BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title : Neurobiology

Neurotransmitters

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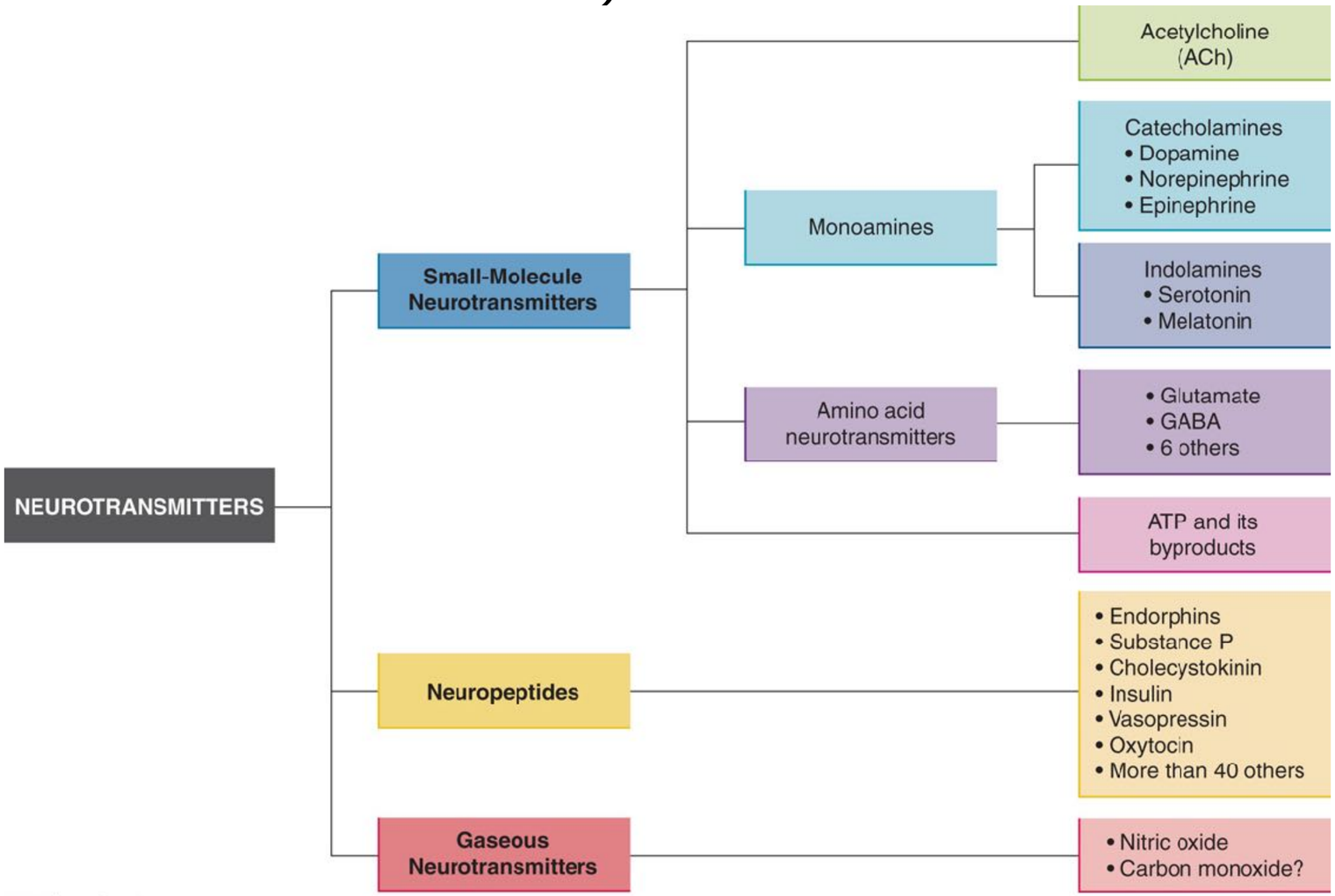
Neurotransmitters, Neuro hormones and Neuro modulators

Definition

Chemical messengers released by one neuron that affects another neuron or an effector organ

(*e.g.*, muscle, gland, blood vessel)

Major Categories of Neurotransmitters, Neuromodulators, and Neurohormones



Neurotransmitters (NT) & Neuromodulators (NM)

1. Acetylcholine (NT)
2. Monoamines (NT; NM)
   - A. Catecholamines
     - Dopamine
     - norepinephrne
     - epineprine
   - B. Indolamines
     - Serotonin
3. Amino Acids (NT; NM)
   - Glutamate
   - GABA
   - Glycine
4. Peptides (NT; NM) — Endorphins, enkephalins
5. Lipid-like substances (NT) — Anandamide, leptin
6. Nucleosides (NM) — adenosine
7. Soluble gases (atypical) — Nitric Oxide, Carbon Monoxide

Neurotransmitters

Neurotransmitters are small organic molecules that carry chemical message from axon or dendrite to another cell or nerve

Neurohormones

Neurohormones are chemical messages secreted by the Brain into the circulatory system and alter cellular function at a distance.

Neuromodulators

Neuromodulators are transmitters or neuropeptides that alter endogenous activity of the target cells.

Neurotransmitter criteria

1. **Identity:** Substance must be found in neurons (presynaptic process)
   This is called it Anatomical criteria.
2. **Synthesis** Cell has precursors and enzymes necessary for synthesis and degradation, must be present in the synapses
   This is called Biochemical criteria.
3. **Release** Must be released from terminals; upon stimulation.
   (collect substance from cleft after nerve stimulation)
   This is called Physiological criteria.
4. **Receptors** Cross desensitization between substance (drug) and suspected n.t. Blockade of n.t. action by receptor antagonists. Applicaton of suspected n.t. mimics action of nerve stimulation. This is called Pharmacological criteria
5. **Inactivation** Inactivation mechanism,enzymatic degradation, reuptake
   This is called Biochemical criteria.

Table 2. Major Neurotransmitter Receptors in the CNS

Neurotransmitter	Receptor Subtypes	G Protein-Coupled (G) vs. Ligand-Gated Ion Channel (LG)
DA DOPAMINE	D_1 D_2 D_3 D_4 D_5	G G G G G
NE/EPI	α_1 α_2 β_1 β_2 β_3	G G G G G
5-HT	5-HT_{1A} 5-HT_{1B} 5-HT_{1D} 5-HT_{2A} 5-HT_{2B} 5-HT_{2C} 5-HT_3 5-HT_4	G G G G G G LG G
ACETYLCHOLINE (**ACh** for short)	Muscarinic M_1 Muscarinic M_2 Muscarinic M_3 Muscarinic M_4 Nicotinic	G G G G LG
Glutamate	NMDA AMPA Kainate Metabotropic	LG LG LG G
Gamma-aminobutyric acid (**GABA** for short)	A B	LG G

N-methyl-D-aspartate receptor

α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

Kainic acid

Introduction to the Best Known Neurotransmitters

ACETYLCHOLINE
(**ACh** for short)

Neurons which use **ACh** to send their messages are referred to as **cholinergic neurons.**
Key locations and functions:
1) ACh is the transmitter at all **neuromuscular (nerve-to-skeletal muscle) junctions & stimulate muscle contraction**
2) is the transmitter of the **parasympathetic half of the autonomic nervous system.**
3) is a transmitter in many **brain areas (cortex, basal ganglia, hypothalamus** to name a few) and is necessary for normal **memory and cognition** and **motor control.**
The action of ACh released at a synapse is ended via breakdown of ACh by the enzyme **acetylcholinesterase**.

NOREPINEPHRINE
(**NE** for short)
(aka noradrenaline)

Key locations and functions:
1) NE is the primary transmitter carrying messages from the **sympathetic half of the autonomic nervous system** to body organs and glands.
2) is a transmitter in many **brain areas (reticular activating system, hypothalamus appetite areas, limbic system)** and is involved in **nervous system arousal, hunger, and mood control.**
The action of NE at a synapse is brought to an end primarily via **reuptake.** NE may also be broken down by enzymes like **MAO.**
(think "NE and hams" for hunger,arousal, mood, sympathetic)

DOPAMINE
(**DA** for short)

DA is the **precursor** that is turned into NE, so is closely related to NE and often affected by the same drugs. **DA and NE** are members of the transmitter family known as the **CATECHOLAMINES**. In some neurons the synthesis of transmitter stops at the DA step and DA serves as the neurotransmitter.
Key Locations and Functions:
DA is an important transmitter in **several brain systems:**
1) **Extrapyramidal motor system** (posture and movement control)
2) **Mesolimbic/mesocortical system** (midbrain connections to limbic system and cortex) (emotion and cognitive functions)
3) **Hypothalamus-pituitary system** (menstrual and other hormone regulation)
The action of DA at a synapse is brought to an end primarily via **reuptake.**
(think "DAMMM" for motor, mood/mesolimbic, menstrual/hormonal)

SEROTONIN
(aka **5-hydroxytryptamine**)
(**5HT** for short)

Serotonin is a chemical cousin of the "catecholamines" discussed above. **5HT, NE and DA** are sometimes grouped under the heading **MONOAMINES or BIOGENIC AMINES**, and because of their similarities they are influenced by some of the same drugs.
5HT is best known as a transmitter in **several brain areas**:
1) **sleep regions**
2) **limbic system mood control regions**
3) **pain suppression system**
The action of 5HT at a synapse is brought to an end primarily via **reuptake.** 5HT may also be broken down by the enzyme **MAO.**
(think "5HT and SLeeP" for sleep, limbic mood control and pain suppression)

Glutamate

Glutamate, an amino acid, is the single most **widely distributed excitatory neurotransmitter** in the CNS.

Gamma-aminobutyric acid (**GABA** for short)

GABA, another amino acid neurotransmitter widely distributed in the CNS, is the **most important inhibitory transmitter**.

Neurotransmitters

- **Properties of neurotransmitters:**

1) synthesized in the presynaptic neuron

2) Localized to vesicles in the presynaptic neuron

3) Released from the presynaptic neuron under physiological conditions

4) Rabidly removed from the synaptic cleft by uptake or degradation

5) Presence of receptor on the post-synaptic neuron.

6) Binding to the receptor elicits a biological response

Neurotransmitters found in the nervous system

EXCITATORY

Acetylcholine

Aspartate

Dopamine

Histamine

Norepinephrine

Epinephrine

Glutamate

Serotonin

INHIBITORY

GABA

Glycine

Chemical Events at the Synapse

- Major categories of neurotransmitters include the following:
  - Amino acids — glutamate, GABA,
  - Acetylcholine
  - Monoamines – serotonin, dopamine, norephinephrine, epinephrine
  - Purines --adenosine
  - Gases –nitric oxide (not laughing gas!)

Chemical Events at the Synapse

- Metabotropic effects utilize a number of different neurotransmitters and are often called neuromodulators because they do not directly excite or inhibit the postsynaptic cell.
- Instead, neuromodulators:
  - increase or decrease the release of other neurotransmitters
  - alter the response of postsynaptic cells to various inputs.

Drugs and the Synapse

- The study of the influence of various kinds of drugs has provided us with knowledge about many aspects of neural communication at the synaptic level.
- Drugs either facilitate or inhibit activity at the synapse.
  - Antagonistic drugs block the effects of neurotransmitters (e.g., novacaine, caffeine).
  - Agonist drugs mimic or increase the effects of neurotransmitters (e.g., receptors in the brain respond to heroin, LSD and cocaine)
- Drugs alter various stages of synaptic processing.