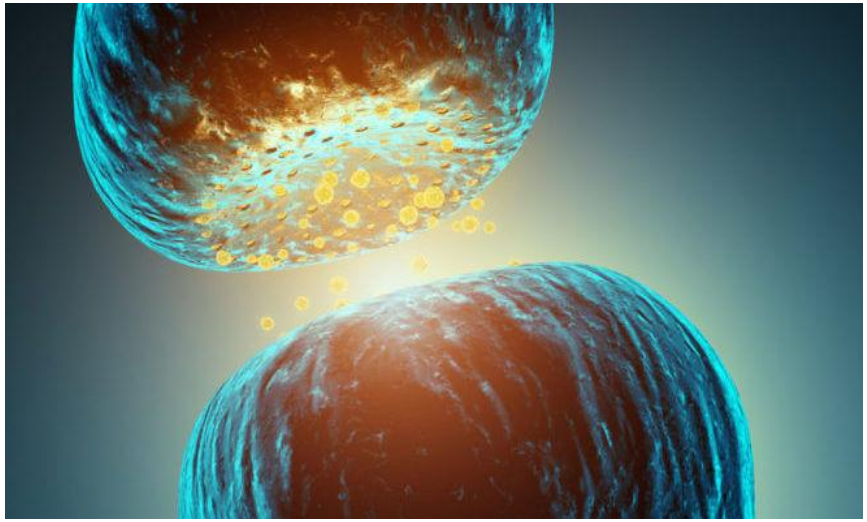
Ural Federal University

NEUROTRANSMITTER SYSTEMS



Speaker
Guryeva A.K.

NEUROTRANSMITTER SYSTEMS

✔ These neurotransmitters are produced by neurons whose cell bodies are located subcortically and in the brainstem, and whose axons project diffusely throughout the cortex.

Monoamines

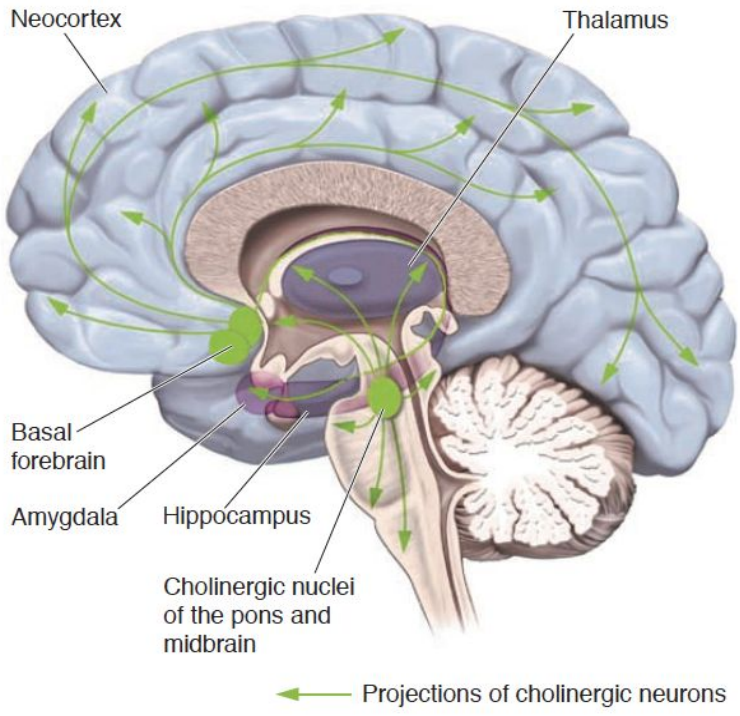
1. acetylcholine
2. dopamine
3. noradrenaline (norepinephrine)
4. serotonin

✔ Each of these neurotransmitters is released by a different set of neurons that together form a *neurotransmitter system:*

- the cholinergic systems
- the dopaminergic systems
- the noradrenergic systems
- the serotonergic systems.

CHOLINERGIC SYSTEM

- ✔ Acetylcholine (ACh) is the neurotransmitter used in the cholinergic system.
- ✔ The cell bodies of neurons of the cholinergic system are located mainly in the basal forebrain nucleus and project to almost all portions of the cortex in a very diffuse and nonspecific manner.
- ✔ There are also cell bodies in the septal nuclei that project to the hippocampus.
- ✔ Because ACh is released in almost every cortical area, it tends to have a very general effect on neuronal and mental functioning.

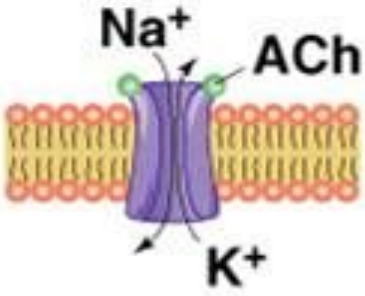


CHOLINERGIC SYSTEM

- ✔ There are two different types of ACh receptors, one ionotropic and one metabotropic, each of which is activated by a different drug.
- ✔ The ionotropic ACh receptor is known as the nicotinic receptor because it can be stimulated by nicotine (the drug found in tobacco leaves).
- ✔ In contrast, the metabotropic receptor is known as the muscarinic receptor because it can be stimulated by muscarine (a drug in the poisonous mushroom Amanita muscaria).

Nicotinic ACh receptors

Postsynaptic membrane of
- All autonomic ganglia
- All neuromuscular junctions
- Some CNS pathways



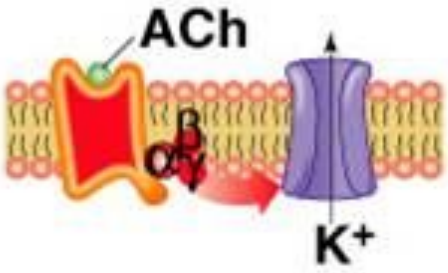
Ligand-gated channels (ion channels are part of receptor)

Depolarization

Excitation

Muscarinic ACh receptors

- Produces parasympathetic nerve effects in the heart, smooth muscles, and glands
- G-protein-coupled receptors (receptors influence ion channels by means of G-proteins)

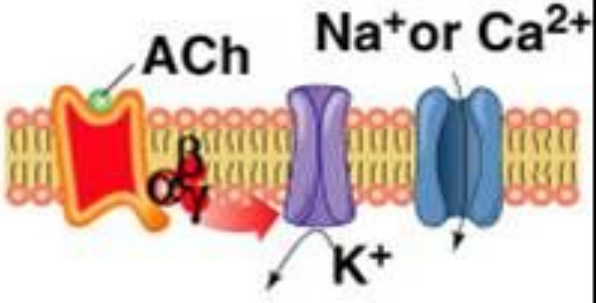


Hyperpolarization

(K^+ channels opened)

Inhibition

Produces slower heart rate



Depolarization

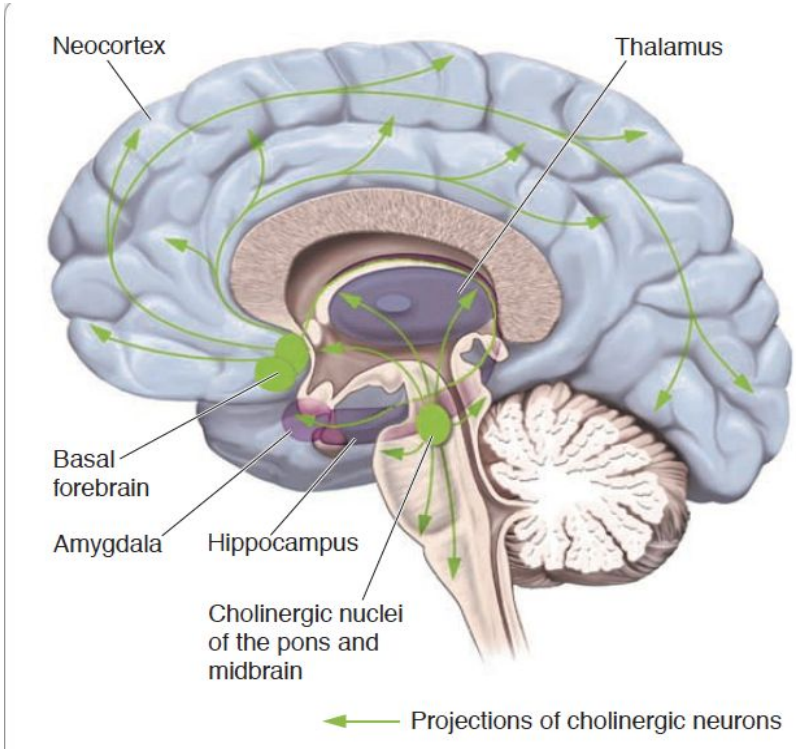
(K^+ channels closed)

Excitation

Causes smooth muscles of the digestive tract to contract

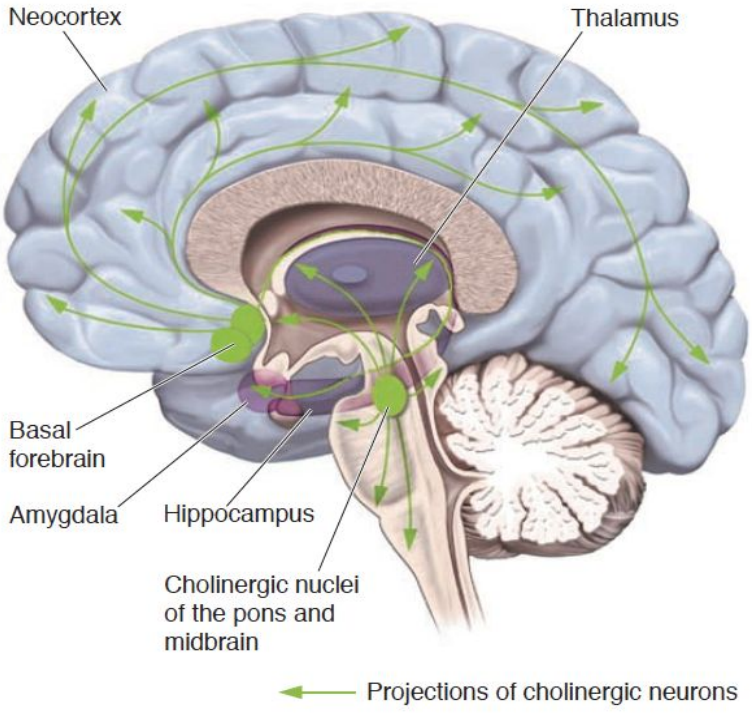
CHOLINERGIC SYSTEM

- ✔ The cholinergic system plays an important role in maintaining overall cortical excitability.
- ✔ ACh levels are decreased during anesthesia (when the brain is less active), and are increased by convulsants (which are drugs that produce seizure activity).
- ✔ ACh has also been linked to the production of rapid eye movement (REM) sleep, which is that portion of sleep when we dream and our minds are relatively active.



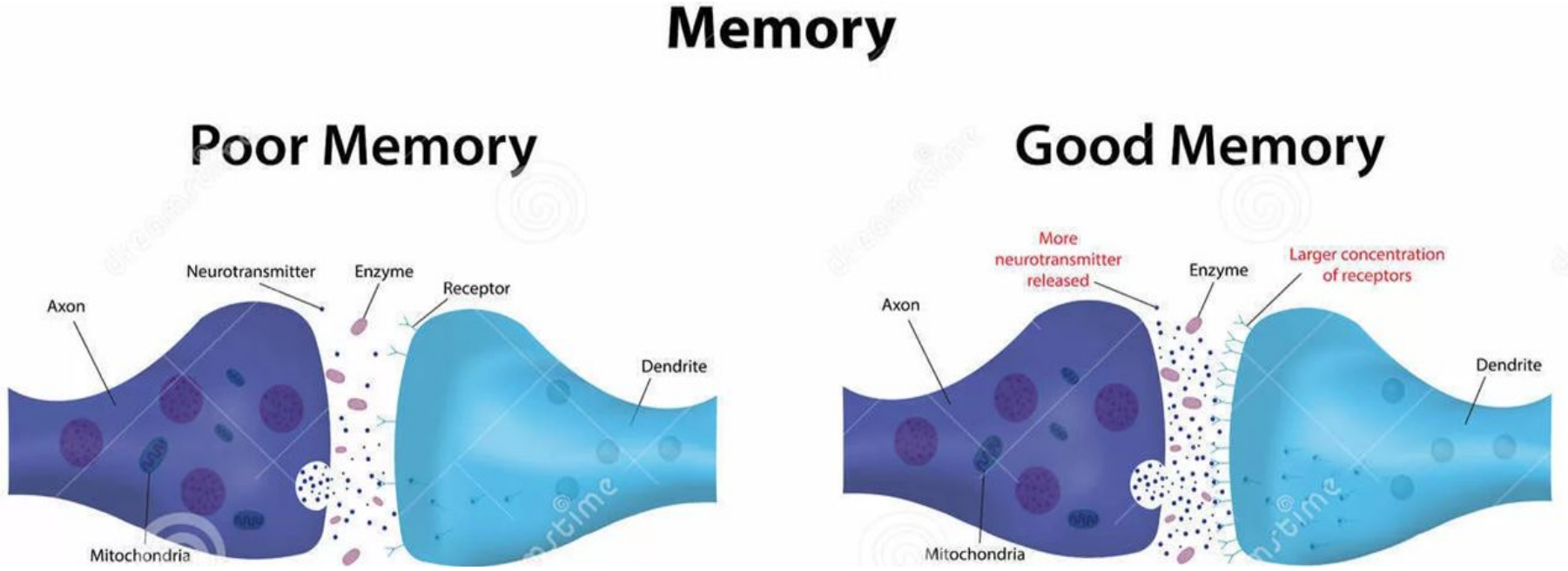
CHOLINERGIC SYSTEM

- ✔ The activity of the cholinergic system has been linked to paying attention.
- ✔ Cholinergic activity appears to be important for overall arousal — the ability to stay alert, especially in boring or monotonous situations or over long periods of time.
- ✔ ACh has also been linked to selective attention, which is the ability to attend to certain information while tuning out other information.



CHOLINERGIC SYSTEM

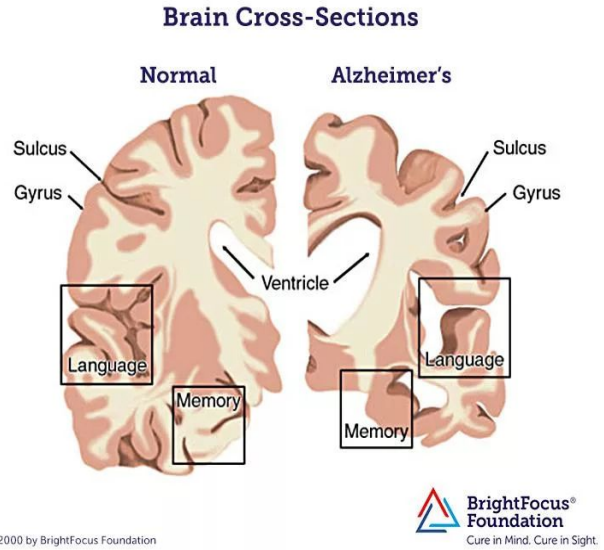
- ✔ ACh has also been linked to memory processing.
- ✔ Acetylcholine depletion is associated with Alzheimer's disease, which has devastating effects on memory as well as other functions.

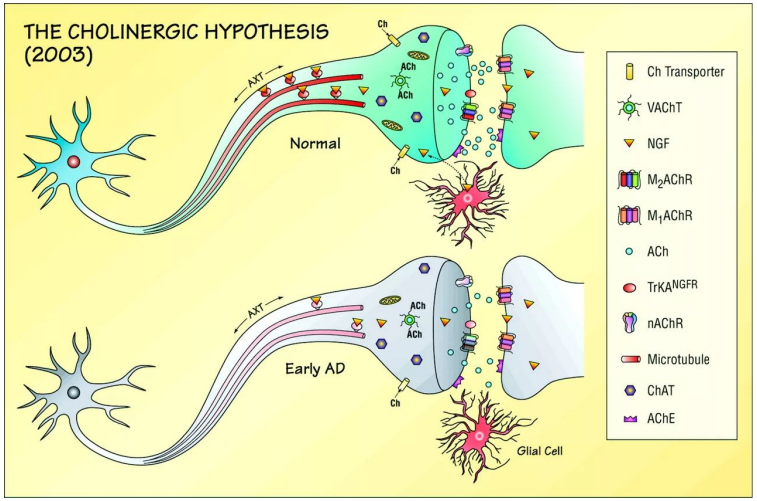


CHOLINERGIC SYSTEM

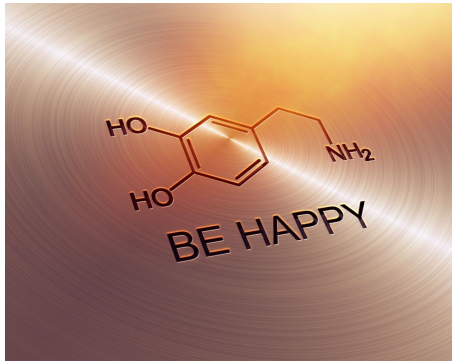
Alzheimer's disease

- ✔ Alzheimer's disease (AD) is a progressive, irreversible brain disorder.
- ✔ Symptoms of the disease include memory loss, confusion, impaired judgment, personality changes, disorientation, and loss of language skills.
- ✔ AD is the most common form of dementia.
- ✔ The correct balance of neurotransmitters is critical to the brain. Three neurotransmitters commonly affected by AD are acetylcholine, serotonin, and norepinephrine. With acetylcholine being the most affected.
- ✔ One of the characteristic changes that occurs in AD is the loss of memory and the loss of acetylcholinesterase (AChE) (the breakdown of the acetylcholine) from both cholinergic and noncholinergic neurons of the brain.





DOPAMINERGIC SYSTEM



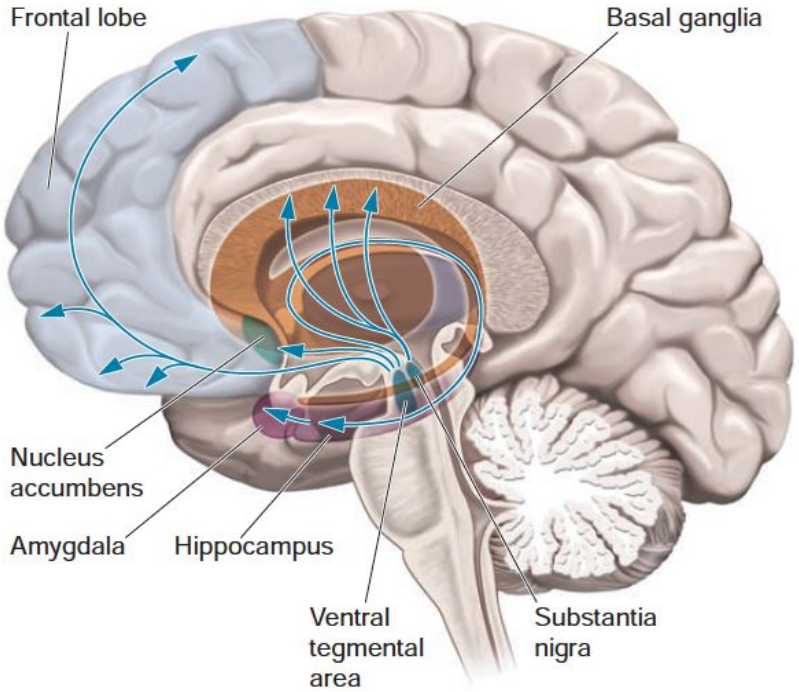
✔ Dopamine is the main neurotransmitter used in the dopaminergic system

There are actually 4 dopaminergic subsystems:

1. The nigrostriatal
2. The mesolimbic
3. The mesocortical
4. The tuberoinfundibular

These subsystems are differentiated by:

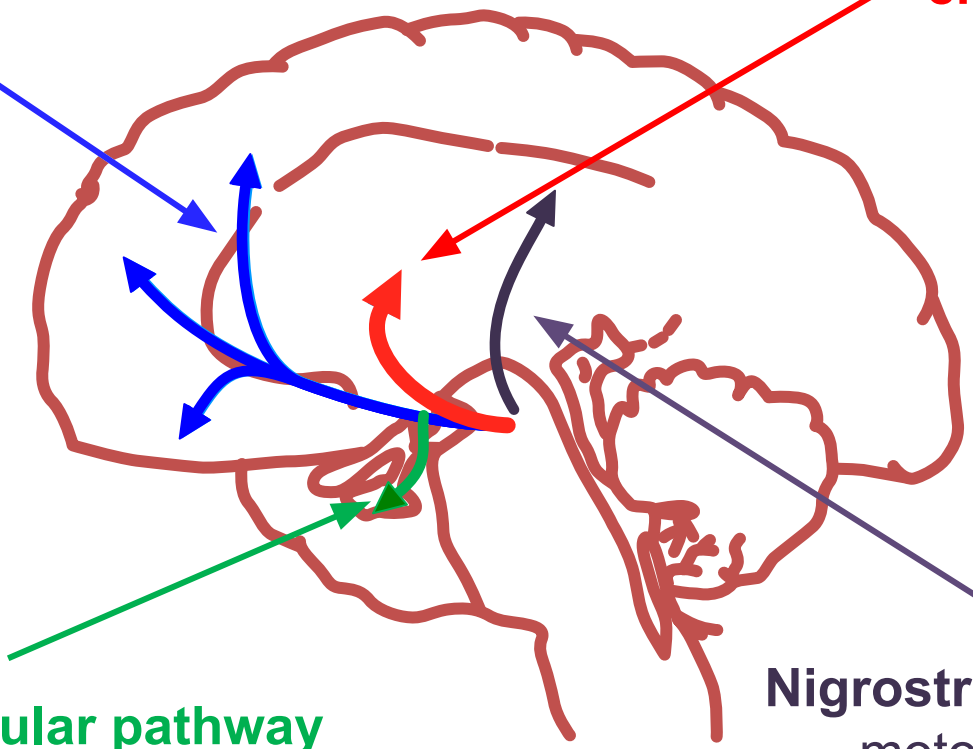
1. the location of their cell bodies
2. the regions of the brain to which they project
3. the effect they have on behavior



DOPAMINERGIC SYSTEM

Mesocortical pathway-
learning and memory

Mesolimbic pathway - emotions



Tuberoinfundibular pathway
regulation of prolactin

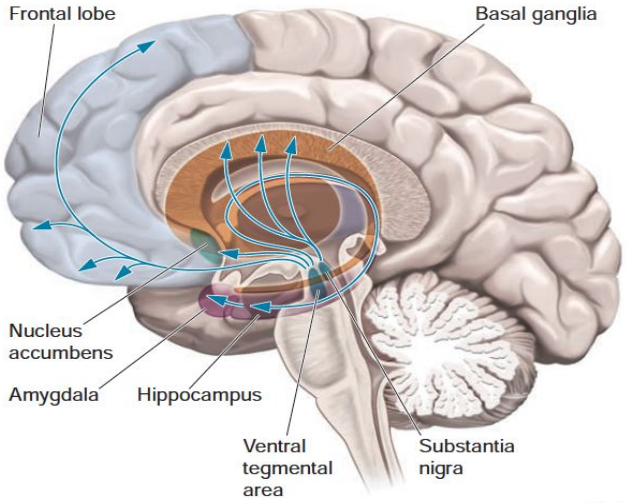
Nigrostriatal pathway -
motor regulation

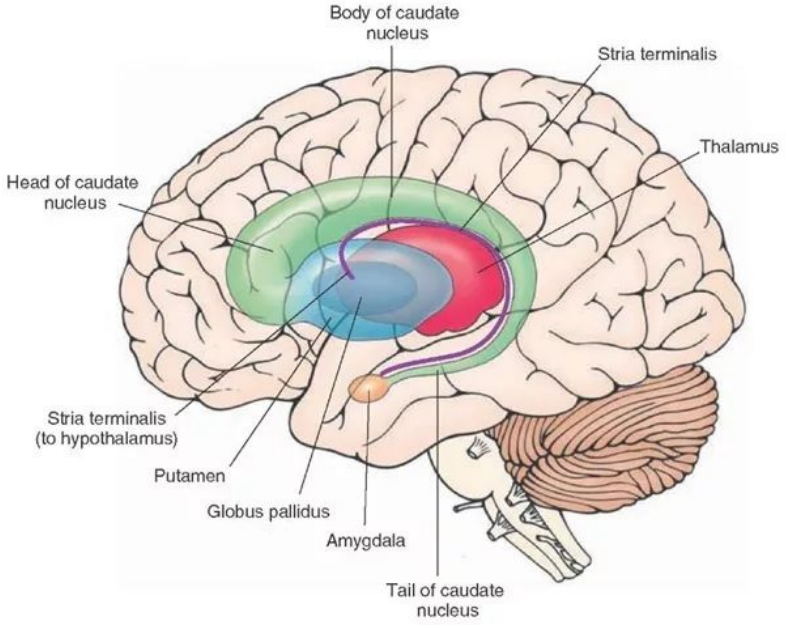
Stahl SM. Essential Psychopharmacology of antipsychotics and mood stabilizers; 1st ed. Cambridge: Cambridge University Press; 2002

DOPAMINERGIC SYSTEM

THE NIGROSTRIATAL SYSTEM

- ✔ The cell bodies of this system are located in the substantia nigra and project to the neostriatum (the caudate nucleus and the basal gang
- ✔ This subsystem regulates the selecti initiation, and cessation of motor behaviors.
- ✔ It is the subsystem that is affected by Parkinson's disease.
- ✔ In that disorder, the dopaminergic neurons in the substantia nigra die, leading to difficulties with motor control.

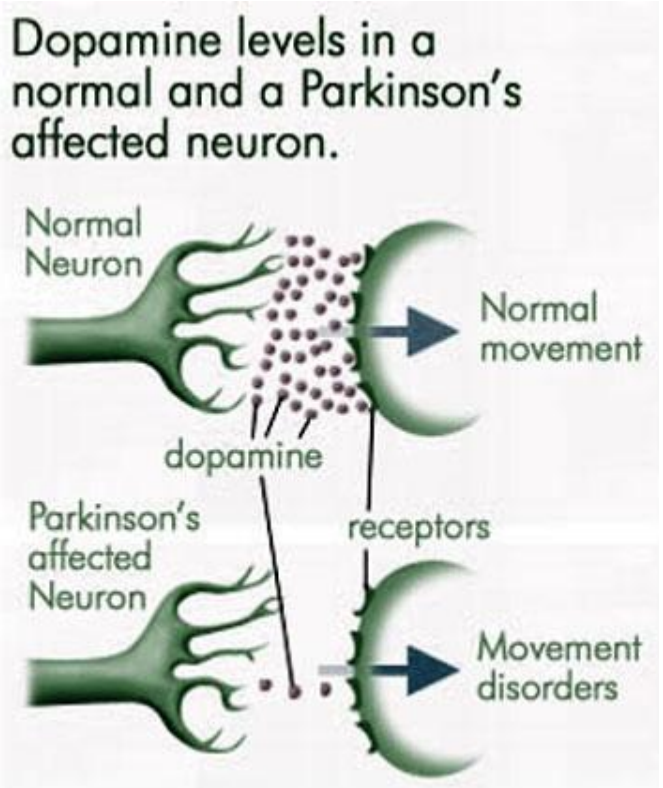




DOPAMINERGIC SYSTEM

PARKINSON'S DISEASE

- ✔ Movement control is accomplished by complex interactions among various groups of nerve cells in the central nervous system. One such important group of neurons is located in the substantia nigra in the ventral midbrain.
- ✔ Neurons of the substantia nigra communicate with neurons of the basal ganglia by liberating the neurotransmitter dopamine (DA). Such an interaction at the biochemical level is responsible for the fine tuning of an organism's movements.
- ✔ Parkinson's disease is a neurological disorder that affects movement control. In Parkinson's disease, neurons of the substantia nigra progressively degenerate; as a result, the amount of DA available for neurotransmission is lowered. The biochemical imbalance manifests with typical clinical symptoms that include resting tremor, rigidity, poor balance and motor coordination.



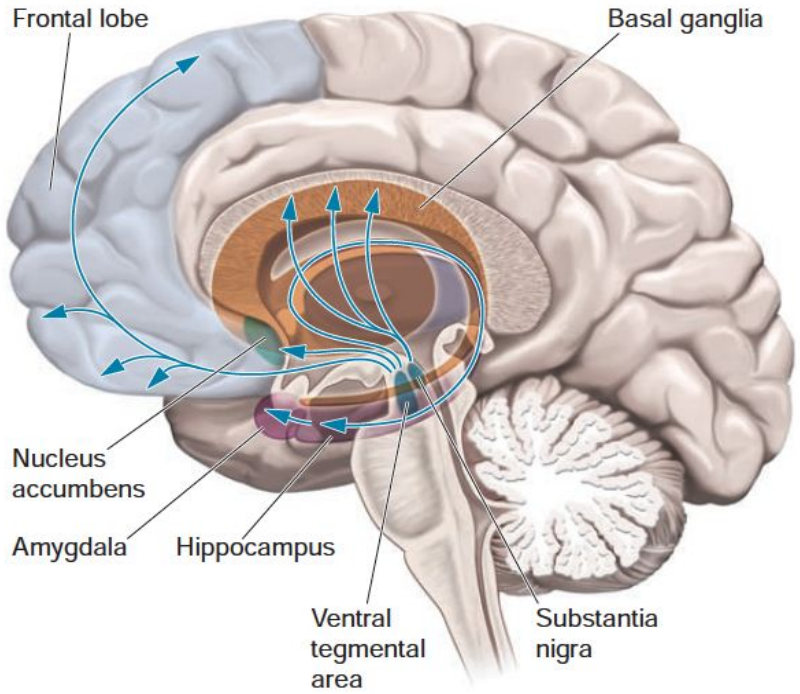
DOPAMINERGIC SYSTEM

THE MESOLIMBIC SYSTEM

✔ It has its cell bodies in the ventral tegmental area.

✔ It projects to several parts of the limbic system, including:

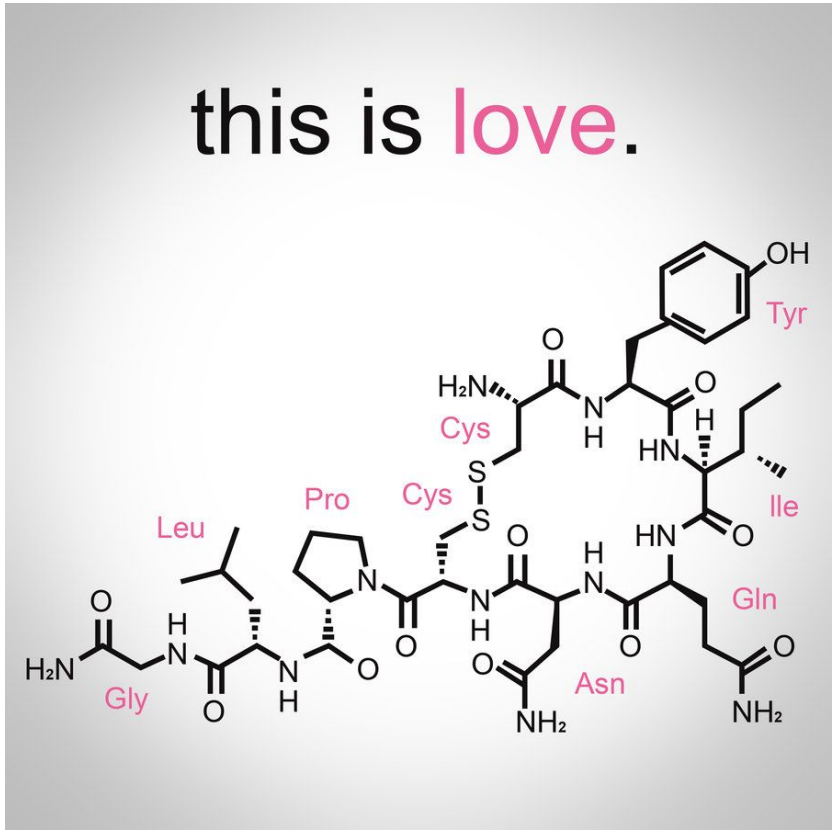
1. nucleus accumbens
2. ventral portions of the striatum
3. amygdala
4. hippocampus
5. prefrontal cortex



DOPAMINERGIC SYSTEM

THE MESOLIMBIC SYSTEM

- ✔ The mesolimbic system has been linked to reward related behavior.
- ✔ Dopamine levels in the nucleus accumbens increase in response to both natural reinforcers (such as food, drink, and sex) and drugs of abuse, such as amphetamine and cocaine.
- ✔ Inputs to prefrontal regions help to integrate what the organism is doing at that time with the appropriate behavioral response to the rewarding stimulus.

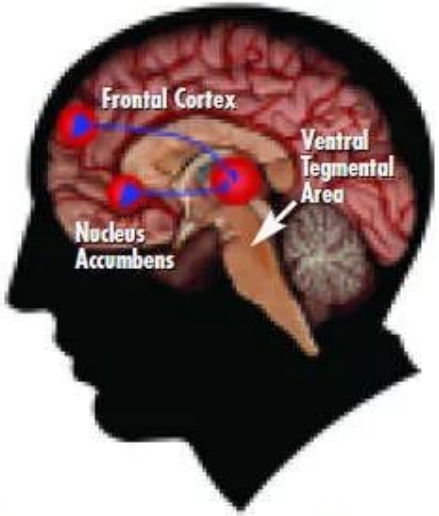


DRUG ADDICTION

- ✔ All drugs directly or indirectly target the reward system by flooding the brain with extracellular dopamine in the limbic regions, including the nucleus accumbens.
- ✔ The body compensates for surges in dopamine by producing less dopamine or decreasing dopamine receptors, reinforcing the user to increase drug intake to bring dopamine levels back to baseline.

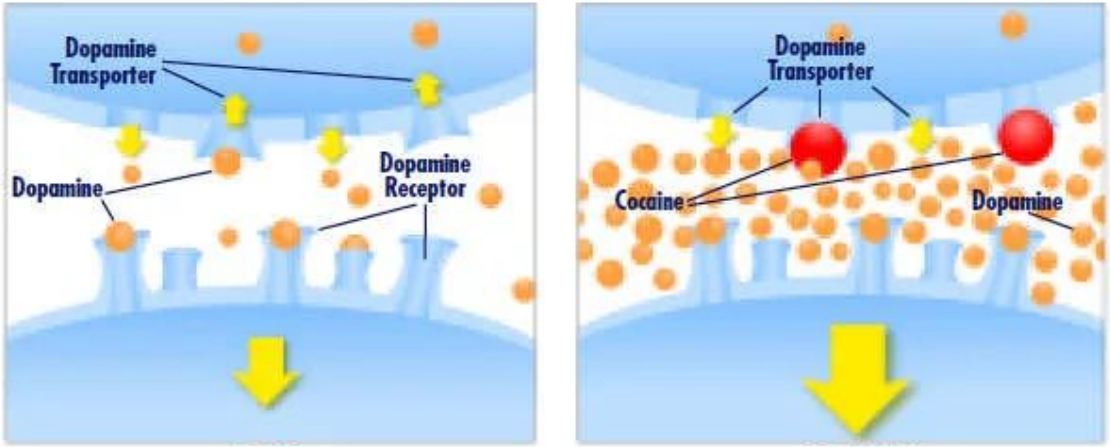
DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

Brain reward (dopamine) pathways



These brain circuits are important for natural rewards such as food, music, and sex.

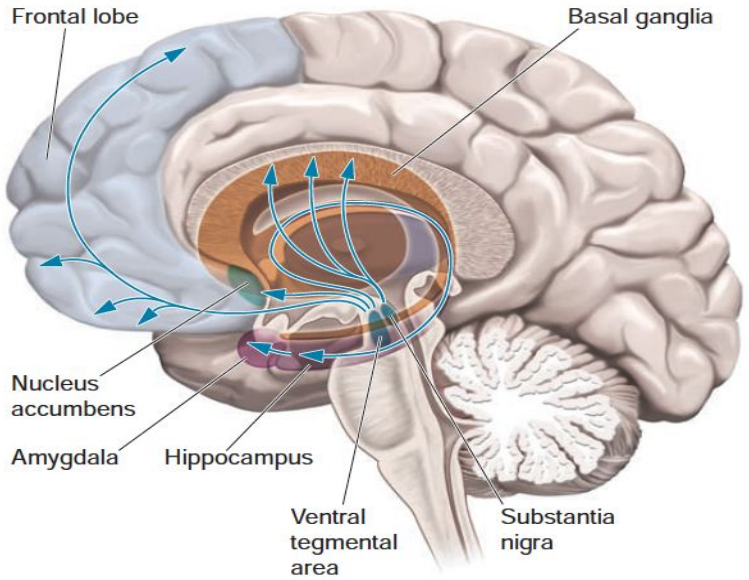
Drugs of abuse increase dopamine



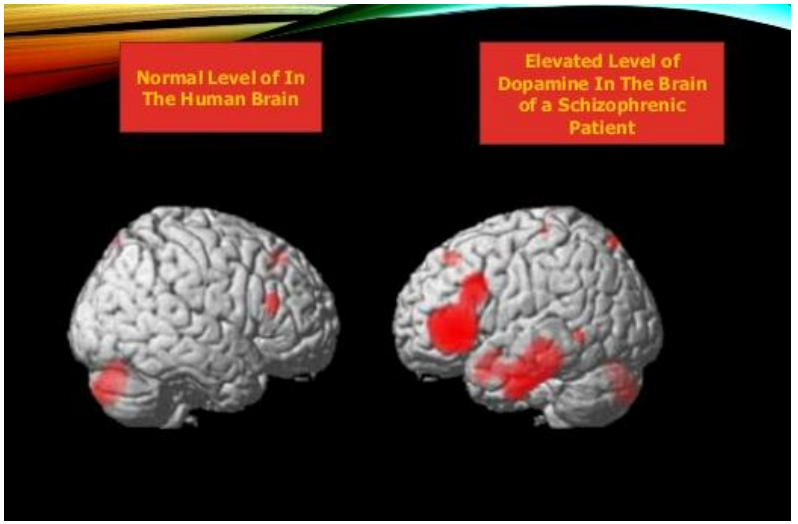
Typically, dopamine increases in response to natural rewards such as food.
When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

DOPAMINERGIC SYSTEM

THE MESOCORTICAL SYSTEM



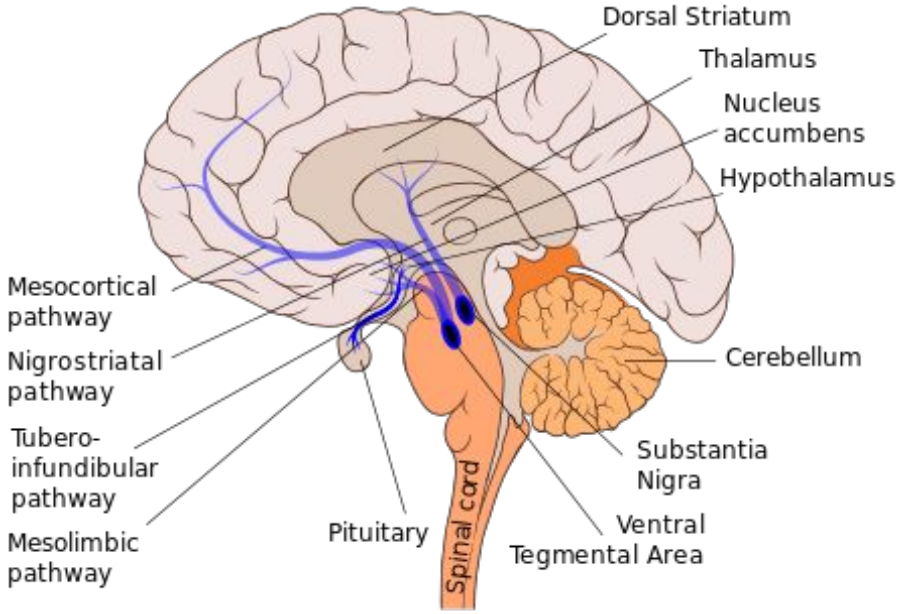
- ✔ The cell bodies are located in the ventral tegmental area.
- ✔ The axons of these cells project to much of the cortex, especially motor and premotor cortex, as well as prefrontal cortex, where they influence a variety of mental functions.
- ✔ One of these functions is working memory, which allows us to keep information “online” for performance of tasks, planning, and strategy preparation for problem solving.
- ✔ This pathway is connected with abnormal functioning in psychoses, such as schizophrenia. It is thought to be associated with the negative symptoms of schizophrenia, which include alogia (marked poverty of speech, or poverty of content of speech), avolition (a lack of motivation).

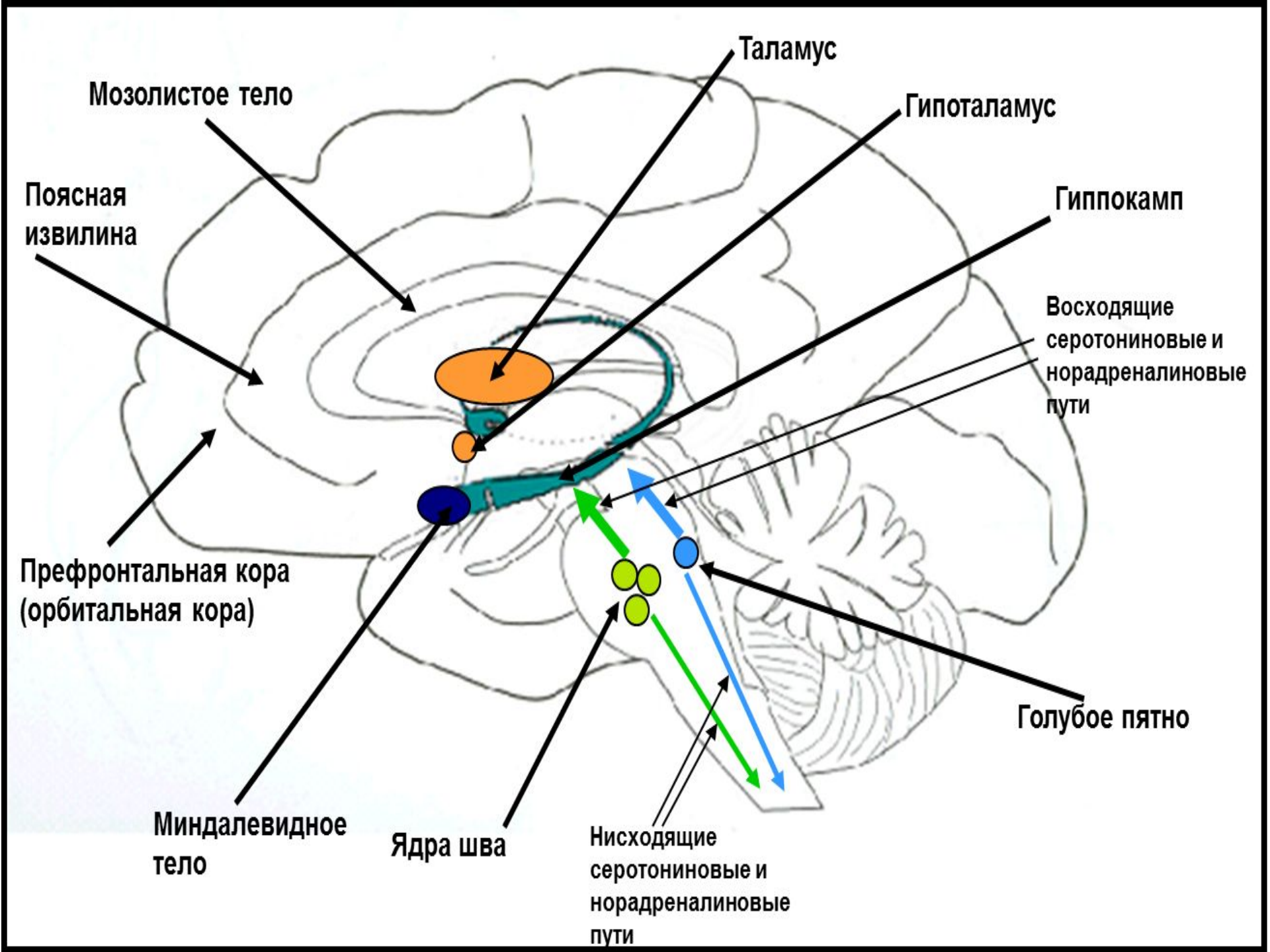


DOPAMINERGIC SYSTEM

THE TUBEROINFINDIBULAR SYSTEM

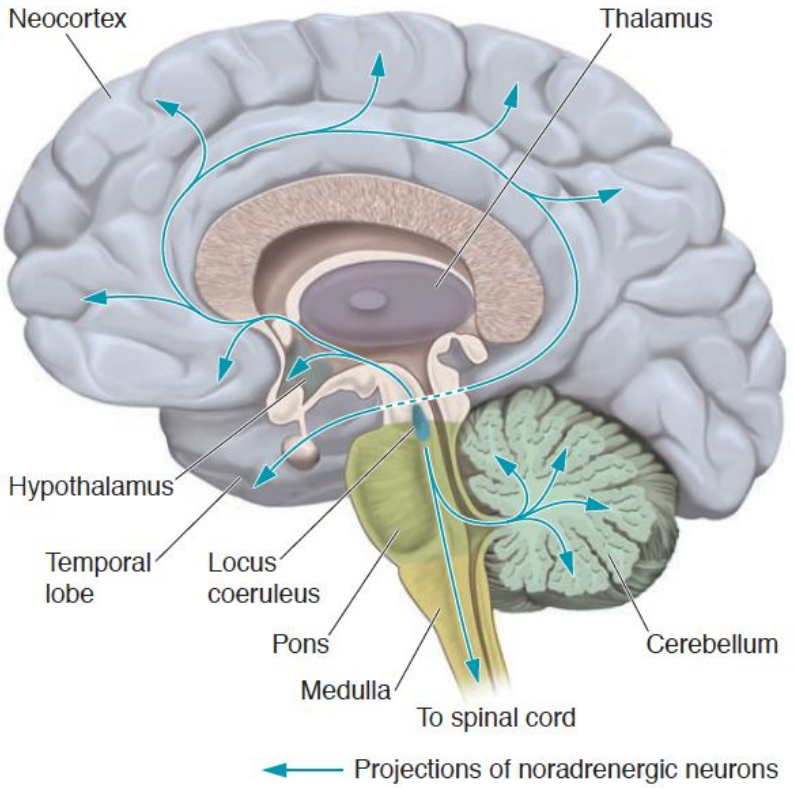
- ✔ The tuberoinfundibular pathway refers to a population of dopamine neurons that project from the arcuate nucleus (the "infundibular nucleus") in the tuberal region of the hypothalamus to the median eminence.
- ✔ Dopamine released at this site regulates the secretion of prolactin from the anterior pituitary gland.
- ✔ Some antipsychotic drugs block dopamine in the tuberoinfundibular pathway, which can cause an increase in blood prolactin levels (hyperprolactinemia). This can cause abnormal lactation (even in men), disruptions to the menstrual cycle in women, visual problems, headache and sexual dysfunction.




Таламус
Мозолистое тело
Гипоталамус
Поясная извилина
Гиппокамп
Восходящие серотониновые и норадреналиновые пути
Префронтальная кора (орбитальная кора)
Голубое пятно
Миндалевидное тело
Ядра шва
Нисходящие серотониновые и норадреналиновые пути

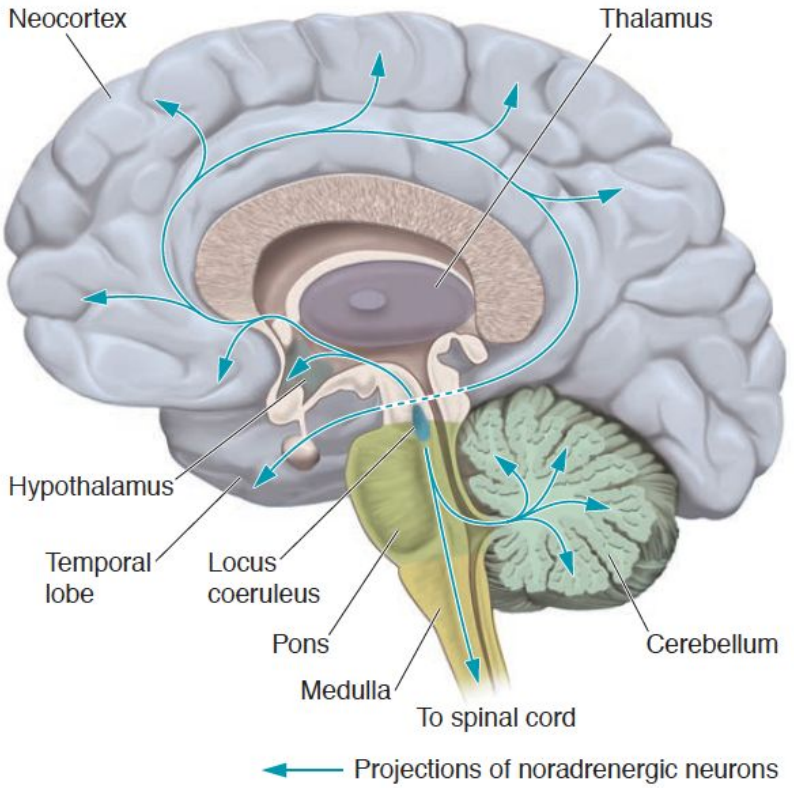
NORADRENERGIC SYSTEM

- ✔ Noradrenaline (or norepinephrine) is the neurotransmitter emitted by cells of the noradrenergic system.
- ✔ The central noradrenergic system originates primarily in the locus coeruleus.
- ✔ Neurons in the locus coeruleus project to
  - the thalamus,
  - the hypothalamus,
  - the cortex (most notably the prefrontal cortex).



NORADRENERGIC SYSTEM

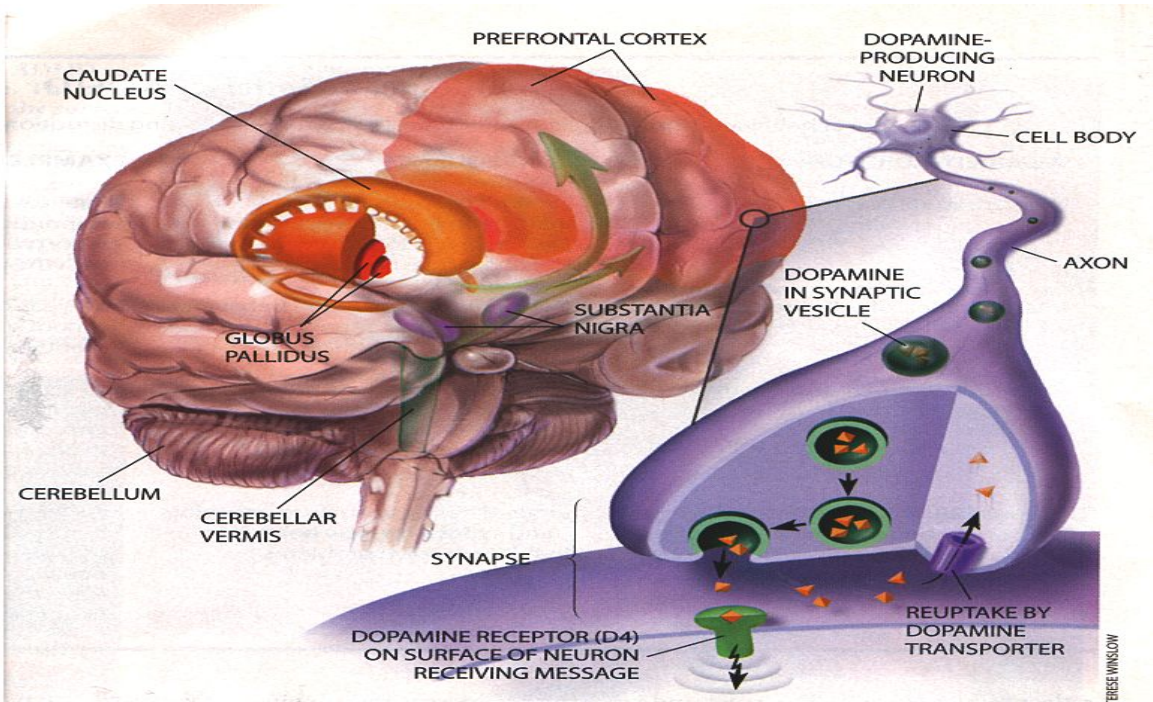
- ✔ The primary cognitive effect of increased activity in the noradrenergic system is to influence arousal and attention.
- ✔ Noradrenaline also plays a role in sleep.
- ✔ Functioning of the noradrenergic system in the prefrontal cortex has also been linked to working memory.
- ✔ The functioning of noradrenaline also may be disrupted in attention deficit hyperactivity disorder (ADHD).
- ✔ Drugs that affect the noradrenergic system have been used clinically to treat ADHD.



NORADRENERGIC SYSTEM

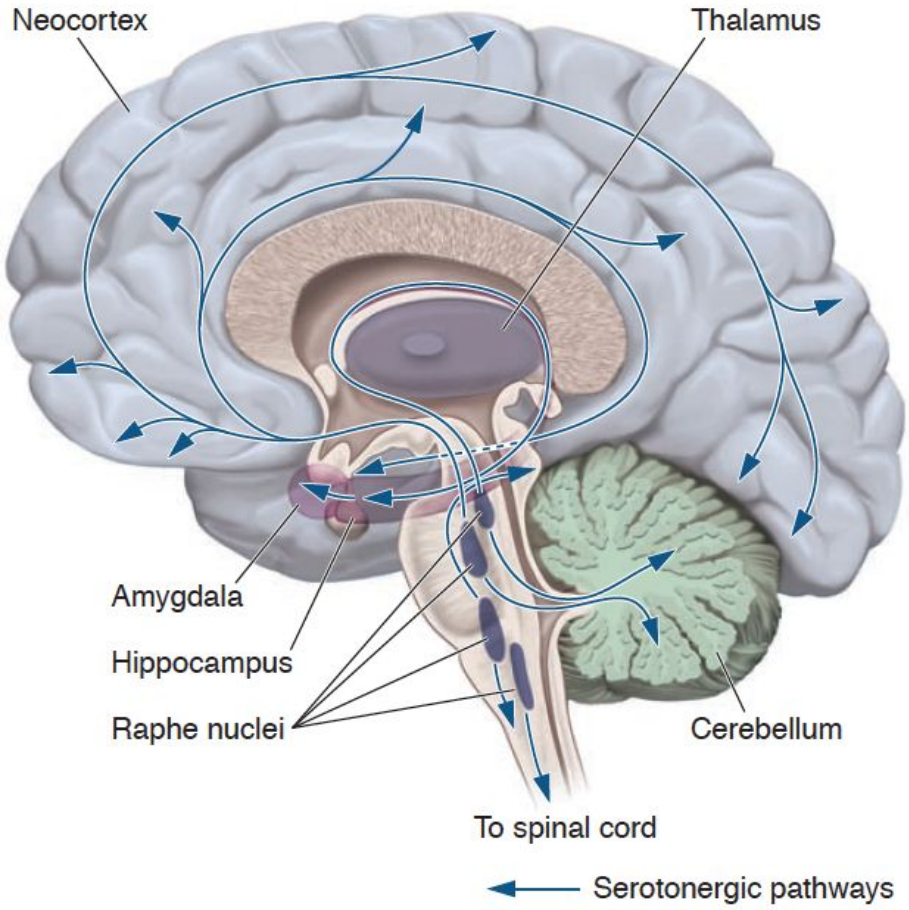
ATTENTION DEFICIT HYPERACTIVITY DISORDER

- ✔ Functional impairments in some of the brain's neurotransmitter systems, particularly those involving dopamine and norepinephrine.
- ✔ The dopamine and norepinephrine pathways which project to the prefrontal cortex and striatum are directly responsible for modulating executive function (cognitive control of behavior), motivation, reward perception, and motor function.
- ✔ In children with ADHD, there is a general reduction of volume in certain brain structures, with a proportionally greater decrease in the volume in the left-sided prefrontal cortex.



SEROTONERGIC SYSTEM

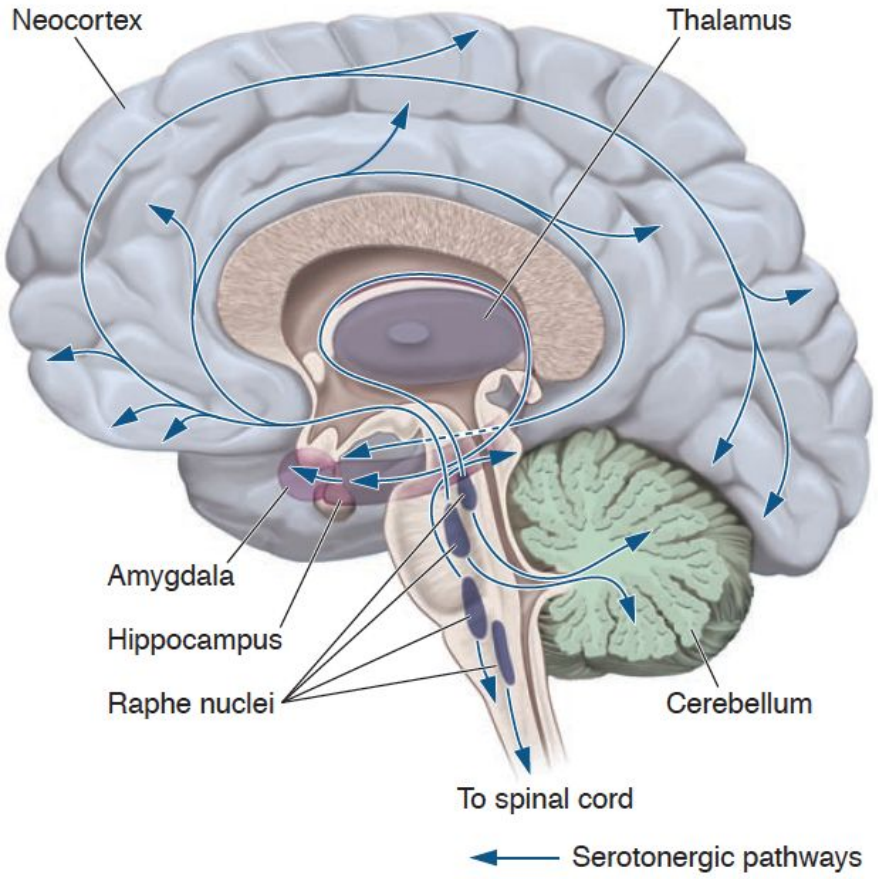
- ✔ Serotonin is the neurotransmitter released by the serotonergic system.
- ✔ The cell bodies of the serotonergic system are found in several clusters located in the raphe nuclei of the midbrain, pons, and medulla.
- ✔ Cells from the dorsal raphe project with greater density to the striatum, cortex, cerebellum, and thalamus.
- ✔ Cells from the medial raphe project more to the hippocampus and other limbic structures.



SEROTONERGIC SYSTEM

✔ This system influences a large variety of behaviors, including:

1. arousal
2. mood (most notably depression)
3. anxiety and aggression
4. the control of eating
5. sleeping and dreaming
6. pain
7. sexual behavior
8. memory (specifically the function of putting ne memories into long-term storage)



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TRIPARTITE MODEL OF DEPRESSION

Deficiency of serotonin 5-HT

- anxiety
- panic attacks
- tachycardia
- excessive sweating
- dryness of mucous membranes
- digestive disorders
- pain

Deficiency of norepinephrine NA

- tiredness
- deficit of attention
- concentration difficulties
- slowing of thought processes
- motor retardation
- pain

Deficiency of dopamine D

- violation of smoothness and pithiness of thinking
- digestive disorders

Clark L.A., Watson D.J. // Abnorm Psychol. 1991;100:316-336.

THANK YOU FOR YOUR ATTENTION