Introduction to Bioelectricity

Week 2: Chemical basis of electrical signals
Lecture 2.5: Neurotransmitters and pathology

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Week 2: Chemical basis of electrical signals

- Lecture 2.5: Neurotransmitters and pathology

### Table 6.1

Functional Features of the Major Neurotransmitters *(Part 1)*

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Postsynaptic effect</th>
<th>Precursor(s)</th>
<th>Rate-limiting step in synthesis</th>
<th>Removal mechanism</th>
<th>Type of vesicle</th>
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<tbody>
<tr>
<td>ACh</td>
<td>Excitatory</td>
<td>Choline + acetyl CoA</td>
<td>CAT</td>
<td>AChEase</td>
<td>Small, clear</td>
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<td>Glutamate</td>
<td>Excitatory</td>
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<td>Glutaminase</td>
<td>Transporters</td>
<td>Small, clear</td>
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<td>GAD</td>
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<td>Glycine</td>
<td>Inhibitory</td>
<td>Serine</td>
<td>Phosphoserine</td>
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</tr>
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<td>Catecholamines</td>
<td>Excitatory</td>
<td>Tyrosine</td>
<td>Tyrosine hydroxylase</td>
<td>Transporters, MAO, COMT</td>
<td>Small dense-core, or large irregular dense-core</td>
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*(epinephrine, norepinephrine, dopamine)*
Lecture 2.5: Neurotransmitters

- Small molecule neurotransmitters

**Small-Molecule Neurotransmitters**

**Amino Acids**
- Glutamate
- Aspartate
- GABA
- Glycine

**Small-Molecule Neurotransmitters**

**Biogenic Amines**
- Dopamine
- Norepinephrine
- Epinephrine

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Lecture 2.5: Neurotransmitters

- **Neurotransmitter effects**

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<td>Transporters, MAO,COMT</td>
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<td>norepinephrine, dopamine)</td>
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*The most common postsynaptic effect is indicated; the same transmitter can elicit postsynaptic excitation or inhibition depending on the nature of the ion channels affected by transmitter binding (see Chapter 7).*
Lecture 2.5: Neurotransmitters

- Large molecule neurotransmitters

**PEPTIDE NEUROTRANSMITTERS**

Example: Methionine enkephalin (Tyr–Gly–Gly–Phe–Met)

![Methionine Enkephalin Structure](image-url)
Lecture 2.5: Neurotransmitters

- Neurotransmitter effects

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<td>Serotonin (5-HT)</td>
<td>Excitatory</td>
<td>Tryptophan</td>
<td>Tryptophan hydroxylase</td>
<td>Transporters, MAO</td>
<td>Large, dense-core</td>
</tr>
<tr>
<td>Histamine</td>
<td>Excitatory</td>
<td>Histidine</td>
<td>Histidine decarboxylase</td>
<td>Transporters</td>
<td>Large, dense-core</td>
</tr>
<tr>
<td>ATP</td>
<td>Excitatory</td>
<td>ADP</td>
<td>Mitochondrial oxidative phosphorylation; glycolysis</td>
<td>Hydrolysis to AMP and adenosine</td>
<td>Small, clear</td>
</tr>
<tr>
<td>Neuropeptides</td>
<td>Excitatory and inhibitory</td>
<td>Amino acids (protein synthesis)</td>
<td>Synthesis and transport</td>
<td>Proteases</td>
<td>Large, dense-core</td>
</tr>
<tr>
<td>Endocannabinoids</td>
<td>Inhibits inhibition</td>
<td>Membrane lipids</td>
<td>Enzymatic modification of lipids</td>
<td>Hydrolasis by FAAH</td>
<td>None</td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>Excitatory and inhibitory</td>
<td>Arginine</td>
<td>Nitric oxide synthase</td>
<td>Spontaneous oxidation</td>
<td>None</td>
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Lecture 2.5: Neurotransmitters

• **Dopamine**
  • Excitatory
  • Small in number
  • Outsized influence
  • Plays a role in:
    - Ventral Tegmental Area
      » motivation
      » reinforcement/reward
    - Substantia Nigra
      » motor control

• **Clinical:**
  - Parkinson’s and L-DOPA
  - anti-psychotics
  - cocaine
Lecture 2.5: Neurotransmitters

• Norepinephrine
  • Excitatory
  • Plays a role in:
    – Locus Coeruleus
      » attention
    – Sympathetic Nervous System
      » fight or flight
  • Clinical:
    – attention deficit hyperactivity disorder, amphetamines
    – depression and SNRI
    – schizophrenia
    – methamphetamine
Lecture 2.5: Neurotransmitters

- Epinephrine
  - Excitatory
  - Third type of catecholamine
  - Plays a role as:
    - neurotransmitter & hormone
    - fight or flight response
    - raises resting heart rate
    - increases respiratory rate
    - vasoconstriction
    - muscle contraction

- Clinical
  - cardiac arrest
Lecture 2.5: Neurotransmitters

- **Histamine**
  - Excitatory
  - Acts in the hypothalamus
  - Works through metabotropic receptors
  - Plays a role in:
    - immune response
      - capillary permeability (white blood cells)
    - inflammatory response
    - allergic reactions
- **Clinical**
  - regulating sleep
  - stomach acid
  - addiction
Lecture 2.5: Neurotransmitters

• Serotonin
  • Excitatory
  • Derived from tryptophan
  • Acts in the pons and upper brainstem
  • Mostly metabotropic receptors
  • Plays a role in:
    – Sleep/wakefullness
    – Mood
    – Appetite

• Clinical
  – depression and SSRIs
  – ecstasy, amphetamines, and cocaine
Lecture 2.5: Neurotransmitters

- **Acetylcholine**
  - Excitatory
  - Broken down by AChE
  - Post-synaptic receptors are often nicotinic
  - Plays a role in:
    - neuromuscular junction
      - somatic
      - autonomic
  - Clinical
    - tobacco leads to relaxation and sense of euphoria
    - myasthenia gravis targets ACh receptors
    - sarin gas inhibits AChE
Lecture 2.5: Neurotransmitters

• Other small molecule NTs
  • Glutamate
    – primary excitatory NT, half of all synapses
    – ionotropic
  • GABA and glycine
    – primary inhibitory NT
    – excitatory in the developing brain
    – Epilepsy
Lecture 2.5: Neurotransmitters

- Other drugs affecting neurotransmitters
  - Opioids
    - modulate pain/pleasure pathways
    - dopamine and opioid (peptide) receptors
  - Cannabis
    - hypothalamus
    - cannabinoid receptors
      » metabotropic
      » most common g-protein receptors
    - Clinical use
      » nausea and vomiting
      » IOP