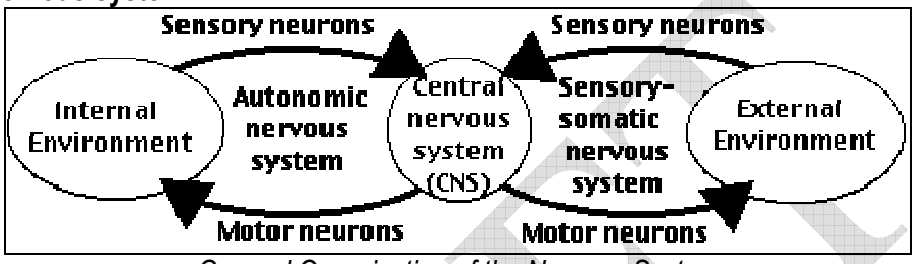
Chapter 3
Central Nervous System

2.1. Organization of the Nervous System

The nervous system is divided into the **peripheral nervous system** (**PNS**) and the **central nervous system** (**CNS**). The **CNS** consists of the **spinal cord** and the **brain.** The **PNS** consists of **sensory neurons** running from stimulus **receptors** that inform the CNS of the stimuli and **motor neurons** running from the CNS to the **muscles and glands** - called **effectors** - that take action. The **peripheral nervous system** is subdivided into the **sensory-somatic nervous system** and the **autonomic nervous system**



General Organization of the Nervous System

2.1.1. White Matter vs. Grey Matter

Both the spinal cord and the brain consist of white matter = bundles of **axons** each coated with a sheath of **myelin**. The grey matter = masses of the **cell bodies** and **dendrites** — each covered with **synapses**. In the spinal cord, the white matter is at the surface, the grey matter inside. In the brain of **mammals**, this pattern is reversed. However, the brains of "lower" vertebrates like fishes and amphibians have their white matter on the outside of their brain as well as their spinal cord.

2.1.2. The Meninges

Both the spinal cord and brain are covered in three continuous sheets of connective tissue, the meninges. From outside in, these are the **dura mater** — pressed against the bony surface of the interior of the vertebrae and the cranium the **arachnoid** and the **pia mater**. The region between the arachnoid and pia mater is filled with **cerebrospinal fluid** (**CSF**).

2.1.3. Extracellular Fluid (ECF) of the CNS

The cells of the central nervous system are bathed in a fluid that differs from that serving as the ECF of the cells in the rest of the body. The fluid that leaves the capillaries in the brain contains far less protein than "normal" because of the **blood-brain barrier**, a system of **tight junctions** between the **endothelial cells** of the capillaries. This barrier creates problems in medicine as it prevents many therapeutic drugs from reaching the brain. **Cerebrospinal fluid** (**CSF**), a secretion of the **choroid plexus**. CSF flows uninterrupted throughout the central nervous system, through the central **cerebrospinal canal** of the spinal cord and through an interconnected system of four **ventricles** in the brain. **CSF returns to the blood through veins draining the brain.**

2.2. The Human Central Nervous System

The central nervous system is made up of the **spinal cord** and **brain**

2.2.1. The Spinal Cord

The spinal cord conducts **sensory information** from the **peripheral nervous system** (both somatic and **autonomic**) to the brain. It conducts **motor information** from the brain to our various effectors such as **skeletal muscles, cardiac muscle, smooth muscle** and glands. It also serves as a minor reflex centre. The 31 pairs of **spinal nerves** arise along the spinal cord. These are **"mixed" nerves** because each contains both sensory and motor axons. However, within the spinal column, all the **sensory axons** pass into the **dorsal root ganglion** where their cell bodies are located and then on

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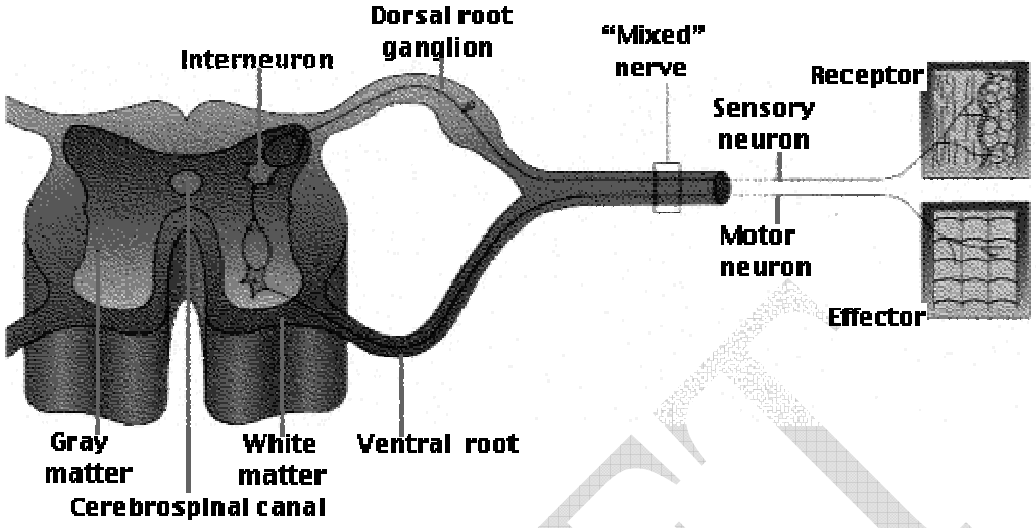
into the spinal cord itself and all the **motor axons** pass into the **ventral roots** before uniting with the sensory axons to form the mixed nerves.



The Structure of Spinal Cord

The spinal cord carries out two main functions:

1. It connects a large part of the peripheral nervous system to the brain. Information (nerve impulses) reaching the spinal cord through sensory neurons are transmitted up into the brain. Signals arising in the motor areas of the brain travel back down the cord and leave in the motor neurons.
2. The spinal cord also acts as a minor coordinating centre responsible for some simple reflexes like the **withdrawal reflex**.

The **interneurons** carrying impulses to and from specific receptors and effectors are grouped together in **spinal tracts**. Impulses reaching the spinal cord from the left side of the body eventually pass over to tracts running up to the right side of the brain and vice versa. In some cases this crossing over occurs as soon as the impulses enter the cord. In other cases, it does not take place until the tracts enter the brain itself.

2.2.2. The Brain

The brain receives sensory input from the spinal cord as well as from its own nerves (e.g., **olfactory and optic nerves**). It devotes most of its volume (and computational power) to processing its various sensory inputs and initiating appropriate — and coordinated — motor outputs.

The brain of all vertebrates develops from three swellings at the anterior end of the **neural canal** of the embryo. From front to back these develop into the **forebrain** (also known as the prosencephalon), **midbrain** (mesencephalon) and **hindbrain** (rhombencephalon). The brain receives nerve impulses from the spinal cord and 12 pairs of **cranial nerves**. Some of the cranial nerves are "mixed", containing both sensory and motor axons. Some, e.g., the optic and olfactory nerves (numbers I and II) contain sensory axons only. Some, e.g. number III that controls eyeball muscles, contain motor axons only.

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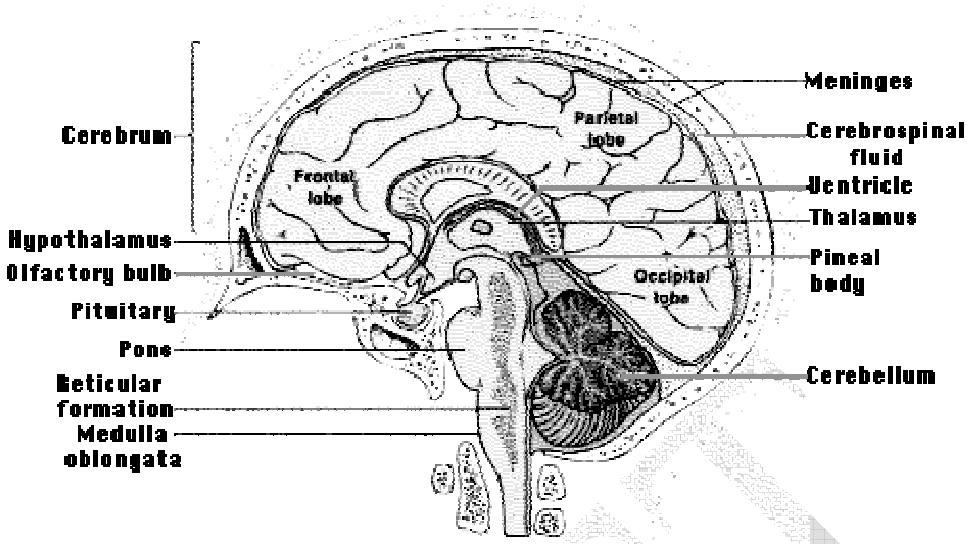

Structure of the Human Brain

(a) The Hindbrain

The main structures of the hindbrain (rhombencephalon) are the **medulla oblongata**, **pons** and **cerebellum.**

(i) Medulla oblongata

The medulla looks like a swollen tip to the spinal cord. Nerve impulses arising here rhythmically stimulate the intercostal muscles and diaphragm — making breathing possible, regulate heartbeat and the diameter of arterioles thus adjusting blood flow.

The neurons controlling breathing have **mu (μ) receptors**, the receptors to which **opiates**, like heroin, bind. This accounts for the suppressive effect of opiates on breathing. Destruction of the medulla causes instant death.

(ii) Pons

The serves as a relay station carrying signals from various parts of the cerebral cortex to the cerebellum. Nerve impulses coming from the **eyes, ears,** and **touch receptors** are sent on the cerebellum. The pons also participates in the reflexes that regulate breathing.

The **reticular formation** is a region running through the middle of the hindbrain (and on into the midbrain). It receives sensory input (e.g., sound) from higher in the brain and passes these back up to the thalamus. The reticular formation is involved in sleep, arousal (and vomiting).

(iii) Cerebellum

The cerebellum consists of two deeply-convoluted hemispheres. Although it represents only 10% of the weight of the brain, it contains as many neurons as all the rest of the brain combined.

Its most clearly-understood function is to **coordinate body movements**. People with damage to their cerebellum are able to perceive the world as before and to contract their muscles, but their motions are jerky and uncoordinated. So the cerebellum is the centre for learning motor skills (**implicit memory**). Labouratory studies have demonstrated both **long-Term Potentiation** (**LTP**) and **long-Term Depression** (**LTD**) in the cerebellum.

(b) The Midbrain

The midbrain (mesencephalon) occupies only a small region in humans (it is relatively much larger in "lower" vertebrates). We shall look at only three features:

1. The **reticular formation**: collects input from higher brain centres and passes it on to motor neurons.
2. The **substantia nigra**: helps "smooth" out body movements; damage to the substantia nigra causes Parkinson's disease.
3. The **Ventral Tegmental Area** (**VTA**): packed with **dopamine**-releasing neurons that are activated by **nicotinic acetylcholine receptors** and whose projections synapse deep within the forebrain.

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The VTA seems to be involved in pleasure: nicotine, amphetamines and cocaine bind to and activate its dopamine-releasing neurons and this may account — at least in part for their addictive qualities.
The midbrain along with the medulla and pons are often referred to as the "brainstem".

(c) The Forebrain

The human forebrain (prosencephalon) is made up of a pair of large **cerebral hemispheres**, called the **telencephalon**. Because of crossing over of the spinal tracts, the left hemisphere of the forebrain deals with the right side of the body and vice versa. It is also made up of a group of unpaired structures located deep within the cerebrum, called the **diencephalon**.

(i) Diencephalon

We shall consider 4 of its structures: the

(1) Thalamus: All **sensory** input (except for olfaction) passes through it on the way up to the **somatic-sensory regions** of the cerebral cortex and then returns to it from there signals from the cerebellum pass through it on the way to the **motor areas** of the cerebral cortex.

(2) Lateral Geniculate Nucleus (LGN): All signals entering the brain from the optic nerves enter the LGN and undergo some processing before moving on the various visual areas of the cerebral cortex.

(3) Hypothalamus: This is the seat of the **autonomic nervous system**. Damage to the hypothalamus is quickly fatal as the normal homeostasis of **body temperature,** blood chemistry, etc. goes out of control. The source of 8 hormones, two of which pass into the posterior lobe of the pituitary gland.

(4) Posterior Lobe of the Pituitary**:** It receives antidiuretic hormone (ADH) and oxytocin from the hypothalamus and releases them into the blood.

(ii) The Cerebral Hemispheres

Each hemisphere of the cerebrum is subdivided into four lobes visible from the outside: **frontal**, **parietal**, **occipital** and **temporal.** Hidden beneath these regions of cerebral cortex are the **olfactory bulbs** which receive input from the olfactory epithelia, The **striatum** that receives input from the frontal lobes and also from the limbic system (below). At its base is the **Nucleus Accumbens** (NA). The pleasurable (and addictive) effects of amphetamines, cocaine, and perhaps other psychoactive drugs seem to depend on their producing increasing levels of dopamine at the synapses in the nucleus accumbens (as well as the **VTA**). **The limbic system** which receives input from various association areas in the cerebral cortex and passes signals on to the **nucleus accumbens**. The limbic system is made up of the: **hippocampus**. It is essential for the formation of long-term memories. The **amygdala** is the centre of emotions (e.g., fear). It sends signals to the hypothalamus and medulla which can activate the **flight or fight response** of the **autonomic nervous system**. In rats, at least, the amygdala contains receptors for **vasopressin** whose activation increases aggressiveness and other signs of the flight or fight response and **oxytocin** whose activation lessens the signs of stress. The amygdala receives a rich supply of signals from the olfactory system, and this accounts for the powerful effect that odour has on emotions (and evoking memories).

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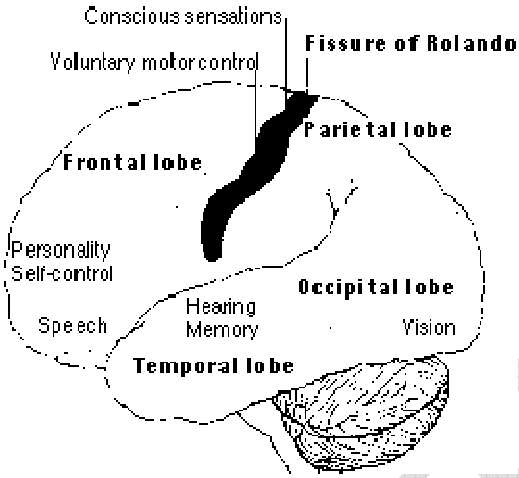

Areas of the Cerebral Hemispheres

2.2.3. Mapping the Functions of the Brain

It is estimated that the human brain contains 100 billion (10^{11}) neurons averaging 10,000 synapses on each; that is, some 10^{15} connections. How to unravel the workings of such a complex system? Several methods have been useful.

(a) Histology

Microscopic examination with the aid of selective stains has revealed many of the physical connections created by axons in the brain.

(b) The Electroencephalograph (EEG)

This device measures electrical activity (brain "waves") that can be detected at the surface of the scalp. It can distinguish between, for example, sleep and excitement. It is also useful in diagnosing brain disorders such as a tendency to epileptic seizures.

2.2.4. Damage to the Brain

Many cases of brain damage from, for example, strokes (interruption of blood flow to a part of the brain), tumours in the brain or mechanical damage (e.g., bullet wounds)
have provided important insights into the functions of various parts of the brain.
e.g. Battlefield injury to the left temporal lobe of the cerebrum interferes with speech.

2.2.5. Stimulating Exposed Brain with Electrodes

There are no pain receptors on the surface of the brain, and some humans undergoing brain surgery have volunteered to have their exposed brain stimulated with electrodes during surgery. When not under general anaesthesia, they can even report their sensations to the experimenter. Experiments of this sort have revealed a band of cortex running parallel to and just in front of the **fissure of Rolando** that controls the contraction of **skeletal muscles**. Stimulation of tiny spots within this **motor area** causes contraction of the muscles. The area of motor cortex controlling a body part is not proportional to the size of that part but is proportional to the number of motor neurons running to it. The more motor neurons that activate a structure, the more precisely it can be controlled. Thus the areas of the motor cortex controlling the hands and lips are much larger than those controlling the muscles of the torso and legs.

A similar region is located in a parallel band of cortex just behind the fissure of Rolando. This region is concerned with **sensation** from the various parts of the body. When spots in this **sensory area** are stimulated, the patient reports sensations in a specific area of the body. A map can be made based on these reports. When portions of the **occipital lobe** are stimulated electrically, the patient reports light. However, this region is also needed for associations to be made with what is seen. Damage to regions in the occipital lobe results in the person's being perfectly able to see objects but incapable of recognizing them. The centres of hearing — and understanding what is heard — are located in the **temporal lobes**.

(i) CT = X-ray Computed Tomography: This is an imaging technique that uses a series of x-ray exposures taken from different angles. Thanks to computers, these can be integrated to produce a picture of the brain. CT scanning is routinely used to quickly diagnose strokes.

(ii) PET = Positron-Emission Tomography; This imaging technique requires that the subject be injected with a radioisotope that emits positrons.

Water labelled with **oxygen-15** ($H_2{}^{15}O$) is used to measure changes in blood flow (which increases in parts of the brain that are active). The short half-life of ^{15}O (2 minutes) makes it safe to use. D**eoxyglucose** labelled with fluorine-18. The brain has a voracious appetite for glucose. When supplied with deoxyglucose, the cells are tricked into taking in this related molecule and phosphorylating it in the first step of **glycolysis.** But no further processing occurs so it accumulates in the cell. By coupling a short-lived radioactive isotope like ^{18}F to the deoxyglucose and using a PET scanner, it is possible to visualize active regions of the brain.

Most cancers consume large amounts of glucose (**cellular respiration** is less efficient than in normal cells so they must rely more on the inefficient process of **glycolysis**). Therefore PET scanning with ^{18}F-fluorodeoxyglucose is commonly used to monitor both the primary tumour and any **metastases**.

(iii) MRI = Magnetic Resonance Imaging : This imaging technique uses powerful magnets to detect magnetic molecules within the body. These can be endogenous molecules or magnetic substances injected into a vein.

(iv) fMRI = Functional Magnetic Resonance Imaging: fMRI exploits the changes in the magnetic properties of haemoglobin as it carries oxygen. Activation of a part of the brain increases oxygen levels there increasing the ratio of **oxyhaemoglobin** to **deoxyhaemoglobin.**

The increased demand for neurotransmitters must be met by increased production of ATP. Although this consumes oxygen (needed for **cellular respiration**), it also increases the blood flow to the area. So there is an increase — not a decrease — in the oxygen supply to the region, which provides the signal detected by fMRI.

(v) Magnetoencephalography (MEG)

MEG detects the tiny magnetic fields created as individual neurons "fire" within the brain. It can pinpoint the active region with a millimeter, and can follow the movement of brain activity as it travels from region to region within the brain. MEG is noninvasive requiring only that the subject's head lie within a helmet containing the magnetic sensors.

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