Pathophysiology

2024-2025

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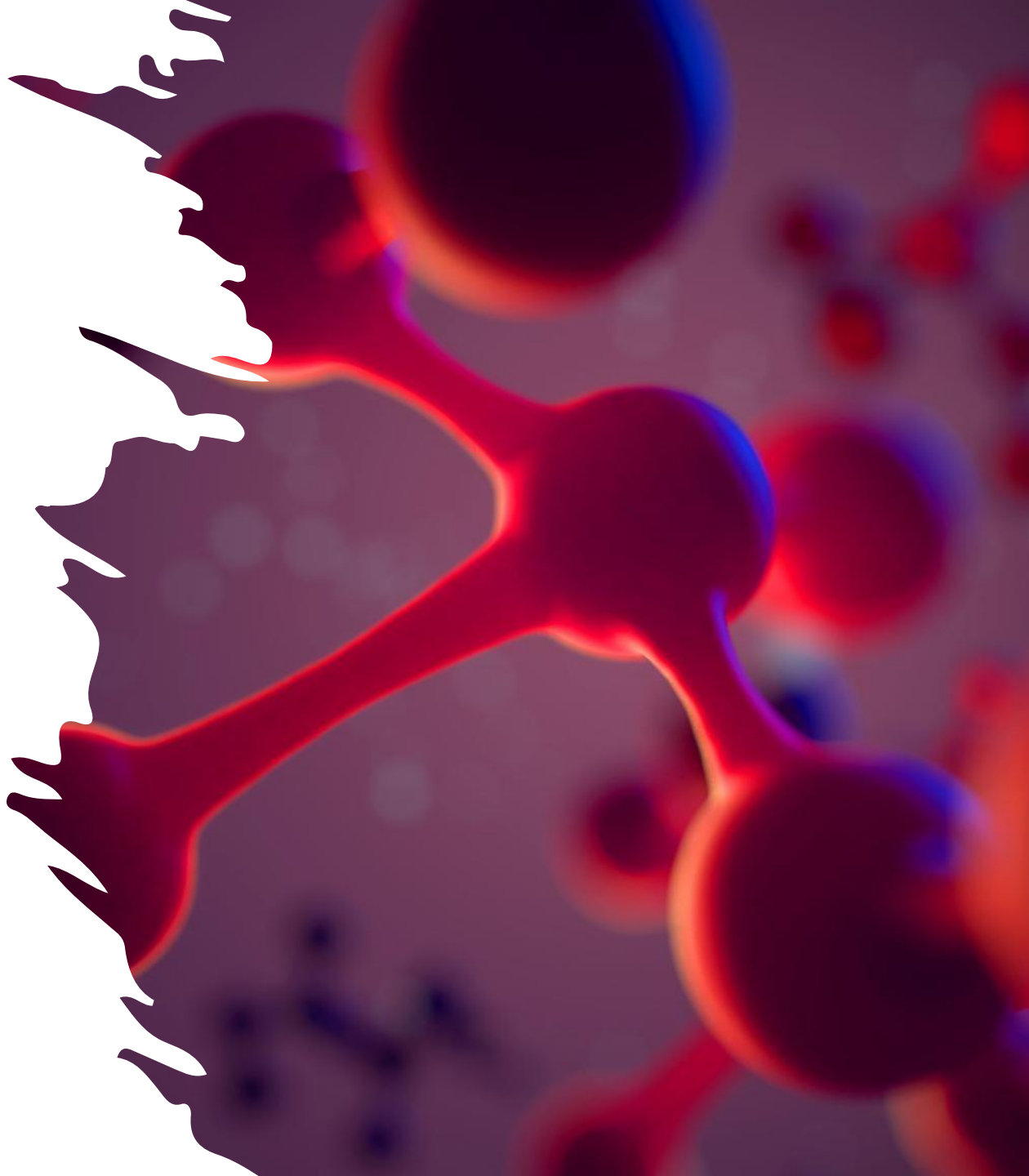
NERVOUS SYSTEM

DR. SHAHIRA



The Structural Organization of the Nervous System

- The nervous system is divided into two parts: the central nervous system (CNS), consisting of the brain and spinal cord, which are located in the skull and spinal column, and the peripheral nervous system (PNS), which is located outside these structures.
- The nervous system contains two major types of cells: neurons, which are functioning cells of the nervous system, and supporting cells, which protect the nervous system and supply metabolic support.
- There are two types of neurons: afferent neurons or sensory neurons, which carry information to the CNS, and efferent neurons or motoneurons, which carry information from the CNS to the effector organs.

Nerve Cell Communication

Action Potentials

- Action potentials can be divided into three phases: the resting or polarized state, depolarization, and repolarization.
- The *resting membrane potential* (approximately 90 mV for large nerve fibers) is the undisturbed period of the action potential during which the nerve is not transmitting impulses. During this period, the membrane is said to be *polarized* because of the large separation of charge (i.e., positive on the outside and negative on the inside). The resting phase of the membrane potential continues until some event causes the membrane to increase its permeability to sodium. A *threshold potential* (approximately 60 mV in large nerve fibers) represents the membrane potential at which neurons or other excitable tissues are stimulated to fire. When the threshold potential is reached, the gatelike structures in the ion channels open. Below the threshold potential, these gates remain tightly closed. The gates function on an all-or-none basis; they are either fully open or fully closed.

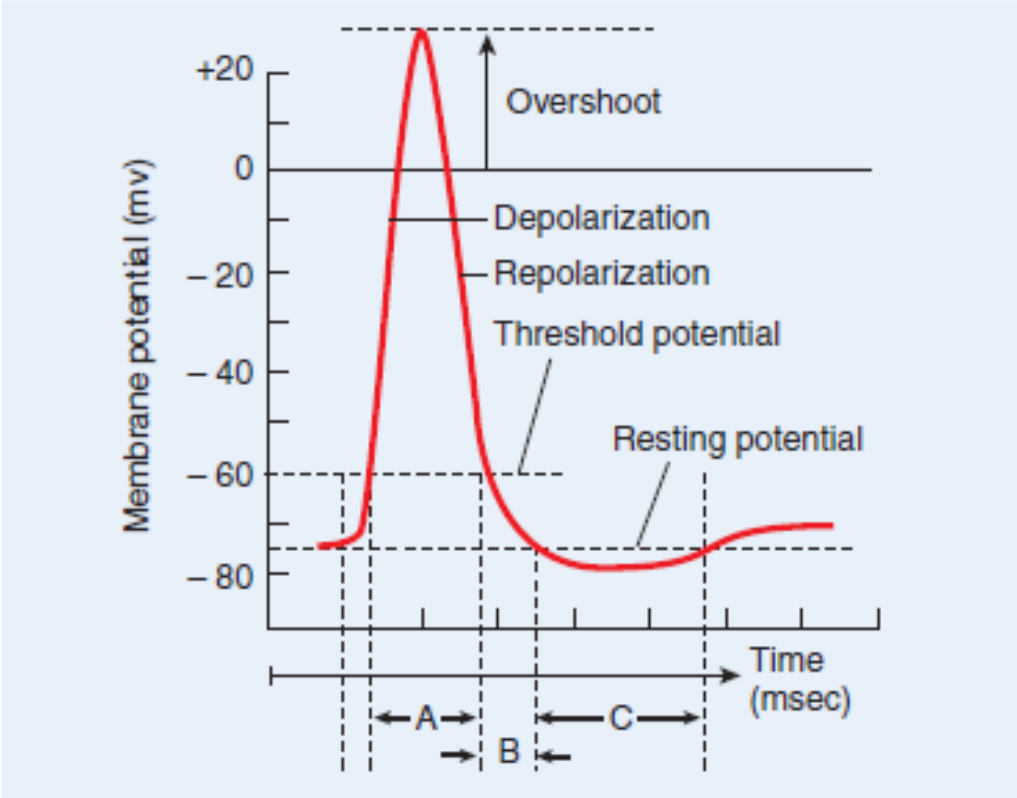
Nerve Cell Communication

Action Potentials

- *Depolarization* is characterized by the flow of electrically charged ions. During the depolarization phase, the membrane suddenly becomes permeable to sodium ions; the rapid inflow of sodium ions produces local currents that travel through the adjacent cell membrane, causing the sodium channels in this part of the membrane to open. In neurons, sodium ion gates remain open for approximately a quarter of a millisecond. During this phase of the action potential, the inner face of the membrane becomes positive (approximately 30 to 45 mV).
- *Repolarization* is the phase during which the polarity of the resting membrane potential is reestablished. This is accomplished with closure of the sodium channels and opening of the potassium channels. The outflow of positively charged potassium ions across the cell membrane returns the membrane potential to negativity. The sodium/potassium–adenosine triphosphatase (Na/K-ATPase) pump gradually reestablishes the resting ionic concentrations on each side of the membrane.

Nerve Cell Communication

Action Potentials



Nerve Cell Communication

Synaptic Transmission

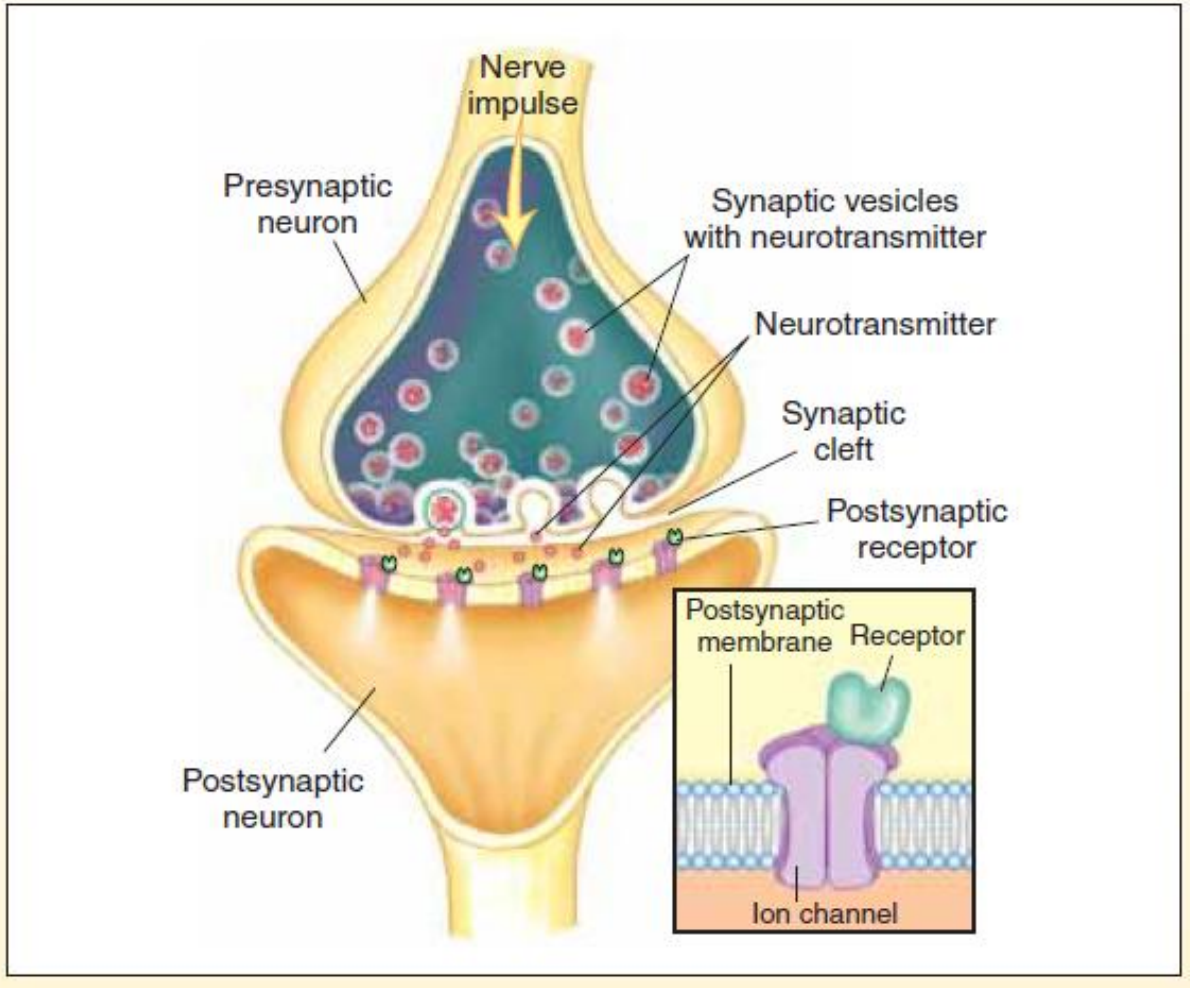
- Neurons communicate with each other through chemical synapses and the use of neurotransmitters. Chemical synapses consist of a presynaptic neuron, a synaptic cleft, and a postsynaptic neuron. The communication process relies on (1) synthesis and release of the neurotransmitter from a presynaptic neuron, (2) binding of the neurotransmitter to receptors in the postsynaptic neuron, and (3) removal of the neurotransmitter from the receptor site.

Nerve Cell Communication

Synaptic Transmission

1

Neurotransmitter Synthesis and Release. Neurotransmitters are synthesized in the presynaptic neuron, and then stored in synaptic vesicles. Communication between the two neurons begins with a nerve impulse that stimulates the presynaptic neuron, followed by movement of the synaptic vesicles to the cell membrane and release of neurotransmitter into the synaptic cleft.

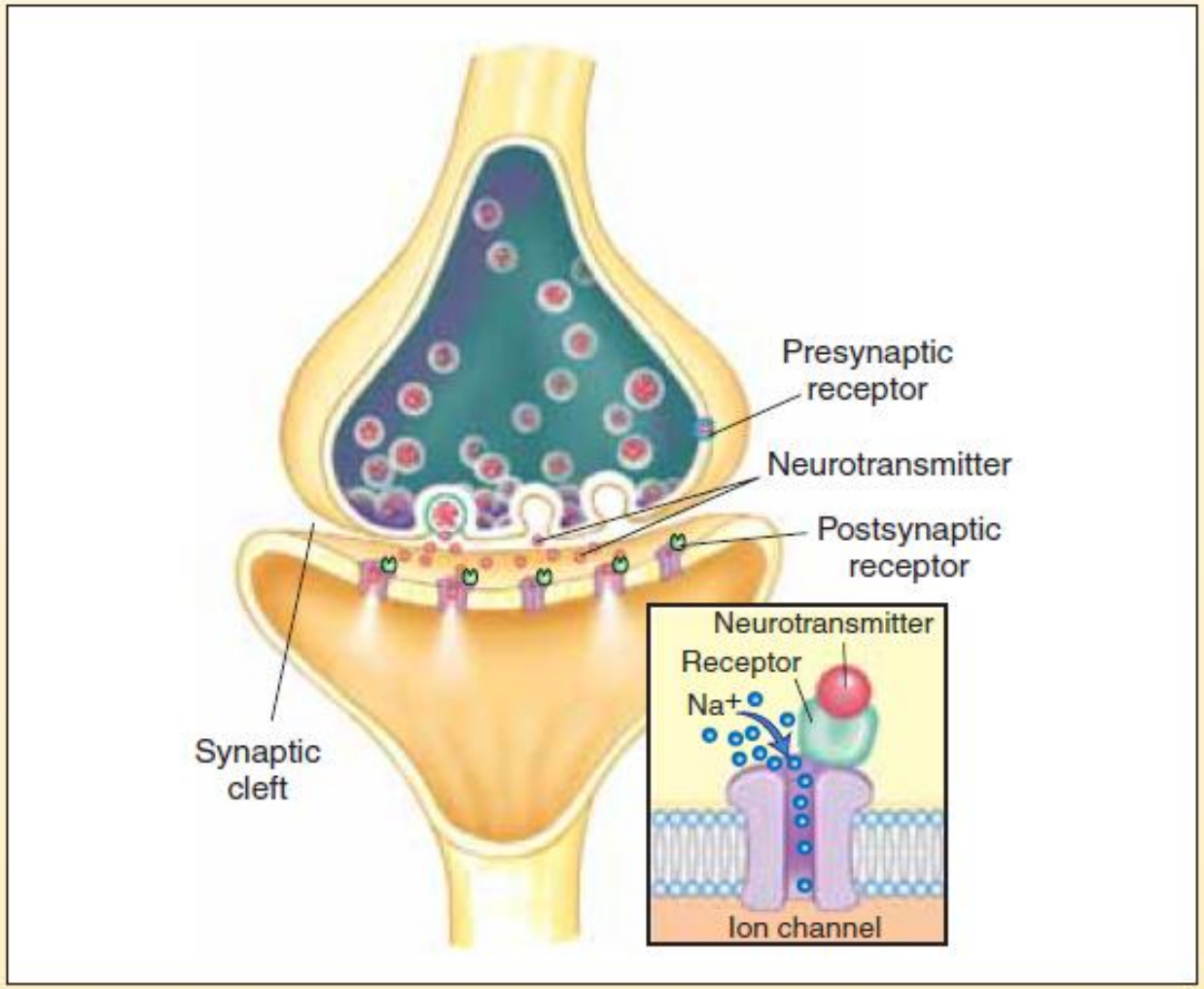


Nerve Cell Communication

Synaptic Transmission

2

Receptor Binding. Once released from the presynaptic neuron, the neurotransmitter moves across the synaptic cleft and binds to receptors on the postsynaptic neuron. The action of a neurotransmitter is determined by the type of receptor (excitatory or inhibitory) to which it binds. Binding of a neurotransmitter to a receptor with an excitatory function often results in the opening of an ion channel, such as the sodium channel. Many presynaptic neurons also have receptors to which a neurotransmitter binds. The presynaptic receptors function in a negative feedback manner to inhibit further release of the neurotransmitter.

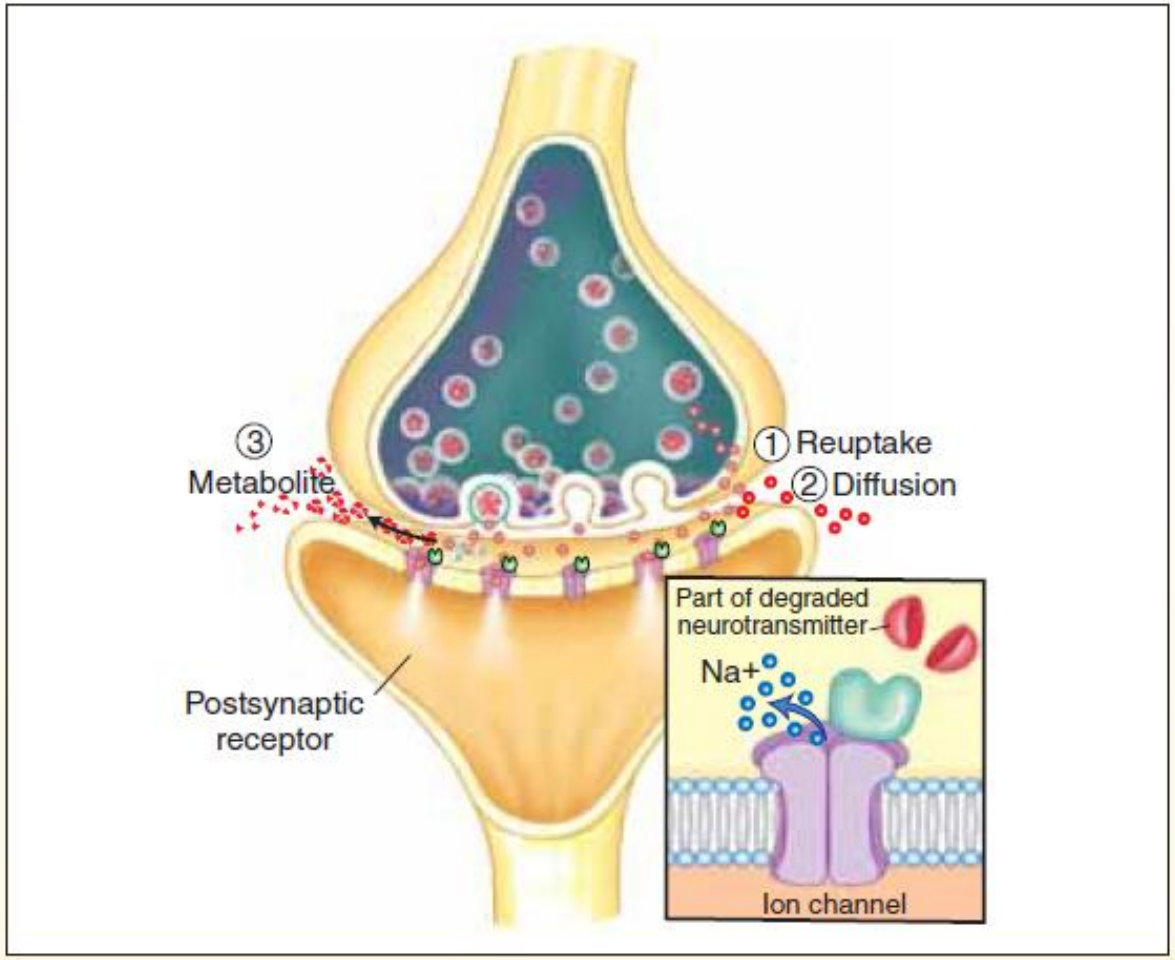


Nerve Cell Communication

Synaptic Transmission

3

Neurotransmitter Removal. Precise control of synaptic function relies on the rapid removal of the neurotransmitter from the receptor site. A released neurotransmitter can (1) be taken back up into the neuron in a process called reuptake, (2) diffuse out of the synaptic cleft, or (3) be broken down by enzymes into inactive substances or metabolites. The action of norepinephrine is largely terminated by the reuptake process, in which the neurotransmitter is taken back into the neuron in an unchanged form and reused. It can also be broken down by enzymes in the synaptic cleft or in the nerve terminals. The neurotransmitter acetylcholine is rapidly broken down by the enzyme acetylcholinesterase.

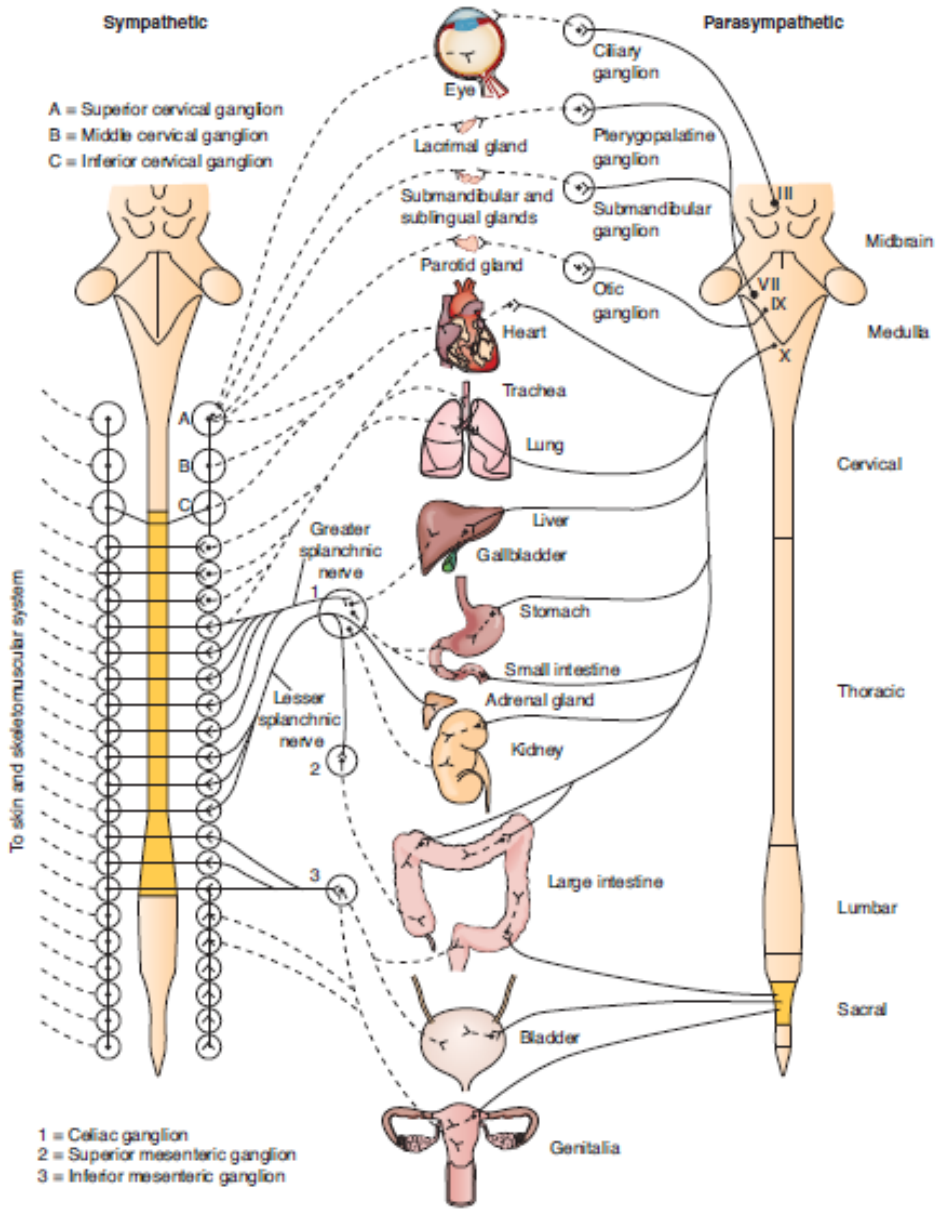


Nerve Cell Communication

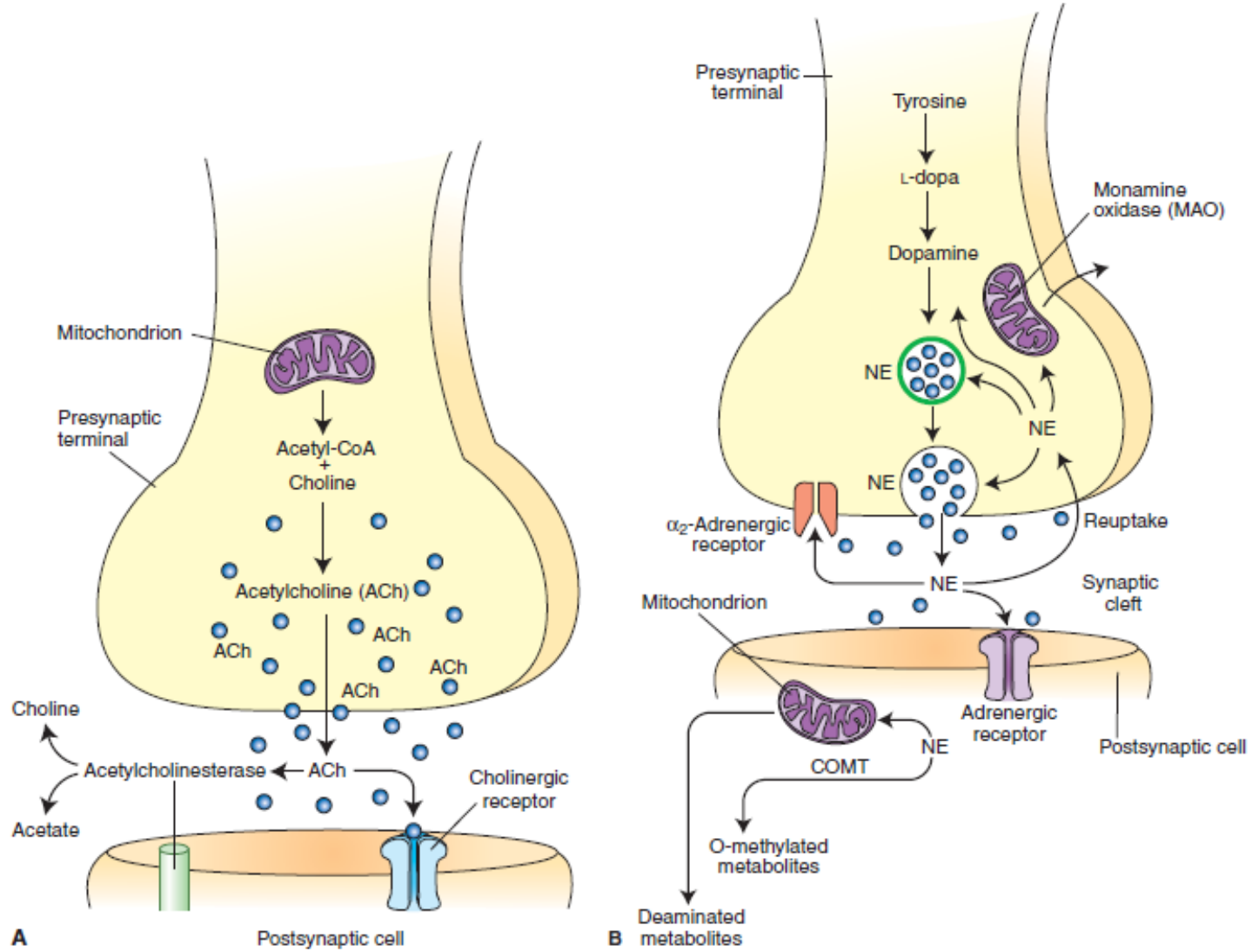
Synaptic Transmission

- Neurotransmitters are chemical messengers that control neural function; they selectively cause excitation or inhibition of action potentials. Three major types of neurotransmitters are known: amino acids such as glutamic acid and GABA, peptides such as the endorphins and enkephalins, and monoamines such as epinephrine and norepinephrine. Neurotransmitters interact with cell membrane receptors to produce either excitatory or inhibitory actions.
- Neuromodulators are chemical messengers that react with membrane receptors to produce slower and longer-acting changes in membrane permeability.

Division of autonomic nervous system



Division of autonomic nervous system



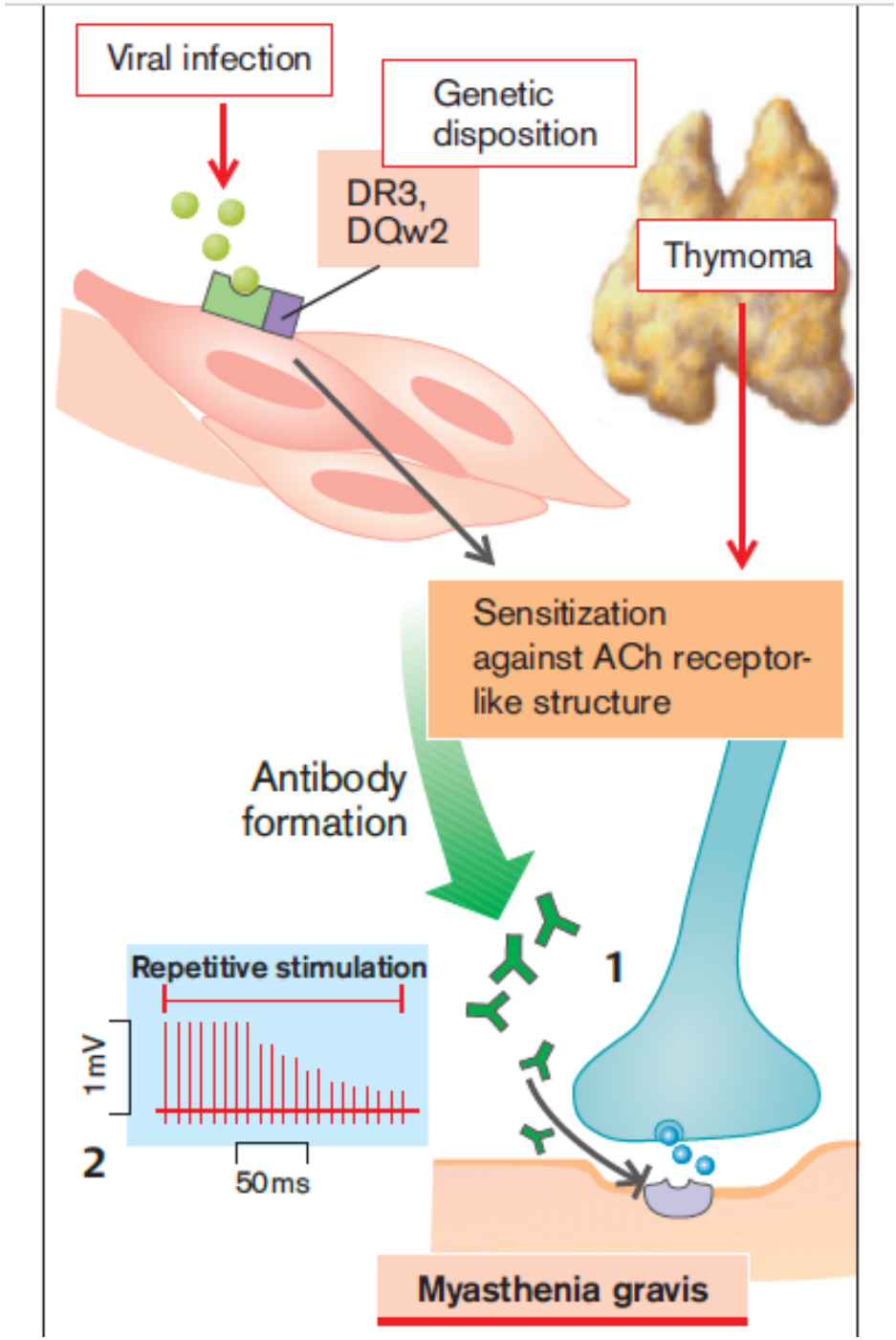
Myasthenia Gravis

- Myasthenia gravis is a disorder of the neuromuscular junction that affects impulse transmission between the motor neuron and the innervated muscle cell.
- Now recognized as an autoimmune disease, the disorder is caused by an antibody-mediated loss of acetylcholine receptors in the neuromuscular junction
- Three mechanisms are thought to underlie the loss of functional acetylcholine receptors: (1) complement mediated injury to the postsynaptic muscle membrane, (2) accelerated acetylcholine receptor degradation by receptor specific antibodies, and (3) blockade of the receptors by antibodies attached to the acetylcholine-binding sites.

Myasthenia Gravis

Clinical manifestations:

- muscle weakness and fatigability with sustained effort.
- The disease may progress from ocular muscle weakness to generalized weakness, including respiratory muscle weakness.



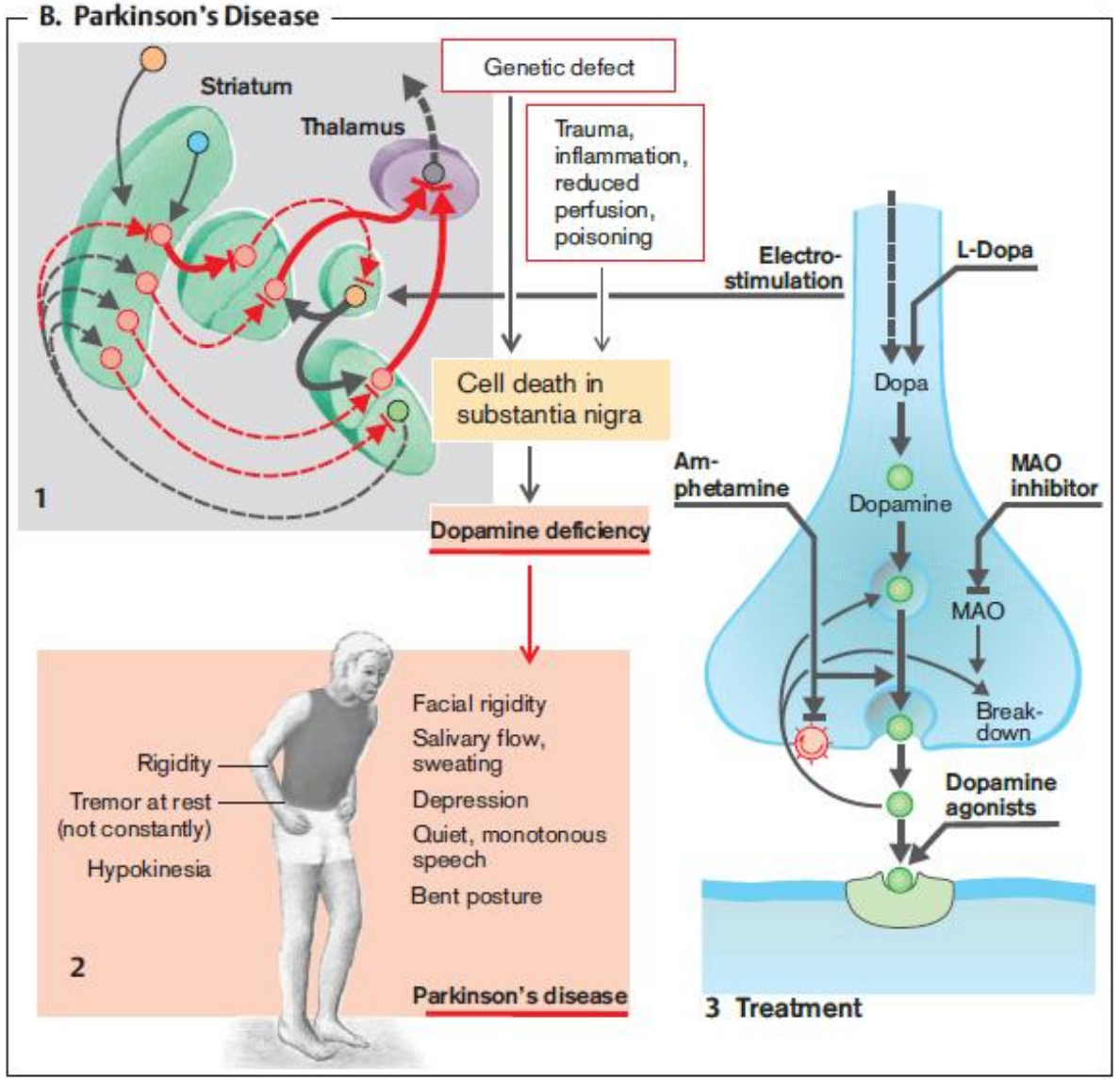
Myasthenia Gravis take home message?

- Thymus?
- Antibodies?

Parkinson Disease

- Parkinson disease is a progressive degenerative disorder of basal ganglia function that results in variable combinations of tremor, rigidity, and bradykinesia
- Parkinson disease is the second most common neurodegenerative disease after Alzheimer disease.
- The primary brain abnormality found in persons with Parkinson disease is degeneration of the nigrostriatal pathway, with subsequent reduction in striatal concentrations of dopamine.

Parkinson Disease



Parkinson Disease take home message?

- Dopamine?

Multiple Sclerosis

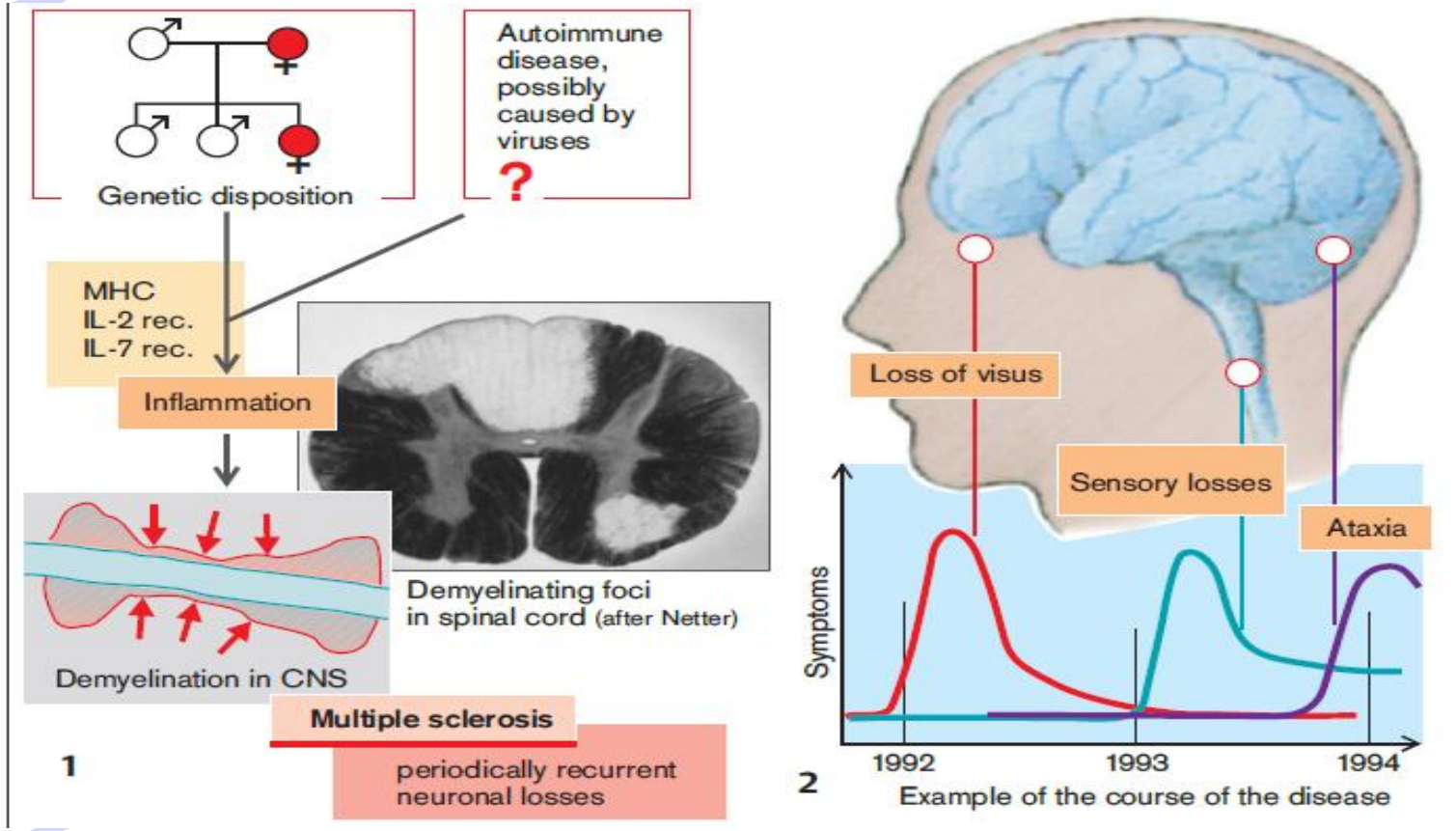
- Multiple sclerosis (MS) is a demyelinating disorder characterized by inflammation and selective destruction of CNS myelin.
- Multiple sclerosis is thought to be an immune-mediated disorder that occurs in genetically susceptible people.
- Demyelinated nerve fibers display a variety of conduction abnormalities, ranging from decreased conduction velocity to conduction blocks.

Multiple Sclerosis

- The lesions of MS consist of hard, sharp-edged, demyelinated or sclerotic patches that are macroscopically visible throughout the white matter of the CNS.
- These lesions, which represent the end result of acute myelin breakdown, are called plaques. The lesions have a predilection for the optic nerves, periventricular white matter, brain stem, cerebellum, and spinal cord white matter.

Multiple Sclerosis

- Paresthesias are evidenced as numbness, tingling, burning sensations, or pressure on the face or involved extremities, with symptoms ranging from annoying to severe.
- Fatigue is one of the most common problems for persons with MS.



Multiple Sclerosis take home message?

- Immunity?
- Symptoms?
- Inflammation?