MEDS 371, Systems Neuroscience

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**Neurochemical Modulatory Systems**

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Reading: Purves 5th Ed – Ch. 6 pp. 111-115, 125-131, Ch. 18 pp. 407-410, Ch. 28 pp. 637-641, and Ch. 29 pp. 663-666

# **Lecture Objectives**

These lectures will provide of an overview of the structure and function of the major monoamine neurotransmitter systems (norepinephrine, dopamine, and serotonin) as well as acetylcholine. We will review their anatomical organization, biochemistry, synaptic effects, and electrophysiology, and discuss the roles of these transmitter-defined functional systems in physiology and behavior.

# Catecholamines - involved in regulation of movement, mood, attention, and visceral function

* Dopamine
* Norepinephrine (Noradrenaline)
* Epinephrine (Adrenaline)

# Indoleamines - involved in regulation of mood, emotional behavior, and sleep

* Serotonin
* Melatonin

# Common features shared by these neurotransmitter systems:

* Small number of neurons
* Cell bodies contained in discrete brainstem nuclei
* Widespread projections – single cell can make up to 100,000 synaptic connections
* Postsynaptic effects mediated by metabotropic (G-protein coupled) receptors
* Modulatory signaling in functionally diverse areas of the CNS, serving an integrative function.
* Strongly implicated in neuropsychiatric disease - both as a potential underlying cause and/or as therapeutic target of psychoactive drugs.

### Anatomy

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### Where in the brain are the pathways that use these neurotransmitters?

### Synaptic Receptors

### Monoamine receptors are metabotropic receptors - postsynaptic effects are mediated by intracellular G-proteins (only exception - the 5-HT3 receptor is an ionotropic receptor)

Receptor activation leads to:

* changes in adenyl cyclase leading to increases or decreases in cAMP
* activation of phospholipase C
* direct effects of G-proteins subunits on voltage-gated K+ and Ca++ channels

Norepinephrine *(same receptors are used for epinephrine)*

* α1 - excitatory, increases IP3
* α2 - inhibitory, decreases adenyl cyclase, cAMP - (also presynaptic autoreceptor)
* ß1,2,3 - excitatory, increases cAMP

*Dopamine*

* D1-like (D1, D5) - increases cAMP
* D2-like (D2, D3, D4) - inhibitory, decreases cAMP, increases K+ channel activity

*Serotonin*

* 5-HT1 - inhibitory, decreases cAMP (5-HT1A - autoreceptor)
* 5-HT2 - excitatory, increases IP3, stimulates phospholipase C
* 5-HT3 - ionotropic, excitatory, similar to nicotinic receptor
* 5-HT4-7 - ??

## Electrophysiology in behaving animals

*Noradrenergic neurons* (Locus Coeruleus) –implicated in sleep & arousal, attention, learning and memory, stress, depression, anxiety, mania

* Tonically active during waking, decreased during sleep, off during REM sleep
* Increased activity during arousal, stressful stimuli (CNS homolog of peripheral sympathetic system)
* Phasic sensory-evoked responses, not pain-specific
* Conditioned responses to aversive, not rewarding, stimuli

*Serotonergic neurons* (Raphe Nuclei) *-* implicated in sleep and arousal, aggression, stereotyped motor behaviors, depression, obsessive-compulsive disorder, panic disorder

* Tonically active during waking, decreased during sleep, off during REM sleep
* Neuronal activity not increased during stress
* Increased activity during stereotyped motor behavior

*Dopaminergic neurons* (Substantia Nigra/VTA) -implicated in motor behavior, motivation, reward, reinforcement, cognition, schizophrenia, Parkinson’s Disease, drug addiction

* Neuronal firing related to motor behavior
* reward, reinforcement