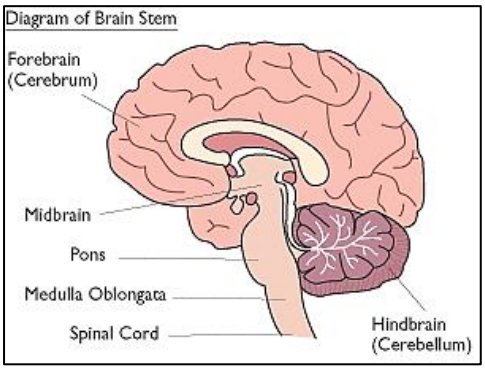
CNS stimulant drugs

CNS stimulants are those agents which stimulate central nervous system. Central nervous system (CNS) stimulants are medicines that speed up physical and mental processes.

Stimulants (also referred to as psychostimulants) are psychoactive drugs that induce temporary improvements in either mental or physical functions or both. Examples of these kinds of effects may include enhanced alertness, wakefulness, and locomotion, among others. Due to their rendering a characteristic "up" feeling, stimulants are also occasionally referred to as "uppers" whereas depressants or "downers" that decrease mental and/or physical function.

Classification

On the basis of their **site of action**.



A. Directly acting

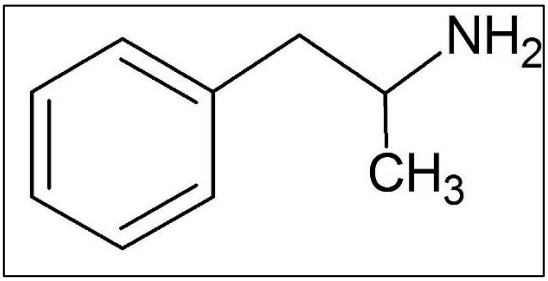
1. **On cortex** (cerebrum or cortex is the largest part of the human brain, associated with higher brain function such as thought and action)
    a. Xanthine group of drugs-e.g. Xanthine and methyl xanthine.
    b. Others- e.g. amphetamine and ephedrine.
2. **On medulla** (center for respiration and circulation)

    E.g. Picrotoxin and nikethemide.
3. **On spinal cord**-e.g. Strychnine.

B. Reflexly acting on CNS-e.g. Nicotine.

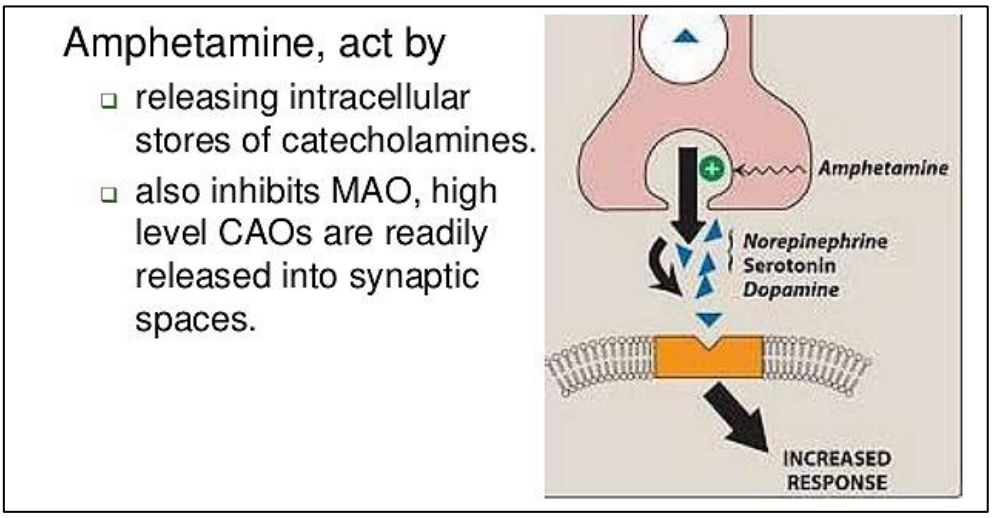
Amphetamine

It is a powerful CNS stimulant drug. It is **adrenergic agonist**. Unlike adrenaline, it is effective after oral administration and its effects last for several hours. It is a popular drug for abuse.



Mode of action

Amphetamine causes release of noradrenaline from the noradrenergic neurons of the brain. In addition, it releases some other neurotransmitters like dopamine and serotonin (5-HT) from dopaminergic and serotoninergic neurons.



Pharmacological effects

1. Amphetamine increases both systolic and diastolic pressure and heart rate is often slowed down. It can develop cardiac arrhythmia at a high dose.
2. 10-30 mg of amphetamine may cause elevation of mood, self-confidence and ability to concentrate, wakefulness, alertness and often elation and euphoria.
3. It delays fatigue in all persons especially in army and athletics. Physical performance in athletes is improved and the drug is often abused for this purpose.
4. It inhibits sleep which results in wakefulness.
5. It has been widely used in the treatment of obesity.
6. It stimulates respiratory centre resulting in increased rate and depth of respiration.

Toxicity

Acute toxicity is as a result of overdose of amphetamine. CNS toxicity includes insomnia, talkativeness, and hallucination (both auditory and visual). CVS toxicity includes cardiac arrhythmia, hypertension or hypotension.

Treatment of acute poisoning

Acute overdose is treated by –

- Acidification of urine by administering ammonium chloride **(Solutions of ammonium chloride are mildly acidic, $NH_3 + HCl \rightarrow NH_4Cl$)**. This increases rate of elimination of amphetamine.
- Antihypertensive drugs like labetalol **(mixed alpha/beta adrenergic antagonist**).

Therapeutic uses

It may be used in-

- Narcolepsy [An extreme tendency to fall asleep whenever in relaxing surroundings.]
- Attention deficit hyperactivity disorder (ADHD)
- Noctural enuresis (Involuntary discharge of urine at night by children old enough to be expected to have bladder control)

1. **Dependence**

Dependence to amphetamine is common and psychological dependence often occurs when amphetamine or dextroamphetamine is used chronically.

2. **ADHD (**Attention deficit hyperactivity disorder**)**

This disorder is seen in children. The child is hyperactive (hyper motile) and has little attention to his studies and is a back bencher in the class. This disorder continues and may persist in adulthood.

3. **Noctural enuresis**

Nocturnal enuresis or nighttime urinary incontinence, commonly called **bedwetting** or sleep wetting, is involuntary urination while asleep after the age at which bladder control usually occurs.

Strychnine

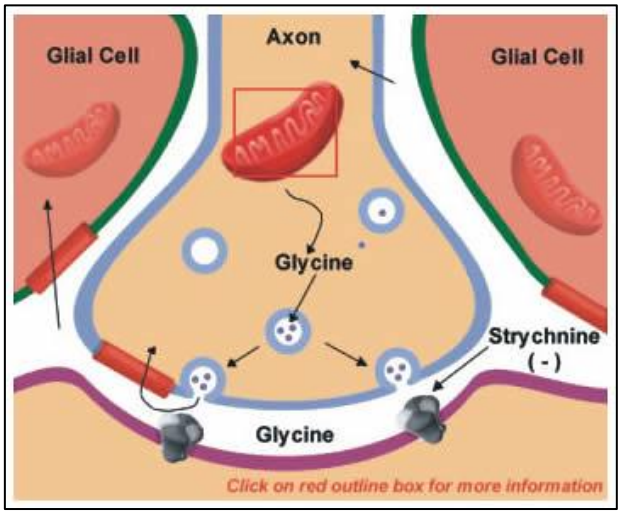
Source

Strychnine is a principle alkaloid present in nux vomica, the seed of strychnose nux vomica. It is first introduced into Germany in the sixteenth century as a poison for rats and other animal pests. It is still used as a pesticide now-a-days. Strychnine is a source of accidental poisoning in children.

Mechanism of action

The convulsant effect of strychnine is due to an interference with the post synaptic inhibition that is mediated by glycine. Glycine is an inhibitory neurotransmitter present in the spinal cord.

Strychnine acts as a selective, competitive antagonist to block the inhibitory effect of glycine at all glycine receptor.



Pharmacological action

It produces excitation of all portion of CNS. It increases the level of neuronal excitability by selectively blocking inhibition.

Strychnine is a powerful convulsant and the convulsion has a characteristic motor pattern. In most experimental animal, the convulsion is characterized by tonic extension of the body and whole limbs.

Strychnine poisoning

The first effect of Strychnine poisoning is stiffness of the face and neck muscle. In the convulsion, the body is arched in hyperextension so that the crown of the head and the heel can touch the ground.

Respiration ceases. Normally, death occurs after 2^{nd} to 5^{th} full convulsion.

Treatment

The main targets of the treatment of strychnine poisoning are-

- Prevention of convulsion and
- Support of respiration.

Diazepam may be used as it is the most useful agent for this purpose because it antagonizes convulsion without causing respiratory depression.

Adequate respiratory ventilation is necessary for support of respiration.

Uses

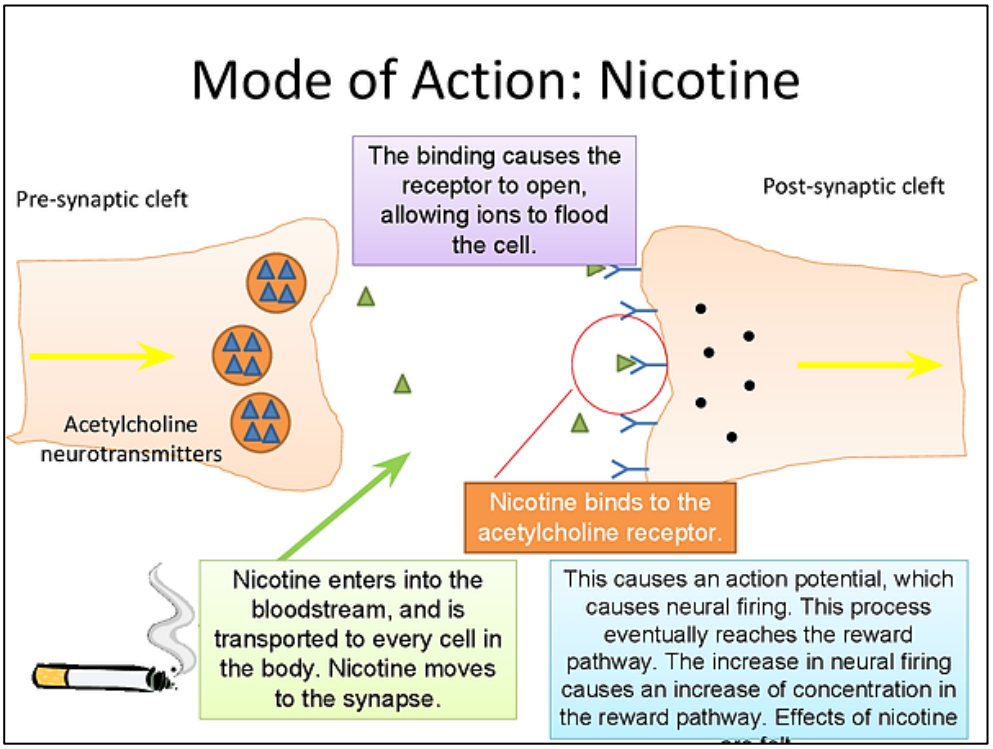
- It has no therapeutic use now. It may be used in nonketotic hyper glycinemia in infant.
  (Nonketotic hyper glycinemia is a metabolic disorder characterized by abnormally high concentration of glycine in infants and cerebrospinal fluid.)
- It is used as a pesticide.

Nicotine

Nicotine is the active ingredient in tobacco. Nicotine remain important because it is second only to caffeine as the most widely used CNS stimulant & is second to alcohol as the most abused drug.

Mechanism of action

Nicotine is a stimulant drug that acts as an agonist at nicotinic acetylcholine receptors. In the brain, nicotine binds to nicotinic acetylcholine receptors on dopaminergic neurons causes release of dopamine into the synapse. Nicotine also binds to nicotinic acetylcholine receptors on the chromaffin cells in the adrenal medulla and triggers the release of epinephrine into the bloodstream.



Pharmacological effects/ actions

- Cigarette smoking or administration of low doses of nicotine produces some degree of euphoria & arousal as well as relaxation & improve attention (due to release of dopamine). High doses of nicotine result in central respiratory paralysis & severe hypotension caused by medullary paralysis.
- Nicotine causes vasoconstriction, increased blood pressure, increased heart rate, and increased blood sugar (due to release of dopamine). At higher doses, Blood pressure falls.

Side Effects

The CNS effects of nicotine include irritability & tremors. Nicotine may also cause intestinal cramps, diarrhea, increases the rate of metabolism of a number of drugs. It is not known which of over 3000 components of cigarette smoke are responsible for this phenomena.

Withdrawal Syndrome

Nicotine is an addictive substance physical dependence on nicotine develops rapidly & is severe withdrawal is characterized by irritability, anxiety, restlessness, difficulty in concentrating, headache & insomnia. Appetite is affected & GIT pain often occur.