Drugs and the Brain

Five Main Types of Neurotransmitters
- Cholinergic
- Catecholamines
- Indoleamines
- Amino Acid NTs
- ATP and byproducts
  - Substance P

Cholinergic Neurons
- Use Acetylcholine as their major NT
- Found at neuromuscular junctions
- Also found in the brain in lower level structures
  - Believed to be involved in learning and memory
  - Alzheimer's Disease

Catecholamines and Indoleamines
- Catecholamines
  - Dopamine
  - Adrenaline
  - Noradrenaline
- Indoleamines
  - Serotonin
  - Melatonin

How to make catecholamines
- Tyrosine (an amine acid)
- Turns to L-Dopa
- Turns to Dopamine
- Turns to Noradrenaline
- Turns to Adrenaline
- They all have the same starting material
  - They're just different steps in the process
  - Steps occur when enzymes are added to the molecules
Dopaminergic Neurons
- Use dopamine
  - Movement
  - Parkinson's disease
  - Feelings of reward
  - May play a role in addiction
  - Higher level cognitive functions
  - Planning behavior

Noradrenaline and Adrenaline
- Both are NTs and hormones
  - Noradrenaline
    - Important for attention and focus
    - Important in sympathetic nervous system
    - Increases confidence
  - Adrenaline
    - Important for short-term stress
    - Also important in sympathetic nervous system
    - Increases energy
  - Side note: ACh is the NT for the parasympathetic nervous system

Indoleamines
- Tryptophan → 5HTP → Serotonin - Melatonin
- Serotonin
  - Widespread throughout the brain, few in number
  - Important for sleep, mood, and appetite
- Melatonin
  - Hormone secreted by the pineal gland
  - Important for sleep wake cycles

Amino acid neurotransmitters
- Glutamate and GABA most important
- Glutamate
  - The most used excitatory NT in the CNS
  - Linked to Long term memory
- GABA
  - The most used inhibitory NT in the CNS
  - Inhibits dopamine

ATP
- Involved in perception of pain
- Major byproduct adenosine is also a NT
- Acts upon autonomic nervous system
  - Vas deferens, bladder, heart, gut
- Frequently coexists with other enzymes
- Also the bodies major source of energy
**Substance P**
- Neuropeptide involved in the perception of pain
- Works in conjunction with endorphins
  - Endorphins inhibit substance P

**Addiction, Tolerance and Withdrawal**
- **Addiction**
  - Compulsive need for repeated use of the drug
- **Tolerance**
  - Changes in the body’s response to the drug to maintain a constant environment
    - i.e., if a drug causes an increase in heart rate, the body may prepare for the drug by decreasing its heart rate
    - This causes users to gradually increase the amount of the drug to get the same effects
- **Withdrawal**
  - Occurs after a user stops using because the body is trying to maintain a constant environment and is preparing for the drug (that never comes)

**Genetic and Environmental contributions to addiction**

**So…**
- If you know the symptoms of a specific drug, and you know what the various neurotransmitters do, you should be able to know what neurotransmitter the drug works on

**Brief Recap**
- **Dopamine**
  - Addiction, movement, planning
- **Acetylcholine**
  - Learning and Memory, movement
- **Adrenaline**
  - Increases energy, heart rate
- **Noradrenaline**
  - Increases confidence
- **Glutamate**
  - Long term memory
- **GABA**
  - Inhibition of dopamine
- **Serotonin**
  - Hunger, mood, sleep
- **Melatonin**
  - Sleep
- **ATP/etc**
  - Pain, reaction time
- **Substance P**
  - Perception of pain

**Uppers**
- **Cocaine and Methamphetamine**
  - Increases catecholamines, serotonin, and acetylcholine
Long term effects of these uppers

- Too much dopamine
  - Linked to the frighten response
  - May cause paranoia
- Too much Adrenaline and Noradrenaline
  - Exhaustion, lethargy, anhedonia (no pleasure), low blood pressure
- Too much Serotonin
  - Insomnia, agitation, depression
- Too much Acetylcholine
  - Muscle tremors, memory lapses, confusion, hallucination

Downers

- Heroin and Opium
  - Works at mu, kappa, and sigma opioid receptors
  - Same place endorphins work
  - Also found in GI tract
  - Inhibits GABA
    - Reduces the inhibition of dopamine

Other issues

- Alcohol
  - Initially elevates serotonin, then depletes it
    - Causes pleasure followed by depression
  - Dopamine is released
    - Reward pathway activated
  - Norepinephrine is released
    - Increased confidence; also leads to reward feelings
    - Remember dopamine and norepinephrine are part of the same family of NTs
What else?

- Releases endorphins
  - Lessens pain
- Inhibits glutamate release
  - Memory problems
- Most importantly: increases GABA
  - Slows down the brain processes

Ecstasy

- Serotonin
  - Forces the release of serotonin from the axons
- Norepinephrine and Epinephrine
  - Probably account for the physical effects of ecstasy
  - Probably due to brainstem activity
- Dopamine
  - Increases release of dopamine as well
  - Addictive
Long term ecstasy effects
- Destroys serotonin receptors
  - Also down regulation makes them unavailable

What about LSD?
- Comes from ergot on rye
- Similar in structure to serotonin

Marijuana?
- Found cannabinoid receptors in the brain
  - But, we can’t have natural receptors just for marijuana
  - There must be a natural NT that binds to these receptors
- Anandamide and 2AG were discovered in the late 80s
  - Neurotransmitters that fit into these receptors
  - THC also uses these receptors
- Receptors found in the immune system as well
- Hippocampus, hypothalamus, amygdala, reward system, cerebellum

Cannabinoid receptors are all over

What do those brain areas mean?
- Hippocampus, hypothalamus, and amygdala deal with emotions and the limbic system
- Major part of the reward pathway
- Cerebellum
  - Slower reaction times in marijuana users probably due to this
- Few cannabinoid receptors found in the brainstem
  - Probably why physical overdose is rare with marijuana

Why the munchies?
- Probably due to the hypothalamus
- Food taste does not change
  - Users may just pay more attention to the specific properties of the food that they are eating
- Recent dietary drugs try to block cannabinoid receptors in the hypothalamus
  - Acomplia
Mental Effects

- Regulates pain
- Gives a feeling of detachment
- Exaggerates mood
- Probably due to the effects on the amygdala

A sense of novelty

- Boring objects seem interesting
- Normally
  - When you encounter an unknown object, anandamides are released
  - THC causes this to happen when the object isn’t unknown
  - Cells react by becoming less responsive
  - Causes even new things to become boring because the body doesn’t respond like it should

Long term marijuana effects

- Lower activity overall

Presence and severity of characteristic withdrawal symptoms

- Reinforcement: A measure of the addictive ability, in human and animal tests, of a substance to enable the user to take it again and again, and its preference to other substances.
- Tolerance: How much of the substance is needed to satisfy cravings over time, and the level of tolerance is eventually reached.
- Dependence: How difficult it is for users to stop using the substance, and the degree of craving and the level of biological need that is eventually reached.
- Intoxication: Associated with addiction and increases the personal and societal damage a substance may do.


Herbal Treatments