Ch. 45 Continues (Have You Read Ch. 45 yet?)

- Central Nervous System Synapses
  - Synaptic functions of neurons
    - Information transmission via nerve impulses
    - Impulse may be blocked in its transmission one neuron to the next
    - Impulse may be changed from a single impulse into repetitive impulses
    - Impulse may be integrated with impulses from other neurons to cause highly intricate patterns of impulses
- Types of synapses – chemical and electrical
  - Chemical synapses
    - Almost all synapses are chemical
    - Neurotransmitter or transmitter substances
    - Acts on receptor proteins to excite the neuron or inhibit it or modify its sensitivity
    - 40 transmitter substances such as acetylcholine, norepinephrine, histamine, GABA, glycine, serotonin, and glutamate
  - Electrical synapses
    - Direct open fluid channels that conduct electricity
    - Protein tubular structures called gap junctions that allow free movement of ions
  - One-way conduction at chemical synapses
    - Transmit the signals in one direction: presynaptic neuron to postsynaptic neuron
    - Principle of one-way conduction

- Physiologic Anatomy of the Synapse
  - Presynaptic terminals
    - Some are excitatory: they secrete a transmitter substance that excites the postsynaptic neuron
    - Many others are inhibitory: they secrete a transmitter substance that inhibits the postsynaptic neuron
    - Fig. 45-6
    - Synaptic cleft
    - Transmitter vesicles: contain transmitter substance that is released into the synaptic cleft to excite or inhibit the postsynaptic neuron
    - Excites with excitatory receptors at the membrane or inhibits with inhibitory receptors
  - Action potentials cause transmitter release from the presynaptic terminals: role of calcium ions
    - Presynaptic membrane contains voltage-gated calcium channels
    - When an action potential depolarize the terminal, the channels open and allow large numbers of calcium ions move into neurons.
    - Calcium ions binds with special protein molecules at release site
    - This binding causes transmitter vesicle to fuse with the release site and open to exterior by exocytosis

As many as 10,000 to 200,000 presynaptic terminals!!!

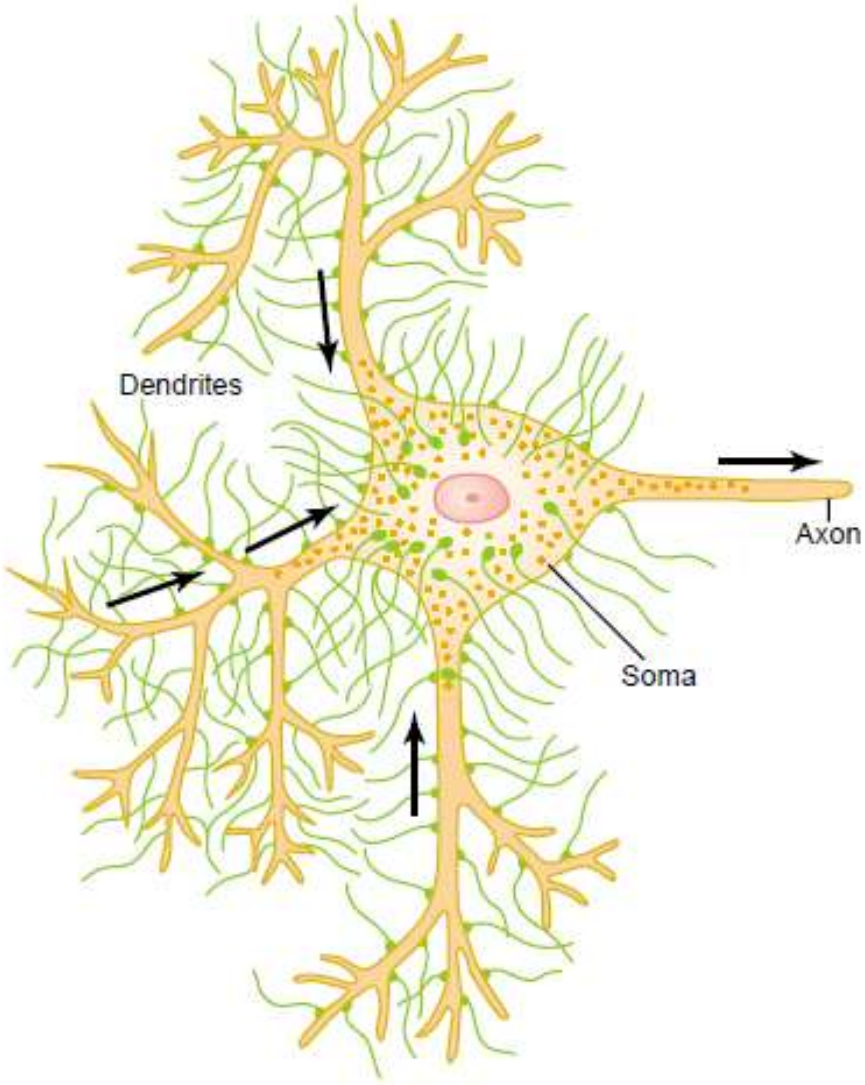


Figure 45–5

Typical anterior motor neuron, showing presynaptic terminals on the neuronal soma and dendrites. Note also the single axon.

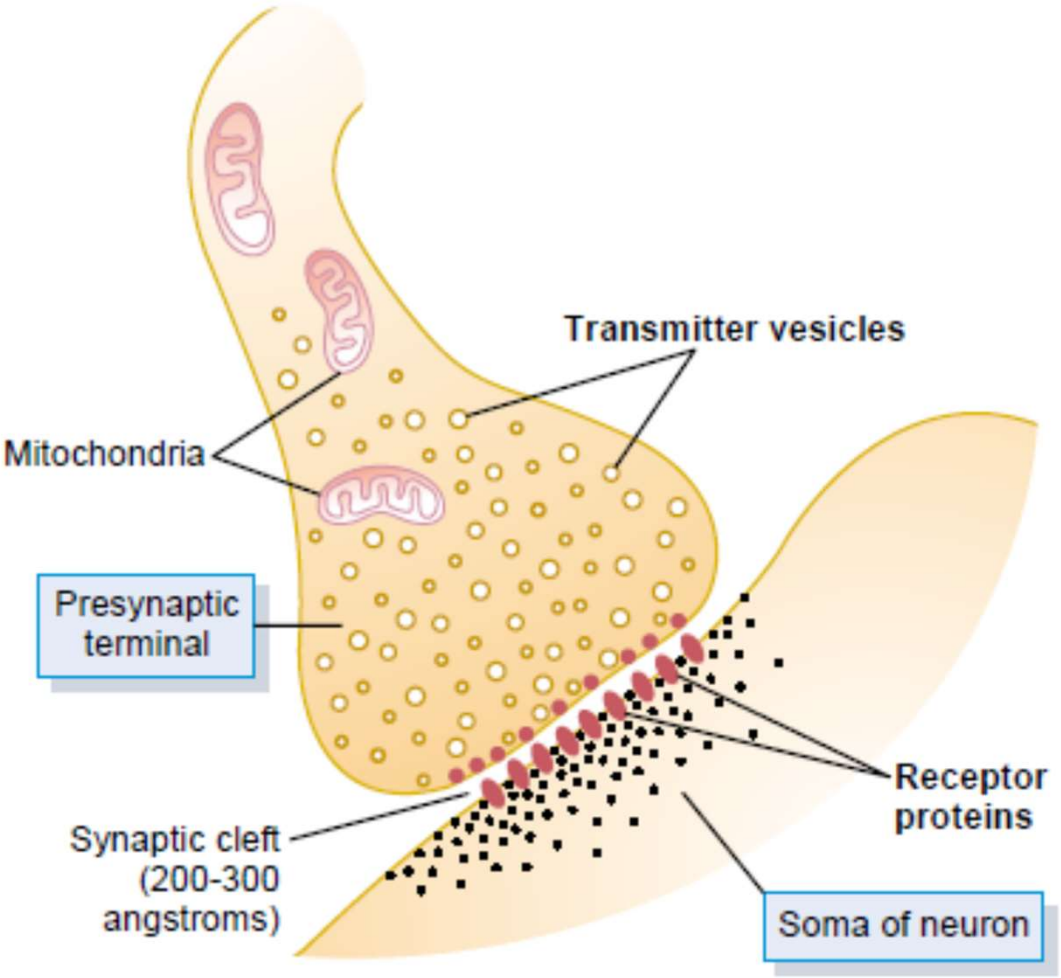
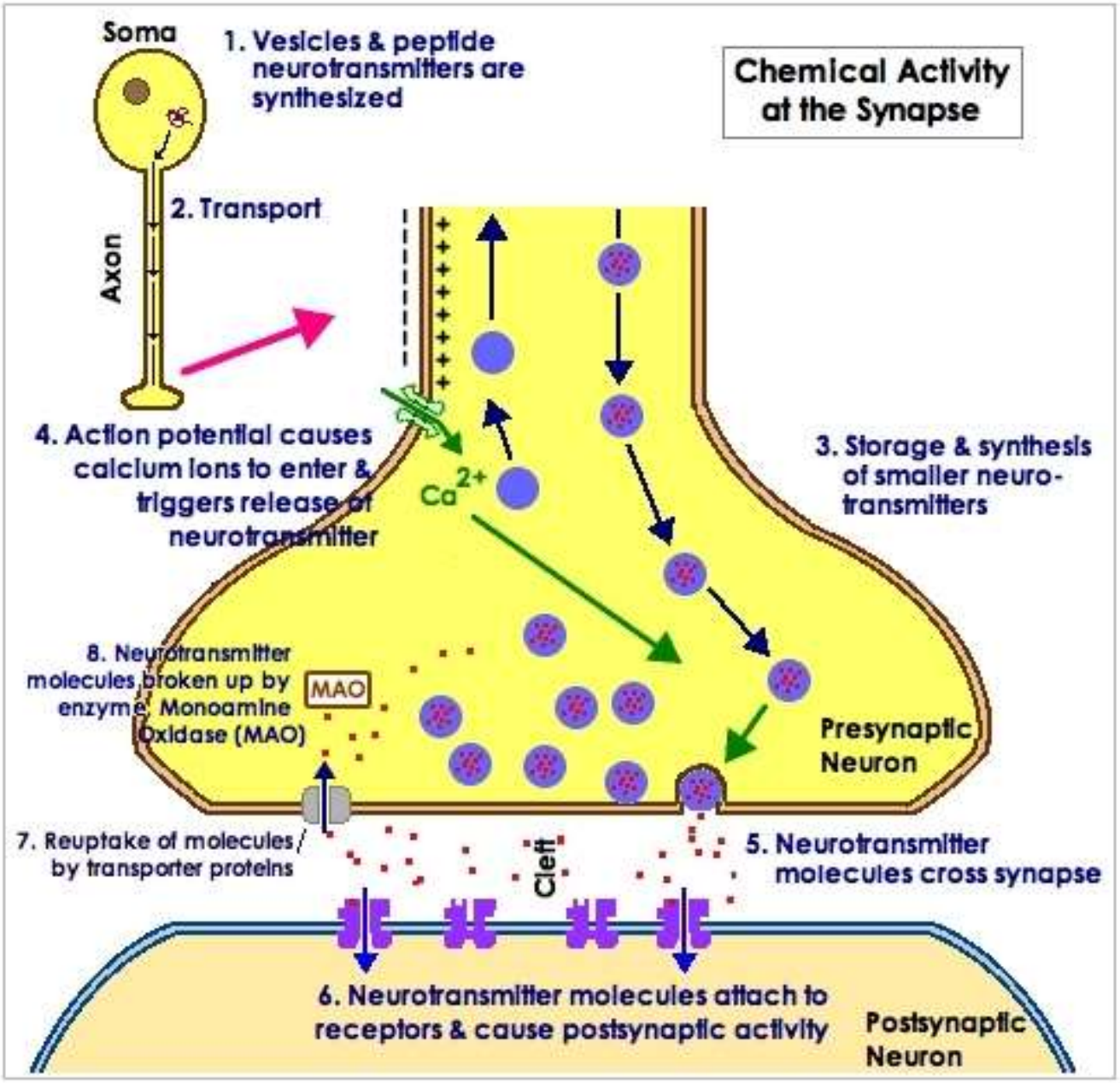


Figure 45–6

Physiologic anatomy of the synapse.


Chemical Activity at the Synapse
Soma
1. Vesicles & peptide neurotransmitters are synthesized
Axon
2. Transport
4. Action potential causes calcium ions to enter & triggers release of neurotransmitter
Ca^{2+}
3. Storage & synthesis of smaller neuro-transmitters
8. Neurotransmitter molecules broken up by enzyme, Monoamine Oxidase (MAO)
MAO
Presynaptic Neuron
7. Reuptake of molecules by transporter proteins
Cleft
5. Neurotransmitter molecules cross synapse
6. Neurotransmitter molecules attach to receptors & cause postsynaptic activity
Postsynaptic Neuron

- Action of the transmitter substance on the postsynaptic neuron – function of receptor proteins
  - **Receptor proteins** in Fig. 45-6
  - Two importance components

    (1) binding component: protrudes outward from the membrane into the cleft, binds with neurotransmitter

    (2) Ionophore* component: passes all the way through the membrane to the interior of the postsynaptic neuron. Two types (i) **ion channels** (ii) **second messenger**

* An ionophore is a lipid-soluble molecule usually synthesized by microorganisms to transport ions across the lipid bilayer of the cell membrane.

  - **(i) Ion Channels**
    - Allows passage of specified types of ions
    - Two types (i) cation channels that most often allow sodium ions to pass, but allow potassium and/or calcium ions (ii) anion channels that allow mainly chloride ions
    - Cation channels: lines with negative charges. Attract positively charged sodium ions and repel chloride ions and other anions
    - Anion channels: chloride ions pass whereas sodium, potassium and calcium cations are blocked
    - A transmitter that opens cation channels called excitatory transmitter since opening cation channels allow sodium ions enter which excites postsynaptic neuron
    - Inhibitory transmitters open anion channels, allow negative ions enter which inhibits the neuron
    - Channels open and close in millisecond.
    - Opening and closing of ion channels provide a means of rapid control of postsynaptic neurons

- **(ii) Second messenger** system in the postsynaptic neuron
  - Prolonged neuronal action is achieved by second messenger chemical system
  - Responsible for prolonged changes in neurons for seconds to months such as memory
  - Uses special proteins called G-proteins
  - Fig. 45-7
  - Four changes (*read textbook for more details*)

  (1) Opening specific ion channels
  (2) Activation of enzyme system in the neuron's membrane
  (3) Activation of intracellular enzyme system
  (4) Activation of gene transcription

- Excitatory and inhibitory receptors in the postsynaptic membrane
  - Excitation is caused by

  (1) opening of sodium channels to allow positively charged ions flow into the interior of the postsynaptic cell. This raises the membrane potential in the positive direction
  (2) Depressed conduction through chloride or potassium channels or both
  (3) Various changes in the internal metabolism of the cell
  - Inhibition is caused by

  (1) Opening of chloride ion channels
  (2) Increase in the conductance of potassium ions through the cell receptor
  (3) Activation of receptor enzymes that inhibit cellular metabolic functions

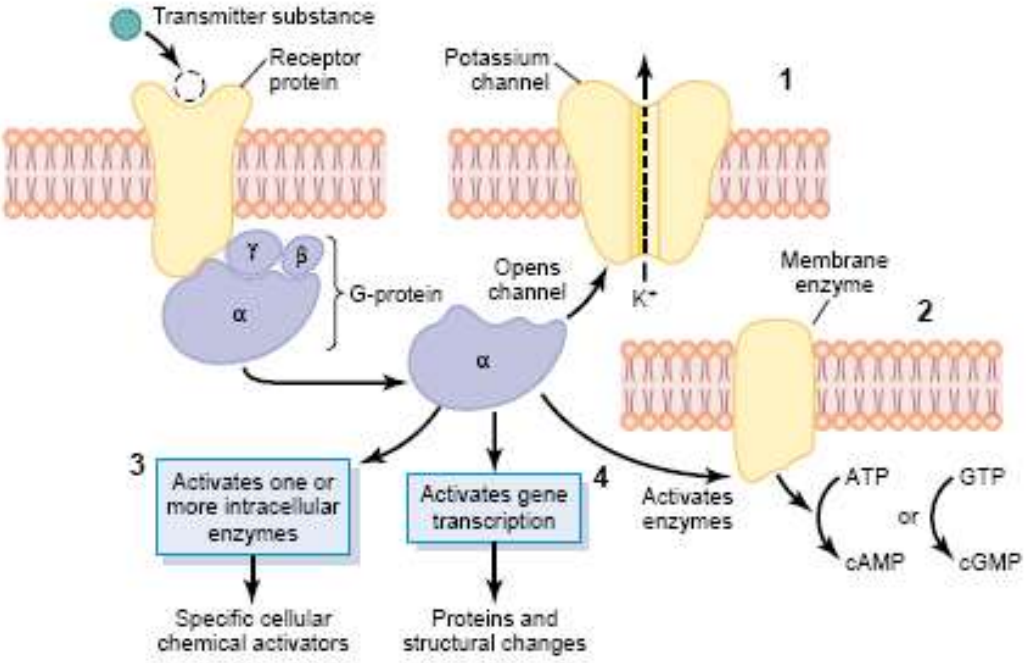
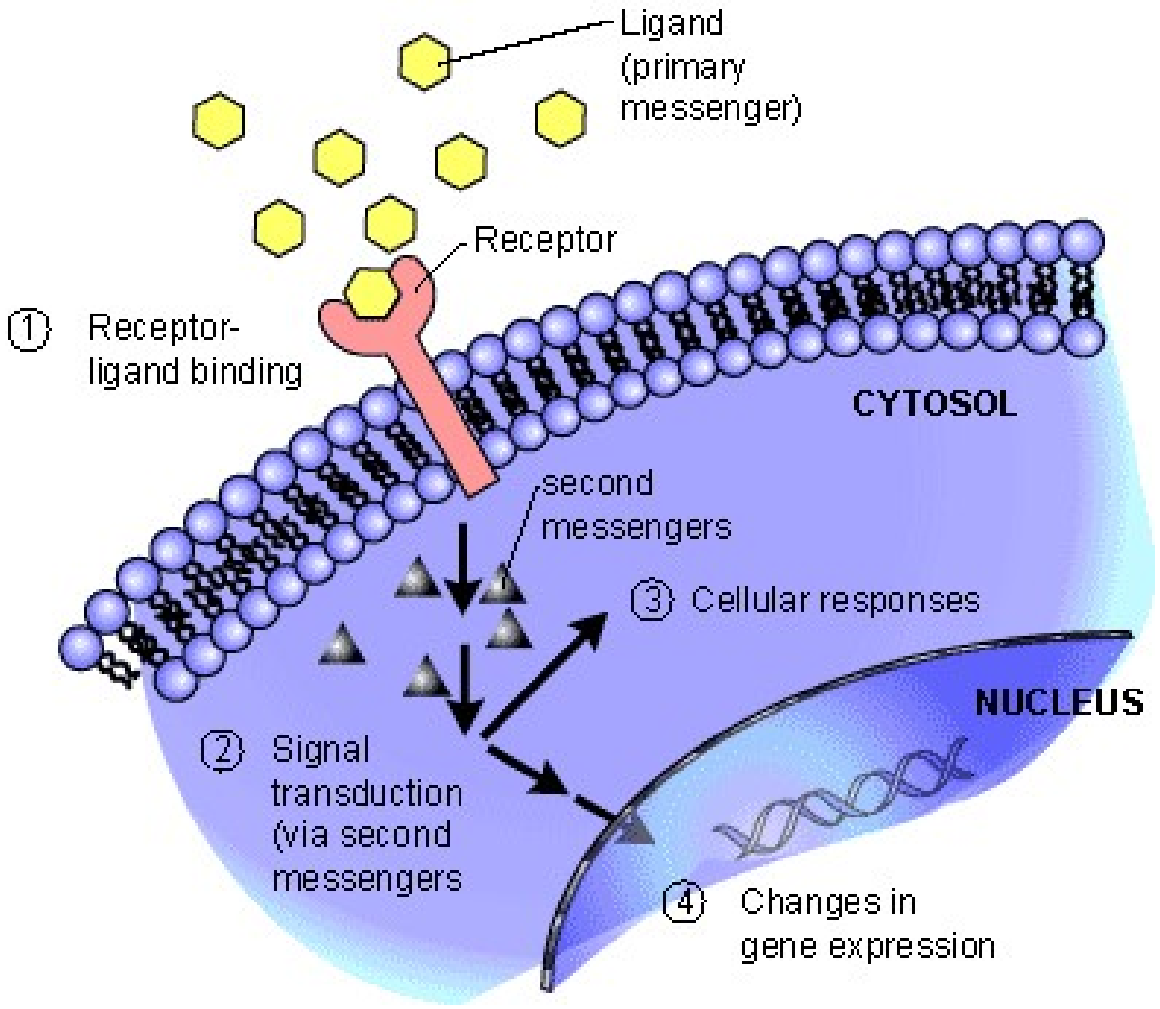


Figure 45–7

"Second messenger" system by which a transmitter substance from an initial neuron can activate a second neuron by first releasing a "G-protein" into the second neuron's cytoplasm. Four subsequent possible effects of the G-protein are shown, including 1, opening an ion channel in the membrane of the second neuron; 2, activating an enzyme system in the neuron's membrane; 3, activating an intracellular enzyme system; and/or 4, causing gene transcription in the second neuron.


Ligand
(primary
messenger)
Receptor
① Receptor-
ligand binding
CYTOSOL
second
messengers
③ Cellular responses
NUCLEUS
② Signal
transduction
(via second
messengers
④ Changes in
gene expression

W사1

– Chemical substances that function as synaptic transmitters
  - 50 chemical substances
  - Tables 45-1 and 45-2
  - Two groups

1. Small-molecule, rapidly acting transmitters – cause most of the acute responses of the nervous system

2. Neuropeptides of larger molecular size – cause more prolonged actions

(1) Small-molecule, rapidly acting transmitters

1. Acetylcholine or Ach (mostly excitatory)
- First neurotransmitter to be identified (by Henry Hallett Dale who got the Nobel Prize in 1936)
- At the neuromuscular junction, activate muscles
- Also works on autonomic nervous system

2. Norepinephrine (excitatory)
- Neurotransmitter in CNS and sympathetic nervous system
- As a stress hormone, it increases heart rate (rate of contractions) released from sympathetic neurons.
- Also increases systolic and diastolic pressure
- Clinically used for attention-deficit, depression, and vaso-constriction.

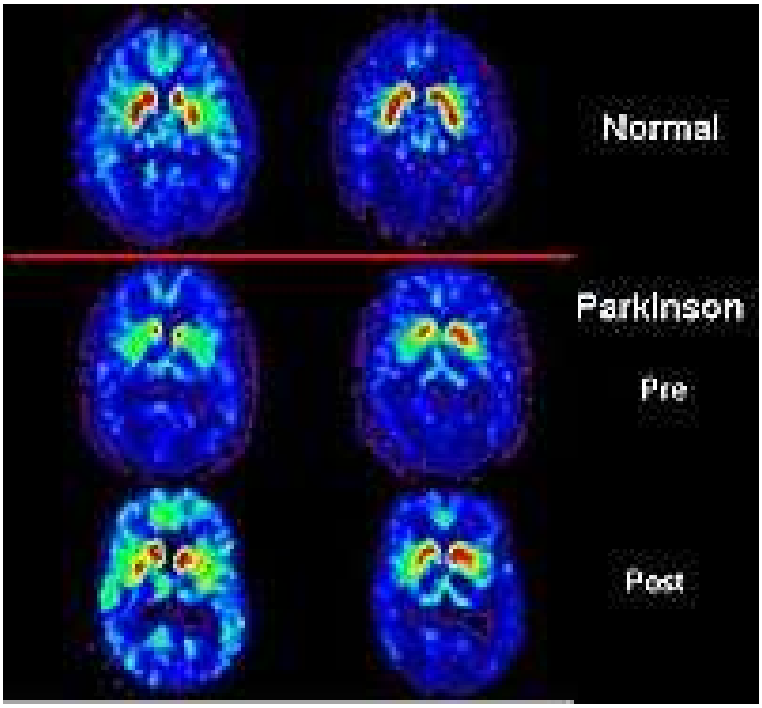
3. Dopamine (inhibitory in general, but also excitatory depending on where and which receptor)
- Problems if it is too low or too high.
- Released from substantia nigra and hypothalamus.
- On sympathetic nervous system, it increases heart rate and blood pressure
- Related Parkinson's disease.
- Again Nobel prize to the founder, Arvid Carlsson in 2000.

슬라이드 10

W사1 Windows 사용자, 2024-03-21

Parkinson's Disease

The term Parkinsonism is used for symptoms of tremor, stiffness, and slowing of movement caused by loss of dopamine.



18F PET scan shows decreased dopamine activity in the basal ganglia, a pattern which aids in diagnosing Parkinson's disease.

Table 45–1

Small-Molecule, Rapidly Acting Transmitters

Class I
- Acetylcholine

Class II: The Amines
- Norepinephrine
- Epinephrine
- Dopamine
- Serotonin
- Histamine

Class III: Amino Acids
- Gamma-aminobutyric acid (GABA)
- Glycine
- Glutamate
- Aspartate

Class IV
- Nitric oxide (NO)

What is the difference between epinephrine and norepinephrine?
Epinephrine and norepinephrine are very similar neurotransmitters and hormones. While epinephrine has slightly more of an effect on your heart, norepinephrine has more of an effect on your blood vessels.

히스타민은 외부자극에 대하여 신체가 빠른 방어 행위를 하기 위하여 분비하는 유기 물질 중의 하나이다. 즉, 상처가 난 곳이 붉게 부어오르며 통증을 느끼게되는 염증반응이 일어나게 하는 물질
Histamine stimulates four subtypes of post-synaptic receptors.
Histamine is also known as a neuromodulator, since it regulates the release of other neurotransmitters, like acetylcholine, norepinephrine, and serotonin.

Aspartate is the most abundant excitatory neurotransmitter in the CNS.
Aspartate is an excitatory neurotransmitter, which increases the likelihood of depolarization in the postsynaptic membrane
Aspartate opens an ion channel and is inactivated by reabsorption into the presynaptic membrane.

Table 45–2

Neuropeptide, Slowly Acting Transmitters or Growth Factors

Hypothalamic-releasing hormones
Thyrotropin-releasing hormone
Luteinizing hormone–releasing hormone
Somatostatin (growth hormone inhibitory factor)
Pituitary peptides
Adrenocorticotropic hormone (ACTH)
β-Endorphin
α-Melanocyte-stimulating hormone
Prolactin
Luteinizing hormone
Thyrotropin
Growth hormone
Vasopressin
Oxytocin
Peptides that act on gut and brain
Leucine enkephalin
Methionine enkephalin
Substance P
Gastrin
Cholecystokinin
Vasoactive intestinal polypeptide (VIP)
Nerve growth factor
Brain-derived neurotropic factor
Neurotensin
Insulin
Glucagon
From other tissues
Angiotensin II
Bradykinin
Carnosine
Sleep peptides
Calcitonin

4. Glycine (inhibitory in CNS)
- One of the 20 amino acids commonly found in proteins.
- Causes IPSP

5. GABA (inhibitory)
- Gamma-aminobutyric acid (GABA)
- Chief inhibitory neuro-transmitter in CNS and in retina.

6. Glutamine (excitatory)
- One of the 20 amino acids
- Aids for recovery after surgery (healing aids)

7. Serotonin (inhibitory)
- Found in many mushrooms, plants, fruits, and veges.
- Regulator of anger, aggression, body temperature, mood, sleep, sexuality, and appetite.
- If low, gets aggressive, angry, depressed.

8. Nitric Oxide (excitatory)
- An important gas molecule for signaling in the mammals. 혈관확장기능.
- Also toxic air pollutant produced by automobile engines and power plants.

(2) Neuropeptide

(1) Prolonged closure of calcium pores
(2) Prolonged changes in the metabolic machinery of cells
(3) Prolonged changes in activation or deactivation of specific genes
(4) Prolonged alterations in numbers of excitatory and inhibitory receptors

- Electrical events during neuronal excitation
  - Resting membrane potential of the neuronal soma is about -65 mV, not -90mV
  - It allows the membrane more excitable and less excitable
  - Concentration differences of ions across the neuronal soma membrane
  - Fig. 45-8
  - Nernst Potential for Na+
  - Effect of synaptic excitation on the postsynaptic membrane – the excitatory postsynaptic potential (EPSP)
  - Fig. 45-9 B
- Electrical events in neuronal inhibition
  - Effect of inhibitory synapses on the postsynaptic membrane – the inhibitory postsynaptic potential (IPSP)
  - Inhibitory synapses open mainly chloride channels
  - Nernst Potential for Cl-
  - Fig. 45-9 C
  - Presynaptic inhibition: caused by discharge of inhibitory synapses. This inhibitory transmitter substances released is GABA (gamma-aminobutyric acid) which has the specific effect of opening anion channels. The negative charge ions cancel excitatory effect of positively charged sodium ions

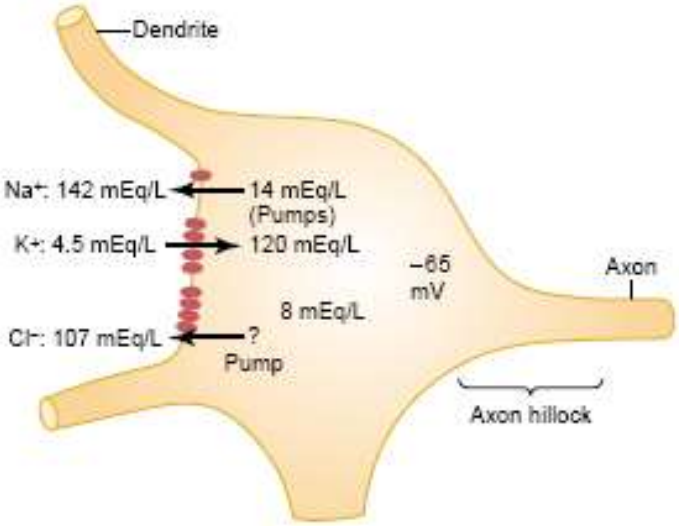


Figure 45–8

Distribution of sodium, potassium, and chloride ions across the neuronal somal membrane; origin of the intrasomal membrane potential.

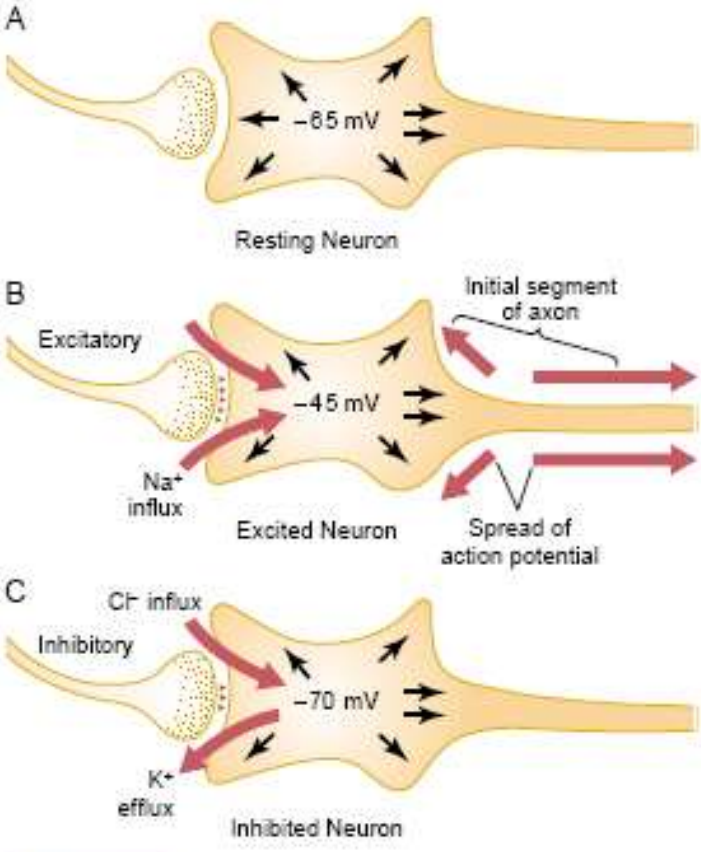


Figure 45–9

Three states of a neuron. *A*, *Resting neuron*, with a normal intraneuronal potential of –65 millivolts. *B*, Neuron in an *excited state*, with a less negative intraneuronal potential (–45 millivolts) caused by sodium influx. *C*, Neuron in an *inhibited state*, with a more negative intraneuronal membrane potential (–70 millivolts) caused by potassium ion efflux, chloride ion influx, or both.

Superposition of Action Potentials

Time course of postsynaptic potentials: Fig. 45-10

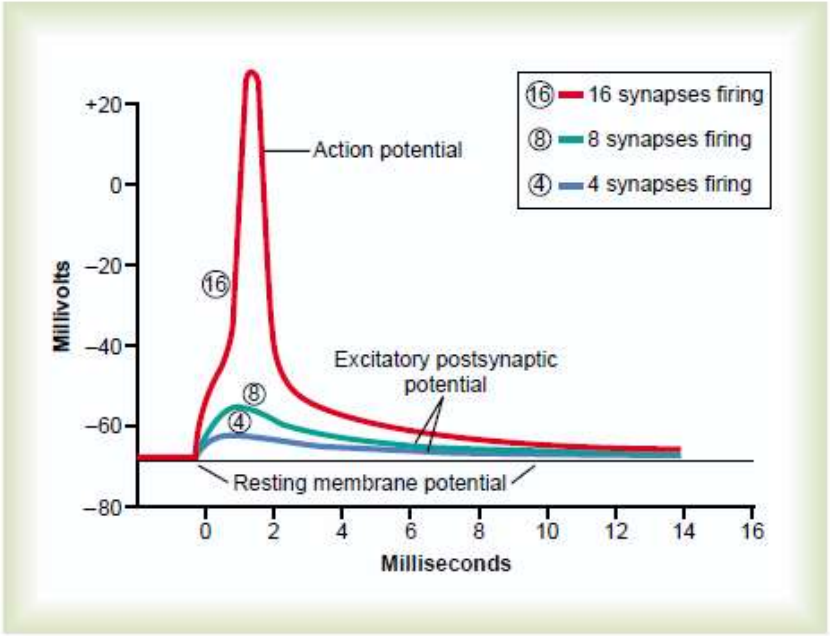
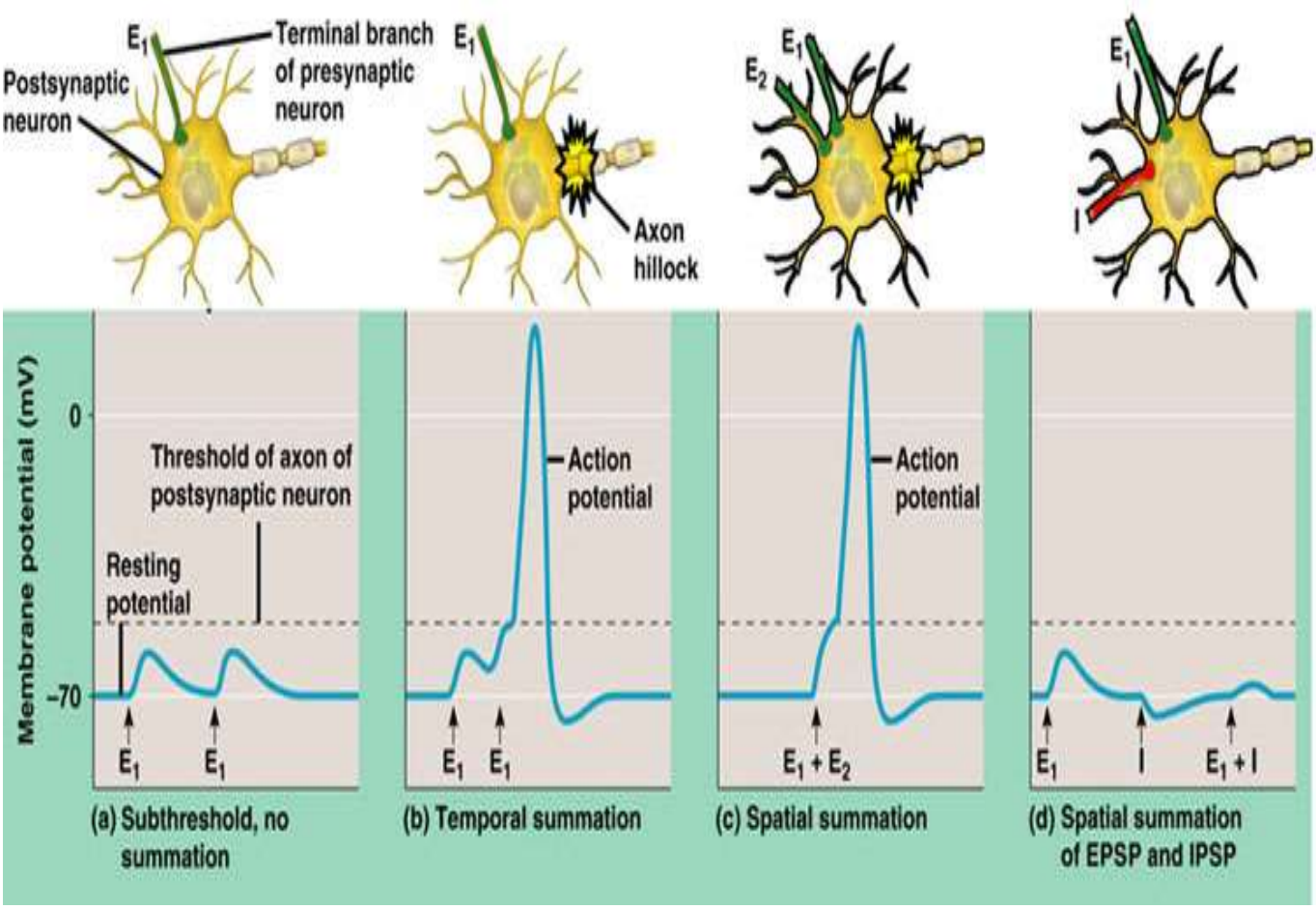


Figure 45–10

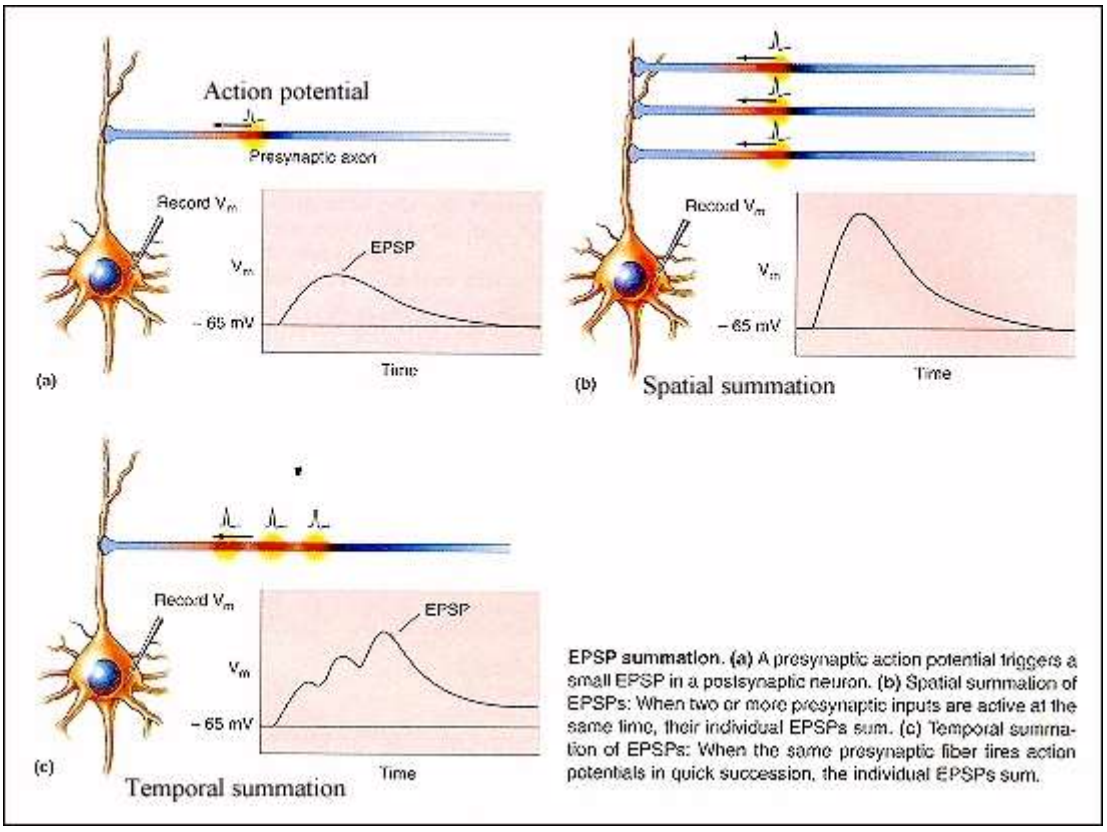
Excitatory postsynaptic potentials, showing that simultaneous firing of only a few synapses will not cause sufficient summated potential to elicit an action potential, but that simultaneous firing of many synapses will raise the summated potential to threshold for excitation and cause a superimposed action potential.

Temporal & Spatial Summation

- **Spatial summation** in neurons – the threshold for firing: Fig. 45-10
- **Temporal summation** in neurons



Spatial & Temporal Summation



EPSP summation. (a) A presynaptic action potential triggers a small EPSP in a postsynaptic neuron. **(b)** Spatial summation of EPSPs: When two or more presynaptic inputs are active at the same time, their individual EPSPs sum. **(c)** Temporal summation of EPSPs: When the same presynaptic fiber fires action potentials in quick succession, the individual EPSPs sum.