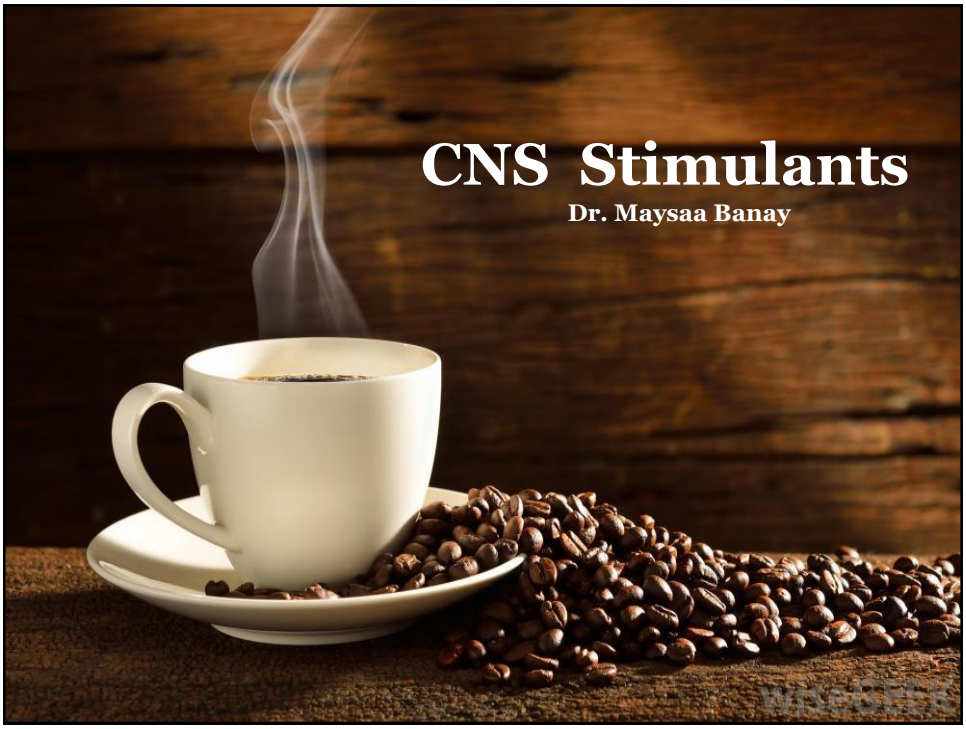

❖**The psychomotor stimulants** cause excitement and euphoria, decrease feelings of fatigue, and increase motor activity.

❖ **PSYCHOMOTOR STIMULANTS**

❖Theophylline , Varenicline, Nicotine, Caffeine, Cocaine, Amphetamine, Methamphetamine, Dextroamphetamine, Methylphenidate

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1. Methylxanthines

Include:

1. ***Theophylline****:* which is found in tea

2. ***Theobromine****:* found in cocoa

3. ***Caffeine****:* found in highest concentration in coffee products, tea, cola drinks, energy drinks, chocolate candy, and cocoa.

3

Mechanism of action

1. Translocation of extracellular calcium
2. Inhibition of phosphodiesterase enzyme lead to increase in cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP)
3. Blockade of adenosine receptors.

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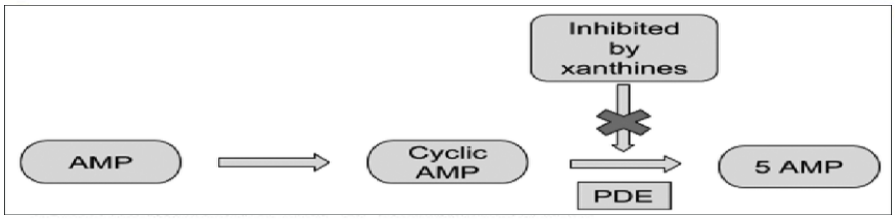

1-It inhibits phosphodiesterase enz. → ↑ cAMP

↑ calcium in CNS & heart

↓calcium in Smooth muscles

(Broncodiltation)

2- Adenosine (A1, A2 and A3) receptors antagonist almost equally, which explains many of its cardiac effects **(↑ catecholamine)**

A2 receptors antagonist responsible for CNS stimulation & smooth muscles relaxation (Broncodiltation)

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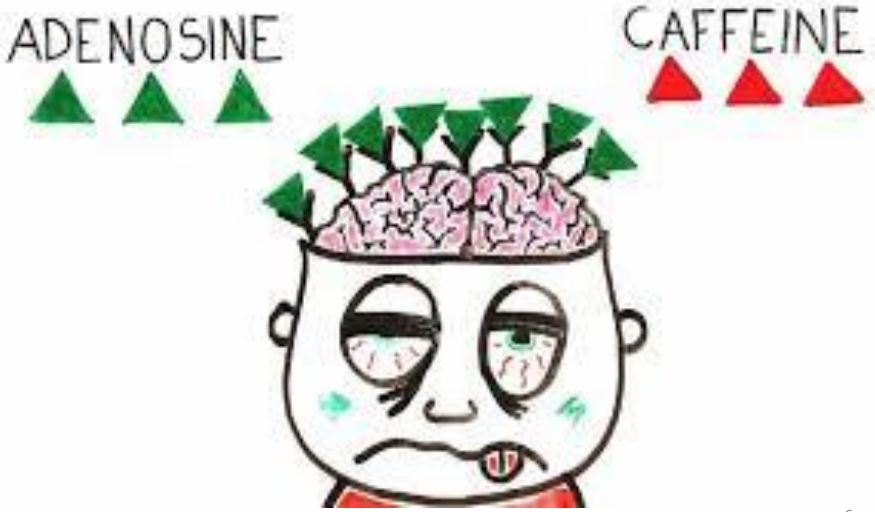
When adenosine binds to its receptors, neural activity slows down, and you feel sleepy.



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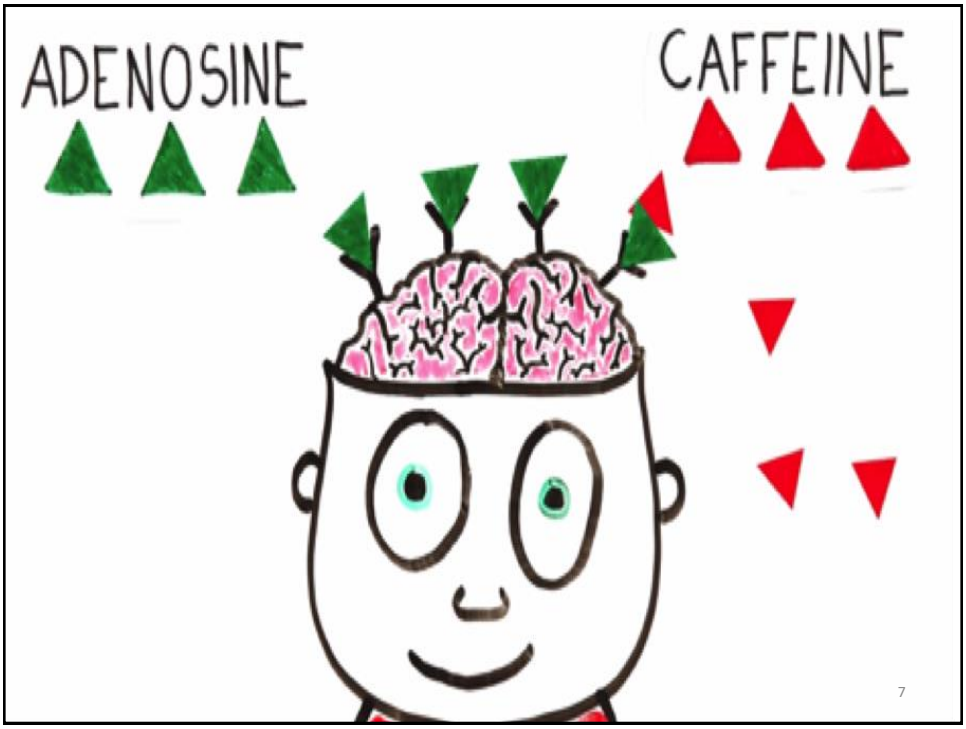

Actions

a. CNS: The *caffeine* contained in one cups of coffee (100 mg) causes a decrease in fatigue and increased mental alertness as a result of stimulating the cortex of the brain.

- Consumption of 1.5 g of *caffeine* (15 cups of coffee) produces anxiety and tremors. The spinal cord is stimulated only by very high doses of *caffeine*.
- Tolerance can rapidly develop to the stimulating properties of *caffeine*, and withdrawal consists of feelings of fatigue and sedation.

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b. Cardiovascular system: A high dose of *caffeine* has positive inotropic and chronotropic effects on the heart, harmful to patients with angina pectoris.

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

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d. Gastric mucosa: Because methylxanthines stimulate gastric acid secretion, individuals with peptic ulcers should avoid foods and beverages containing methylxanthines.

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Therapeutic uses

1. Relax the smooth muscles of the bronchioles, ***theophylline*** replaced by β2 agonists and corticosteroids for the treatment of asthma
2. Caffeine is used in combination with the analgesics *acetaminophen* and *aspirin* for the management of headaches.

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- **Pharmacokinetics:** well absorbed orally. *Caffeine* distributes throughout the body, including the brain and placenta to the fetus and are secreted into the breast milk.

- **Adverse effects:** insomnia, anxiety, and agitation.
- Toxicity (high dosage): emesis and convulsions.
- The lethal dose is 10 g of *caffeine* (about 100 cups of coffee), which induces cardiac arrhythmias.

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2. Nicotine

- ***Nicotine*** is the active ingredient in tobacco, used in smoking cessation therapy.
- In combination with the tars and carbon monoxide found in cigarette smoke, *nicotine* represents a serious risk factor for lung and cardiovascular disease, cancers.

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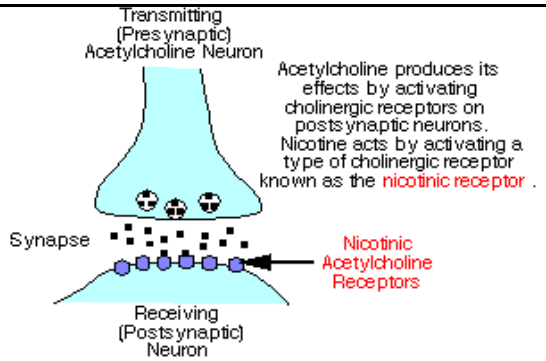

- **Mechanism of action:** *Nicotine* receptors exist in the CNS, *Nicotine is a* full agonist at these receptors
- **In low doses**, *nicotine* causes ganglionic stimulation by depolarization.
- **At high doses**, *nicotine* causes ganglionic blockade.

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Actions

a. 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, arousal, and relaxation.

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

❖*Nicotine* is an appetite suppressant.

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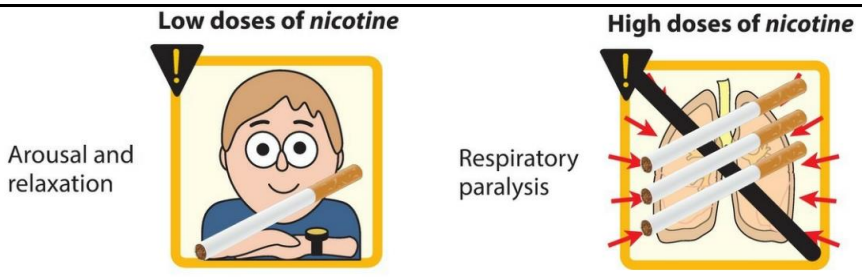

b. Peripheral effects: Stimulation of **sympathetic ganglia** and adrenal medulla increases blood pressure and heart rate, vasoconstriction. (harmful in hypertensive patients and angina).

- Stimulation of **parasympathetic ganglia** also increases motor activity of the bowel.
- **At higher doses**, blood pressure falls and activity stop in GI tract and bladder as a result of block of parasympathetic ganglia.

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- **Pharmacokinetics:** *nicotine* is highly lipid soluble, absorption occurs via the oral mucosa, lungs, GI mucosa, and skin. crosses the placental membrane and is secreted in the breast milk.
- **Adverse effects**

1. CNS: irritability and tremors
2. GIT: Intestinal cramps, diarrhea
3. CVS: increased heart rate and blood pressure
4. Cigarette smoking increases the rate of metabolism for a number of drugs.

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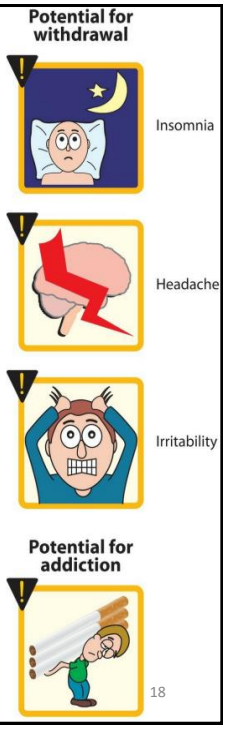
- **Withdrawal syndrome:** *nicotine* is an addictive substance, physical dependence develops rapidly.
- Withdrawal is characterized by irritability, anxiety, restlessness, difficulty concentrating, headaches, and insomnia.
- The transdermal patch and chewing gum containing *nicotine* reduce *nicotine* withdrawal symptoms and to help smokers stop smoking.
- Other forms of *nicotine* replacement used for smoking cessation include the inhaler, nasal spray, and lozenges.
- *Bupropion* (antidepressant), can reduce the craving for cigarettes.



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3. Varenicline (champix)™

- *Varenicline* is a partial agonist at neuronal nicotinic acetylcholine receptors in the CNS so, it produces less euphoric effects than *nicotine*.
- It is useful as an adjunct in the management of smoking cessation in patients with *nicotine* withdrawal symptoms.
- Patients taking *varenicline* should be monitored for suicidal thoughts, nightmares, and mood changes.

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4. Cocaine

- *Cocaine* is a highly addictive drug.
- **The mechanism of action**: blockade of reuptake of the monoamines (norepinephrine, serotonin, and dopamine) into the presynaptic terminals. This prolongs the CNS and peripheral actions of these monoamines.
- Prolongation of dopaminergic effects in the brain's pleasure system (limbic system) produces euphoria.
- Chronic intake of *cocaine* depletes dopamine, triggers craving for cocaine

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5. Amphetamine

Amphetamine is a sympathetic amine
(Dextroamphetamine, Methamphetamine)

- **Mechanism of action:** As with *cocaine*, indirect elevation of the level of catecholamine neurotransmitters in synaptic spaces by:

1) Inhibit reuptake into noradrenergic neurons
2) Releasing intracellular stores of catecholamines
3) Inhibits (MAO)

so high levels of catecholamines are readily released into synaptic spaces.

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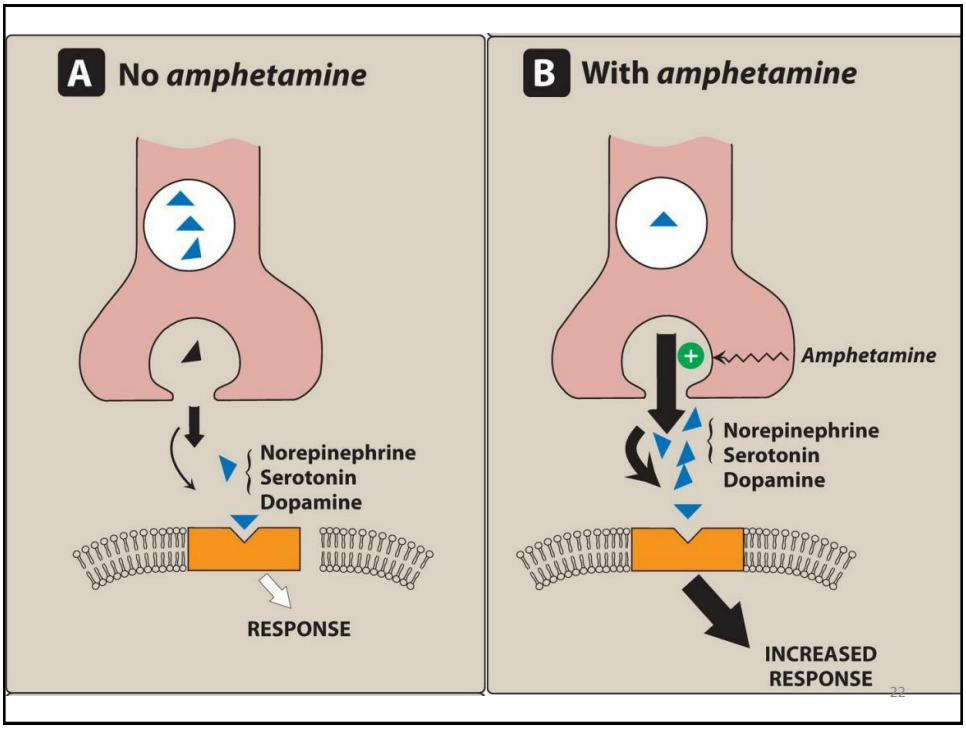

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Actions

- **CNS:** The major behavioral effects result from a combination of its dopamine and norepinephrine release enhancing properties.

❖*Amphetamine* stimulates the cerebrospinal axis, cortex, brainstem, and medulla. This leads to increased alertness, decreased fatigue, depressed appetite, and insomnia.

❖As CNS stimulant: use in therapy for hyperactivity in children, narcolepsy, and obesity.

❖At high doses, psychosis and convulsions can occur.

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Therapeutic uses

a. Attention deficit hyperactivity disorder (ADHD): Some young children are hyperkinetic and cannot concentrate for very long.

- *Dextroamphetamine*, the *mixed amphetamine salts (*Adderall *)™*, *methamphetamine* and *methylphenidate* can help improve attention span and alleviate many of the behavioral problems associated with this syndrome.

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b. Narcolepsy: is rare sleep disorder characterized by uncontrollable bouts of sleepiness during the day. treated with drugs, such as the *mixed amphetamine salts* or *methylphenidate.*

❖**Modafinil** is first-line agents for the treatment of narcolepsy. The mechanism of action unclear but involve the adrenergic and dopaminergic systems

c. Appetite suppression: *Phentermine* and *diethylpropion* are sympathomimetic amines that are related structurally to *amphetamine*. used in the management of obesity.

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Adverse effects

1) Addiction, dependence, and tolerance
2) **CNS effects:** insomnia, irritability, tremor, and hyperactive reflexes, suicidal tendencies. ***lorazepam***, used in the management of agitation and CNS stimulation secondary to *amphetamine* overdose.
3) **Cardiovascular effects:** palpitations, cardiac arrhythmias, hypertension, and circulatory collapse
4) **GIT effects:** anorexia, nausea, vomiting, abdominal cramps.

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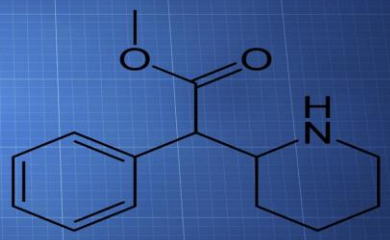
6. Methylphenidate



- CNS-stimulant properties similar to those of *amphetamine* and may also lead to abuse.
- *Methylphenidate* is presently one of the most prescribed medications in children.

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Mechanism of action

- Children with ADHD may produce weak dopamine signals.
- *Methylphenidate* is a dopamine and norepinephrine transport inhibitor and may act by increasing both dopamine and norepinephrine in the synaptic cleft.
- *Methylphenidate* have less potential for abuse than *cocaine*, because it enters the brain more slowly than *cocaine* and does not increase dopamine levels as rapidly.

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- **Therapeutic uses:** treatment of ADHD, narcolepsy.
- **Pharmacokinetics:** *Methylphenidate* is available in extended-release oral formulations and as a transdermal patch for once-daily application.

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Adverse effects

1. GIT are the most common and include abdominal pain and nausea
2. Anorexia, insomnia, nervousness, and fever.
3. In seizure patients, *methylphenidate* may increase seizure
4. Contraindicated in patients with glaucoma.
5. *Methylphenidate* can inhibit the metabolism of *warfarin*, *phenytoin*, *phenobarbital*, *primidone*, and the tricyclic antidepressants.

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