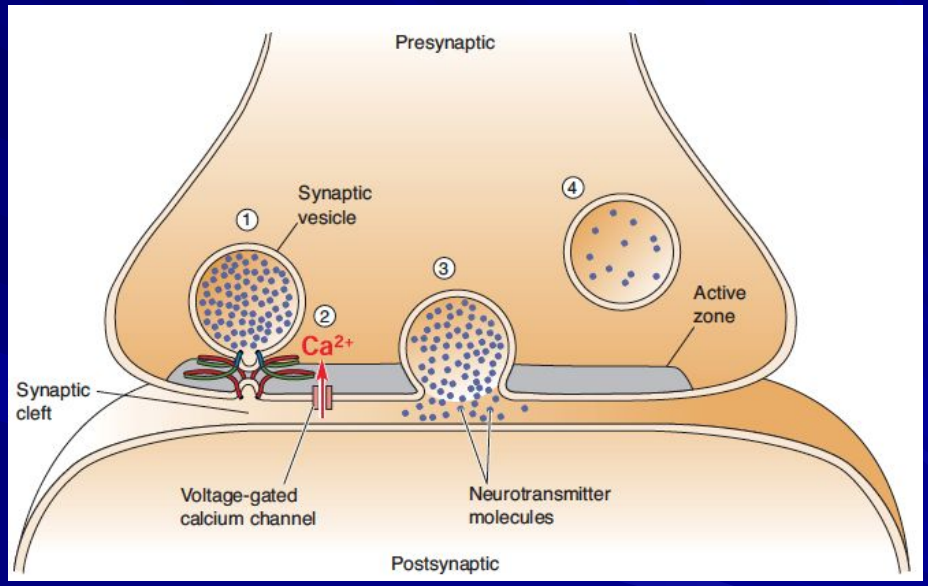
Neurotransmitters

Neurotransmitters are the chemicals that neurons release that allow them to communicate with one another.

In this section we discuss

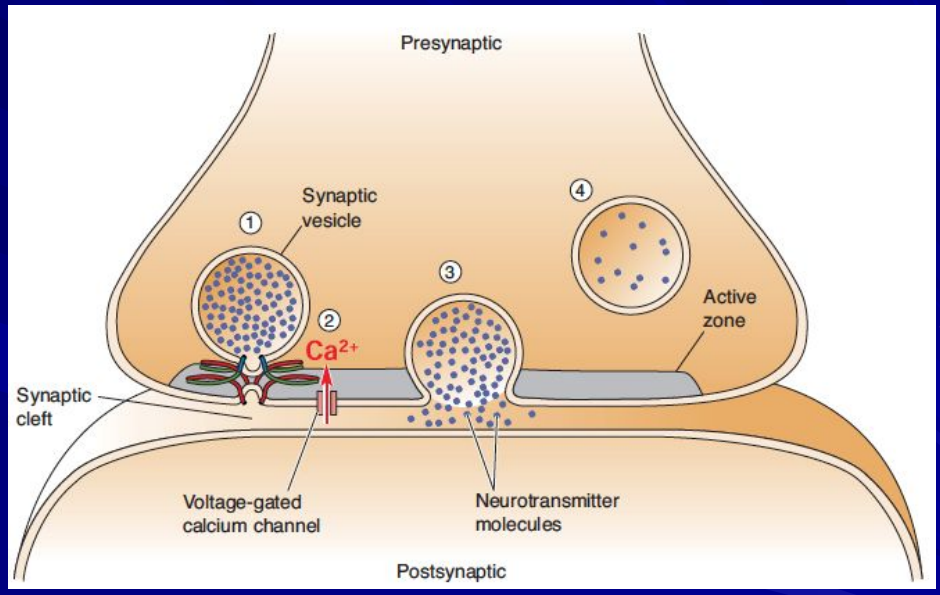
1. Different types of neurotransmitters
2. The characteristics of neurotransmitters
3. The type of receptors to which neurotransmitters bind
4. Influence of the neurotransmitters on mental function



Neurotransmitters

Major characteristics of neurotransmitters

1. They are chemicals synthesized within the neuron.
2. They are released when the cell is activated by an action potential
3. They have an effect on a target cell (neuron or muscle cell).
4. When the release of the neurotransmitter is blocked, an action potential will not result in activity in the postsynaptic neuron.
5. One neuron can release one, two or more neurotransmitters.



Neurotransmitters

Two major classes of neurotransmitters in the CNS

1. Amino acids

- the smallest and most basic building blocks of proteins
- act as the main excitatory and inhibitory neurotransmitters in the brain

2. Neurotransmitter Systems

- these neurotransmitters are produced by specific sets of neurons whose cell bodies are located subcortically and whose axons project diffusely throughout the cortex.

Neurotransmitters

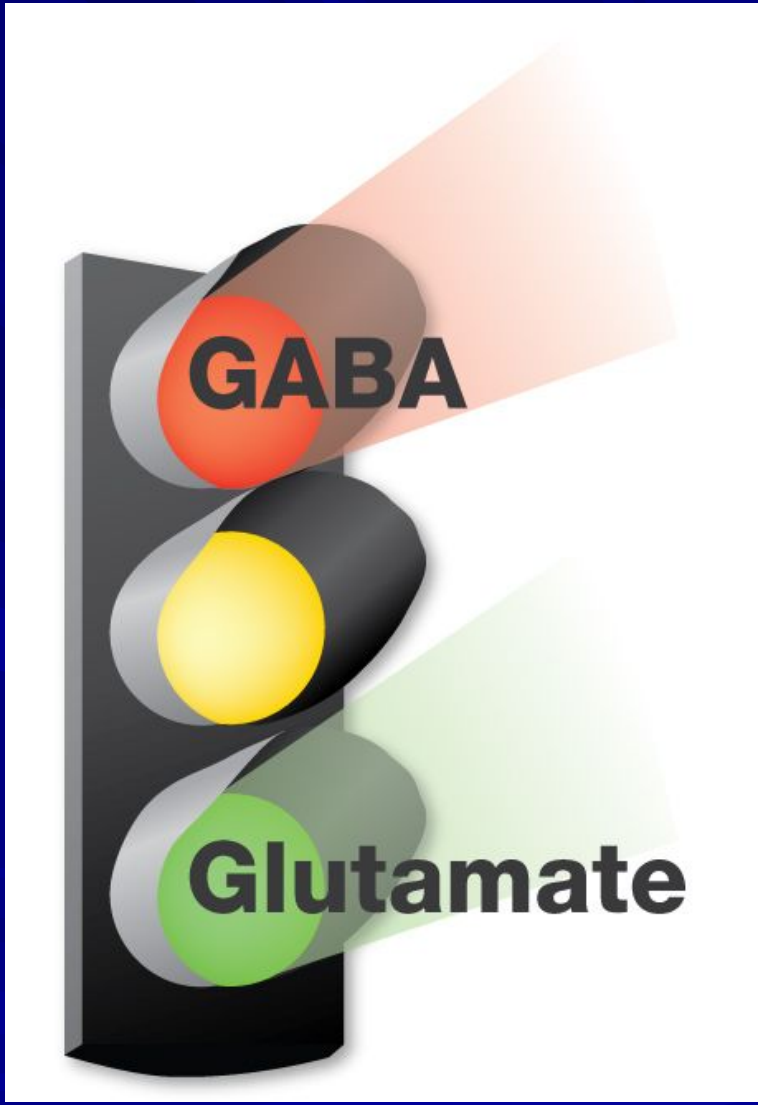
Amino acids

The two main amino acids

1. Glutamate, which has an excitatory effect,
2. GABA (gamma-aminobutyric acid), which has an inhibitory effect.

- Two other amino acids that also serve as neurotransmitters

1. Aspartate, which is excitatory
2. Glycine, which is inhibitory.



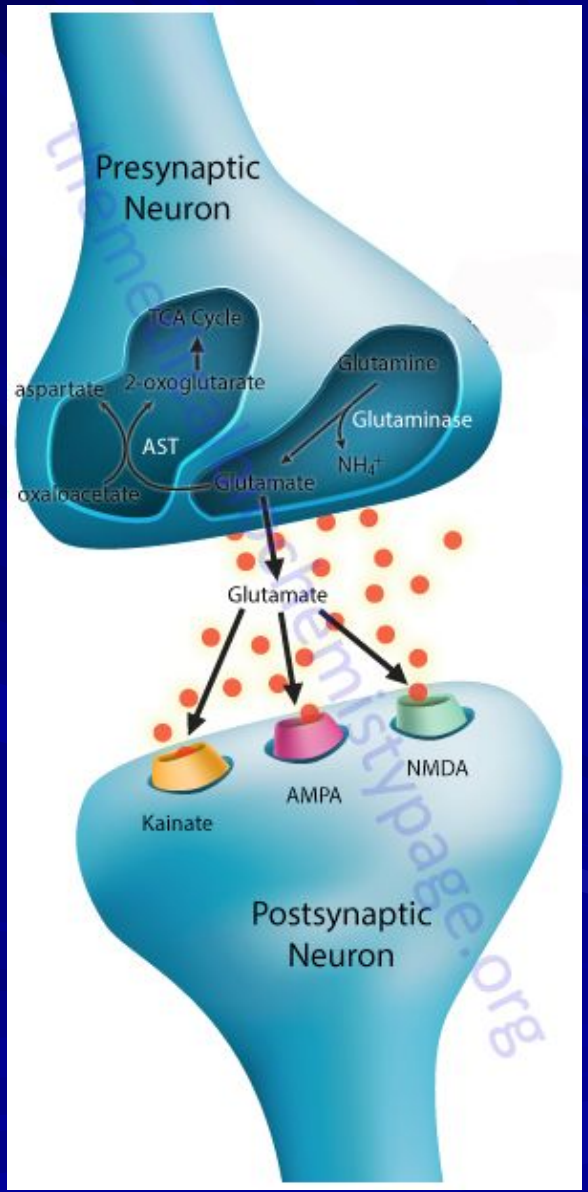
Neurotransmitters

Glutamate

- The main excitatory amino acid neurotransmitter in the CNS.
- This neurotransmitter is used at approximately 15 to 20% of synapses in the CNS.

- There are four major glutamatergic receptors.

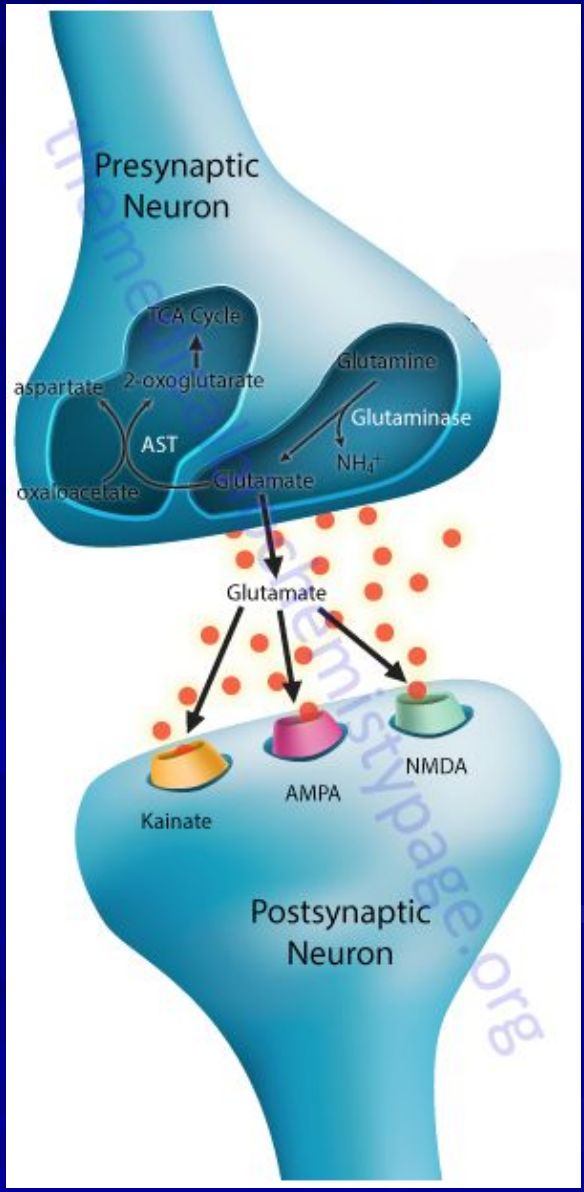
1. Three are ionotropic (NMDA, AMPA, kainate)
2. The fourth is the metabotropic glutamate receptor.



Neurotransmitters

Glutamate

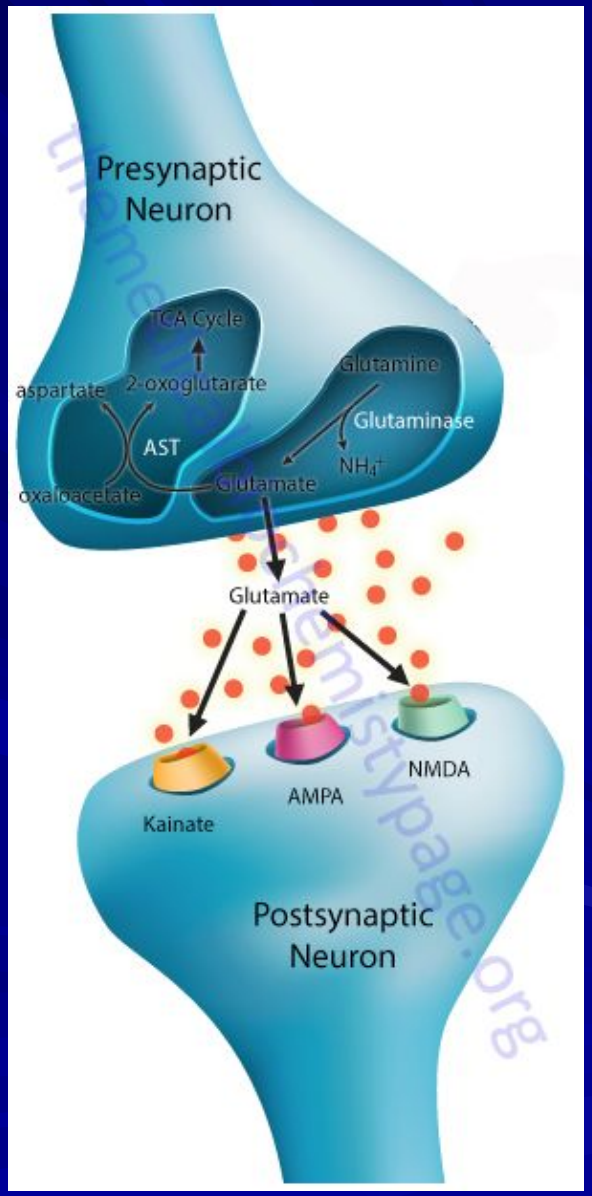
- Binding of glutamate to the AMPA and kainate receptors produces EPSPs.
- Binding of glutamate to the NMDA receptor has special properties that allow it not only to regulate the entry of ions, but also to allow those ions to act as second messengers to change the biochemical and structural properties of the cell.
- These changes are important for the production of new memories, as they initiate a cascade of events that leads to changes in the shape and number of spines at synaptic sites.



Neurotransmitters

Glutamate

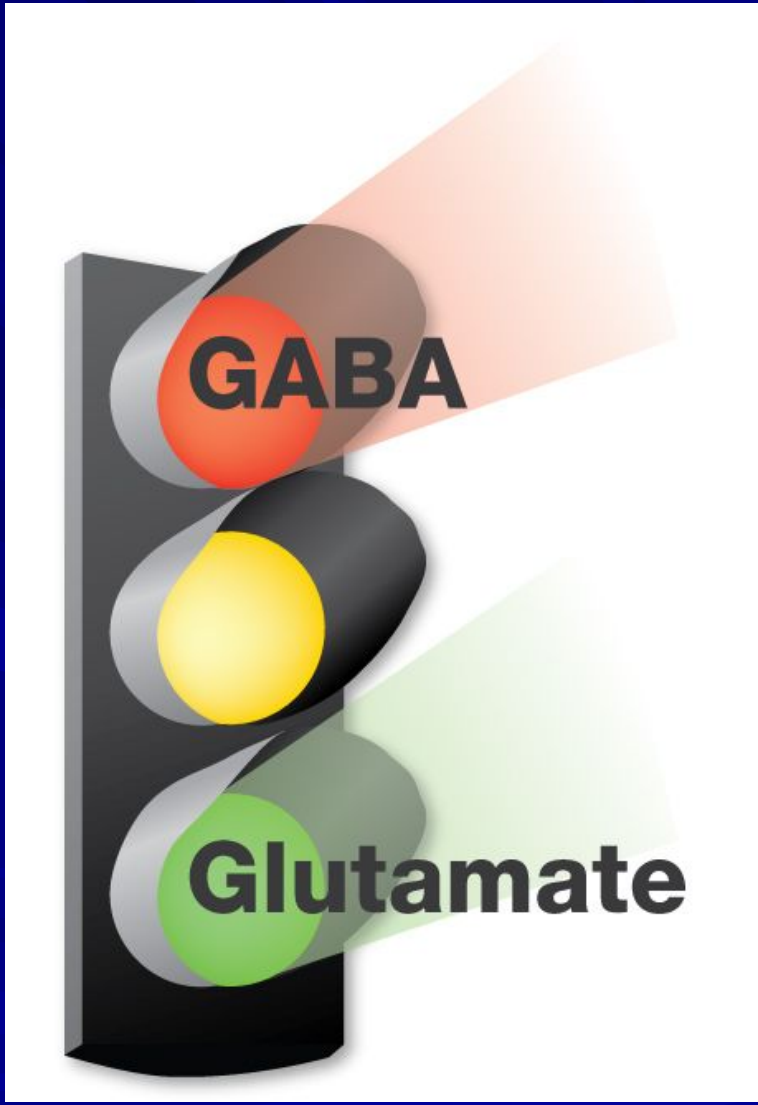
- Overactivity of glutamate in the brain is thought to play a role in the development of epilepsy.
- Too much glutamate can produce excitotoxicity, which is excessive activity of receptors that can literally excite neurons to death.
- Excitotoxicity appears to be an unfortunate consequence of a particular form of brain damage, known as ischemia.



Neurotransmitters

Gamma-Aminobutyric Acid (GABA)

- The main inhibitory amino acid neurotransmitter
- About 40% of receptors in the CNS are GABAergic
- The inhibitory control provided by GABA is thought to be important for “fine-tuning” the pattern of activation across the nervous system.

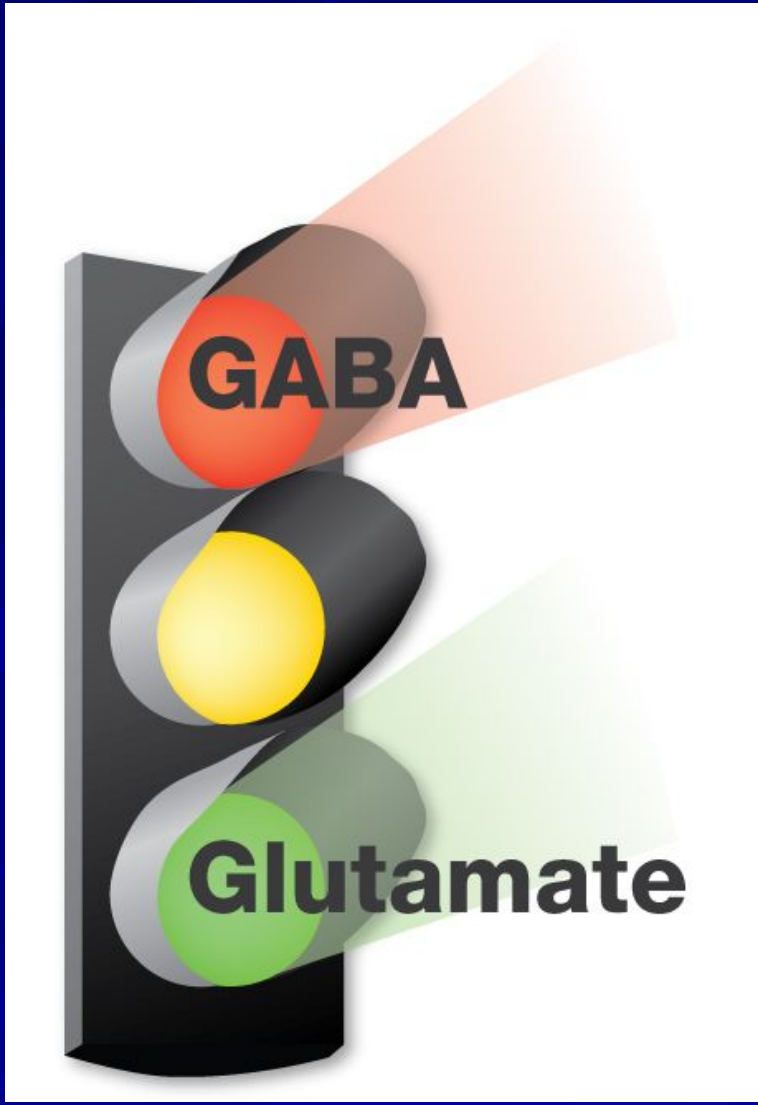


Neurotransmitters

Gamma-Aminobutyric Acid (GABA)

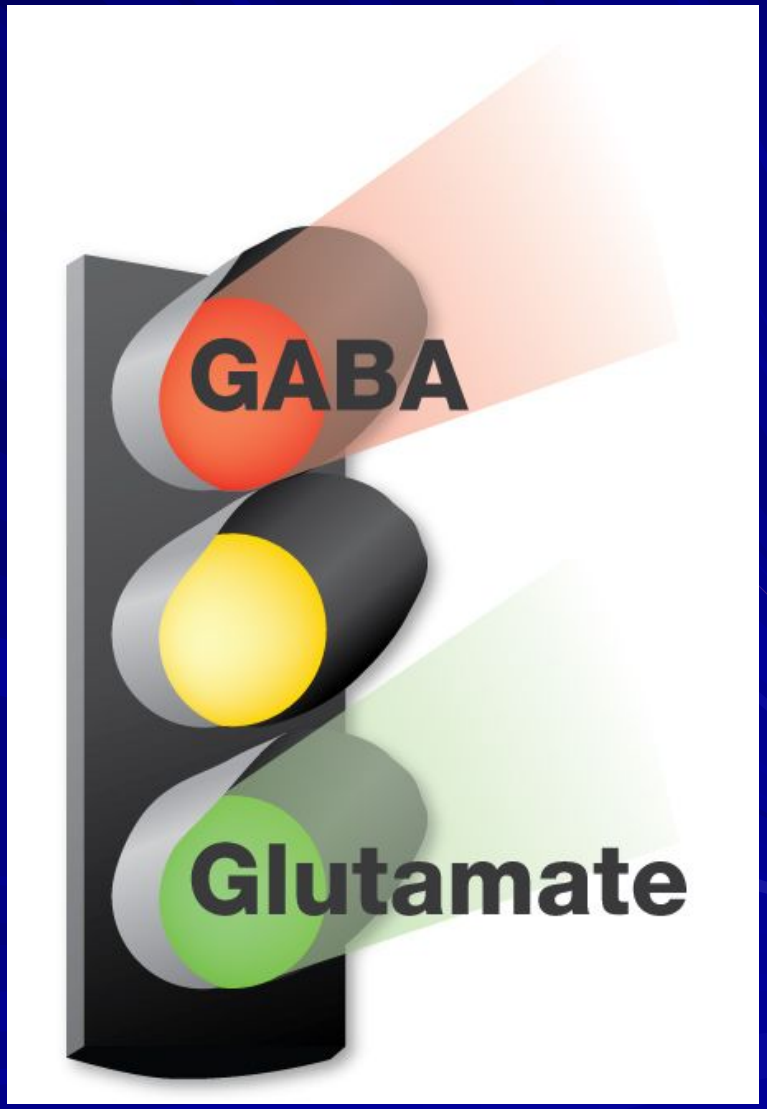
- There are two main types of GABA receptors:
- $GABA_a$ is an ionotropic receptor
- $GABA_b$ is metabotropic receptor

- Both appear to be important in dampening oscillatory, reverberatory excitation between the thalamus and cortex



Neurotransmitters

- Many substances that reduce the activity of the CNS bind to GABA receptors.
- One such group of substances is barbiturates (a class of CNS depressants)
- These drugs reduce seizure activity and induce sedation and sleep.
- Other substances that bind to GABA receptors are tranquilizing drugs called benzodiazepines (Valium and Librium).
- These drugs are generally used to treat anxiety disorders, but can also be used as antiseizure medication and to promote sleep and muscle relaxation.



Neurotransmitters

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

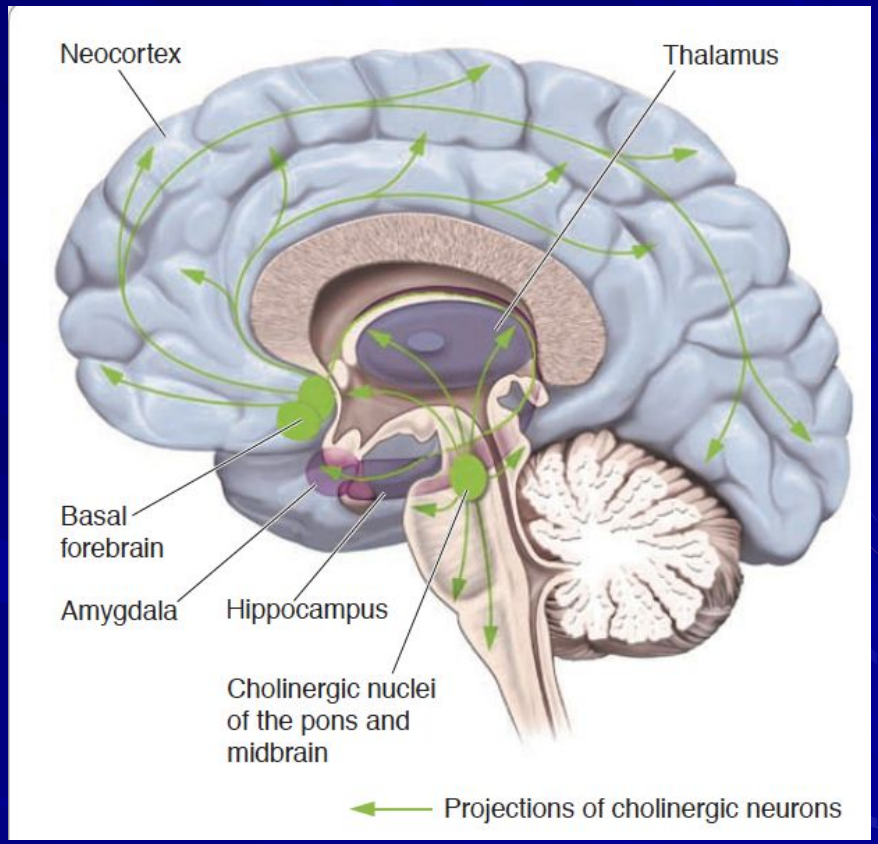
1. acetylcholine
2. dopamine
3. noradrenaline (norepinephrine)
4. serotonin

- 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.

Neurotransmitters

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.



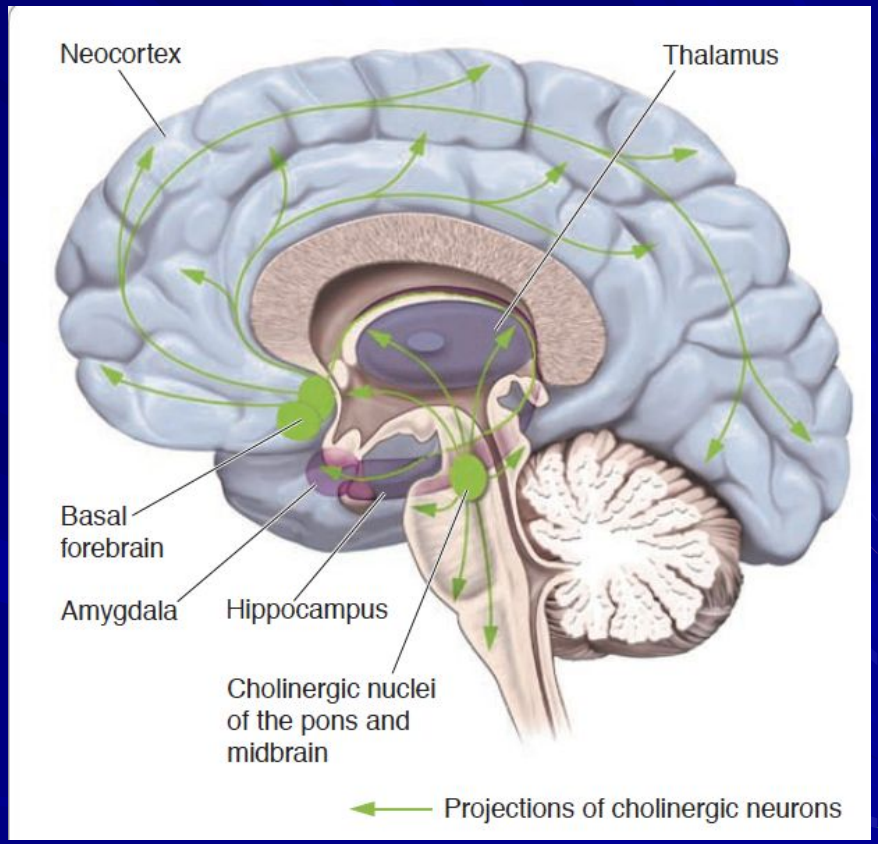
Neurotransmitters

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 muscariam).



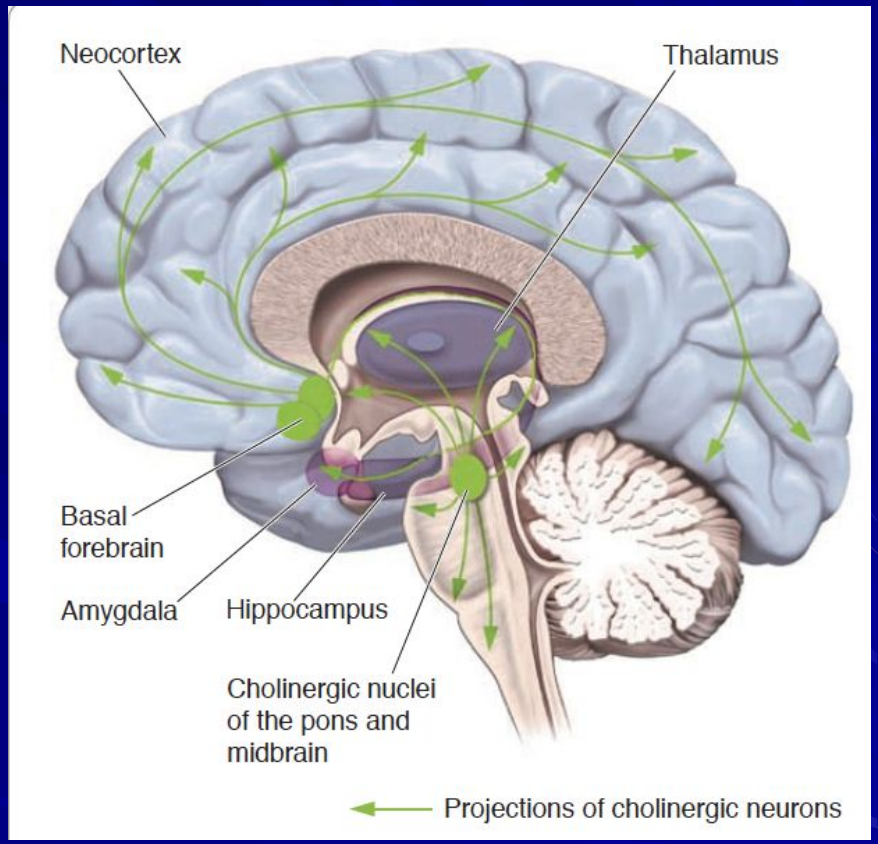
Neurotransmitters

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).

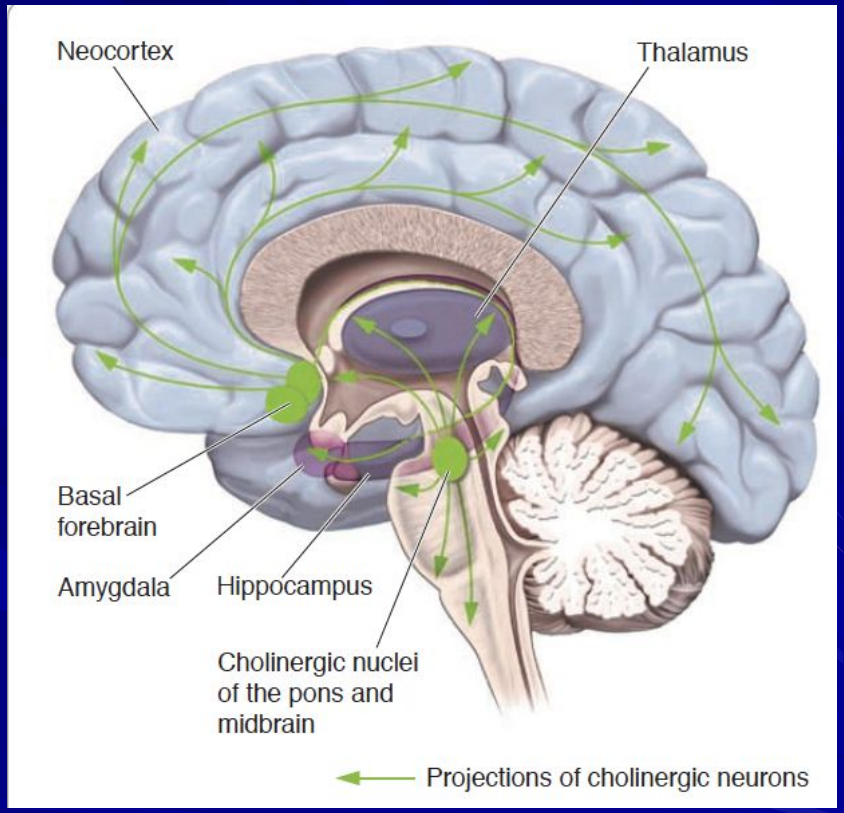
- ACh has also been linked to the production of rapid eye movement (REM) sleep, which is that portion of sleep when we dream and our minds are relatively active.



Neurotransmitters

Cholinergic System

- The activity of the cholinergic system has been linked to paying attention
- Cholinergic activity appears to be important for overall arousal or vigilance — 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.
- ACh appears to sharpen the responses of cells to the features of stimuli that are most likely to make them fire, while suppressing responses to less prominent features of a stimulus



Neurotransmitters

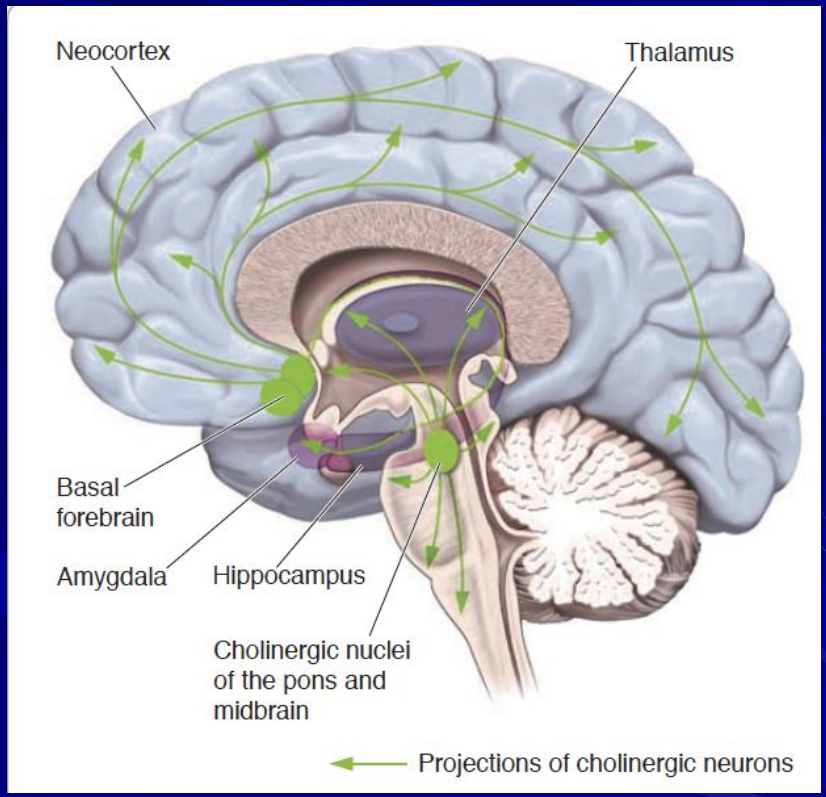
Cholinergic System

- 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.

Conclusion

- ACh may affect both attentional and memory processes because it modulates an operation required in both: that of selecting certain types of information while ignoring other types.



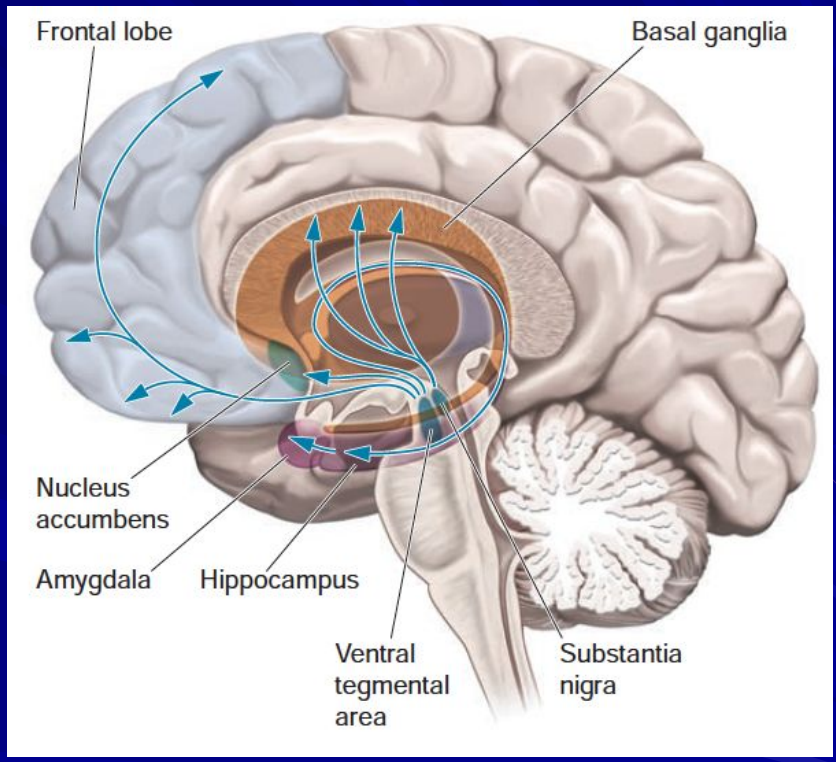
Neurotransmitters

Dopaminergic System

- Dopamine is the main neurotransmitter used in the dopaminergic system.

- There are actually three dopaminergic subsystems:
  1. the nigrostriatal
  2. the mesolimbic
  3. the mesocortical

- 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

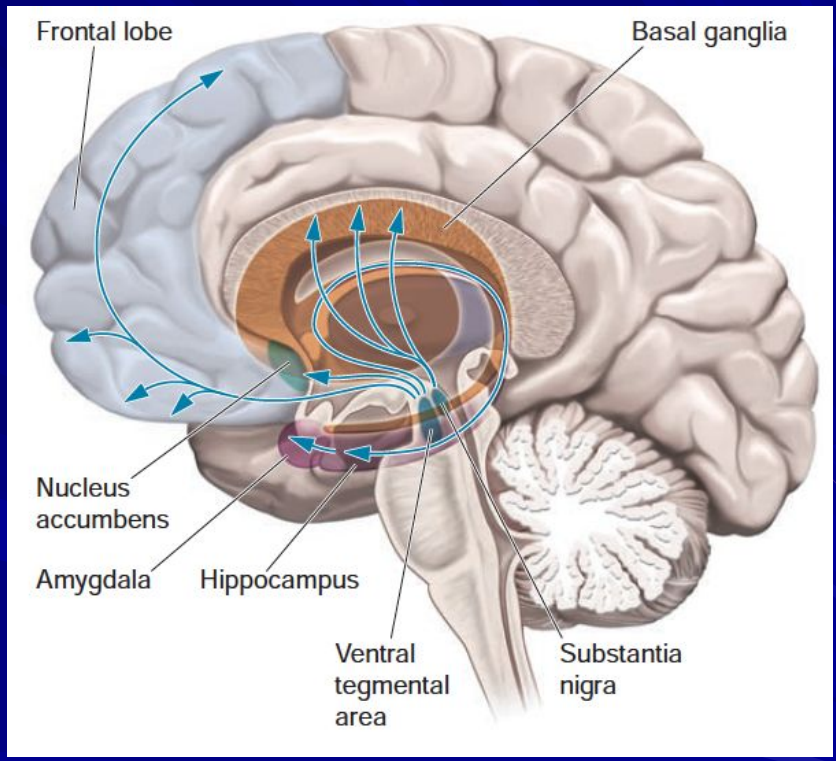


Neurotransmitters

Dopaminergic System

The nigrostriatal system

- The cell bodies of this system are located in the substantia nigra and project to the neostriatum (i.e., the caudate nucleus and putamen, also known as the basal ganglia).
- This subsystem regulates the selection, 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.



Neurotransmitters

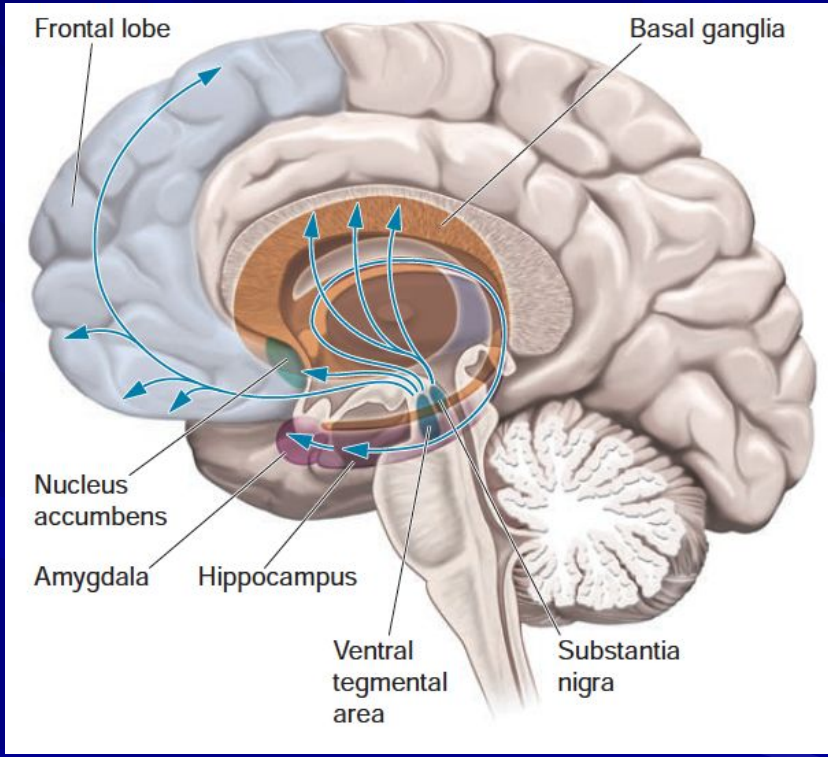
Dopaminergic System

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

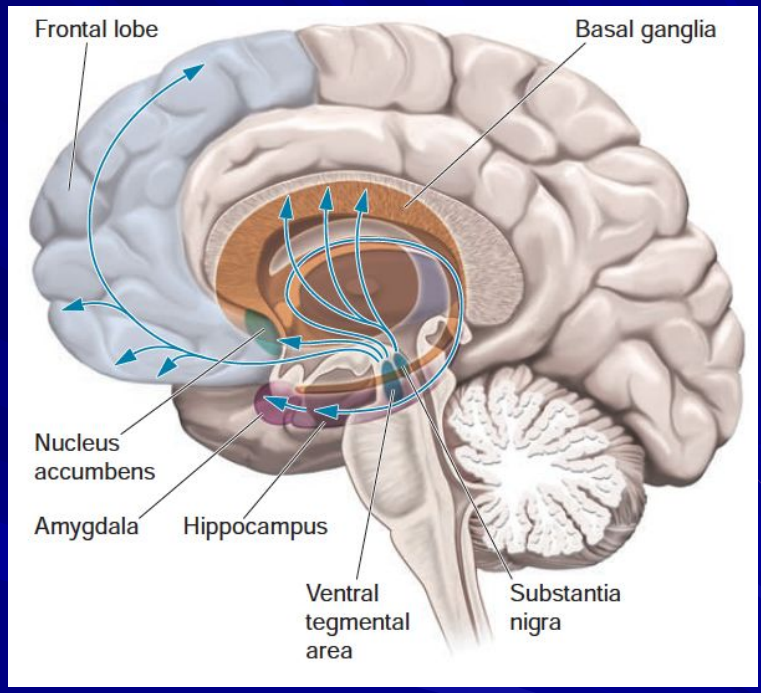


Neurotransmitters

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.
- Activity within the ventral portion of the striatum has been linked to a wide variety of reinforcers.
- The portion of the mesolimbic system that projects to the amygdala appears to be important for linking predictive cues to either a rewarding or aversive stimulus.
- Inputs to prefrontal regions help to integrate what the organism is doing at that time with the appropriate behavioral response to the rewarding stimulus.

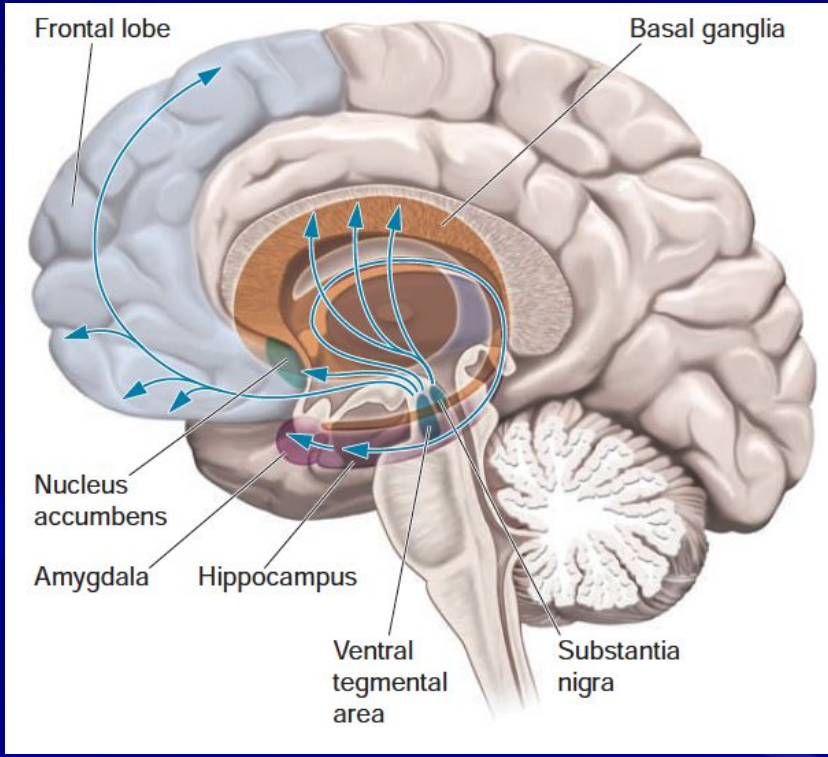


Neurotransmitters

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.



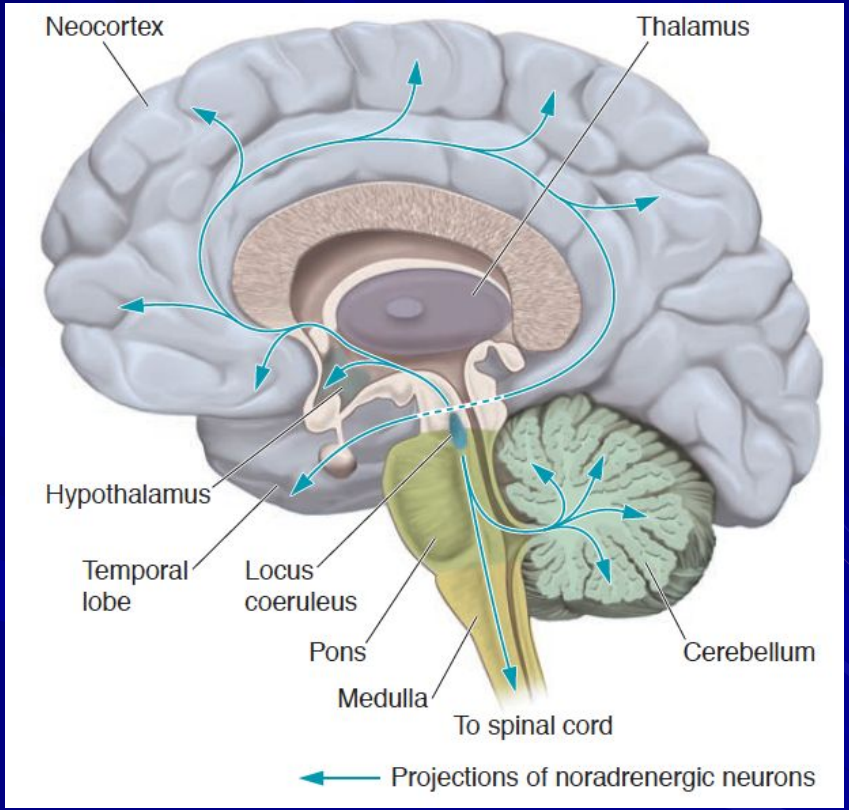
Neurotransmitters

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

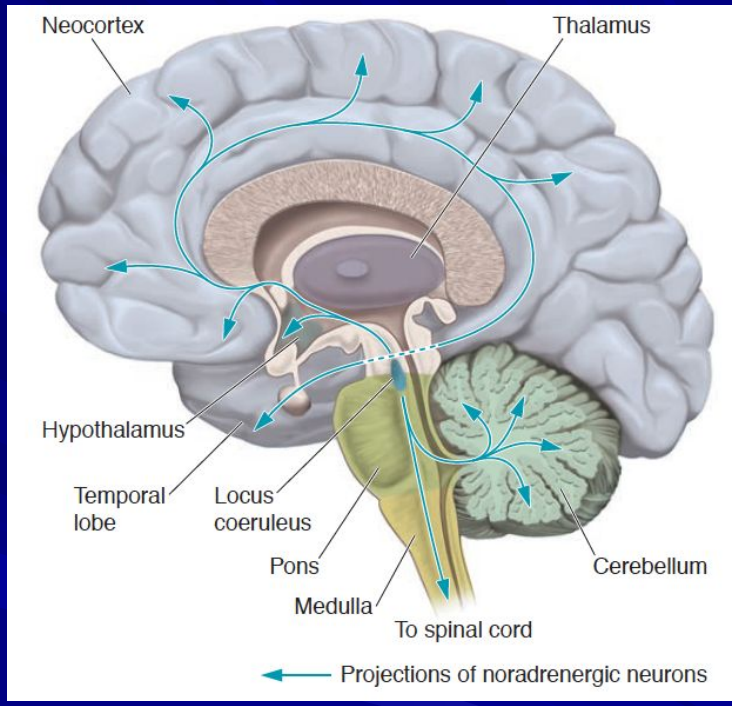
- Neurons in the locus coeruleus project to
- the thalamus,
- the hypothalamus,
- the cortex (most notably the prefrontal cortex).



Neurotransmitters

Noradrenergic System

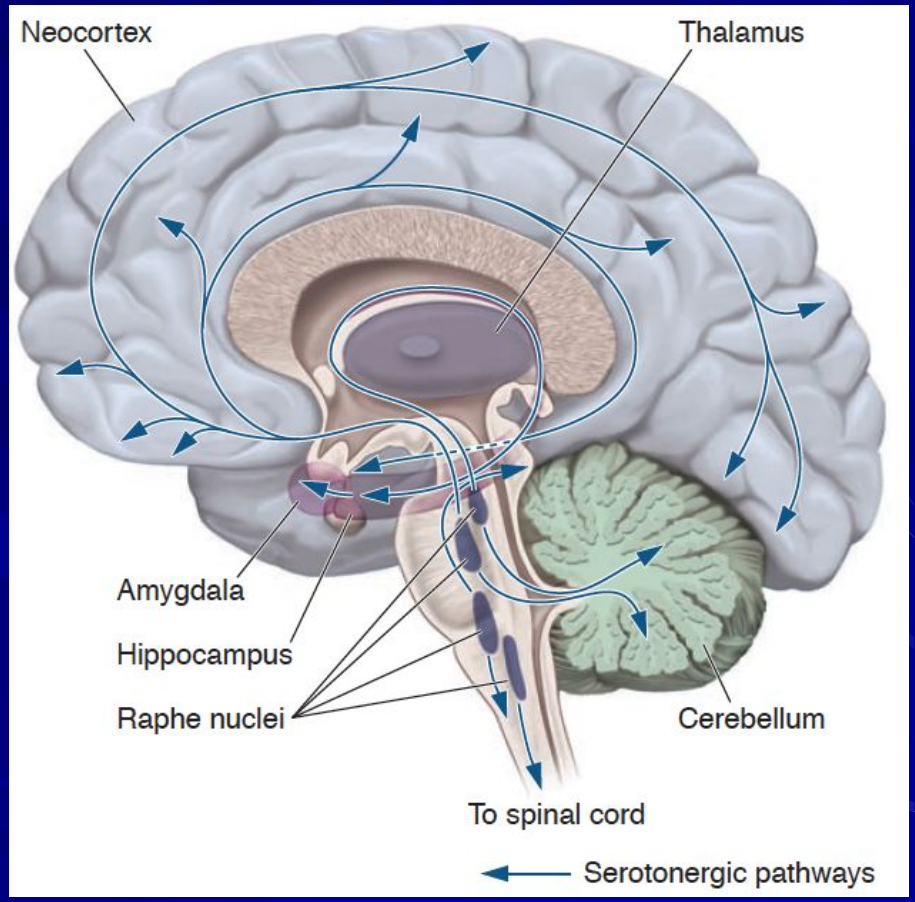
- The primary cognitive effect of increased activity in the noradrenergic system is to influence arousal and attention.
- Noradrenaline also plays a role in sleep.
- The functioning of noradrenaline also may be disrupted in attention deficit hyperactivity disorder (ADHD).
- Drugs that affect the noradrenergic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



Neurotransmitters

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 from the medial raphe project more to the hippocampus and other limbic structures.



Neurotransmitters

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 new memories into long-term storage)

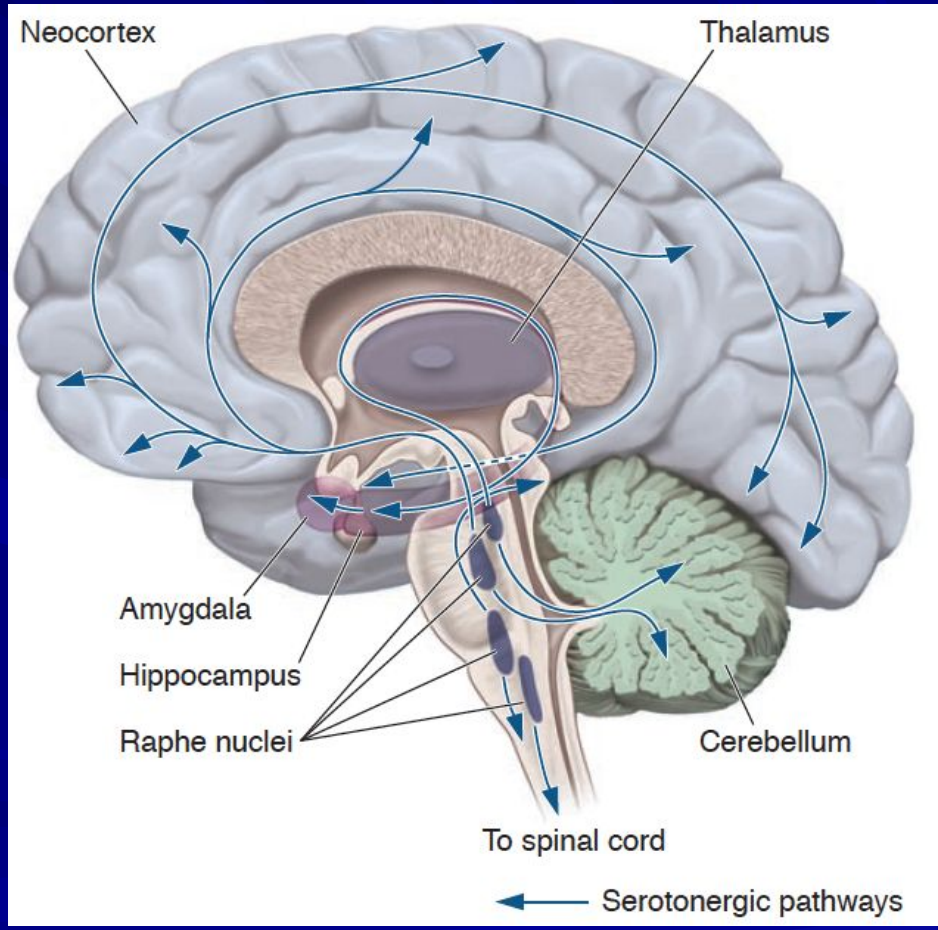


TABLE 2.1 The Four Main Neurotransmitter Systems

Neurotransmitter System	Transmitter	Site of Origin	Projection Sites	Main Receptor Types	Main Behavioral Effects
Cholinergic	Acetylcholine	Basal forebrain	Diffuse cortical regions	a. Muscarinic b. Nicotinic	Overall cortical excitability, attention, memory
Dopaminergic	Dopamine			a. D_1 family (D_1 & D_5) b. D_2 family (D_2, D_3, & D_4)	Working memory, novelty seeking, attention, psychotic symptomatology
Subsystems NIGROSTRIATAL		Substantia nigra	Dorsal striatum		Motor activity
MESOLIMBIC		Ventral tegmental area	a. Limbic regions b. Ventral striatum		Reward
MESOCORTICAL		Ventral tegmental area	Prefrontal cortex		Working memory, planning
Noradrenergic	Noradrenaline (norepinephrine)			α_1, α_2, $ß_1$, $ß_2$	
		Ventrolateral tegmental area	Hypothalamus		Feeding, sexual behavior
		Locus coeruleus	a. Thalamus b. Hypothalamus c. Cortex		Attention, sleep, working memory
Serotonergic	Serotonin			At least nine different receptors	Sleep, mood, sexual behavior, eating, pain, memory, arousal
		Dorsal raphe nucleus	a. Cortex b. Thalamus		
		Medial raphe nucleus	Limbic system		