

Here are some things to keep in mind before we start our discussion of:

Annual Review of Psychology

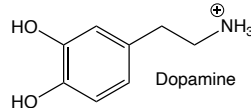
Dopamine and Addiction

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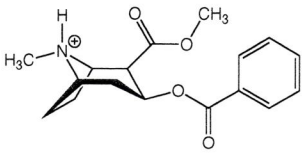
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- 1) Dopamine neurons respond to rewards such as food with reflexive, linked, **bursts of discharges**.
 - Dopamine neurons also come to respond with bursts of discharges to stimuli that immediately precede and reliably predict the reward.
 - Bursts of discharges (also called phasic firing) of dopamine-containing neurons are necessary to establish long-term memories associating predictive stimuli with rewards.
- 2) Actual dopamine neuron activity is very complicated as there can be shifts in so-called tonic activity (the overall baseline of activity) as well as phasic activity, that is the bursts of discharges associated specifically with an event.
- 3) Within the striatum, close to half of the output neurons express only D₁-type receptors, and the other half express only D₂-type receptors.
 - D₁ receptors have low or loose binding to dopamine and are thus infrequently occupied by dopamine molecules.
 - Current thinking is that D₁ receptors activate when high dopamine is released due to a **reward** being received and repeated activation leads to **learning how to anticipate and seek the reward**.
 - D₂ receptors have high or tight binding to dopamine and are usually occupied by dopamine molecules.
 - Current thinking is that D₂ receptors activate to stop a behavior associated with a **punishment** and repeated activation of D₂ receptors leads to **learning how to avoid that punishment**.
 - **LOSS of D₂ receptors therefore leads to risk-taking and an ignoring of negative consequences.**
 - Schizophrenia is a disabling psychiatric disorder with many positive, negative and cognitive symptoms that can be attributable to an imbalance between dopaminergic pathways that signal D₂ and D₁ receptors.
- 4) Addiction is commonly identified with habitual nonmedical self- administration of drugs. It was usually defined by characteristics of intoxication or by characteristics of withdrawal symptoms.
 - Addiction is caused by molecules that act to release dopamine.
 - **Unusually high levels of dopamine caused by drugs of addiction activate D₁ receptors and decrease the number of D₂ receptors on neurons**
 - **Both of these effects are amplified with increased or longer use.**

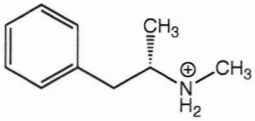
Cocaine



Cocaine activates the dopamine system by blocking reuptake of dopamine, serotonin, and norepinephrine. As a psychomotor stimulant, cocaine elevates extracellular dopamine levels 3-5 times. When given to rats, cocaine activates D1 pathways and when abstinent, their D2 pathways were activated because of an absence of cocaine.

In the experiment, the rats preferred places where they could get cocaine and avoided places without it. The rats approached places with immediate cocaine injections and avoided places where they have to wait 15 minutes. Cocaine addicted humans have decreased D₂ receptors which leads to reduced sensitivity to non-habitual rewards.

Amphetamines



Methamphetamine

Amphetamine, methamphetamine & related drugs are psychomotor stimulants that elevate dopamine levels and are habit forming. Direct effects include elevated mood, increased alertness & relief from fatigue. The baseline dopamine level is elevated and causes rapid dopamine release & causes one to avoid cues that predict delayed access to amphetamine. Methamphetamine causes long term decreases in D_2 receptors, which leads to reduced sensitivity from infrequent rewards and a lack of acknowledgement for punishments.

-elevated mood, increased alertness, relief from fatigue
-baseline dopamine is elevated; rapid dopamine release

Methamphetamine causes

• Long term decreases in D_2 receptors → As a result, those with this addiction possess

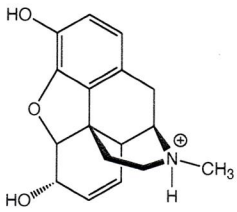
As a result, those with this addiction possess

reduced sensitivity to infrequent rewards →

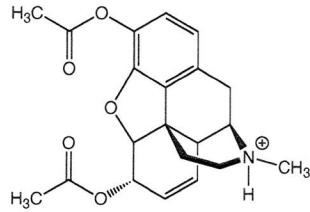
avoid cues that predict delayed access to amphetamine

This loss of D_2 receptors leads to lack of acknowledgement for punishments

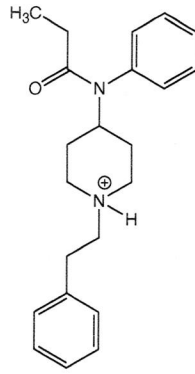
Opiates



Morphine



Heroin



Fentanyl

- Opiates are sedative hypnotics that increase dopamine levels in the brain, leading to a decrease in tension + pain, along with addiction
- Affects μ -opioid receptors in the ventral tegmental area, which contributes to habit-forming nature.
- Inhibits (takes up) GABA-containing neurons that usually keep the dopamine system under control, leading to uncontrolled firing of the system.
- Long-term use of opioids leads to the loss of D_2 receptors,
- Mice learned to predict reward as well as avoid conditions where opiates aren't available.

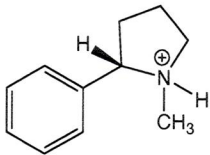
Alcohol



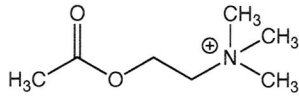
Ethanol

- Is a depressant drug that, at lower doses, gives immediate effects of euphoria and a decrease in inhibitions. At higher doses, gives experiences of depression
- Alcohol can activate temporary increases in dopamine levels, which can reach over about 50% over normal baseline
- Unlike other addictive drugs, there is no single receptor for alcohol and therefore is connected to multiple sites of rewarding action.
- Alcoholics develop a long term decrease in D_2 dopamine receptors, making them less aware of consequences to their actions.

Nicotine



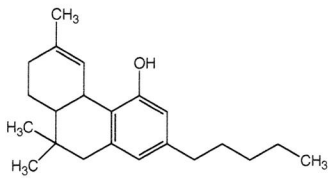
Nicotine



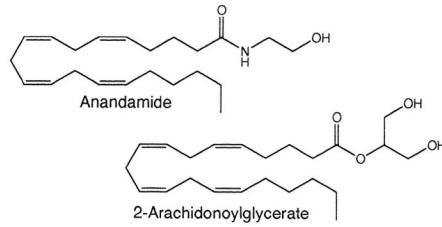
Acetyl Choline

- Nicotine is a stimulant that causes a burst firing of dopamine neurons, and is habit-forming
- Nicotine elevates dopamine levels in the brain by acting on receptors localized in specific brain regions
- Acts at subsets of acetylcholine receptors
- initially, for new users, nicotine is unpleasant, after a delay it hits dopamine receptors
- long-term decrease in the expression of D₂ dopamine receptors
- impacts sensitivity to rewards → nicotine-addicted individuals may find it more challenging to derive satisfaction from rewards that are not associated w/ their addiction

Marijuana



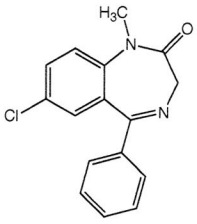
THC



Endocannabinoids

[The addictive agent in marijuana is THC which is a depressant and causes feelings of relaxation and euphoria by elevating extracellular dopamine levels. The result of cannabinoid treatment is increased burst firing of dopamine neurons and increased dopamine flow into the striatum and prefrontal cortex.]
[Cannabinoids are rewarding but pharmaceuticals can block the CB1 cannabinoid receptor, inhibiting rewarding effects of other drugs and food seeking. Sudden withdrawal ~~through~~ via treatment with a CB1 receptor antagonist leads to a withdrawal state and symptoms in humans. Similar to other drugs, human addicts develop long-term decreases in expression of D₂ receptors, leading to risk-taking and ignoring of negative consequences.]

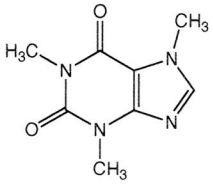
Barbiturates and Benzodiazepines



Diazepam ("Valium")

Barbiturates and Benzodiazepines are depressants that produce withdrawal symptoms. They also activate and disinhibit the dopamine system. They target the centrally nervous system to cause drowsiness. It is sometimes used to treat insomnia and seizures. An overuse of these chemicals can suppress brain activity and the withdrawal suppresses dopamine signaling. This leads to more irrational decision making and violence (D2) and less drive (D7).

Caffeine



Caffeine produces the feelings of well-being & happiness as it suppresses adenosine & adenosine receptors while elevating dopamine levels. Caffeine produces similar rewarding effects to alcohol & nicotine, as well as non-drug reinforcement. It binds to both the D₁ & D₂ receptors, proposing the common question as to whether or not caffeine is actually addictive. Withdrawal overlaps with symptoms of anxiety, depression & insomnia. An aggressive amount of caffeine exposure leads to induces changes in the D₂ receptor in the striatum.

Other Forms of Addiction

- gambling, eating, anything else that presents reward can become an addiction
- food-seeking is decreased when dopamine in the brain is decreased
- food causes a burst of dopamine release, people who overeat use much of their dopamine while eating, so when they're not eating, they have low dopamine levels and are therefore depressed
- mirrors the effect of drug use, when not using, dopamine no longer fires, increasing ~~depression~~ depression.
- overeaters have decreased D_2 receptors, reducing their sensitivity to negative punishment
- ~~low~~ increase dopamine correlates with increased impulsivity - gambling and substance abuse.