The sympathetic and parasympathetic nervous system uses noradrenaline and acetylcholine respectively as an electrical impulse, except the sweat glands, which use acetylcholine.

For example; during exercise (perceived to the body as a stressful situation) one does not feel hungry since the sympathetic NS is activated to a greater extent than the parasympathetic NS.
There are two types of neurons that carry information to and from the CNS:

1. Afferent neurons relay information from the body to the CNS.
2. Efferent neurons transmit information from the CNS to the body.

The CNS is divided into 7 anatomical regions:

1. Spinal cord – 1 billion neurons. Its major function is to connect the body to the brain. It is the only way of communication. If you mess with the spinal cord you will be paralyzed, this is because no signal can pass from the brain to that part of the body. Its job is to conduct sensory information from the body to the brain and motor actions from the brain to the body. The spinal cord is not passive; it participates in processes on its own without involving the brain. These are reflex actions, where the spinal cord reacts without consulting the brain. For example; the knee jerk.

   Reflex actions are there for a purpose, if you are going to grab something jot the body needs to get rid of it immediately. The faster you get rid of it the less damage is made. Damage of the medulla, respiration stops, and blood pressure rises, this leads to death.

   It is made up of whit matter (mainly myelinated sheathes) and grey matter (mainly cell bodies).

   For example; during injury, the spinal cord transmits the sensation of pain from the site of injury to the brain, where it is perceived. The brain will then instruct the spinal cord to release endorphins (endogenous morphine) that will powerfully suppress the pain.

2. Medulla oblongata – a portion of the hindbrain that controls the autonomic functions such as breathing, digestion, heart, and respiratory system and blood vessel function, swallowing and sneezing. Motor and sensory neurons from the midbrain and forebrain travel through the medulla.

The GABA(A) receptor may be reversible or irreversible. Most drugs on the market bind reversibly to receptors. However, some drugs, such as chemical nerve gas used in warfare, snake venom (α bungarotoxin) and botox, bind irreversibly to receptors.

Botox is an injection of Botilium toxin A. It irreversibly binds with the acetylcholine receptor in facial muscles. Its effect lasts 5-6 months, until the receptors replenish themselves. If injected in blood it is fatal.

GABA (A) receptors contain:

- Ion channels
- 2 binding sites for GABA
- Single binding site for benzodiazepines, promotes binding of GABA, increase conduction of Cl ions
- Alcohol-binding site

Synapses

Neurons communicate via synapses. Most drugs used to treat disease of the CNS act on synaptic transmission.

	CHEMICAL	ELECTRICAL
Cytoplasmic Continuity	Absent	Present
Distance of synapse (between pre- and post- membrane)	30-50nm	2-5nm
Presence of ligands (drugs)	Influenced	Not influenced
Speed of transmission	Fast	Slow
Direction of transmission	Unidirectional (pre to post only)	Bidirectional

Electrical impulses

Gap junctions. They are most commonly found in astrocytes (glia cells). They enable communication between one cell and another and form direct cytoplasmic continuity between one cell and another. They are composed of 6 connexons each of which has 4 trans membrane domains.

Selecting the correct NT can be divided into 4 steps:

1. Synthesis of NT in cell body/pre-synaptic terminal
2. Storage in synaptic vesicles and release by exocytosis
3. Interaction between NT and its respective receptor
4. Removal of NT from synaptic area.

A substance can only be considered a NT if:

- Synthesized in the neuron.
- Present in pre-synaptic terminals and released in sufficient amounts to produce an effect on the post-synaptic neuron.
- If it is administered exogenously, it must mimic the effect as the endogenous molecule.
- There should be a specific mechanism by which the substance is removed from the synaptic cleft.

The nervous system makes use of 2 classes of neurotransmitters:

1. Small molecule NT:
   - Ach
   - Biogenic amines
   - Amino acids

2. Neuropeptides

Acetylcholine

Acetylcholine is a small molecule found in the brain, motor neurons of the spinal cord, autonomic nervous system, all skeletal nerve junctions and synapses in the brain, especially around the area known as the nucleus basalis, which feeds cholinergic projections into the cerebral cortex. It plays an important role in the contraction of skeletal muscles, and cognitive function.

Acetyl CoA + Choline → Acetylcholine + CoA

Acetyl CoA is formed through the Kreb's cycle during glucose metabolism.

Choline is obtained from diet, it is found in foods such as animal products, animal derivatives and some vegetables.

M4 receptor

- Location: mainly in the brain
- Agonists: Ach, muscarin
- Antagonists: atropine, hyoscine

M5 receptor

- Not well known

The non-selective antagonists are known to cause adverse effects such as dry mouth and blurred vision.

The nicotinic acetylcholine receptors (nAchRs)

- Two types: neural (brain) – cognitive processing and skeletal (rest of the body) movement of muscle.
- Inotropic, therefore fast synaptic events
- Bring about depolarization
- Allow the passage of Na+, K+ and Ca2+ ions
- Occur along the entire width of the cell membrane

How is muscle contraction brought about?
This is done by the release of Ach into the synaptic cleft. Ach diffuses through the cleft until it reaches the motor end plate of the muscle fiber, where it binds to the nAch receptors. The binding of Ach to these receptors alone is not enough for the end plate to reach threshold. However, the depolarizing effects are enough to open the Na+ voltage gated channels. Na+ enter the cell, producing significant depolarization to result in an end plate, which will in turn lead to muscle contraction.

The skeletal nAchRs (peripheral) are composed of 4 different subunits but 5 in all (2 alpha, beta, delta and gamma). Alpha and beta can only be of one variant.

The neuronal is composed of 2 subtypes but 5 in all (2 alpha and 3 beta). Alpha can be of 8/9 different variants (alpha 8 has only been found in chickens) while beta can be of 3 different types. The neuronal receptor can be further divided into two:

- Heteromer: composed of more than one subunit (most common in nicotine addicts there is upregulation of this particular receptor.

GABA-T inhibitors (increasing GABA):

1. These are drugs that are used in epilepsy to lower glutamate concentrations and reduce the incidence of seizures such as;
    - Gamma-vinyl GABA
    - Sodium valproate – also used in mania

There are those, which inhibit the re-uptake of GABA, they also increase the GABA concentration in the synaptic cleft and is therefore useful in controlling epilepsy and seizures. These are experimental drugs like – 2-4,diaminobutyric acid.

GABA receptors

Two main GABA receptors:

- GABA (a) – ionotropic
- GABA (b) – metabotropic

GABA (c) also exists but is only present in the retina, it is shown to be very similar to GABA (a), they are both ionotropic and have similar structures.

GABA(a)

GABA (a) receptor is ionotropic and forms part of a multi-receptor complex, that is, a large protein complex that contains a number of receptor sites gating a channel.

It gates a chloride channel. Binding of GABA will result in opening of the chloride channel. Chloride ions will enter the intracellular space, bringing about a hyperpolarization. Although the diameter of channel is very narrow, when it opens, large quantities of ions are able to pass through.

It's a multi-complex channel, other than the GABA site there are other sites, which include:

- Benzodiazepine site
- Barbiturate site
- Anesthetic site
- Picrotoxin site
- Neurosteroid site
- Alcohol site

Binding a particular ligand with its receptor site changes the conformation in such a way that it will hate the channel.

People who are deprived of REM tend to show very aggressive behavious.

REM sleep is sleep that is characterized by rapid eye movement. The functins of REM sleep are not fully understood but theories include its role in memory consolidation and importance of neural development, especially in neonatal development. It is the time we spend dreaming.

Drugs of abuse

SSRIs reduce alcohol intake in alcohol-dependent rates. Also, 5HTA agonists, such as buspirone, reduce alcohol intake in humans.

Anxiolytic Activity

5-HT-1A agonists such as buspirone and gepirone, have these effects.

Depression (MOOD)

SSRIs are usually clinically as antidepressants, as well as in the treatment of OCD.

Aggression

5-HT-1A and to a lesser extent 5-HT-1B and 5-HT1C agonists suppress aggression in animal models.

Obesity

Fenfluramine a potent 5-HT 2B agonist was used as an anti-obesity drug. It was subsequently withdrawn due to cardiac valve damage.

Dopamine

Dopamine is a NT implicated in a number of diseases. It is most important is schizophrenia and Parkinson's and attention deficit disorders.

Schizophrenia is one of the most devastating illnesses and is characterized by disjointed thoughts, auditory and visual hallucinations (most are negative).

Similar effects of schizophrenia are encountered with the administration of some drugs like LSD. In fact, a number of people who take these drugs end up developing schizophrenia. It comes out at the age of about twenty and is more common in males.

There are 3 pathways of dopamine in the brain:

1. Nigro-striatal pathway

This is associated with locomotive activity. This area of the brain is extremely rich in melatonin, thus appears darkish in color. It starts from the substantial