1 Drugs Have Been Widely Used, and Abused, for a Long Time

2 Drug Abuse and Addiction
   - Drug abuse is often defined as harmful drug use
   - 6% of Americans, roughly 15 million people abuse drugs on a regular basis
   - Continued drug abuse can eventually alter the structure of the brain, producing a brain
disorder called drug addiction or drug dependence
   - Drug addiction is defined as having lost much control over drug taking, even in the
face of adverse physical, personal or social consequences
   - At least 60 million Americans are addicted to alcohol, nicotine, or both; another 5-6
million are addicted to illegal drugs; prescription drugs?

3 Why Do People Abuse Drugs?
   - Drugs produce feelings of pleasure, or they remove feelings of stress or emotional pain
   - Almost all abused drugs produce pleasure by activating a specific network of brain
neurons called the reward system
   - This circuit is normally activated when we fulfill survival functions - eating when
hungry, drinking when thirsty, etc - the brain rewards us with pleasurable feelings that
  teach us to repeat the task
   - Because drugs inappropriately turn on this reward circuit, people may want to repeat
  the drug use

4 Rats will also self-administer addictive drugs directly into their brains
   - However, this is true only if the drugs go into a specific area of the reward system
   - If the injection needle is moved less than a millimeter away from this crucial area, the rat won't press the lever for more
drug.

5 Drug Abuse and Addiction
   - The structures involved in the human brain reward system vary depending on the stimulus, but are
likely to include:
   - Ventral tegmental area (VTA) – contains dopamine neurons that project through the
   - Medial forebrain bundle (MFB) to the
   - Nucleus accumbens (NA)
   - Prefrontal Cortex

6 Drug Actions / Effects: Determinants
   I. Route of administration (just a few)
      A. Oral
         - Advantages - high compliance, safe, cheap
         - Disadvantages - effects are slow (min to hrs) and variable because of unpredictability of
           absorption from the stomach (alcohol) or small intestine (most drugs)
      B. Intravenous
         - Advantages - rapid action (seconds to min) and little variability; effects are strong
         - Disadvantages - effects are strong and can be dangerous (e.g. increased risk of overdose,
           impure drugs, or allergic reactions); limited sites are appropriate for IV injection, thus addicts
           frequently develop infections and scar tissue

7 Drug Actions / Effects: Determinants
   I. Route of administration (just a few)
      C. Drug inhalation
- Advantages - rapid onset (absorbed directly into bloodstream from the lungs), similar to i.v.
- Disadvantages – dose is hard to regulate, possible lung damage

Absorption Through Mucous Membranes
- Advantages – some drugs readily absorbed through mucous membranes of nose, mouth, rectum
- Disadvantages – membranes are easily damaged

8 Drug Actions / Effects: Determinants
- **Mechanisms of Drug Action**
  - Can act diffusely on neural membranes
  - Alcohol and many general anesthetics
- **Metabolism** (How quickly drug is broken down)
  - Is drug broken down into ACTIVE or INACTIVE metabolite?
  - Diazepam (Valium) metabolized into desmethyl-diazepam which is also anxiolytic
  - MOST drugs break down into INACTIVE metabolites

9 Tolerance
- **Drug Tolerance** - decreased susceptibility to a drug that develops as a result of repeated exposure to a drug; compensatory mechanisms opposite to initial drug effect
- Exposure to one drug can lead to the development of tolerance to another drug’s effects (cross tolerance)
- Tolerance does not always develop equally to all the effects of a drug
  - Tolerance may develop to some effects of a drug while sensitivity to other effects increases (sensitization)

10 Tolerance
- Multiple mechanisms can underlie drug tolerance
  - **Metabolic Tolerance** (any tolerance effect that results from a decrease in the amount of the drug reaching the target cells)
  - **Functional Tolerance** (any tolerance that results from a decrease in the ability of the drug to influence the target cells)
    - Tolerance to most psychoactive drugs is largely functional
    - May be due to several types of neural changes, including changes in the number of receptors, or the way drug interacts with those receptors
  - **Behavioral Tolerance** (learning to perform some tasks under the influence of drug)

11 Learning Can Influence the Development of Tolerance
- Addicts may develop tolerance to drug effects that are repeatedly experienced in the same environment
- Consequently, they must start taking larger doses of the drug to maintain the effects
- If they take the elevated dose in a novel environment in which they are not tolerant, they run the risk of a drug overdose

12 Learning Can Influence the Development of Tolerance
Drug Dependence and Withdrawal

- **Drug dependence** – the adaptive physiological state that results in withdrawal symptoms when drug use stops
- The physiological changes that compensate for a drug’s effects on the nervous system (the basis of tolerance) are no longer balanced if the drug is withdrawn – withdrawal symptoms are the result – these are generally opposite to the original effects of the drug

Learning Can Also Influence the Development of Withdrawal

- Withdrawal effects can be elicited by the environment associated with the drug or other drug-associated cues
  - May reflect the expression of a conditioned response to drug-predictive cues in the absence of the drug itself

Learning Can Also Influence the Development of Withdrawal

Addiction

- **Addicts** are habitual drug users who continue to use the drug despite its adverse effects on their health and relationships, and often, despite repeated attempts to stop using.
- Addiction does not always equal physical dependence (though addicts are frequently physically dependent on the drug)

Commonly Abused Drugs: Tobacco

- Approximately 70 million Americans currently use tobacco products
- Highly addictive; approximately 70% of people who try it end up addicted (10% for alcohol, 30% for cocaine)
- Kills more than 430,000 Americans/year – more than alcohol, cocaine, heroin, homicide, suicide, car accidents, fire, and AIDS combined

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Commonly Abused Drugs: Tobacco

- Nicotine is the major psychoactive ingredient, but tobacco contains thousands of other chemicals
- Nicotine acts through nicotinic acetylcholine receptors (nicotinic receptors are a subtype of acetylcholine receptors)
- Has mostly stimulant effects:
  - Stimulates adrenal glands and release of epinephrine (adrenaline) – increases blood pressure, respiration and heart rate
  - Suppresses insulin output from the pancreas (smokers often slightly hyperglycemic)
– Can cause transient boost in memory
– Indirectly causes release of dopamine in the brain’s reward system (particularly the nucleus accumbens)

• Studies in rats suggest that after repeated exposure to nicotine, if nicotine use is stopped, the cells in the nucleus accumbens that are responsible for reinforcement become less responsive.

23 Treatment of Tobacco Addiction
• Nicotine gum, dermal patch, nasal spray and inhaler
  – used to relieve withdrawal symptoms
  – all appear to be equally effective
• Antidepressants (e.g. Zyban)
• Behavioral treatments
  – Can provide coping skills useful in avoiding relapse

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25 Commonly Abused Drugs: Alcohol

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1

2 • Annual cost of alcohol abuse and addiction estimated at $185 billion

2 • Estimated that alcohol is involved in about 3% of all deaths in US (birth defects, ill health, accidents, and violence)

27 Commonly Abused Drugs: Alcohol
• Ethanol (the active ingredient) reduces anxiety, tension and inhibitions
  – At low doses it may act as a stimulant
  – At higher doses it acts as a depressant
  – In both cases, it significantly alters mood and behavior
• Clouds thinking
• Impairs motor skills, and delays reaction times
• It can also cause heat loss (hypothermia) through vasodilation and dehydration (alcohol is a diuretic)
• Can disrupt sleep patterns

28 Continuum of Alcohol Effects

29 Commonly Abused Drugs: Alcohol

30 Commonly Abused Drugs: Alcohol
31 Commonly Abused Drugs: Alcohol
- At higher doses, alcohol also decreases the function of NMDA (glutamate) receptors – can cloud thinking and eventually lead to coma

32 Chronic Alcohol Abuse Can Produce Brain Damage
- Korsakoff's Syndrome
- Fetal Alcohol Syndrome (young brains particularly vulnerable during period of synaptogenesis – the last trimester)

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34 Commonly Abused Drugs: Alcohol
- Can produce tolerance and physical dependence
- Withdrawal symptoms can range from the headache and nausea of a hangover, to severe tremors, nausea, hallucinations, convulsions, and delirium tremens (DTs)
  - DTs are characterized by disturbing hallucinations, bizarre delusions, agitation, confusion, hyperthermia, and tachycardia (rapid heart beat))
  - DT's can be severe enough to be fatal

35 Genetic and Environmental Factors Contribute to Alcoholism
- No single factor or combination of factors can be used to predict who will become an alcoholic
- Most researchers believe genetics contributes to alcoholism, but disagree on how much
  - some estimates put heritability at about 55%, some lower
  - early-onset alcoholism (before 25) seems to have a stronger genetic basis than late onset alcoholism
  - Several genes have been found to be more common in alcoholics, but each of these genes appears to be, by itself, a minor contributor (e.g. found in 5% of alcoholics, 2% of other people)

36

37 Does a Sensation-Seeking Personality Predispose an Individual to Alcohol Abuse?
- Researchers have identified families in which one sibling scored high in sensation-seeking, and another score low.
- They found that the sensation-seeker was consistently more likely to be a heavy drinker
- Further studies are needed to determine if the correlation will hold up

38 Treatment of Alcohol Addiction
- Antabuse
  - antagonizes the liver enzyme that breaks down acetaldehyde (a poisonous metabolite of ethanol)
  - People taking it can't drink without getting sick
- Naltrexone
  - Reduces euphoric feelings produced via the opioid system
  - Helps cut cravings in some alcoholics
- Several drugs may help to rebalance the glutamate system (e.g. acamprosate, topiramate, memantine)
- Counseling techniques
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Commonly Abused Drugs: Marijauna

- Marijauna is the single most used illicit drug in the US
- An estimated 11 million Americans currently use marijauna, and more than 71 million admit using marijuana at least once in their lifetime

Effects of Marijauna Can Include:

- Euphoria
- Intense anxiety
- Distortion of perception (e.g. colors appear more intense), and alterations in the sense of time, space and self
- Impaired judgment, short-term memory, learning and problem solving
- Problems with coordination
• Impaired judgment, short-term memory, learning and problem solving
• Problems with coordination

44 Commonly Abused Drugs: Marijuana
- Effects on the brain are largely due to THC (delta-9-tetrahydrocannabinol), but marijuana contains more than 400 chemicals
- Acts through cannabinoid receptors - normally bind a chemical called anadamide (anada = Sanskrit “bliss”)
  - Cannabinoid receptors are especially common in the basal ganglion, cerebellum, hippocampus, and areas of the hypothalamus that influence feeding

45 Commonly Abused Drugs: Marijuana
- Active ingredients dissolve in the body’s fats, and leave slowly. Metabolites of THC can sometimes be detected in urine weeks after last marijuana use
  - Quitting marijuana does not generally produce intense withdrawal symptoms (but heavy users who abstain have reported moderate irritability, anger, restlessness, anxiety, depression, sleep disruption, and changes in appetite) — psychological addiction is not uncommon
- Marijuana smokers are vulnerable to smoking-related health problems
  - Lung damage and disease, heart problems, eye irritations, oral cancers, etc.