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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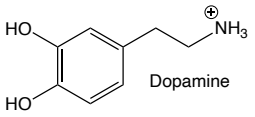


1) Dopamine neurons respond to rewards such as food with reflexive, linked, **bursts of discharges**.

   - 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.

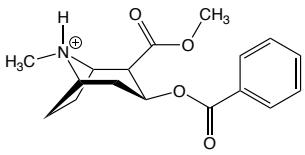
3) Within the striatum, close to half of the output neurons express only D1-type receptors, and the other half express only D2-type receptors.

   - 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 elevates extracellular dopamine level. It causes a form of euphoria but is different from other drugs' euphoria

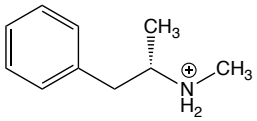
It blocks the reuptake of dopamine by the dopamine transporter
Also blocks the reuptake of norepinephrine and serotonin

Elevates basal dopamine levels "several fold"

Cocaine addicted humans develop long-term decreases in expression of D_2 dopamine receptors, leaving them with reduced sensitivity

when it becomes a conditioned aversive stimulus, it has an established aversive state which then creates a negative conditioning situation

Amphetamines



Methamphetamine

psychomotor stimulants
elevates dopamine levels
found in cocaine
↳ ↑ mood, increased alertness, relief from fatigue,
withdrawal symptoms
↳ depressed mood/activity ? lack of motivation

How it functions

↳ elevate extracellular dopamine levels by releasing dopamine from vesicles and reversing the dopamine transporter.

Low doses of dopamine receptor antagonists → ↑ amphetamine intake

↑ Adderall

Desoxyn

↑ Methamphetamine vs amphetamine = Class II / Schedule II

↳ 2nd line for severe cases

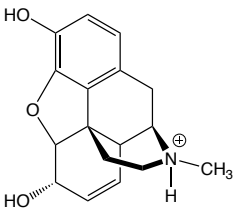
↳ common in Attention medications

↳ more in medical context

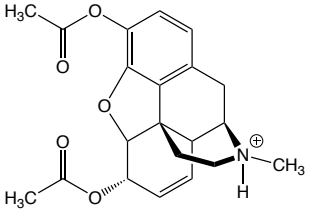
Long term methamphetamine addicts = ↓ D_2 dopamine receptors

reduced sensitivity to nonnatural rewards

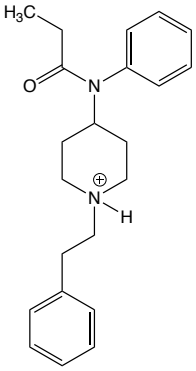
Opiates



Morphine



Heroin



Fentanyl

- Opiates are sedative-hypontic drugs that reduce Pain while increasing dopamine (Produce euphoria, overlaping with alcohol)
- It's self administrated and elevate dopamine level to approximately same as Cocaines.
- Opiates activate dopamine system by trans-symaptic Mechanism. It inhibit AABA-containing neurons, which normally hold dopamine in normal condition

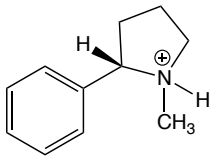
Alcohol

CH_3CH_2OH

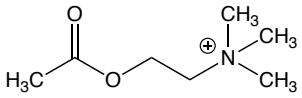
Ethanol

Alcohol is a depressant drug that increases your dopamine baseline. Low doses cause euphoria and a decrease in inhibition, activating the dopamine system. Unlike other drugs however it has no specific receptor and it is not well understood. A strong possibility is that activation of the dopamine system depends on glycine receptor interactions. Once addicted D2 receptors decrease leaving cravings, anxiety, and behavioral distress.

Nicotine



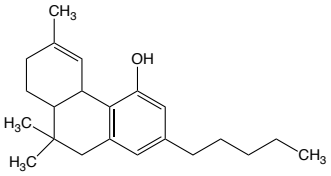
Nicotine



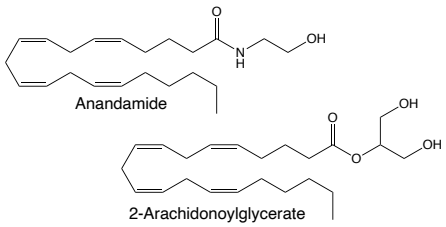
Acetyl Choline

- psychomotor stimulant that causes burst firing of dopamine neurons, elevates extracellular dopamine levels, and is habit forming
- acts at subsets of acetylcholine receptors in the brain
- primary nicotinic dopamine-elevating action involves receptors localized in the medial portion of the ventral tegmental area
- nicotine causes dopaminergic neurons to discharge, and nicotinic effects in the striatum, influencing release of dopamine from axon terminals
- nicotine addicted people develop long-term decreases in D2 receptors, leaving them w/ reduced sensitivity to nonnabitual rewards.

Marijuana



THC

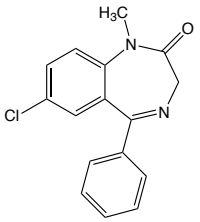


Endocannabinoids

THC is a depressant and causes relaxation and a sense of euphoria. THC acts on the cannabinoid receptors in the brain and increases extracellular dopamine levels. THC also increases dopamine signaling in the basal ganglia. Those who struggle with marijuana missuse have a decreased expression of D_2 dopamine receptors. This leaves users with reduced sensitivity to rewards and unique experiences.

CB1 and CB2: receptors for endogenous cannabinoids
- anandamide and 2-arachidonoylglycerol
- → + functions as retrograde neurotransmitters
  - : synthesized, released by dopaminergic neurons
  - : act presynaptically on local axon terminals
  - : cannabinoid treatment increases burst firing of dopamine neurons, increased dopamine efflex into striatum and prefrontal cortex
  - : withdrawal symptoms in humans; decreased appetite, nervousness, weight loss, etc.

Barbiturates and Benzodiazepines



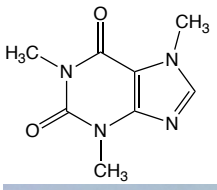
Diazepam ("Valium")

-They are depressants producing withdrawl symptoms.

-It inserts a slight increase dopamine in Certan brain regions, while inhibiting stress

- Relaxant, Binds to GABA receptors

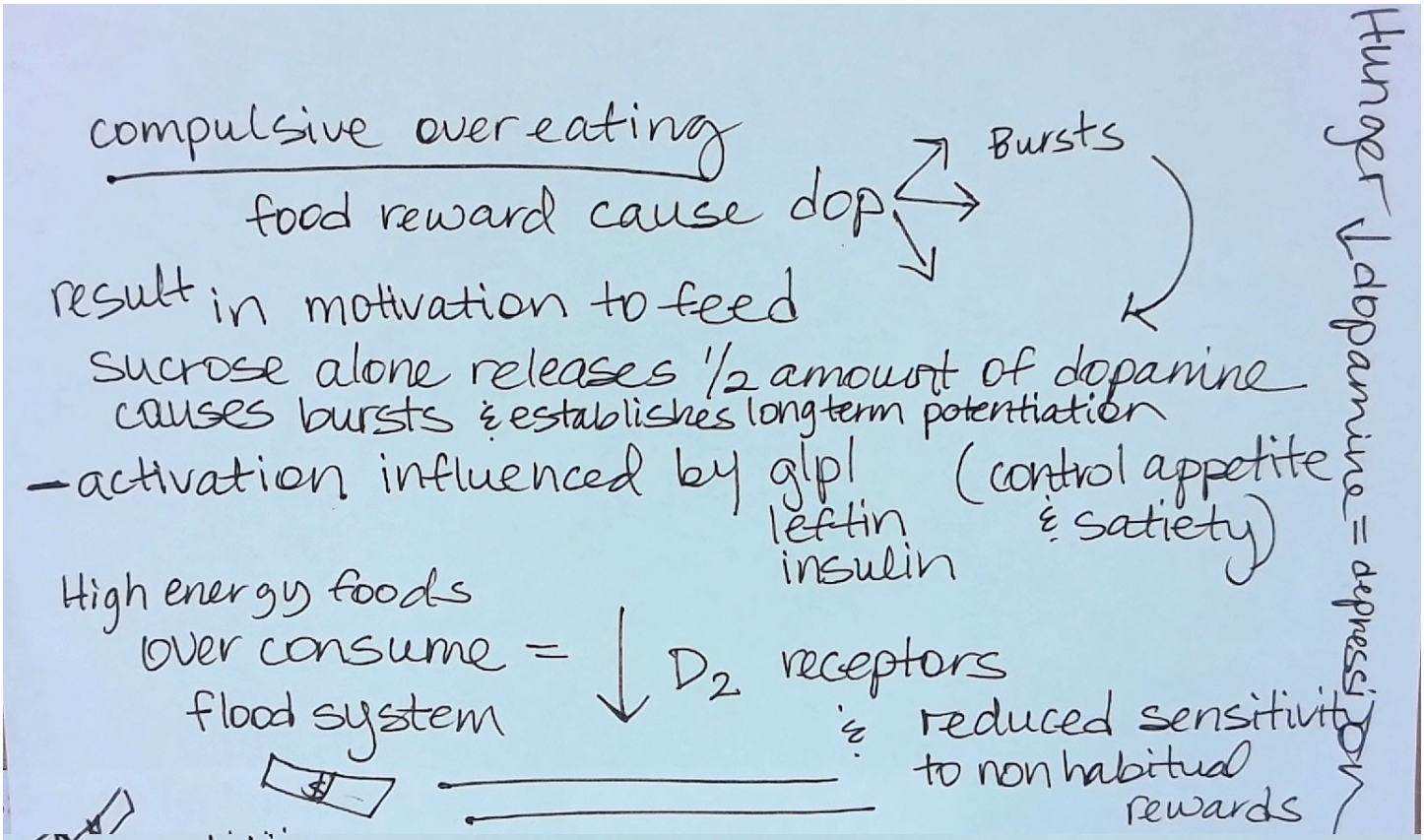
Caffeine



Caffine produces feelings of well-being, happiness, alertness, and sociability. It potentiates or increase the chances of rewarding effects of alconol & nicotine. Caffine blocks effects of adenosine at adenosine receptors = increase alertness & wakefulness. Affects on mood!! Withdrawls = anxiety, depression, insomnia. Minimally effective at activating dopamine system -human [High doses: it can elevate dopamine levels Heteromers with D_1 receptors & D_1 striatal output neurons regulate things like learning, and addiction

Low doses

Other Forms of Addiction



gambling

Long periods of uncertainty of reward release dopamine Boost

maybe other reward seeking activities also cause similar reward system dioruption