



Amphetamines

Psychology 472
Pharmacology of Psychoactive Drugs

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Background

- Used for numerous disorders
 - Schizophrenia
 - Addictions (morphine and nicotine)
 - Head Injury
 - Hypotension
 - Severe hiccups
 - Others

Terms

<h3>Slang</h3> <ul style="list-style-type: none"> • Bennies, Speed, Pep pills, Uppers • Black beauties • Bumble bees • Co-pilots • Cross tops • Dexies, Midnight runners • Footballs • Hearts • Crank • Hot Ice • Ice • Tweak, • Glass • L.A. glass • Meth 	<h3>Medical</h3> <ul style="list-style-type: none"> • Benzedrine, <ul style="list-style-type: none"> • Amphetamine Sulphate • Dexedrine <ul style="list-style-type: none"> • Dextroamphetamine • Amphet. Sul. + Dex. Amp. = Aderall • Methedrine <ul style="list-style-type: none"> • Methamphetamine "Meth" • Most potent
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Amphetamines

- Synthesized in 1887.
 - Isolated from ma-huang (cone-bearing shrub found in China)
 - In 1924, its structure was determined
 - Effects similar to epinephrine.
 - Ephedrine replaced Epinephrine for asthma

Problem

- Concerns that supplies would run out.
- Search made for a synthetic made in 1887, Tested in 1910, (Barger and Dale) wrote about its actions.
- Drug (Amphetamine) had been forgotten until 1927
 - Alles suggested amphetamine would be a cheap alternative to ephedrine.

Medical Possibilities

- Not known until 1927
- Found to stimulate nervous system, increase blood pressure, and enlarge the bronchioles.
 - 1932: Sold as benzedrine inhaler for bronchial congestion and asthma.
 - 1935: Treatment for narcolepsy
 - 1937: Paradoxical effect in "calming" hyperactive children noted.
 - Also prescribed for weight reduction.

Ephedrine

- Increases NE in the synapse
- Increases BP
- Weight Loss
- Many side effects
- Pulled from OTC substances

Amphetamines

- During WWII was used to overcome fatigue.
- After the war, used (inappropriately) for weight control and depression.
- Epidemic of abuse (especially in Japan)
 - "Speed freak" (users who took IV for days).
- Fatal doses anywhere from 30–1700 mg.

Danger Decreases

- Users saw dangers of compulsive use ("speed kills").
- Government exerted pressure on drug companies to decrease their production.
- Medical use was inhibited and unethical physicians prosecuted.
- Medical alternatives to depression were discovered.

Medical Use Today

- Narcolepsy (better drugs today)
- Attentional Disorders (ADD / ADHD)
 - Mixed Results
- Obesity (ineffective long-term)

Pharmacokinetics

- Oral
- Inhalation
- Injection

Absorption

- Easily crosses mucosal barriers
- Easily crosses the BBB
- Easily crosses the placental barrier
- Goes to multiple systems

Pharmacological Effects

- Metabolized in the liver
 - Excreted through the urine
 - Detectable for up to 48 hours
 - 40% of methamphetamine is excreted unchanged.

Pharmacodynamics

- Work similar to Cocaine
- Causes release of dopamine and norepinephrine from presynaptic nerve terminals.
- Blocks reuptake of Dopamine and NE
- Impacts MFB.

Behavioral Effects

- Hyperactivity
- Task performance may improve
- Dexterity deteriorates
- Increased flight/fight/fright response that is dose-related

Psychological Effects

- Euphoria
- Excitement
- Mood elevation
- Increased motor/speech activity
- Feeling of power

Pharmacological Effects

- At moderate doses
 - Respiratory stimulation
 - Slight tremors
 - Restlessness
 - Greater increase in motor activity
 - Insomnia
 - Agitation

Pharmacological Effects

- At high doses
 - Repetitive purposeless acts
 - Sudden outbursts of aggression/violence
 - Paranoid delusions
 - Severe anorexia
 - Overall psychosis and abnormal mental conditions
 - Amphetamine Psychosis: paranoid ideation
 - Primarily with meth users

Health Effects

- Infections from neglected health care
- Poor eating habits
- Use of unsterile equipment
- Great deterioration in social, personal, occupational affairs

Psychological Problems

- Harmful effects follow from exaggerated doses and responses:
 - Insomnia, restlessness, agitation, stereotyped behaviors, purposeless/repetitive acts, violence, paranoia, delusions, anorexia, psychosis, progressive deterioration in physical and mental well-being.
 - Amphetamine psychosis with paranoid ideation (persistent?).

Pharmacological Effects

- Long Term evidence shows...
 - Poor academic performance
 - Behavioral problems
 - Cognitive slowing
 - General maladjustment
- The effects on this list are permanent.

Methamphetamine

- d-N-methylamphetamine
- Is a hydrochloride salt
- Absorbs water from the air very fast and can be diluted and injected.
- Can be smoked as is, or grown into crystals and smoked
 - Considered to be freebase but the term is inaccurate
Freebase is actually an oil form.
Not commonly found on the street
- Crystalline form is easier to smoke.
- Is very pure.

Slang Terms

- Tweek or Tweak
- Glass
- Uppers
- Yaba
- Crank
- Ice

Pharmacological Effects

- Physiological Effects
 - Increased BP
 - Increased HR
 - Increased alertness
 - Psychomotor stimulant
 - Loss of appetite

Tolerance

- Develops from down regulation
- Develops rapidly
- Necessitates the need for markedly higher doses
- Use becomes compulsive
 - Affects MFB
 - Causes prolonged binging
 - Physical dependence follows a classical conditioning model
 - Psychological dependence follows an operant conditioning model
 - Negative Reinforcement Model

Withdrawal

- Withdrawal occurs but not as dramatic as with narcotics and barbiturates
 - Symptoms opposite of drugs effects
- May require treatment with:
 - Antidepressants
 - Antipsychotics
 - Mood stabilizers

ICE

- Crystallized form of methamphetamine
- Extremely potent
- High is intense and long lasting
- Chronic use can result in serious psychiatric, cardiovascular, metabolic and neuromuscular changes

ICE: Pharmacokinetics

- Smoking causes immediate absorption
- Biological half-life around 11 hours
- 60% metabolized in the liver after distribution to the brain
- 40% excreted unchanged

Pharmacodynamics

- Effects similar to other amphetamines and cocaine at receptor sites
- Is a potent psychomotor stimulants
 - Same effects on MFB as methamphetamine
- Repeated high doses associated with paranoid psychosis

Acute Neurotoxicity of Methamphetamine

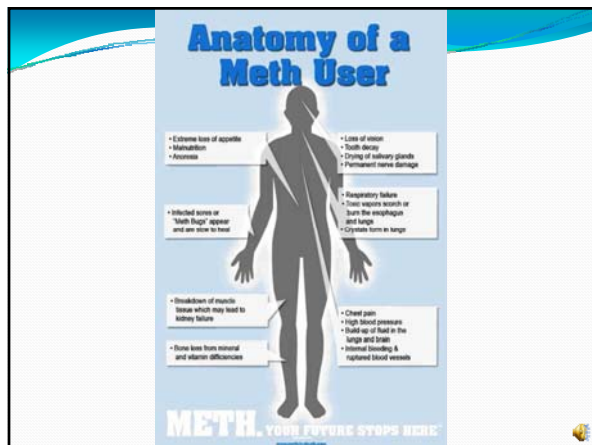
- Strokes and psychosis
- Dopamine reductions cause problems with:
 - Sleep
 - Sexual functioning
 - Depression
 - Movement disorders
 - Frontal lobe "executive functioning"

Problems Increase as Use Continues

- Violence, psychosis, and personality changes
 - Can last months or years after stopping use
- Problems with frontal lobe and executive functioning
 - Major reductions (6-8%) frontal cortical and basal ganglia neuronal.
 - Cannot process information as well
 - Reductions remain even after abstinence
- Dopamine receptors reductions
 - Occurs in multiple sites
 - prefrontal cortex, nucleus accumbens and caudate nuclei;
 - Longer the use, greater the decrease

Ice Problems

- Same as other forms of Methamphetamine
- Also causes changes in brain chemistry
 - Reductions of neurons in frontal lobe and basal ganglia
 - Also found after remaining abstinent for years
- Can cause permanent symptoms
 - Sleep functions
 - Sexual functions
 - Mood (permanent depression)
 - Schizophrenia
 - Movement disorders



Results of Vasoconstriction



Methylphenidate (Ritalin)

- Lots of hype around this drug
- Is a nonamphetamine behavioral stimulant
 - Acts similarly to amphetamines
- Regular release half life = 2 - 4 hours
- Time release half-life = 3 - 8 hours
- Medical Uses
 - Attention Deficit Disorder
 - Attention Deficit Hyperactivity Disorder
 - Narcolepsy

Actions

- Increase vascular flow in the brain
- Increase Dopamine levels in frontal cortex
- Enhance the inhibitory systems of the brain
 - Increase Serotonin and Norepinephrine levels.
- Result
 - Shuts down stimulation in frontal lobe
 - Allows you to concentrate better
- Drug does work
 - Problem: Often overprescribed
 - Should be recommended when other techniques do not work
 - Should not be given lightly or because some teacher recommends it.

Side Effects

- Reduced appetite
- Drug Rebound:
 - Similar to withdrawal of other stimulants
 - Apathy
 - Depression
 - Irritability
- Difficulty sleeping
- Others

Pharmacokinetics

- Medically
 - Taken orally or used transdermal
 - Not much euphoria
- Illicitly
 - Often ground up and injected
 - Can be taken IV with cocaine:
 - Gives an extra kick
 - Used within youth groups

Medical Effects

- Shuts down the frontal lobe
 - Gives greater focus
 - Why used for ADD and ADHD
 - Note: These are different disorders
- Stimulates other brain areas
 - LC
 - NA
 - Others

Injection Effects

- Like other stimulants
 - Increased Alertness
 - Excitation
 - Euphoria
 - Increased HR & BP
 - Insomnia
 - Loss of appetite

Pharmacodynamics

- Neuronal effects are more similar to cocaine than amphetamines
 - Blocks reuptake of Dopamine and NE
- Causes release of dopamine
 - Similar to amphetamines but at lower levels

Conclusions

- Lots of different Amphetamines and Amphetamine-like drugs
- Generally causes stimulation
- Not used as often as in the past
- Effects are more pronounced when used in combination
- Hard to kick due to brain biochemistry changes and deterioration.