

Cocaine

Psychology 472

Pharmacology of Psychoactive
Drugs


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Cocaine – Background Info

- From the leaves of Erythroxylan coca
- Used for centuries (maybe 5,000 years) in South America: Peru, Bolivia, Ecuador
- Used for
 - Religious
 - Social
 - Euphoriant
 - Medicinal

History

- Used to reduce hunger and increase energy.
- Under Inca rulers it was sacred; restricted to priests and aristocrats.
- Spanish conquerors first tried to ban it, but then realized it would improve work capacity of the Indians .
- 1749: Samples sent to Europe. Linnaeus gave the plant its own family and Lamarck named most important species in 1786 (Erythroxylon coca)



More History

- Isolated by Albert Niemann (1855) Named *cocaine*, published in 1860.
- Robert Louis Stevenson reportedly wrote “The strange case of Dr. Jekyll and Mr. Hyde” with cocaine use in mind.
- Sherlock Holmes’ keen powers of observation were due to his 7 percent solution of cocaine.
- Paranoia of Holmes being pursued by criminal Professor Moriati resembles cocaine paranoia.



Medicine

- Proven to be one of the 1st local anesthetics for surgery
- Sigmund Freud obtained and studied cocaine’s psychological effects
 - Advocated its use and prescribed cocaine for depression and chronic fatigue.
 - Later he realized its adverse side effects

Medicine Cont.

- Cocaine incorporated into numerous medicines and beverages
- Physicians thought it might be antidote to alcohol and opiate addiction
 - Produced effects opposite to CNS depression

Other Products

- Used in:
 - Lozenges and pastilles,
 - Elixirs
 - Pills.



More History

- Angelo Mariani patented a wine containing coca and became wealthy.



- Cocaine praised by Edison, Czar of Russia, Prince of Wales, Jules Verne, Emile Zola, Henrik Ibsen, the Pope, others

Coca-Cola

- Originally had 60 mg / 8 oz.
- John Styth Pemberton made his version of Mariani wine drink in 1881.
 - He was moderately successful,
- 1885, Atlanta bans the sale of alcohol.
- Pemberton took out the alcohol
 - Sold his new drink under the name Coca-Cola.
 - Profits were good, but not great.
- Disillusioned he sold the entire operation to Asa Griggs Candler for \$2,300.
- Rest is history

Included in Harrison Narcotic Act (1914)

- Banned its use
- Drove it underground until around the 1960s.
- By the 1920's,
 - Limited to cultural "avant-garde."
 - Was expensive and glamorous.
- Recreational use increased dramatically in the late 1960's
- Inexpensive "crack" cocaine use spread in the late 1970's
- Later use decreased and replaced with amphetamines

Cocaine in Medicine

- Was the 1st local anesthetic (topical, regional and spinal).
- Toxicity was marked with regional blocks.
- Still occasionally used, primarily in nasal surgery.

Statistics

- Use peaked in 1980's
- Decreased in 1990's
- Currently increasing
 - 2 million users
 - 22-25 million used at least once
 - Males are more likely to use than females
 - 0.7 million new male users each year
 - 0.5 million new females each year.
 - > 400,000 infants born addicted to cocaine each year.

Forms of Cocaine

- E. coca contains about 0.5-1.0% cocaine
- Leaves are soaked in kerosene and gasoline and mashed
- Cocaine extracted in the form of coca paste
- Paste approx 50-60% purity



Cocaine Hydrochloride

- Paste is treated with numerous chemicals to oxidize and purify the paste to form the water soluble cocaine hydrochloride powder.
- Can be close to 100% pure
- Can be injected, inhaled as powder, or ingested orally
- Cannot be smoked

Freebase Form

- Crack Cocaine
- Similar to the unpurified insoluble coca paste.
- Made by reversing the oxidation process
- Cannot be inhaled (as powder) or injected because it is not water soluble
- Forms a stable vapor when heated and inhaled (smoked)



Pharmacokinetics

- Absorbed from all sites of application
 - Mucous membranes, lungs, stomach
- Potent Vasoconstrictor
 - crosses mucosal membrane poorly
- Peak plasma levels in 30-60 minutes
- Inhalation causes slow absorption
 - Prolongs effects

Pharmacokinetics

- IV injection
 - Bypasses all barriers to absorption
 - Total dosage goes into blood stream and eventually the brain
- Smoking Cocaine Base
 - Absorption is rapid and complete at the lungs
 - Effects onset in seconds, peaks in 5 minutes and lasts about 30 minutes

Pharmacokinetics

- Distribution
 - Penetrates brain rapidly
 - Brain concentrations far exceed plasma levels
 - Freely crosses the placental barrier

Pharmacokinetics

- Metabolism & Excretion
 - Half-life 30-90 min.
 - Metabolized by enzymes in both plasma and liver to benzoylecognine
 - Slowly removed from brain
 - Positive urine tests for 12 hours

Use With Alcohol

- In the presence of ethanol a different metabolite is produced – cocaethylene
- Cocaethylene has the same physiological effect on the brain as cocaine but more toxic

Alcohol + Cocaine = Cocaethylene

- Active metabolite of cocaine
- Produced in liver when cocaine and alcohol used together.
- Half-life is about 2.5 hours
- Is a indirect dopamine agonist like cocaine
 1. Alcohol inhibits cocaine metabolism
 2. Resulting in production of cocaethylene,
 3. Further inhibits hepatic metabolism
 4. Further increases cocaethylene levels
- Is longer lasting and more toxic than cocaine.

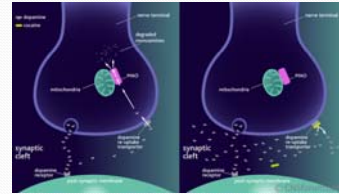
Cocaethylene

- Euphoric effects last longer
 - Increases risk of dual dependency
 - Increases severity of withdrawal
 - Probably the reason 85-90% of cocaine users are alcohol dependent
- **Alcohol/Cocaine is the largest two drug combination resulting in death**

Pharmacodynamics

- Attaches to and blocks presynaptic dopamine reuptake transport proteins
- Result - Dopamine stays in the synapse longer
- Potentiates the synaptic actions of dopamine, norepinephrine and serotonin

Blocks Dopamine Reuptake Transport



Reinforcing Action

- Increases the sensitivity of D₃ dopamine receptors in MFB
 - Increased density of D₃ receptors
 - More Dopamine in synaptic cleft
 - Get Down Regulation
- Responsible for craving

Psychological Effects

- Immediate euphoria
- Giddiness
- Enhanced self-consciousness
- Forceful boastfulness
- These last approx 30 min.

More Effects

- Increased alertness
- Motor hyperactivity
- Tachycardia
- Pupils dilate
- Increased glucose availability
- Shifts of blood flow from internal organs to muscles
- Numerous cardiovascular complications can occur with prolonged or single use

Effects in the CNS

- Depletion of Oxygen
- Cerebral Atrophy
- Seizures
- Others

Effects of Short Term Use

- Moderate euphoria lasts for 60-90 min
- A state of anxiety lasts for hours
- Thoughts race, rapid speech
- Sleep delayed
- Appetite suppressed
- A depressive state follows

Physiological Responses

- Responses are exaggerated
 - Anxiety, sleep deprivation, hypervigilance, suspicious/paranoia, fearful
 - Develop an altered perception of reality
 - Can become aggressive or homicidal in response to imagined persecution
 - Toxic paranoid psychosis

Cocaine: Urine Testing

- Urine can test positive for cocaine for up to 12 hours.
- Benzoyllecognine can be detected for up to 48 hours; even to a week or more in chronic users.
- Therefore, urine presence of metabolite is not an indicator of recent use; nor does it "prove" that one was under the influence of cocaine at the time of commission of a crime.
- Cocaethylene is also tested for in urine.

Tolerance and Sensitization

- Tolerance occurs due to downregulation
- Get sensitization of the anesthetic and convulsant effects
 - Explains deaths after low doses

Medical Complications

- Many cardiovascular effects
 - Heart attacks
 - Irregular heart rhythm
- Respiratory failure
- Seizures

Cocaine and Pregnancy

- Many indirect effects from the vasoconstriction of mothers blood vessels
 - Decreased blood flow and oxygen to Uterus
 - Associated with
 - Placental detachment
 - Preterm labor
 - Stillbirth
 - Low birth weight
 - Others

Kids Effects from Cocaine

- Direct effects from cocaine in the fetus
 - Neonatal neurological syndrome
 - Abnormal sleep patterns, tremors, seizures
 - Increased incidence of SIDS
- Some problems
 - Difficulty developing attachments
 - Difficulty dealing with multiple stimuli
 - Often behave aggressively
 - High incidence of ADHD

Cocaine Today

- Use will be determined by price and availability.
 - Today methamphetamine is cheaper and more available.
 - As we stop methamphetamine, cocaine may return.

Treatment

- No consensus on a generally accepted successful pharmacological treatment.
- Three problems that complicate therapy
 1. Intensity of the drug effect and reinforcing action
 2. Pronounced tendency toward relapse
 3. Most addicts have a coexisting disorder

Treatment

- Psychosocial treatment offers the most promise
 - Cognitive Behavioral Therapy
 - Individual/Group counseling
 - Behavior Reinforcement strategies
- Self Help Groups
 - Cocaine Anonymous
- Some medicines can help with craving

Summary

- Very powerful drug
- Use is increasing again
- Can cause death the first time using it.