

Pharmacology II

4th stage

Lec. 2

CNS Stimulants

CNS Stimulants

A type of drug that increases the levels of certain chemicals in the brain and **increases alertness, attention, energy, and physical activity.**

CNS stimulants also **raise blood pressure and increase heart rate and breathing rate.**

CNS Stimulants

two groups of drugs that act primarily to stimulate the central nervous system (CNS).

The first group, the psychomotor stimulants, cause excitement and euphoria, decrease feelings of fatigue, and increase motor activity.

The second group, the hallucinogens, produce profound changes in thought patterns and mood.

Psychomotor Stimulants include

- A. Methylxanthines*
- B. Nicotine*
- C. Cocaine*
- E. Amphetamine*
- F. Dextroamphetamine*
- G. Methylphenidate*

A. Methylxanthines

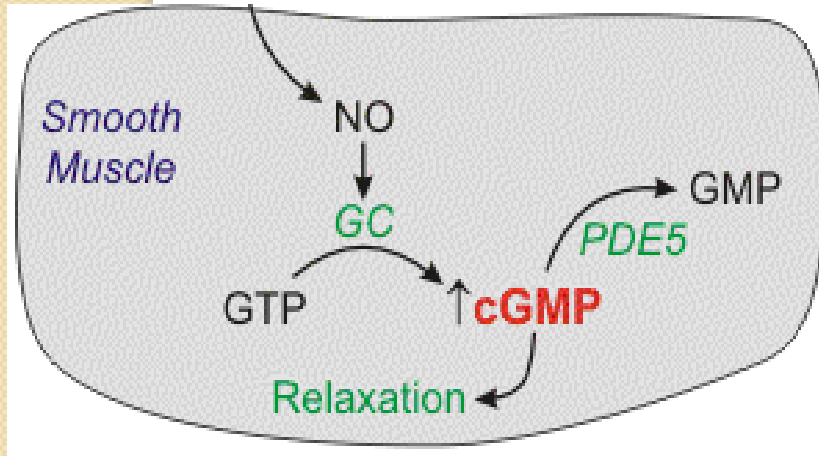
The methylxanthines include

- ***Theophylline*** which is found in tea;
- ***Theobromine***, found in cocoa; and
- ***Caffeine*** found in coffee, tea, cola drinks, chocolate, and cocoa.

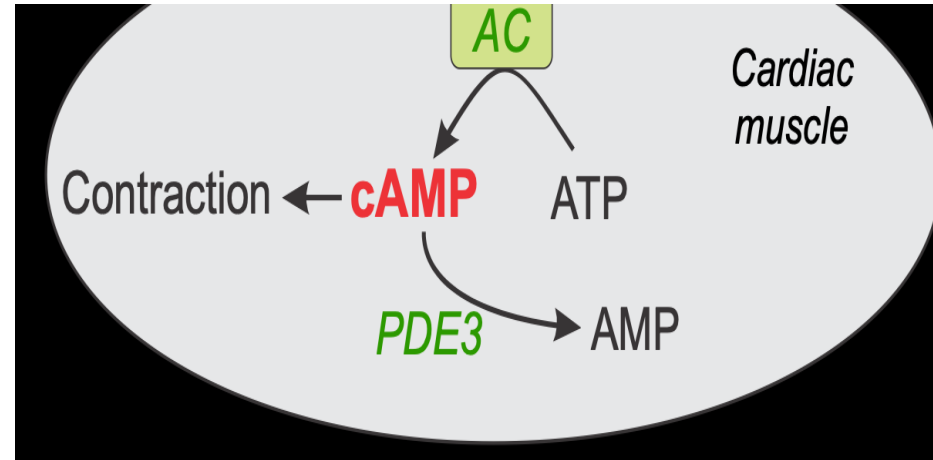
Mechanism of action: includes,

- **inhibition of phosphodiesterase enzyme :**
lead to increase cyclic adenosine
monophosphate **cAMP** and cyclic guanosine
monophosphate **cGMP** .
- **blockade of adenosine receptors.**

inhibition of phosphodiesterase enzyme



- No:** nitric oxide
- GC:** guanylyl cyclase
- AC:** Adenylyl cyclase
- PDE:** phosphodiesterase



Actions : CNS: The *caffeine* contained in one to two cups of coffee (100-200 mg) **causes a decrease in fatigue and increased mental alertness.** Consumption of 1.5 g of *caffeine* (12 to 15 cups of coffee) **produces anxiety and tremors.**

Tolerance can rapidly develop to the stimulating properties of *caffeine*; **withdrawal** consists of feelings of fatigue and sedation.

Cardiovascular system: A high dose of *caffeine* has positive inotropic and chronotropic effects on the heart.

Diuretic action: *Caffeine* has a mild diuretic action that increases urinary output of sodium, chloride, and potassium.

Gastric mucosa: Because all methylxanthines stimulate secretion of hydrochloric acid from the gastric mucosa, individuals with peptic ulcers should avoid beverages containing methylxanthines.

Therapeutic uses: *Caffeine* and its derivatives relax the smooth muscles of the bronchioles so it can be used in asthma.

Pharmacokinetics: The methylxanthines are well absorbed orally. All the methylxanthines are metabolized in the liver and excreted in the urine.

Adverse effects: Moderate doses of *caffeine* cause insomnia, anxiety, and agitation.

B. Nicotine

Nicotine is the active ingredient in tobacco. In low doses, *nicotine* causes ganglionic stimulation by depolarization. At high doses, *nicotine* causes ganglionic blockade.

Actions:

CNS: *Nicotine* is highly lipid soluble and readily crosses the blood-brain barrier. Cigarette smoking or administration of low doses of *nicotine* produces **some degree of euphoria and relaxation. It improves attention, learning, problem solving.**

High doses of *nicotine* result in central respiratory paralysis and severe hypotension caused by medullary paralysis .

Nicotine is an appetite suppressant.

Peripheral effects: Stimulation of **sympathetic ganglia** as well as the adrenal medulla increases blood pressure and heart rate. Stimulation of **parasympathetic ganglia** also increases motor activity of the bowel.

At higher doses, the activity ceases in both the gastrointestinal tract and bladder musculature as a result of a *nicotine*-induced block of parasympathetic ganglia.

Pharmacokinetics: Because *nicotine* is highly lipid soluble, absorption readily occurs via the oral mucosa, lungs, gastrointestinal mucosa, and skin.

Nicotine crosses the placental membrane and is secreted in the milk of lactating women.

Clearance of *nicotine* involves metabolism in the lung and the liver and urinary excretion.

Adverse effects: irritability, tremors, intestinal cramps, diarrhea, and increased heart rate and blood pressure.

Withdrawal syndrome: *nicotine* is an addictive substance. Withdrawal is characterized by irritability, anxiety, restlessness, difficulty concentrating, headaches, and insomnia.

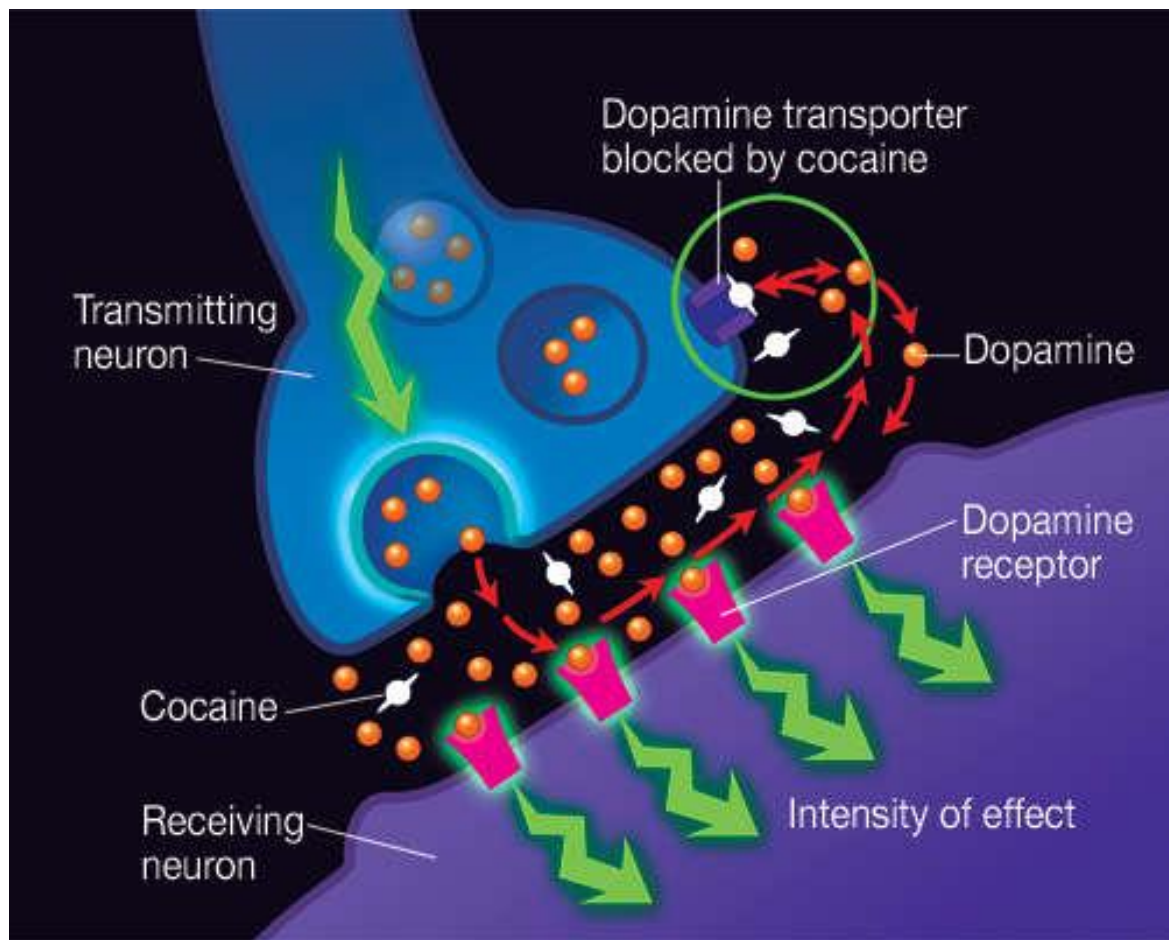


Nicotine patch

C. Cocaine

Cocaine is a widely available and highly addictive drug. The primary mechanism of action is blockade of reuptake of the monoamines (*norepinephrine*, *serotonin*, and *dopamine*) into the presynaptic terminals from which these neurotransmitters are released.





Actions:

CNS: Cocaine acutely increases mental awareness and produces a feeling of well-being and euphoria. at high doses, it causes tremors and convulsions, followed by respiratory depression.

Sympathetic nervous system: Peripherally, cocaine potentiates the action of *norepinephrine* ,this is associated with tachycardia, hypertension, pupillary dilation, and peripheral vasoconstriction.

D. Amphetamine

Amphetamine shows effects quite similar to those of *cocaine*.

Mechanism of action

As with *cocaine*, the effects of *amphetamine* on the CNS and peripheral nervous system are indirect; that is, both depend upon an elevation of the level of catecholamine neurotransmitters in synaptic spaces. *Amphetamine*, however, achieves this effect by releasing intracellular stores of catecholamines. *Amphetamine* also inhibits monoamine oxidase (MAO).

Actions:

CNS: increasing the release of *dopamine* and *norepinephrine* leads to increased alertness, decreased fatigue, depressed appetite, and insomnia.

These CNS stimulant effects of amphetamine and its derivatives have led to their use in therapy for **hyperactivity in children, narcolepsy, and for appetite control.**

Narcolepsy is a relatively **rare sleep disorder** that is characterized by uncontrollable bouts of sleepiness during the day. It is sometimes accompanied by **cataplexy**, a loss in muscle control, or even **paralysis** brought on by strong emotions, such as laughter. However, it is the sleepiness for which the patient is usually treated with drugs such as **amphetamine** , **methylphenidate** and **modafinil**.

Attention deficit hyperactivity disorder (ADHD)

Some young children are hyperkinetic and lack the ability to be involved in any one activity for longer than a few minutes.

F. Methylphenidate

Used for the treatment of ADHD. Children with ADHD may produce weak *dopamine* signals, *methylphenidate* is a more potent *dopamine* transport inhibitor than *cocaine*, thus making more *dopamine* available.

Adverse reactions: Gastrointestinal effects include anorexia, insomnia, nervousness, and fever.

Hallucinogens

The individual under the influence of these drugs is incapable of normal decision making, because the drug interferes with rational thought.

A. Lysergic acid diethylamide:

B. Tetrahydrocannabinol

C. Phencyclidine

A. Lysergic acid diethylamide:

The drug shows **serotonin (5-HT) agonist** activity, **activation of the sympathetic** nervous system occurs.

low doses of LSD can induce **hallucinations**, **High doses** may produce **long-lasting psychotic changes** in susceptible individuals.

B. Tetrahydrocannabinol: present in marijuana.

THC can produce euphoria, followed by drowsiness and relaxation. In addition to affecting short-term memory and mental activity, appetite stimulation and visual hallucinations.

It is indicated as an appetite stimulant, It is also sometimes given for the severe emesis caused by some cancer chemotherapeutic agents .

The CBI-receptor antagonist, rimonabant, is effective in the treatment of obesity and has been found to decrease appetite and body weight in humans.

Adverse effects include increased heart rate, and reddening of the conjunctiva.

Which of the following CNS stimulants occurs naturally and can be found in certain candies?

A. Amphetamine.

B. Modafinil.

C. Caffeine.

D. Atomoxetine.



Thank You