Psychoactive drugs are chemicals that affect consciousness and behavior. This includes social or recreational drugs as well as drugs that are prescribed for various purposes in medicine and psychiatry. In this course we will take a comprehensive look at psychoactive drugs, the basis of their effects, their medical and nonmedical uses, and the controversies surrounding them.

Classification of Psychoactive Drugs

An important first step in examining psychoactive drugs is to find some useful way of classifying them. A number of different classification schemes have been proposed for psychoactive drugs, but none of these is perfect. The simplest ones divide the drugs into a few basic categories that are intended to roughly describe the drugs’ effects: e.g., stimulants tend to speed us up, whereas depressants tend to slow us down. But such categories can be simplistic and misleading because they actually tell us little about the effects of specific drugs.

For ex., alcohol is classified as a depressant, yet low to moderate doses can have a stimulating effect in social situations such that people become more talkative and sociable. Conversely, amphetamine is classified as a stimulant, yet low doses are commonly prescribed to calm hyperactive children. Nicotine is classed as a stimulant yet smokers commonly say a cigarette calms them down. Thus, whether a particular drug acts as a stimulant or a depressant in terms of its behavioural or subjective effects can depend on the dose taken and even the context in which it is taken. The point is that the categories used to classify psychoactive drugs should not be taken too literally - they are at best a general starting point for understanding various drugs.

A Simple Classification Scheme for Psychoactive Drugs

I. **Depressants** - drugs that promote relaxation, drowsiness or sleep, depending on the dose. Examples include alcohol, barbiturates (“downers”), GHB (“Fantasy”), and benzodiazepines (also called minor tranquilizers or anxiolytics; commonly prescribed for their anxiety-reducing effects, e.g., valium). Depressant drugs are also sometimes called sedatives, referring to their sedating action, or hypnotics, which refers to their ability to induce sleep. Note that the term “depressant” does not mean that these drugs will make you feel depressed in terms of mood; in fact, some depressant drugs can have a mood-elevating effect (e.g., alcohol). Depressant here refers to a slowing down of behavior and physiological functions, not depression of mood.

II. **Stimulants** - drugs that promote alertness and wakefulness. Examples include cocaine, nicotine, caffeine, and amphetamines. Note that although these drugs are classified as stimulants, their subjective effects and mechanisms of action are all quite different. For example, cocaine has a powerful mood elevating effect whereas caffeine has none.

III. **Opioids** - drugs related to morphine (the main drug in opium). Opioids have analgesic (pain relieving), calming, and mood-elevating effects, with depressant actions becoming prominent as the dosage is increased. This category includes drugs derived from the opium poppy, called opiates, their many derivatives such as heroin, and synthetic analogues such as methadone.

IV. **Hallucinogens** - drugs that primarily alter perception and cognition. This diverse category includes psychedelic (“mind-manifesting”) drugs such as LSD (“acid”), psilocybin (from “magic” mushrooms), and mescaline (from peyote and other cacti); dissociatives such as PCP (“angel dust”), ketamine (“k”), nitrous oxide (“laughing gas”), and dextromethorphan (DXM or “robo”); delirients such as atropine and scopolamine from the Datura family of plants, and salvinorin from the hallucinogenic plant salvia divinorum; and cannabis or marijuana, which contains the psychoactive drug THC. The popular synthetic drug MDMA (“Ecstasy”) is usually classed as a mild psychedelic.
V. **Antidepressants** - drugs prescribed for clinical depression. This category includes commonly prescribed drugs such as fluoxetine (Prozac), paroxetine (Paxil/Aropax), sertraline (Zoloft), and others. Side effects of these drugs often include a mixture of stimulant and depressant actions. Their antidepressant effects are not immediate, and require about 2-6 weeks to kick in.

VI. **Antipsychotics** - drugs prescribed for psychotic disorders such as schizophrenia and mania. Psychotic disorders are major mental illnesses in which the patient suffers from delusions and/or hallucinations. Drugs in this category are also sometimes called major tranquilizers (because they are prescribed for major mental illnesses) or neuroleptics. Thorazine, Haldol and Zyprexa are examples of antipsychotic drugs. Most antipsychotics have depressant side effects.

**Note:** Many drugs have a generic name, one or more brand names, and sometimes several street names as well. For ex., the generic drug diacetylmorphine (often contracted to diamorphine) was given the brand name Heroin by the Bayer pharmaceutical company in the late 19th century, and this drug has many street names such as H, horse, smack, junk, etc.

In order to understand how psychoactive drugs work, first some knowledge of how the brain works is required. All psychoactive drugs affect consciousness and behavior by temporarily altering brain activity in some way. Specifically, psychoactive drugs affect the information processing cells of the brain, called neurons (or nerve cells), generally by altering or disrupting their communication with other neurons.

**NEURON STRUCTURE AND FUNCTION**

There are about 100 billion neurons in the human brain, each of which typically has thousands of connections with other neurons, making for literally trillions of connections. We’ve got a long way to go before we can claim to have a thorough understanding of such a complex system, but in recent years substantial progress has been made.

A typical neuron has 4 main parts:

1) **dendrites** collect incoming messages from other neurons. A typical neuron may receive thousands of messages from other neurons via its many dendrites, which typically form a complex branching pattern called a **dendritic tree**.

2) the **cell body or soma** contains the basic metabolic machinery common to all cells - e.g., genetic instructions are contained in the nucleus; mitochondria are present for energy production; etc. The cell body is also the **summation point** for all incoming signals received by the dendrites. The summation process ultimately determines the message that will be sent to other cells.

3) the **axon** is a long cable-like structure that conducts nerve impulses, also called **action potentials**, to other cells. Axons can range up to a meter in length in humans. Bundles of many thousands of axons are commonly called **nerves**. Axons convey information by means of their **firing rate**, which means the frequency of action potentials; this can vary from 0 to about 500 action potentials per second, depending on how excited or inhibited the neuron is by the messages it receives from other cells at any given time.

4) **synapses** are sites where information is sent from one neuron to another cell, and are the usual sites of action of psychoactive drugs. Most neurons have thousands of synapses, thus there are trillions of synapses in the human brain. Synapses typically consist of the **axon terminal** of the sender (or presynaptic) cell, and an area of **receptor** sites on the receiver (or postsynaptic) cell. Receptors are most often located on the dendrites or cell body of a postsynaptic neuron. Information is transferred across synapses by means of specialized chemical messengers called **neurotransmitters** - the brain’s own psychoactive drugs.
Synapses occur not only between one neuron and another, but also between neurons and other kinds of body cells. These synapses are classed as neuroeffector junctions and neuromuscular junctions.

**Neuroeffector junctions** are synapses between autonomic neurons and internal organs and glands. Release of neurotransmitter at these synapses alters organ or glandular activity. Such synapses are found on the heart, gut, blood vessels, adrenal glands, sweat glands, etc.

**Neuromuscular junctions** are synapses between motor neurons and skeletal muscles, which mediate bodily movement. The axons of motor neurons innervate muscle fibers; release of neurotransmitter induces muscular contraction. This is how we move.

**Neurotransmitter Release**

The presynaptic terminal and postsynaptic membrane are separated by a tiny gap called the **synaptic cleft** that is only around 30 nanometers (billionths of a meter) across. Despite its small size the nerve impulses carried by the presynaptic axon cannot jump across the synaptic cleft; instead, the electrical signal carried by the axon (the action potential) is converted into a chemical signal at the synapse in the form of neurotransmitter release.

The presynaptic axon terminal contains many little packets of neurotransmitter called **synaptic vesicles**. When an action potential reaches the axon terminal, it triggers a process called **exocytosis** in which some of the vesicles fuse with the cell membrane, spilling a limited amount of neurotransmitter into the synaptic cleft. It then only takes a fraction of a millisecond for the released neurotransmitter molecules to diffuse across the synaptic cleft through the extracellular fluid to the postsynaptic cell.

The amount of neurotransmitter released in a given period of time depends on the **firing rate** of the presynaptic cell – the number of action potentials per unit time. The higher the firing rate of the presynaptic cell, the more neurotransmitter it will release at that time, and the stronger the effect it will have on the postsynaptic cell.

**Postsynaptic Receptor Binding**

The postsynaptic cell membrane contains imbedded protein molecules called **receptors**. The shape of these receptors is such that they only bind specific neurotransmitters that have a matching shape (**lock and key arrangement**). When a neurotransmitter key binds to its receptor lock, the receptor changes shape, opening little doors called **ion channels** in the postsynaptic cell membrane. These channels when open allow ions to flow across the cell membrane, either into or out of the cell.

**Ions** are atoms or molecules with an electric charge. Thus the opening of ion channels causes a flow of charged particles across the cell membrane which **alters the electric charge** of the postsynaptic cell, potentially altering its activity.

Neurons in the resting state are negatively charged like little batteries. This resting charge is called the **resting potential**. An influx of **positive ions** into the cell reverses this negative charge, which has an **excitatory** effect - meaning that the neuron tends to increase its firing rate. Conversely, an influx of **negative ions** into the neuron strengthens its negative charge, which has an **inhibitory** effect – meaning that the neuron becomes more resistant to firing. So reversing the resting potential of a neuron tends to increase its firing rate, whereas increasing the resting potential of a neuron tends to decrease its firing rate.

Neurotransmitters that increase the amount of positive charge inside the postsynaptic cell (thus reversing the negative resting potential) are called **excitatory neurotransmitters**. An example is **glutamate** which increases the flow of positive ions such as sodium (Na+) and calcium (Ca++) into...
the postsynaptic cell. The resulting increase in positive charge inside the cell is called **depolarization**, **excitatory post-synaptic potential (EPSP)** or simply **excitation**.

Neurotransmitters that increase the amount of negative charge inside the postsynaptic cell are called **inhibitory neurotransmitters**. An example is **GABA** (gamma amino butyric acid) which increases the flow of negative chloride ions (Cl\(^-\)) into the cell. The resulting increase in negative charge inside the cell is called **hyperpolarization**, **inhibitory post-synaptic potential (IPSP)** or simply **inhibition** because this type of electrical change decreases the postsynaptic cell’s activity or firing rate.

Glutamate and GABA are exclusively excitatory or inhibitory, but many other neurotransmitters can have either excitatory or inhibitory effects depending on the type of receptor they bind to. An example is the first neurotransmitter ever identified, **acetylcholine (Ach)**. The human nervous system contains two general types of Ach receptors, each of which is named after a drug that binds to it. **Nicotinic** receptors are named after the drug nicotine in tobacco; when Ach binds to the nicotinic receptor, the result is **excitation** of the postsynaptic cell due to opening of sodium channels allowing sodium (Na\(^+\)) to enter the cell. **Muscarinic** receptors are named after the drug muscarine, which comes from a colorful but poisonous mushroom, *Amanita Muscaria*. When Ach binds to the muscarinic receptor, the usual result is **inhibition** of the postsynaptic cell due to opening of potassium channels allowing potassium (K\(^+\)) to flow out of the cell – increasing the cell’s negative charge due to loss of positively charged potassium ions from the cell. **Nicotinic and muscarinic receptors are found in different synapses**; you’d never find both in the same synapse, otherwise they would just cancel each other out. Many other neurotransmitters also have both excitatory and inhibitory types of receptors.

**Electrical Summation of Postsynaptic Potentials**

A typical neuron receives simultaneous input from thousands of other cells. Some of this input is excitatory, some is inhibitory. These inputs all summate at the cell body and the net result of this summation process is the **firing rate** of the neuron at any given time. When excitatory messages predominate, the cell will show a relatively high firing rate; when inhibitory messages predominate, the cell will show a relatively low firing rate, or it may not fire at all. Thus the firing rate of a neuron at any given time depends on the balance of excitation and inhibition coming in from many other neurons simultaneously.

**Dale’s Principle**

A simplifying rule in understanding how neurotransmitters work is Dale’s Principle, which says that any given neuron manufactures and releases only one neurotransmitter from all its axon terminals even though it may possess receptors for many different neurotransmitters on its dendrites. Since at least 100 different neurotransmitters have been discovered so far, there must be at least 100 different types of neurons by this criterion.

Some neurons release more than one synaptic chemical, seemingly violating Dale’s Principle. In most of these cases, though, only one neurotransmitter is released along with another chemical that modulates (enhances or dampens) the neurotransmitter’s effect; such chemicals are called **neuromodulators**. They have no effect by themselves, and only serve to modulate the effect of the neurotransmitter they are released with.

An inhibitory neuromodulator, for ex., might be released when the firing rate of the presynaptic cell is too high; this serves to dampen the effect of the high amount of neurotransmitter released onto the postsynaptic cell, which might otherwise be toxic at such high levels.
Deactivation of Neurotransmitters

Soon after neurotransmitters have been released into the synaptic cleft, they are rapidly deactivated. If this was not the case, the message would be permanent, like making a phone call and never hanging up. Thus the synapse must be quickly cleared to allow new messages to come through. This is accomplished by either of two mechanisms depending on the neurotransmitter:

(1) enzymatic breakdown of the neurotransmitter, i.e., the neurotransmitter molecules are broken down by special enzymes released into the synapse by the postsynaptic cell. An example is the enzyme acetylcholinesterase (AchE) found at Ach synapses. This destroys Ach very soon after it is released. If AchE is blocked by drugs called AchE-inhibitors, there is a rapid buildup of Ach in the synapse which results in overstimulation of the body’s muscles. This is because Ach is the neurotransmitter released at all neuromuscular junctions between motor neurons and muscle fibers. Thus in a high enough dose an AchE-inhibitor causes all the muscles in the body to contract simultaneously, leading to death by suffocation or cardiac arrest. Because of their lethal effects, AchE-inhibitors are the active constituents of some nerve gases and insecticides.

(2) reuptake – many axon terminals have transport systems that pull certain neurotransmitter molecules back into the presynaptic cell for recycling. Many neurotransmitters are cleared from the synaptic cleft by reuptake. Some drugs work by blocking the reuptake process for certain neurotransmitters. These include cocaine, which blocks reuptake of dopamine, and prozac, which blocks reuptake of serotonin. Blocking reuptake increases the level of neurotransmitter in the synaptic cleft, increasing the effects of that neurotransmitter.

Common Mechanisms of Psychoactive Drug Action

In most cases, psychoactive drugs alter neural activity in either of 2 general ways and can be classified accordingly:

(1) Agonists: Drugs that increase neurotransmission at particular synapses. They can do this in several ways. Some drugs bind to and activate postsynaptic receptors in the same way that a particular neurotransmitter does, thus in effect making the brain operate as though it has become flooded with that neurotransmitter. This is called a direct agonist action. There are many examples of this type of drug action: e.g., nicotine binds to nicotinic receptors and activates cells the same way Ach does; LSD activates serotonin receptors the same way serotonin does; opiates such as heroin and morphine activate opioid receptors in the same way that endorphins do. But there are other types of agonist action as well, collectively called indirect agonist actions. Some drugs block the deactivating mechanisms that remove neurotransmitter from the synapse. Examples include the nerve gases that block AchE; cocaine, which blocks reuptake of dopamine; and prozac, which blocks reuptake of serotonin. Other indirect agonist drugs promote release of a particular neurotransmitter, e.g., methamphetamine triggers release of dopamine and norepinephrine; MDMA or ecstasy triggers release of serotonin.

(2) Antagonists: Drugs that reduce or block neurotransmission at particular synapses. One way an antagonist can work is to block receptors for a particular neurotransmitter, thus preventing that neurotransmitter from working. For example, the antipsychotic drugs used to treat schizophrenia are dopamine antagonists: they bind to dopamine receptors without activating them, thus blocking dopamine from binding to and activating dopamine receptors in the brain. The opiate antagonists naltrexone (Narcan) and naltrexone (Revia) block opioid receptors, thus a naltrexone injection can quickly reverse the effects of a heroin overdose by knocking heroin off its receptors in the brain. Caffeine blocks receptors for an inhibitory neuromodulator called adenosine. Other antagonists work in more indirect ways, such as inhibiting release of a neurotransmitter or promoting reuptake.
The mechanisms and effects of individual drugs will be covered in more detail in the coming weeks.

WEEK TWO
Psychoactive drugs vary in their effects depending on which neurotransmitter systems they influence and the areas of the nervous system affected. Thus an understanding of the various nervous system structures and their functions is necessary in order to understand drug actions and effects.

OVERVIEW OF THE NERVOUS SYSTEM

The vertebrate nervous system consists of 2 main divisions:

1) **central nervous system (CNS)** - brain and spinal cord;
2) **peripheral nervous system (PNS)** - all neurons located outside the brain and spinal cord.

**PERIPHERAL NERVOUS SYSTEM** - has 2 main functions:

1) to carry sensory information from the body to the CNS for processing; and
2) to carry commands from the CNS to the muscles, internal organs and glands.

Sensory axons are called **afferent**; they carry information into the CNS. Axons that carry **commands** to muscles or organs (away from CNS) are called **efferent**. Most nerves contain both afferent and efferent axons.

The PNS consists of 2 basic divisions: somatic and autonomic.

1) **somatic nervous system** - consists of sensory and motor nerves. Motor nerves control skeletal muscle activity and therefore bodily movement. They release the neurotransmitter acetylcholine (Ach) at neuromuscular junctions with muscle cells, which contain nicotinic (excitatory) receptors for Ach. Release of Ach by motor nerves excites muscle cells, triggering contraction of the muscle. Drugs that antagonize this process, such as **curare** (which blocks nicotinic receptors on muscles) and **botulinium toxin (Botox)** (which blocks release of Ach), are called **paralytics** because they induce paralysis.

2) **autonomic nervous system (ANS)** - controls activity of internal organs and glands. It is called “autonomic” because this system of nerves functions autonomously without conscious effort required. The ANS consists of 2 opposing systems of nerves:

1) **sympathetic nervous system** - prepares the body for vigorous muscular activity by initiating the **fight-flight reaction**: heart rate goes up; respiration becomes rapid; the pupils dilate; sweating increases; blood pressure rises; the adrenal glands secrete the hormone epinephrine (adrenaline), which further amplifies the fight-flight reaction; and the process of digestion is inhibited. All of these changes happen simultaneously in a situation of perceived threat. It is called “sympathetic” because of the simultaneous changes in many different organ systems, as if they are in synchrony with each other. Sympathetic nerves release the neurotransmitter **norepinephrine (NE)** at the neuroeffector junctions with their target organs (heart, sweat glands, pupils, blood vessels, etc.).
Some drugs have **sympathomimetic effects** in addition to their effects on consciousness and mood. This means they increase sympathetic nervous system actions, generally by increasing NE neurotransmission. Such drugs include **amphetamines, MDMA (ecstasy), nicotine and cocaine.**

2) **parasympathetic nervous system** – controls the same internal organs as the sympathetic nervous system, but has the opposite effect: it slows down heart rate and respiration, constricts the pupils, increases digestive activity, etc. It basically promotes restoration and recovery of the body and energy storage. At the neuroeffector junctions with their target organs, parasympathetic axons release the neurotransmitter Ach. The target organs have inhibitory **muscarinic receptors** for Ach, which means organ functioning slows down when parasympathetic nerves are highly active (with the exception of digestive processes, which are stimulated by an excitatory subtype of muscarinic receptor). Thus for ex., electrical stimulation of the **vagus nerve**, a major parasympathetic nerve, will slow down heart rate.

The balance of activity between the sympathetic and parasympathetic nervous systems determines how activated or aroused our bodies are at a given time. In a stressful situation, such as a final exam, the balance favors sympathetic nervous system activity and thus heart rate and respiration rate are elevated, sweating may occur, etc. Once the stressful event is over, the balance shifts in favor of parasympathetic activity and you may feel tired or burned out – or at least more relaxed.

**CENTRAL NERVOUS SYSTEM**

**SPINAL CORD** - carries sensory information from the PNS to the brain, and carries commands from the brain to the PNS; it also mediates simple unlearned behaviors called **spinal reflexes**. The **central canal** of the spinal cord contains **cerebrospinal fluid (CSF)**, as do the ventricles of the brain. This is surrounded by **gray matter** - mostly cell bodies and dendrites. Surrounding the gray matter is **white matter**, consisting of vast numbers of axons conveying messages vertically between brain and body. The white color comes from **myelin**, a fatty substance surrounding most axons in the mammalian nervous system, and which acts as an electrical insulator to enhance the speed of conduction of nerve impulses.

**THE BRAIN**

At the base of the skull, the spinal cord merges into the brain at an area called the **medulla**. The medulla is the lowest part of the **brainstem**, the bottom part of the brain. The medulla controls a number of basic physiological functions such as breathing and heart rate. The potentially lethal effects of **overdose** for many psychoactive drugs are due to their inhibitory effects on the medulla. For ex., a **heroin** overdose can be fatal due to the drug’s inhibitory effect on the respiratory center in the medulla, causing death by respiratory arrest.

Above the medulla is the **pons**, the middle part of the brainstem. The pons is largely concerned with sensory and motor functions. Connected to the pons is the **cerebellum** (“little brain”), which is the center for motor coordination and balance. **Alcohol** impairs coordination and balance in high doses due to its inhibitory effect on cerebellar function, causing effects such as staggering, “spinning room syndrome” and slurring of speech.

The top of the brainstem is called the **midbrain**, which contains several important structures. The **ventral tegmental area (VTA)** contains neurons whose axons make up the **mesolimbic (text: mesotelencephalic) dopamine system** - which releases the neurotransmitter dopamine at several sites higher in the brain, including the **nucleus accumbens** and the prefrontal cortex. This system of axons is also sometimes called the **pleasure system** or **reward system**. Researchers in the 1950s discovered that if a rat had an electrode implanted here, and learned he could press a lever to deliver a pulse of electrical stimulation to this area, the rat would press the
lever thousands of times until he collapsed from exhaustion. The rat would ignore all other rewarding stimuli including food, water, and sex partners in favor of the lever. Mother rats would even ignore their infants, and rats addicted to this brain stimulation would cross a highly electrified grid to get to the lever – something even starving rats would not do for food! It turns out that addictive drugs such as heroin and cocaine exert an effect similar to that of direct electrical stimulation here, so this area plays a central role in most current theories of addiction. This circuit in the brain, the mesolimbic dopamine system innervating the nucleus accumbens, appears to signal “do this again” whenever it becomes highly activated, and drug-induced changes in this system over time are thought to underlie drug addiction.

Also in the midbrain, adjacent to the VTA, is the substantia nigra, a structure which is crucial for voluntary movement. The substantia nigra is the part of the brain that degenerates in Parkinson’s disease, a neurological disorder of movement that most often afflicts the elderly. The substantia nigra sends axons to a major motor area higher up called the basal ganglia, which fails to function properly if the dopamine input from the substantia nigra is insufficient. This is called the mesostriatal dopamine system. Drug treatments for Parkinson’s Disease consist of drugs that boost brain dopamine levels to help compensate for the loss of dopamine due to the degeneration of the substantia nigra.

Forming the core of the brainstem throughout its length is a structure called the reticular formation or reticular activating system (RAS). The RAS sends axons throughout the brain, releasing activating neurotransmitters such as serotonin and NE. The reticular formation controls level of arousal (wakefulness). Electrical stimulation of the reticular formation will wake up a sleeping animal, whereas damage to the reticular formation produces coma, a level of unconsciousness deeper than deep sleep. Drugs that stimulate this system, including amphetamines, promote wakefulness and physiological arousal.

Deep inside the brain are the 4 large, fluid-filled chambers called ventricles. The ventricles are filled with CSF, which circulates through the brain and also fills the central canal of the spinal cord. CSF is essentially blood plasma and results from the filtering action of cells in a specialized tissue lining the ventricles called the choroid plexus. The ventricles function as shock absorbers by absorbing much of the energy of a blow to the head.

Sitting on top of the midbrain is the thalamus, which controls the amount of sensory information reaching the highest level of the brain - the cerebral cortex - for processing. The thalamus is sometimes called a sensory gate for this reason. Psychedelic drugs such as LSD and psilocin override the gating function of the thalamus, resulting in excessive sensory stimulation of the cerebral cortex and producing the bizarre hallucinations characteristic of these drugs.

The largest and most obvious structures of the brain are the cerebral hemispheres. As with nearly everything else in the brain, there is a left hemisphere and a right hemisphere. The left hemisphere controls the right side of the body, while the right hemisphere controls the left side of the body - an arrangement that is termed contralateral (opposite side). The two hemispheres communicate with each other by means of a very large system of axons called the corpus callosum. If this connection is destroyed, the result is two independently functioning minds in the same skull – a condition known as split brain syndrome.

Deep within the cerebral hemispheres are two groups of interconnected structures. One group of structures, the basal ganglia, plays a crucial role in voluntary movement. Dysfunction of the basal ganglia results in severe movement disorders such as Parkinson’s disease and Huntington’s disease (a rare and fatal genetic disease).
The other large group of structures situated within the cerebral hemispheres is called the **limbic system**. Important structures of the limbic system include the *amygdala*, *nucleus accumbens*, *hippocampus*, and *hypothalamus*. Functions of the limbic system include emotions, basic drives, and memory. Damage to the limbic system can produce dramatic changes in behavior. For ex., extensive damage to the *amygdala* causes loss of fear and anxiety, whereas stimulation of the amygdala causes anxiety or panic. **Benzodiazepines** such as Valium and Xanax relieve anxiety by inhibiting activity of the amygdala.

The **hippocampus** is crucial for memory, specifically the transfer of new information from short-term into long-term memory storage. Damage to the hippocampus results in a severe memory deficit called [anterograde amnesia](https://en.wikipedia.org/wiki/Anterograde_amnesia), such that the individual is incapable of learning new information (as in the movie “Memento”). Chronic severe alcoholism can permanently damage the hippocampus, resulting in a syndrome called **Korsakoff’s psychosis** which is characterized by severe memory loss and an inability to retain new information.

The **hypothalamus** controls a variety of basic drives, including hunger, thirst, sex drive, and aggression, and it regulates body temperature as well. In addition the hypothalamus controls the **pituitary gland** located just below it. The pituitary is often called the master gland because the hormones it secretes control the activity of many other endocrine glands in the body. Note that **hormones** are chemical messengers that are released into the bloodstream and travel throughout the body, unlike neurotransmitters, which only travel across the synaptic cleft. Another difference between hormones and neurotransmitters is that hormones generally produce long-lasting structural and functional changes in their target cells, whereas neurotransmitters produce only very brief changes in activity. But both hormones and neurotransmitters are chemical messengers that act on their target cells by binding to receptors.

The outer surface of the each cerebral hemisphere or **cerebrum** consists of a 1 mm thick layer of cells called the **cerebral cortex**. The cerebral cortex is made up of **gray matter**, i.e., mostly cell bodies and dendrites. Beneath the cerebral cortex is **white matter**, which consists of axons that carry information from one part of the brain to another. The cortex is highly convoluted, with numerous folds which increase the surface area of the cortex by a factor of about 2/3. This is basically nature’s way of cramming more cerebral cortex into a skull of limited size.

The largest folds in the cortical surface divide the cerebral cortex of each hemisphere into **4 lobes**:

- **Occipital lobe** at the back of the head carries out initial processing of visual information in the so-called **visual cortex**. Damage to the occipital lobe produces **cortical blindness**. The eyes are perfectly functional, but the patient is blind because the main part of the brain for processing visual information is non-functional.

- **Temporal lobe**, located close to the temples, carries out processing of auditory information in the area called **auditory cortex**. In addition, high-level visual processing takes place in the temporal lobe as well - in **inferotemporal cortex** on the underside of the temporal lobe, which mediates visual recognition of objects and faces. A patient with damage to the inferotemporal cortex can still see shapes and patterns but they can’t determine what the shapes or patterns are. For ex., they can describe the face of a person in front of them quite accurately, but cannot tell who it is, even if it is a close family member. The neurologist Oliver Sacks described a severe case of this syndrome, called **visual agnosia**, in his popular book “The Man Who Mistook his Wife for a Hat.”

- **Parietal lobe** at the top of the cerebrum carries out processing of sensory information from the skin, the muscles, the joints, and internal organs. This takes place in the **somatosensory (“body sense”) cortex** located just across the central sulcus from the frontal lobe. Some drugs that affect