

CNS Stimulants & Drugs of abuse



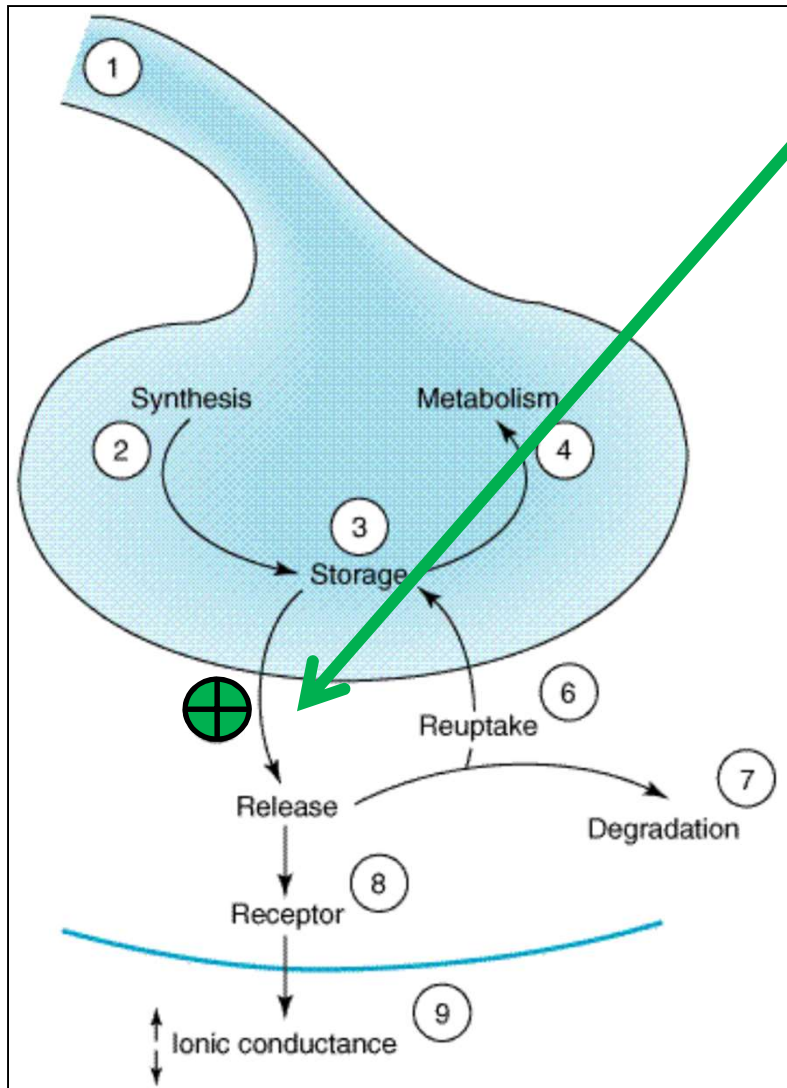
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PhD

Stimulants vs. Depressants

- Alertness
- Wakefulness
- Locomotion
- Examples
 - Amphetamine
 - Barbiturates
 - Opioids
 - Cocaine
 - Benzodiazepine



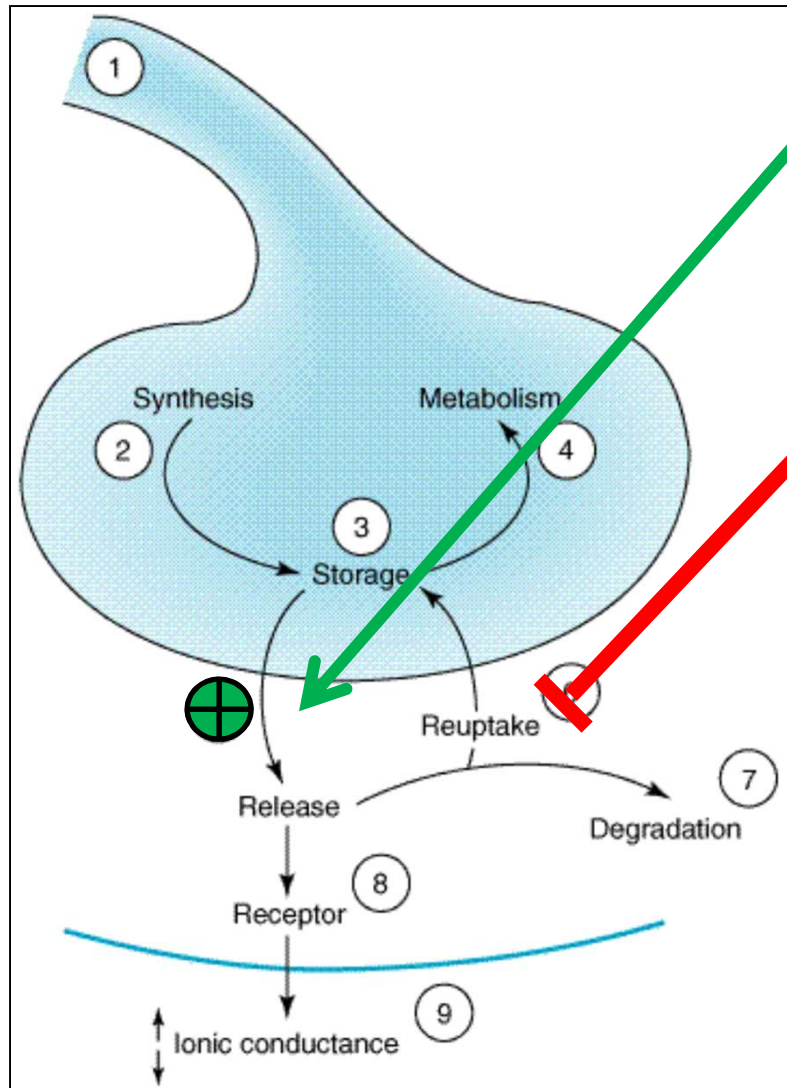
Excitatory Neurons



1) Enhance Neurotransmitter release:

- Amphetamine

Excitatory Neurons



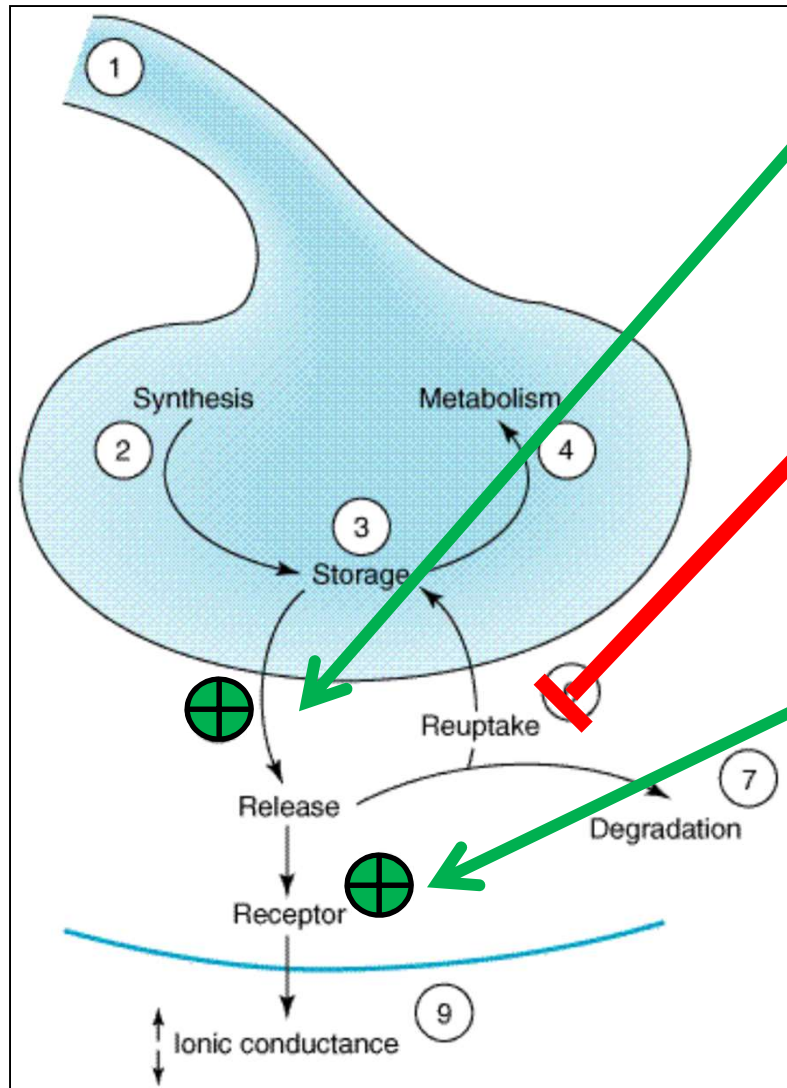
1) Enhance Neurotransmitter release:

- Amphetamine

2) Inhibit Neurotransmitter Uptake:

- Cocaine

Excitatory Neurons



1) Enhance Neurotransmitter release:

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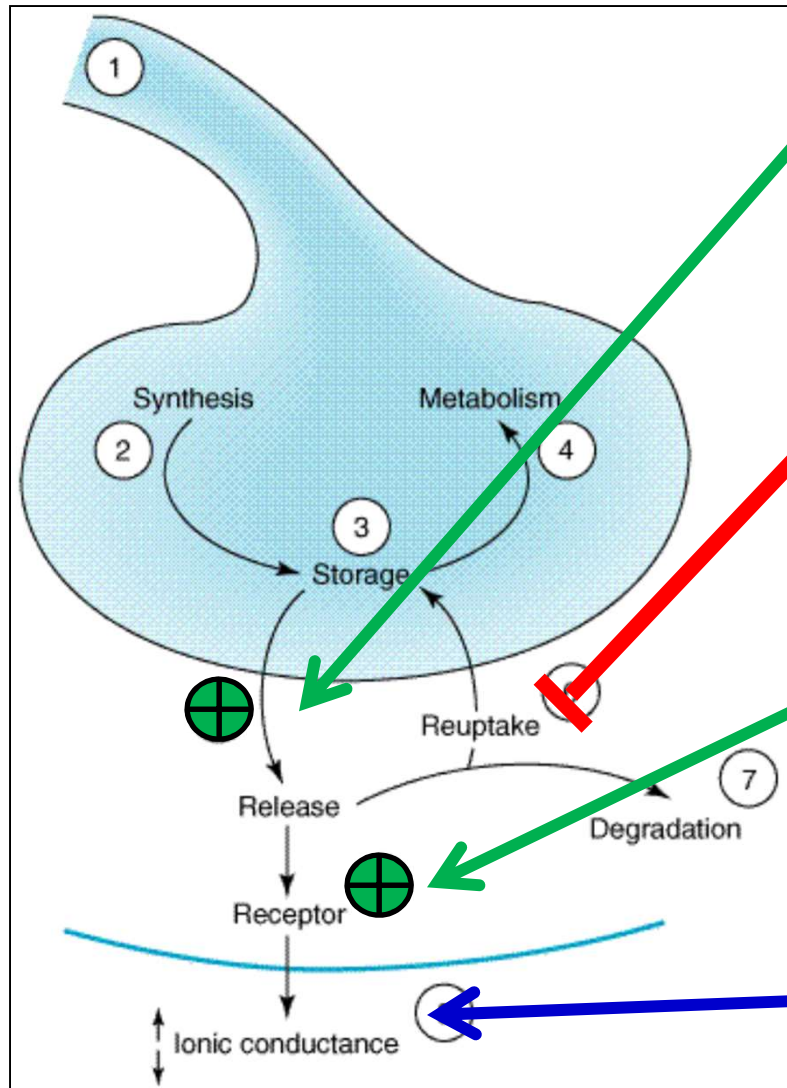
2) Inhibit Neurotransmitter Uptake:

- Cocaine

3) Activate postsynaptic receptors

- Nicotine

Excitatory Neurons



1) Enhance Neurotransmitter release:

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2) Inhibit Neurotransmitter Uptake:

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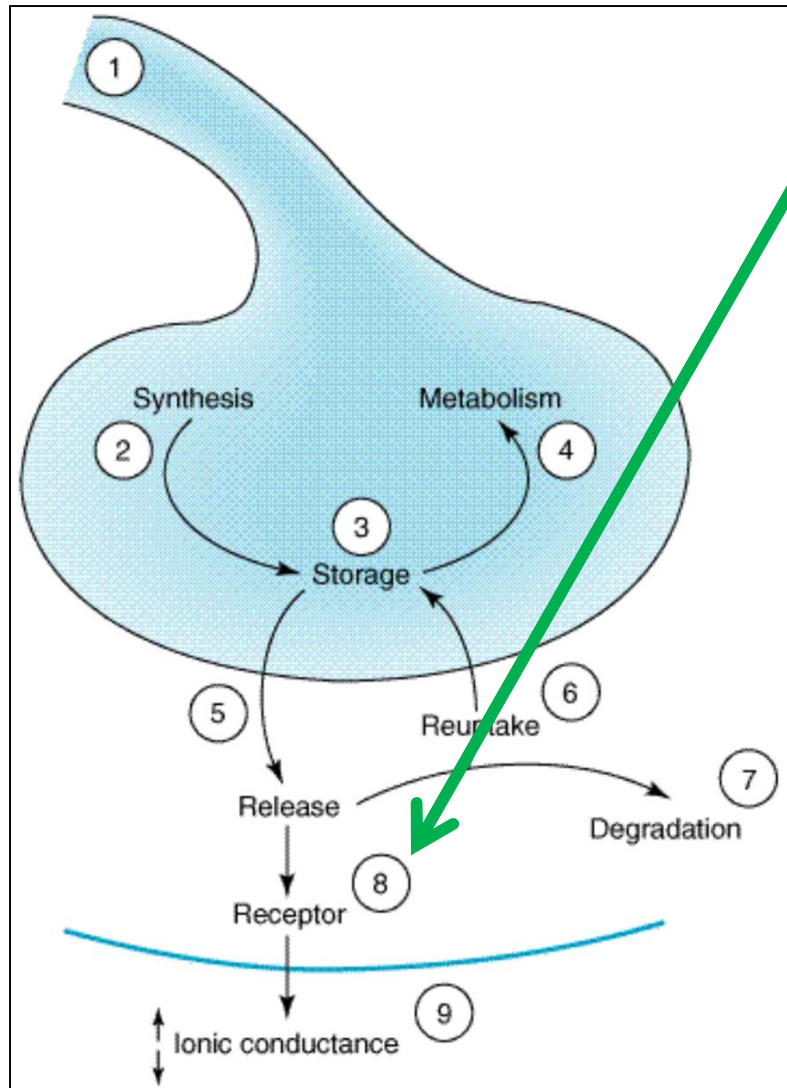
3) Activate postsynaptic receptors

- Nicotine

4) Interfere with 2nd messenger

- Caffeine

Inhibitory Neurons



1) Inhibit postsynaptic receptors:

- Strychnine (inhibit glycine receptors)

CNS Stimulants



Definitions

- **Drug abuse:**
 - A pattern of drug intake in which the user consumes the drug against its medical indication



Definitions

- **Withdrawal symptoms:**
 - The emergence of unwanted signs and symptoms after cessation of drug intake



Definitions

- **Dependence:**
 - Compulsive drug using behavior in which the individual uses the drug to avoid unwanted side effects



Definitions

- Physiological Dependence:
 - Diarrhea
 - Sweating
 - Nausea
 - Headache
 - Hypertension
 - etc



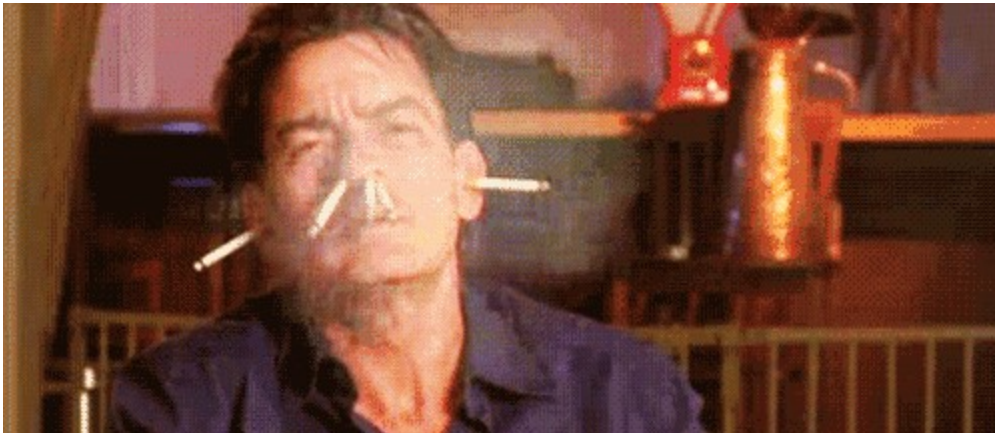
Definitions

- **Psychological Dependence:**
 - Continuous drug intake for personal satisfaction.
 - Emotional connection to the abused substance



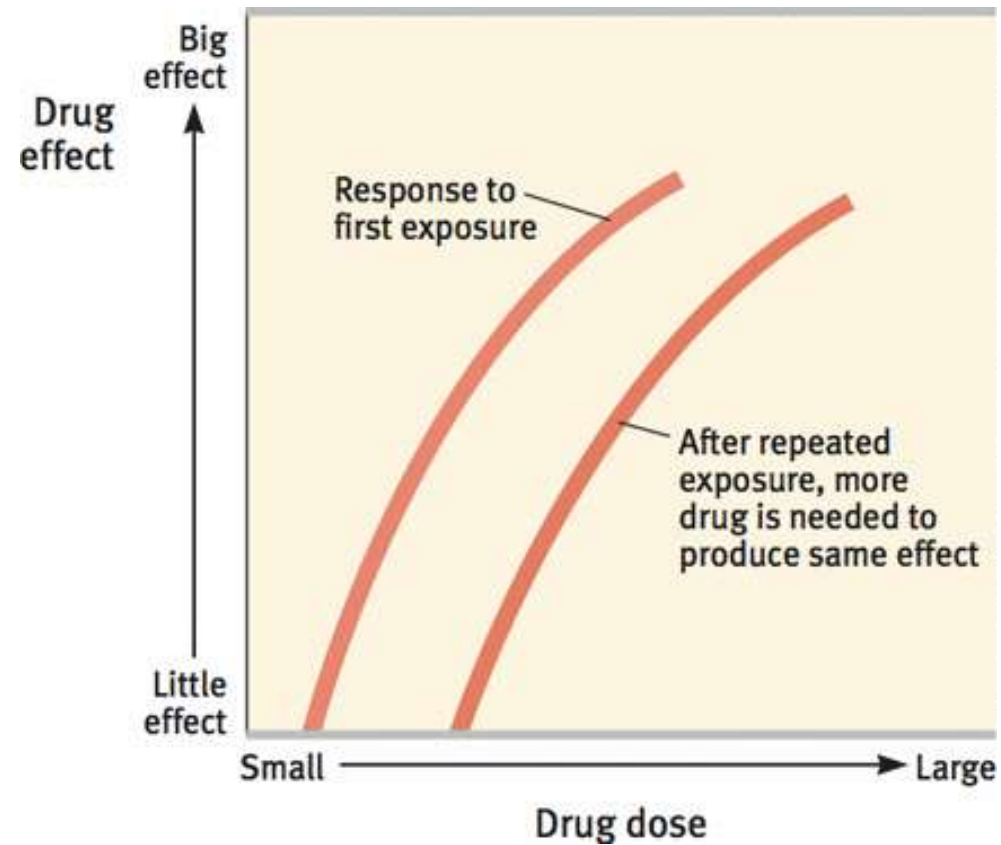
Definitions

- **Addiction**
 - Continuous repetition of a behavior despite adverse consequences.

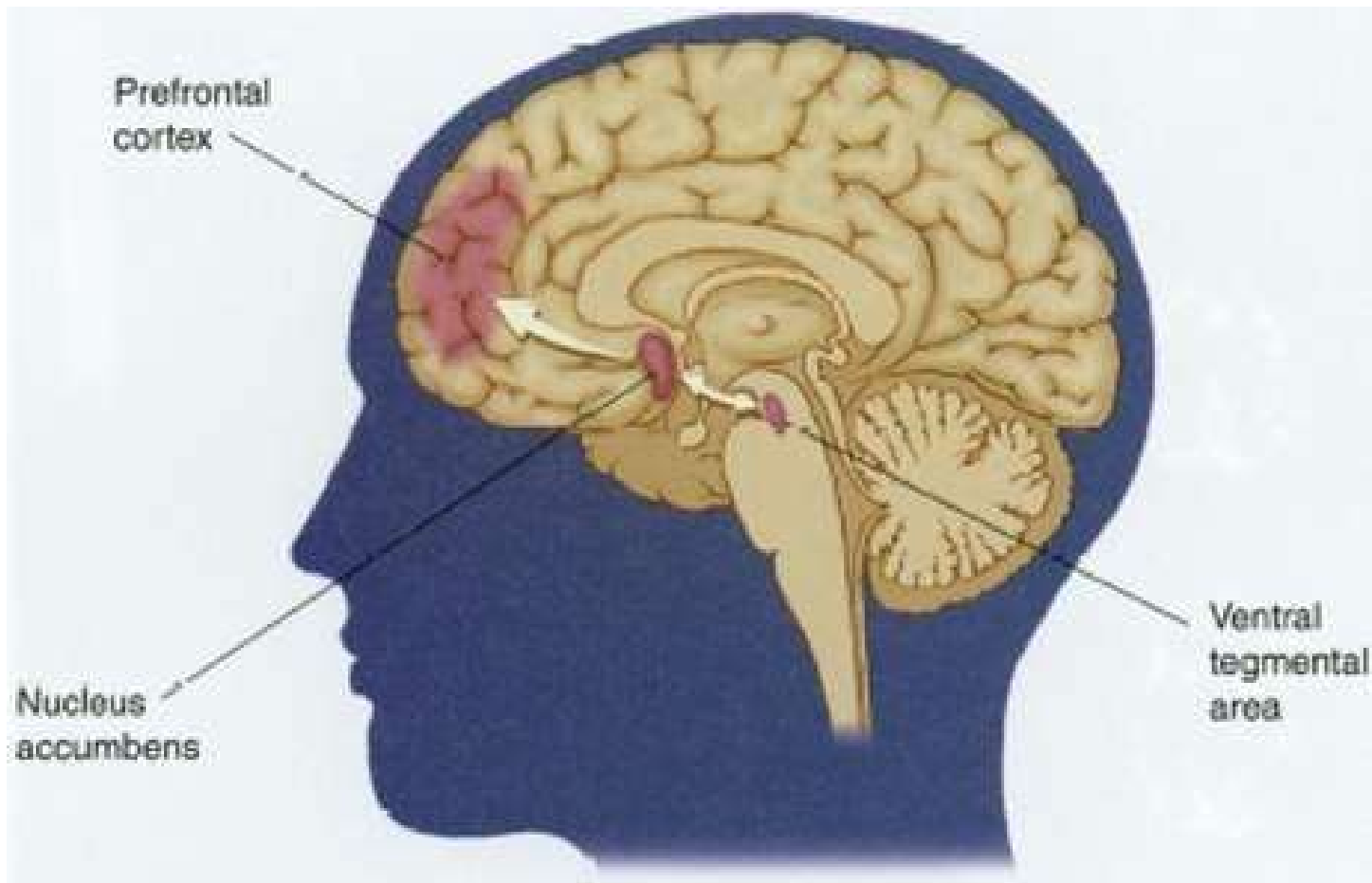


Definitions

- Tolerance

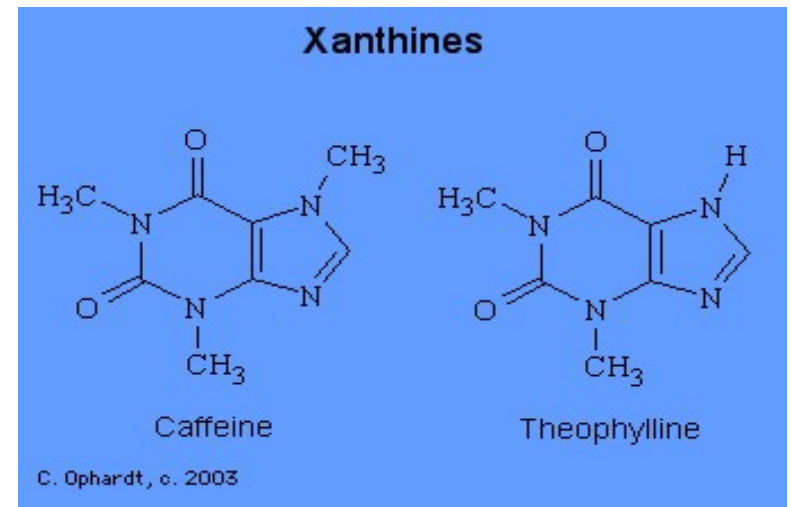


Mesolimbic Dopamine Pathway

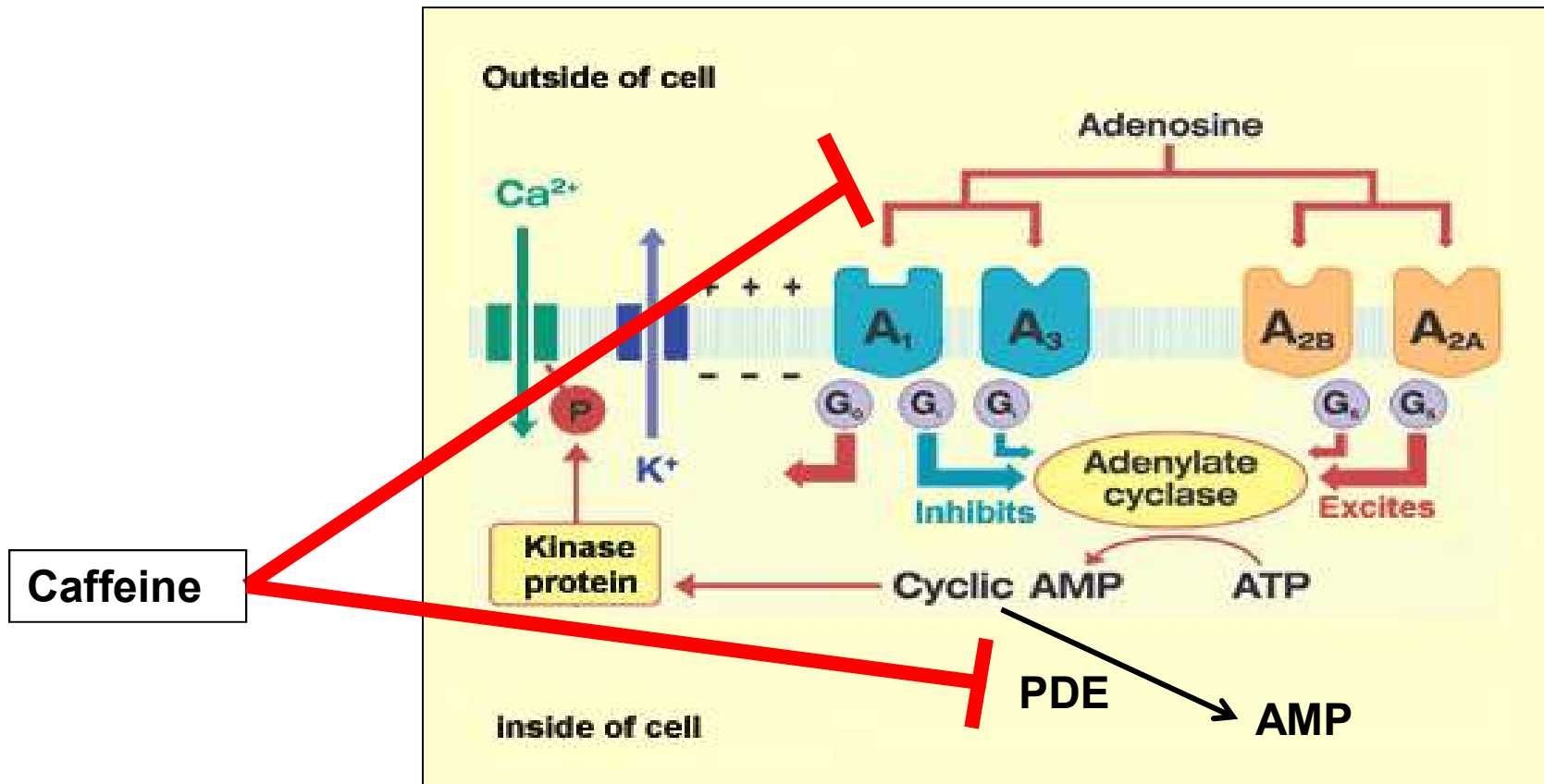


Methylxanthines

- Improve alertness and enhance wakefulness and mental performance
- No stereotyped behavior or psychosis even in large doses
- Act by inhibition of adenosine receptors and PDE.



Methylxanthines



PDE = Phosphodiesterase

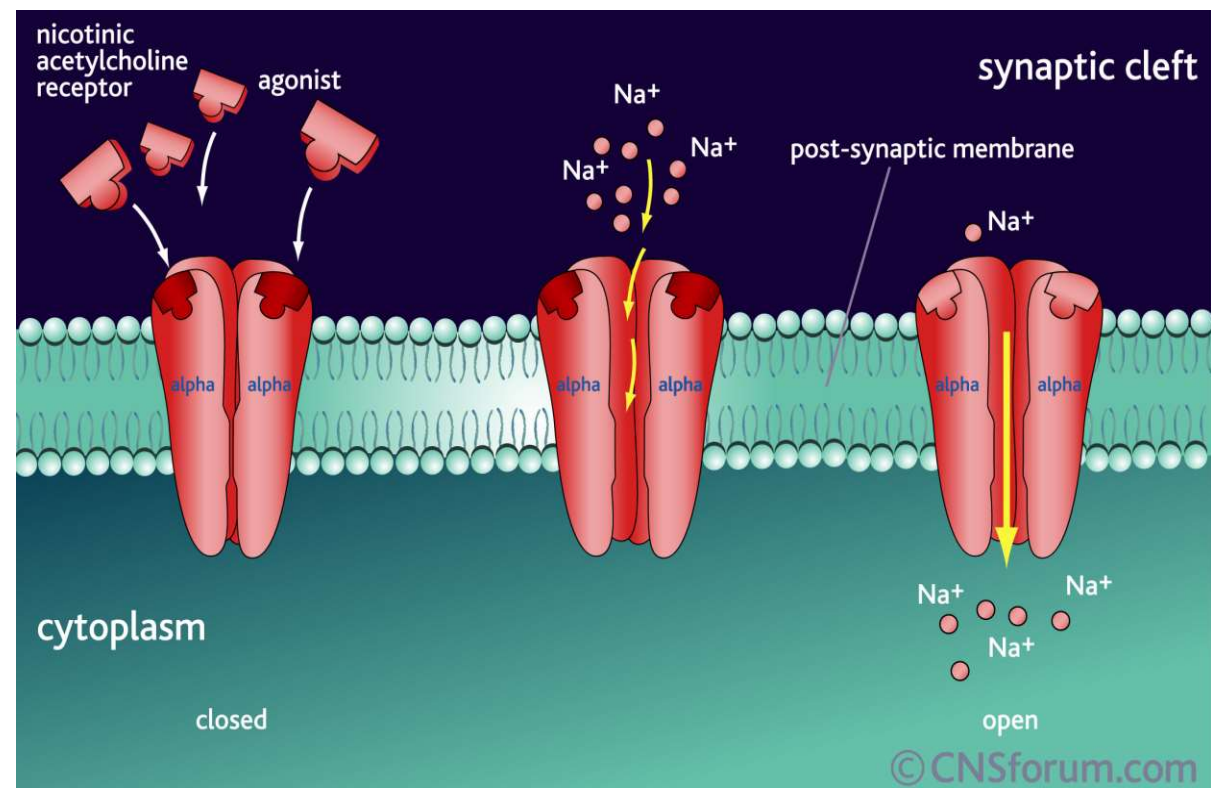
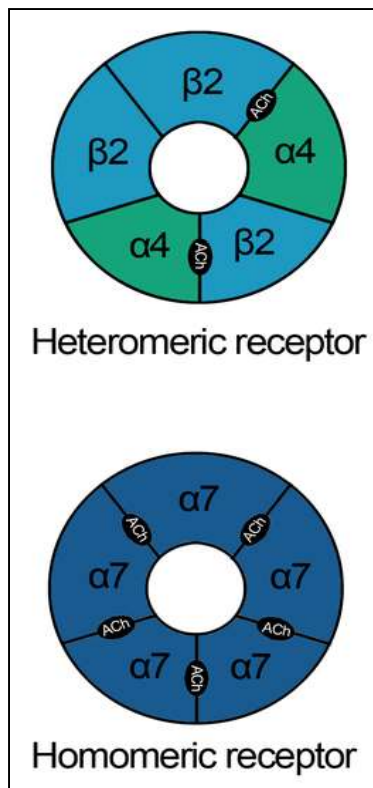
Methylxanthines

- CNS:
 - Low dose:
 - High dose:
 - Tremor, anxiety insomnia, nervousness, cardiac stimulation and arrhythmia.
 - Withdrawal:
 - Lethargy, fatigue, and headache.

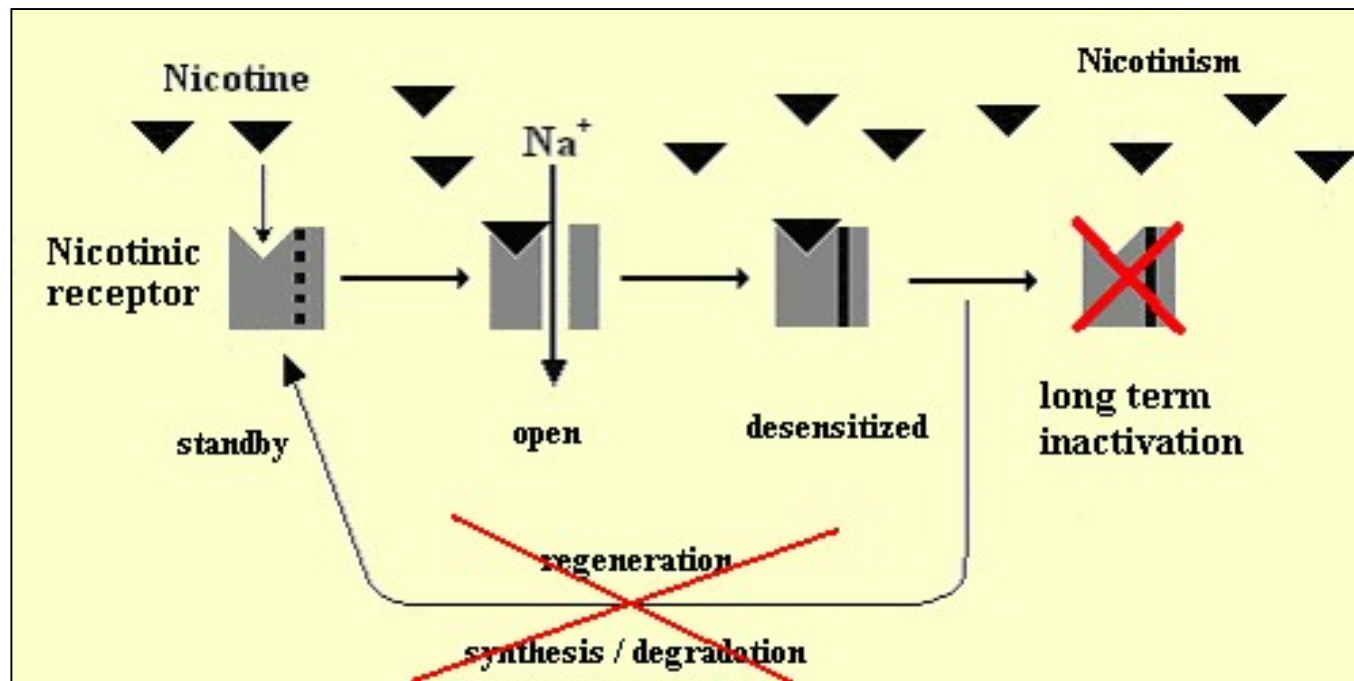
Nicotine

- Is the active ingredient of tobacco.
- Second only to caffeine as the most widely used CNS stimulant.
- Second only to alcohol as the most abused substance. (in US)
- Low doses stimulate and high doses block the ganglia.
 - Why?

Nicotinic Receptors



Nicotinic Receptors (Desensitization)



Nicotine

- Is the active ingredient of tobacco.
- Second only to caffeine as the most widely used CNS stimulant.
- Second only to alcohol as the most abused substance. (in US)
- Low doses stimulate and high doses block the ganglia.
 - Why?
- Q: What is the difference between nicotine and Acetylcholine?

Effects of nicotine

- Low dose:
 - Euphoria, arousal, relaxation, and improvement of attention, learning, problem solving and reaction time, anxiolytic.
- High doses:
 - Respiratory depression and severe hypotension.

Nicotine

- Nicotine is an appetite suppressant .
- Physical and psychological dependence.
- Withdrawal:
 - Irritability, anxiety, restlessness.
 - Headache and difficulty in concentration
 - Insomnia, weight gain (?).
- Withdrawal symptoms could be relieved by:
 - Transdermal patches
 - Chewing gum
 - Varenicline: Partial agonist. ??
 - Bupropion:?

Cocaine

- Chewing, intranasal, snorting, smoking and IV.
- Acts by inhibition of catecholamines uptake, especially dopamine.

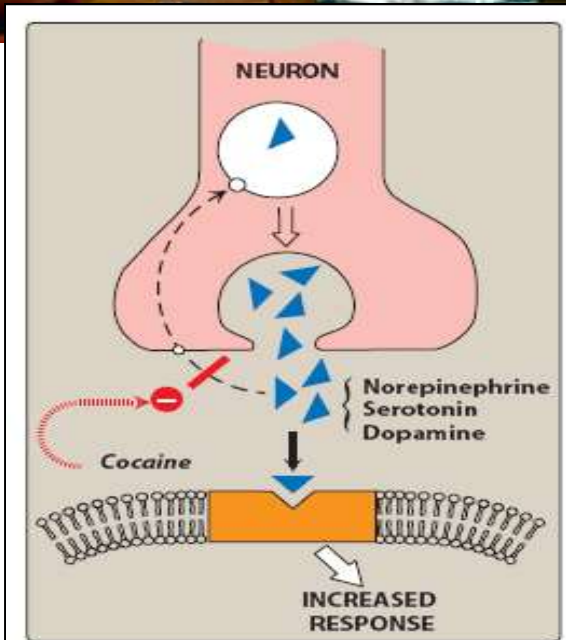
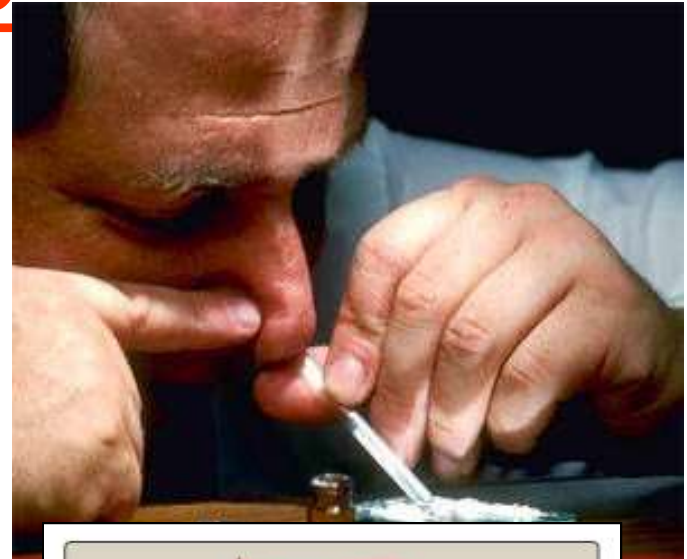
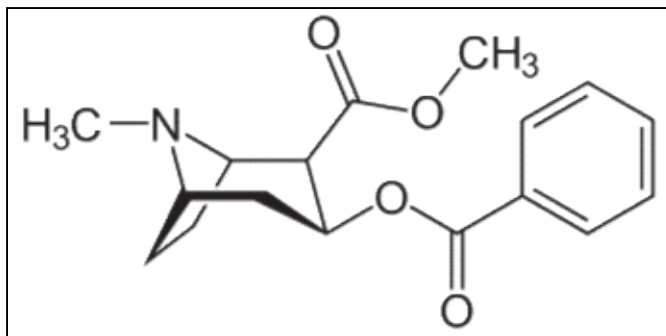


Figure 10.6
Mechanism of action of cocaine.

Cocaine

- Produces euphoria, self-confidence, mental alertness for short period.
 - Produces tolerance, physical and psychological dependence.
- Overdose:
 - death from arrhythmia, seizures, respiratory depression
 - severe hypertensive episodes which can lead to MI and strokes, and hyperthermia.

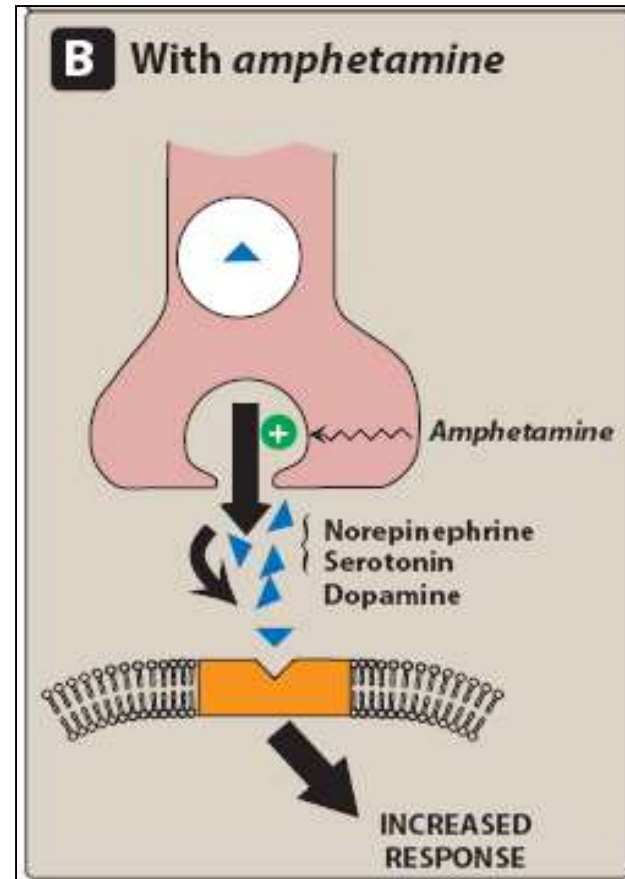
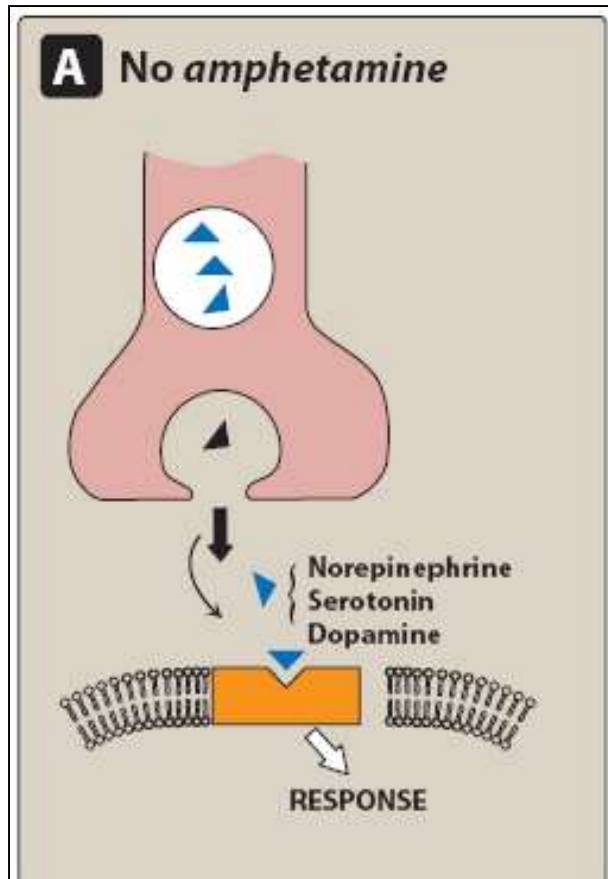
Cocaine

- Therapeutic use:
 - Local anesthesia (esp. ENT and eye)
 - Vasoconstrictive effect
- Pharmacokinetics:
 - Fast onset of action (susceptibility of overdose)
- Withdrawal:
 - Depression of mood (anhedonia)
 - Apathy, irritability.

Amphetamines

- D-amphetamine, methamphetamine and methylphenidate.
- Main effects:
 - Similar to cocaine
 - Increase motor activity
 - Euphoria and excitement
 - Anorexia
 - Stereotyped and psychotic behavior – after prolonged use.
- The effects are mainly due to release of NE & Dopamine.

Amphetamine (MOA)



Amphetamines

- Therapeutic uses:
 - ADHD
 - Narcolepsy
- Longer effect than Cocaine
- Tolerance to the stimulant effect develops rapidly.

CNS Hallucinogens

- Psychotomimetic Drugs
- Produce profound changes in thought patterns and mood
 - Delusion; illusion; hallucination
- Examples:
 - LSD
 - MDMA (Ecstasy)

Hallucinogens

- Affect thoughts, perceptions and mood with no marked psychomotor stimulation or depression.
- Mood change is very complex “not euphoria nor depression”.
- They do not produce dependence.

Hallucinogens

- Mechanism of actions:
 1. Interfere with 5-HT (serotonin):
 - a. 5-HT₂ agonists as LSD
 - b. 5-HT uptake inhibitors as: Methylene DioxyMethAmphetamine(MDMA).
 2. Antagonist at NMDA receptors
 - Glutamate receptors
 - Phencyclidine
 3. Activate cannabinoid receptors
 - Marijuana

LSD

Lysergic acid diethylamide



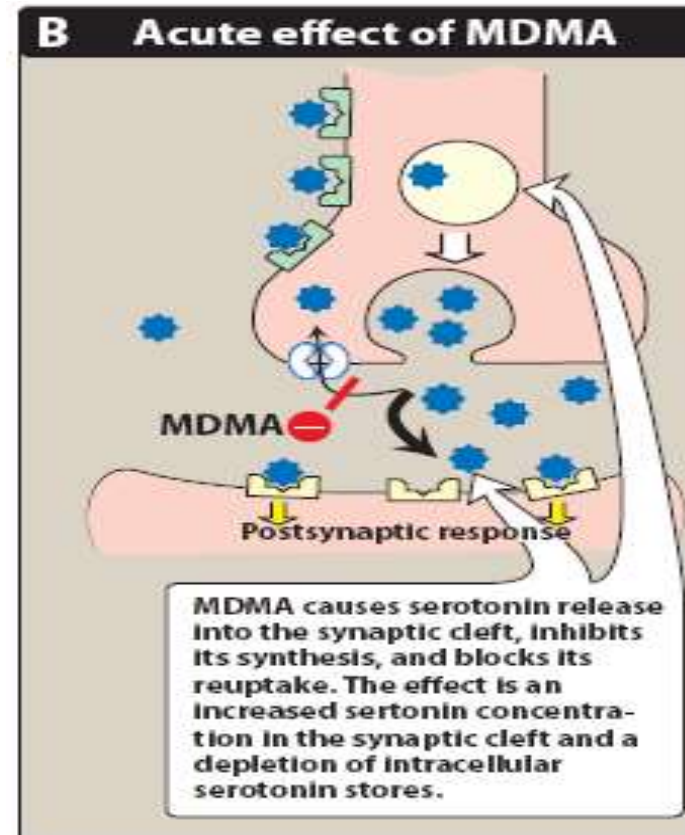
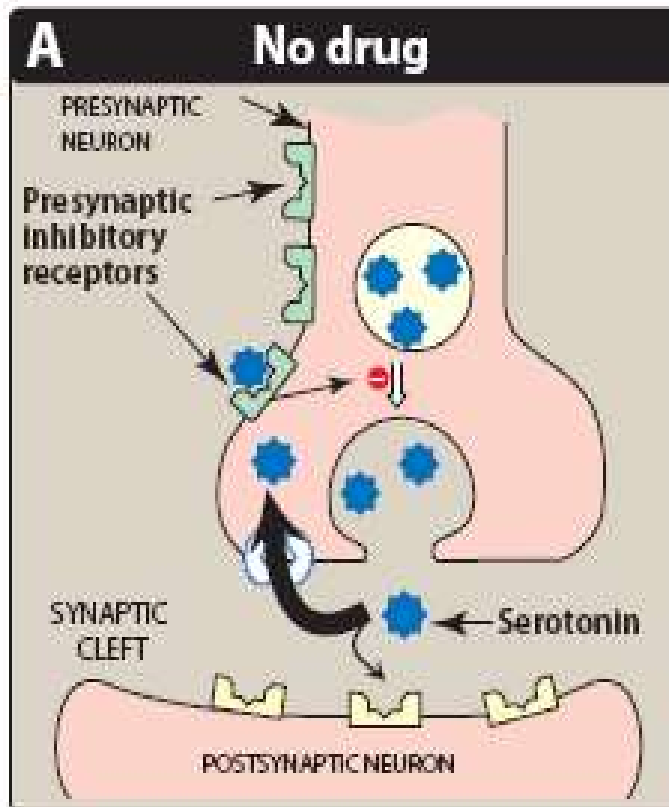
LSD

- 5-HT₂ Receptor agonist.
- Potent and long duration of action (5-12 hrs)
- Effects:
 - Hallucination with brilliant color
 - Alteration of mood
 - Sympathomimetic:
- High doses may produce psychotic changes

MDMA(ecstasy)

- Methylenedioxymathamphetamine
- Widely used as “party drug”.
- Has severe long term psychotic effect.
- Effects:
 - Sympathomimetic
 - Sense of well-being, euphoria, empathy.
 - Serotonin syndrome
 - Teeth and jaw grinding

MDMA (MOA)



Marijuana



Marijuana

- Hashish or Canabis sativa.
- The active ingredient is THC (Tetrahydrocannabinol)
- Effects:
 - Produce euphoria?
 - Disinhibition
 - Uncontrollable laughing
 - Enhance appetite
 - Change in time perception
- Alcohol potentiates these effects.
- Uses:
 - Agonist: Antiemetic; appetite enhancer.
 - Antagonist: Obesity

Marijuana (MOA)

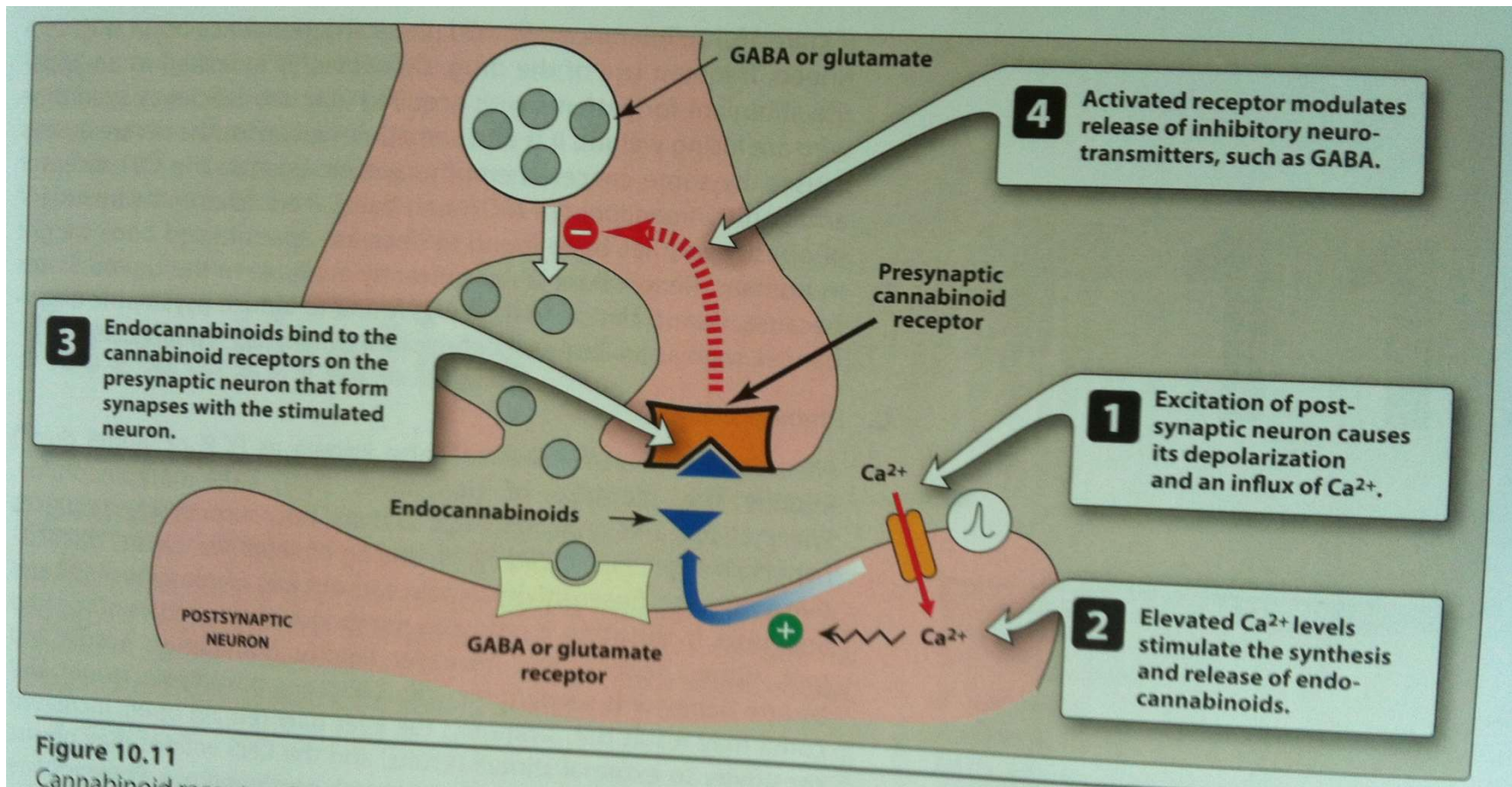


Figure 10.11

Cannabinoid receptor

Others?

- Captagon?
- Joker?



Videos

- Mouse party
 - <http://learn.genetics.utah.edu/content/addiction/mouse/>
- Spiders on drugs
 - <http://www.youtube.com/watch?v=sHzdsFiBbFc>
- Drugs and driving
 - <https://www.youtube.com/watch?v=bWLksTAnuFE>

Thank you

