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Limbic system

Dr Devendra Save

Introduction

- Named by Paul Broca .
- Limbic = border (Greek word)
- It is structure forming border between hypothalamus and cerebral cortex
- Is functional anatomic system of interconnected cortical and sub cortical structures
- Area of intimate processing between hypothalamus and cortical information processing
- Plays role in emotions, learning, autonomic regulation
- Broad functional divisions



Rostral limbic system

caudal system

Old theories and concepts

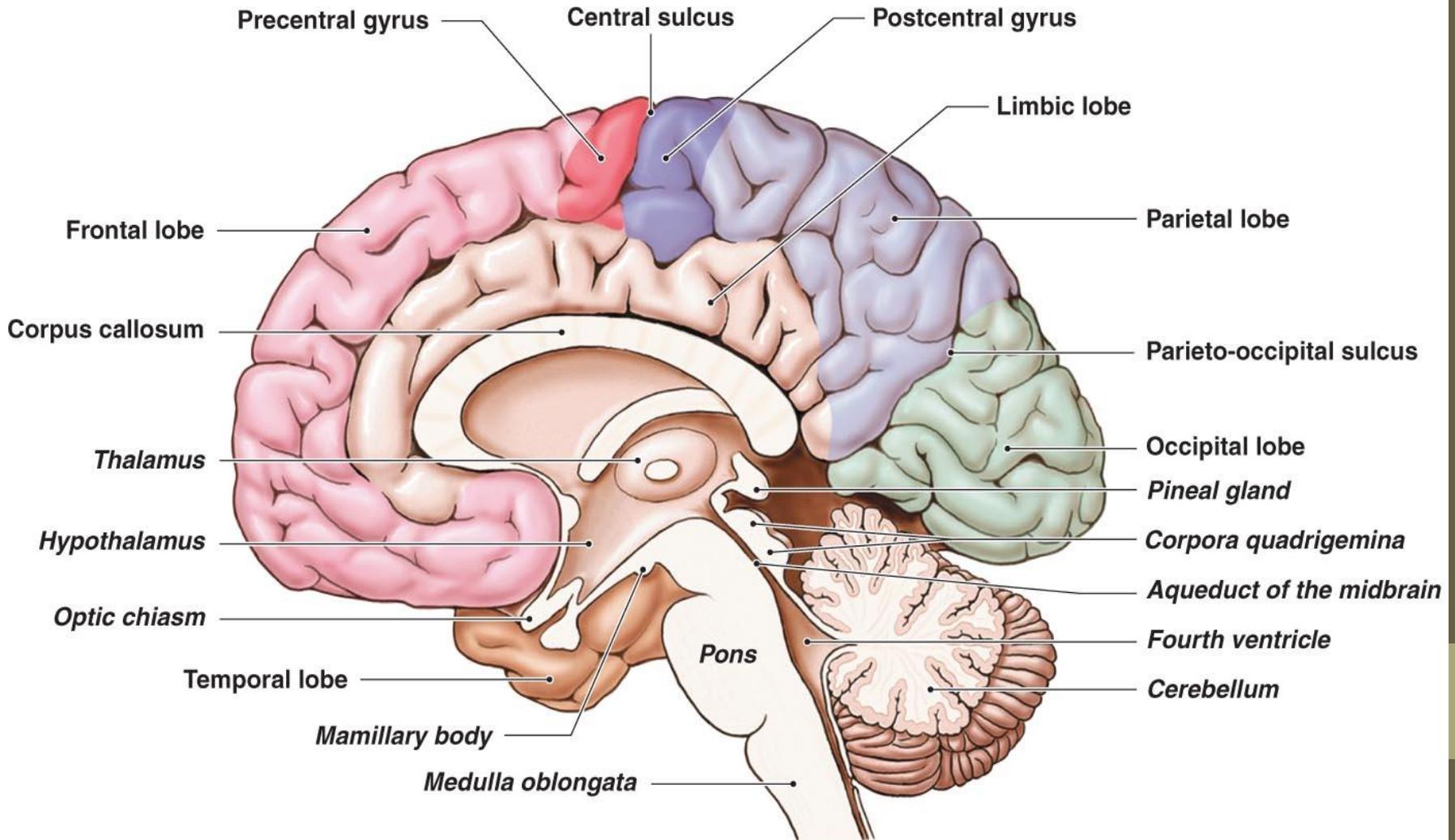
- **Hypothalamus** -important role in generating emotional behaviors
- **Amygdala** -important role in integrating information and coordinating emotional behaviors in response to sensory stimuli, events, and memories.
- These findings were demonstrated in animal studies
- Reward processing occurs in distinct brain circuits.
 - Stimulation of these circuits can provide powerful reinforcement signals.
 - Dopaminergic neurons in the ventral tegmental area provide a learning signal that reflects a computation comparing the reward received to the reward expected.
 - Drugs of abuse act on reward circuits.
- **Limbic system**- Psychiatric disorders such as depression, anxiety disorders, and addiction are related to it

Table 15–1. Components of the limbic system.

Major brain division	Structure	Component part
Cerebral hemisphere (telencephalon)	Limbic association cortex	Orbito-frontal Cingulate Entorhinal Temporal pole
	Hippocampal formation	Hippocampus (Ammon's horn) Subiculum
	Amygdaloid complex	Dentate gyrus Corticomedial Basolateral
	Ventral striatum	Central nucleus ¹ Nucleus accumbens Olfactory tubercle Ventromedial caudate and putamen
Diencephalon	Thalamus	Anterior nucleus Medial dorsal nucleus Midline nuclei
	Hypothalamus	Mammillary nuclei Ventromedial nucleus Lateral hypothalamic area
	Epithalamus ²	Habenula
Midbrain	Portions of the periaqueductal gray matter and reticular formation	

Anatomy of brain

A midsagittal view showing the inner boundaries of the lobes of the cerebral cortex
(Structures outside of the cerebrum are labeled in italics.)



Limbic system- broad functional divisions

Rostral limbic system

- **Important for emotion**
- Amygdala
- Septum
- Orbitofrontal cortex
- Anterior insula
- Anterior cingulate

Caudal system

- **Important For memory and visual-spatial functions**
- Hippocampus
- Posterior cingulate
- Posterior para hippocampal cortex

Limbic lobe v/s Limbic system

Limbic lobe

- **Cortical areas of limbic system**
- Para hippocampal gyrus
- Hippocampus
- Orbital frontal
- Cingulate gyrus
- insula

Limbic system

- **Nuclei-**
 - Amygdala
 - Septal nuclei
 - Mammillary body
 - Anterior thalamus
- **Connection-**
 - Fornix
 - Median forebrain bundle
 - Stria terminalis
 - Mamillothalamic tract

Components of limbic system

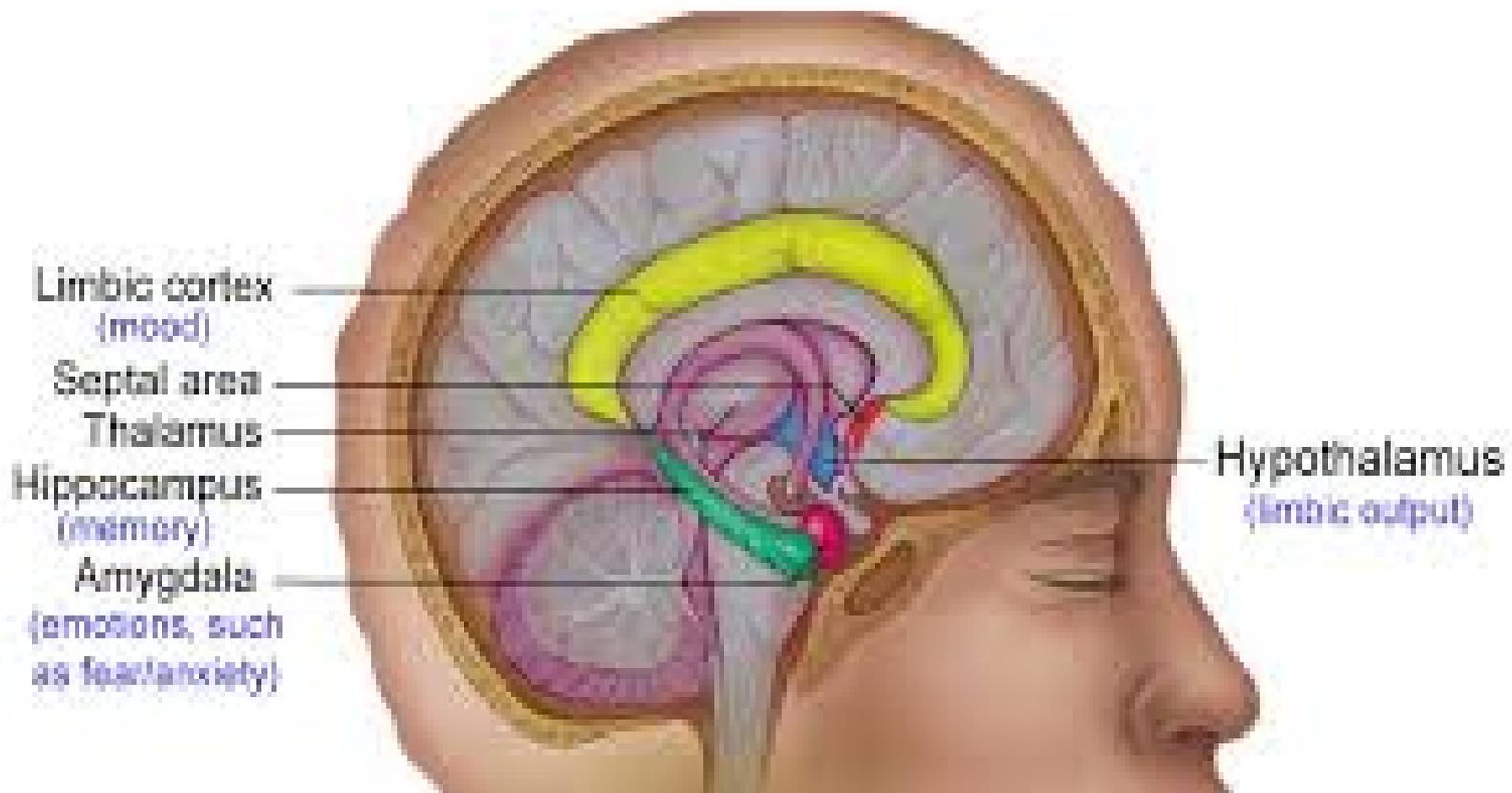
- Olfactory pathways
- Anterior perforated substance
- Piriform lobe
- Septal area
- Amygdaloid body
- Limbic cortex
- Hippocampal formation
- Elements of diencephalon
- Bundles of axons connecting above regions

Functions of limbic system

- Olfaction
- Autonomic responses BP, Respiration
- Appetite and eating behavior
- Sleep and dreams
- Emotional responses like fear, rage & placidity, autonomic & endocrine responses
- Sexual behavior
- Addiction & motivation
- Memory
- Social cognition

Anatamico –functional correlation

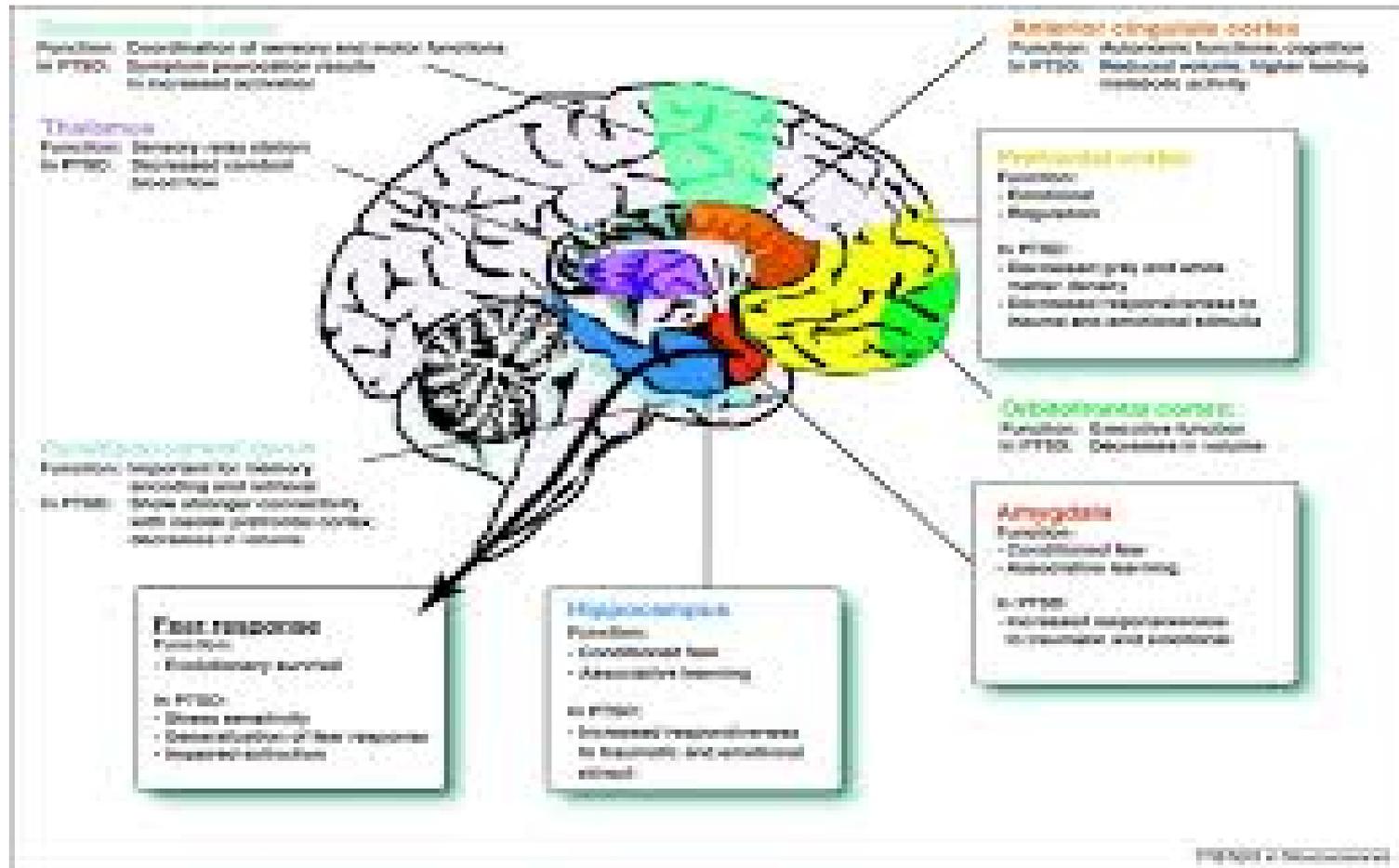
Limbic System

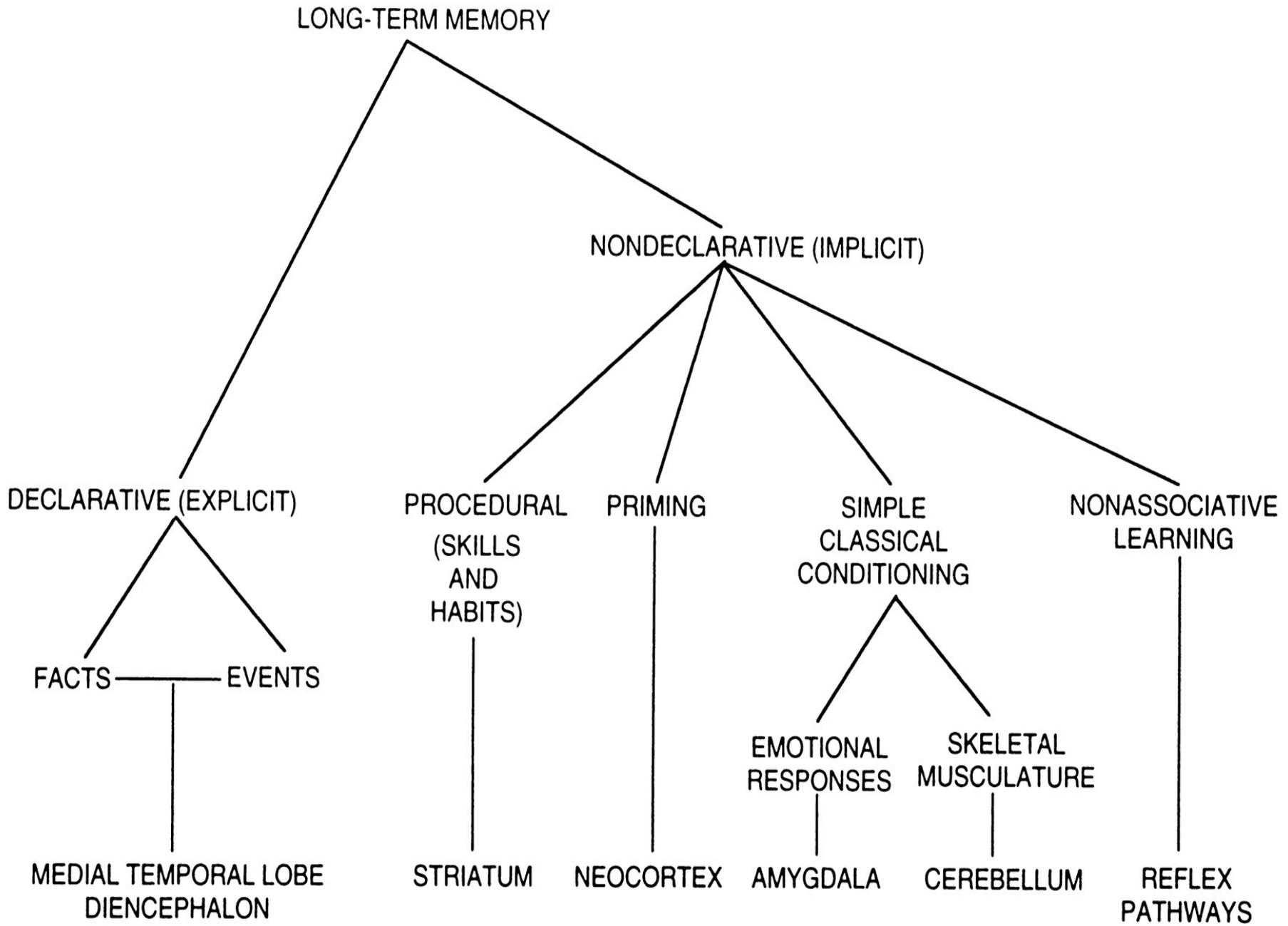


Functions of areas of limbic system

- **Cingulate gyrus-** autonomic functions regulating HR,BP. Cognitive, attentional, emotional processing
- **Para hippocampal gyrus-** spatial memory
- **Hippocampus** – long term memory
- **Amygdala** – anxiety ,aggression, emotional memory, social cognition, fear conditioning
- **Hypothalamus-** regulation of autonomic nervous system via hormone production and release. Also affects& regulates BP, HR, hunger, thirst , sexual arousal, circadian rhythm of sleep& wake cycle
- **Mammillary body** - memory
- **Nucleus Accumbens** - reward , addiction

Functional division of limbic system





Limbic lobe

- At inferomedial aspect of cerebral hemispheres
- Consists of 2 concentric gyri surrounding corpus callosum
- As per Broca , larger outer gyrus is limbic gyrus and inner smaller gyrus is intra limbic gyrus
- Limbic gyrus (lobe) consists of isthmus of cingulate gyrus , parahippocampal gyrus and sub callosal area

Cingulate gyrus and para hippocampal gyrus

- **Cingulate gyrus-**

- Situated dorsal to corpus callosum
- Heavily interconnected with association area of cerebral cortex
- Inputs from- anterior nucleus of thalamus, neo cortex , somatosensory areas of cerebral cortex Via cingulum , projects to entorhinal cortex
- Related to emotion formation, processing, learning, memory, important role in attention, feeling of safety and security

- **Parahippocampal gyrus-**

- Situated in medial temporal lobe
- Imp role in memory encoding
- ERC funnels highly processed cortical information to hippocampal formation & serves as a major output pathway

The limbic system

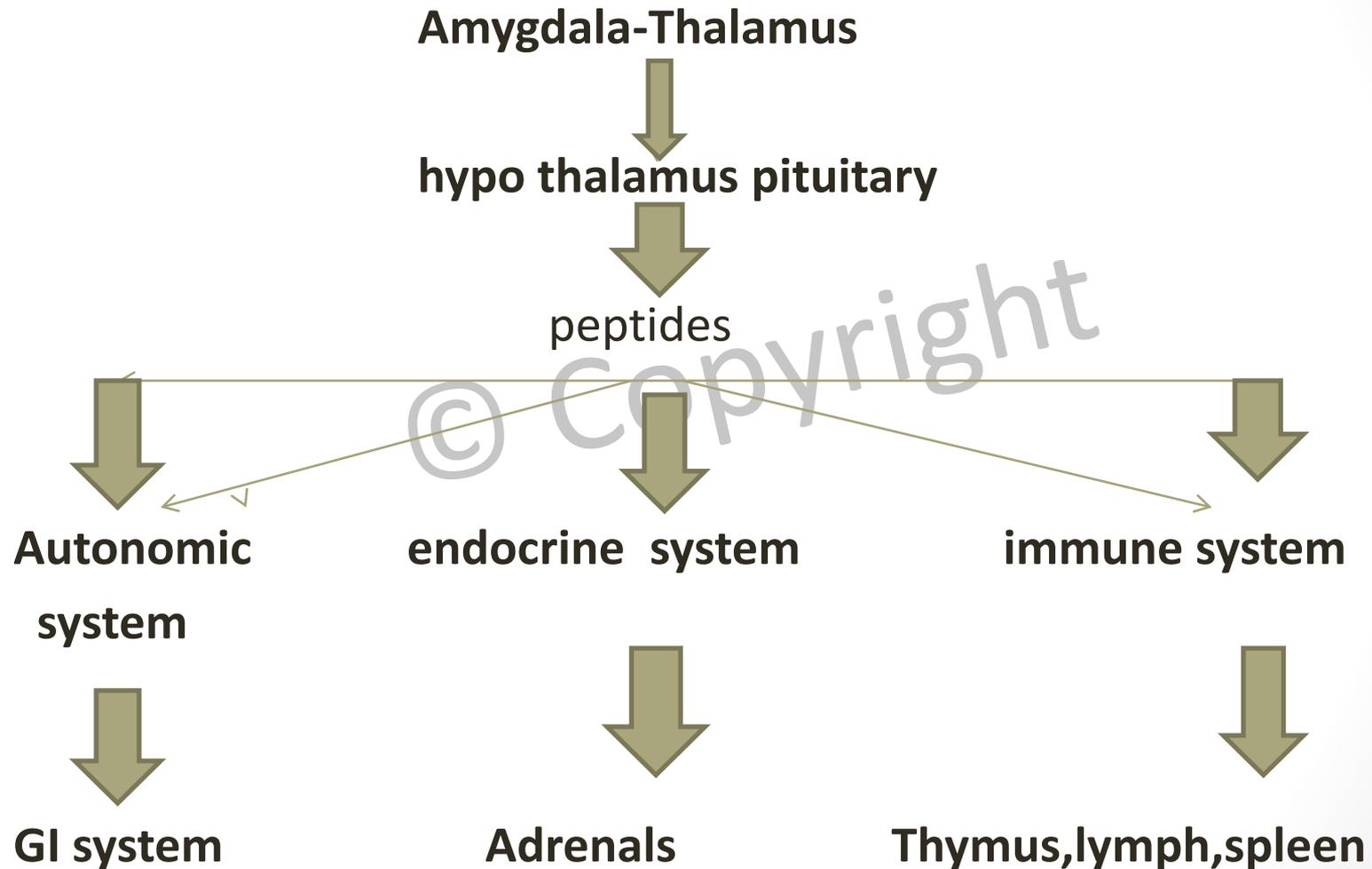
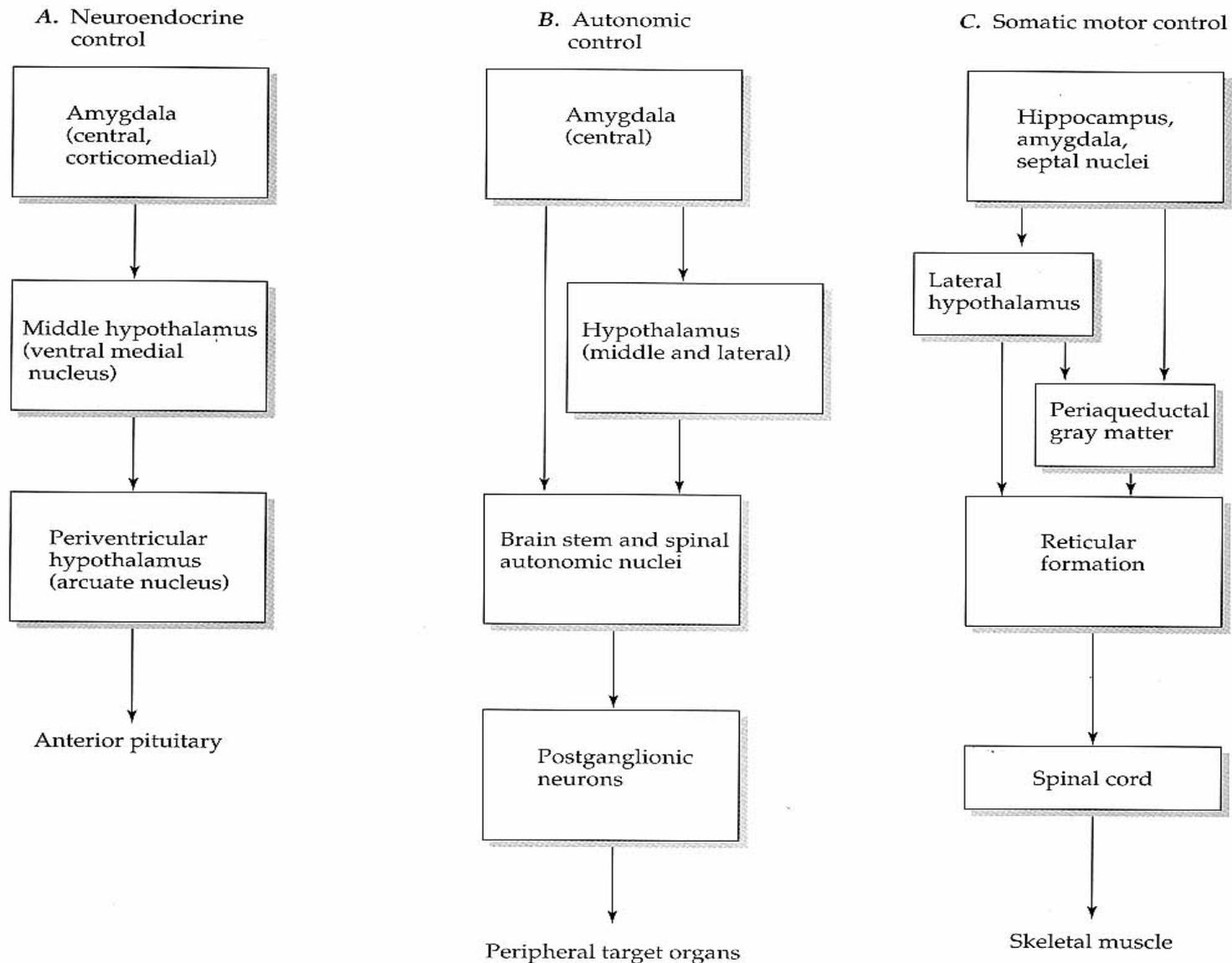
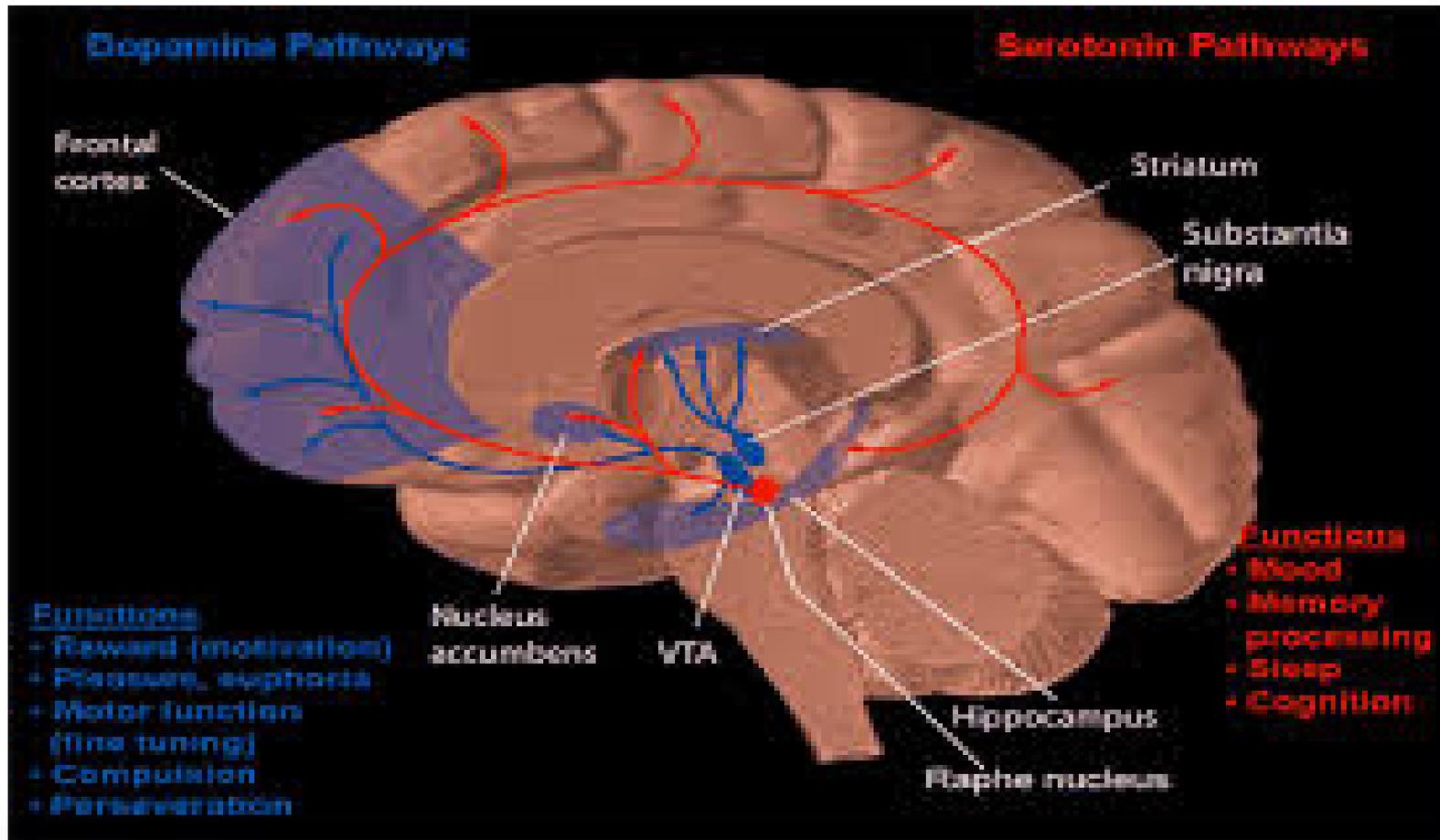


Fig. 16-9: Links between Limbic System and Effector Systems

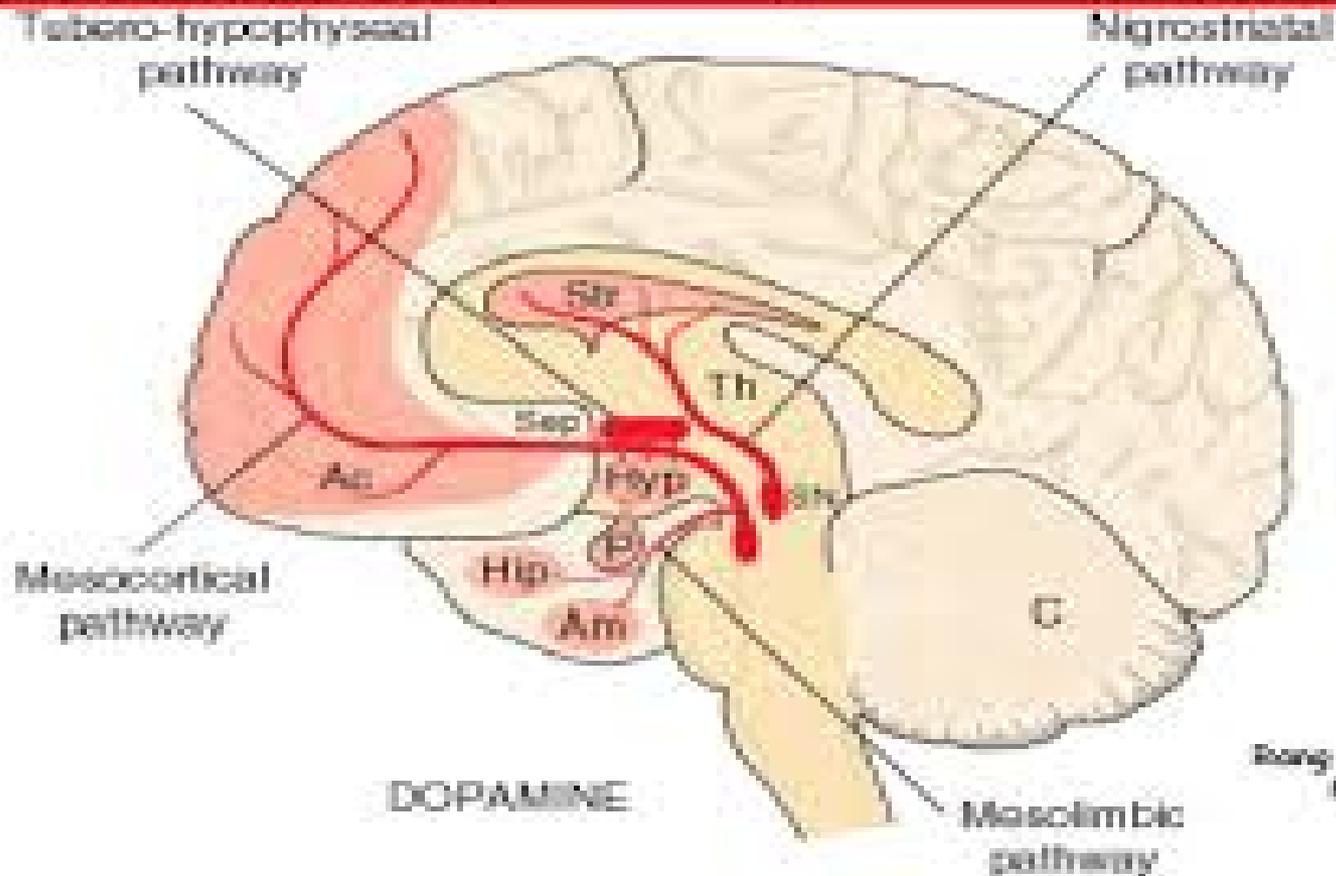


Pathways in limbic system



Dopaminergic pathways in CNS

Dopaminergic pathways in the CNS



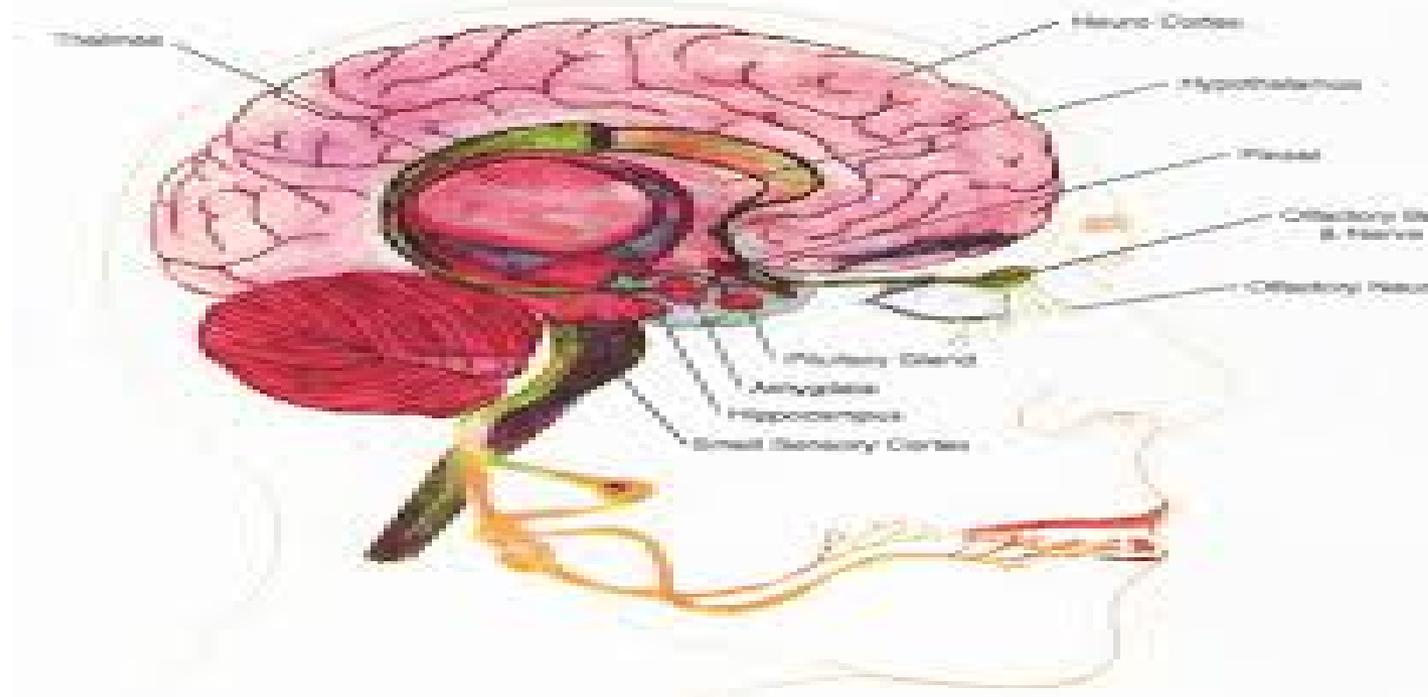
Song et al. (2012)
Fig. 28.3

Significance of dopaminergic pathway

- Mesolimbic pathway- associated with pleasure , rewards, goal directed behavior-
- Nigrostriatal pathway- associated with coordination of movement (it is part of basal ganglia motor loop)
- Tuberofundibular pathway-associated with maternal behavior and in regulation of prolactin secretion by pituitary gland
- Mesocortical pathway- associated with emotional and motivational responses.

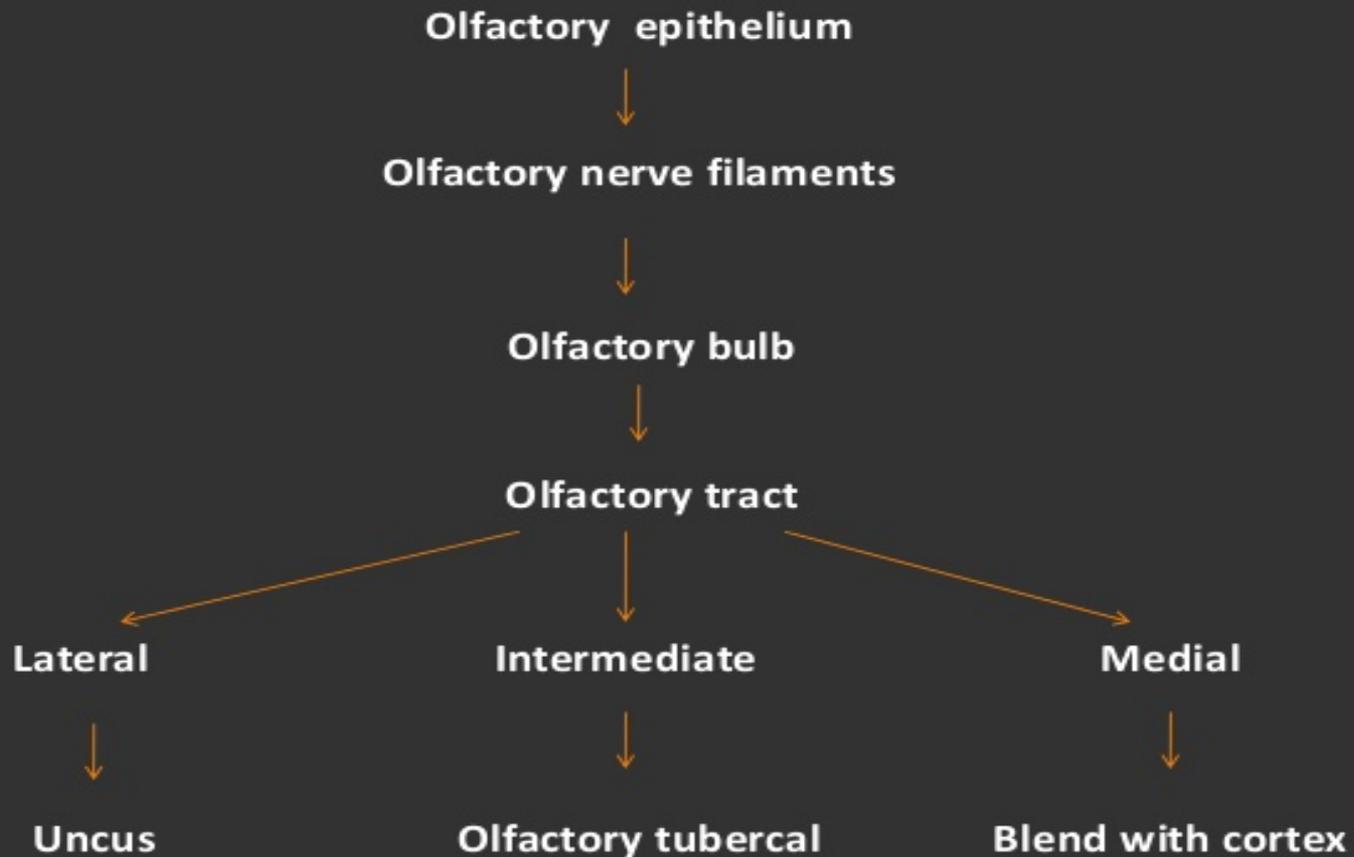
Smell and emotional responses

Limbic System Smell and Emotional Responses



Olfactory pathway

Olfactory pathway



Parts of limbic system

- **Anterior perforated substance-**

mass of grey matter situated on either side of optic chiasma and perforated by central branch of MCA

- **Pyriform lobe-**

- Uncus-principal region for olfactory awareness
- Limen insulae-most medial part of insula
- Entorhinal cortex-ant part of parahippocampal gyrus
BA28

- **Septal area-**

- Situated ventrally to corpus callosum
- Includes paraterminal gyrus and septum pellucidum
- Receives olfactory fibres from medial olfactory stria
- Through fornix, has reciprocal connections with hippocampus

- **Amygdala**

- Almond shaped collection of nuclei & lies above Inferior horn of lateral ventricle and has wide efferent connections
- Major function: Responding to stimuli with an emotional component.

-

- 3 Nuclear components:

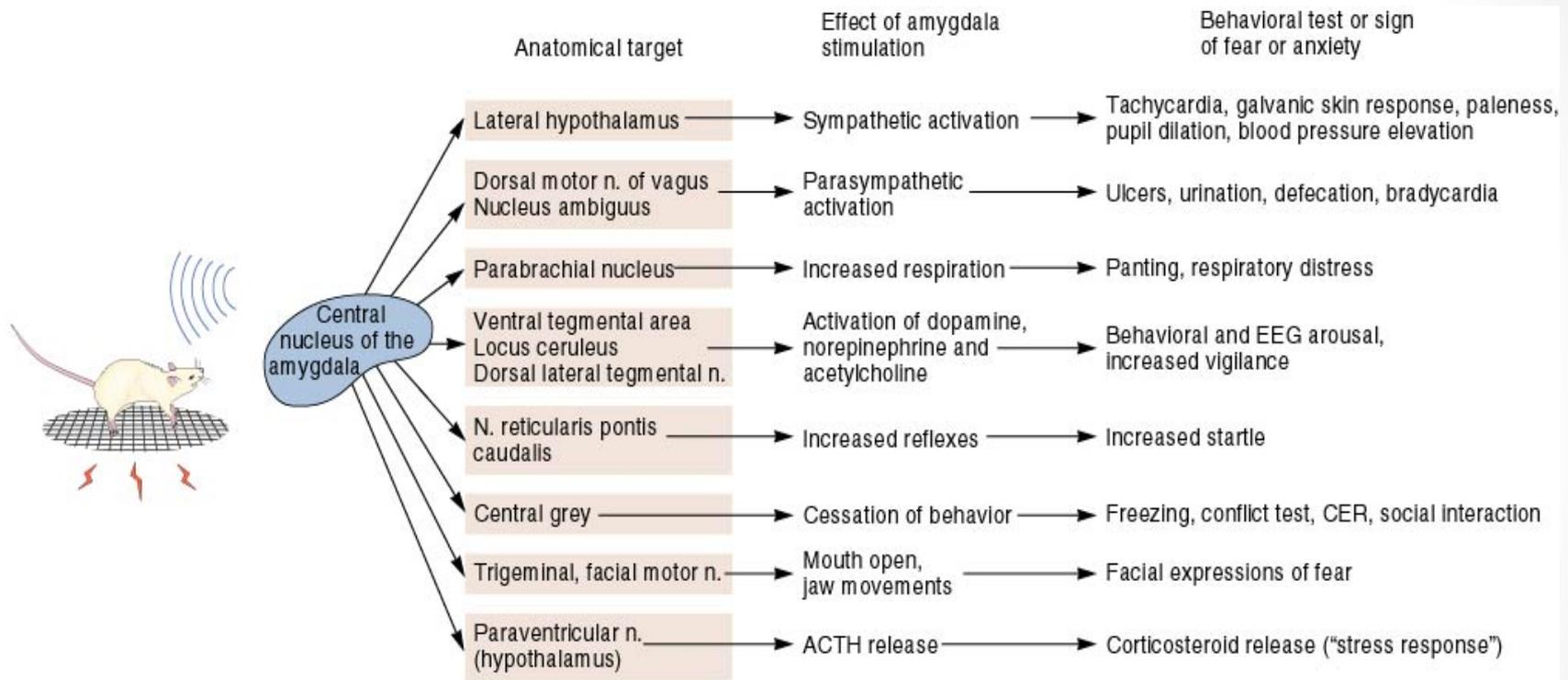
A) Basolateral – attaching emotional significance to a stimulus.

Sensory cortices (higher-order) → BL → limbic association cortex, prefrontal cortex, hippocampal formation (for learning emotional significance). B. Central Nucleus – mediates emotional responses.

B) Visuosensory input from solitary, para brachial nuclei → CN → dorsal motor n. of X, other parasympathetic n. reticular formation and hypothalamus → autonomic responses.

C) Cortico medial nuclei – mediates behaviors triggered by olfactory stimuli. Olfactory bulb → CM → hypothalamus (lateral zone) → regulation of “appetitive behaviors”; *i.e.*, eating in response to smells

Amygdala stimulation produces emotional behaviors through subcortical pathways



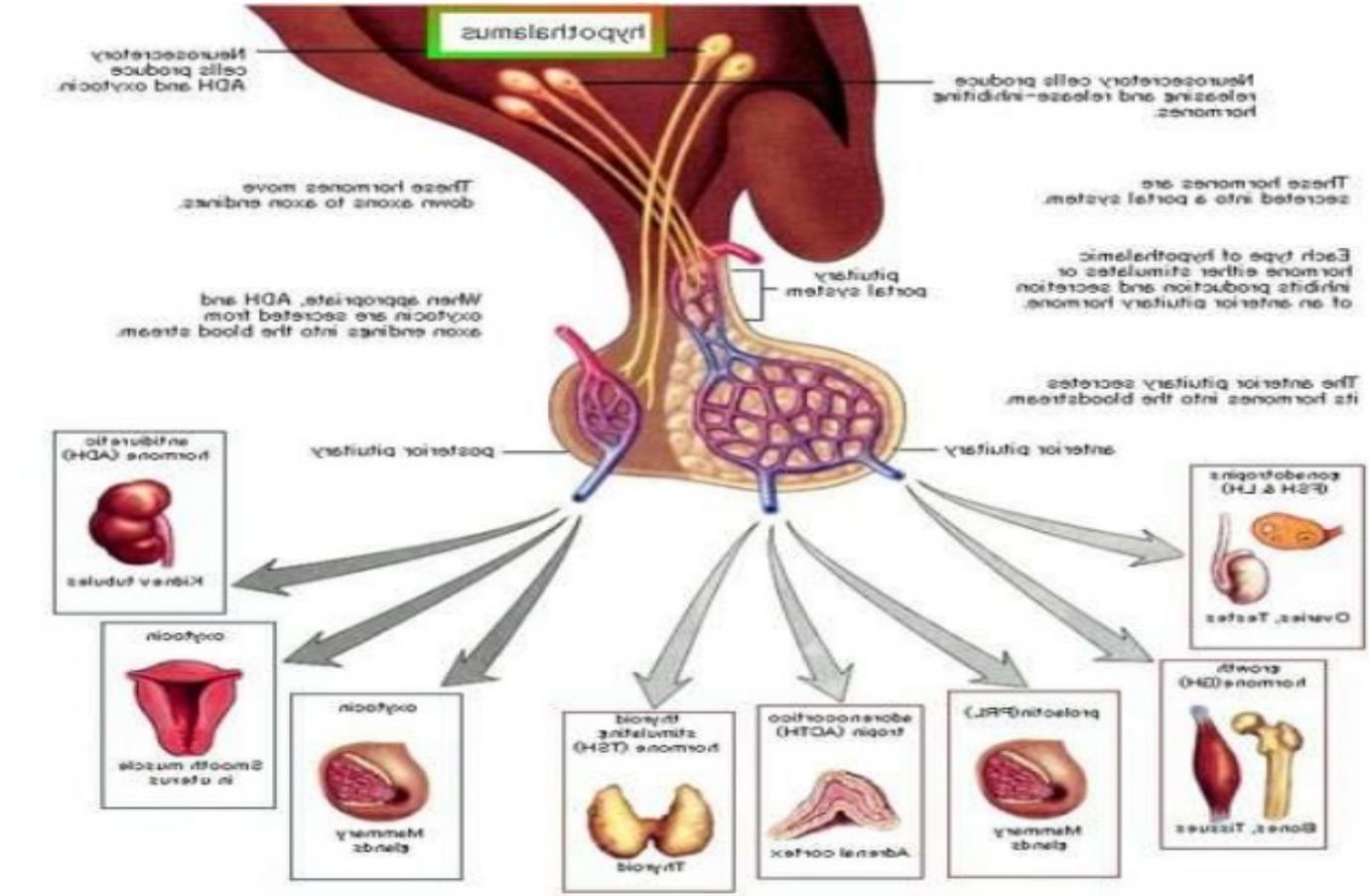
Appleton & Lange

Kandel/Schwartz/Jessell

Principles of Neural Science

Fig. 50.09

Hypothalamus and effects



Links Between Limbic System and Effector (Behavioral) Systems

- A. Neuroendocrine – by amygdala (central and CM) via para ventricular n. of hypothalamus.
- B. Autonomic – by amygdala (central n.?) lateral hypothalamus → descending pathways via autonomic nuclei.
- C. Somatic Motor – by several limbic components → reticular formation → stereotypic behaviour via reticulospinal tract.

Substances and their effects

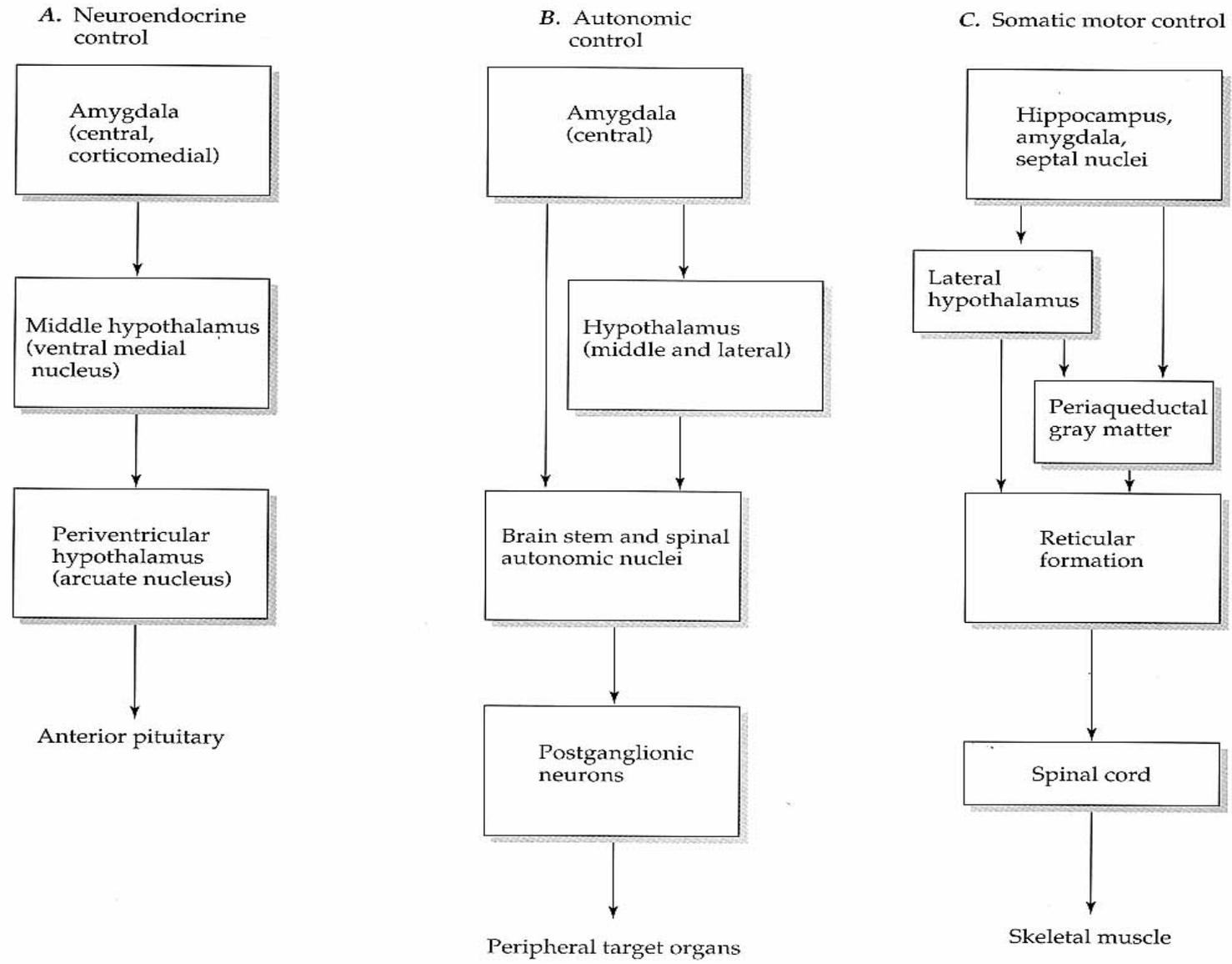
Dopamine: Excessive transmission in limbic structures may contribute to schizophrenia.

5-HT: Ascending projections control mood; increase appears to help in many forms of anxiety and depression (mood disorders).

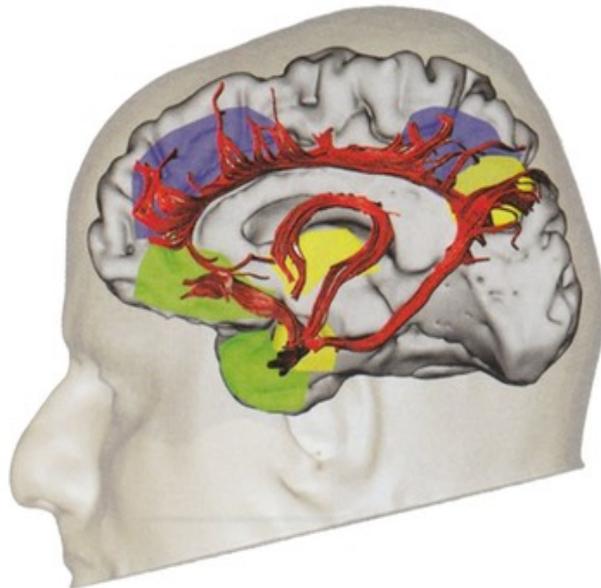
Norepinephrine: Excessive transmission may contribute to anxiety and aggression. Under-reaction, along with that of 5-HT, may contribute to depression.

Acetylcholine: Important in cognition, activating a number of neocortical, as well as limbic areas – the 1st system to degenerate in Alzheimer's Disease.

Links between Limbic System and Effector Systems



Network , functions and related disorders



■ retrosplenial-hippocampal-diencephalic network

■ temporo-amygdala-orbitofrontal network

■ medial 'default network'

Network	Functions	Disorder
Retrosplenial-hippocampal-diencephalic	<ul style="list-style-type: none"> •spatial orientation •memory 	<ul style="list-style-type: none"> •Amnesias •Korsakoff's syndrome •Mild Cognitive impairment •Alzheimer's disease (early) •Balint syndrome
Temporo-amygdala-orbitofrontal	<ul style="list-style-type: none"> •Olfactory-gustatory-visceral functions •Multimodal sensory integration •Behavioural inhibition •Outcome monitoring •Object-reward association learning •Memory for temporally complex visual information 	<ul style="list-style-type: none"> •Depression •Temporal lobe epilepsy •Semantic dementia •Alzheimer's Disease (advanced) •Klüver-Bucy syndrome •Geschwind's syndromes •Psychopathy
Default network	<ul style="list-style-type: none"> •Attention •Mentalizing •Response selection and action monitoring •Autobiographical memory •Self-knowledge •Pain perception •Empathy •Person perception 	<ul style="list-style-type: none"> •Mild Cognitive Impairment •Alzheimer's Disease (early) •Autism •Attention Deficit Hyperactivity Disorder •Schizophrenia •Depression •Anxiety •Obsessive compulsive disorder

Figure 11.5 The medial limbic structures participating in the activity of three distinct but partially overlapping networks. The main connections of the retrosplenial-hippocampal-diencephalic network are the ventral cingulum, the fornix, and mammillo-thalamic tract; the endstations of this network are indicated in yellow, while its functions and corresponding clinical disorders are listed in the table. The nodes of the temporo-amygdala-orbitofrontal network (indicated in green) are connected by the uncinate fasciculus. The dorsal cingulum is the main connection of the medial default network, whose cortical projections are shown in blue.

Limbic system clinical syndromes

- Hyper limbic- mania, OCD
- Hypo limbic-depression, apathy, amnesia(hippocampus), anxiety/panic, psychosis, kluver- Bucey syndrome(amygdala) , social disdecorum
- Limbic epilepsy
- Limbic encephalitis
- Rage (hypothalamus and amygdala)

Limbic system - clinical implications

Temporal lobe epilepsy

Form of focal epilepsy

Recurrent seizures arising from one or both temporal lobes

Types- Mesial (MTLE) and lateral Temporal lobe epilepsy (LTLE)

Mesial temporal sclerosis-

- 47-70% of all temporal lobe epilepsy
- severe neuronal loss in CA1, may spread to CA3 & CA4
- CA2 & dentate – only mildly involved
- Pathological abnormalities- specific hippocampal neuronal cell loss pattern, associated hippocampal atrophy & gliosis,
- Patient complains- fear. Deja vu., jamaisvu , elementary & complex visual hallucinations, forced thinking, emotional distress

Limbic encephalitis

Form of encephalitis

Inflammatory process involving hippocampi, amygdala, insular, etc

C/F-

- severe impairment of short term memory
- Confusion
- Changes in behavior & mood, irritability, depression, sleep disturbances
- seizures

60% times is para neoplastic in origin which is commonly associated with small cell lung carcinoma but majority of encephalitis are viral

Alzheimer's disease

- Neurogenerative changes in limbic system
- Hippocampus first area to degenerate >> leads to anterograde amnesia
- Early cortex degeneration >> retrograde amnesia , dementia
- Pathology-

Amyloid proteins build up & form plaques

Neurofibrillary tangles(inside cells) >>neuronal death

Kluver – Bucy syndrome

Neurobehavioral syndrome associated with bilateral lesions in medial temporal lobe, especially amygdala

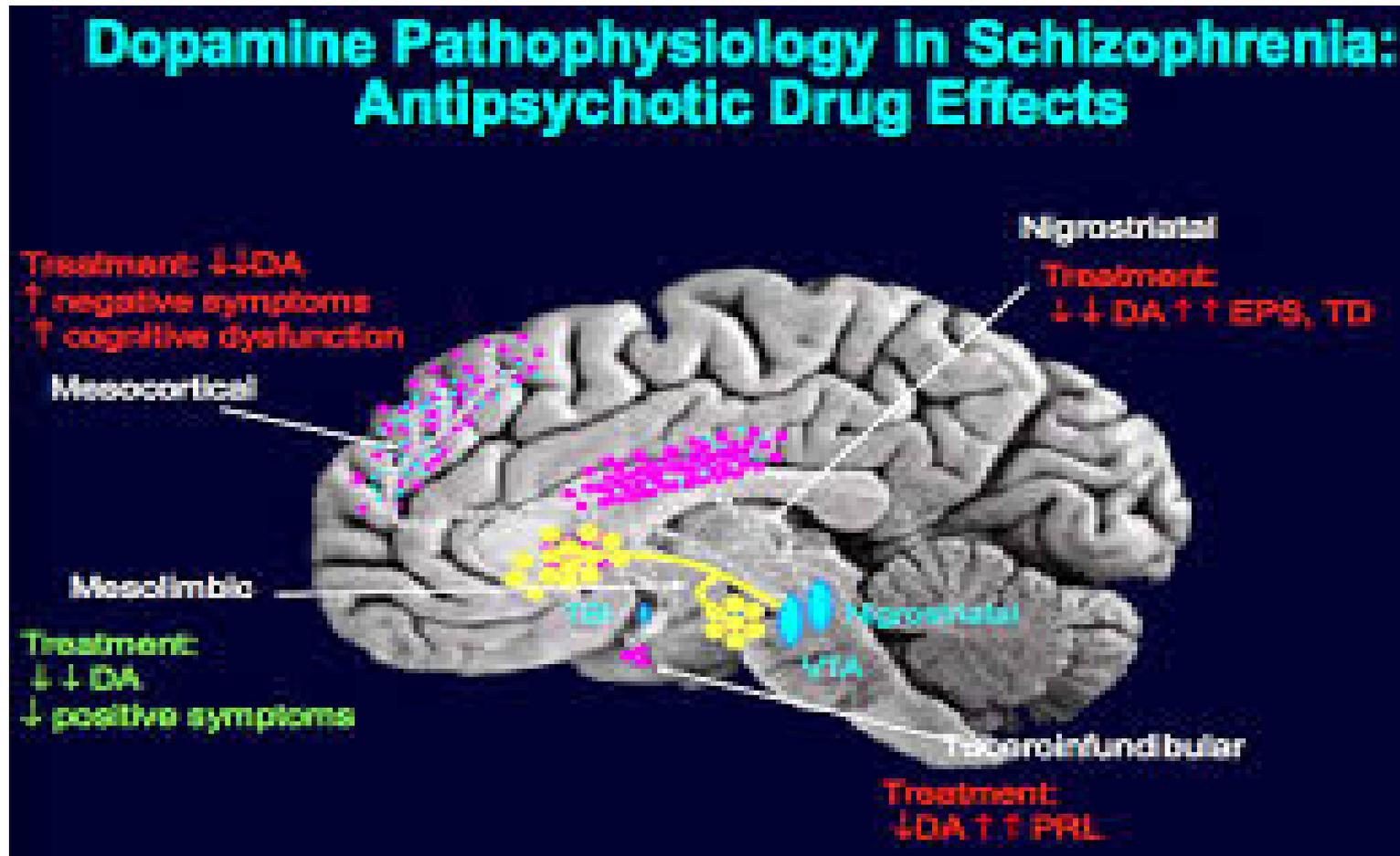
C/F-

- Facial blunting (may not respond appropriately to stimuli)
- Hyperphagia
- Hyperorality
- Hypermetamorphosis
- Inappropriate sexual behavior
- Visual Agnosia / psychic blindness

Limbic system in schizophrenia

- Ventricular enlargement
- Reduced limbic volumes
- Decreased size of hippocampus and thalamus
- Decreased amygdala response during facial recognition tasks
- Decreased activity in dorsolateral pre frontal cortex (PET)
- Papez circuit – probably involved in schizophrenia
- Distortion of cortical neuronal organization of layer II of ERC
- Reduced number of GABAergic cells in cingulate and anterior thalamus with resultant glutamatergic excitotoxicity

Schizophrenia- pathophysiology& drug effects



Limbic system in bipolar disorder & ADHD

Limbic system in bipolar disorder

- Reductions in volumes of frontal lobes, basal ganglia , amygdala, hippocampus
- Functional studies revealed decreased activity in prefrontal cortex and anterior cingulate gyrus which is center for integration of attentional and emotional output and helps effortful control of emotional arousal

Limbic system in ADHD

Disrupted connections between amygdala and orbitofrontal cortex >> may contribute to behavioral disinhibition

Limbic system in OCD and autism

OCD-

- **Neuro imaging** has implicated the cortical-striatal-thalamic circuit
- **PET imaging** shows increased glucose metabolism in orbital gyri
- **Postulation-** orbitofrontal-thalamic hyperactivity gives rise to obsessive thoughts

Autism-

Involvement of cingulate gyrus, amygdala (mediate cognitive & affective processing)

In autism spectrum disorders, basolateral circuit (imp for social recognition) is disrupted

Limbic system in anxiety disorders

- May be result of failure of anterior cingulate and hippocampus to modulate activity of amygdala (tap down regulation)
- A fear circuitry involving amygdala, prefrontal and anteriorcingulate (bottoms up regulation)
- Limbic system (involved in storing memories & creating emotions) thought to play central role in all anxiety related information
- People with OCD often show increased activity in basal nuclei, particularly striatum and other frontal lobe areas of forebrain

references

**Squire L, Zola S PNAS 1996;93:13515-13518
Adapted from Squire, Knowlton 1994**

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