CNS Stimulants
Cerebral Stimulants (Psychostimulants)
Hallucinogens
Analeptics or Convulsants
Psychostimulants
Agents that increase psychomotor activity and induce temporary improvements in either mental or physical function or both. Low to moderate doses, generally have the following effects:
- Heightened mood (euphoria).
- Improve concentration
- Increase vigilance and alertness.
- Reduce fatigue.
- Keep you awake.

In order of prevalence of use:
- Caffeine
- Nicotine
- Amphetamines
- Cocaine
Caffeine

- The most widely consumed stimulant in the world.
- Caffeine, an alkaloid of the methylxanthine such as theophylline and theobromine.

A cup of instant coffee or strong tea contains 50-70mg of caffeine

Average daily consumption is about 200mg

Nuts of cola plant also contain caffeine
Mechanism of action

- Caffeine antagonizes the adenosine A1 receptor & inhibits phosphodiesterase resulting in an increase in both adenylyl cyclase activity and cAMP formation.
- Further, voltage-gated calcium channels are open which allows calcium entry and potassium channels are blocked.
- This allows the cell to be more easily depolarized, thereby increasing neurotransmitter release.
CNS Effects of Xanthenes
Caffeine > theophylline > theobromine
Cortical level: remove fatigue and improve mental performance.
  High doses stimulate medulla.

Effects on different body function
CVS: positive inotropic & chronotropic effects on heart.
Bronchodilation, theophylline is used in asthma
Diuresis: mild diuretic action & increase urinary output of electrolytes. Theophylline most potent due to inhibition of Na tubular reabsorption.
Increase gastric secretions.
Therapeutic uses of Caffeine:
- Apnea in newborns
  Caffeine helps regularize breathing.
- Migraine headaches when combined with aspirin.

Adverse Reactions:
Habituation.
Nervousness, delirium, insomnia.
Tachycardia, cardiac arrhythmias.
Diuresis.
Tachypnea (increase in the rate of respiration)
Nicotine

Nicotine is named after the tobacco plant **Nicotiana tabacum**

A nicotinic acetylcholine receptor agonist.

Average 1 cigarette yields about **1 mg** nicotine.

Nicotine reaches the brain within 10-20 seconds after inhalation.

Elimination half life is 2 hrs

Metabolized in liver by cytochrome P450 enzyme.

Major metabolite is **cotinine**.
Nicotine increases the extracellular level of dopamine in nucleus accumbens, which is responsible for the reinforcing behaviour, stimulant & dependence properties of nicotine.

- Nicotine increases the level of several neurotransmitters in the brain.
- Tobacco contains naturally-occurring MAOI compounds in addition to the nicotine.

**Withdrawal**

Mild compared to opioids and involves irritability with insomnia.

Nicotine is among the most addictive drugs and relapse after attempted cessation is common.
Effects of Nicotine

Positive:
• Anxiolytics
• Cognitive Enhancement
• Cerebro-vasodilation
• Neuroprotection
• Analgesia
• Anti-psychotic

Negative:
• Gastrointestinal Distress
• Hypothermia
• Emesis
• Hypertension
• Seizures
• Respiratory Distress

- Tobacco can cause cancer, heart disease and lung disease.
Amphetamine & Amphetamine Like Drugs

amphetamine, methamphetamine methylphenidate, Methylenedioxymethamphetamine. (*MDMA; ecstasy*) Synthetic, cause the release of DA, NE & serotonin.

**Amphetamine**

One of the most abusable drugs.

The *dextro* isomer is considerably more potent (*Dexedrine*).

**Mechanism**

1- Act indirectly by releasing monoamines in the brain.
2- Inhibit neuronal amine uptake.
3- Direct stimulation of dopamine & serotonin receptors.
4- Inhibition of MAO.
High doses deplete monoamines, causing the development of tolerance and mood disturbances.
Chronic use leads to marked tolerance and the administration of very high doses.
Extremely high doses or chronic use can lead to amphetamine-induced psychosis, indistinguishable from paranoid schizophrenia.

Amphetamine psychosis is often associated with anxiety and fear.
Pharmacological effects

CNS: Psychic stimulation resulting in feeling of euphoria, self confidence, wakefulness, alertness with increase mental and physical activities.

It has anti-fatigue & analeptic action

It **depress appetite** by central action on hypothalamus feeding centers by reduction sense of smell & taste.

Chronic abuse leads to psychotic state with delusion and paranoia like schizophrenia.

**CVS:** increase BP and reflex bradycardia with large doses may cause arrhythmias.
Clinical uses
Narcolepsy
Methylphenidate is better.
Hyperkinetic syndrome
(attention deficit disorder)
Nocturnal enuresis
Adverse effects
Dysphoria, confusion, headache, mental depression, psychosis, confusion, arrhythmia, anginal pain, dry mouth, anorexia, vomiting.
(MDMA; “ecstasy”) Has both amphetamine-like effects and hallucinogenic effects. Synthesized from ephedrine. MDMA produces in the user feelings of euphoria, empathy, openness, and love.

**mechanism of action:**

binding to serotonin transporters (and to a lesser extent DA & NE transporters) and causing them to work in reverse, effectively dumping serotonin into the synapse and keeping it there. **MDMA hallucinogenic properties depend on the agonist activity at the 5-HT2A-receptor** considered neurotoxic in humans **MDMA destroys axonal processes in serotonergic cell.**
Cocaine
Alkaloid found in the leaves of *Erythroxylon coca*. A shrub endogenous to the Andes. For more than 100 years it has been used a local anesthetic & to dilate the pupil in ophthalmology.

**Mechanism of action**
Blocks the uptake of DA, NE & 5HT
The reward effect of cocaine is due to the increase of DA concentration in the nucleolus accumbens. induces very strong psychological dependence in the short term effects and users may have very strong cravings when the effects wear off.
Effects are very similar to amphetamines, except that cocaine is much shorter acting. Cross-tolerance can develop with amphetamine. Not well absorbed from the GIT, so it’s usually taken intranasal.

**Adverse effects**
Loss of appetite, Hyperactivity, Intracranial hemorrhage, Ischemic stroke, Myocardial infarction, Seizure, Hyperthermia, coma & death on high doses.
Khat, qat, (Catha edulis)

Khat chewing is a social custom dating back thousands of years. Khat contains a monoamine alkaloid called **Cathinone**, an amphetamine-like stimulant, which cause excitement, loss of appetite and euphoria. In 1980, (WHO) classified it as a drug of abuse that can produce mild-to-moderate psychological dependence.

**Methedrone**
A synthetic derivative of **Cathinone**. Its effects are similar to cocaine or amphetamine. The first toxicologically confirmed fatal case directly linked to mephedrone use was recorded in Sweden in 2008.
HALLUCINOGENS

Hallucination: is a sense or perception (sight, touch, smell, sound or taste) that has no basis of external stimulation.

Hallucinogens are characterized as agents which produce hallucinations.
Cannabinoids
1) Endogenous cannabinoids
Bind to CB1 receptors where they inhibit release of either Glutamate or GABA transmitters. Due to this backward signaling they are called retrograde Messengers.

2) Exogenous cannabinoids: Marijuana which contains Tetrahydrocannabinol (THC) A powerful psychoactive substance. Causes release of DA mainly by pre-synaptic inhibition of GABA Neuron in the VTA
Half life of THC is about 4 hrs
Onset after smoking marijuana occur within minute.

**Effects:**
euphoria, relaxation, feelings of well being, grandiosity & altered perception of passage of time.
Drowsiness, diminished coordination and memory impairment, visional hallucination, & psychotic episodes.
Increase appetite, nausea, decrease intraocular pressure and relief of chronic pain
Chronic use of marijuana produce dependency with mild withdrawal symptoms, like restlessness, irritability, mild agitation and insomnia.
Lysergic acid diethylamide (LSD)

Agonist at presynaptic 5HT1 receptors in the midbrain and stimulates 5H2 receptors.

Physical effects

LSD can cause pupil dilatation, reduce or increase appetite, increased wakefulness, numbness, hypo or hyperthermia, elevated blood sugar, increase heart rate, jaw clenching.

LSD is not considered addictive drug

Psychological effects

Vary greatly from person to person.

radiant bright colors behind the closed eye lids and altered sense of time & space.

Clinical uses: End of life anxiety
Phencyclidine (PCP)

It is also called **angel dust**.

NMDA receptor antagonist.

Inhibit the reuptake of DA, 5HT, and NE.

PCP, like Ketamine, also acts as a D2 receptor partial agonist.

It causes dissociative anesthesia (insensitivity to pain without loss of consciousness).

Induces symptoms in humans that mimic schizophrenia.

Tolerance produced with continued use
Analeptics or Convulsants
Strychnine:

*Nux vomica* seeds.

Used as rat poison in 1500s, also as a tonic.

Competes with Glycine in the spinal cord, but can affect all levels of CNS.

Reduces postsynaptic inhibition of Renshaw cell.

Produces fatal convulsions (tonic – clonic)

Causes coordinated extensor thrusts progressing to full tetanic convulsions = Opisthotonus.

Convulsions increased by sensory stimuli.
Picrotoxin
*Alkaloid from Anamirta cocculus seeds.*
A non-competitive blocker for **GABAA chloride channels** receptors.
Blocks presynaptic inhibition.
has stimulant and convulsant effects.
Was used to counter **barbiturate** poisoning

**Pentylenetetrazole**
Synthetic, medullary stimulant, was used as a respiratory stimulant.
High doses cause convulsions

**Nikethamide** (Coramine) **Bemegride**
Respiratory stimulant were used as CNS stimulants and antidote for barbiturate poisoning.