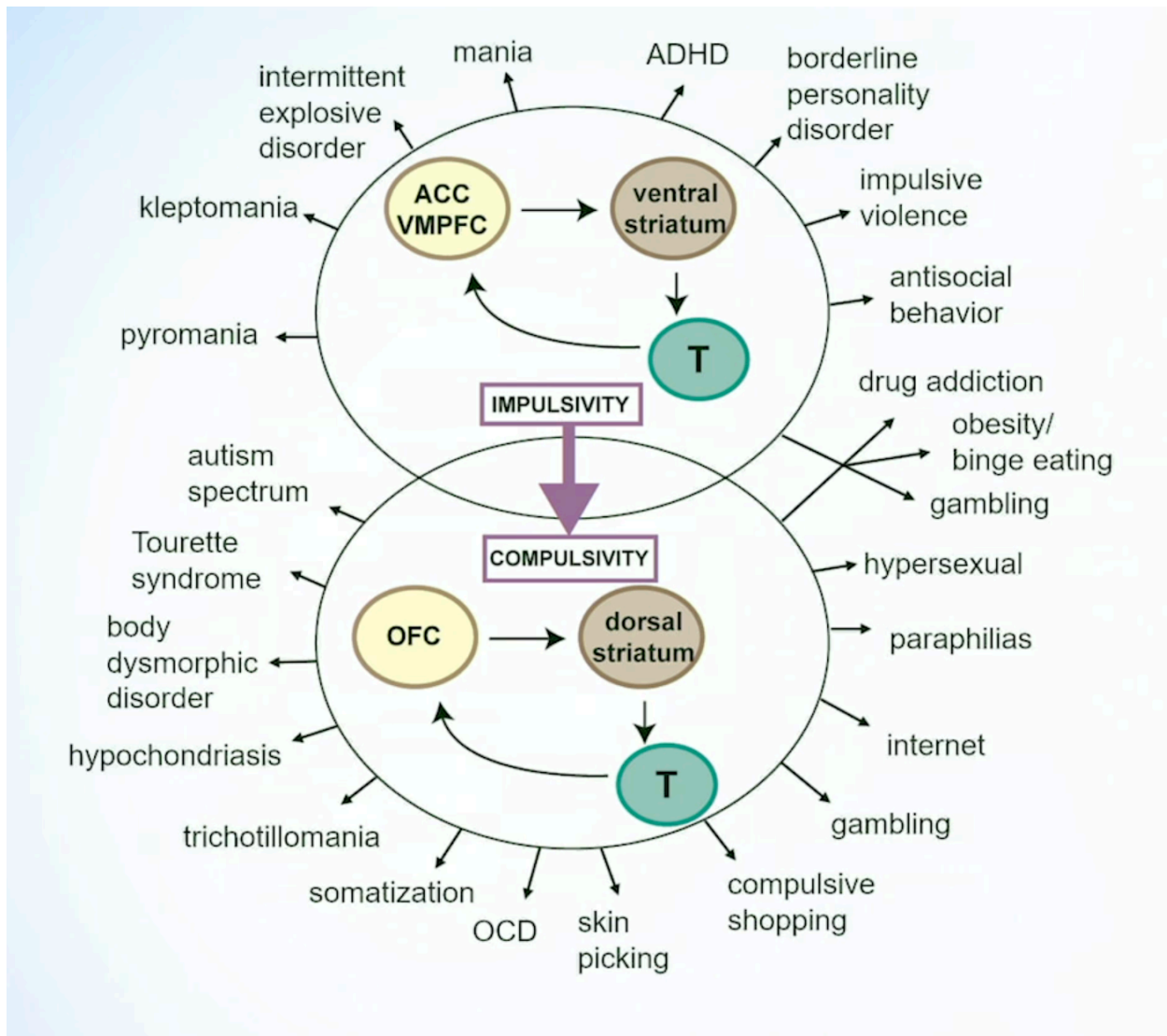


Impulsivity, Compulsivity, and Addiction

Impulsivity and Reward

- Impulsive is to get an award
 - Thalamus- ACC VMPFC- ventral striatum-Thalamus
- Compulsivity is you do it because you've gotten a reward in the past
 - Thalamus-OFC- Dorsal striatum- thalamus
 - OFC: is where sensory motor
 - Now it's not for a reward, about rewards in the past
 - Ex. Pavlov dogs (ring bell and salivate)
 - On PET Scans of addicts, it is not the hit that lights up the scan, its holding the drugs, or holding the pipe. It is the sensory motor



Dopamine theory of reward

- Dopamine mesolimbic pathway
 - Natural highs like winning a race, hearing a good opera,
 - Behaviorally induced highs like gambling
 - Substance induced highs

Impulsive-compulsive disorders

- Substance use
 - Cannabis
 - Nicotine
 - Alcohol
 - Opioids
 - Stimulants
 - Hallucinogens
 - Empathogens
 - Dissociative
- Behavioral addictions
 - Binge eating disorder
 - Gambling disorder
 - Internet gaming disorder

Stimulant Actions on mesolimbic dopamine circuit

- Works by increasing dopamine which leads to joy
 - At the end you are in a dopamine deficient state
- Progress of stimulant abuse
 - Take it have fun
 - Then you crave the dopamine release
 - Then reverse tolerance/addiction
 - Anhedonia, sleepiness, and withdrawal due to not much dopamine
 - Compulsive use: will do anything to have it.
 - You can lose 50% or more of brains dopamine permanently, burns the synapses

Nicotine Actions

- Nicotine receptors
 - Alpha 4 beta 2
 - Alpha 7
- Nicotine indirectly activates dopamine release
 - Nicotine activates Ach receptor
 - Activates dopamine release
 - Get joy, addiction cycle begins
- Nicotine receptor resting, have a cigarette and they open and dopamine is releases, then cigarette finished, then nicotine receptor desensitized, then takes 45min to hour for re-sensitization, then cycle begins again.
- If chronically desensitized they make more, leads to increased craving, drug seeking behaviors, impulse choices, and reward sensitivity.

Molecular actions of a nicotinic partial agonist

- Nicotinic full agonist: channel frequently open
- Nicotinic partial agonist (NPA): stabilizes channel in less frequent open state, not desensitized
- Nicotinic antagonist: stabilizes channel in closed state, not desensitized.

Varenicline

- Partial agonist for nicotinic receptors

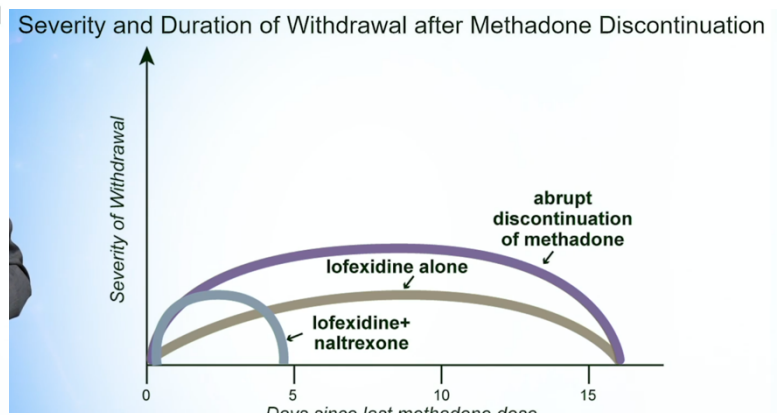
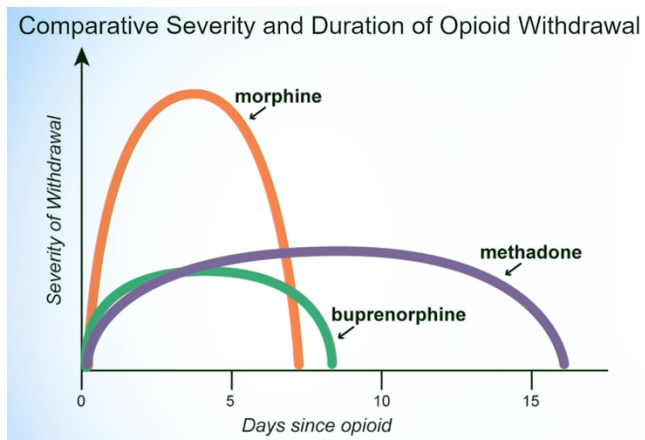
Bupropion

- works to make sure the dopamine levels stay up, bupropion blocks the dopamine pump.

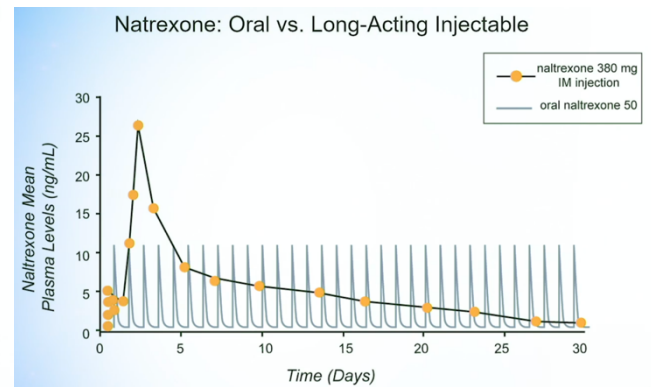
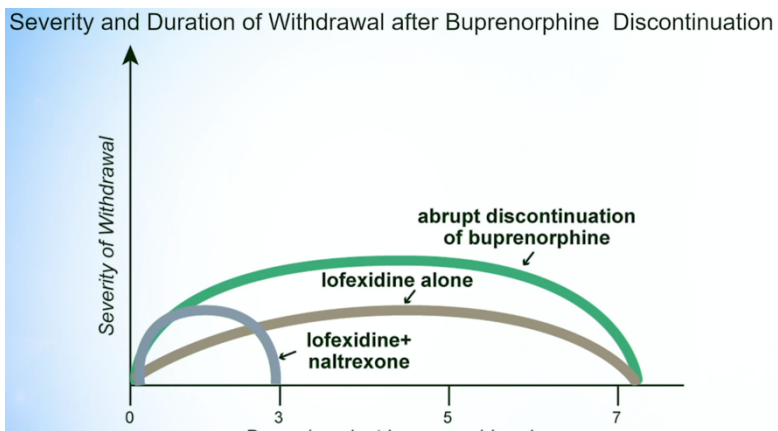
Alcohol

- stimulates the mu opioid receptor (weak)
- also works on GABA neurons
- High- is the impulsivity
- The joy of drinking is the compulsion
 - **Naltrexone** (U-opioid antagonistic) reduce the reward (pleasure) of drinking
 - **Acamprosate** reduces excessive glutamate release to relieve alcohol withdrawal

Opioids






- If you give lofexidine or clonidine it will bring down the detox
- If you give lofexidine and naltrexone shorten



- To start naltrexone shot must be fully detoxed.

Marijuana

- In the body we have endocannabinoid system: receptors and Ligands
 - CNS and peripheral neuron terminals
 - 2AG= 2arachidonoylglycerol
 - High efficacy agonist at CB1
 - Anandamide
 - Low efficacy agonist at CB1
 - Immune cells
 - 2AG= 2arachidonoylglycerol
 - High efficacy agonist at CB2
 - Anandamide
 - Low efficacy agonist at CB2
- Side effects: the brain has endocannabinoids which come out and talk to CB1 letting the brain know to release less
 - THC
 - Potential Therapeutic Properties
 - Ant inflammatory
 - Euphoria
 - Opioid type pain relief
 - Cannabidiol
 - Neuropathic pain relief
 - Anti-inflammatory
 - Patient specific

THC vs. CBD: Psychiatric Effects			
	 Cannabis with Low CBD Content	 Cannabis with High CBD Content	 CBD Alone
Psychosis symptoms	Higher risk of hallucinations and delusions	Lower risk of hallucinations and delusions	Possible antipsychotic effects
Psychotic disorder	Earlier age of onset	Later age of onset	
Cognition	Higher risk of acute memory impairment	Lower risk of acute memory impairment	
Anxiety	Anxiogenic Increased amygdalar activity		Anxiolytic Reduced amygdalar activity

- Growing in green houses, what is grown now (high THC low CBD) High potency
- Associated high evidence
 - benefits:
 - Chronic pain
 - Chemotherapy induced nausea
 - Spasticity in MS
 - Risks

- respiratory symptoms
 - MV crashes
 - Low birth weight
 - psychosis
- Moderate evidence
 - Benefits
 - Sleep, obstructive sleep apnea, fibromyalgia, chronic pain, MS
 - Airway dynamics
 - Forced vital capacity
 - Cognition in psychosis
 - Risks
 - Overdose injuries in pediatric populations
 - Impaired learning memory and attention
 - Increased (hypo)mania in bipolar
 - Depressive disorders
 - Suicidality
 - Social anxiety disorder
 - Development of substance use disorder for other substances

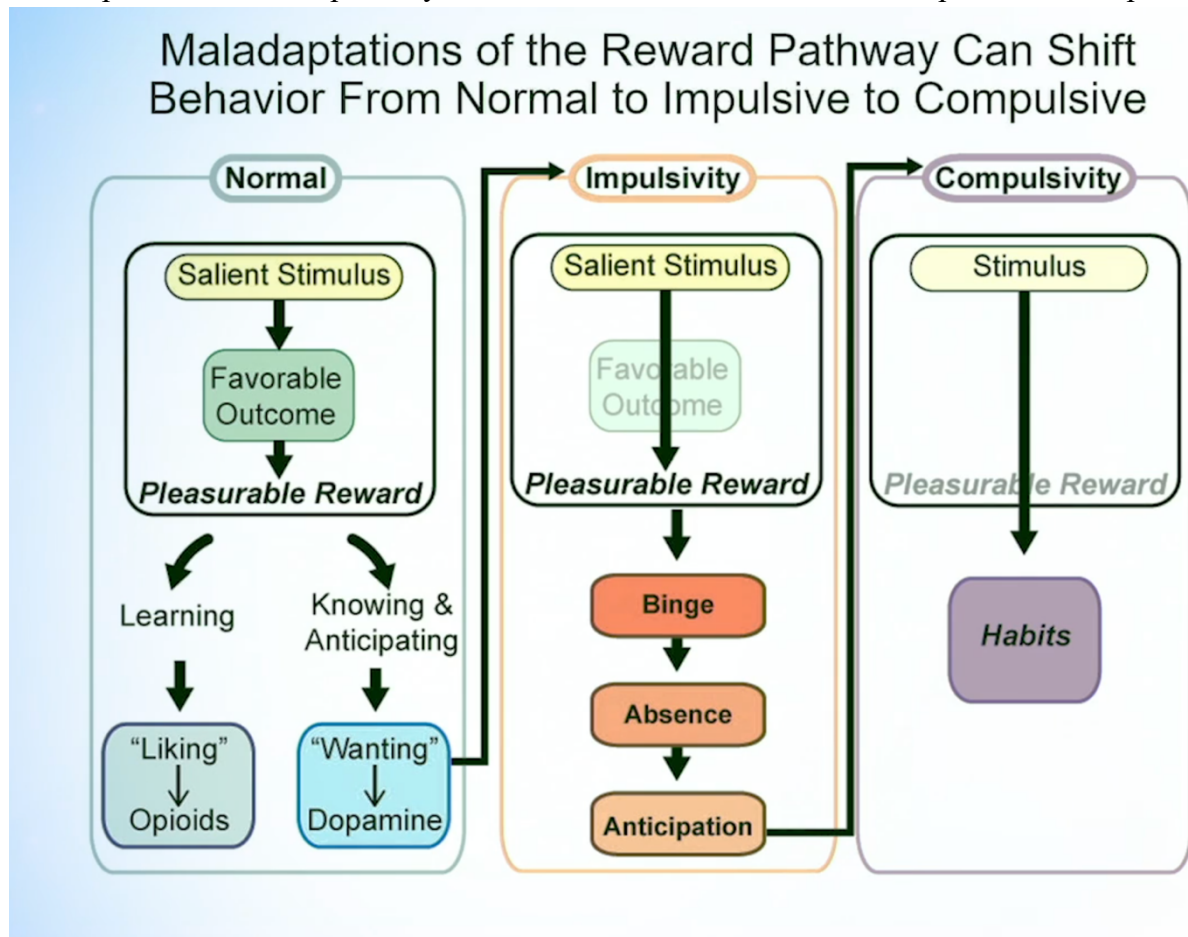
Approved Uses for THC and CBD

				Schedule
Dronabinol	Synthetic THC	Oral capsule or solution	Chemo-induced nausea and vomiting (US) Appetite boost in AIDS wasting syndrome (US)	III
Nabilone	Synthetic THC analogue	Oral capsule	Chemo-induced nausea and vomiting (US)	II (due to its potency)
Nabiximols	Purified ~1:1 THC:CBD	Spray	Spasticity caused by multiple sclerosis (UK, Canada, Europe, Australia, New Zealand, Israel) Pain in multiple sclerosis and in cancer (Canada, Israel)	N/A
Epidiolex	CBD purified from marijuana	Oral solution	Seizures associated with two rare and severe forms of epilepsy, Lennox–Gastaut syndrome and Dravet syndrome, in patients 2 years of age and older (US)	Not a controlled substance

Hallucinogens

- LSD
- psilocybin
- mescaline
- MDMA
 - Goes into the serotonin synapses, at high doses it will open a channel.
 - Can cause hyperthermia due to increase temp.

Maladaptation of reward pathway that can shift behavior from normal to impulsive to compulsive



We can give long acting injectable naltrexone may in fact enhance this process of habit extinction. Because you cannot get high or drunk you may be able to reverse these compulsions

Impulsive-compulsive disorders

- Obsessive compulsive disorder
 - Anxiety or fear about obsessions or compulsions
 - Worry obsessions
 - compulsions
- Body dysmorphic disorder
- Trichotillomania
- Skin picking
- Hoarding
- Shopping
- Hypochondriasis
- Somatization
- Agitation in Alzheimer's
- Motor and behavioral impulsivity in ADHA
- Provocative behaviors in mania
- Disruptive mood dysregulation disorder

- Pyromania
- Kleptomania
- Paraphilias
- Hypersexual disorder
- Autism spectrum disorders
- Tourette's
- Stereotyped movement disorder
- Borderline
- Self-harm and parasuicide behaviors
- Conduct disorder
- Antisocial
- Oppositional defiant disorder
- Intermittent explosive disorder
- Aggression and violence