

Tribal Law and Policy Institute: 5th Annual Tribal Healing to Wellness Court
Enhancement Training

Neuropharmacology of Addiction

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I. Background

A. Why do people use drugs?

1. Feel good
2. Feel better
3. Experimentation
4. Moral failing/lack of will power/habit

B. Definitions:

Drug addiction: a relapsing cycle of intoxication, bingeing, withdrawal and craving that results in excessive drug use despite adverse consequences.

1. Drug Use: taking a psychoactive substance for non-medical purposes
2. Drug Abuse: drug use that leads to problems (e.g. drunk driving)
3. Drug Dependence:
 1. Drug use causes significant impairment and inability to stop using, including withdrawal and tolerance
 2. Needing a drug to function normally
4. **Substance Use Disorder:** DSM-5 defines a substance use disorder as the presence of at least 2 of 11 (or 10 for some drugs of abuse) criteria, which are clustered in four groups:
 - a. **Impaired Self-control:** (1) taking more or for longer than intended, (2) wanting to stop or cut down use but not being able to, (3) spending a great deal of time obtaining, using, or recovering from use, (4) craving and urges to use substance.
 - b. **Social impairment:** (5) failure to fulfill major obligations (home, work, school) due to substance use, (6) continued use despite relationship problems caused by use, (7) important social, occupational or recreational activities given up or reduced because of substance use.
 - c. **Risky use:** (8) recurrent use in hazardous situations (drunk driving), (9) continued use despite physical or psychological problems that are caused or exacerbated by substance use (blackouts, anxiety).
 - d. **Pharmacologic dependence:** (10) tolerance to effects of the substance (needing more of the substance to get the desired

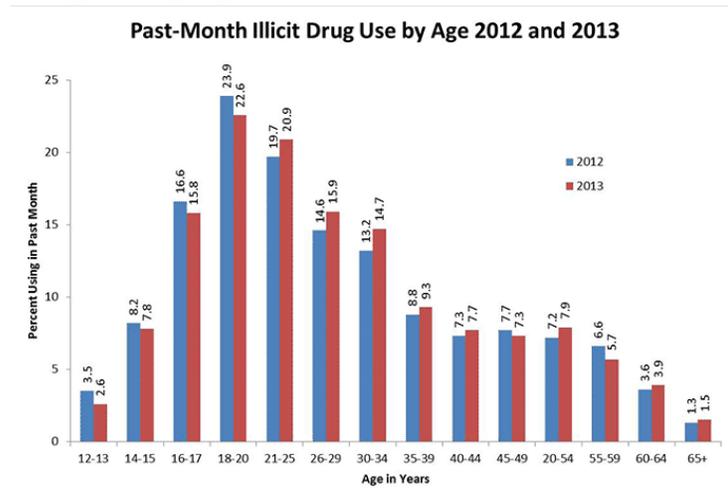
effect), (11) withdrawal symptoms when not using or using less, which can be relieved by taking more of the substance.

e. **Diagnosis of substance use disorder must include a pattern of use leading to significant impairment or distress.**

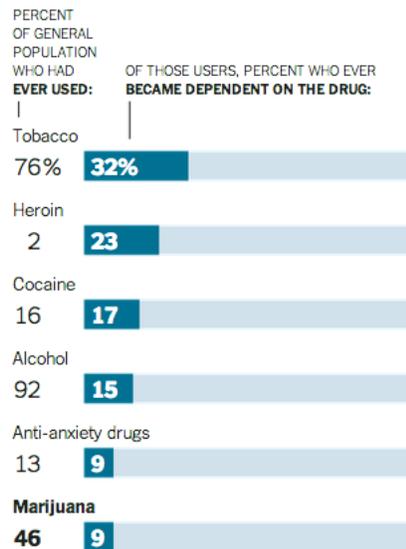
C. Rate of substance abuse by race/ethnicity

1. American Indian/Alaska Natives 12.5%
2. African Americans 10.5%
3. Anglo/European Americans 9.5%
4. Hispanic Americans 8.8%
5. Asian Americans 3.1%

D. Illegal drug use by age



E. What percent of users become addicts?



(1999- Institute of Medicine Study)

F. Relapse rates

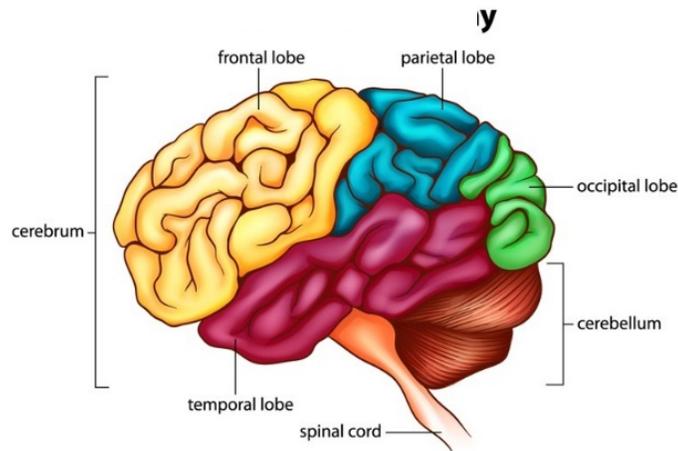


II. Vulnerability to addiction

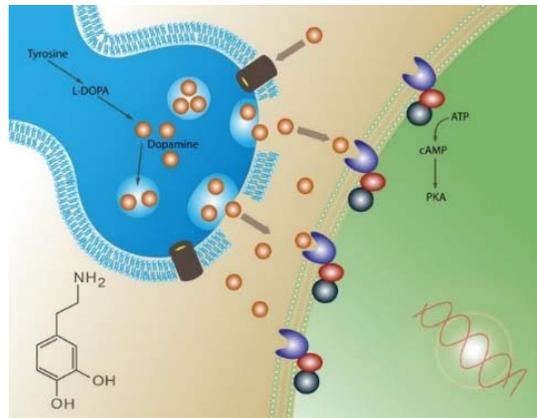
- A. Some people can use casually or just socially (even heroin).
- B. Some correlation with low level of D2 receptors
- C. Genetics and alcoholism: increased substance abuse use if family history
- D. Do AI/AN have a predisposition to addiction?
 1. No clear research at this time to support this hypothesis
 2. Alcoholism is caused by a combination of genetics, cultural, an environmental factors.
 3. Trauma, violence, poverty, hopelessness factors in increased risk for alcoholism/addiction
- E. Self-medication theory:
 1. Use of substances to compensate for untreated mental illness/medical problem.
 2. Hedonic tone: theory that addicts do not have normal level of happiness and use substances to create “normal” feelings.
 3. Thrill-seeking personalities: hyperactive dopamine system
 4. Reward deficiency syndrome: hypoactive dopamine system
 5. “addictive personality”
- F. Environmental (e.g., *in utero* drug exposure)

III. Basic brain anatomy and physiology

- A. Cerebrum:
 1. Frontal lobe: problem solving and judgment (executive function); movement; memory.
 2. Parietal lobe: intelligence; sensation; language.
 3. Temporal lobe: behavior; hearing; speech; memory.
 4. Occipital lobe: vision.



B. Neurons: cell body (soma), axon, dendrites/Synapse

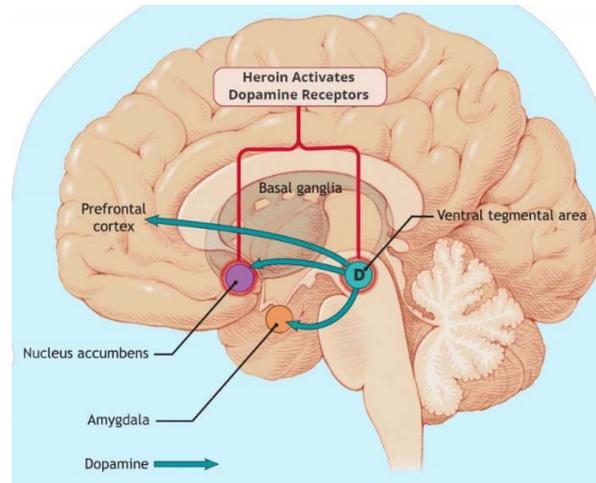


1. Synaptic cleft
2. Neurotransmitter binds with receptor specific for that neurotransmitter on post-synaptic cell and leads to downstream chemical reaction

C. Abused substances disrupt normal neurotransmission

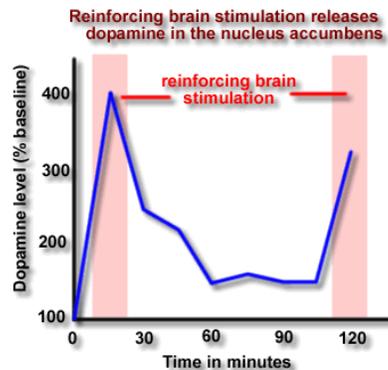
1. Bind to receptors that they match by coincidence
2. Produce feelings of pleasure in the reward system by altering neurotransmission of dopamine neurons and increasing dopamine release
3. Other effects (pain relief, hallucinations) due to action at other areas in the brain.

IV. Main parts of the brain involved in addiction



- A. **Pleasure/Reward center:** Generates pleasure sensation so that we will do what is necessary to survive: eat, drink water, procreate.
1. Many things stimulate reward center without creating substance use disorder: chocolate, caffeine
 2. Drug induced euphoria linked to release of dopamine in the nucleus accumbens (pleasure center)
 3. Ventral Tegmental Area (VTA)
 - a. Receives information from other regions that tells it how well fundamental needs are being taken care of
 - b. Uses the neurotransmitter dopamine to relay message to the nucleus accumbens
 - c. Message also sent to prefrontal cortex
 4. Nucleus Accumbens relays feeling of pleasure
- B. **Prefrontal cortex:** focuses attention, planning and motivating action; inhibited by use of addictive substances; planning and forethought inhibited
- C. **Hippocampus:** memories about the substances and pleasure
- D. **Amygdala:** emotions; conditioned response—intense craving—when person encounters cues associated with the substance
- E. **Locus coeruleus:** an alarm center (fight or flight); releases norepinephrine (adrenaline) at times of stress such as lack of drug;
- V. Reward Pathway and other areas of brain are changed by addiction
- A. Addictive drugs, alcohol, pornography, gambling, leads to surge of DA in pleasure center (different substances create DA increase by different mechanisms).
 - B. In addiction: pleasure circuit is hijacked by addictive drug

1. Dopamine release is higher with addictive stimulus than with healthy stimulation, like healthy food and sex.
2. Enjoy using substance then crave it
3. Representation of DA levels in NA after stimulation with addiction substance:



C. Judgment impaired:

1. Frontal cortex inhibited:
2. In non-addicted brain: frontal cortex helps make good decisions and dampens messages from nucleus accumbens [stop drinking; don't get high or you will get arrested]

D. Dopamine release also affects learning and memory: Seeing a photo of drug or encountering environment where drug abuse occurred will release DA into NA

E. With substance abuse, brain will decrease production of dopamine because it is being flooded with it. When brain senses lack of dopamine, it will kick into gear to get the drug.

1. When lack of drug, locus coeruleus drives the addict to do anything necessary to obtain it.
2. Prefrontal cortex hijacked to figure out how to get drugs and make bad decisions

VI. Chronic drug effects

A. Executive function deficits:

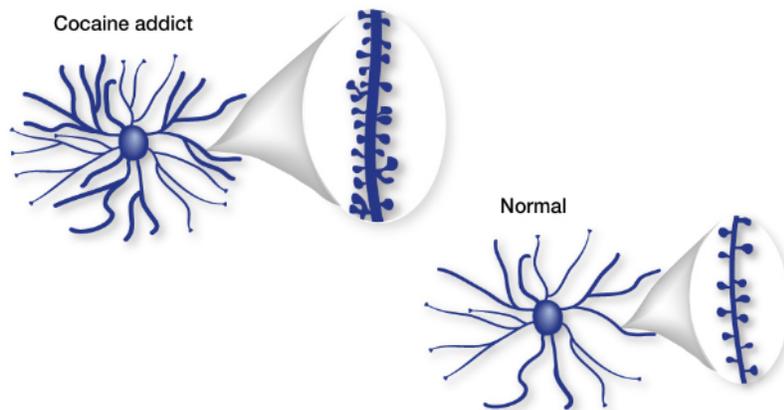
1. Physical change in cortex: thinning
2. lower attention, memory, ability to understand, problem solving
3. unable to learn as well

B. Drug seeking behavior

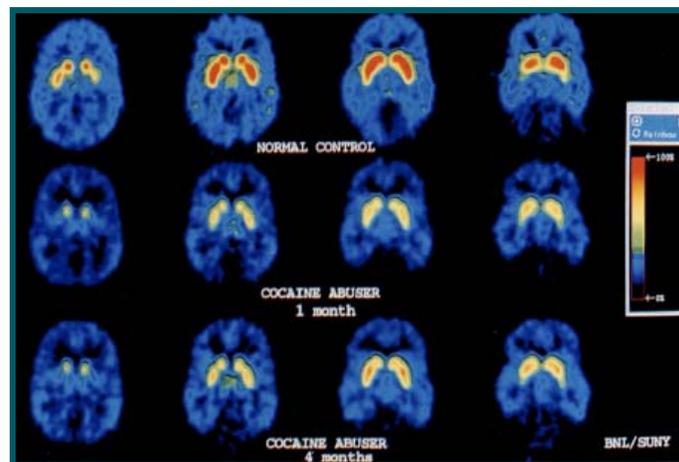
C. Development of tolerance:

1. Use more of the drug to maintain euphoria or to avoid dysphoria or withdrawal
2. Receptor number increases to counter the constant presence of the drug of abuse

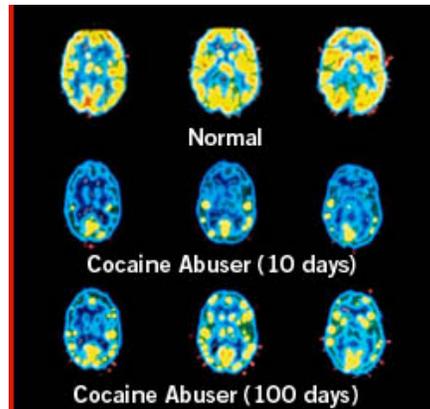
3. The amount of DA gradually decreases through *depletion* (components are used up) and *feedback inhibition* (too much there so brain signals to stop making it)
 4. Need to increase dose for same effect
 5. Decreased response to normal reward
- D. Controls vs sober addicts: still low brain activity after 100 days later: still brain damaged 100 days out
1. Reduced brain metabolism measured by glucose use in substance abusers
 2. Can take 1.5 years of sobriety to recover brain function
- E. Changes in connections between neurons: decreased in some areas, increased in other areas
- Neurons in nucleus accumbens increase connections



- F. Lower D2 receptor availability in substance abusers:



G. Lower glucose metabolism=lower brain activity



VII. Pharmacological treatment/harm reduction

A. Methadone

B. Buprenorphine (Subutex)

C. Suboxone (buprenorphine + naloxone): naloxone included to prevent abuse by injecting suboxone

D. Long term implants

1. Probuphine (buprenorphine implant)

2. Naltrexone (Vivitrol, Revia)

E. Naloxone (Narcan): used for overdose

