

Drugs affecting the CNS

Major Neurotransmitters in CNS :

1. Noradrenaline → mood , B.P.regulation
wakefulness

2. Dopamine → ↓ dopamine → Parkinson's
↑ dopamine → schizophrenia

3. serotonin (5-HT) → Many functions

4. Acetylcholine → ↓ Ach → dementia - Alzheimer's
serotonin → depression

5. GABA → Major inhibitory transmitter

6. Glutamate → Major excitatory transmitter

CNS drugs

↓
Stimulants

↓
Depressants

C N S Stimulants

1. Cortical stimulants
2. Brainstem stimulants
3. Spinal cord stimulants

Cortical Stimulants

1) **Psychomimetics**

- Amphetamine and related drugs
- Cocaine

2) **Psychotomimetics (Hallucinogens)**

3) **Methylxanthines**

4) **Nootropic drugs e.g.Piracetam**

C N S stimulants

Examples :

Amphetamine and related drugs (khat , captagon , Ephedrine etc.)

Mechanism of action:

- Indirectly acting sympathomimetics
- action in CNS and periphery
- taken up by Noradrenergic neurons and cause release of NA

(Also cause release of dopamine and serotonin in the brain by similar mechanisms).

* Blocks NA reuptake, inhibits MAO & has direct effect on receptors .

Actions :

a) In the periphery :

Cardiovascular effects :

↑ blood pressure

cardiac arrhythmias

b) In the CNS :

- ↑ wakefulness
- ↑ Alertness
- ↓ fatigue
- euphoria and ↑ mood
- ↑ physical performance
- ↓ mental performance

- Hallucinations followed by depression and fatigue ,after large doses .
- ↓ appetite (causing loss of weight)
- Tolerance and psychic dependence
(but no or little physical dependence)

Side effects (toxic effects) :

Insomnia

Cardiac arrhythmias

Dependence

Drug abuse

Clinical uses :

- Narcolepsy
- To reduce body weight (fenfluramine is better)
- Attention – deficit hyperactivity disorder (ADHD)

Cocaine HCl

Mechanism :

Prevents reuptake of NA in the CNS and periphery
(prolongs the action of NA).

Actions :

- Similar to amphetamine
- Also has local anaesthetic action .

Side effects :

- Similar to amphetamine
- Abused drug by sniffing and by injection
 - Sniffing → Leads to nasal puncture .
 - Injection → Risk of AIDS and Hepatitis .
- Abortion → and premature labour in women .
- Cocaine base (Crack) is more toxic than the salt

Clinical uses :

- Local anasesthesia (eye, nose & throat surgery)
- Eye drops cause mydriasis (used in eye examination).

Psychotomimetics

(Hallucinogens)

- * Methoxylated amphetamines
(mescaline; dimethoxyamphetamine)
- * High doses of amphetamine & analogus
- * High doses of cocaine
- * L S D → inhibits firing of serotonergic
neurons via stimulation of 5-HT₂
receptors
- * Cannabis (marihuana and Hashish)
contains δ -9- tetrahydrocannabinol
(antiemetic in cancer patients)

*Nitrous oxide

- auditory → through endogenous morphine
- Anaesthetic

* Pentazocine → visual → endogenous morphine

- Analgesic

Mechanism of hallucination : via serotonin
(except Nitrous oxide and pentazocine) .

- Abused drugs
- Cause tolerance and psychic dependence

Methylxanthines (theophylline ,caffeine
theobromine)

Clinical uses :

- Theophylline → asthma
- Aminophylline (theophylline + ethylene diamine)
used in asthma
- Caffeine → headache
caffeine + ergot alkaloids → migraine
- Pentoxiphylline (derivative of theobromine) for
vascular disorders

Pharmacological properties :

1- Smooth muscle relaxation (esp. bronchi)

Theophylline → most effective .

- antiinflammatory in asthmatic lung .

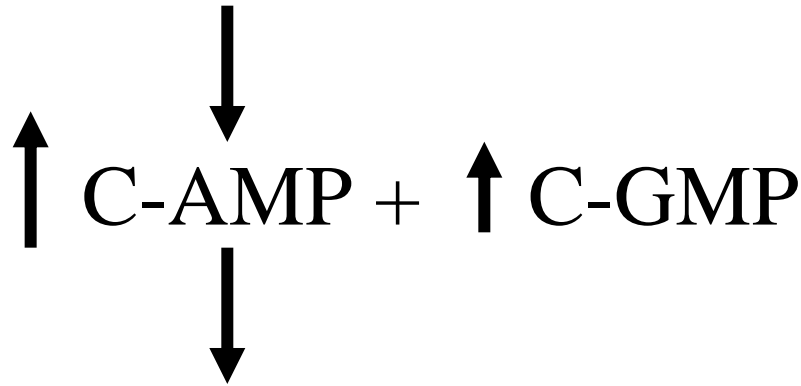
2- CNS stimulant (theophylline > caffeine) .

3- Cardiovascular → Tachycardia & dysrhythmias at high doses .

4- Mild diuresis → inhibits Na^+ reabsorption .

Mechanisms :

1. Inhibition of phosphodiesterase



smooth muscle relaxatoin

2. Causes Ca^{++} release Ca^{++} depletion from cells

& prevents Ca^{++} influx into cells .

3. Antagonism of adenosine receptors (inhibitory transmitter in CNS + autacoid in GIT)

Adverse effects :

- Insomnia
- Tachycardia
- Tolerance and withdrawal syndrome (headache + sleepiness)
- Reports of sudden death from I.V aminophylline .

Piracetam :

Nootropic drug (effects intellect)

M.O.A. Not clear

- Improves microcirculation in CNS

No central vasodilatation

causes peripheral vasodilatation

Clinical uses :

- Loss of memory , vertigo , Alzheimer's disease
- Learning difficulties in children
- Chronic alcoholism and alcohol withdrawal
- Coma

adverse effects :

- few

Nervousness

anxiety

sleep disturbances .

Brainstem Stimulants

(analeptics)

Picrotoxin : Clonic asymmetric convulsions
antagonist at postsynaptic GABA A receptors .

Pentylentetrazole :

induces convulsions

Mechanism not clear

Respiratory stimulant

Doxapram :

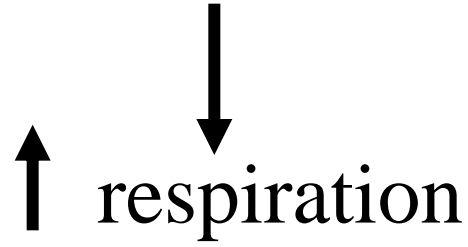
Respiratory stimulant

Induces convulsions at high dose

Used in recovery from general anaesthesia

Mechanism :

- Peripheral stimulation of chemoreceptors



- potentiates glutamate (excitatory transmitter)

Spinal cord stimulants

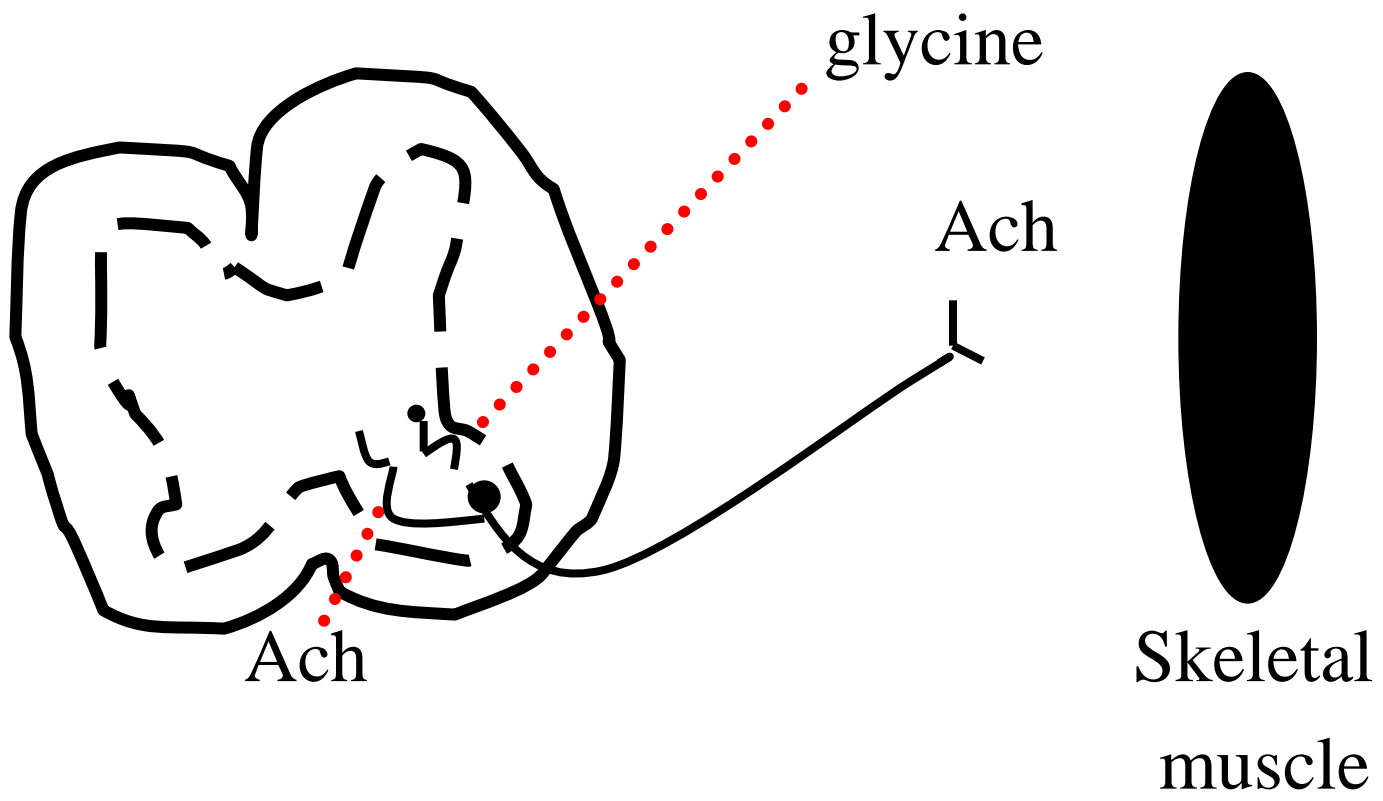
Strychnine :

Natural poison

Causes tonic symmetrical convulsions due to antagonism of glycine (inhibitory transmitter) of Renshaw cells in spinal cord

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Spinal
Cord



glycine

Ach

Ach

Skeletal
muscle

 Reshow cell

 α -motoneuron