

DRUGS THAT ACT IN THE CNS

CNS Stimulants

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CNS Stimulants / E. Amphetamine

Amphetamine is a sympathetic amine that shows neurologic and clinical effects quite **similar to those of cocaine**.

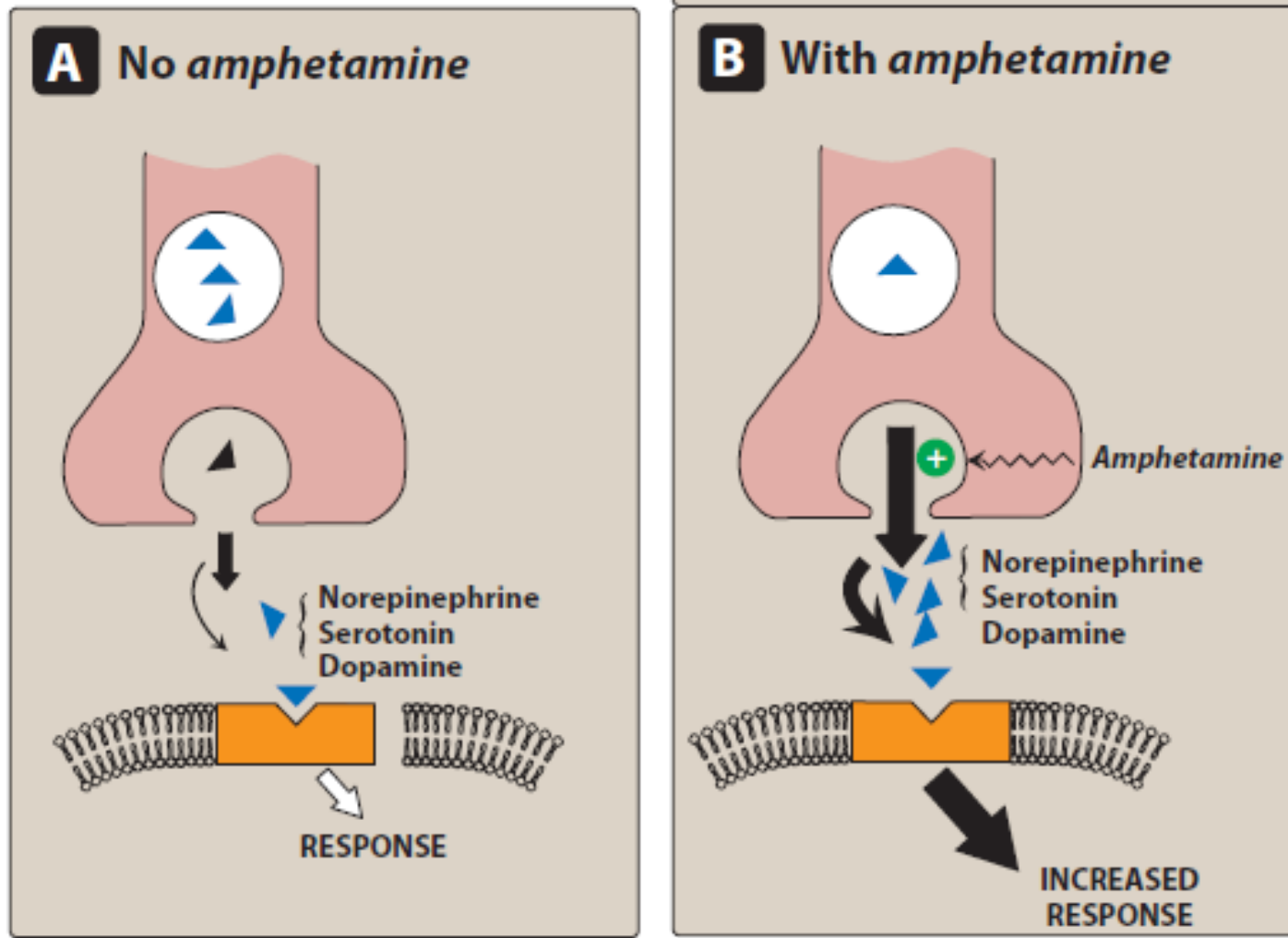
Dextroamphetamine is the major member of this class of compounds.

Methamphetamine (also known as “**speed**”) is a derivative of amphetamine available for prescription use. It can also be smoked and is preferred by many abusers.

3,4-ethylenedioxyamphetamine (also known as **MDMA**, or **Ecstasy**) is a synthetic derivative of methamphetamine with both stimulant and hallucinogenic properties

CNS Stimulants

E. Amphetamine/Mechanism of action



CNS Stimulants/ E. Amphetamine/ 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 .

Because amphetamine also **inhibits monoamine oxidase (MAO)** and is a weak **reuptake transport inhibitor**, high levels of catecholamines are readily released into synaptic spaces.

CNS Stimulants/ E. Amphetamine/ Actions:

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

This leads to increased alertness, decreased fatigue, depressed appetite, and insomnia.

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

At high doses, psychosis and convulsions can ensue.

b. Sympathetic nervous system: In addition to its marked action on the CNS, amphetamine acts on the **adrenergic system**, indirectly stimulating the receptors through norepinephrine release.

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

a. 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.

The **dopamine pathways and norepinephrine pathways** are directly responsible for modulating executive function (cognitive control of behavior), motivation, reward perception, and motor function.

These pathways are known to play a central role in the pathophysiology of ADHD

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

a. Attention deficit hyperactivity disorder (ADHD):

Inattention	Hyperactivity-impulsivity
<ul style="list-style-type: none">•gives no close attention to details•has trouble holding attention on tasks•has trouble organizing tasks and activities•loses things necessary for tasks•appears forgetful in daily activities•has a short attention span and is easily distracted•makes careless mistakes – for example, in schoolwork•is unable to stick at tasks that are tedious or time-consuming•appears unable to listen to or carry out instructions	<ul style="list-style-type: none">•unable to sit still•fidgets, squirms in seat•leaves seat in inappropriate situations•takes risks with little thought for the dangers•"on the go" or "driven by a motor"•talks excessively•blurts out answers too early•has trouble waiting their turn•interrupts or intrudes on conversations

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

a. Attention deficit hyperactivity disorder (ADHD):

Dextroamphetamine, methamphetamine, the mixed amphetamine salts, and methylphenidate can help improve attention span and alleviate many of the behavioral problems associated with this syndrome, in addition to reducing hyperkinesia.

Lisdexamfetamine is a **prodrug** that is converted to the active component dextroamphetamine after GI absorption and metabolism.

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

a. Attention deficit hyperactivity disorder (ADHD):

Atomoxetine is a nonstimulant drug **approved for ADHD** in children and adults.

Unlike methylphenidate, which blocks dopamine reuptake more than norepinephrine reuptake, atomoxetine is more selective for inhibition of **norepinephrine** reuptake.

Therefore, it is not considered habit forming and is not a controlled substance.

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

b. Narcolepsy:

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, and even paralysis brought on by strong emotions such as laughter.



CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

b. Narcolepsy:

The sleepiness can be treated with drugs, such as the mixed amphetamine salts or methylphenidate.

Modafinil and its R-enantiomer derivative, armodafinil, are considered first-line agents for the treatment of narcolepsy.

CNS Stimulants/ E. Amphetamine/ Therapeutic uses:

b. Narcolepsy:

- ✓ Modafinil promotes wakefulness, but it produces fewer psychoactive and euphoric effects and fewer alterations in mood, perception, thinking, and feelings typical of other CNS stimulants.
- ✓ The mechanism of action remains unclear, but may involve the adrenergic and dopaminergic systems.
- ✓ Modafinil and armodafinil may have some potential for abuse and physical dependence, and both are classified as controlled substances.

c. Appetite suppression:

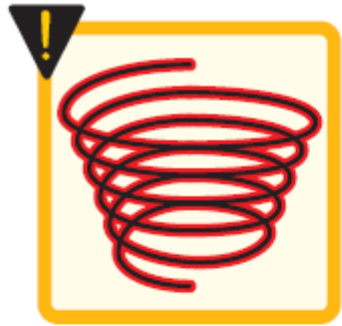
- ✓ Phentermine and diethylpropion are sympathomimetic amines that are related structurally to amphetamine.
- ✓ These agents are used for their appetite-suppressant effects in the management of obesity

CNS Stimulants/ E. Amphetamine/ Pharmacokinetics:



- ✓ Amphetamine is completely absorbed from the GI tract, metabolized by the liver, and excreted in the urine.
- ✓ Administration of urinary alkalinizing agents such as sodium bicarbonate will increase the nonionized species of the drug and enhance the reabsorption of dextroamphetamine from the renal tubules into the bloodstream.
- ✓ The euphoria caused by amphetamine lasts 4 to 6 hours, or four- to eightfold longer than the effects of cocaine.

CNS Stimulants/ E. Amphetamine/ Adverse effects:



Vertigo



Confusion



Diarrhea



Hypertension



Potential for addiction



Insomnia



Nausea

CNS Stimulants/ E. Amphetamine/ Adverse effects:



- ✓ a. CNS effects: Adverse effects of amphetamine usage include insomnia, irritability, weakness, dizziness, tremor, and hyperactive reflexes.
- ✓ Benzodiazepines are often used in the management of agitation and CNS stimulation secondary to amphetamine overdose.
- ✓ Chronic amphetamine use produces a state of “amphetamine psychosis” that resembles the psychotic episodes associated with schizophrenia.
- ✓ Whereas long-term amphetamine use is associated with psychic and physical dependence, tolerance to its effects may occur within a few weeks.
- ✓ The anorectic effect of amphetamine is due to its action in the lateral hypothalamic feeding center.

CNS Stimulants/ E. Amphetamine/ Adverse effects:



b. Cardiovascular effects: In addition to its CNS effects, amphetamine causes palpitations, cardiac arrhythmias, hypertension, anginal pain, and circulatory collapse. Headache, chills, and excessive sweating may also occur.

c. GI system effects: Amphetamine acts on the GI system, causing anorexia, nausea, vomiting, abdominal cramps, and diarrhea..

Contraindications:

- Patients with hypertension,
- Cardiovascular disease,
- Hyperthyroidism, glaucoma,
- History of drug abuse
- Those taking MAO inhibitors

CNS Stimulants/ F. Methylphenidate



Methylphenidate has CNS-stimulant properties similar to those of amphetamine and may also lead to abuse, although its addictive potential is controversial.

Methylphenidate is presently one of the most prescribed medications in children.

It is estimated that **4 to 6 million** children in the United States take methylphenidate daily for **ADHD**.

The pharmacologically active isomer, dexamethylphenidate, is also used for the treatment of ADHD.

CNS Stimulants/ F. Methylphenidate/ Mechanism of action:



Children with ADHD may produce **weak dopamine signals**, which suggests that once-interesting activities provide fewer rewards to these children.

Methylphenidate is a dopamine and norepinephrine transport inhibitor and may act by increasing both **dopamine and norepinephrine** in the synaptic space.

Methylphenidate may have **less potential for abuse** than cocaine, **because it enters the brain much more slowly than cocaine** and, thus, does not increase dopamine levels as rapidly.

CNS Stimulants/ F. Methylphenidate/ Therapeutic uses:



Methylphenidate has been used for several decades in the treatment of **ADHD**.

It is also effective in the treatment of **narcolepsy**.

Unlike methylphenidate, dexamethylphenidate is not indicated in the treatment of narcolepsy.

CNS Stimulants/ F. Methylphenidate/ Adverse effects:



GI adverse effects are the most common and include abdominal pain and nausea.

Other reactions include anorexia, insomnia, nervousness, and fever.

In seizure patients, methylphenidate may increase seizure frequency, especially if the patient is taking antidepressants.

It is contraindicated in patients with glaucoma.

Methylphenidate can inhibit the metabolism of warfarin, phenytoin, phenobarbital, primidone, and the tricyclic antidepressants.

HALLUCINOGENS



A few drugs have, as their primary action, the ability to induce altered perceptual states reminiscent of dreams.

Many of these altered states are accompanied by visions of bright, colorful changes in the environment and by a plasticity of constantly changing shapes and color.

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

These compounds are known as hallucinogens, and **lysergic acid diethylamide (LSD)** and **tetrahydrocannabinol** (from marijuana) are examples of agents in this class.