Brain Neurotransmitters

* Chemical substances released by electrical impulses into the synaptic cleft from synaptic vesicles of presynaptic membrane
* Diffuses to the postsynaptic membrane
* Binds to and activates the receptors
* Leading to initiation of new electrical signals or inhibition of the post-synaptic neuron

Classification of Neurotransmitters

Amines		
Acetylcholine (ACh)	Dopamine (DA)	Norepinephrine (NE)
Serotonin (5-HT)	Histamine	Epinephrine

Amino Acids		
Gamma-aminobutyric acid (GABA)	Glycine	Glutamate
Aspartate		

Neuroactive Peptides - 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
gonadotropnin-releasing hormone	growth hormone-releasing hormone	luteinizing hormone	vasoactive intestinal peptide

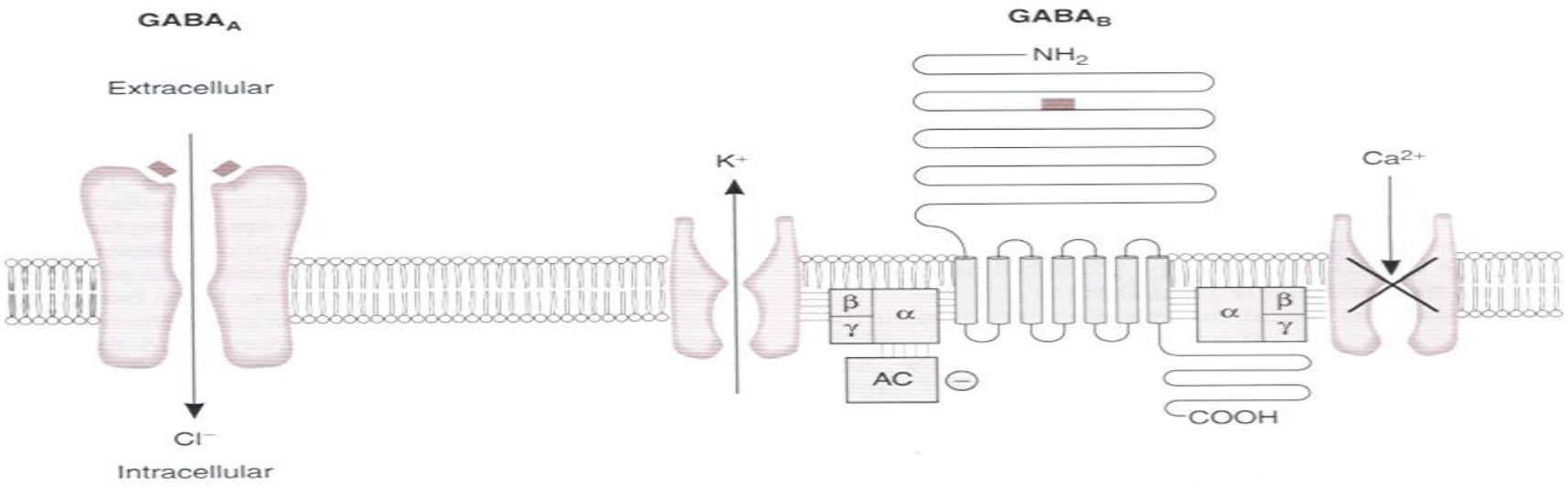
Soluble Gases	
Nitric Oxide (NO)	Carbon Monoxide

1- Adrenaline / NE
2- Ach
3- Glutamate
4- GABA
5- Serotonin
6- Dopamine

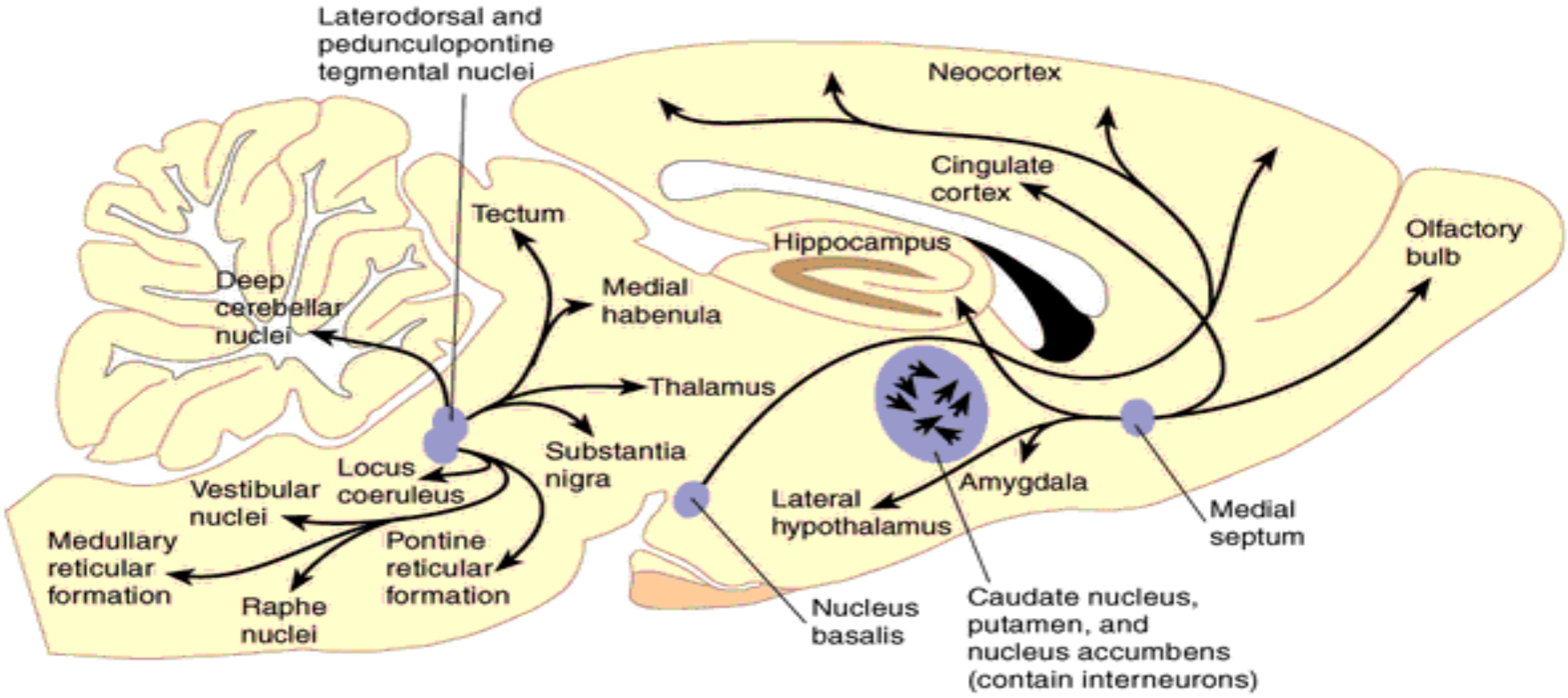
Classes of Receptors

* Metabotropic = trans membrane receptor acts through a secondary messenger

* Ionotropic = Ligand gated ion channel



1- Norepinephrine System



Nucleus Coeruleus in the pons, involved in physiological responses to stress and panic

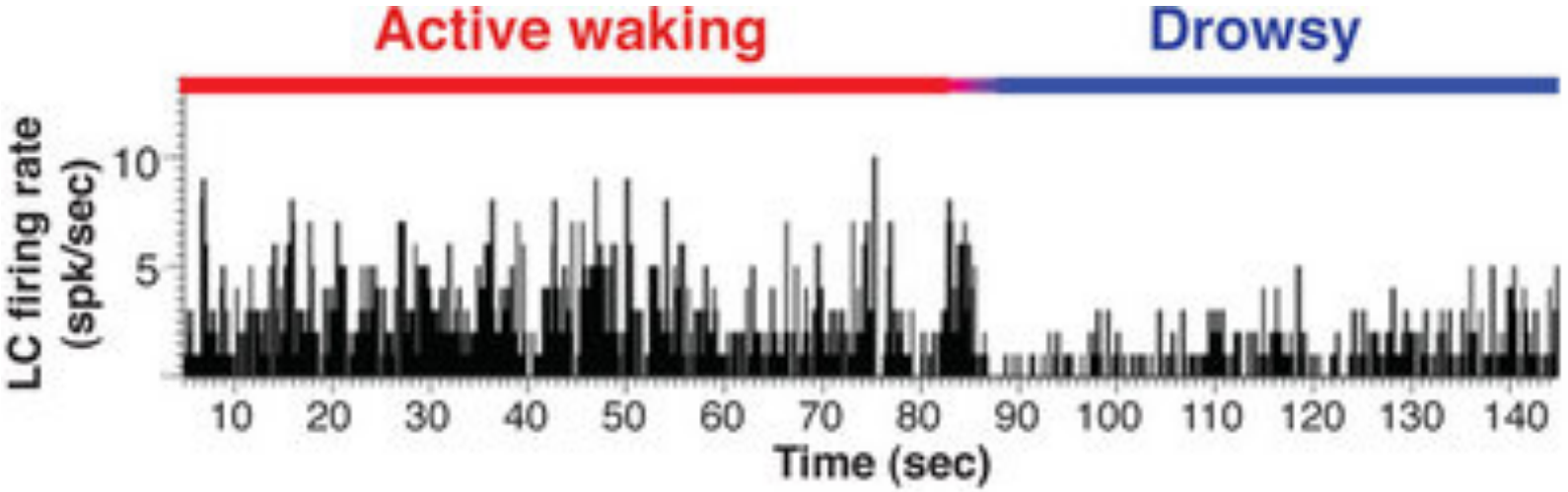
The Locus Coeruleus/Norepinephrine System

- Very wide-spread projection system
- LC is activated by stress and co-ordinates responses via projections to thalamus, cortex, hippocampus, amygdala, hypothalamus, autonomic brainstem centers, and the spinal cord
- Sleep
- Attention/Vigilance

Locus coeruleus neurons fire as a function of vigilance and arousal

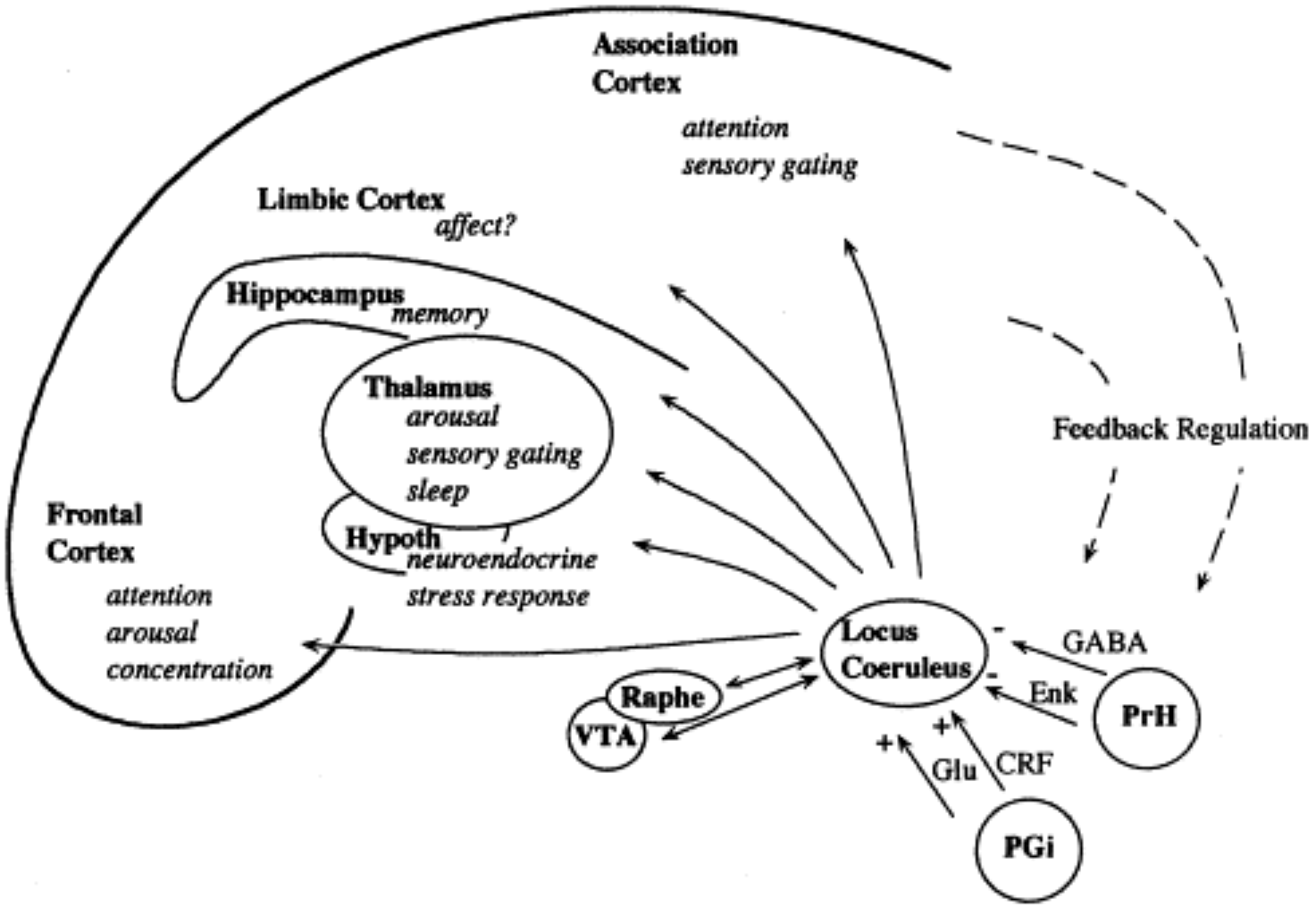
Irregular firing during quiet wakefulness
Sustained activation during stress

Their firing decreases markedly during slow-wave sleep
and virtually disappears during REM sleep.

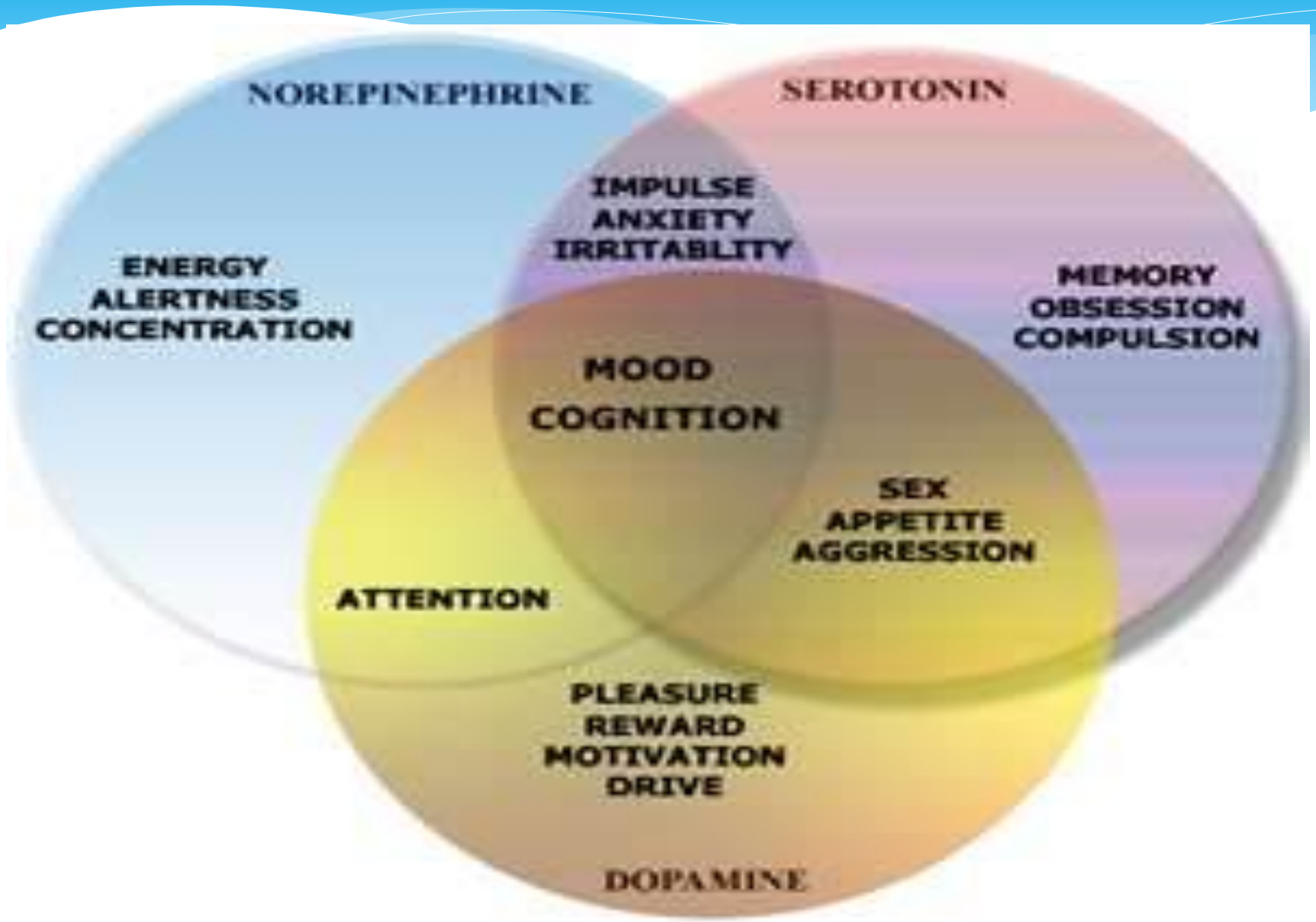


Norepinephrine (NE) Implicated in Stress-Related Disorders

- Depression
- Withdrawal from some drugs of abuse
- Other stress-related disorders such as panic disorder.



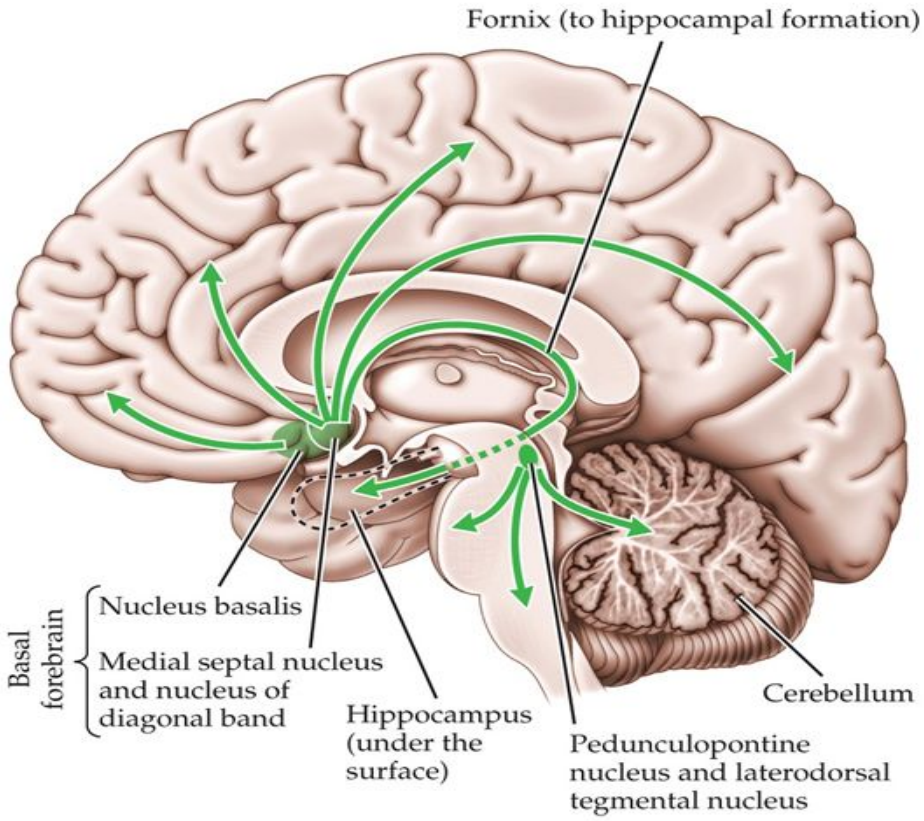
PGi: Nucleus paragigantocellularis
PrH: Perirhinal Cortex


NOREPINEPHRINE
SEROTONIN
IMPULSE
ANXIETY
IRRITABLITY
ENERGY
ALERTNESS
CONCENTRATION
MEMORY
OBSESSION
COMPULSION
MOOD
COGNITION
SEX
APPETITE
AGGRESSION
ATTENTION
PLEASURE
REWARD
MOTIVATION
DRIVE
DOPAMINE

2- Acetylcholine

Cholinergic Pathways in the Brain

Cholinergic nerve cell bodies and projections contain ACh.

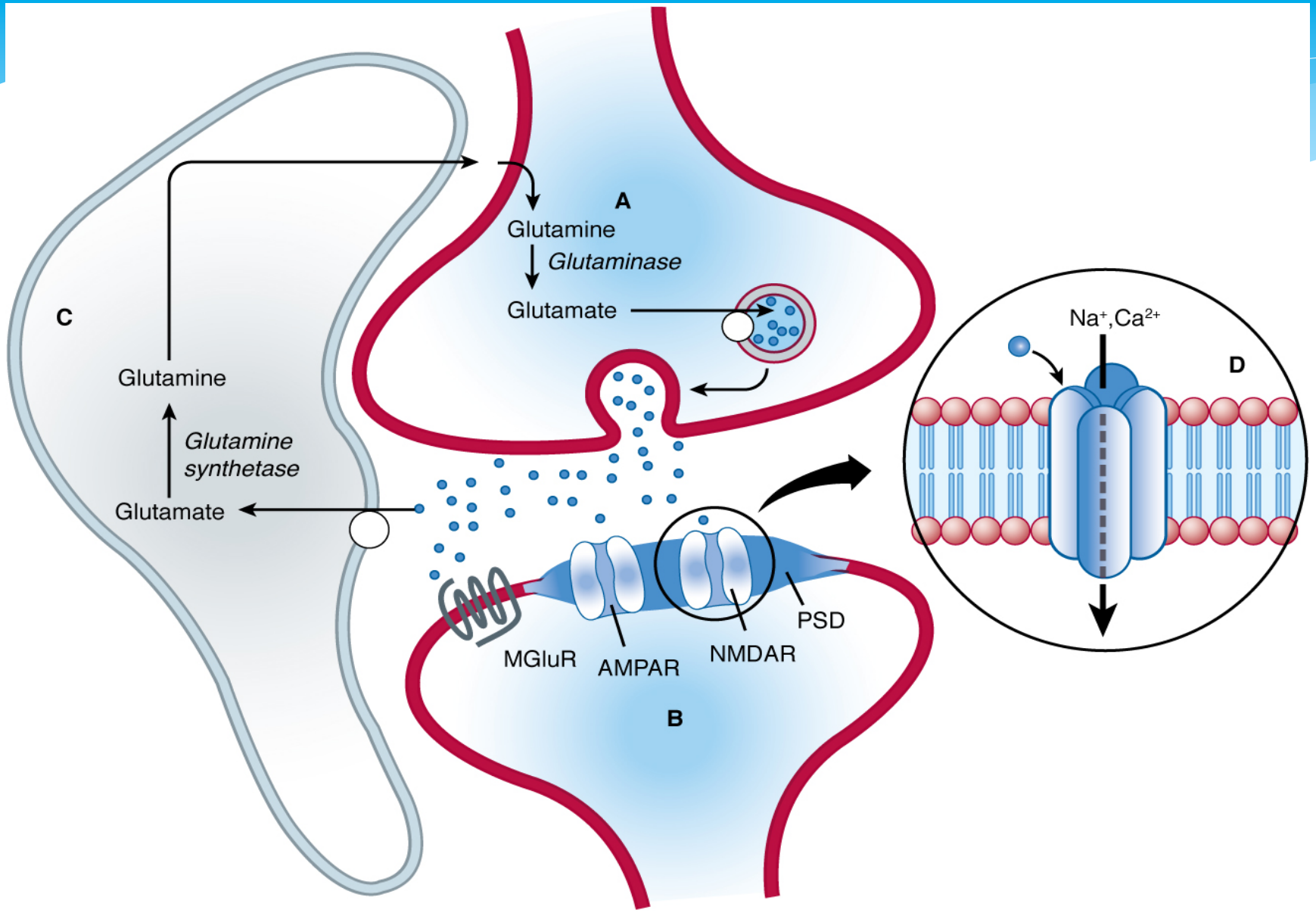


***BIOLOGICAL PSYCHOLOGY 7e*, Figure 4.3**

* Major neurotransmitter in the peripheral nervous system

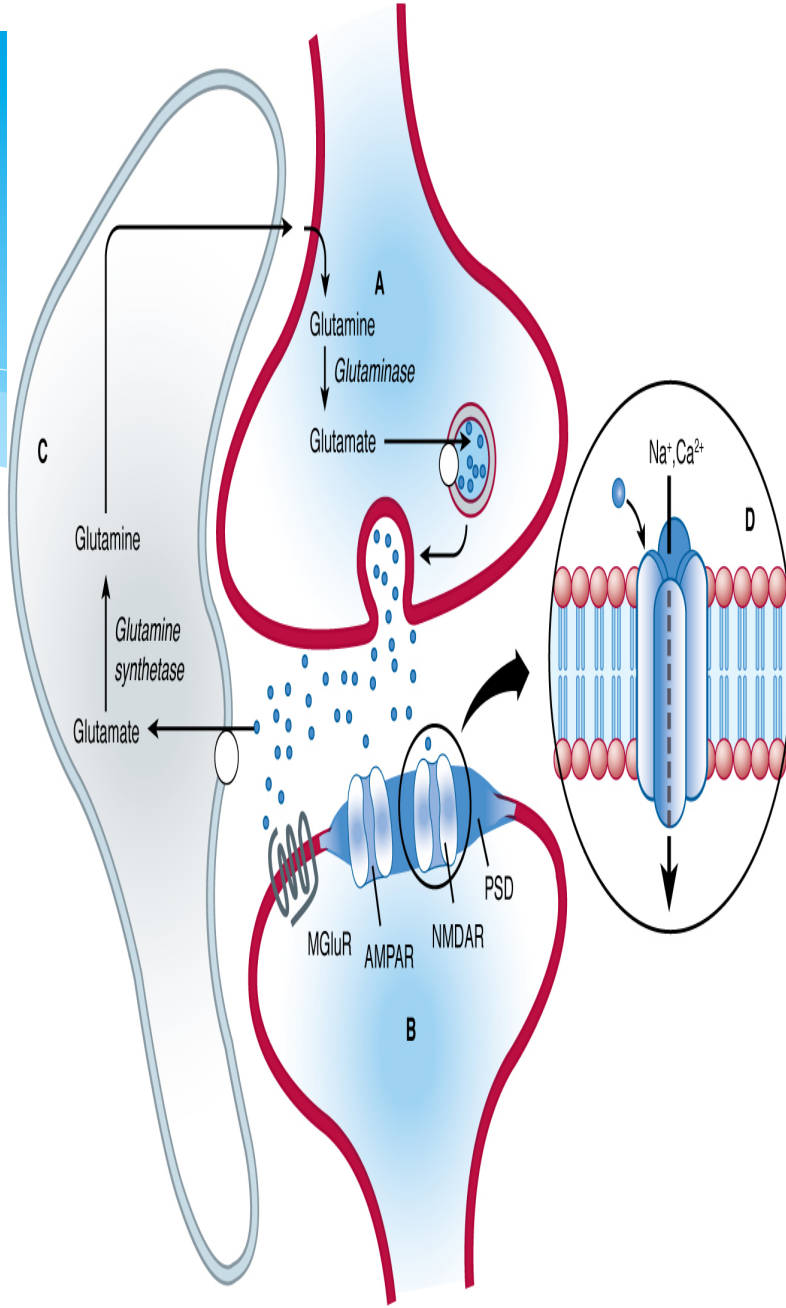
* Associated with:
* Thought
* Memory
* Muscular coordination
* Speed of information processing in the brain
* Production of myelin sheath

* ACh influences mental processes such as:
  * Learning
  * Memory
  * Sleeping
  * Dreaming.
* Alzheimer's Disease- the most common form of dementia that is associated with acetylcholine Damage to Ach producing cells in the basal forebrain
* Bipolar disorder
* Mood swings
* Depression
* Mental attension


A
Glutamine
Glutaminase
Glutamate
C
Glutamine
Glutamine synthetase
Glutamate
B
MGluR
AMPAR
NMDAR
PSD
D
Na+,Ca2+

3- Glutamate

* It is the most commonly found neurotransmitter in the brain.
* It is always excitatory.
* Glutamate is formed (alpha ketoregulation) Kreb's cycle
* > > > carried into astrocytes > > > converted to glutamine > > > passed on to glutaminergic neurones



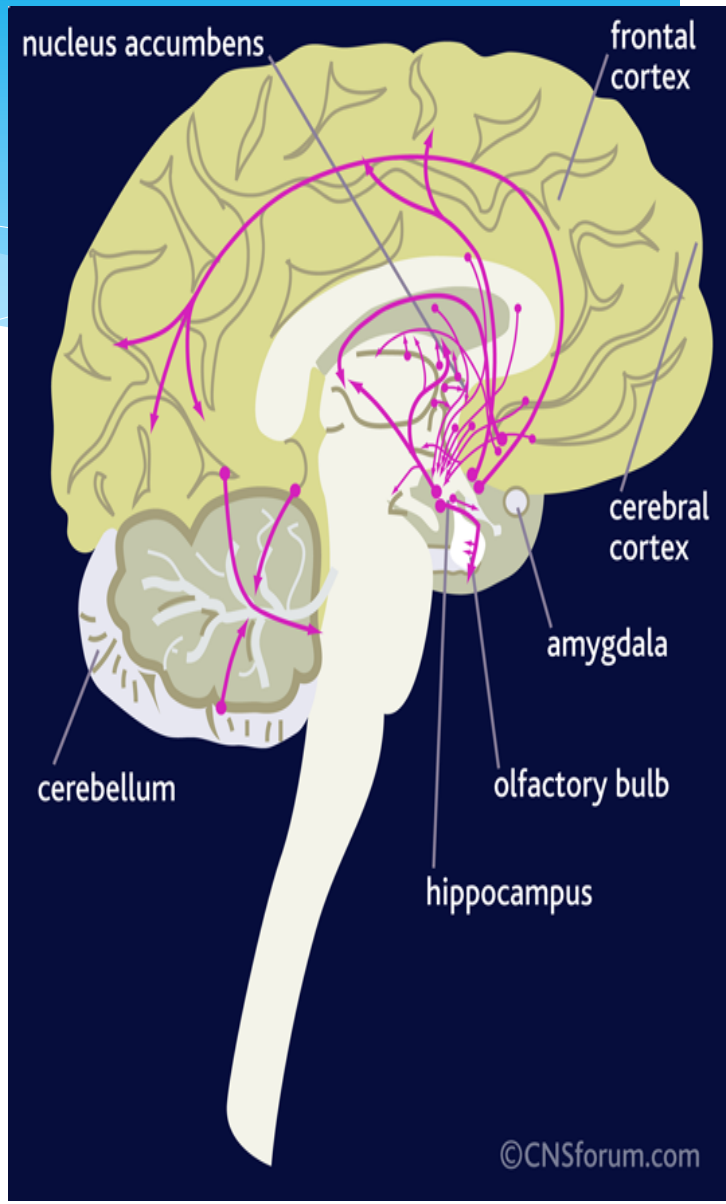
* Important role in
* Learning and memory

Reduced level in:

* Stroke
* Autism
* Intellectual disability
* Alzheimer's disease

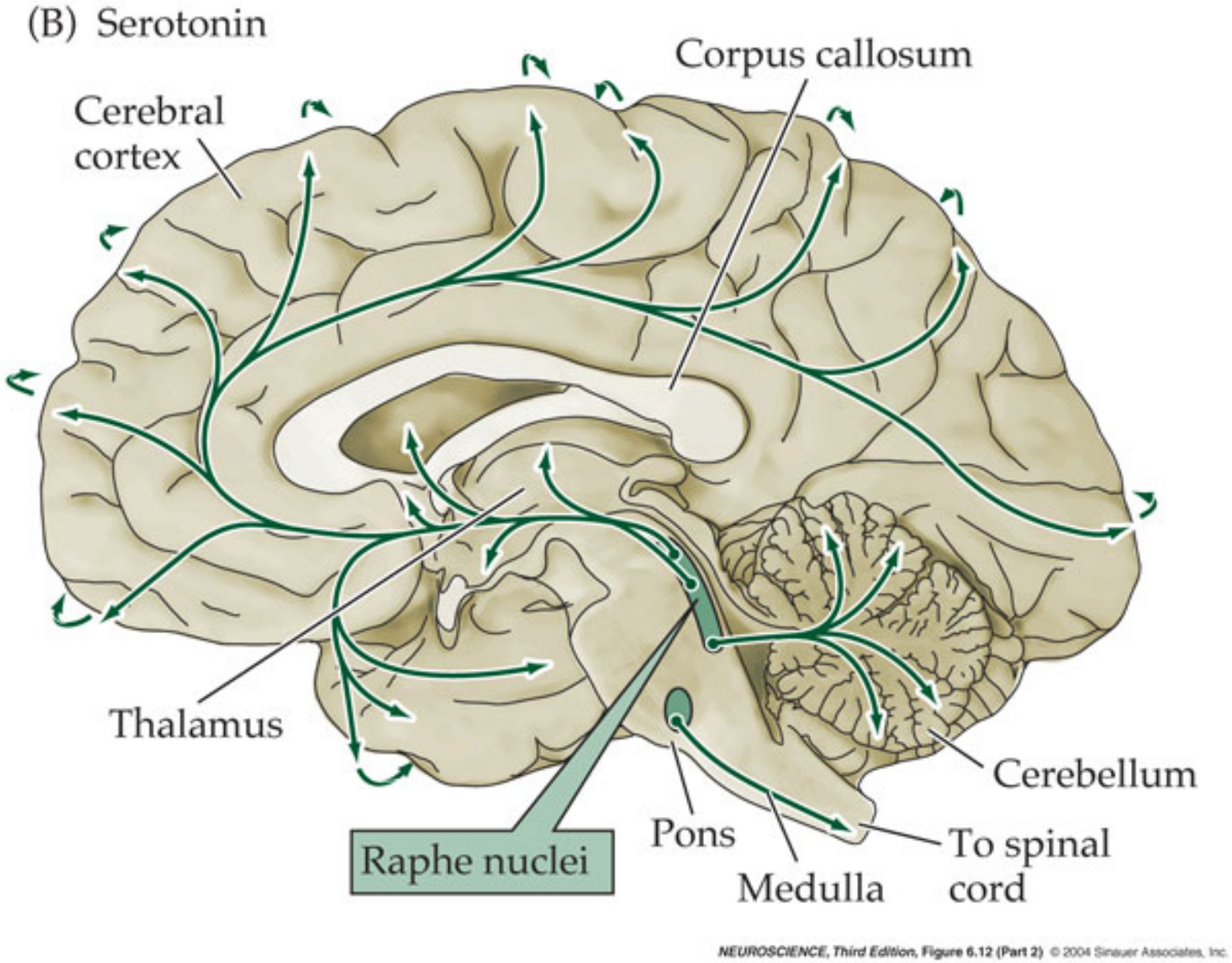
4-Gamma Aminobutyric acid (GABA)

* Inhibitory neurotransmitter of CNS and is also found in retina.
* Formed by decarboxylation of glutamate.
* Three types of GABA receptors e.g. $GABA_{A\ B\ \&\ C.}$
* $GABA_{A\ \&\ B}$ receptors are widely distributed in CNS.
* $GABA_{C}$ are found in retina only
* $GABA_{B}$ are metabotropic (G-protein) in function.



* GABA is the main inhibitory neurotransmitter in the central nervous system (CNS).
* GABAergic inhibition is seen at all levels of the CNC:

  Hypothalamus, hippocampus, cerebral cortex and cerebellar cortex
* GABA interneurones are abundant in the brain, with 50% of the inhibitory synapses in the brain being GABA mediated.



NEUROSCIENCE, Third Edition, Figure 6.12 (Part 2) © 2004 Sinauer Associates, Inc.

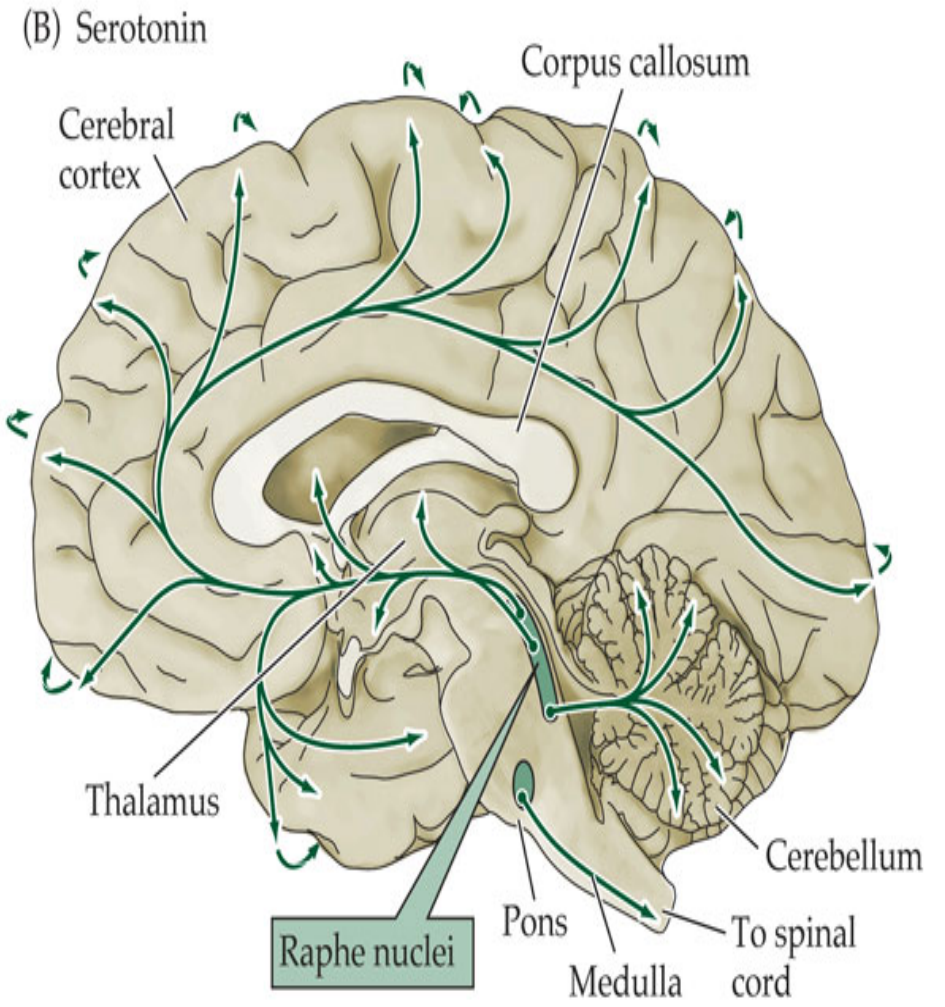
5- Serotonin

The serotonin pathways in the brain:

The principal centers for serotonergic neurons are the rostral and caudal raphe nuclei

>>>> axons ascend to the cerebral cortex, limbic & basal ganglia

Serotonergic nuclei in the brain stem >>>> descending axons (terminate in the medulla& spinal cord



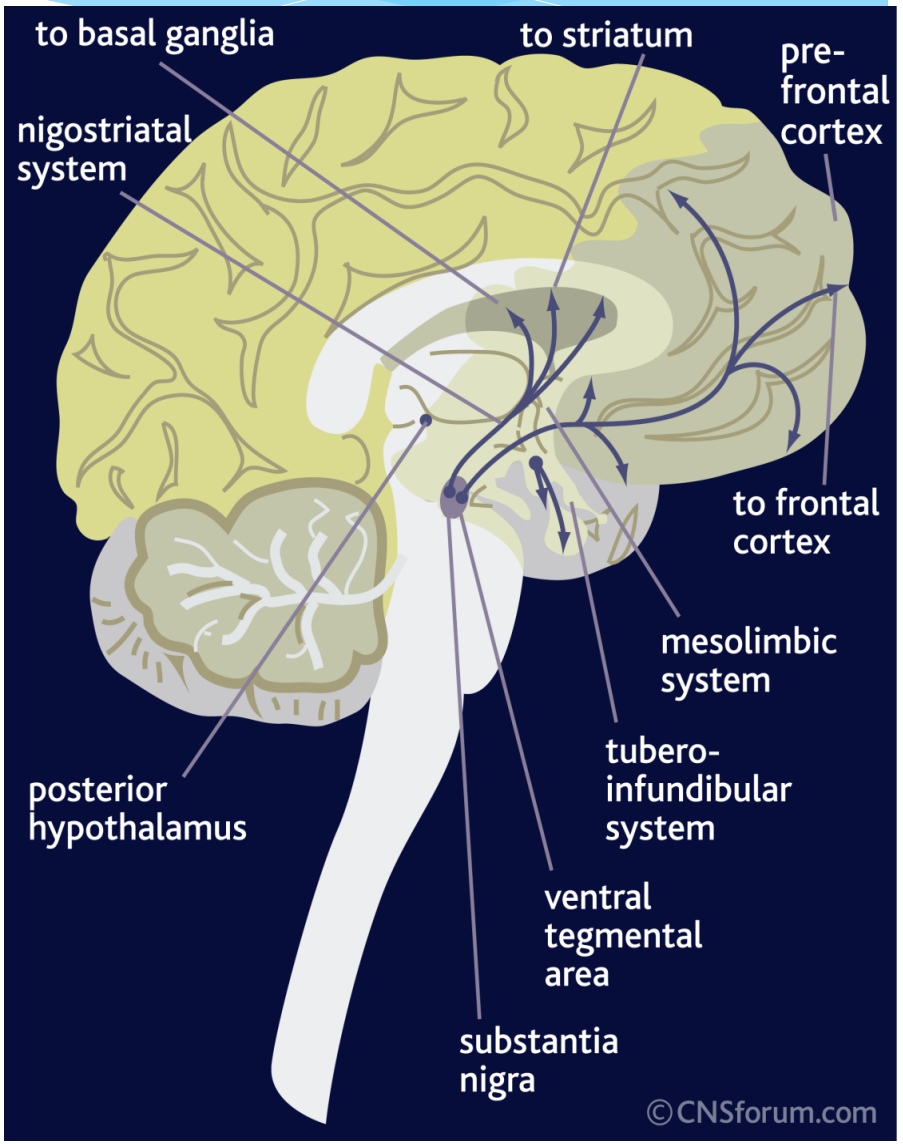
Serotonin (5-HT) Disorders

- Depression
- Anxiety

6-Dopaminergic Pathways

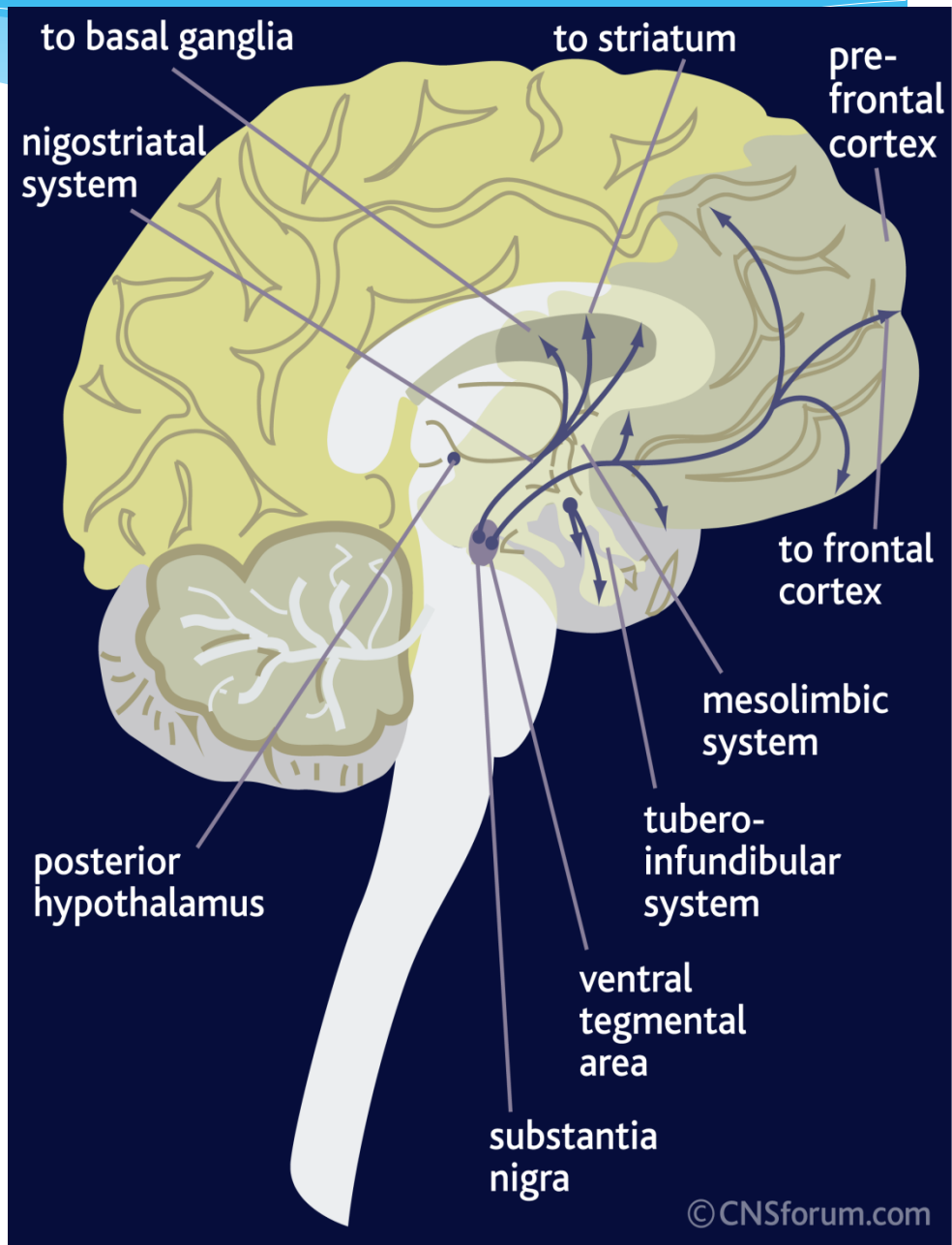
Dopamine is transmitted via three major pathways:

1- The first extends from the substantia nigra to the caudate nucleus-putamen (neostriatum) and is concerned with sensory stimuli and movement.



* 2- The second pathway prject to the mesolimbic forebrain
* Related to cognitive, reward and emotional behavior

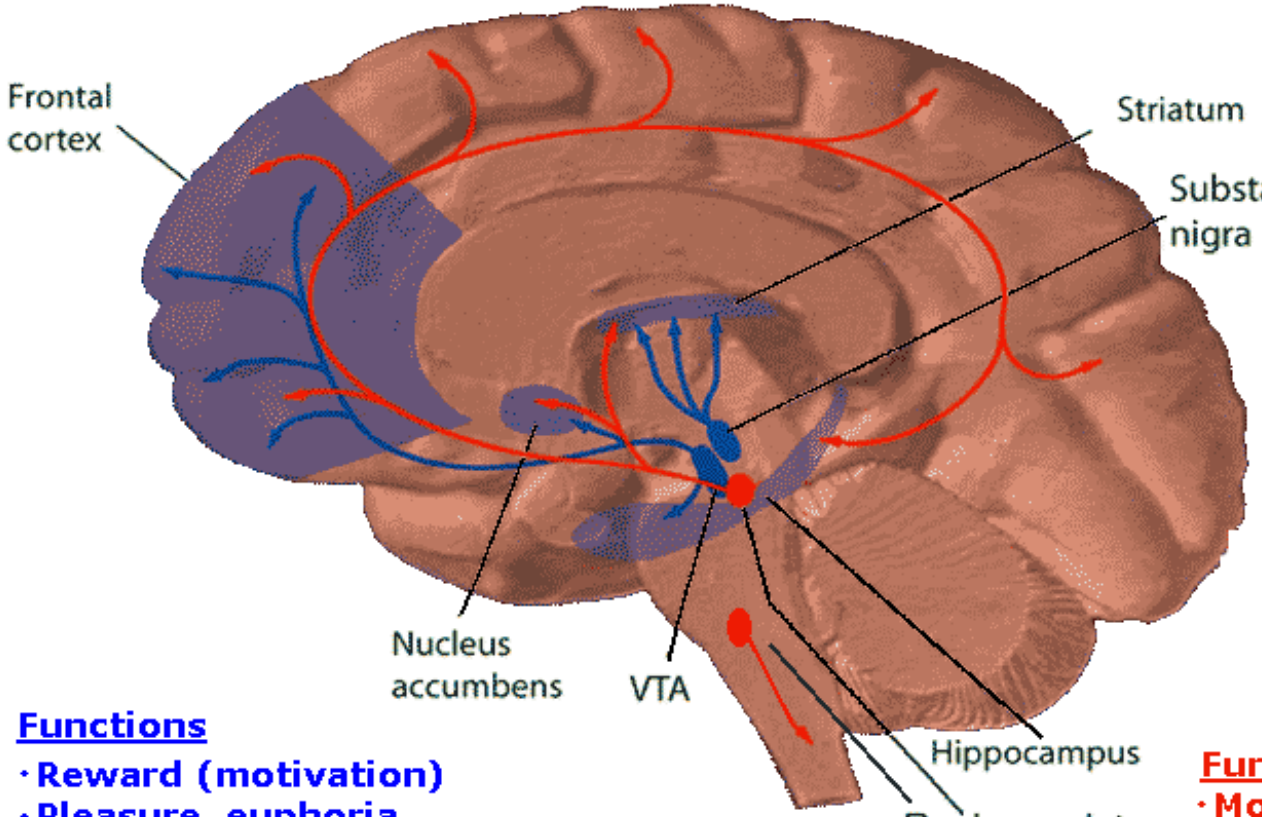
* 3- The third pathway, known as the tubero-infundibular system
* Rleated to neuronal control of the hypothalmic-pituatory endocrine system.



Dopaminergic Pathways/Functions

Dopamine Pathways

Serotonin Pathways



Functions

- **Reward (motivation)**
- **Pleasure, euphoria**
- **Motor function (fine tuning)**
- **Compulsion**
- **Perseveration**

Functions

- **Mood**
- **Memory processing**
- **Sleep**
- **Cognition**

Dopaminergic neurons disorders

Schezophrenia.

Parkinson's Disease.

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
1.Acetyl choline (Ach)	Excitatory	Acetyl co-A + Choline	Cholinergic nerve endings Cholinergic pathways of brainstem	1.Nicotinic 2.Muscarinic	Broken by acetyl cholinesterase	Cognitive functions e.g. memory Peripheral action e.g. cardiovascular system
2. Catecholamines i. Epinephrine (adrenaline)	Excitatory in some but inhibitory in other	Tyrosine produced in liver from phenylalanine	Adrenal medulla and some CNS cells	Excites both alpha α & beta β receptors	1.Catabolized to inactive product through COMT & MAO in liver 2.Reuptake into adrenergic nerve endings 3.Diffusion away from nerve endings to body fluid	For details refer ANS. e.g. fight or flight, on heart, BP, gastrointestinal activity etc. Norepinehrine controls attention & arousal, sleep/ wake cycle.
ii.Norepinephrine	Excitatory	Tyrosine, found in pons. Reticular formation, locus coerules, thalamus, mid-brain	Begins inside axoplasm of adrenergic nerve ending is completed inside the secretary vesicles	α_1 α_2 β_1 β_2		
iii. Dopamine	Excitatory	Tyrosine	CNS, concentrated in basal ganglia and dopamine pathways e.g. nigrostriatal, mesocorticolimbic and	D_1 to D_5 receptor	Same as above	Sensory motor Cognetive/ emotional behavior Endocrine Hypothalamic Decreased

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
3. serotonin (5HT)	Excitatory	Tryptophan	CNS, Gut (chromaffin cells) Platelets & retina	5-HT_1 to 5-HT_7 5-HT_2 A receptor mediate platelet aggregation & smooth muscle contraction	Inactivated by MAO to form 5-hydroxyindoleacetic acid(5-HIAA) in pineal body it is converted to melatonin	Mood control, sleep, pain feeling, temperature, BP, & hormonal activity
4. Histamine	Excitatory	Histidine	Hypothalamus	Three types H_1, H_2, H_3 receptors found in peripheral tissues & the brain	Enzyme diamine oxidase (histaminase) cause breakdown	Arousal, pain threshold, blood pressure, blood flow control, gut secretion, allergic reaction (involved in sensation of itch)
5. Glutamate	Excitatory 75% of excitatory transmission in the brain	By reductive amination of Kreb's cycle intermediate α – ketoglutarate.	Brain & spinal cord e.g. hippocampus	Ionotropic and metabotropic receptors. Three types of ionotropic receptors e.g. NMDA, AMPA and kainate receptors.	It is cleared from the brain ECF by Na^+ dependent uptake system in neurons and neuroglia.	Long term potentiation involved in memory and learning by causing Ca^{++} influx.

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
6. Aspartate	Excitatory	Acidic amines	Spinal cord	Spinal cord	Aspartate & Glycine form an excitatory / inhibitory pair in the ventral spinal cord	
7. Gama amino butyric acid(GABA)	Major inhibitory mediator	Decarboxylation of glutamate by glutamate decarboxylase (GAD) by GABAergic neuron.	CNS	GABA – A increases the Cl^- conductance, GABA – B is metabotropic works with G – protein GABA transaminase catalyzes. GABA – C found exclusively in the retina.	Metabolized by transamination to succinate in the citric acid cycle.	GABA – A causes hyperpolarization (inhibition) Anxiolytic drugs like benzodiazepine cause increase in Cl^- entry into the cell & cause soothing effects. GABA – B cause increase conductance of K^+ into the cell.
8. Glycine	Inhibitory	Is simple amino acid having amino group and a carboxyl group attached to a carbon atom	Spinal cord	Glycine receptor makes postsynaptic membrane more permeable to Cl^- ion.	Deactivated in the synapse by simple process of reabsorbtion by active transport back into the presynaptic membrane	Glycine is inhibitory transmitted found in the ventral spinal cord. It is inhibitory transmitter to Renshaw cells.