Sally: 41-year-old female - 80 lbs. overweight (BMI of 32)
She came to our office for help with overeating and depression.

History:

Growing up, Sally's father was an alcoholic and her parents were always arguing, which was extremely stressful. Sally's mother felt horrible about their situation and often gave Sally sugary treats, such as candy or ice cream, to help her feel better amidst the chaos.

Sugar made Sally feel happier, so she continued eating it whenever she felt stressed and/or anxious. She started to gain weight once she had her first child at the age of 26, and the weight gain never stopped.

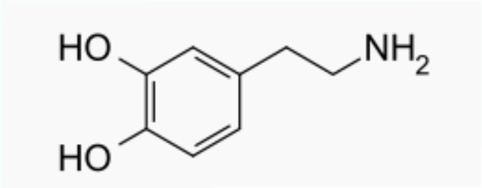
At 40 lbs. overweight, she decided to make some changes. She switched to diet soda, started exercising 3 days per week and drank healthy smoothies for breakfast, but she never lost much weight or felt good about herself. She confessed that she was in the habit of rewarding her exercise efforts with bagels or donuts—just like she had always done. Eventually, she gave up.

Sally told our intake nurse:

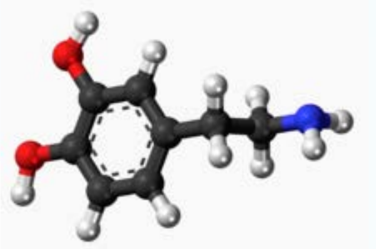
"I am sad every single day and I don't know why. Nothing makes me happy anymore. I never want to leave the house because I just don't have enough energy or motivation. Sometimes I will spend all day planning a sugar binge, which is exciting, but I never actually feel good when I'm done. I feel so empty inside. I want to know why."

Sally has been self-medicating her uncomfortable emotions with food, which has resulted in food addiction and significant downregulation of the D2 dopamine receptors in her brain. Essentially, her brain's pleasure and reward system has been hijacked and can no longer function properly.

The following presentation outlines dopamine function and food-related dopamine downregulation, then ends with suggestions for helping the brain upregulate dopamine receptors once again.



Dopamine Overview



Dopamine is a water-soluble monoamine catecholamine hormone in the same class as epinephrine and norepinephrine.

The precursor for dopamine is the amino acid tyrosine, which is an essential amino acid that must be obtained from the diet.

Dopamine is a major signaling neurotransmitter that helps sustain life by controlling certain life-sustaining behaviors, in addition to involvement in mood, movement and learning.

Activation of dopamine receptors give rise to pleasurable, rewarding feelings associated with goal-directed behaviors, food consumption and drug use; conversely when not stimulated, it motivates seeking behavior.

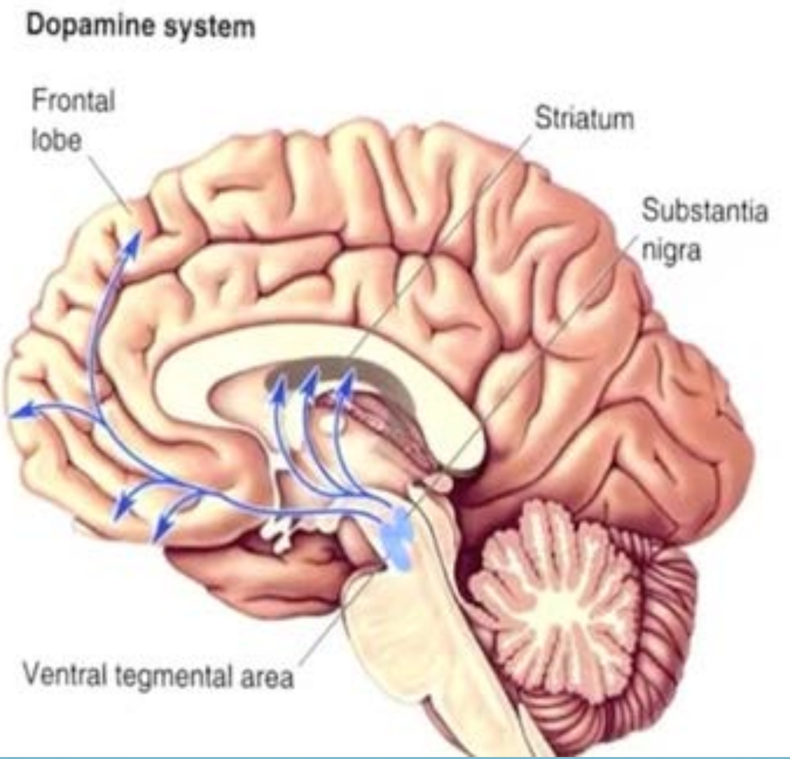
Drugs of abuse—alcohol, cocaine, methamphetamine, heroin, cannabis and even sugar—hijack the reward system, turn a person's needs into drug needs.

Dopamine Reward Pathways

The dopamine reward system originates in the ventral tegmental area (VTA) and substantia nigra, with projections ending in the nucleus accumbens and striatum.

Several inputs feed into this system, including cannabinoid and opiate systems, as well as signaling molecules (insulin and leptin) that are regulated by food consumption.

- **Insulin** is a hormone made by the pancreas, which allows the body to use sugar as energy.
- **Leptin** is a hormone made by adipose cells, which helps regulate energy balance by inhibiting hunger.



The 4 Major Dopamine Pathways

Mesocortical Pathway

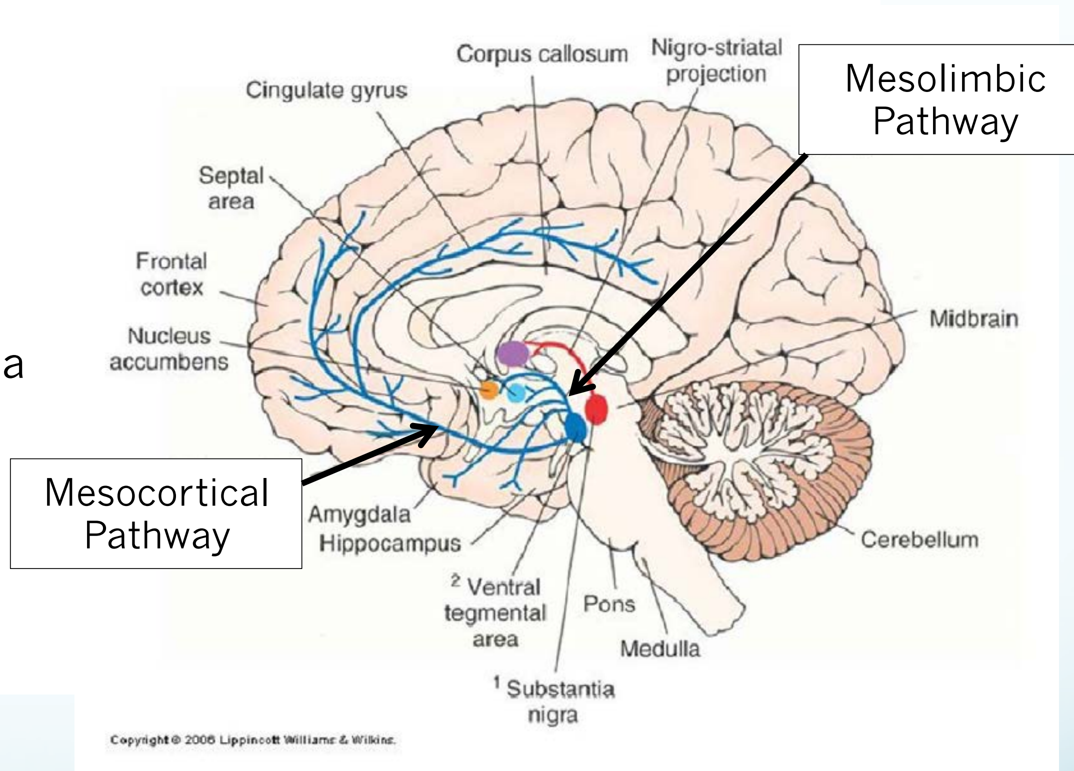
Connects the ventral tegmentum to the frontal lobes of the cerebral cortex (PFC) and is involved in cognitive control (inhibition, focus, attention), learning, memory, motivation and emotional response.

Dysregulation of this pathway is often connected to ADD/ADHD, Schizophrenia and "flat affect," often recognized in Autism Spectrum Disorder.

Mesolimbic Pathway

Also called "the reward pathway," carries dopamine from the VTA to the nucleus accumbens via the amygdala and hippocampus.

Dysregulation of this pathway is most often implicated in addiction.



The 4 Major Dopamine Pathways

Nigrostriatal Pathway

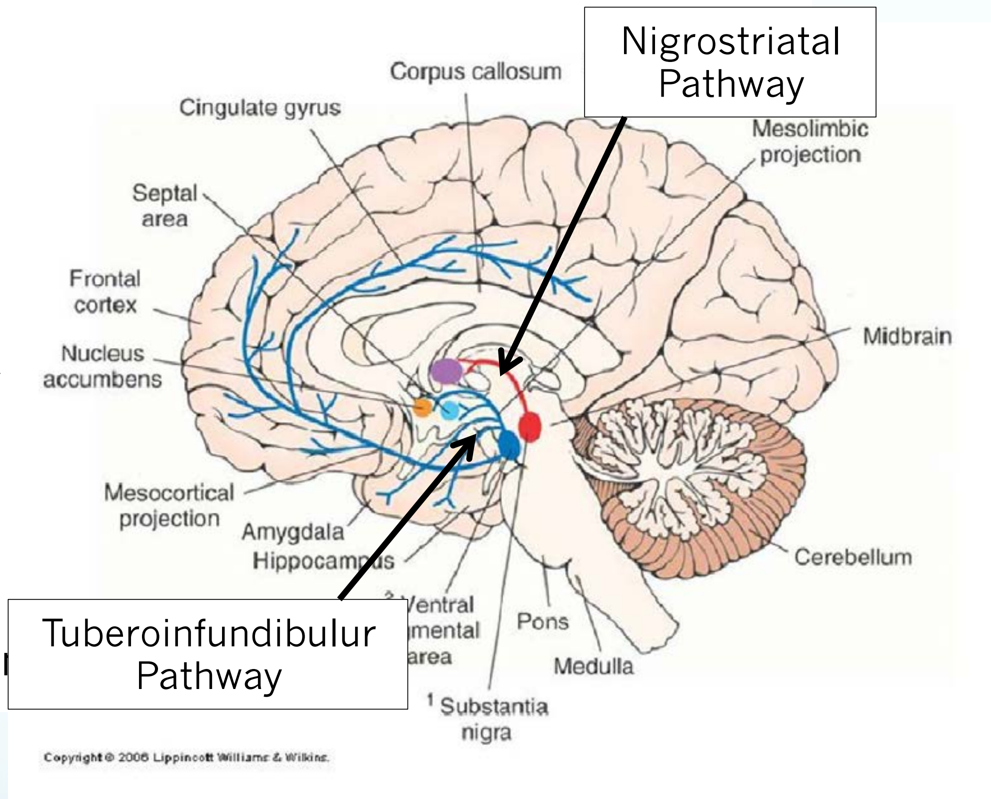
Connects the sustantia nigra with the striatum and is associated with the production of movement and part of the basal ganglia motor loop. DA releasing neurons of this pathway release several other neurotransmitters, including glutamate and GABA.

Loss of dopamine neurons in this pathway is the root cause of Parkinson's Disease.

Tuberoinfundibulur Pathway

A group of dopamine neurons in the infundibulum, which regulates the secretion of prolactin from the adenohypophysis.

Dysregulations in this pathway are associated with male lactation, sexual dysfunction and menstrual cycle disruption, just to name a few.



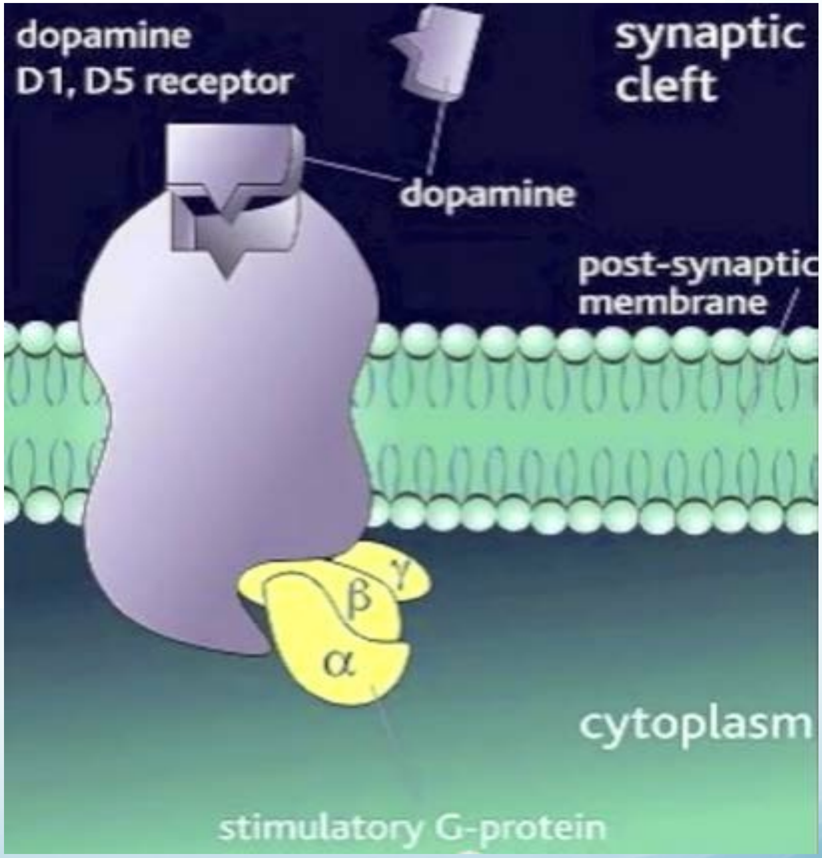
The 5 Types of Dopamine Receptors

There are two families of receptors: D1-like and D2-like, which function in somewhat of an inverse relationship: stimulatory and inhibitory.

D1-like family - *stimulatory*

Activation of D1-like receptors is coupled to G protein, which activates adenylyl cyclase, increasing the intracellular concentration of cAMP.

Includes D1 (along with D2, most prevalent in the brain) and D5



The 5 Types of Dopamine Receptors

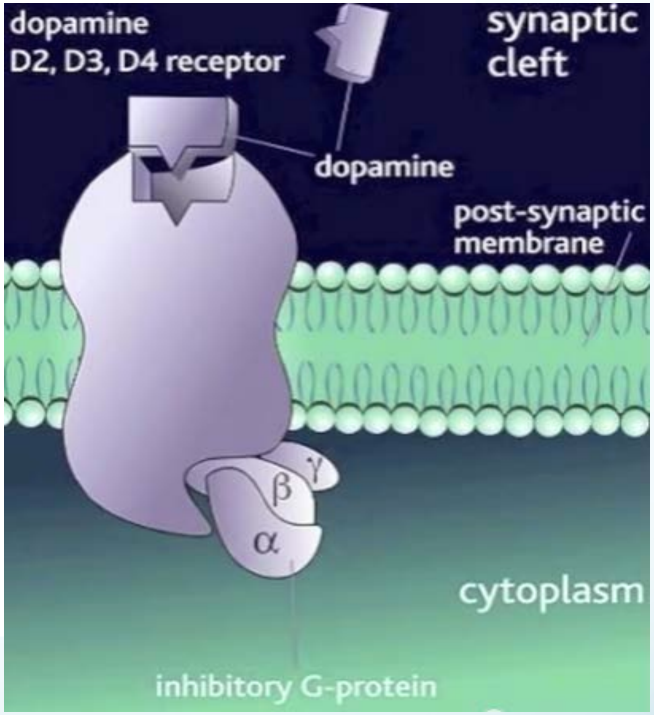
There are two families of receptors: D1-like and D2-like, which function in somewhat of an inverse relationship: stimulatory and inhibitory.

D2-like family - *inhibitory*

addiction dysregulation occurs in D2 receptors (mostly)

Activation of D2-like receptors is coupled to G protein, which inhibits the formation of cAMP by inhibiting adenylyl cyclase.

> **D2***short* **is pre-synaptically situated**, with modular functions—autoreceptors—that regulate neurotransmission via feedback mechanisms. **Affects synthesis, storage and release of dopamine into the synaptic cleft.**
>
> **D2***long* **may function as a post-synaptic receptor**, transmitting information in either an excitatory or inhibitory fashion, unless blocked by a receptor antagonist (cocaine) or a synthetic partial agonist (Abilify).



D2 (and D1) are the most prevalent receptors

D3, D4, D5 are considerably more restricted and weaker than that of D1 and D2

D3 – maximum expression noted in the islands of Calleja and nucleus accumbens.

D4 – receptor gene that displays polymorphisms that differ within the coding sequence of exon 3. Some alleles are associated with great incidence of certain disorders, such as the D4.7 in ADHD.

Movement of Dopamine

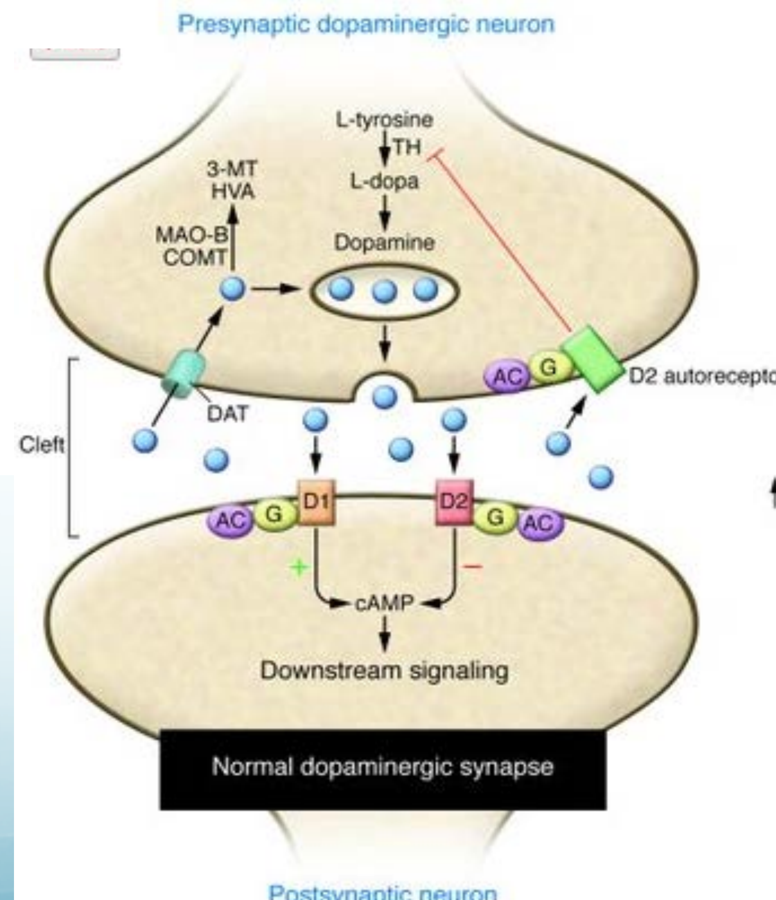
After dopamine is synthesized, it is stored in the synaptic vesicles where it awaits an action potential (influx of calcium ions) to arrive in the terminal for release of dopamine into the synapse via exocytosis.

(Several thousand molecules of dopamine are stored in each synaptic vesicle… normally.)

After release, dopamine interacts with dopaminergic receptors on the postsynaptic neuron.

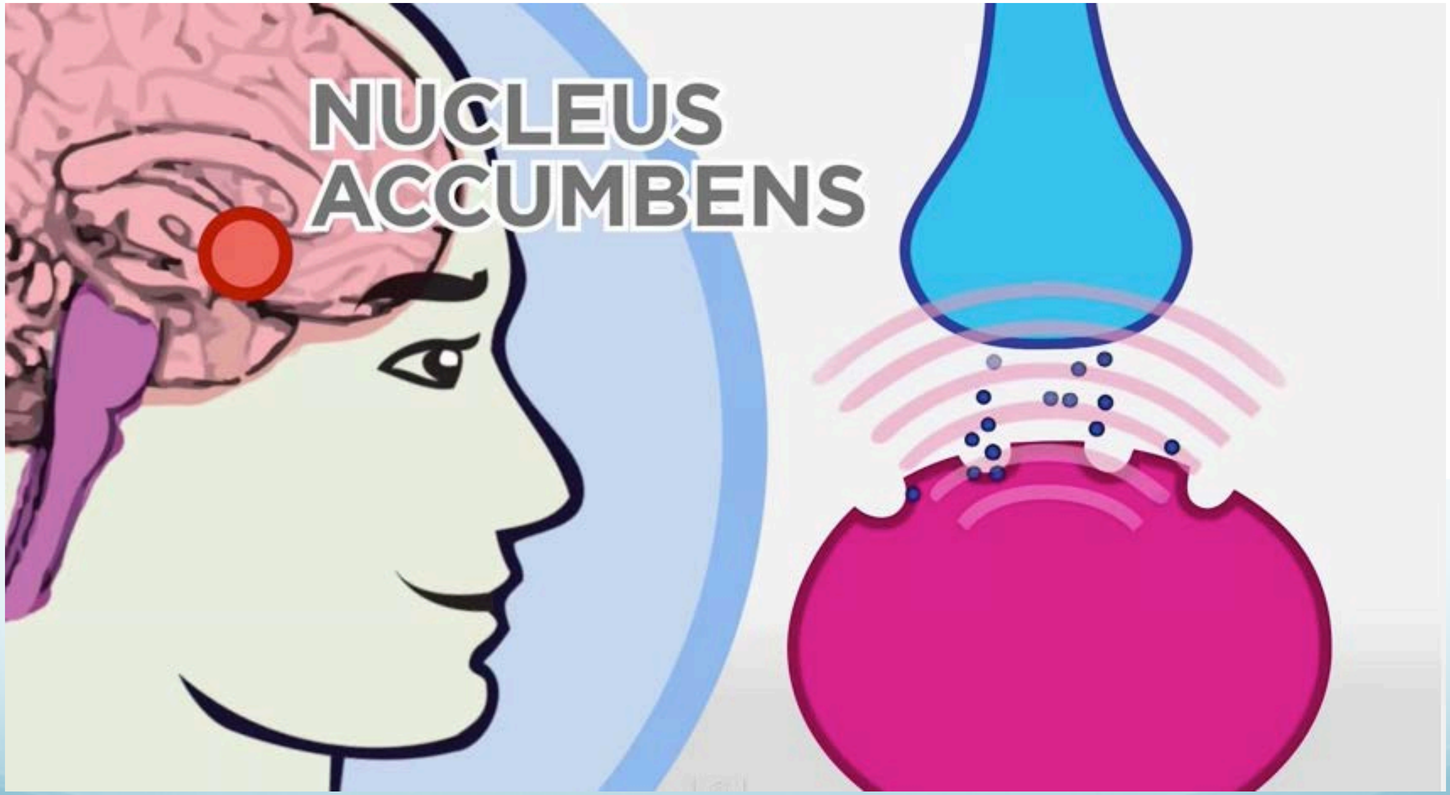
During normal functioning, there is a dopamine transporter reuptake process that pumps excess dopamine back into the presynaptic neurons for reuse.

(Reuptake is blocked by some certain drugs of abuse and pharmaceuticals.)



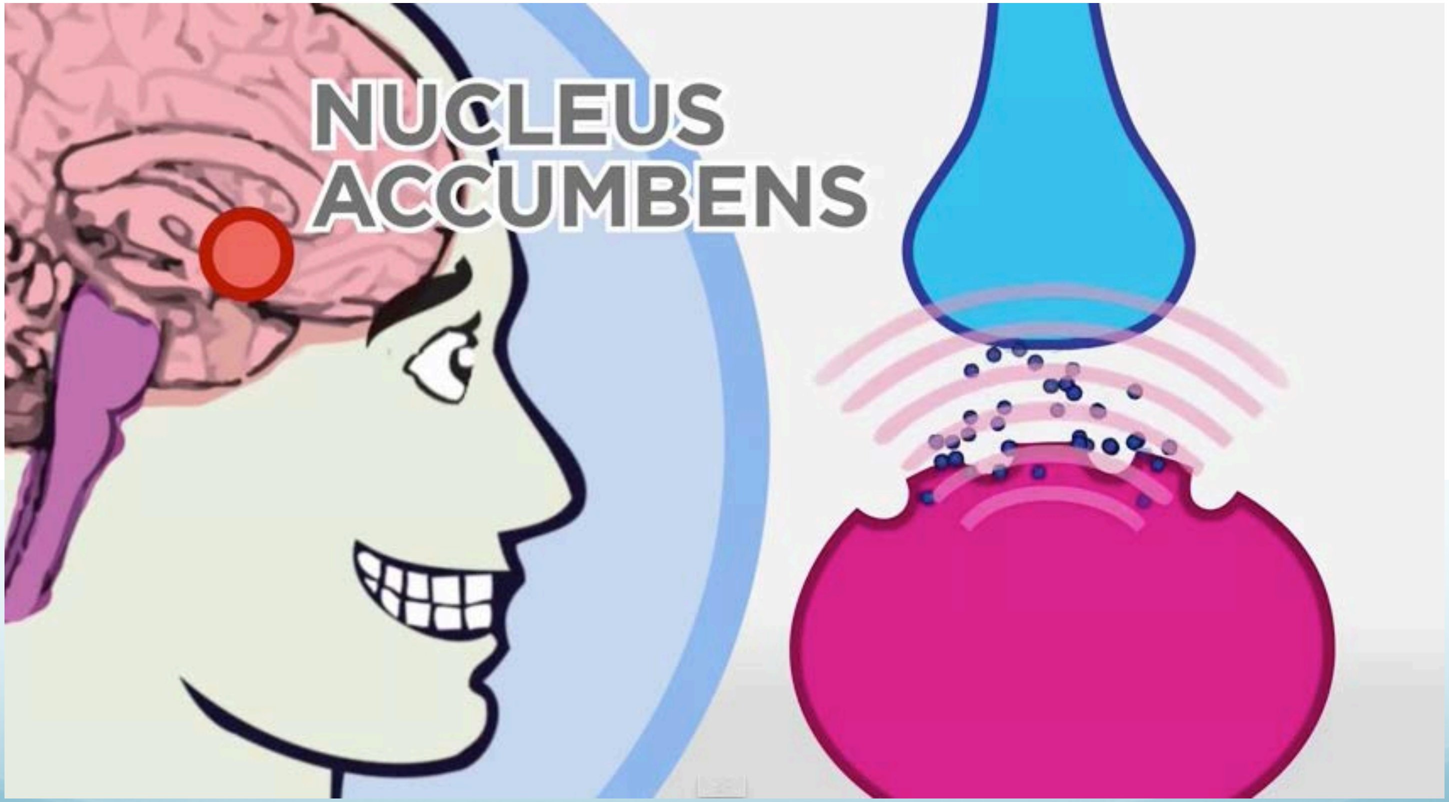
Process of Food-Related Dopamine Downregulation

During neuronormal eating behaviors, released dopamine is taken up by the dopaminergic receptors in the nucleus accumbens, and the person experiences pleasure (dopamine) and satiety (leptin).



Process of Food-Related Dopamine Downregulation

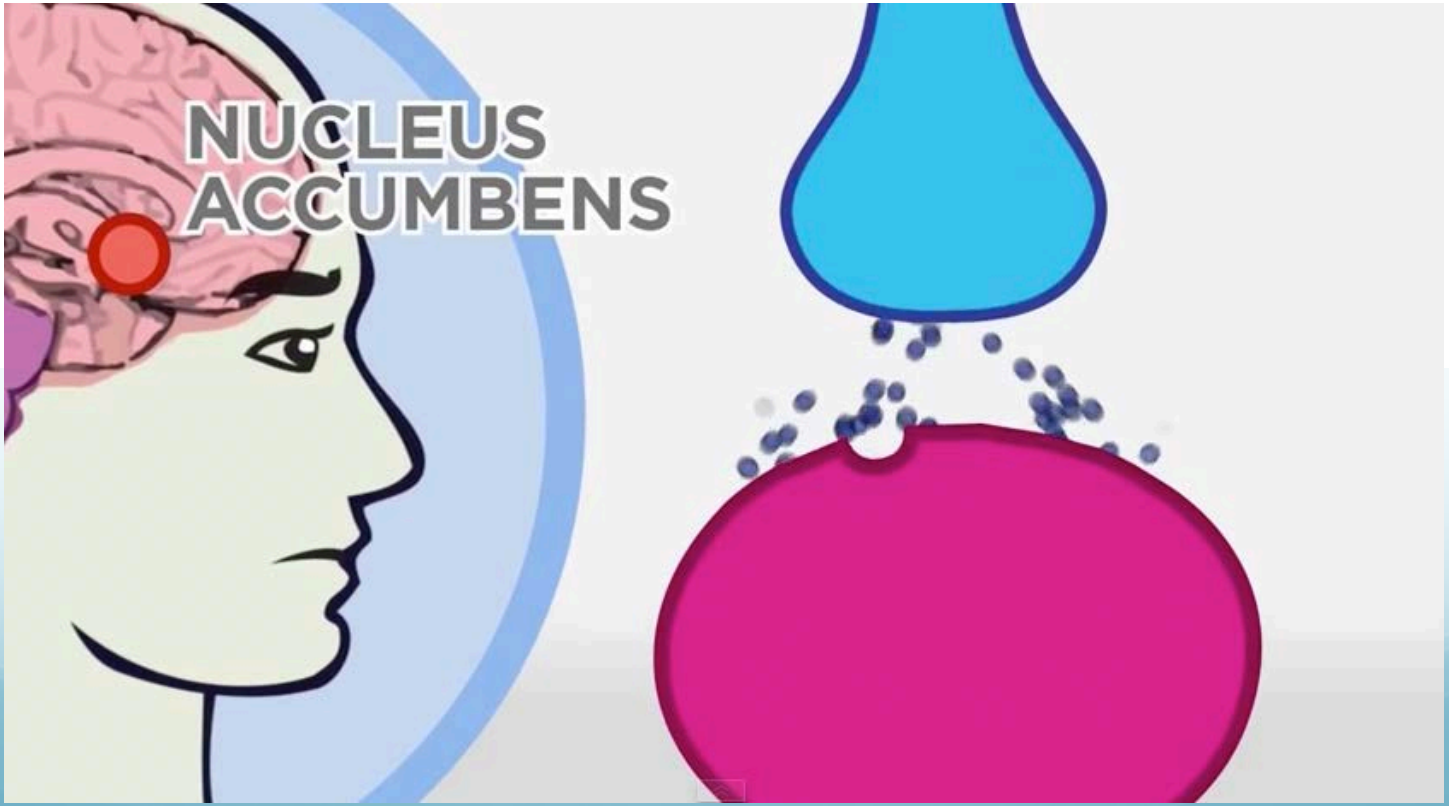
However, when a person—such as Sally—continues to trigger dopaminergic neurons to release dopamine through pleasure-seeking eating behaviors, the synaptic cleft becomes inundated with dopamine.



Process of Food-Related Dopamine Downregulation

After stimulating this system chronically—again and again and again—by eating for pleasure, the dopamine system begins to change as dopamine receptors downregulate.

According to Robert Lustig, MD, Pediatric Endocrinologist and Professor at UCSF, it only takes 3 weeks of chronic stimulation for dopamine receptor downregulation to begin.



Outcome of Food-Related Dopamine Downregulation

According to research by Elissa Epel, PhD, Associate Professor of Psychiatry at UCSF School of Medicine:

> **"The brain's of people with obesity respond differently to food. In the reward center, when they see palatable food, some parts of the brain light up a lot—the wanting part—but the liking part, once they taste the food, it's blunted. It's not that they're getting more pleasure or reward, they're getting less. That's like living with an urge that you can't satisfy. That is causing people to overeat to get that dopamine that they're missing …**
>
> **… Food can be just like a drug to certain people with a predisposition to addiction.**
>
> **Is it that becoming obese has changed their brain chemistry, or that they were born with this predisposition that caused them to become obese? It's probably a little bit of both."**

Food Addiction = Drug Addiction

Both Dr. Epel and Dr. Lustig agree that **sugar (in particular) is no different than other drugs of abuse in its ability to cause brain changes that blunt the reward system, leading to tolerance and withdrawl.**

<u>ADDICTION:</u>

"A state in which an organism engages in a compulsive behavior."

- Behavior is reinforcing (rewarding or pleasurable)
- Loss of control in limiting intake

Drugabuse.gov

Is Willpower Enough?

Knowing that these issues are biochemical in nature—going on every minute of every day—explains a lot when it comes to Sally's inability to exert "willpower" over her urge to self-medicate with food… along with millions of other overweight, depressed people.

While the United States government and food companies would like to pin the blame for obesity and food addiction on citizens, no amount of exercise alone is going to overpower these drives that are hard-wired in the brain.

So, how can the millions of sugar-addicted, food-addicted people begin the process of rewiring their habituation patters and upregulating dopamine receptors?

7 Diet & Lifestyle Tips to Regain Your Brain!

1. Cut out ‘‘discretionary’’ calories – ALL OF THEM.

This means “empty calories” without protein, fiber or nutrients: sweetened beverages, highly processed carbohydrate foods (french fries, chips, cookies, etc.). No cheating! Sugar is a slippery slope, so give yourself 3 months to kick the habit.

Food nutrition labels don’t provide a daily reference value for sugar (coincidence?), so follow this general rule:

Women: 6 tsp. (25 g)
Men: 9 tsp. (38 g)
Children: 3-6 tsp. (12-25 g)

Wondering how much that is? One Coca-Cola contains a whopping 39 g

How much sugar is in your drink?
Monster Energy 16 oz.
200 calories
vitaminwater 20 oz.
125 calories
Mountain Dew 20 oz.
290 calories
Snapple Lemon Tea 16 oz.
160 calories
Gatorade 20 oz.
130 calories
Nantucket Nectars Cranberry 17.5 oz.
280 calories
13.5 teaspoons
8 teaspoons
19.25 teaspoons
10.5 teaspoons
8.5 teaspoons
17.5 teaspoons
Consumption of sugar sweetened beverages may be the single largest driver of the obesity epidemic according to a 2009 study in the New England Journal of Medicine.
Average sugar sweetened beverage consumption by youth
BOYS
Ages 2-5: 47 gallons/year
Ages 6-11: 65 gallons/year
Ages 12-19: 108 gallons/year
GIRLS
Ages 2-5: 41 gallons/year
Ages 6-11: 51 gallons/year
Ages 12-19: 77 gallons/year
The extra calories from adding just one 20 oz Mountain Dew to your regular diet every day for a year would be enough calories to cause a 30 pound weight gain.
Alliance for a
Healthier
Rhode Island
c/o Rhode Island Medical Society
This artwork was created by our colleagues from the Alliance for a Healthier Vermont. We thank them for sharing!

7 Diet & Lifestyle Tips to Regain Your Brain!

2. Diligently check labels and reject foods with added sugars

Did you know that 80% of processed foods in the grocery store contains added sugar? Yep—your food addiction means BIG profits for food companies! Don't let them get away with it any longer.

Keep an eye out for:

> Corn sweetener, corn syrup, dextrose, fructose, fruit juice concentrates, glucose, high-fructose corn syrup, invert sugar, lactose, maltose, malt syrup, raw sugar, sucrose, sugar syrup, cane crystals, cane sugar, crystalline fructose, evaporated cane juice, corn syrup solids, malt syrup.

7 Diet & Lifestyle Tips to Regain Your Brain!

3. Begin training your neurons to derive pleasure from non-food experiences:

- Goal-setting/achievement – make lists and check-off items when complete
- Spirituality
- Volunteer work
- Healthy social connections

4. Reward yourself for long-term goals, but not with food!

Take "me time," enjoy a hot bath, buy yourself a gift and wrap it—the possibilities really are endless!

5. Cook meals at home

On average, Americans eat 70% of their meals away from home. Preparing meals at home re-establishes a conscious connection to food and is healthier in myriad ways.

7 Diet & Lifestyle Tips to Regain Your Brain!

6. Walk 3-4 days per week, for 30-45 minutes—OR, whenever stress, anxiety or worry strike!

Vigorous physical activity releases pain-reducing, bliss-enhancing “feel-good” endorphins and promotes new brain cell growth via BDNF.
DO IT—you’ll be happy that you did!

7. Replace packaged snack foods with protein and healthy fats.

They take longer to break down and trigger very little insulin release, plus they contain nutrients that are slower to metabolize—leaving you feeling fuller, longer!

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