Psychomotor Stimulants

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The psychomotor stimulants are a diverse group of drugs which share certain pronounced effects upon behavior. The term “psychomotor stimulant” does not accurately describe the behavioral actions of these drugs. The most extensively studied group of psychomotor stimulants are the amphetamines and related drugs.
Ephedra sinica – Ma Huang
Amphetamines

- **Amphetamine**

- **Methamphetamine**

Chemical structures of amphetamines.
## Psychomotor Stimulants

<table>
<thead>
<tr>
<th>Stimulant</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>d-Amphetamine (Obetrol®)</td>
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<tr>
<td>Cocaine</td>
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<tr>
<td>Fenfluramine (Pondimin®)</td>
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<tr>
<td>Methylphenidate (Ritalin®)</td>
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<td>Caffeine</td>
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<td>Diethylpropion (Tenuate ®)</td>
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<tr>
<td>Methamphetamine (Desoxyn®)</td>
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<tr>
<td>Phenmetrazine (Preludin®)</td>
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B. F. Skinner
1904 - 1990
Behavioral effects of the amphetamines and related psychomotor stimulants

Rate-dependent effects. These drugs might not change the overall rate of occurrence of behavior. However, their effects upon specific behaviors are dependent upon the rates at which each behavior occurs. They tend to:

A. increase the frequency of occurrence of behavior which tends to occur normally at low rates.

B. decrease the frequency of occurrence of behavior which tends to occur normally at high rates.

C. decrease the frequency of occurrence of behavior which is punished.
Other Behavioral Effects

Psychomotor stimulants as discriminative stimuli. These drugs develop the characteristics of conditioned, discriminative stimuli.

These drugs have reinforcing properties. Because these drugs are powerful positive reinforcers, behavior which results in the self-administration of these drugs will rapidly develop into a predominant form of behavior.

Effects of amphetamines motor and intellectual performance.
Other Behavioral Effects

Cause a slight but significant improvement in the physical endurance and capacity of trained athletes. Consistent effects cannot be demonstrated upon unskilled individuals.

Increase the motor coordination and control, as well as the vigilance of fatigued individuals. Similar improvements of performance cannot be demonstrated in rested individuals.

Improve the performance of fatigued or bored individuals upon simple and complex verbal and arithmetic tasks.
Other Behavioral Effects

Do not improve learning or memory when administered to normal individuals.

Have powerful effects upon subjective states, the dominant ones being an increase in reports of alertness and well-being. In an aversive environment, individuals who take amphetamines may report feeling irritable and aggressive.
Amphetamines and Related Psychomotor Stimulants

The action of these drugs in the central nervous system are complicated.

Reserpine does not antagonize the behavioral effects of the amphetamines.

Inhibitors of norepinephrine synthesis cause complex shifts in dose-response curves for the behavioral effects of these drugs.
Amphetamines and Related Psychomotor Stimulants

Withdrawal of the drug does not result in a clear abstinence syndrome.

The withdrawn abuser becomes depressed, sleeps for long periods of time and is apathetic.

There are disturbances of REM sleep which last for as long as two months after withdrawal of amphetamines.
Amphetamines and Related Psychomotor Stimulants

Direct toxic effects are sudden death, cerebral hemorrhage from increased blood pressure, cardiac arrhythmias, etc. Abusers also have an extremely high incidence of abscesses, thrombophlebitis, tetanus, bacterial endocarditis and infectious hepatitis. Today in certain metropolitan areas AIDS is associated most commonly with intravenous drug use.
Amphetamines and Related Psychomotor Stimulants

Anorexic effects

The amphetamines decrease appetite. Tolerance develops very rapidly to the anorexic properties of these drugs.
Amphetamines and Related Psychomotor Stimulants

**Acute Intoxication:** dizziness, tremor, irritability, confusion, hallucinations, ideas of reference, paranoia, chest pain, palpitations, hypertension, sweating, and cardiac arrhythmias.

Death is preceded by hyperpyrexia, convulsions, and shock.

Treatment is the administration of chlorpromazine.
Tolerance develops to both the physiological and behavioral effects of most psychomotor stimulants.

Tolerance develops only to those behavioral effects which are highly disruptive to the patient's ability to function in his environment.
Amphetamines and Related Psychomotor Stimulants

Therapeutic Uses

Treatment of obesity
Narcolepsy
Fatigue States
ADHD
Mental Retardation
Amphetamines and Related Psychomotor Stimulants

Drug Interactions

MAO Inhibitors
α-Methyl Dopa
Barbiturates
Reserpine
Tricyclic Antidepressants
Narcotic Analgesics
Noradrenergic Synapse

MAO Inhibition

Tyrosine $\leftrightarrow$ DOPA $\leftrightarrow$ DA $\rightarrow$ NE

NE $\rightarrow$ NMN

COMT
After Treatment with $\alpha$-Methyl-DOPA

$\alpha$-me-DOPA $\rightarrow$ $\alpha$-me-DA $\rightarrow$ $\alpha$-me-NE
Amphetamines and Related Psychomotor Stimulants

Drug Interactions

Barbiturates
Reserpine
Tricyclic Antidepressants
Narcotic Analgesics
Chlorpromazine
Fenfluramine (Pondamin®)
Dexfenfluramine (Redux®)

- Serotonin reuptake inhibitor
- CNS depressant
- Produces sedation
- Reduces appetite
- Little or no tolerance to anorexic actions
- Withdrawn from market because of association with valvular regurgitation and pulmonary hypertension
“Woe to you, my Princess, when I come, I will kiss you quite, red and feed you till you are plump. And if you are forward you shall see who is the stronger, a gentle little girl who doesn't eat enough or a big wild man who has cocaine in his body....”

Sigmund Freud, in a letter to his fiancée, Martha Bernays (June, 1884)
Structural Relationship between Cocaine and Atropine
27. Erythroxylum coca
Erythroxylum coca
Cocaine

Local anesthetic actions. The first and only current medical use of cocaine is related to its local anesthetic actions. It blocks initiation or conduction of the nerve impulse after local application. It was first used in ophthalmology but was found to cause a sloughing of the corneal epithelium.

Inhibition of uptake. Most of the pharmacological actions of cocaine can be attributed to an inhibition of monoaminergic neurotransmitter uptake. Cocaine will potentiate the actions of directly acting sympathomimetic amines and will cause a release of neurotransmitter substances. Many of the CNS and cardiovascular actions can be attributed to this property of the drug.
Cocaine

Central nervous system. Cocaine is a potent psychomotor stimulant. Its actions are quite similar to those of the amphetamines. High doses can cause tremors and clonic-tonic contractions. Vomiting may occur. Central stimulation is soon followed by depression. Death can result from respiratory depression.

Cardiovascular system. Small doses of cocaine might slow heart rate due to an effect on central vagal motor centers. But even moderate doses will cause a tachycardia and a hypertension will eventually result. A large intravenous dose of cocaine can cause death from arrhythmias, coronary vasoconstriction leading to myocardial infarction or cardiac failure due to direct depression of heart muscle.
Cocaine

**Body temperature.** Like other psychomotor stimulants cocaine can increase markedly body temperature. This might be a result of actions directly upon central temperature-regulating system in the CNS in addition to increased motor activity and vasoconstriction.

**Cocaine can kill** anyone, even young, apparently healthy individuals, who elect to take this dangerous drug. Treatment includes drugs such as the benzodiazepines to block convulsions and drugs which have the ability to block both α- and β-adrenergic receptors.
Amphetamine-like Psychomotor Stimulants

Methylphenidate

Phenmetrazine
Methylxanthines

- Caffeine
- Theophylline
- Theobromine