has a characteristic hue and is thus referred to as 'grey matter'. Beneath the surface of the cortex run millions of axons that connect the various regions together; as they are covered by a white-coloured protective tissue called myelin this gives rise to the name 'white matter'. The most prominent features of the cortex are the two lateral fissures (the deep grooves which run along each side of the brain), the central sulcus (which runs from the top centre of the brain to join up with the lateral fissures), and the longitudinal fissure (the major gap between the two hemispheres running from front to back). These conveniently clear anatomical divisions are used to help define the different lobes of the brain, and thus the hemispheres are divided into four lobes: frontal, temporal, parietal and occipital.

Functions of the different lobes

While the cortex acts as an integrated whole to coordinate behaviour, evidence from anatomical/histological examinations, animal experiments, human cases of localised brain damage, electrical recording and stimulation experiments, and neuroimaging studies, has shown that specific areas of the cortex are responsible for certain aspects of processing. Cytoarchitectonic (cellular architecture) maps have been developed of these subregions based upon differences in cell density, cell shape, size and connectivity. A commonly used map is that produced by the neuroanatomist Korbinian Brodmann in 1909. He used tissue stains to visualise different cell types in different brain regions and described fifty-two distinct regions that are now referred to as 'Brodmann's areas'. While these areas have experienced some modification and further subdivision, experimental and imaging techniques have broadly confirmed their existence and thus we possess specialised brain regions for touch, perception, movement, and even distinct cognitive processes

(Gazzaniga *et al.*, 1998; Kolb and Whishaw, 2001). A basic summary of the key functions of each lobe is provided below:

Frontal lobes

These extend from the central sulcus to cover the anterior portion of the brain. They contain primary motor cortex (area 4), premotor cortex (area 6), Broca's area (area 44) and the prefrontal cortex. Each area receives input from the thalamic nuclei, limbic system and hypothalamus, and connections from the other lobes, making it a 'control centre'. A key region of frontal cortex is referred to as 'prefrontal cortex', which forms around a third of the entire cortical mantle, and constitutes a larger proportion of the brain in humans than in other species. A major role of prefrontal cortex concerns working memory – the ability to retain pieces of information for short periods of time. Prefrontal cortex is also involved in higher-order cognitive behaviours such as planning, organisation, the monitoring of recent events, the probable outcome of actions and the emotional value of such actions.

Temporal lobes

The temporal lobe comprises all the tissue below the lateral (Sylvian) fissure running backwards to the parietal and occipital cortices. This region is also described by gyri that form it – the superior temporal gyrus, the middle temporal gyrus and the inferior temporal gyrus. The temporal lobe is richly connected to the other lobes, the sensory systems, the limbic system and the basal ganglia, which means that the temporal lobe does not subserve a single unitary function; it seems to have three key functions. First, areas 22, 41 and 42 are concerned with auditory and visual perception, specifically with focussing attention on relevant information and with the perception of speech (left hemisphere), music and faces (right hemisphere). Secondly, the classic case of patient 'H.M.' reported by Scoville and Milner (1957) showed that the hippocampus was critical for the formation of new memories. Finally, the amygdala adjoins the hippocampus and is concerned with emotional control (see later section on the limbic system).

Parietal lobes

These lie between the occipital lobe and the central sulcus. Just behind the central sulcus lies the postcentral gyrus (Brodmann's areas 1–3) which houses primary somatosensory cortex, the region of cortex housing the sensory representation of the body. The right hemisphere contains information about the left side of the body and vice versa. Parietal cortex thus integrates sensory and motor information and so spatial navigation and perception are thought to be key functions of this region of the brain. A common feature of damage to the right parietal lobe is 'sensory neglect' – the tendency to ignore the contralateral side of the body and features of the outside world.

Occipital lobe

Occipital cortex is primarily concerned with visual perception. It is located at the caudal end of the cortex and comprises primary visual cortex (area 17) and visual association (areas 18 and 19). Area 17 is also referred to as striate (striped) cortex or area V1, and is the main target for the thalamic nuclei that receive input from the visual pathways; this information is relayed to secondary visual cortex (area 18 or V2) and then on to additional areas (area 19, V3, V4 and V5). As in the other cortices, the left half of the visual field is relayed to the right hemisphere, though the map is considerably distorted as much of our visual processing concerns the analysis of information from the central visual field (fovea).

The Limbic system

An important group of forebrain structures were defined in the 1930s and their key role was assumed to reflect motivational and emotional processing (Papez, 1937). MacLean (1949) provided further modifications to what was then called 'Papez circuit', and we now refer to it as the limbic ('ring-shaped') system which includes the amygdala, hippocampus, cingulate cortex, fornix, mammillary bodies and septum. The amygdala (means 'almond-shaped') lie at the front end of each of the temporal lobes and are not single structures but in fact consist of around a dozen interconnected nuclei (Aggleton, 1993). Bilateral removal of the amygdala in monkeys leads to profound impairments in social and emotional behaviours, while bilateral amygdala damage in humans leads to similar deficits in emotional processing, with fear and anger being particularly affected (Broks *et al*., 1998; Scott *et al*., 1997). The hippocampus ('seahorse') is a bilateral structure located within the temporal lobes. Many studies involving both experimental animals, human cases of brain damage, and brain functioning in undamaged humans have clearly demonstrated that the hippocampus is crucial for what is called 'declarative memory', i.e. memory for explicit facts and episodes (Squire, 1992; Squire *et al*., 1992).

Lying above the corpus callosum is a large region of cortex formed within the cingulate gyrus; it encircles part of the thalamus (and shares dense interconnections with the various thalamic nuclei) and is referred to as cingulate cortex. Evidence from experimental animal and human case studies demonstrates that damage to cingulate cortex leads to a profound disturbance in the experience and expression of emotion: generally the individual seems completely unresponsive to affective situations or stimuli (Damasio and Van Hoesen, 1983). The fornix ('arch') is a fibre pathway connecting the hippocampus to the mammillary ('breast-shaped') bodies which are part of the hypothalamus, and the septum.

The basal ganglia

The third element of the telencephalon is a collection of individual nuclei that together are involved in the control of voluntary movements. The principal structures of this system include the caudate ('tailed') nucleus and the putamen ('shell'), which are collectively referred to as the striatum ('striped structure'), and the globus pallidus ('pale globe').

The diencephalon

The diencephalon contains two key elements: the thalamus and the hypothalamus. The thalamus is not a single structure but is a two-lobed collection of separate but interconnected nuclei. Most of these nuclei receive input from the sensory systems, process it, and then transmit the information to the appropriate sensory processing areas in the neocortex. The thalamus thus seems to act as a kind of sensory relay centre and can thus influence almost the whole of the brain. Some of the thalamic nuclei may also play a key role in certain aspects of learning and memory. The hypothalamus lies underneath the thalamus at the base of the brain. It too is not a single structure but comprises twenty-two small nuclei, the fibre pathways that pass through it, and the pituitary gland attached to the hypothalamus via the pituitary stalk. This array of nuclei control the autonomic nervous system and the endocrine system. Almost all aspects of basic motivations and survival behaviours (such as fighting, escape, mating, feeding, etc.) are coordinated from here. I shall describe the form and functions of the hypothalamus and pituitary gland in more detail in the next chapter.

The midbrain

The mesencephalon consists of two major parts: the tectum ('roof') and the tegmentum ('covering'). The tectum contains two main structures, the superior colliculus and the inferior colliculus, which appear as four bumps ('colliculus' is Latin for 'mound') on the surface of the brain stem. The inferior colliculus forms part of the auditory system, and the superior colliculus forms part of the visual system, appearing to be important in visual reflexes and reactions to moving stimuli. The tegmentum lies beneath the tectum and it includes portions of the reticular formation, a set of more than ninety interconnected nuclei in the brain stem which play a role in sensory processing, attention, arousal, sleep, muscle tone, movement and reflexes. Two key structures of the tegmentum are the red nucleus and the substantia nigra ('black substance') which are important components of the motor system as they connect to parts of the basal ganglia.

The hindbrain

The hindbrain contains the cerebellum ('little brain'), a two-lobed structure lying directly underneath the cerebral hemispheres and connected to the brain stem. This important structure receives information from the sensory systems and from the muscles and the vestibular system and it coordinates this information, making our movements smooth. Damage to the cerebellum (which occurs in cerebral palsy) leads to impairments in walking, balance, posture and the performance of skilled motor activities. The hindbrain also houses the pons ('bridge'), a bulge on the brain stem which contains part of the reticular formation and seems to play an important role in sleep and arousal. Finally, a key structure is the medulla oblongata ('oblong marrow') which lies at the end of the brain stem bordering the top of the spinal cord. It also contains part of the reticular formation and contains nuclei that control vital functions such as control of breathing and skeletal muscle tone.

Communication systems

The body has evolved three different communication systems: the nervous system, the endocrine system and the immune system, each of which has its own type of specialised chemical messenger. The nerve cells (or neurons) use neurotransmitters (but also use certain hormones), endocrine glands use hormones, and the immune system uses cytokines. The three systems are very closely interlinked: the nervous system controls the release of hormones (this process will be described in detail in the next chapter) and can influence the release of cytokines by the immune system. Hormones in turn can influence nervous system activity (neuroendocrinology) and have close links with the immune system (neuroimmunology).

As described by Gard (1998), possibly the most simple form of communication between cells is for one cell to release a chemical into the extracellular fluid; this chemical can then influence the activity of nearby cells. Such a system of course is not very efficient as it is non-specific, and large amounts of the chemical may have to be released to ensure that the nearby cell can be influenced. Nature seems to have solved this problem by ensuring that cells develop specialised outgrowths towards one another, and that only certain regions of the cells can secrete the chemicals. This process in fact describes how neurons within the central nervous system communicate, and it is referred to as 'neurocrine' communication (and will be described in detail in subsequent sections). In a variation of this type of cell, some neurons release hormones which act within the central nervous system – this is called 'neuroendocrine' communication (and is described in the next chapter). The problem with the neurocrine system is that a single neuron is only able to communicate with a fairly limited number of cells within a short distance.

In order for a cell to communicate with more widely dispersed cells, then, another system is required.

Some cells thus release their chemicals into the bloodstream and are thereby able to influence cells all over the body. However, this system has certain drawbacks in that only molecules under a certain molecular size can be transported through the vascular system; the secretory cells must be linked to the vascular system via the capillaries; and the secreted chemicals may be constantly being depleted by blood arriving from other areas of the body. This means that only a small fraction of the secreted chemical can reach the target cell. These problems have been solved by the fact that cells producing a chemical clump together and form glands; they can thus produce larger amounts of the chemical (in this case a hormone). In addition the chemicals that they secrete are very potent and thus only small amounts are required. This is in fact how the endocrine system works. Note that the endocrine glands also release chemicals which act on adjacent cells (just like neurons). This is referred to as 'paracrine' communication.

Cells of the nervous system

The nervous system consists of two different types of cell.

Glia

These are by far the most prominent in terms of quantity, outnumbering the neurons by around ten to one. For many years it was assumed that all they did was act as support workers to the much more important neurons. Hence, the different types of glial cells – oligodendrocytes, Schwann[2] cells, astrocytes, and microglia – provide the neurons with nutrition, clear waste products from them and hold them in place; the word 'glial' in fact means 'glue' and often these cells are collectively referred to as 'neuroglia' (literally meaning 'nerve glue'). In fact the status of these humble cells is rapidly rising as research is beginning to demonstrate that they also serve important roles in transmitting and receiving information from neurons, and in establishing and maintaining the connections (synapses) between neurons.

Neurons

According to Williams and Herrup (1988) the adult human brain contains around 100 billion neurons which combine to form consciousness, sensory experience and controlled behaviours. Neurons have a high metabolic rate and must be constantly supplied with oxygen and glucose or they will die.

---

[2] Named after German physiologist Theodor Schwann (1810–82).

Unlike other cells of the body, neurons are not replaced when they die and we are born with as many as we will ever have. The role played by the various support cells described previously is thus very important. The neurons are specialised cells that receive and transmit information; they vary in size and shape but all consist of the same basic structures:

Cell body (soma)

The soma contains the machinery which serves to maintain the normal functioning of the cell, and also houses the nucleus which contains the genes housed in twenty-three pairs of chromosomes (thus a genetically 'normal' human will posses forty-six chromosomes). In twenty-two of the chromosomes (referred to as autosomal chromosomes) genes form matched pairs (one inherited from the mother and one from the father). These matched pairs of genes are referred to as alleles. The twenty-third pair of chromosomes are the sex chromosomes – the X and Y chromosomes, designated thus because they roughly resemble these shapes. These special chromosomes determine an individual's sex: normal females possess a pair of Xs, while normal males possess one X and one Y. Since the female always has two X chromosomes her eggs will always carry an X, but a male's sperm can carry either an X or a Y; thus the offspring can be XX (female) or XY (male). Alternatives to this normal pattern of sex chromosomes, and how they affect sex determination, will be discussed in detail in chapter 6.

Each chromosome is a very long molecule of deoxyribonucleic acid (DNA) with many genes along its length, providing a set of instructions for constructing an organism, these instructions being referred to as the 'genome'. The discovery that DNA consists of two helical spirals which can 'unzip' to make copies of itself is attributed to Francis Crick and James Watson in 1953.[3] However, significant credit should also be given to Rosalind Franklin, Maurice Wilkins and Linus Pauling whose research enabled the now famous pair to make the conceptual leap and hence take the bulk of the credit. We now understand that the strands of DNA are composed of a sequence of nucleotide bases attached to a chain of phosphate and deoxyribose. The bases are: adenine (A), cytosine (C), guanine (G) and thymine (T), and they are always linked in a particular fashion (A with T; G with C). Genetic information is copied and transmitted when the two strands became 'unzipped' and collect new complementary bases forming two double-stranded molecules of DNA, each identical to the original.

To assist in the copying process there is another substance in each cell called RNA (ribonucleic acid) composed of adenine, guanine, uracil and cytosine. The number of bases can vary from a thousand to a million, with a sequence of three bases (called a 'codon') along the strand making up a gene.

---

[3] Crick announced the 'secret of life' not to a scientific conference but to the more humble clientele of the Eagle pub in Cambridge!