



Nicotine

Psychology 472

Pharmacology of Psychoactive
Drugs

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NICOTINE

- Primary active ingredient in tobacco
- One of the three most widely used psychoactive drugs
 - Caffeine
 - Alcohol
- Few or no therapeutic applications
- Importance
 - Because of widespread use and toxicity
 - Effects with other drugs

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History

- Indigenous to the Americas
- 1492 Columbus arrives in West Indies
 - Natives offer tobacco as gift
- 1556 First plants are taken to Europe
- 1571 Was believed to have curing properties for 36 different ailments
- 1575-1600 Becomes “duty” of every man of fashion
 - Worth its weight in silver

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More History

- 1881 Cigarette rolling machine invented
- 1889 2.4 billion cigarettes produced annually in U.S.
- 1904 3 billion cigarettes sold in U.S.
- 1912 13 billion cigarettes sold in U.S.
- WWII through mid-1960’s smoking considered cool
- 1970. Smoking and Health – Report from the Surgeon General
- 1990’s Laws regulating smoking
 - Smoking begins to be shunned as unhealthy and unwise
- Today in US Pariahs of the Earth

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Currently

- Responsible for the deaths of 1,100 Americans every day
- Each day
 - 6000 American teenagers try their first cigarette
 - 3000 children become regular smokers
 - 1000 of these will die from smoking related disease
- 9 of 10 smokers become addicted before age 21
 - Girls become addicted faster than boys
 - Women have a harder time “Kicking” than men

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Today

- ½ of all people who have smoked have quit
- % American adults who smoke has fallen from 50 in 1965 to 25 in 1998
- Smoking identified as the major preventable cause death and disability
 - Known for 30 years
- Rates among males are decreasing
- Rates among females are increasing
- US rates decreasing, other countries increasing

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Background Information

- o Nicotine is only one of about 4,000 compounds released by burning tobacco
- o Adverse cardiovascular, pulmonary, and carcinogenic effects are from the other compounds

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Nicotine

- Exerts powerful effects on
 - Brain
 - Spinal cord
 - Peripheral nervous system
 - Heart
 - Various other body structures

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Effects

- Stimulation of the vomit center in the brain stem and sensory receptors in the stomach
 - Nausea in early stages of smoking
 - Tolerance develops rapidly
- Reduces weight gain
 - probably by suppressing appetite
- Stimulates release of ADH (AntiDiuretic Hormone) causing fluid retention

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More Effects

- Reduces activity of afferent nerve fibers from muscles
 - Reduction in muscle tone
 - May be partially involved with relaxation effect
- Higher doses
 - Can induce nervousness and tremors
 - Seizures in toxic overdose
- Smoking associated with increased occurrence of panic attacks and panic disorders

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CNS Effects

- Increases
 - Psychomotor activity
 - Cognitive functioning
 - Sensimotor performance
 - Attention
 - Memory consolidation

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Effect

- Nicotine can improve performance on vigilance and rapid information processing
 - Effects are greater for working memory rather than long term memory
- Nicotine exerts an antidepressant effect
 - High smoking rates among depressed individuals may be an attempt at self medication

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Effects

- Nicotine exerts a potent reinforcing action
 - Indirect activation of midbrain dopamine neurons
 - Greatest in early phases
 - Diminishes over time - Tolerance
 - Then levels off
 - Smoking is continued to avoid withdrawal symptoms -Negative Reinforcement

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Reproductive Effects

- Smoking reduces oxygen delivery to the fetus resulting in varying degree of fetal hypoxia
 - Fetus does not receive as much oxygen
- Smoking may result in irreversible intellectual and physical deficiencies
 - Increased prevalence of ADHD
 - Lower IQ scores

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Reproductive Effects

- Smoking during pregnancy increases rates of
 - Spontaneous abortion
 - Stillbirth
 - Early postpartum death
 - Preterm deliveries
- Intrauterine growth retardation is increased 40%
- 2000 infant deaths per year attributed to smoking

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Tolerance

- Minimal biological tolerance after initial changes
 - Increased use in early stages
 - Usually levels off as smoking is continued
 - Smokers adjust nicotine intake to maintain 20 to 40 Nanograms per milliliter of plasma
- Does induce physiological and psychological dependence
 - Habituation
 - Rebound effect
- Exceptional Classical and Operant Condition effects

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Withdrawal Symptoms

- Intense nicotine craving
- Irritability
- Anxiety
- Anger
- Difficulty concentrating
- Restlessness
- Impatience
- Increased appetite
- Weight gain
- Insomnia

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Pharmacokinetics

- Easily absorbed in the body
 - Lungs
 - Buccal and nasal mucosa
 - Skin
 - Gastrointestinal tract
- Nicotine is suspended in the minute particles (tars) in smoke
- Orally administered blood levels of nicotine are comparable to smoking

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Pharmacokinetics

- Only about 20% of the nicotine in a cigarette is inhaled and absorbed into the bloodstream
- Is rapidly metabolized by the hepatic enzyme CYP2A6
 - 80 to 90% before excretion to the kidneys
 - Primary metabolite is Cotinine
 - Also binds on Ach receptors
 - Half-life = about 2 hours
- Inhalation allows controllability of dose
 - Frequency of breaths
 - Depth of breaths
 - Time in lungs
 - Number of cigarettes

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Pharmacodynamics

- Nicotine is thoroughly distributed in the body
 - No barriers to nicotine distribution
 - Rapid brain penetration
 - Crosses placental barrier
 - Appears in all bodily fluids

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Receptors

- Activates Nicotinic Acetylcholine (ACh) receptors
- Receptors are located throughout the body
 - Skeletal muscle
 - Sympathetic and parasympathetic neurons
 - CNS
- Ach binding has an immediate response

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Mechanism of Action

- Nicotine replaces ACh at Nicotinic receptor
 - Has a greater affinity at the binding site
 - Is an agonist
 - Opens ion channel directly
 - Depolarization occurs

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Result

- Impacts on PNS
 - Increases blood pressure and heart rate
 - Causes the release of epinephrine from the adrenal glands
 - Increases the tone, secretions, and activity of the gastrointestinal tract

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CNS

- Activates release of NT
 - Dopamine
 - Acetylcholine
 - Glutamine
- Dopamine levels are increased in the MFB
 - Ventral tegmentum
 - Nucleus accumbens
 - Forebrain

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Result

- Behavioral reinforcement,
- Stimulant effects
- Antidepressant effects

- Addictive properties of nicotine

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Other CNS Effects

- Increases in Acetylcholine
 - Helps with cognitive potentiation and memory facilitation
- Increases in glutamnergic NT
 - Improvements in memory functioning

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Smoking Diseases

- Accelerates the depositing of fat in the arteries
 - Increased risk of heart attack and stroke
- Weakens the immune system
- Irritates the lining in the lungs impairing respiration
 - Smokers cough
 - Emphysema
- Other effects

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Smoking Diseases

- Lung cancer
 - 90-95% of male deaths
 - 70-75% of female deaths
- Cancer of the mouth and throat
 - Chewing tobacco
- Effects and risks are multiplied when person is an alcoholic

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Cardiovascular disease

- Carbon monoxide decreases amount of oxygen delivered to the heart while nicotine increases the workload
- Carbon monoxide and nicotine increase narrowing (atherosclerosis) and clotting (thrombosis) in the coronary arteries
- Increased risk of coronary heart disease
- Usually what kills you

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Second Hand Smoke

- About 4000 Americans per year die from lung cancer caused by second-hand smoke
- 37,000 deaths per year from heart disease caused by second hand smoke

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Effects with Other Drugs

- Causes synergistic effects
 - Multiple systems are activated
- Have major impacts when people are coming off sedative hypnotic drugs
 - Seizures, agitation, hair trigger personality effects

Therapy

- Nicotine replacement therapy doubles successful quit rates
 - Skin patches
 - Gum
 - Nicotine nasal spray

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Conclusions

- Tobacco is bad stuff
- Lots of problems
- Kicking is extremely difficult
 - Withdrawal takes two years
 - Nicotine removed about a week
 - Cotinine $\frac{1}{2}$ life = 6 months
 - Other compounds