Modulatory Systems of the Brain

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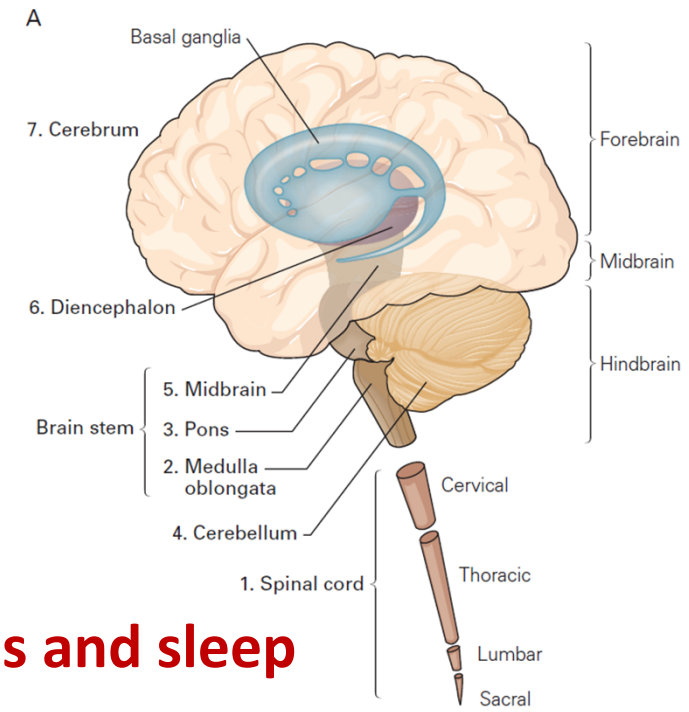
This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Neuroscience exam.

Sources :

- Principles of Neural Science (5th ed.), Kandel et al. (2013)
- Ganong's Review of Medical Physiology, (24th ed.), Barret (2010)
- Textbook of Medical Physiology (11th ed.), Guyton and Hall (2006)
- Color Atlas of Physiology (6th ed.), Silbernagl and Despopoulos (2009)

Brain stem

- contains ascending (**sensory**) tracts and descending (**motor**) tracts
- **nuclei of the cranial nerves**
- contains **centers that control respiration and heartbeat**
- contains **centers** crutial **for consciousness and sleep**



The brain stem is a modulatory center that orchestrates the activity of the rest of the CNS, ensuring that its activity is optimized.

- **six neurochemical modulatory systems**

Brain stem – Modulatory Function

- mediated by small groups of neurons which project widely
- neurotransmitters:
  - acetylcholine
  - monoamines (catecholamines - norepinephrine, epinephrine, dopamine; serotonin; histamine)
- enable and modulate many of the higher-order behaviours – processes localized in the forebrain (memory, language, compassion)
- involved in pathophysiology, drug targets

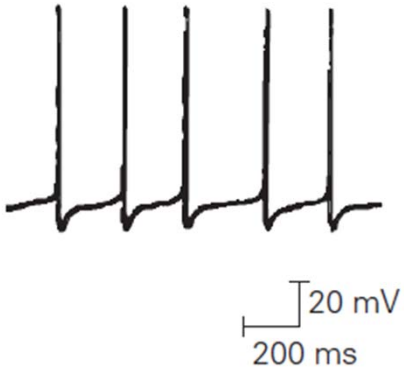
Brain stem – Modulatory Function

Monoamines (catecholamines - norepinephrine, epinephrine, dopamine; serotonin; histamine)

- Neurons using these neurotransmitters fire action potentials in a highly regular pattern.

  (action potentials followed by a slow membrane depolarization that results in the next spike - intrinsic pacemaker currents)

Firing pattern of a locus ceruleus neuron

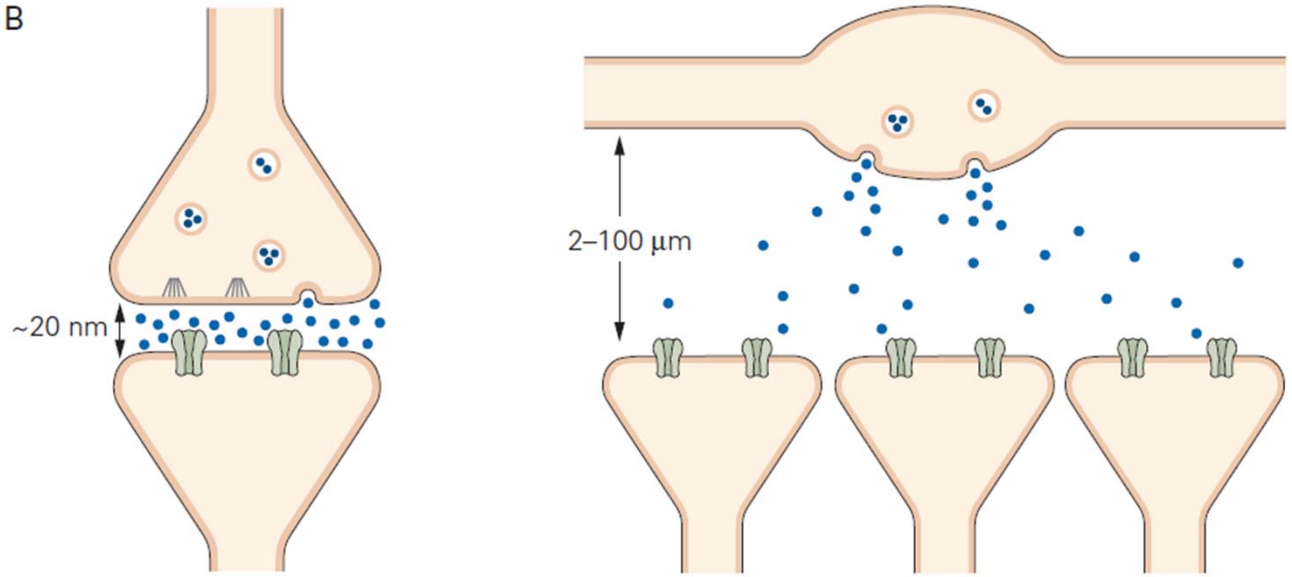


- continuous delivery of monoamines (*e.g.* basal ganglia)

Brain stem – Modulatory Function

Monoamines (catecholamines - norepinephrine, epinephrine, dopamine; serotonin; histamine)

- some axon terminals release neurotransmitter diffusely to many targets at once



Brain stem – Modulatory Function

Monoamines (catecholamines - norepinephrine, epinephrine, dopamine; serotonin; histamine)

- responses both fast and slower

Cholinergic neurons – share some of the properties (*e.g.* acting also through G protein-coupled muscarinic receptors).

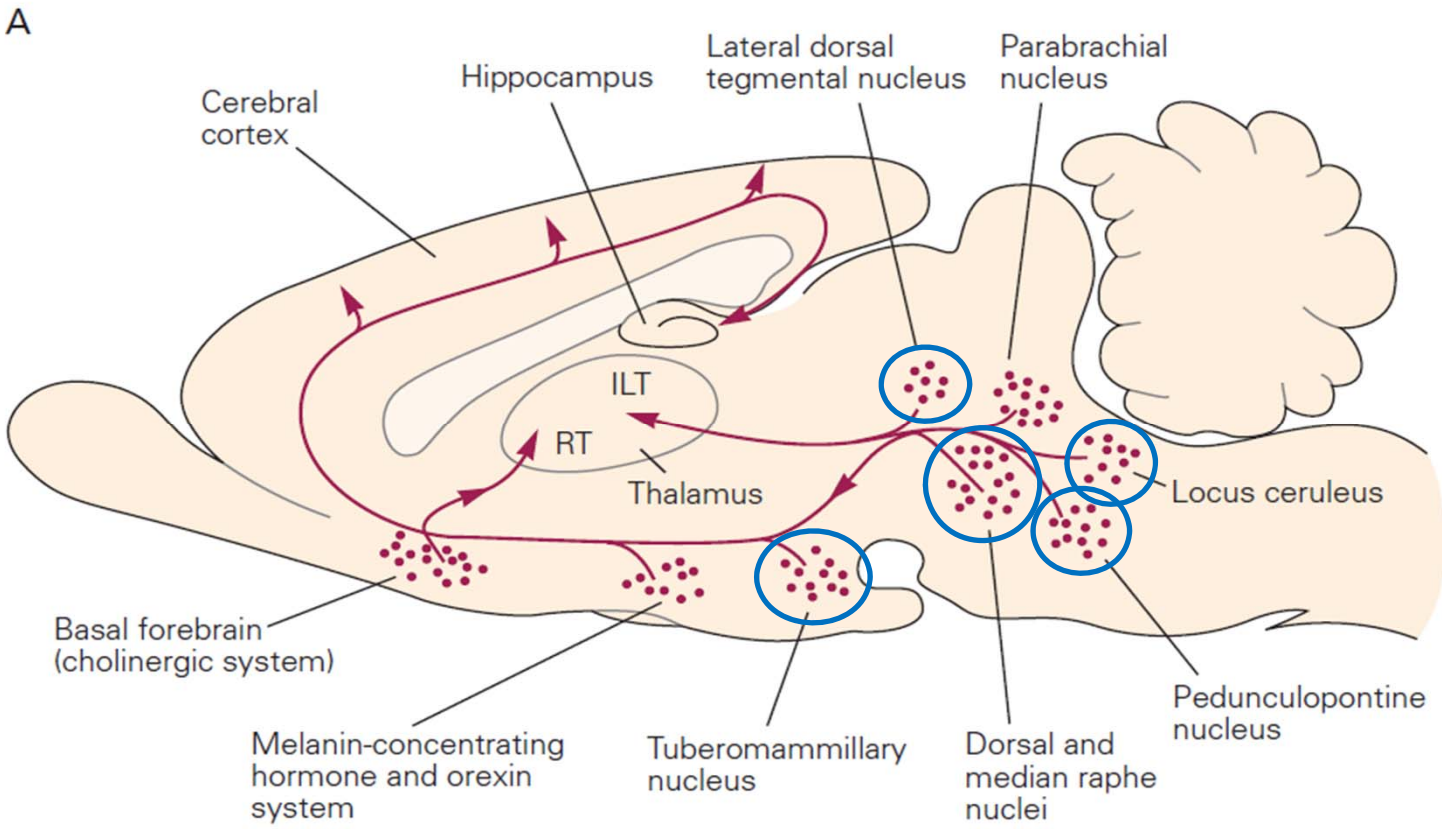
Brain stem – Modulatory Function

- Some neurons in the brain stem that project to the forebrain control wakefulness and sleep by changing arousal.
- located namely in the rostral pons and caudal midbrain
- reticular formation, reticular activating system
- **ascending arousal system (AAS)**
  - remarkable connectivity (widespread projections almost to every part of the CNS)
  - together with sleep-promoting regions in other parts of the brain regulates sleep and waking
  - damage of its projections in the thalamus and hypothalamus leads to coma

Brain stem – Modulatory Function

Arousal – Ascending Arousal System

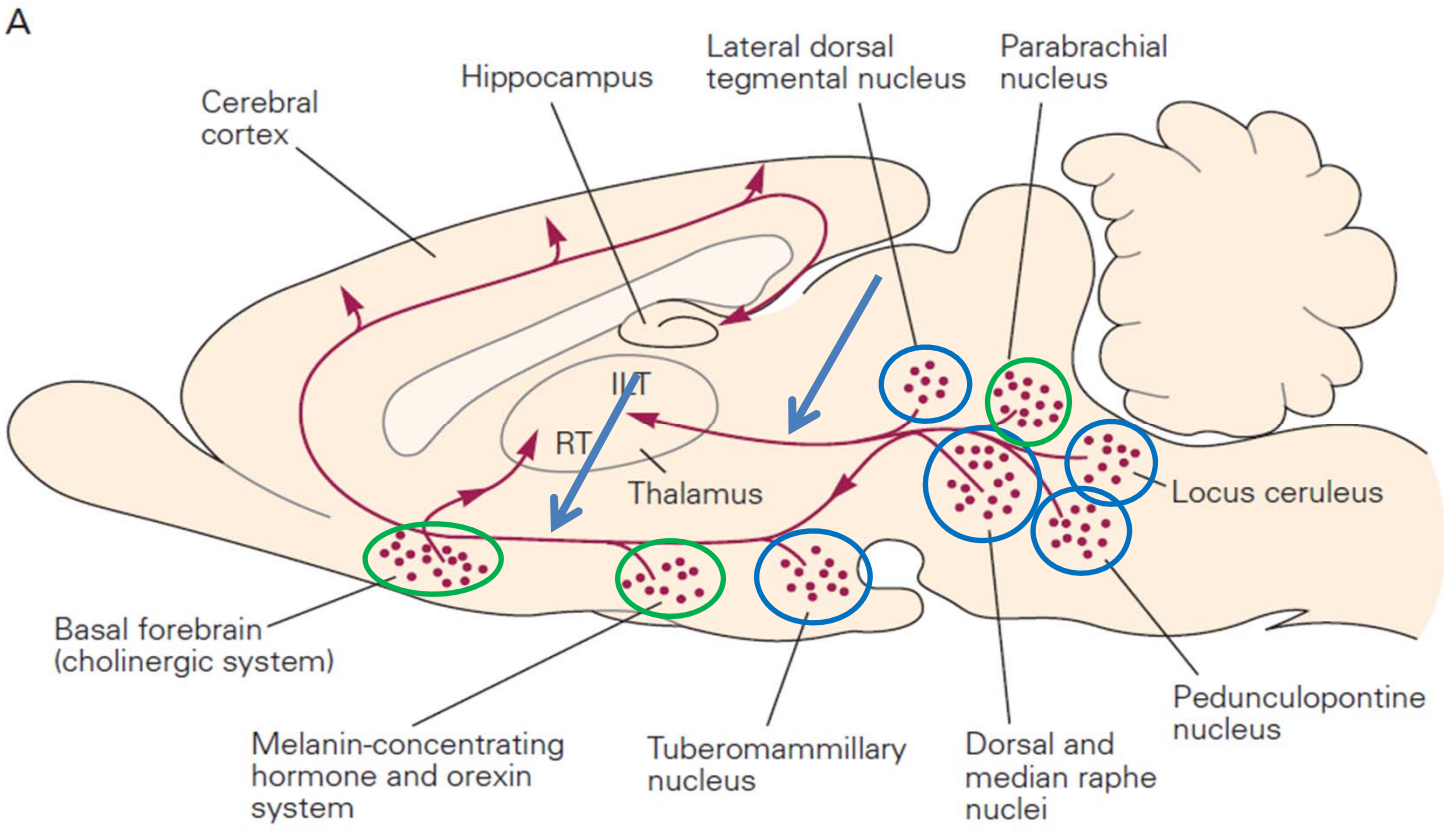
Major parts:



Brain stem – Modulatory Function

Arousal – Ascending Arousal System

Regulate sleep and waking together with other neurons:

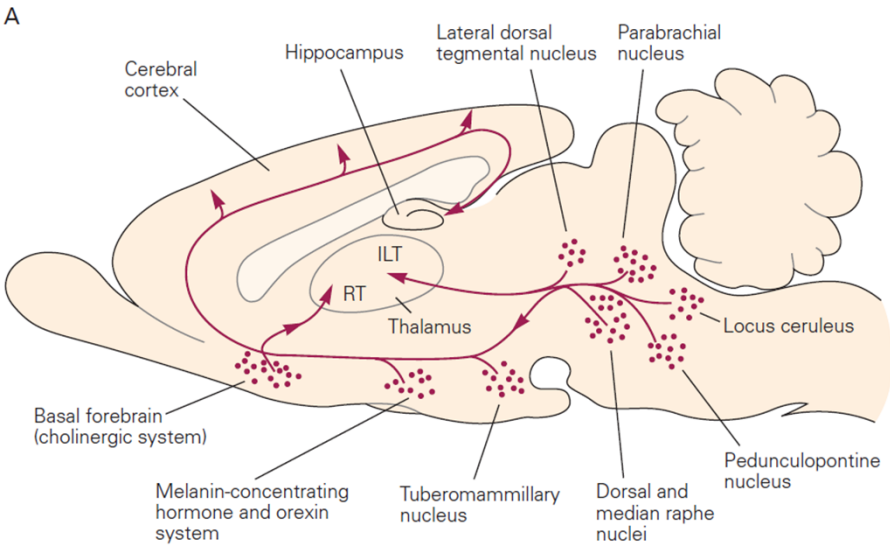


Brain stem – Modulatory Function

Arousal – Ascending Arousal System

AAS activates the cortical neurons:

- **directly**
- **indirectly** – by modulating activity of neurons:
  - in the hypothalamus
  - in the basal forebrain
  - in the thalamus



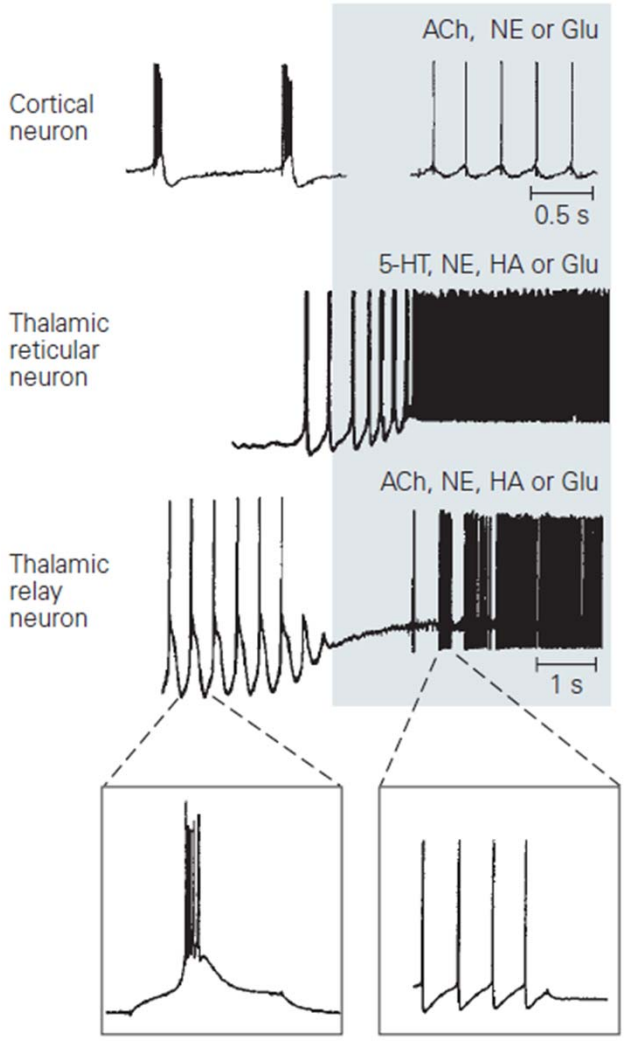
Brain stem – Modulatory Function

Arousal – Ascending Arousal System

Activation of the thalamic and cortical neurons is caused by different mode of firing of the neurons.

- **during sleep – firing in bursts**
- **during wakefullness – firing in single spikes**

  Following application of acetylcholine, norepinephrine, serotonin, and histamine.



Brain stem – Modulatory Function

Regulation of Brain Functions Other than Arousal

1. **Optimization of Cognitive Performance**
2. **Involvement in Autonomic Regulations and Breathing**
3. **Modulation of Pain and Anti-nociceptive Pathways**
4. **Facilitation of Motor Activity**

Brain stem – Modulatory Function

1. Optimization of Cognitive Performance

- **locus ceruleus (NE)** - important role in **attention**
- **monoaminergic inputs to dorsolateral prefrontal cortex improve the working memory**
- **dopamine** is also linked to **reward-based learning**

  increased activity of dopaminergic neurons when a reward is unexpectedly given

  The same pathways are involved in addiction to drugs of abuse.

Brain stem – Modulatory Function

2. Involvement in Autonomic Regulations and Breathing

- maintenance of resting vascular tone
- changes of vascular tone at specific situations:

  e.g. orthostasis disinhibits the neurons – baroreflex depressor reflexes by inhibition of the preganglionic sympathetic neurons - *e.g.* due to deep pain

Brain stem – Modulatory Function

2. Involvement in Autonomic Regulations and Breathing

Serotonin

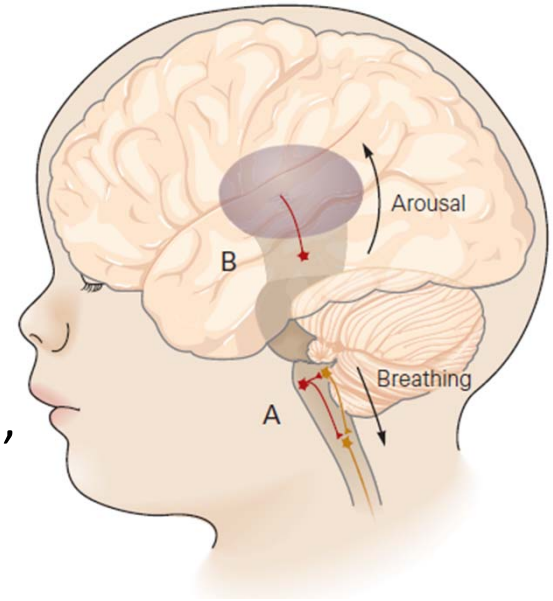
- regulates many autonomic functions
- stimulation of serotoninergic neurons (raphe nuclei in medulla)
  → ↑ heart rate and blood pressure
  → ↑ respiratory motor

Brain stem – Modulatory Function

2. Involvement in Autonomic Regulations and Breathing

Serotonin

- serotoninergic neurons as central chemoreceptors
  (in the medulla, increased firing at higher pCO_2)
  → ↑ ventilation
  (increased firing at higher pCO_2)
  → ↑ arousal, anxiety, changes in the cerebral blood flow
  (important for survival at airways obstruction, SIDS)



Brain stem – Modulatory Function

3. Modulation of Pain and Anti-nociceptive Pathways

- acute pain – beneficial to avoid/reduce injury

- chronic pain – may be maladaptive

Descending monoamine projections to the dorsal horn of the spinal cord modulate pain perception.

Treatment of:

- migraine headaches - agonists of 5-HT_{1B} and 5-HT_{1D} receptors (triptans)
- migraine headaches and chronic pain – blockers of monoamine reuptake (antidepressant drugs including SSRIs)

Brain stem – Modulatory Function

4. Facilitation of Motor Activity

Dopaminergic system – critical for normal motor performance, **release inhibition on motor responses** (Parkinson disease).

Serotoninergic neurons – important for generation of motor programs (serotonin syndrome).

Noradrenergic neurons – facilitates excitatory inputs to motor neurons, namely in stereotypic and repetitive behaviours (through β and α1 receptors; stress – exaggerated motor responses, tremor; β-blockers - to reduce certain type of tremor, musicians)

Brain stem – Modulatory Function

Summary

Ascendent projections

- to the forebrain
- control of various aspects of mood and cognition (AAS - arousal and sleep, attention, memory, reward-based learning)

Descendent projections

- to the spinal cord
- regulation of autonomic, somatosensory (modulation of pain perception), and motor functions

Plays an important role in normal brain function!