Bear: Neuroscience: Exploring the Brain 3e

- Chapter 05: Synaptic Transmission

Introduction

- Synaptic Transmission
  - The process of information transfer at a synapse
  - Plays role in all the operations of the nervous system
  - 1897: Charles Sherrington- "synapse"
  - Chemical and electrical synapses
    - 1921- Otto Loewi

Types of Synapses

- Direction of Information Flow
  - In one direction: Neuron to target cell
  - First neuron = Presynaptic neuron
  - Target cell = Postsynaptic neuron

Types of Synapses

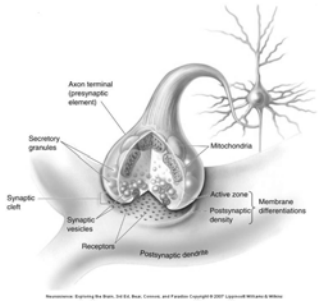
- Electrical Synapses
  - Gap junction
    - Channel
      - Connexon- formed by six connexins
  - Cells are said to be "electrically coupled"
    - Flow of ions from cytoplasm to cytoplasm

Types of Synapses

- Electrical Synapses (Cont'd)
  - Very fast transmission
    - Postsynaptic potentials (PSPs)
  - Synaptic integration: Several PSPs occurring simultaneously to excite a neuron (i.e. causes AP)

Types of Synapses

- Chemical Synapses

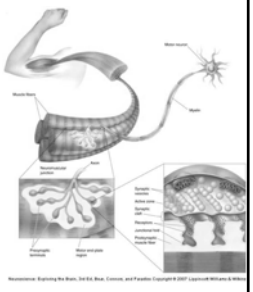


Types of Synapses

- CNS Synapses (Examples)
  - Axodendritic: Axon to dendrite
  - Axosomatic: Axon to cell body
  - Axoaxonic: Axon to axon
  - Dendrodendritic: Dendrite to dendrite
  - Gray's Type I: Asymmetrical, excitatory
  - Gray's Type II: Symmetrical, inhibitory

Types of Synapses

- The Neuromuscular Junction (NMJ)
  - Studies of NMJ established principles of synaptic transmission
  - High clinical relevance



Principles of Chemical Synaptic Transmission

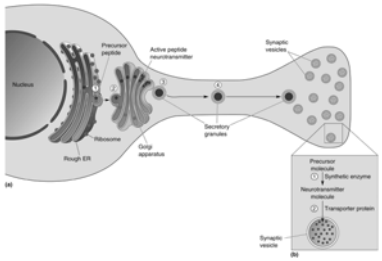
- Basic Steps
  - Neurotransmitter synthesis
  - Load neurotransmitter into synaptic vesicles
  - Vesicles fuse to presynaptic terminal
  - Neurotransmitter spills into synaptic cleft
  - Binds to postsynaptic receptors
  - Biochemical/Electrical response elicited in postsynaptic cell
  - Removal of neurotransmitter from synaptic cleft

Principles of Chemical Synaptic Transmission

- Neurotransmitters
  - Amino acids: Small organic molecules
    - e.g., Glutamate, Glycine, GABA
  - Amines: Small organic molecules
    - e.g., Dopamine, Acetylcholine, Histamine
  - Peptides: Short amino acid chains (i.e. proteins) stored in and released from secretory granules
    - e.g., Dynorphin, Enkephalins

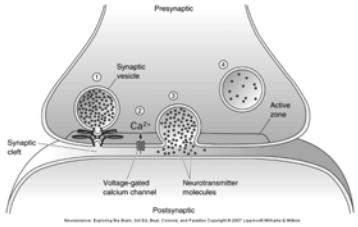
Principles of Chemical Synaptic Transmission

- Neurotransmitter Synthesis and Storage
  - Amines, amino acids, peptides



Principles of Chemical Synaptic Transmission

- Neurotransmitter Release
  - Exocytosis: Process by which vesicles release their contents



Principles of Chemical Synaptic Transmission

- Neurotransmitter Release (Cont'd)
  - Mechanisms
    - Process of exocytosis stimulated by release of intracellular calcium, $[Ca^{2+}]i$
    - Proteins alter conformation - activated
    - Vesicle membrane incorporated into presynaptic membrane
    - Neurotransmitter released
    - Vesicle membrane recovered by endocytosis

Principles of Chemical Synaptic Transmission

- Neurotransmitter Receptors and Effectors
  - Ionotropic: Transmitter-gated ion channels
  - Metabotropic: G-protein-coupled receptor
- EPSP:Transient postsynaptic membrane depolarization by presynaptic release of neurotransmitter
- IPSP: Transient hyperpolarization of postsynaptic membrane potential caused by presynaptic release of neurotransmitter

Principles of Chemical Synaptic Transmission

- G-Protein-Coupled Receptors
  - Steps of neurotransmitter action
    - Bind to receptor proteins
    - Activate small proteins
    - Activate "effector" proteins
  - Second messengers
  - Metabotropic receptors: Metabolic effects
  - Same neurotransmitter: Different postsynaptic actions
  - ACh Effect: Heart, skeletal muscle

Principles of Chemical Synaptic Transmission

- Autoreceptors
  - Presynaptic receptors sensitive to neurotransmitter released by presynaptic terminal
  - Act as safety valve to reduce release when levels are high in synaptic cleft (autoregulation)

Principles of Chemical Synaptic Transmission

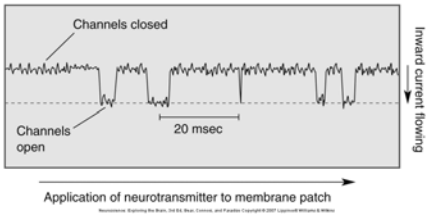
- Neurotransmitter Recovery and Degradation
  - Diffusion: Away from the synapse
  - Reuptake: Neurotransmitter re-enters presynaptic axon terminal
  - Enzymatic destruction inside terminal cytosol or synaptic cleft
  - Desensitization: e.g., AChE cleaves Ach to inactive state

Principles of Chemical Synaptic Transmission

- Neuropharmacology
  - Effect of drugs on nervous system tissue
  - Receptor antagonists: Inhibitors of neurotransmitter receptors
    - Curare
  - Receptor agonists: Mimic actions of naturally occurring neurotransmitters
    - Nicotine
  - Defective neurotransmission: Root cause of neurological and psychiatric disorders

Principles of Synaptic Integration

- Synaptic Integration
  - Process by which multiple synaptic potentials combine within one postsynaptic neuron



Principles of Synaptic Integration

- Quantal Analysis of EPSPs
  - Synaptic vesicles: Elementary units of synaptic transmission
  - Quantum: An indivisible unit
  - Miniature postsynaptic potential ("mini")
  - Quantal analysis: Used to determine number of vesicles that release during neurotransmission
  - Neuromuscular junction: About 200 synaptic vesicles, EPSP of 40mV or more
  - CNS synapse: Single vesicle, EPSP of few tenths of a millivolt

Principles of Synaptic Integration

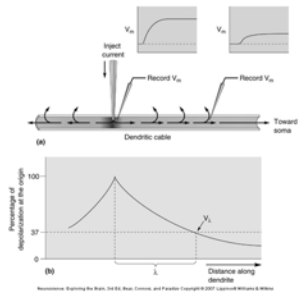
- EPSP Summation
  - Allows for neurons to perform sophisticated computations
  - Integration: EPSPs added together to produce significant postsynaptic depolarization
  - Spatial: EPSP generated simultaneously in different spaces
  - Temporal: EPSP generated at same synapse in rapid succession

Principles of Synaptic Integration

- The Contribution of Dendritic Properties to Synaptic Integration
  - Dendrite as a straight cable
  - Membrane depolarization falls off exponentially with increasing distance
    - $V_x = V_o / e^{x/\lambda}$
  - Dendritic length constant (λ)
  - In reality, dendrites are very elaborate structures that contribute to more complex integrative properties

Principles of Synaptic Integration

- The Contribution of Dendritic Properties to Synaptic Integration



Principles of Synaptic Integration

- Excitable Dendrites
  - Dendrites of neurons of voltage-gated sodium, calcium, and potassium channels
    - Can act as amplifiers (vs. passive)
  - Dendritic sodium channels: May carry electrical signals in opposite direction, from soma outward along dendrites

Principles of Synaptic Integration

- Inhibition
  - Action of synapses to take membrane potential away from action potential threshold
  - Exert powerful control over neuron output

Principles of Synaptic Integration

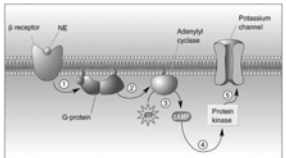
- IPSPs and Shunting Inhibition
  - Excitatory vs. inhibitory synapses: Bind different neurotransmitters, allow different ions to pass through channels
  - Membrane potential less negative than -65mV = hyperpolarizing IPSP
- Shunting Inhibition: Inhibiting current flow from soma to axon hillock

Principles of Synaptic Integration

- The Geometry of Excitatory and Inhibitory Synapses
  - Excitatory synapses
    - Gray's type I morphology
    - Clustered on soma and near axon hillock
  - Inhibitory synapses
    - Gray's type II morphology

Principles of Synaptic Integration

- Modulation
  - Synaptic transmission that modifies effectiveness of EPSPs generated by other synapses with transmitter-gated ion channels
  - Example: Activating NE β receptor



Concluding Remarks

- Chemical synaptic transmission
  - Rich diversity allows for complex behavior
  - Provides explanations for drug effects
  - Defective transmission is the basis for many neurological and psychiatric disorders
  - Key to understanding the neural basis of learning and memory

- End of Presentation