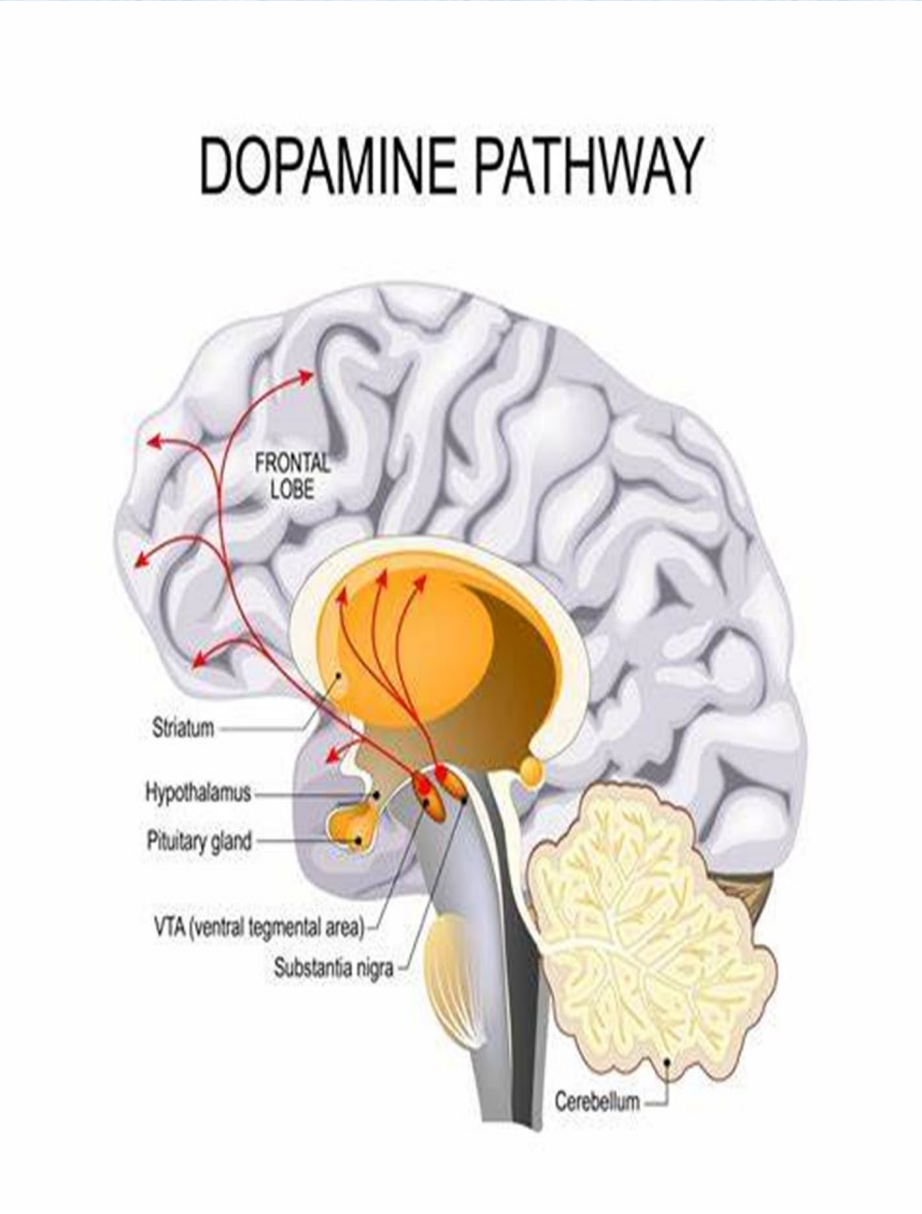
# Dopamine: The pathway to pleasure

- Dopamine is a neuromodulator molecule that plays several important roles in the cell. It is an organic chemical of the catecholamine and phenethylamine families. Dopamine constitutes about 80% of the catecholamine content in the brain.
- Dopamine is a type of monoamine neurotransmitter. It's made in the brain and acts as a chemical messenger, communicating messages between nerve cells in the brain and the  brain and the rest of the body.
- Dopamine also acts as a hormone. Dopamine, epinephrine and norepinephrine are the main catecholamines. These hormones are made by adrenal gland.

- **Where is dopamine produced?**
- Dopaminergic neurons produce dopamine in two different parts of the human brain. The first is called substantia nigra, a tiny strip of tissue on either side of the base of the brain, located in the midbrain. The second is the ventral tegmental area (VTA) lying close by.
- Dopamine produce in a two-step process. First, the amino acid tyrosine is converted into another amino acid, called L-dopa. Then L-dopa undergoes another change, as enzymes turn it into dopamine.



The primary and minor metabolic pathways respectively are:

- Primary: L-Phenylalanine → L-Tyrosine → L-DOPA → Dopamine
- Minor: L-Phenylalanine → L-Tyrosine → p-Tyramine → Dopamine
- Minor: L-Phenylalanine → m-Tyrosine → m-Tyramine → Dopamine

The direct precursor of dopamine, L-DOPA, can be synthesized indirectly from the essential amino acid phenylalanine or directly from the non-essential amino acid tyrosine. These amino acids are found in nearly every protein and so are readily available in food . Because dopamine is made from tyrosine, getting more of this amino acid from food could potentially boost dopamine levels in the brain. There is evidence that a diet rich in tyrosine also may improve memory and mental performance.

Although dopamine is also found in many types of food, it is incapable of crossing the blood–brain barrier that surrounds and protects the brain. The blood–brain barrier (BBB) is a highly selective semipermeable border of endothelial cells that prevents solutes in the circulating blood from non-selectively crossing into the extracellular fluid of the central nervous system where neurons reside. It must therefore be synthesized inside the brain to perform its neuronal activity. L-DOPA on the other hand, is a precursor in the formation of dopamine, norepinephrine, and epinephrine can cross the blood brain barrier, and is prescribed to treat several diseases and symptoms.

Dopamine itself is used as precursor in the synthesis of the neurotransmitters norepinephrine and epinephrine. Dopamine is converted into norepinephrine by the enzyme dopamine β-hydroxylase, with O2 and L-ascorbic acid as cofactors. Norepinephrine is converted into epinephrine by the enzyme phenylethanolamine N-methyltransferase with S-adenosyl-L-methionine as the cofactor.

# Dopamine Receptors

- Dopamine receptors are most abundant in pituitary and brain, particularly in the basal forebrain, but they are also found in the retina and peripheral organs such as the kidney where dopamine binds to the receptor and performs distinct functions depending on the type of the receptor.

- These receptors are encoded by different genes, with there being five types of receptors, including D1, D2, D3, D4, and D5 .
  - ➢D1 is primarily responsible for attention, memory, impulse control, regulating renal function, and movement.
  - ➢D2 assists with attention, memory, learning, sleep, and movement.
  - ➢D3 and D4 are responsible for cognition, attention, sleep, and impulse control.
  - ➢D5 there is a part in cognition, attention, decision making, and renin secretion.

## What's the role of dopamine in the body?

- Dopamine plays a role in many body functions.
- As a neurotransmitter, dopamine is involved in:
- Movement.
- Memory.
- Pleasurable reward and motivation.
- Behavior and cognition.
- Attention.
- Sleep and arousal.
- Mood.
- Learning.
- Lactation.
- As a hormone, dopamine is released into the bloodstream. It plays a small role in the "fight-or-flight" syndrome. The fight-or-flight response refers to your body's response to a perceived or real stressful situation, such as needing to escape danger.

- **Dopamine also:**

Outside the central nervous system, dopamine functions primarily as a local paracrine messenger. In blood vessels, it inhibits norepinephrine release and acts as a vasodilator (at normal concentrations); in the kidneys, it increases sodium excretion and urine output; in the pancreas, it reduces insulin production; in the digestive system, it reduces gastrointestinal motility and protects intestinal mucosa; and in the immune system, it reduces the activity of lymphocytes. With the exception of the blood vessels, dopamine in each of these peripheral systems is synthesized locally and exerts its effects near the cells that release it.

## The best way to increase dopamine naturally

Many plants, including a variety of food plants, synthesize dopamine to varying degrees. The highest concentrations have been observed in bananas—at levels of 40 to 50 parts per million by weight. Potatoes, avocados, broccoli, oranges, tomatoes, spinach, beans, and other plants contain measurable concentrations less than 1 part per million. The dopamine in plants is synthesized from the amino acid tyrosine, by biochemical mechanisms similar to those that animals use .

- As mentioned before the dopamine which consumed in food cannot act on the brain, because it cannot cross the blood–brain barrier. However, there are also a variety of plants that contain L-DOPA, the metabolic precursor of dopamine. The highest concentrations are found in the leaves and bean pods of plants of the genus Mucuna, especially in Mucuna pruriens (velvet beans), which have been used as a source for L-DOPA as a drug.] Another plant containing substantial amounts of L-DOPA is Vicia faba, the plant that produces fava beans (also known as "broad beans"). The level of L-DOPA in the beans, however, is much lower than in the pod shells and other parts of the plant .The seeds of Cassia and Bauhinia trees also contain substantial amounts of L-DOPA.

- In a species of marine green algae Ulvaria obscura, a major component of some algal blooms, dopamine is present in very high concentrations, estimated at 4.4% of dry weight. There is evidence that this dopamine functions as an anti-herbivore defense, reducing consumption by snails and isopods.

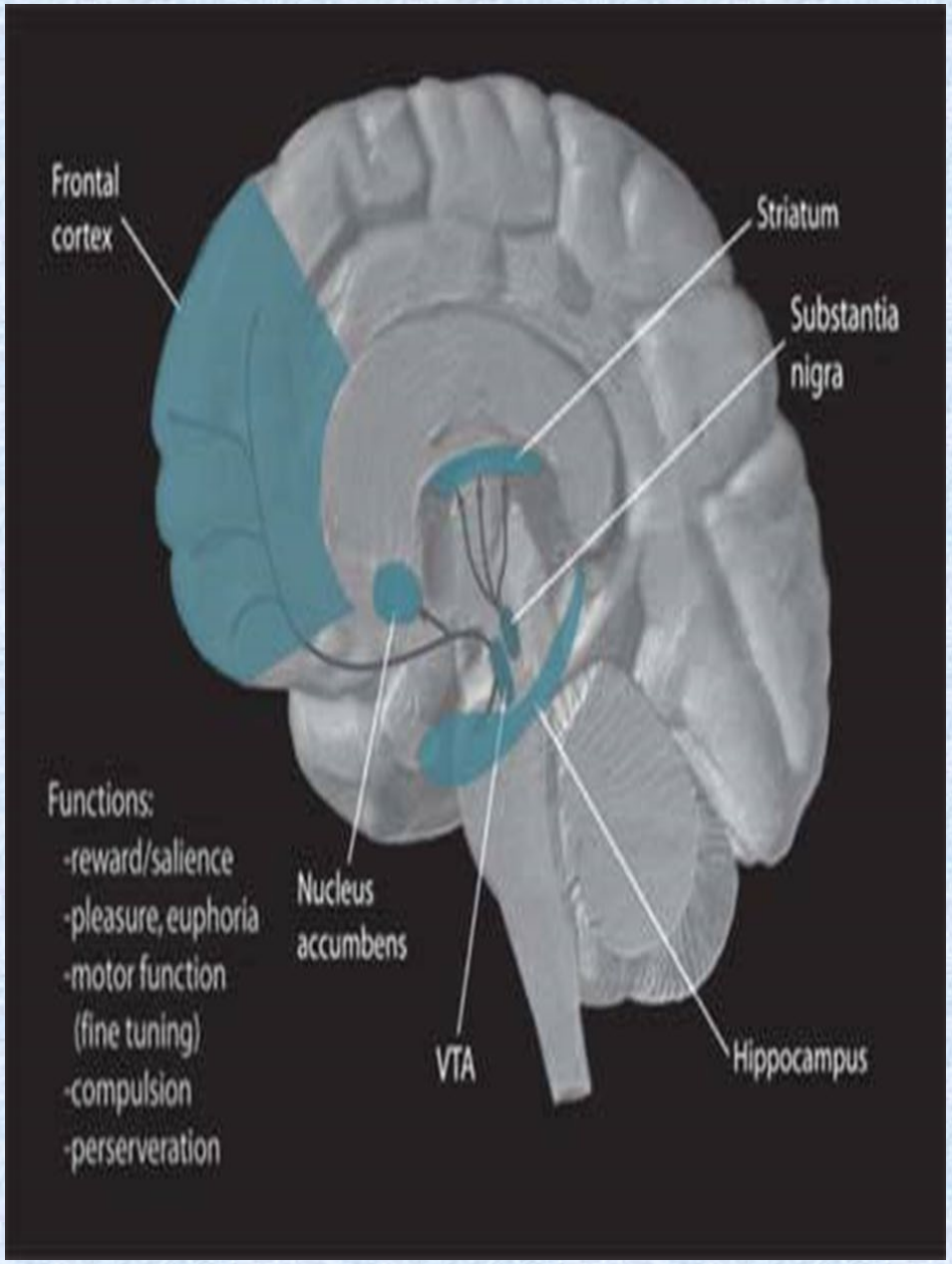
# How does dopamine make someone feel happy?

- Dopamine is known as the “feel-good” hormone. It gives a sense of pleasure. It also gives the motivation to do something when you’re feeling pleasure.

- Dopamine is a neurotransmitter that involved in reward pathway, motivation, and addiction.
- When dopamine binds to five subtypes of dopamine receptors: D1, D2, D3, D4, and D5, a flow of signaling responsible for activating functions in the associated brain regions where each receptor type is most dominant.

- Dopamine was activated during the rewarding brain stimulation. With an influx of dopamine reaching the brain regions involved in reward and pleasurable feelings.

- In the reward pathways, specifically the mesolimbic pathway, dopamine is released during pleasurable experiences and binds to dopaminergic receptors located in the nucleus accumbens.
- The ventral tegmental area sends dopamine to other areas of the brain like the nucleus accumbens and the prefrontal cortex. When we are exposed to pleasurable things like brownies, new clothes, a shiny new car, or drugs, dopamine is shunted to the nucleus accumbens. This area of the brain is highly associated with pleasure, motivation, and the reward system. (i.e. I did this thing. I got the awesome reward. Lots of feel good dopamine hormone was sent to the nucleus accumbens. I'm motivated to do that again. And again. And again.)



- The perspective on dopamine's role has shifted slightly. Once believed to be the neurotransmitter responsible for directly causing pleasurable experiences, it is now thought to be involved with aspects of reward rather than the experience of enjoyment.
- This is why junk food and sugar are so addictive. They trigger release of large amount of dopamine into your brain, which gives you the feeling that you're on top of the world and you want to repeat that experience
- For instance, is has been suggested that dopamine is involved in encoding the memories associated with a reward, such as understanding how to achieve the experience again.

- **Obesity**. Most of the time, if you take in more calories than you burn, you'll gain weight. So why can't obese people simply eat less and slim down? The answer isn't that simple. They may face obstacles that others don't. They could have problems with their natural reward systems. This can affect the amount of food they eat before they feel satisfied. The body may not release enough dopamine and another feel-good hormone, serotonin.

- **Dopamine needs to remain within the natural range. If dopamine levels fall too low or get too high, specific health problems may occur.**

- **What does lack of dopamine feel like?**

- Dopamine Deficiency - Low levels of dopamine have been linked to Parkinson's disease, restless legs syndrome and depression. Low levels of dopamine can make you feel tired, moody, unmotivated and many other symptoms.

- **What happens when dopamine levels are too high?**
- While sufficient dopamine can actually help some people stay calm, abnormally high levels can make a person feel internally nervous and knotted. It may be difficult to sit still for long periods of time. Some people may feel more anxious when dopamine levels increase in certain parts of the brain.

- **Which vitamin increases dopamine?**

- Vitamin B12 Vitamin B12 also helps regulate the levels of dopamine in the brain, and consuming adequate amounts of the vitamin may increase dopamine. According to the University of Maryland Medical Center, vitamin B12 aids in the production and metabolism of several brain chemicals, including dopamine.

# Addiction

- As indicated, dopamine is secreted by the brain during many activities that bring pleasurable feelings, activated the dopamine reward pathways.
- Drugs such as stimulants, Cocaine, opioids, ethanol, and nicotine trigger the release of more dopamine in the brain.
- At the earliest stage, genetic differences that alter the expression of dopamine receptors in the brain can predict whether a person will find stimulants appealing or aversive.

- These drugs will typically bind to receptors of the brain in regions associated with rewards, e.g. nucleus accumbens ,with drugs, they will force the brain to release a large amount of dopamine than would be released by healthy activities. Consumption of stimulants produces increases in brain dopamine levels that last from minutes to hours

- They will also prevent the brain from reabsorbing the dopamine, making the pleasurable experience last unnaturally longer. **Overstimulating** the reward systems in the brain can eventually result in addiction.

- **Addiction** is the result of reinforcing or rewarding behaviors being carried out compulsively, despite any negative consequences, a main feature being that there is a loss of control over the amount of the addictive substance.

- In a further study of rats, they were dispensed cocaine if they pushed a lever. The rats quickly learnt to keep pushing the lever to get more cocaine and would also engage in drug-seeking behaviors and would increase their dosage if given the opportunity to.

- Over time, with repeated use of addictive substances, the body becomes reliant on this to maintain rewarding feelings. A negative consequence is that although a lot of dopamine is stimulated around the brain and there are strong feelings of euphoria, this also causes serotonin levels to decrease.

- Serotonin is an essential neurotransmitter associated with feelings of happiness. Due to addictive substances like drugs affecting serotonin levels, this can get to a point where everyday activities which an individual would have found pleasurable before do not bring them happiness anymore and could result in feeling very low in mood over continued use of drugs.

- This can also be because these activities do not produce the same amount of dopamine that they are now accustomed to.

Stimulants such as nicotine, cocaine and methamphetamine promote increased levels of dopamine which appear to be the primary factor in causing addiction. For other addictive drugs such as the opioid heroin, the increased levels of dopamine in the reward system may play only a minor role in addiction

## Why the treatment of stimulant addiction is very difficult?

The chronic elevation in dopamine that comes with repetitive high-dose stimulant consumption triggers a wide-ranging set of structural changes in the brain that are responsible for the behavioral abnormalities which characterize an addiction.

When people addicted to stimulants go through withdrawal, they do not experience the **physical suffering** associated with alcohol withdrawal or withdrawal from opiates; instead they **experience craving**, an intense desire for the drug characterized by irritability, restlessness, and other arousal symptoms. Treatment of stimulant addiction is very difficult, because even if consumption ceases, the craving that comes with psychological withdrawal does not .Even when the craving seems to be extinct, it may re-emerge when faced with stimuli that are associated with the drug, such as friends, locations and situations. Association networks in the brain are greatly interlinked

# Drug addiction and psychostimulants

The effects of psychostimulants include increases in **heart rate**, **body temperature, and sweating; improvements in alertness, attention, and endurance; increases in pleasure produced by rewarding events;** but at higher doses agitation, anxiety, or even loss of contact with reality. Drugs in this group can have a high addiction potential, due to their activating effects on the **dopamine-mediated reward system** in the brain .The mesolimbic dopaminergic system is known as a major reward-related center in the brain. However some can also be useful, at lower doses, for treating **attention deficit hyperactivity disorder (ADHD) and narcolepsy.**

# Diseases associated with dopamine disfunction

Several important diseases of the nervous system are associated with dysfunctions of the dopamine system, and some of the key medications used to treat them work by altering the effects of dopamine. **Parkinson's disease,** a degenerative condition causing tremor and motor impairment, is caused by a **loss of dopamine-secreting** neurons in an area of the midbrain called the substantia nigra. Its metabolic precursor L-DOPA can be manufactured; **Levodopa**, a pure form of L-DOPA, is the most widely used treatment for Parkinson's

- There is evidence that **schizophrenia** involves altered levels of dopamine activity, and most antipsychotic drugs used to treat this are **dopamine antagonists** which reduce dopamine activity. Similar dopamine antagonist drugs are also some of the most effective anti-nausea agents. Restless legs syndrome and **attention deficit hyperactivity disorder (ADHD)** are associated with decreased dopamine activity. **Dopaminergic stimulants** can be addictive in high doses, but some are used at lower doses to treat ADHD. Dopamine itself is available as a manufactured medication for intravenous injection: although it cannot reach the brain from the bloodstream, its peripheral effects make it useful in the treatment of heart failure or shock, especially in newborn babies.

## How to increase dopamine levels?

Spending more time outdoors. Science consistently shows that low exposure to sunshine can reduce levels of mood-boosting neurotransmitters including dopamine. Similarly, increased sunlight exposure can help raise dopamine levels. Of course, addictive substances greatly affect our dopamine levels.

# Tips and advices that I hope you will find useful.

- Wake up and sleep at regular intervals.
- Eat healthy meals at regular times.
- Exercise regularly.
- Set aside time for both work and rest..
- Allocate some time for your favorite activities..
- If you think you are experiencing any medical condition, you should seek immediate medical consultation from a doctor or other professional healthcare provider.
- Finally life is beautiful ..every day is a gift …enjoy it.


THANK
YOU