Neurobiology of Addiction: *the rewired system*.

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Post Acute Withdrawal Syndrome is a framework that helps explain the Biological changes people go through in recovery.

This allows the Therapist to explain how the brain and biology relate to what the client feels.

Thoughts…Feelings…Actions

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Post Acute Withdrawal Syndrome

Racing Thoughts	Frustration	Sleep Disorders
Confusion	Moodiness	Exhaustion
Easily Overloaded	Pink Cloud	Pain Issues
Memory Problems	Anger	Over/Under Eating
Loss of Skills	Anxiety	Digestion Issues
Obsession	Hopeless	Accident Prone
Distractibility	Depression	Compulsive Actions
Dissociation	Alexithymia	Agitation

Why are these symptoms grouped this way?

What do all these things have in common?

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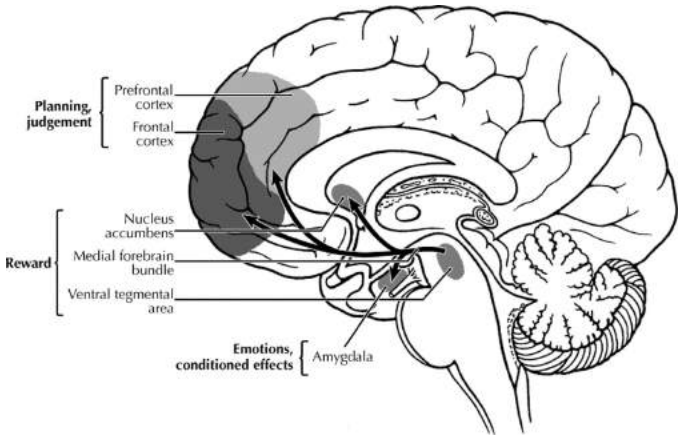
- The Brain Is…Biological



Yes…you really need to know these parts of the brain.
The Reward System, where addiction starts.

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There are many myths about the brain.

- **'We only use only 10% of our brain.'**
  There is no scientific basis for this assertion. This misconception most likely arose from a misunderstanding of neurological research in the late 1800s and early 1900s when researchers either discovered that only about 10% of the neurons in the brain are firing at any given time and announced that they had only mapped the functions of 10% of the brain up to that time. Another possible origin of the misconception is that only 10% of the cells in the brain are neurons; the rest are *glial cells* that, despite being involved in learning, do not function in the same way that neurons do.

- **'Someplace in our brain we remember everything that ever happened to us.'**
  There is no proof we can remember that much. We have plenty of proof that we forget, permanently, lots of thing. We also have good proof that when we recall memories we are *re-writing and changing* those memories each time we access them. There *are a few* people who have Hyperthymesia, an extraordinary recall for most of the events in their lives.

- **'We don't really know how the Brain works.'**
  We understand very well how the major areas and functions of the brain work. We know how most of those interact and we are quickly learning the fine details about the remaining areas. We know a huge amount about how individual neurons work.

Please do not state *myths* to your clients as *facts*.
That is malpractice!

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And some more myths about the brain.

- **'We kill thousands of Brain cells when we drink alcohol (use drugs).'**
  It is very hard to examine the effects of drug abuse on a living brain. We have to rely on scanning and other non-invasive techniques. While we can see more and less activation in some areas due to substance abuse we cannot accurately say how many nerve cells are being damaged or destroyed.

- **'I'm a left/right brain thinker.'**
  Some mental functions such as speech and language tend to be localized to specific areas in one hemisphere. If one hemisphere is damaged at a very early age, however, these functions can often be recovered in part or even in full by the other hemisphere. Other abilities such as motor control, memory, and general reasoning are spread equally across the two hemispheres.

- **'Once you are an adult you don't get new brain cells, they only die as you get older.'**
  In fact, new neurons can grow within the mature adult brain; this process is known as neurogenesis. The scientific consensus, however, is that neurogenesis only occurs in the hippocampus and the olfactory bulb (and maybe Cerebellum). Regardless of neuron growth or death, brain *function* and capabilities can be learned and developed throughout life.

Please do not state *myths* to your clients as *facts*.
That is malpractice!

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Human Brain: Facts, Anatomy & Mapping Project

by Tanya Lewis, LiveScience Staff Writer

Date: 06 May 2013 Time: 06:28 PM ET

– **Brain mapping project**

- In April 2013, President Barack Obama announced a new research program known as the *Brain Research through Advancing Innovative Neurotechnologies* (BRAIN) Initiative, which will provide $100 million in funding starting in 2014 to map the structure and function of the human brain.
- Sometimes called the Brain Activity Map, the project has been planned for some time. In June 2012, six scientists put forth general proposals for developing sensors and protocols for experimenting on single cells within neural networks. Obama first referenced the project in his 2013 State of the Union address in February, and in March 2013, the project's backers outlined their goals in the journal Science, calling for a sustained effort over several years to create tools to understand how brain networks function.
- Supporters of the project argue that it will provide the missing piece in how the brain operates at a level between that of single neurons and the whole brain.

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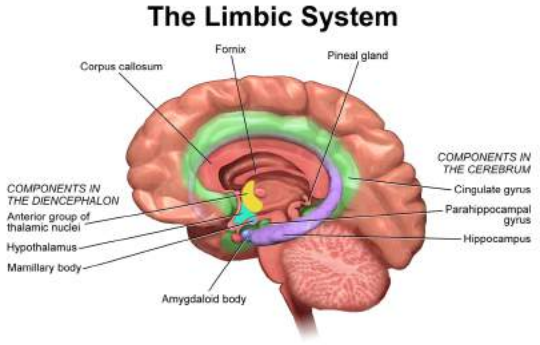
The Reward System is several different structures deep in the brain between the top of the spinal cord and the Cerebrum (the big part of the rest of the brain). It manages many different basic functions like hunger, thirst, sleep, sex, motivation, and rewarding successful behaviors. It also regulates our emotions and attaches emotions to memories.

The Reward System is part of the Limbic System, which manages all of the above as well as many of the basic operations of our brains that are below our level of awareness and control. These are deep structures that are shared by all mammals, and run the basic functions needed to keep us alive. Elephants, mice, whales, marmosets, dogs, whatever, all have these structures in their brains. Non-mammals do have similar structures as well.



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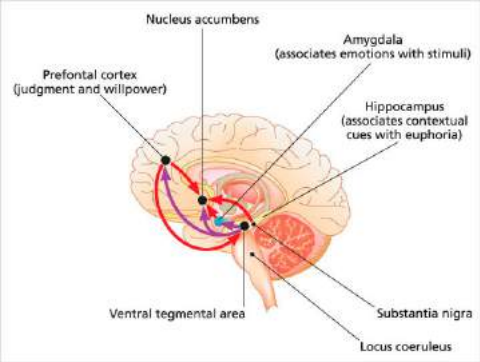
Why a Reward System.

Rewards come from different sources…

Natural Rewards
- Food
- Water
- Nurturing
- Sex



Natural Rewards stimulate the Reward System of the Brain. That system tells us what feels good or relieves a need, and makes us want to *repeat the same behavior* when needed to relieve the need again (**Reinforcement**). When things don't feel good, we don't *usually* repeat the behavior.

This is real important; if we didn't have a reward system there could be no such thing as addiction.

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Addiction

- A state in which an organisms engages in repeated, compulsive behaviors.
- The behaviors are Reinforced by the brain. (Labeled as Pleasurable, or they relieve Displeasure such as Anxiety or Withdrawals.)
- There is a *loss of control* in limiting the behaviors despite damage to the organism.

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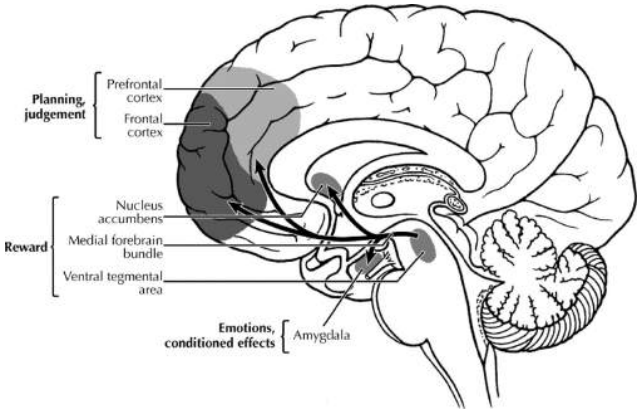
The Reward System cannot use words to communicate with the rest of the brain. **It uses feelings and emotions**. Feelings like Hunger, Craving, Pain and Fear are the ways the it tries to influence us to satisfy it. It will send a ***craving*** for the drug, or the gambling, or whatever to the Frontal Lobes of the brain, our center for planning and judgment. It uses the only language it has, feelings. This is why addicts may have trouble finding words to describe what they are going through. The Reward System has been rewired and is now an **Addiction System**(copyright).



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Time to talk about Vocabulary. You really need to know these words and get comfortable using them all the time. These are the words of our profession.

- Central Nervous System (CNS)
- Frontal Lobes
- Neuron
- Axon
- Dendrite
- Synapse
- Receptor Site
- Neurotransmitter
- Reuptake
- Addiction
- Post Acute Withdrawal Syndrome (PAWS)
- Harm Reduction
- Reward System
- Reinforcement
- Extinguish
- Synaptic Pruning
- Neuroplasticity

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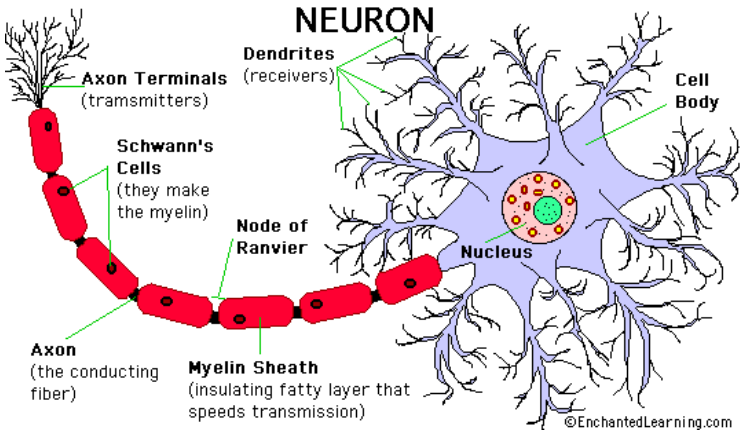
Neuroplasticity

- The ability of the brain to continually rewire itself through changes in Synapses, Neural pathways and Neural Networks. These changes are ongoing and are from numerous causes. Changes in behavior, environment, thinking, emotions, as well as bodily injury lead to changes in the neural networks. Recovery from Stroke damage is a good example of Neuroplasticity.
- A 2005 study found that the effects of neuroplasticity can occur rapidly. Medical students' brains were imaged during the period when they were studying for their exams. In a matter of months, the students' gray matter increased significantly in the posterior and lateral parietal cortex.
- Drug addiction and obsessive-compulsive disorder are deemed examples of "negative plasticity" as the synaptic rewiring resulting in these behaviors is highly maladaptive and difficult to change.
- A surprising consequence of neuroplasticity is that the brain activity associated with a given function can move to a different location; this can result from normal experience and also occurs in the process of recovery from brain injury.
- "neurons that fire together, wire together, neurons that fire apart, wire apart,"

But what are these Systems made from? *Really tiny parts*. Neurons!



One Hundred Million Neurons in One Cubic Milliliter of Brain.
86 Billion Neurons in the total Human Brain.

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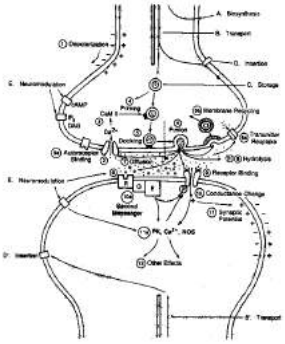
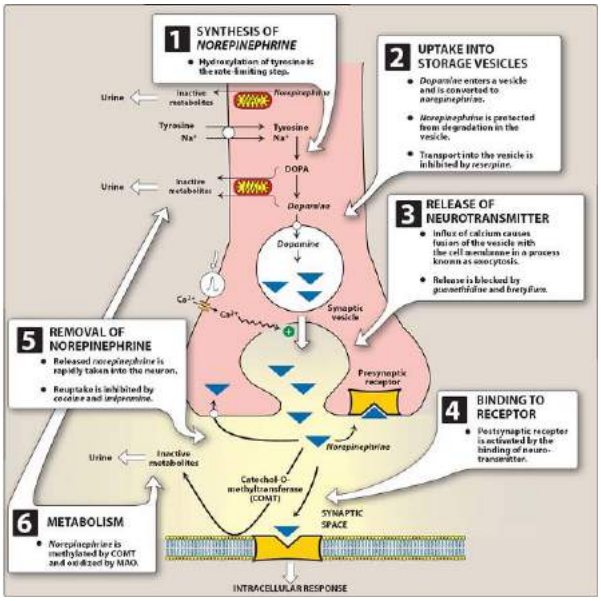
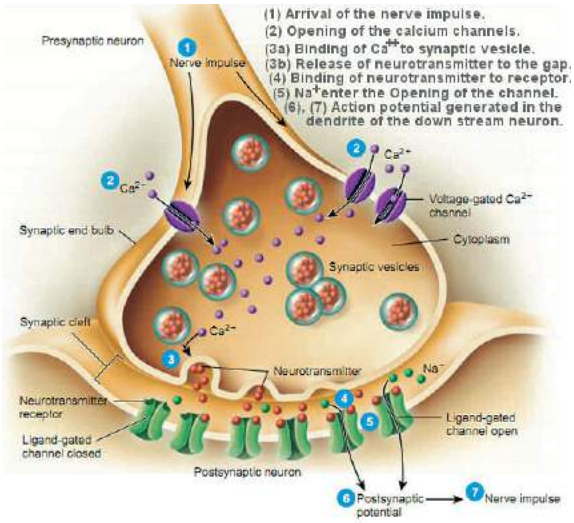
Synapses



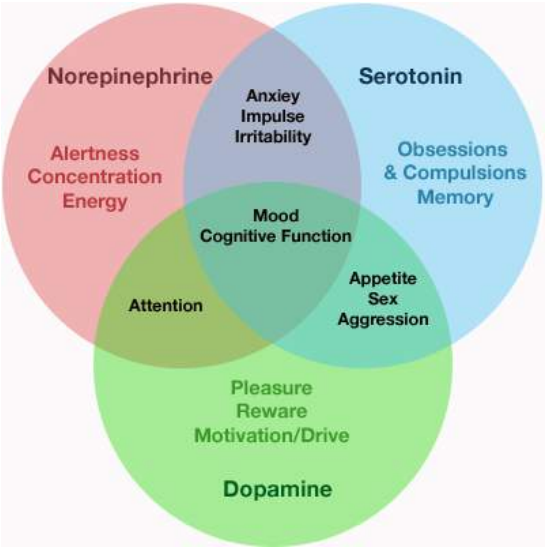


Which are understood in great detail.

Simpler can be better. The basic structure of a synapse, the connection between two neurons.



Lets get back to the basics…



Neurons talk to each other using chemicals at their Synapses.

Neurotransmitters

Here's how three important Neurotransmitters may interact to create our moods.

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We have lots of Neurotransmitters. No, don't try to memorize these.

Small Molecule Neurotransmitter Substances.	Acetylcholine (ACh)	Dopamine (DA)	Norepinephrine (NE)	
	Serotonin (5-HT)	Histamine	Epinephrine	
Amino Acids	Gamma-Aminobutyric acid (GABA)	Glycine	Glutamate	
	Aspartate			
Neuroactive Peptides –it's a partial list.	bradykinin	beta-endorphin	bombesin	calcitonin
	cholecystokinin	enkephalin	dynorphin	insulin
	gastrin	substance P	neurotensin	glucagon
	secretin	somatostatin	motilin	vasopressin
	oxytocin	prolactin	thyrotropin	angiotensin II
	sleep peptides	galanin	neuropeptide Y	thyrotropin-releasing hormone
	gonadotropins-releasing hormone	growth hormone-releasing hormone	luteinizing hormone	vasoactive intestinal peptide
Soluble Gases	Nitric Oxide (NO)	Carbon Monoxide		

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More about Neurotransmitters.

- Different types of cells secrete different neurotransmitters. Each brain chemical works in widely spread but fairly specific brain locations and may have a different effect according to where it is activated. Some 60 neurotransmitters have been identified and many more suspected, but some of the most important, seem to be:
- **Dopamine**
- Controls arousal levels in many parts of the brain and is vital for giving physical motivation. Your ability to generate ideas and take action is regulated by dopamine. Dopamine is the master power switch controlling our drive to pursue life and all it has to offer. Abundant dopamine in the brain gives you a feeling that you can do anything and feelings of euphoria. When levels are severely depleted, as in Parkinson's disease, people may find it impossible to move voluntarily. Drugs of addiction tend to increase levels of dopamine.
- **Serotonin**
- Serotonin is key to regulating sleep, appetite, happiness, sexual arousal and very important for regulating emotions. It helps defend against both anxiety and depression. Shortages of serotonin can cause depressed moods, anxiety, panic attacks, low energy, migraines, sleeping problems, obsession or compulsions, irritability, sweets cravings, and reduced sex drive. This is the neurotransmitter enhanced by Prozac, and has thus become known as the 'feel-good' chemical. It has a profound effect on mood and anxiety -- high levels of it, or sensitivity to it, are associated with serenity and optimism.
- **Acetylcholine (ACh)**
- This plays an essential role in enabling us to learn and remember. Acetylcholine helps regulate the plasticity of our neural network. It helps manage how our brain re-wires connections between neurons in response to new activities and experiences. People with Alzheimer's disease typically have low levels of ACh, and drugs that boost its action may improve their memory.
- **Adrenalin and Noradrenalin**
- Mainly excitatory chemicals that induce attention, mental focus, physical/mental arousal, and cognition. When levels are too low in the brain, you can experience fatigue, lack of focus, and low motivation. Production is centered in an area of the brain called the Locus Coeruleus, which is one of several components of the brain's 'pleasure' center.
- **GABA (Gamma Aminobutyric acid)**
- The chief inhibitory neurotransmitter in the CNS. It plays a role in regulating Neuron excitability throughout the nervous system; similar to the brakes on a car it can slow things down.
- **Glutamate**
- The brain's major excitatory neurotransmitter, vital for forging the links between neurons that are the basis of learning and long-term memory. Makes it more likely any neuron affected will send a signal. Can be thought of as a gas pedal for the brain.
- **Enkephalins and Endorphins.**
- These are internal opioids that, like the drugs heroin and morphine, modulate pain, reduce stress and promote a sensation of floating, oceanic calm. They also depress physical functions like breathing and may produce physical dependence.

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There are many ways that a drug can act to enhance (**Agonize**) a given neurotransmitter:

An **agonistic drug** can increase the production of particular neurotransmitters. When those neurotransmitters are then released into the synapse, they are more numerous than they would normally be, and more of the neurotransmitter molecules find their way over to the post-synaptic receptors on the dendrites of the next neuron (L-Dopa and L-Tryptophan).
An **agonistic drug** can interfere with the re-uptake of neurotransmitter molecules which has the effect of forcing them to remain in the synapse and interacting with receptors longer than normal (an excellent example is Cocaine).
An **agonistic drug** can bypass the neurotransmitter entirely, and simply float out into the synapse and itself bind with and activate the neurotransmitter's receptors (Heroin).

Similarly, there are many ways that a drug can act to interfere with (**Antagonize**) a given neurotransmitter:
An **antagonistic drug** can interfere with the release of neurotransmitters into the synapse. (Alcohol suppresses Glutamate and increases the effect of GABA).
An **antagonistic drug** can compete with the neurotransmitter for binding to the neurotransmitter's receptor. The antagonistic drug binds to the receptor but does not activate it, thus *blocking* receptors from being activated by the neurotransmitter (Naloxone/Narcan).
An **antagonistic drug** can causes neurotransmitters to leak out of their containers in the terminal button, into the fluid of the pre-synaptic neuron itself, making the neurotransmitter substance unavailable for release into the synapse. When the neuron is activated, there is less neurotransmitter available to be released into the synapse (Reserpine).

Most of the drugs that get abused are **agonists** of various neurotransmitters - they work to enhance the natural effect of neurotransmitters.

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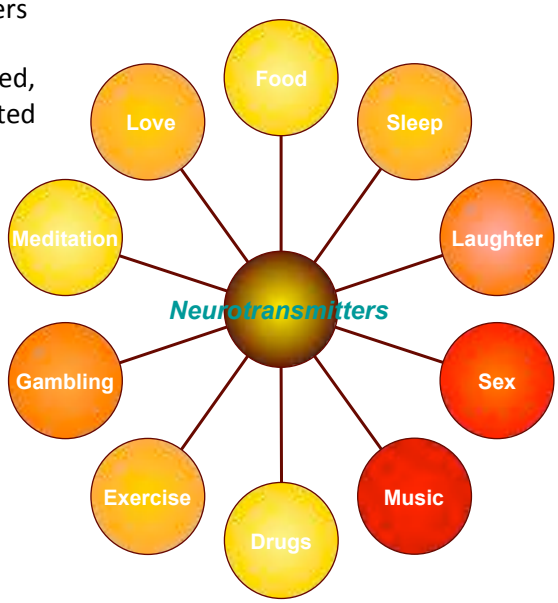
Neurotransmitters are released, enhanced, reduced, imitated or affected by…



Everything we experience is because of, and affects, our Neurotransmitters.

All of our reality is a dance of chemicals in our brain.

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Addiction

A state in which an organisms engages in a repeating, compulsive behavior.

The behavior is initially reinforcing.	"Wow…that was great!" "Thank god…my anxiety is going away!"
There is a loss of control in delaying or offsetting the behavior.	"Just one more hit." "Of course I can stop anytime I want." "This machine is ready to pay off."
The behavior is often continued when there is no further reinforcement.	"I musta got some bad stuff." "I don't get why I keep using, I don't even like it anymore."
The behavior is often continued to the point of damaging or destroying the organism.	"My wife left me, I'm going to jail and my liver is shot…but I can stop anytime I want to."

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Alcohol

CH3CH2OH

•Alcohol affects the brain's neurons in several ways. It alters their membranes as well as their ion channels, enzymes, and receptors. Alcohol also binds directly to the receptors for **acetylcholine, serotonin, GABA**, and the NMDA receptors for **glutamate**.

•**GABA**'s effect is to reduce neural activity by allowing chloride ions to enter the post-synaptic neuron. These ions have a negative electrical charge, which helps to make the neuron less excitable. This physiological effect is amplified when alcohol binds to the GABA receptor, probably because it enables the ion channel to stay open longer and thus let more Cl- ions into the cell.

•The neuron's activity would thus be further diminished, this explains the sedative effect of alcohol. This effect is accentuated because alcohol also reduces glutamate's excitatory effect on NMDA receptors.

•However, chronic consumption of alcohol gradually makes the NMDA receptors hypersensitive to glutamate while desensitizing the GABAnergic receptors. It is this sort of adaptation that would cause the state of excitation, up to seizures, characteristic of alcohol withdrawal.

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Endorphins

- At least 20 types of endorphins have been demonstrated in humans. Endorphins can be found in the pituitary gland, in other parts of the brain, or distributed throughout the nervous system.
- Stress and pain are the two most common factors leading to the release of endorphins. Endorphins interact with the opiate receptors in the brain to reduce our perception of pain and act similarly to drugs such as morphine and codeine. In contrast to the opiate drugs, however, activation of the opiate receptors by the body's endorphins does not lead to addiction or dependence.
- In addition to decreased feelings of pain, secretion of endorphins leads to feelings of euphoria, modulation of appetite, release of sex hormones, and enhancement of the immune response.

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Opiates

- The reason that opiates such as heroin and morphine affect us so powerfully is that these ***exogenous*** substances bind to the same receptors as our ***endogenous*** opioids. There are many kinds of opiate receptors widely distributed throughout the brain.
- These receptors, through second messengers, influence the likelihood that ion channels will open, which in certain cases reduces the excitability of neurons. This reduced excitability is the likely source of the euphoric effect of opiates.
- This euphoric effect also appears to involve another mechanism in which the GABA-inhibitory interneuron's of the **ventral tegmental area** come into play. By attaching to their receptors, exogenous opioids reduce the amount of GABA released.
- Normally, GABA reduces the amount of dopamine released in the **nucleus accumbens**. By inhibiting this inhibitor, the opiates ultimately increase the amount of dopamine produced and the amount of pleasure felt.

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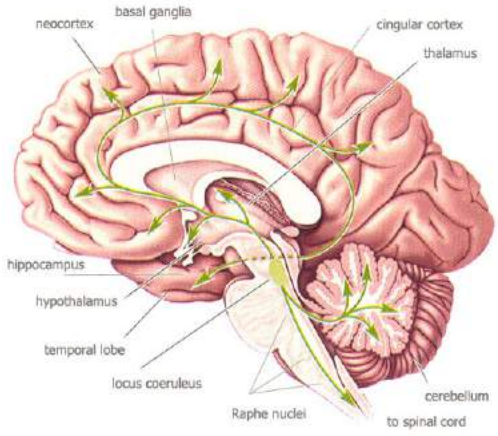
The Locus Coeruleus is one of the centers of brain activation. It is intimately connected to PTSD and Opiate withdrawals. Opiates inhibit the firing of neurons in the locus coeruleus. When opioid consumption is stopped, the increased activity of the locus coeruleus contributes to the symptoms of opiate withdrawal. The alpha2 adrenoceptor agonist Clonidine is used to counteract this withdrawal effect by decreasing adrenergic neurotransmission from the locus coeruleus.



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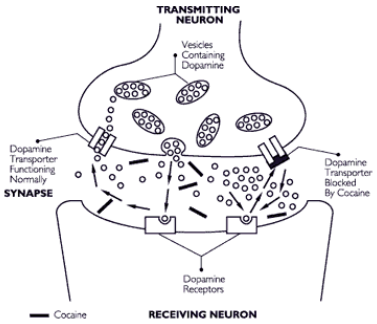
Cocaine



- Cocaine acts by blocking the reuptake of certain neurotransmitters such as **dopamine**, **norepinephrine**, and **serotonin**. By binding to the transporters that normally remove the excess of these neurotransmitters from the synaptic gap, cocaine prevents them from being reabsorbed by the neurons that released them and thus increases their concentration in the synapses. As a result, the natural effect of dopamine on the post-synaptic neurons is amplified.
- The group of neurons thus modified produces the euphoria (from dopamine), feelings of confidence (from serotonin), and energy (from norepinephrine) typically experienced by people who take cocaine.
- Because the norepinephrine neurons in the **locus coeruleus** project their axons into all the main structures of the **forebrain**, the powerful overall effect of cocaine can be better understood.
- The **Ventral Tegmental Area (VTA) creates the impulse to repeat the behavior**. This is where the "craving" comes from.

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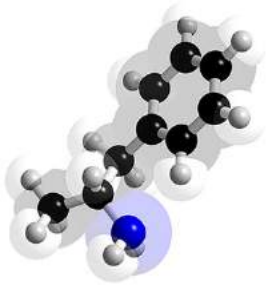
Amphetamines



C9H13N

- Like cocaine, amphetamines increase the concentration of **dopamine** in the synaptic gap, but by a different mechanism. Amphetamines are similar in structure to dopamine, and so can enter the terminal button of the presynaptic neuron via its dopamine transporters as well as by diffusing through the neural membrane directly. Once inside the presynaptic neuron, amphetamines force the dopamine molecules out of their storage vesicles and expel them into the synaptic gap by making the dopamine transporters work in reverse.
- Amphetamines also seem to act by several other mechanisms. For example, they seem to reduce the reuptake of dopamine and, in high concentrations, to inhibit monoamine oxydase A (MAO-A).
- Amphetamines may also excite dopaminergic neurons via glutamate neurons. Amphetamines would thus remove an inhibiting effect. By thus releasing this natural brake, amphetamines would make the dopaminergic neurons more readily excitable.

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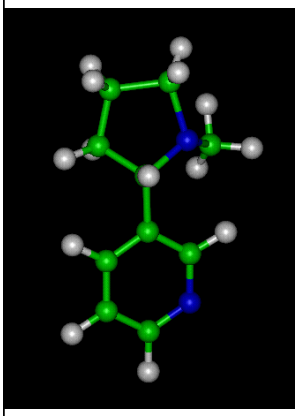
Nicotine



The chemical formula for nicotine is C10H14N2

- Nicotine imitates the action of a natural neurotransmitter called **acetylcholine** and binds to a particular type of acetylcholine receptor, known as the nicotinic receptor.
- Whether it is acetylcholine or nicotine that binds to this receptor, it responds in the same way: it changes its conformation, which causes its associated ion channel to open for a few milliseconds. This channel then allows sodium ions to enter the neuron, depolarizing the membrane and exciting the cell. Then the channel closes again, and the nicotinic receptor becomes temporarily unresponsive to any neurotransmitters. It is this state of desensitization that is artificially prolonged by continual exposure to nicotine.
- Tobacco dependency, which then develops very quickly, arises because nicotinic receptors are present on the neurons of the **ventral tegmental area** which project their terminations into the nucleus accumbens. In smokers, repeated nicotine stimulation thus increases the amount of **dopamine** released in the **nucleus accumbens**.

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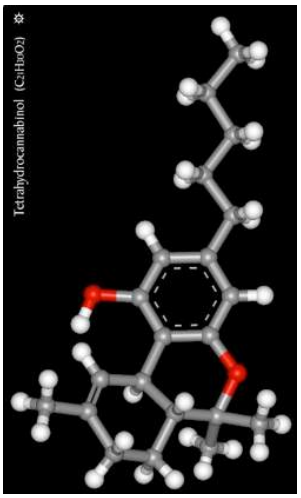
Cannabis



- **Cannabinoid receptors** are present almost everywhere in the brain, and an endogenous molecule that binds to them naturally has been identified: **anandamide**. We are thus dealing with the same kind of mechanism as in the case of opiates that bind directly to the receptors for endorphins, the body's natural morphine.
- Anandamide is involved in regulating mood, memory, appetite, pain, cognition, and emotions. When cannabis is introduced into the body, its active ingredient, **Delta-9-tetrahydrocannabinol (THC)**, can therefore interfere with all of these functions.
- THC begins this process by binding to the CB1 receptors for anandamide. These receptors then modify the activity of several intracellular enzymes, including cAMP, whose activity they reduce. Less cAMP means less protein kinase A. The reduced activity of this enzyme affects the potassium and calcium channels so as to reduce the amount of neurotransmitters released. The general excitability of the brain's neural networks is thus reduced as well.
- However, in the reward circuit, just as in the case of other drugs, more dopamine is released.

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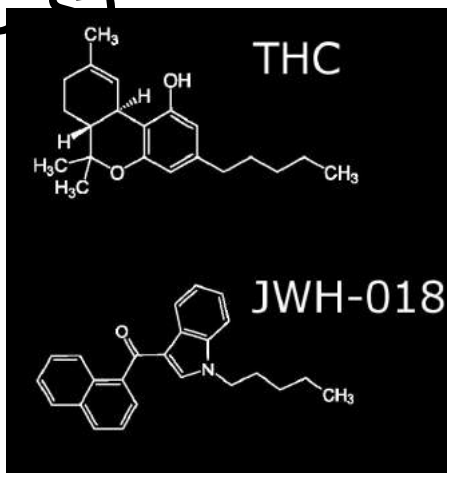
K2 (Synthetic THC's)

- K2 products are synthetic cannabinoid-laced, marijuana-like drugs of abuse, use of which is often associated with clinical symptoms atypical of marijuana use, including hypertension, agitation, hallucinations, psychosis, seizures and panic attacks. JWH-018, a prevalent K2 synthetic cannabinoid, is structurally distinct from Δ^9-THC, the main psychoactive ingredient in marijuana. Since even subtle structural differences can lead to differential metabolism, formation of novel, biologically active metabolites may be responsible for the distinct effects associated with K2 use.



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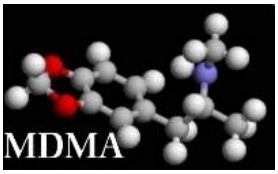
Ecstasy



- Ecstasy (MDMA) is a synthetic drug. It acts simultaneously as a stimulant and a hallucinogen because of its molecular structure, which is similar to that of both amphetamines and LSD. Like amphetamines and cocaine, ecstasy blocks the reuptake pumps for certain neurotransmitters, thus increasing their levels in the synaptic gap and their effect on the post-synaptic neurons' receptors.
- While ecstasy also potentiates the effects of **norepinephrine** and **dopamine**, it is distinguished from other psychostimulants by its strong affinity for **serotonin** transporters. The initial effect of ecstasy is thus an increased release of serotonin by the serotonergic neurons. The individual may then experience increased energy, euphoria, and the suppression of certain inhibitions in relating to other people.
- A few hours later, there is a decrease in serotonin levels. This decrease can last much longer than the initial increase. Once again, an artificial increase in the level of a neurotransmitter exercises negative feedback on the enzyme that manufactures it. As a result, when intake of the drug ceases, the excess turns into a shortage.
- Like all psychoactive drugs that produce a sensation of pleasure, ecstasy also increases the release of dopamine into the **reward circuit**.

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PCP C17H25N Part 1

- PCP affects several major neurotransmitter systems, resulting in many different internal and external consequences. Primarily, PCP is a sympathomimetic drug, causing a high, maintained level of sympathetic nervous system activity (the flight or fight response). Sympathetic activation, though, is also the reason why patients became "unmanageable". The reason for the sympathetic reaction is an increased level of norepinephrine (NE), caused by the blocking of NE reuptake into the presynaptic neuron. In addition to activating the sympathetic reaction, increased NE helps stimulate the reward center of the brain. It also contributes to an irritable mood, heightened general arousal, heightened anxiety, and heightened senses of panic.
- At the same time the sympathetic system is being activated, the parasympathetic system (responsible for relaxation) is inhibited by a decrease in acetylcholine (Ach). The blocked parasympathetic reaction allows high levels of arousal to be maintained without interruption. In addition, decreased Ach levels contribute to increased muscular rigidity, dilated pupils, disorientation and confusion, and amnesia.
- The dopamine (Da) system is also effected. The reuptake of Da is blocked by PCP, and Da levels rise. High levels of Da cause the expansive mood, dissociation, hallucination, and psychosis involved in a PCP high. High levels of Da also are at the root of schizophrenia, hence the similarity of a PCP high to schizophrenic symptoms. Excess Da also creates a risk for seizures and convulsions. High Da levels also have a negative effect on coordination and movement, affecting the nigrostriatal pathway for movement (PCP can remain in the substantia nigra for over three weeks (Palfai & Jankewicz, 1991)). Dopamine is also the foremost neurotransmitter involved in the reward center of the brain through the mesolimbic pathway. Interestingly, monkeys will seek PCP reinforcement just as much as they will seek reinforcement from cocaine or amphetamines (Ray & Ksir, 1999). Other hallucinogens will not support animal self-administration like PCP will. Hence, PCP generates psychological dependence, and uniquely so.

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PCP C17H25N Part 2

- Levels of serotonin also rise under the effects of PCP, though it the exact cause for this is undetermined (it does not seem that the reuptake is blocked) Due to increased serotonin levels, PCP highs do not involve any sleep. Increased serotonin also leads to increased confidence, expansive mood, and delusions involved with the schizophrenic-like symptoms observed in the PCP high. High levels of serotonin are believed to be partially involved in schizophrenia (*American Family Physician*, 1985).
- New discoveries show that the receptors for the neurotransmitter glutamate are the primary sites of action for PCP. There appears to be an endogenous PCP-like substance that PCP, when administered, throws out of balance. The receptor site at which glutamate and PCP are involved is the NMDA (N-methyl-D-aspartate) receptor. PCP acts as an NMDA antagonist, lowering the levels of glutamate in the brain. Lower levels of glutamate add to, and are possibly the most responsible for, the schizophrenic like symptoms of a PCP high.
- The level of GABA, an "inhibitory" neurotransmitter, is raised through its reuptake being blocked by the effects of PCP. Increased levels of GABA are responsible for the inhibition of pain associated with the PCP high. GABA works on the same receptor complex as alcohol and benzodiazepines, and therefore, is responsible for PCP's alcohol-like effects. This is the same reason, though, that there is a deadly synergistic effect between PCP, alcohol, and benzodiazepines. This synergy is the leading cause of PCP overdose.
- Finally, the levels of endorphins are also raised by PCP. Endorphins are the body's natural opiates, creating pleasure. Endorphins also work to mask pain. The absence of pain in a PCP high is one of the most important factors in PCP's risk for behavioral toxicity.

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Benzodiazepine

- Benzodiazepines, such as diazepam (Valium) and clonazepam (Rivotril) are anxiolytics that can also have hypnotic or amnesia-inducing effects. Like alcohol, these drugs increase the efficiency of synaptic transmission of the neurotransmitter **GABA** by acting on its receptors.
- A GABA receptor is actually a macromolecular complex that, in addition to containing sites for binding GABA, also contains sites for binding other molecules such as benzodiazepines that modulate GABA's activity.
- When benzodiazepines bind to a specific site on a GABA receptor, they do not stimulate it directly. Instead, they make it more efficient by increasing the frequency with which the chlorine channel opens when GABA binds to its own site on this receptor. The resulting increase in the concentration of Cl- ions in the post-synaptic neuron immediately hyperpolarizes this neuron, thus making it less excitable.

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Gambling Addiction

- **Serotonin** in the cerebral spinal fluid of problem gamblers is a little deficient from that of people who don't have a gambling addiction. The SSRIs [selective serotonin reuptake inhibitors] are medications that affect serotonin, which are most popularly the antidepressants: Prozac, Paxil. These have shown benefit in gambling addiction. So serotonin may have something to do with gambling addiction.
- Neurotransmitters don't act alone, they act in concert with each other. **Dopamine** is associated with rewarding experiences. When researchers looked again at cerebral spinal fluid dopamine seemed to be a little deficient compared to people who don't have a gambling addiction.
- Most interesting is the case of Parkinson's disease. Parkinson's represents depleted dopamine, so when these patients take medications that increase dopamine, many of them developed a gambling addiction, even people who have never gambled before. An intriguing concept. Why is this?
- **Bupropion** is a medication with a dopamine effect—it's also called Wellbutrin and Zyban. It's used to treat smoking problems. It has also been shown in some early studies to be effective against gambling addiction.
- And then last are **endorphins**, the opiate system of the brain, which gets revved up and tells us something's pleasurable. We've found out that when you look at different parts of the opiate system, metabolites in the cerebral spinal fluid, again, it's a little out of whack in people who have a gambling addiction. And we have used opiate antagonists, the most widely known being Naltrexone, which is a medication to treat alcoholism and the urges of alcoholism, and we've used that in gambling addiction as well. Some people say that when they are on the medicine they gamble and it isn't any fun any more. They don't get that rush.

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Addictions of Impulse Control?

- In some people with Impulse Control issues the ventral medial prefrontal cortex, which is the front part of the lower part of the brain, does not seem to be as activated, and this is the part of the brain that would say, "Don't do it. Not a good idea." It seems to be less activated in people who have a gambling addiction compared to people who don't have a gambling addiction.
- People who have manic depression, which is an illness partly defined by its impulsivity, tend to have the same finding on fMRI brain scans. That's not to say that they're the same illness, but perhaps the same part of the brain is involved when someone cannot control impulses. You could look at this in terms of sexual addictions and other disorders defined by lack of ability to put off rewards, control impulses.
- Of course gambling, eating and sex all activate the reward system as well. They feel good so we want to do them. Does this mean the reward system is altered in these people as well?

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How To Treat the Re-Wired Brain

Use P.A.W.S. as a framework to explain to your client how to repair the changes they have made to their brain.

Abstain!
Decrease Stress.
Teach Coping Skills.
Let them talk, talk, talk.
Take medications *as prescribed*.
Convince them of the value of Learning!
Reframe their experiences as healthy brain growth.
Use P.A.W.S. as one of your tools to explain things.
Remind them this is all temporary.
Meditation. Diet. Exercise. Sun.
Teach clients how to have fun.
Model ways to Laugh.

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