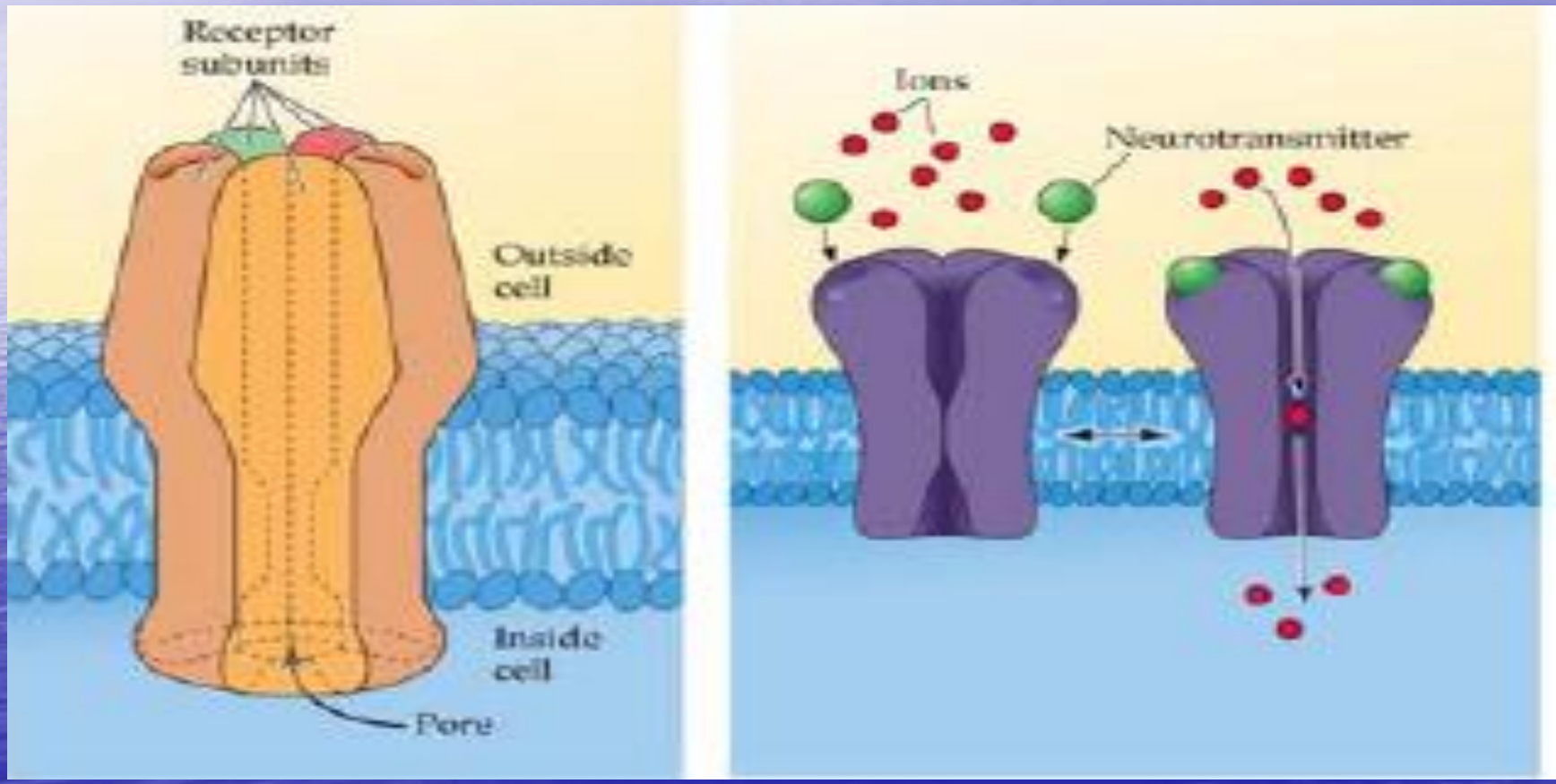
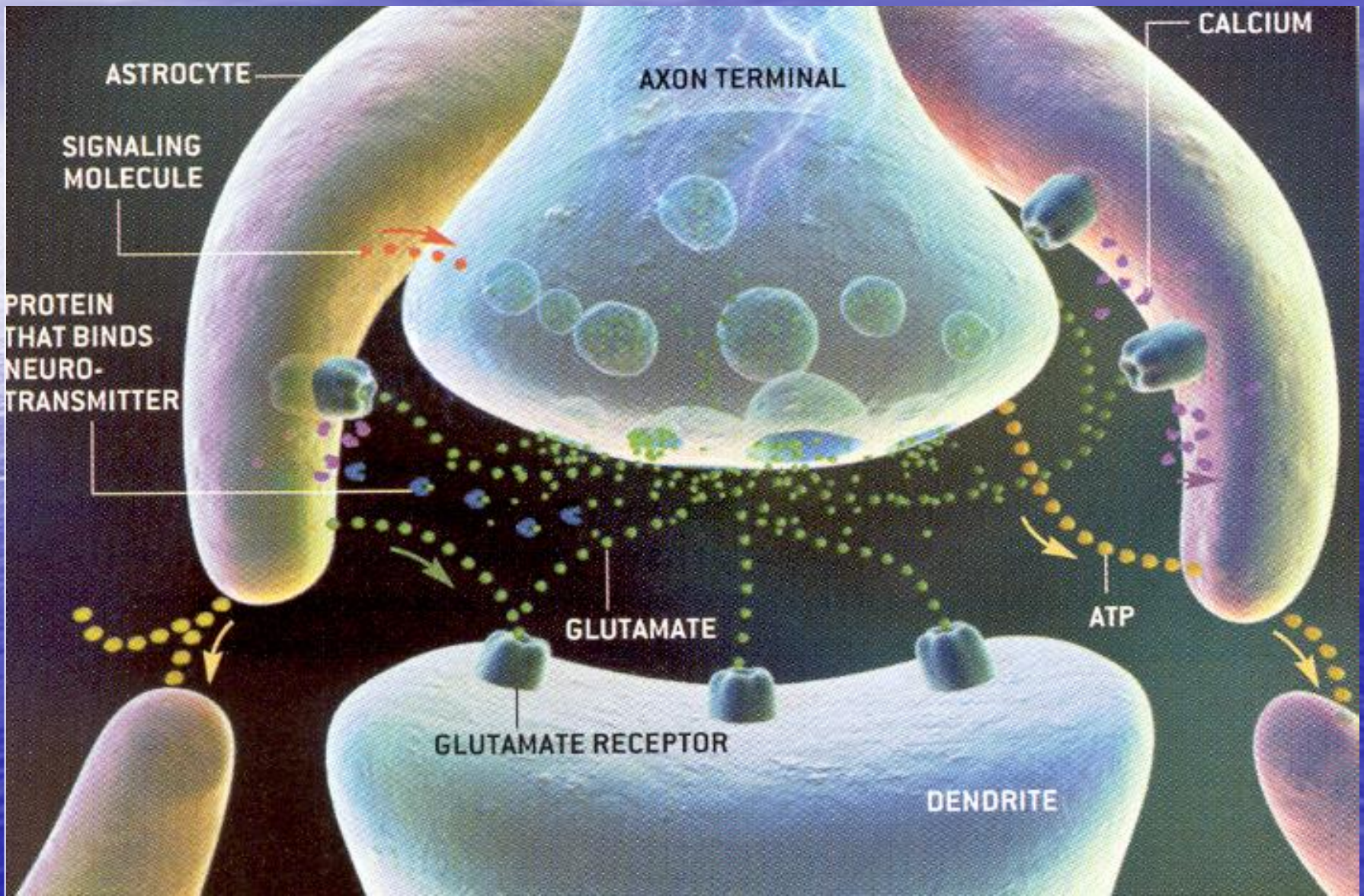
Basic Neuro Anatomy – Part II

Neurotrasmiters

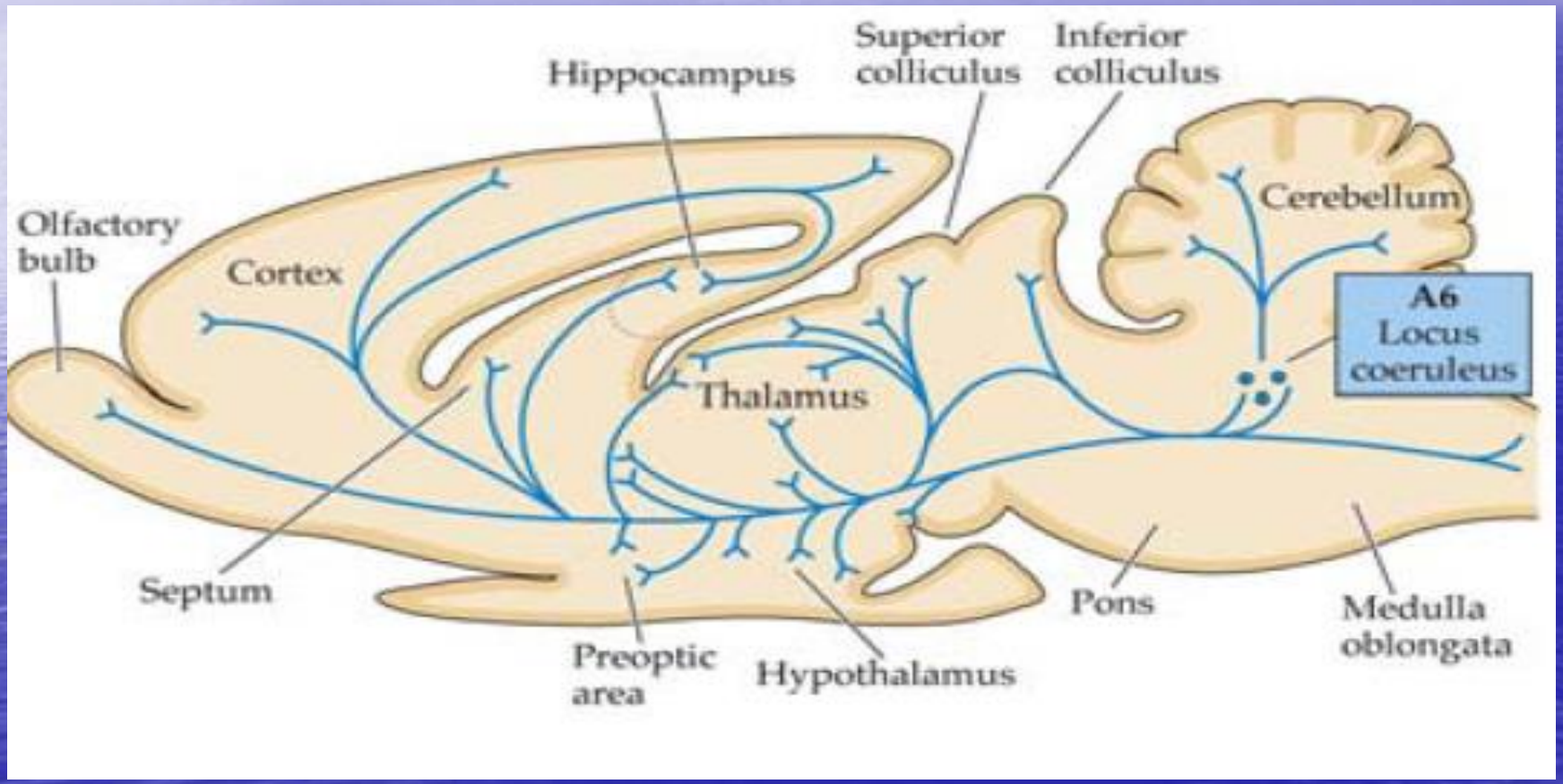
Dr.G.MATHAN
Assistant Professor
Department of Biomedical Science
Bharathidasan University
Tiruchirappalli, Tamil Nadu


Receptor subunits
Outside cell
Inside cell
Pore
Ions
Neurotransmitter

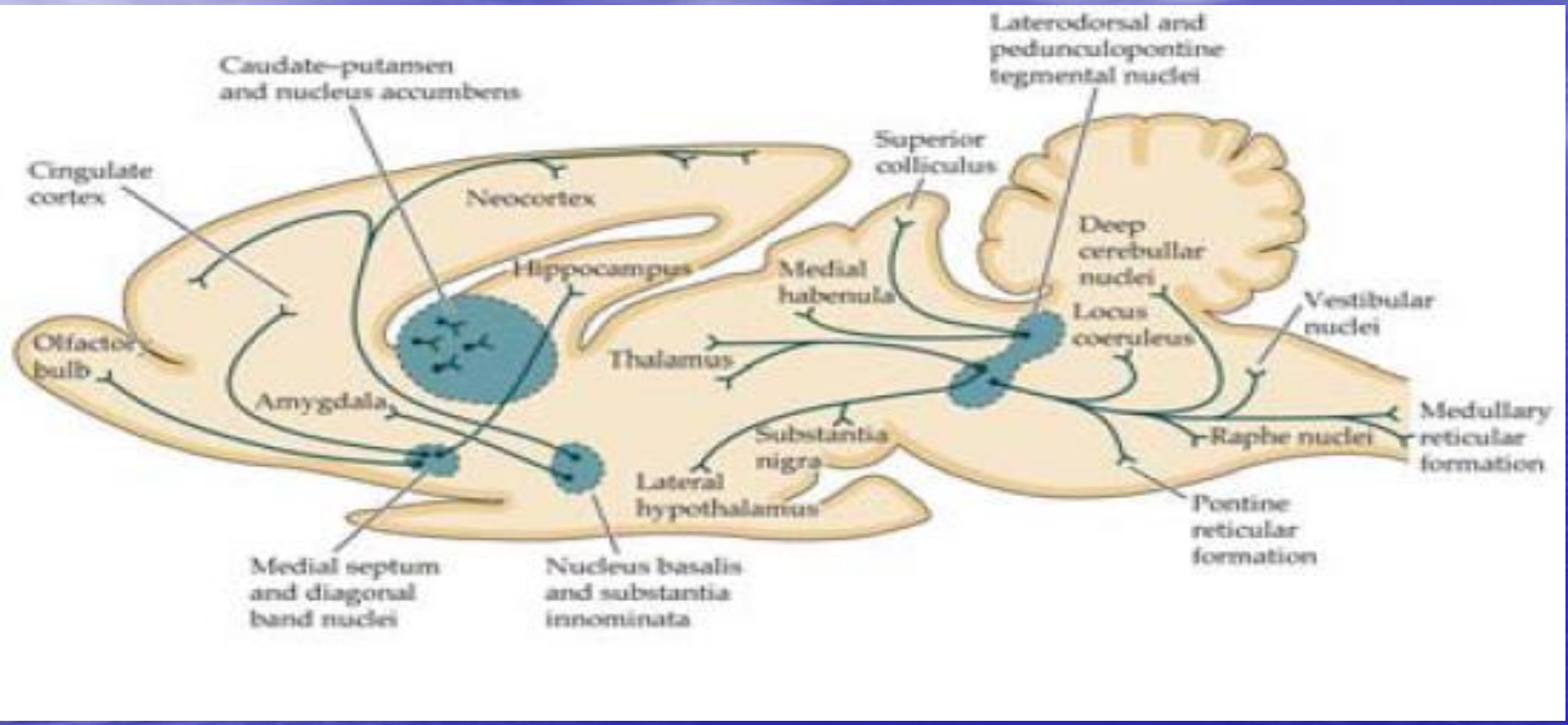
Synapses


CALCIUM
ASTROCYTE
AXON TERMINAL
SIGNALING MOLECULE
PROTEIN THAT BINDS NEURO-TRANSMITTER
ATP
GLUTAMATE
GLUTAMATE RECEPTOR
DENDRITE

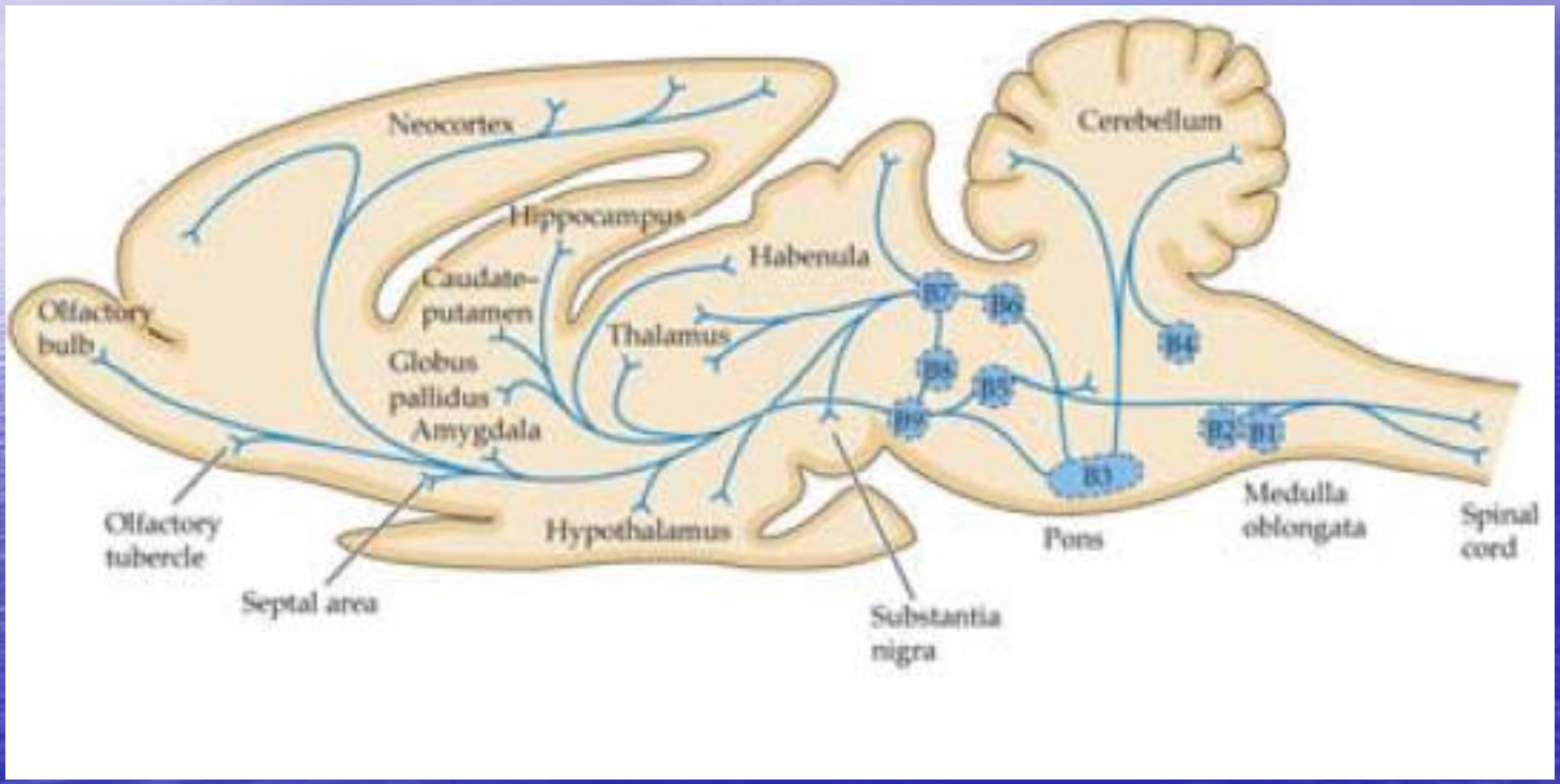
The locus coeruleus (LC) contains a dense cluster of noradenergic neurons



Anatomy of cholinergic pathways in the brain



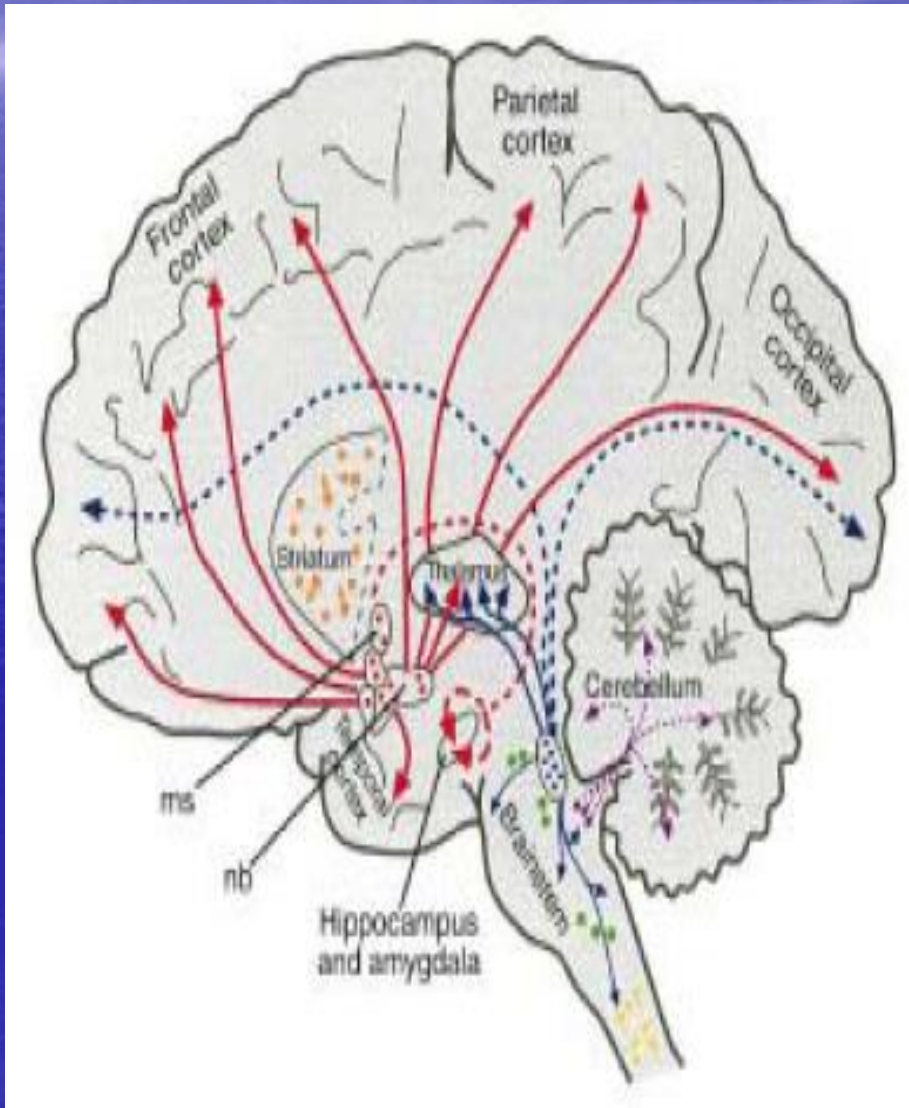
Anatomy of the serotonergic system



Pedunculopontine ACh pathway

Pedunculopontine – lateral dorsal pathway

- Pontine tegmental nucleus (PPTN) & lateral dorsal tegmental nuclei (LDTN)
- Ascending reticular pathway
- Thalamus (lateral geniculate nucleus)
- Occipital cortex, Inferior frontal cortex



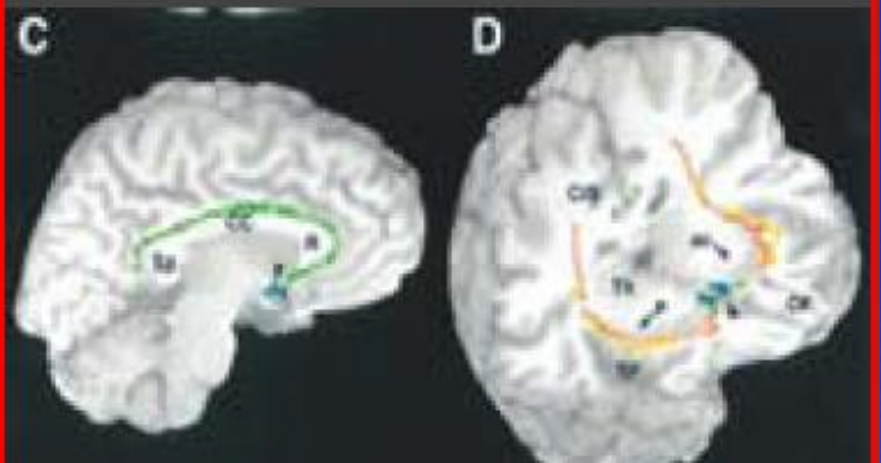
Basal forebrain ACh pathways

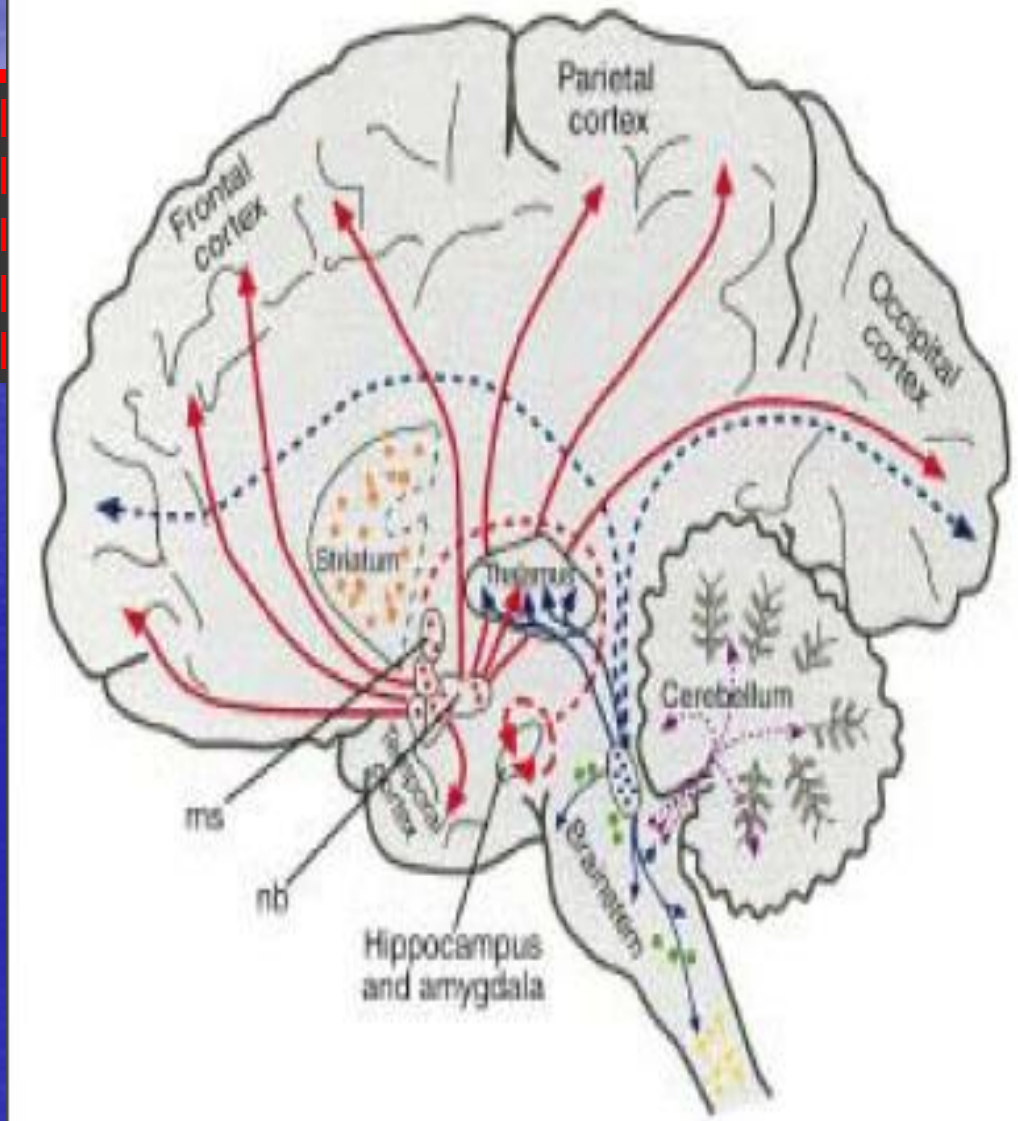
Learning and memory

Medial septal nucleus → HC + amygdala

Nucleus basalis of Maynert → cortex

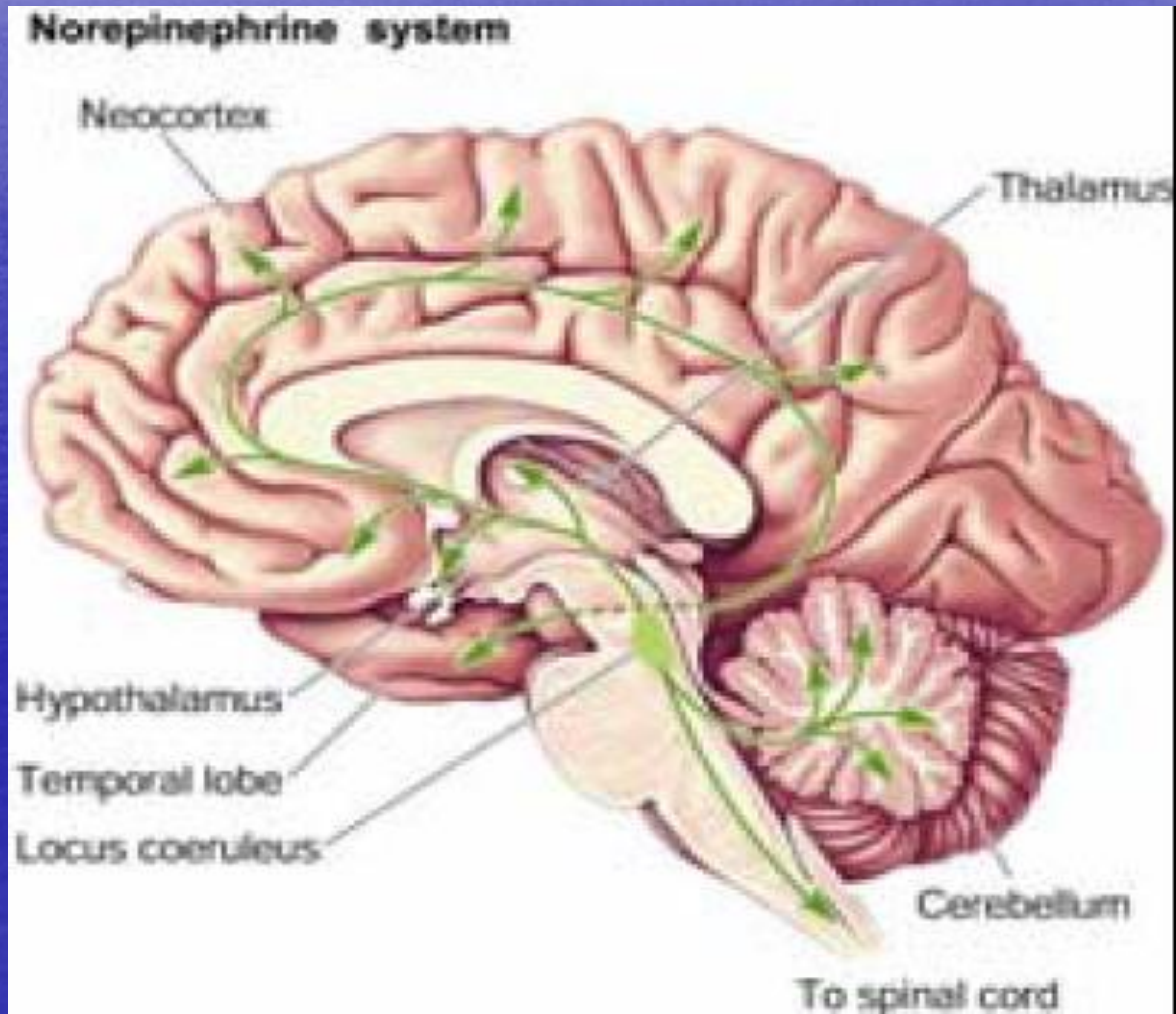
medial (C) & lateral (D) pathways





NE pathways in brain

- 2 major groups of NE neurons ascending from pontine locus coeruleus (LC) and lateral tegmental nuclei (LTN)
  - some overlap, together innervate whole brain



Basal forebrain ACh functions

- Attention: selective attention, vigilance, response inhibition → "signal-to-noise" ratio and suppression of interference (Everitt & Robbins, 1997; McGaughy et al', 2000)

- Learning and memory: long-term potentiation (LTP) in HC, amygdala, cortex [interactions with glutamate]
  - Declarative (semantic and episodic) memory (Everitt & Robbins, 1997; McGaughy et al., 2000; Selden et al., 1998)
  - Consolidation during (REM) sleep (Perry et al, 1999; Webster, 2001)

Attention and memory deficits, dementia following cholinergic pathway damage

- Alzheimer's disease. Standard treatment: AChE inhibitors

DA synthesis and metabolism

Tyrosine (amino acid from diet)

↓ Tyrosine hydroxylase

Dopa ← L-dopa (agonist) tx Parkinson's disease

↓ Dopa decarboxylase on postsynaptic membrane

Dopamine (DA)

↓ Monoamine oxidase (MAO) in presynaptic neuron [after reuptake]

↓ Catechol-O-methyl transferase (COMT)

DOPAC + HVA

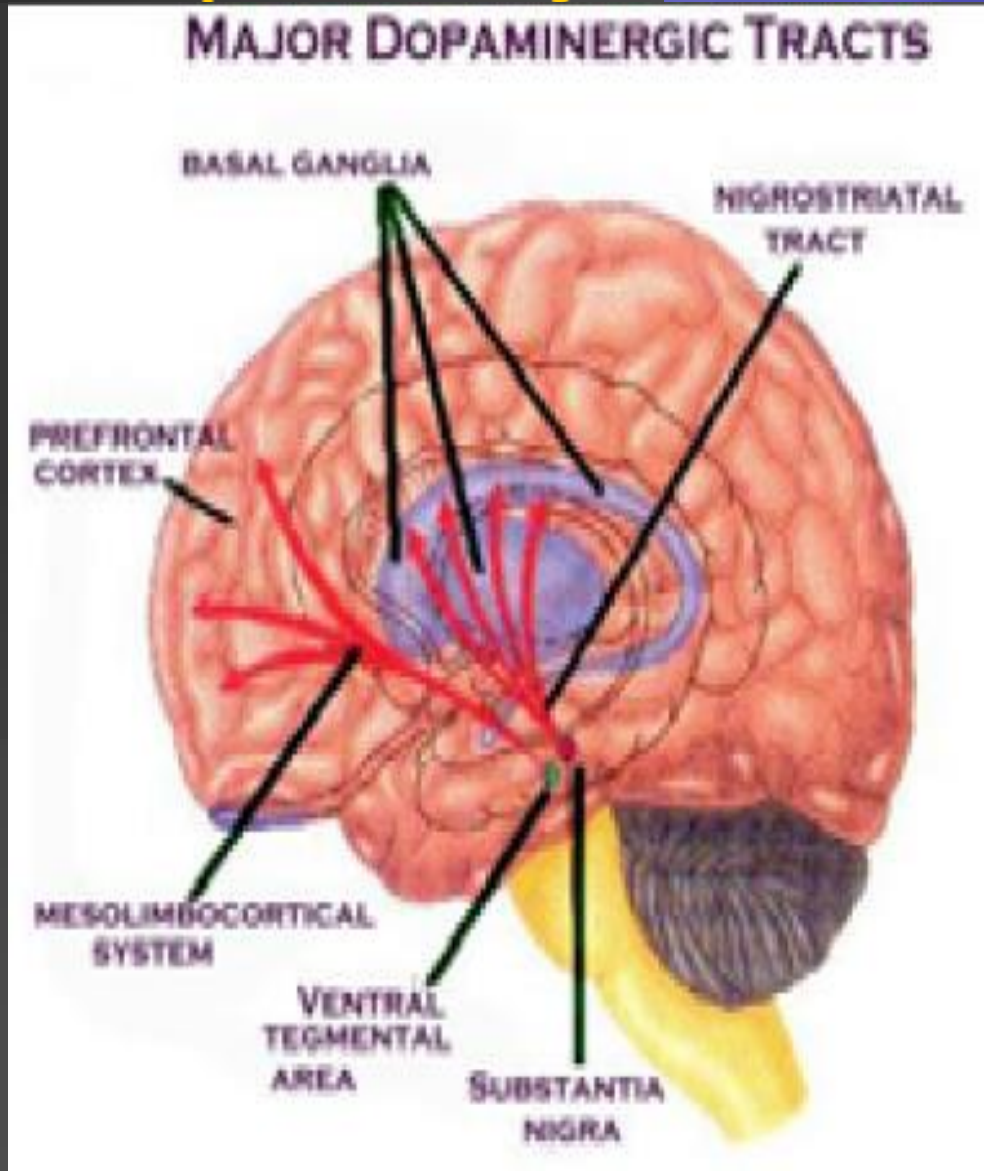
3 Major DA pathways in brain

- Nigrostriatal pathway
  - Motor function
- Mesolimbic and Mesocortical pathways
  - Reward, reinforcement, motivation → attentional and behavioural control
  - Psychosis
    - Schizophrenia, hallucinatory drugs

Nigrostriatal DA pathway

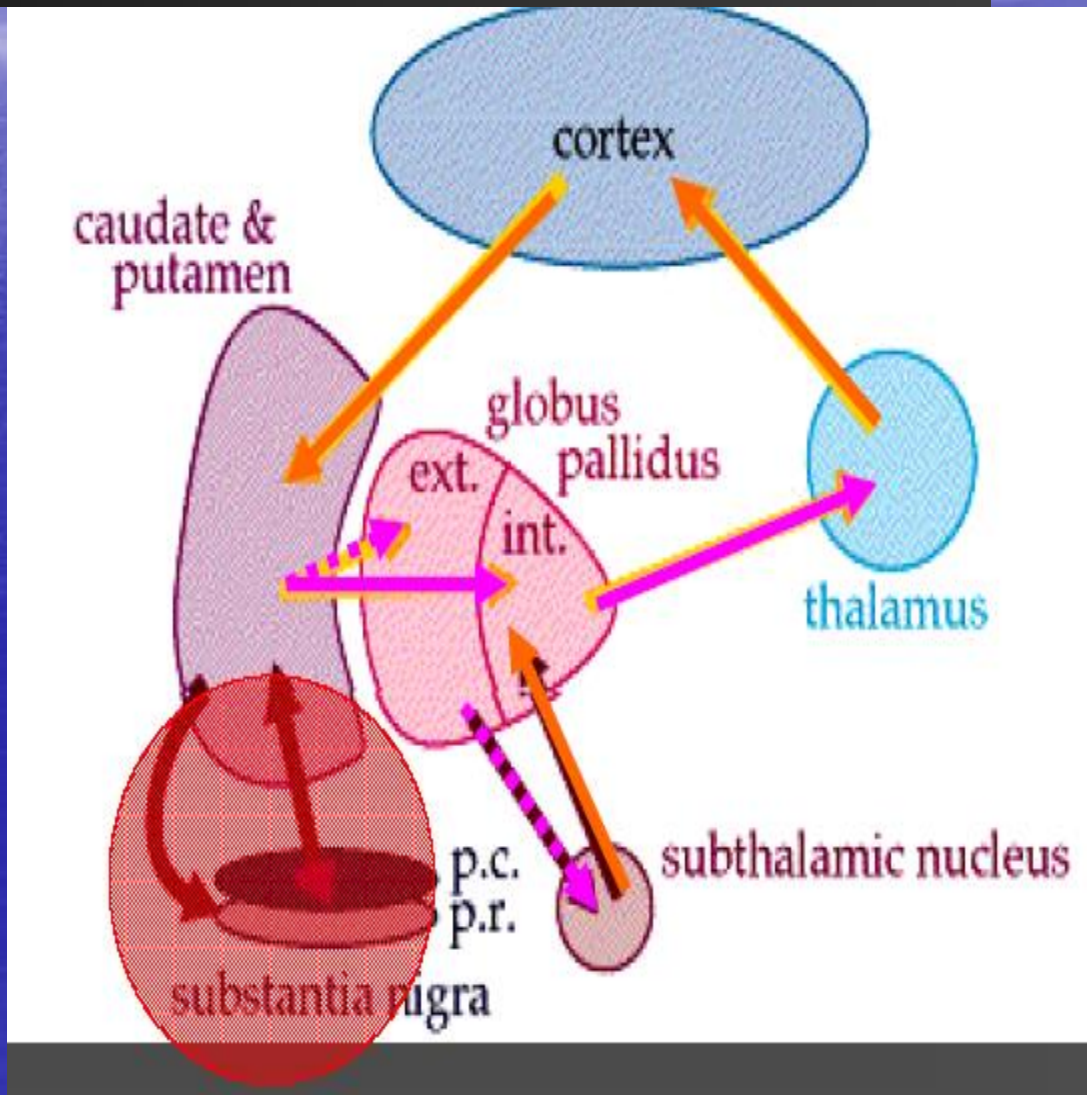
- Substantia nigra (midbrain)
- Striatum (caudate + putamen)

Coordinate movement via basal ganglia, thalamus, cortex by interacting w amino acids (GLT+GABA)



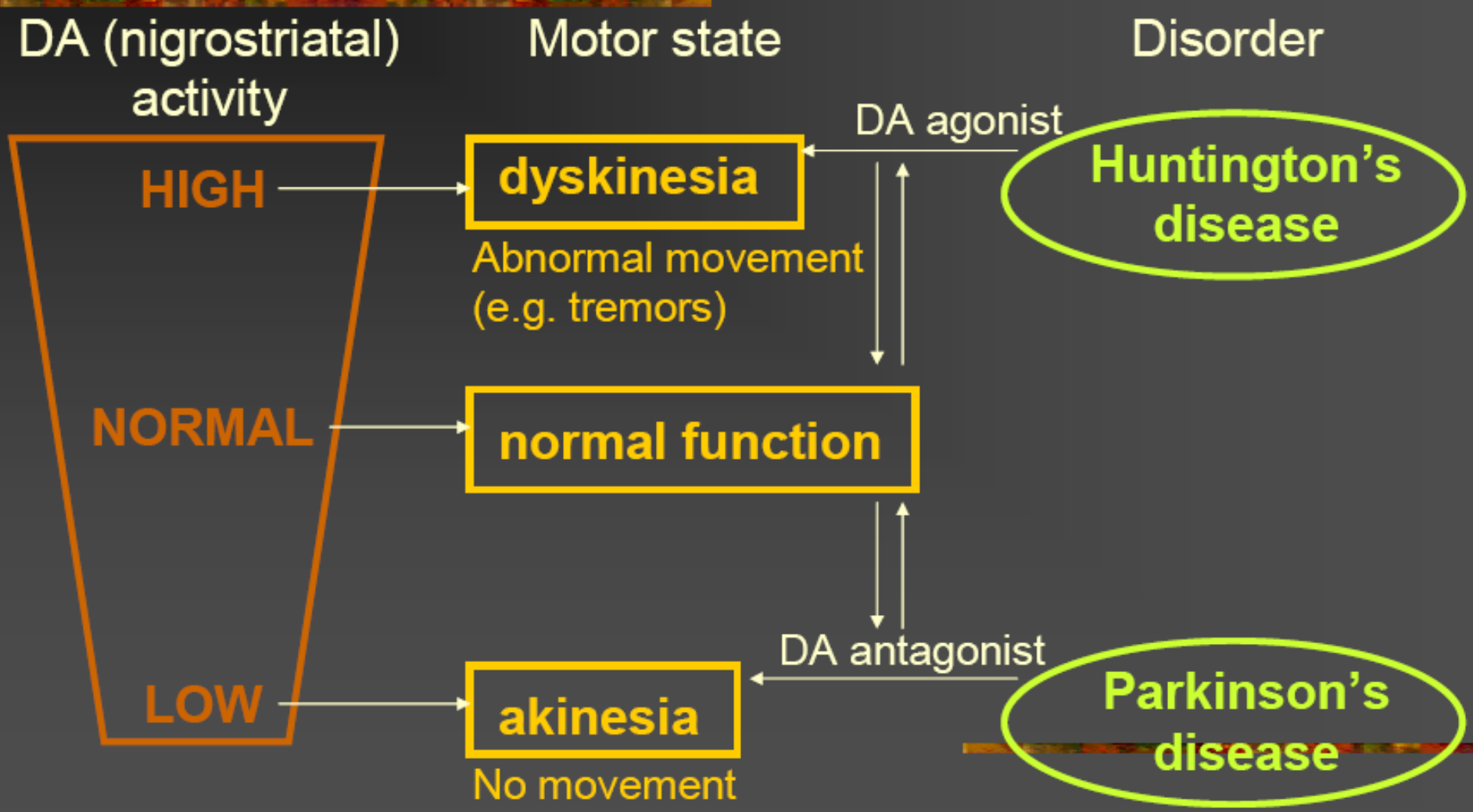
Parkinson's Disease

Degeneration of dopaminergic nuclei in substantia nigra



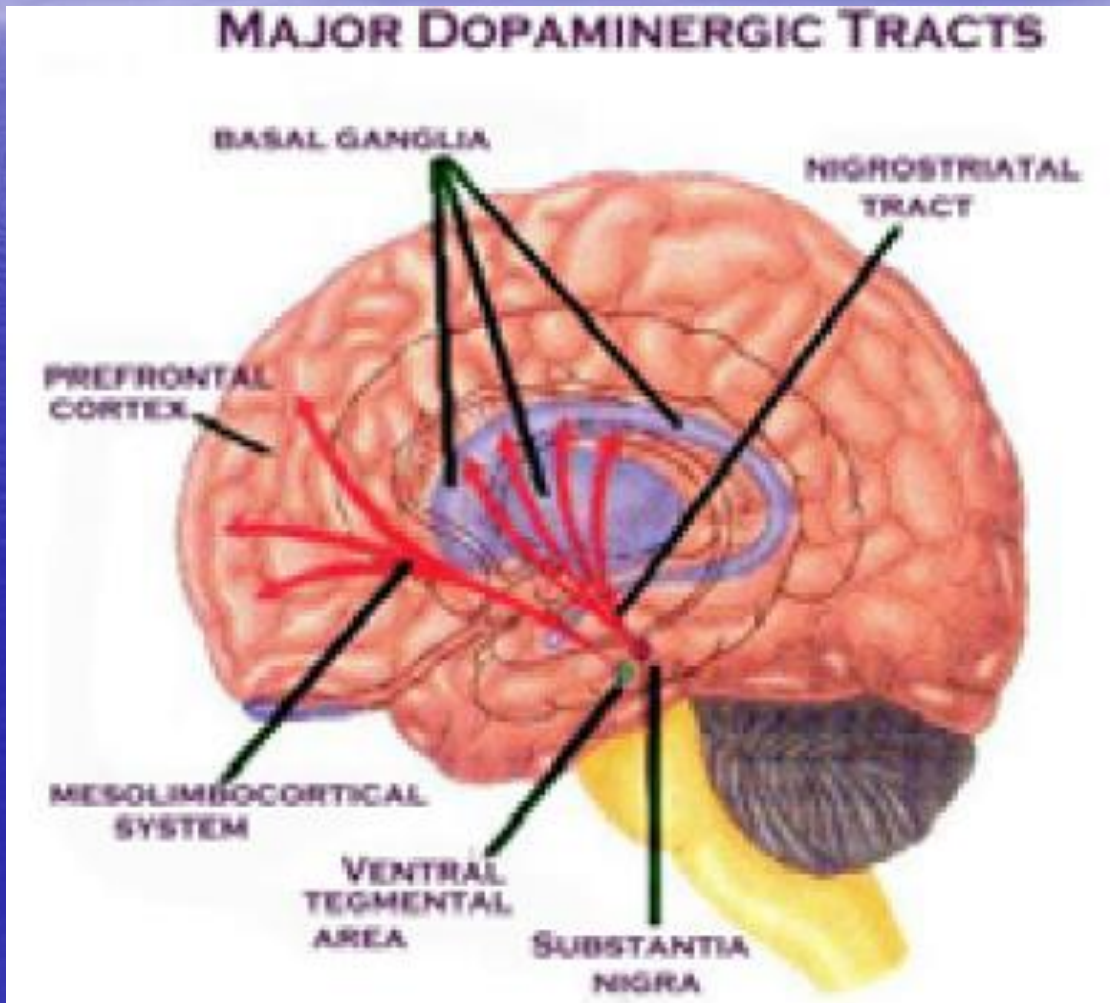
Nigrostriatal DA functions:

Motor control and coordination



Mesolimbic & mesocortical DA pathways (mesolimbocortical system)

- Mesolimbic
  - VTA
  - Nucleus accumbens, olfactory tubercle
  - Amygdala + HC
- Mesocortical
  - VTA
  - Prefrontal cortex



Mesocortical DA functions: motivation (and interference suppression)

D2,4

- Attention Deficit Hyperactivity Disorder (ADHD)
  - Deficits in sustained attention and response inhibition
    - D4 gene (Leung et al, 2005); caudate, PFC (Swanson et al., 1998)
  - Difficulty imposing top-down control on 'boring' tasks
    - Easily distracted

5-HT synthesis and metabolism

Tryptophan (amino acid from diet)

Rate-limiting step: can study effects of 5-HT via dietary tryptophan depletion

↓ Tryptophan hydroxylase

5-hydroxytryptophan

↓ L-aromatic acid decarboxylase

Most antidepressants act on metabolism

Serotonin (5-HT)

↓ Monoamine oxidase (MAO) in presynaptic neuron [after reuptake]

↓ Aldehyde dehydrogenase

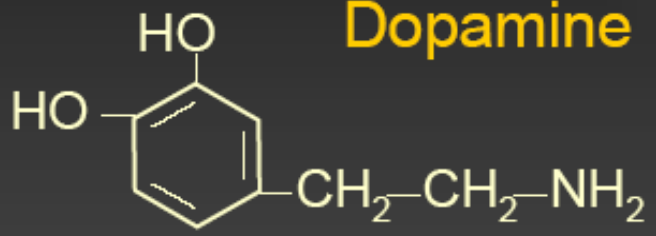
5-HIAA

Major classes of neurotransmitters

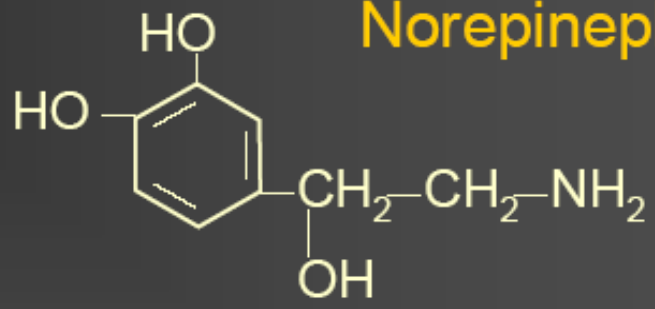
1. Amino Acids
   - Glutamate (excitatory); GABA (inhibitory)
2. Acetylcholine (excitatory)
3. Monoamines (excitatory)
   - Catecholamines: Dopamine, Norepinephrine
   - Indolamine: Serotonin

Neurotransmitters

- Catecholamines



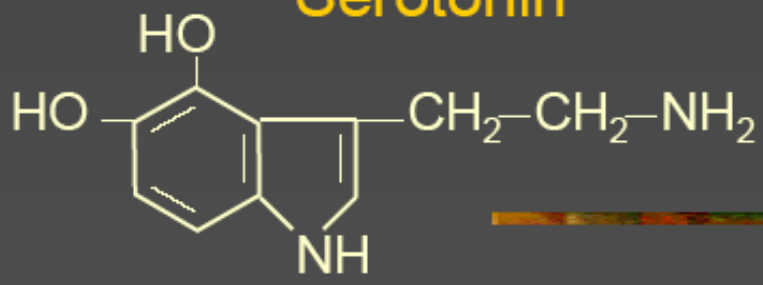
Dopamine



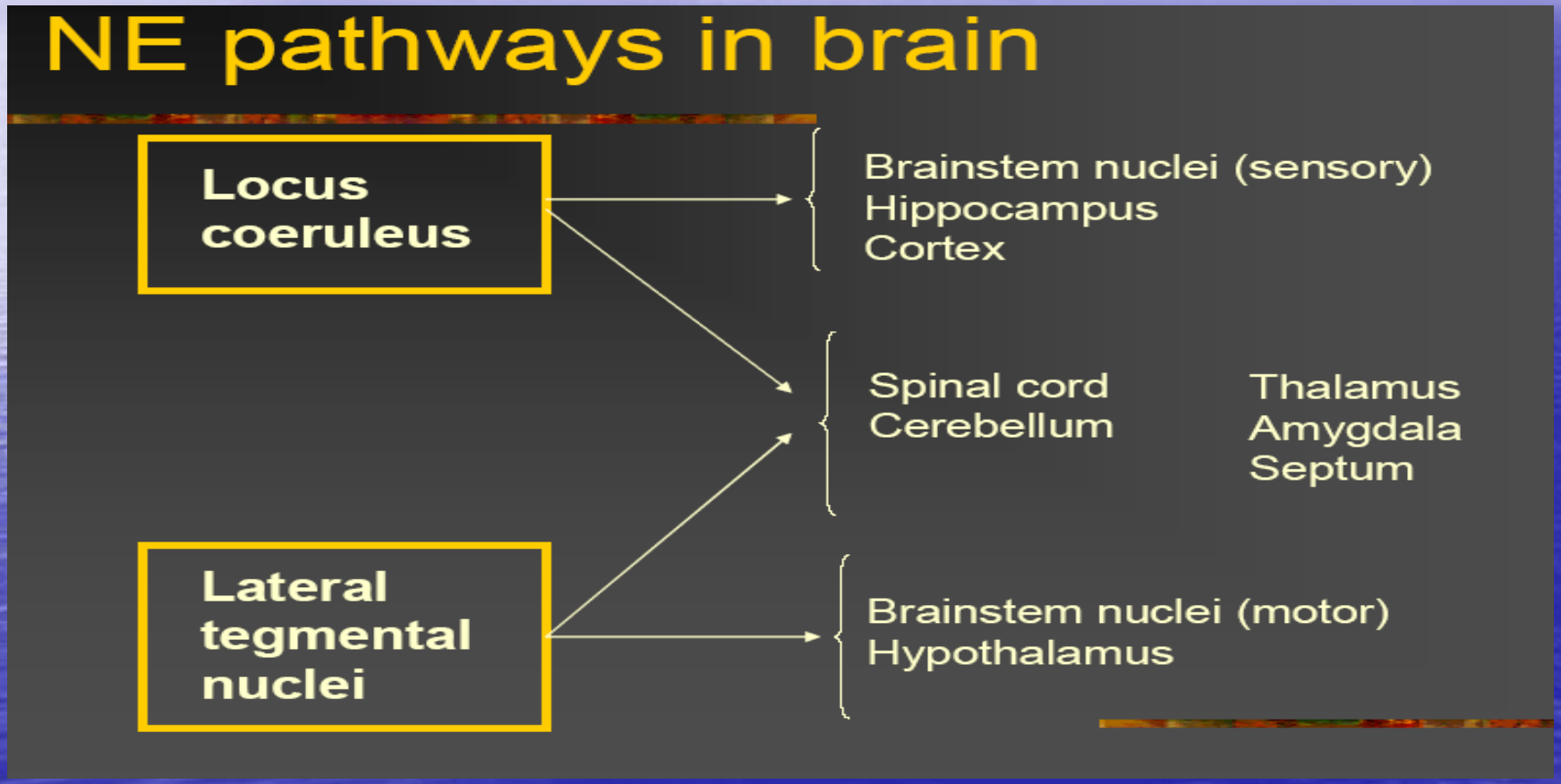
Norepinephrine

- Indolamine(s)

Serotonin



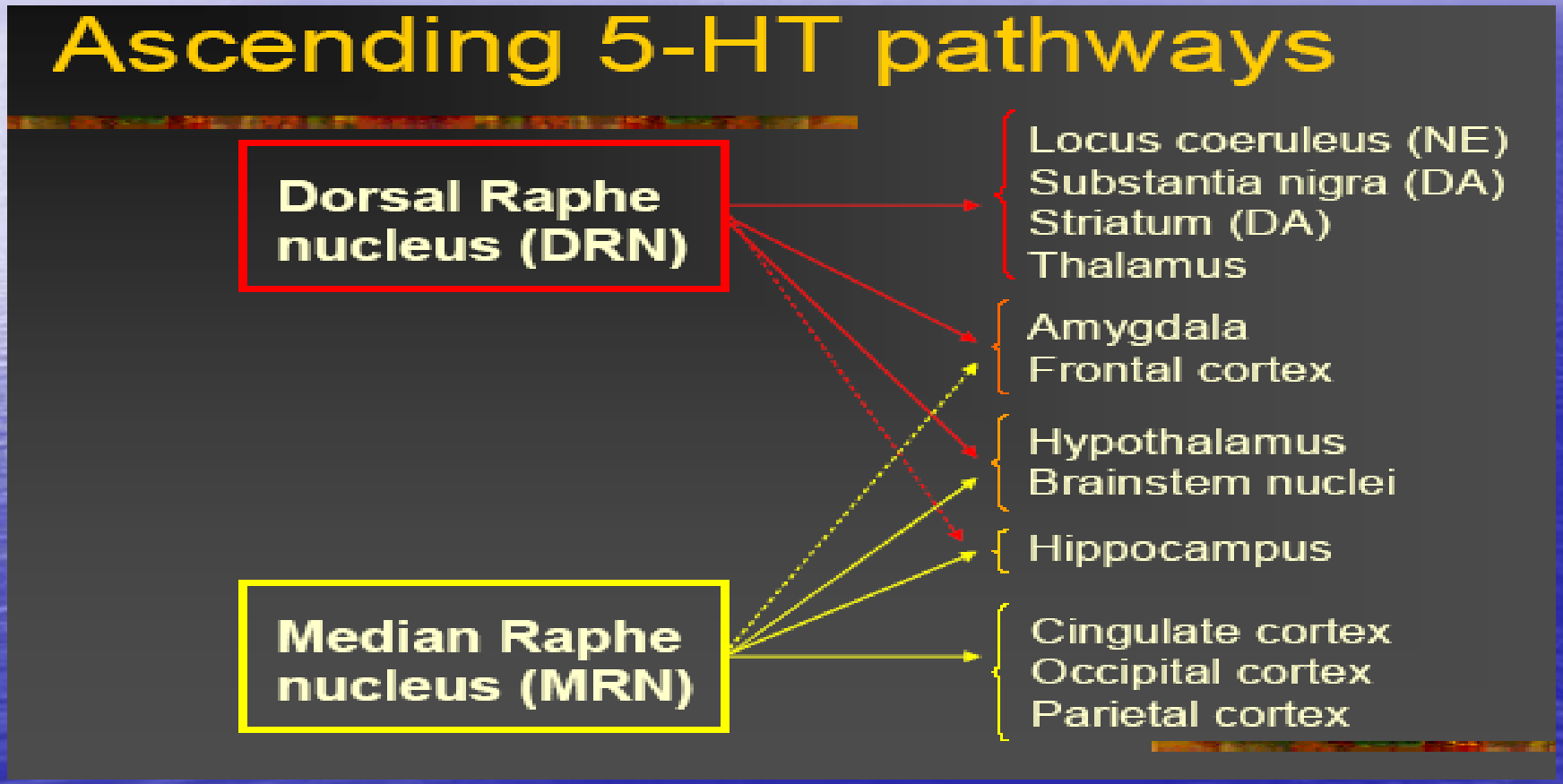
NE pathways in brain



NE functions: Arousal / attention

- Arousal: LC → septal: sleep/wake state (Berridge et al, 2005)
- Arousal ↔ attention (Aston-Jones et al., 1994, 1999)
  - Electrode recordings, monkeys, Go / no-go task
  - Tonic NE activity in LC = vigilant attention
    - Scanning, high behavioural flexibility (but also distractibility)
  - Phasic NE activity in LC = focused attention
    - Selective attention, response inhibition

Ascending 5-HT pathways



5-HT functions: 'body'
coordinated physiological functioning

- Majority (98%) of 5-HT in body is outside CNS
- Physiological regulation (Stanford 2001)
  - Thermoregulation, appetite and digestion, cardiovascular activity, sexual functioning, pain perception
- Circadian rhythms (Stanford, 2001)
  - Sleep/wake cycle: precursor of melatonin (pineal gland)
    - Firing of 5-HT neurons in DRN and MRN is 'clock-like', NOT reactive like LC noradrenergic neurons
    - Changes in activity correspond to phases in sleep/wake cycle

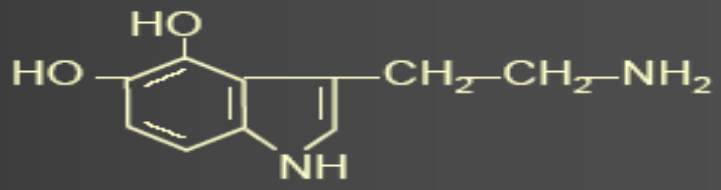
5-HT functions: 'mind'
affect regulation and cognitive function

- Learned helplessness (animal model depression)
  - 5-HT increase following exposure to inescapable stress predicts helpless behaviour (Petty, 1994)
  - Microinjection of 5-HT to prefrontal cortex reverses learned helplessness (Davis et al., 1999)
- Anticipatory anxiety: 5-HT from DRN exaggerates amygdala response to conditioned aversive stimuli (Graeff et al., 1996)
- 5-HT contributes to (declarative) memory, particularly for emotional (mood-congruent) stimuli

Disorders of 5-HT system: mood disorders

- Major depressive disorder (MDD) closely linked to low 5-HT activity (Stanford, 2001)
  - Broad symptom range reflects broad actions of 5-HT in homeostasis, affect, and cognition
  - Antidepressants increase synaptic 5-HT activity, with SSRIs being most specific
  - Acute tryptophan depletion → recurrence of depressed mood and cognitive (memory) impairment in remitted depressed Ps (Booij et al, 2005)
- 5-HT dysfunction also linked to anxiety (obsessive-compulsive and generalized anxiety disorders) (Stanford, 2001)

Serotonin (5-HT)

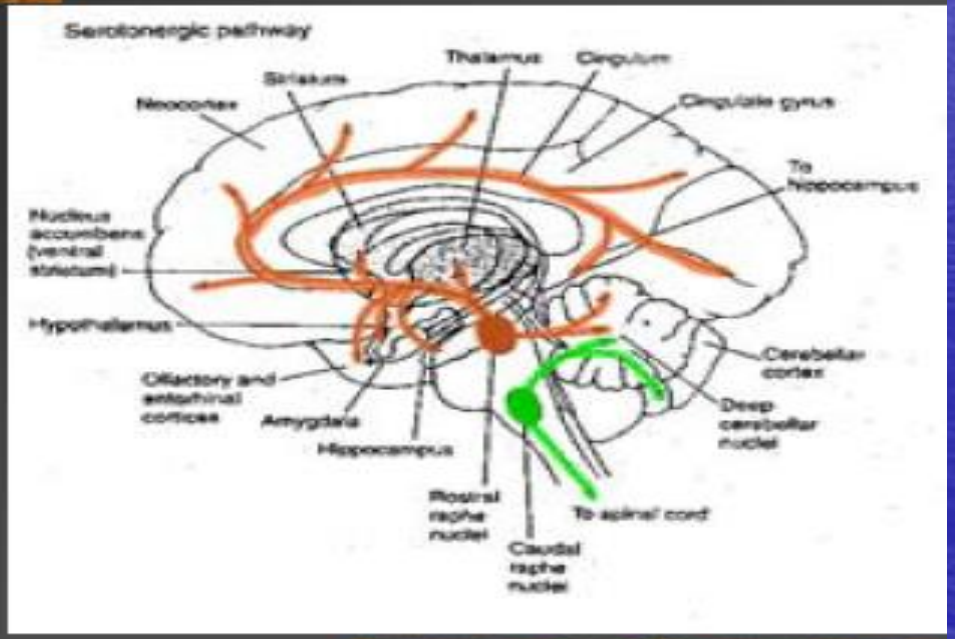


- 5-hydroxytryptamine
- Found in both PNS and CNS
  - CNS contains < 2% total 5-HT in body
  - Outside CNS: broad range physiological functions
    - Cardiovascular regulation, smooth (organ) muscle contraction, gastrointestinal functions
- 7 (!) receptor subtypes (ionotropic and metabotropic)
  - Not clearly associated with specific brain regions
  - Some functional specificity (with overlap)
    - Efforts to isolate receptors in order to improve drug specificity (e.g. busipione, a 5HT-1A anxiolytic with fewer side effects than benzodiazepenes, which affect GABA)

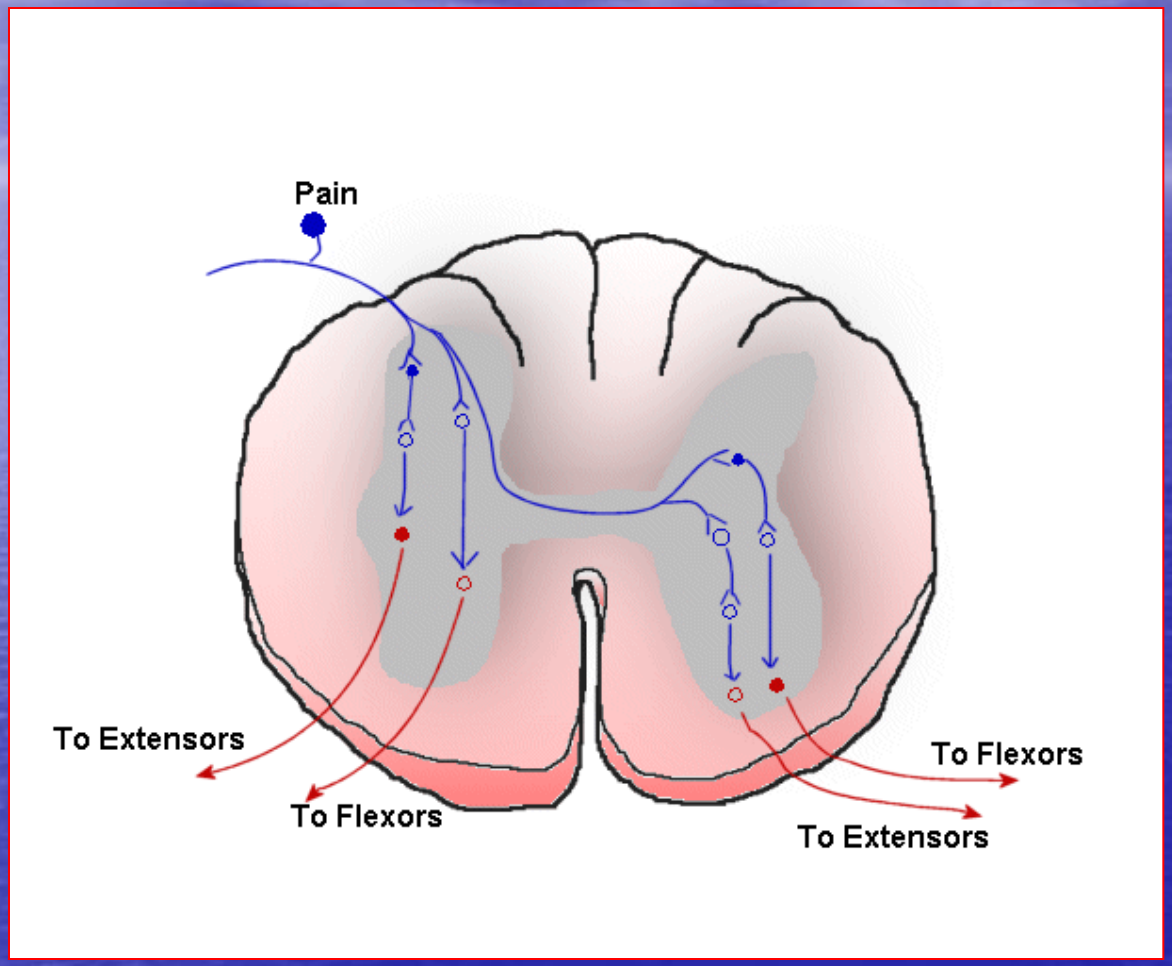
2 major 5-HT pathways in CNS

- Ascending superior
- Limbic, sensory areas, thalamus, hypothalamus, all cerebral cortex

- Descending inferior
- Brainstem nuclei, spinal cord → motor / autonomic functions, pain perception



Withdrawal Reflex



Muscles do not receive direct inhibitory input; motor neurons are inhibited in the spinal cord = less neurotransmitter release, not active inhibition of contraction

- Language and speech
  - *Broca's area* – located at left frontal lobe and is part of the primary motor cortex that controls muscles in the face
  - *Wernicke's area* – posterior portion of the temporal lobe that controls comprehension and generation of speech
  - Frontal & temporal areas become active when meaning must be attached to words (ex. ~ a person generates verbs to go with nouns)
    - Damage in this spot abolishes the ability to comprehend speech, but left speech generation intact

Acknowledgement

- The Presentation is being used for educational and non commercial purpose
- Thanks are due to all those original contributors and entities whose pictures used for making this presentation.