Chapter 32

Neuromuscular Junction

DEFINITION AND STRUCTURE

DEFINITION

Neuromuscular junction is the junction between terminal branch of the nerve fiber and muscle fiber.

STRUCTURE

Skeletal muscle fibers are innervated by the motor nerve fibers. Each nerve fiber (axon) divides into many terminal branches. Each terminal branch innervates one muscle fiber through the neuromuscular junction (Fig. 32.1).

Axon Terminal and Motor Endplate

Terminal branch of nerve fiber is called axon terminal. When the axon comes close to muscle fiber, it loses the myelin sheath. So, the axis cylinder is exposed. This portion of the axis cylinder is expanded like a bulb, which is called motor endplate.

Axon terminal contains **mitochondria** and **synaptic vesicles.** Synaptic vesicles contain the neurotransmitter

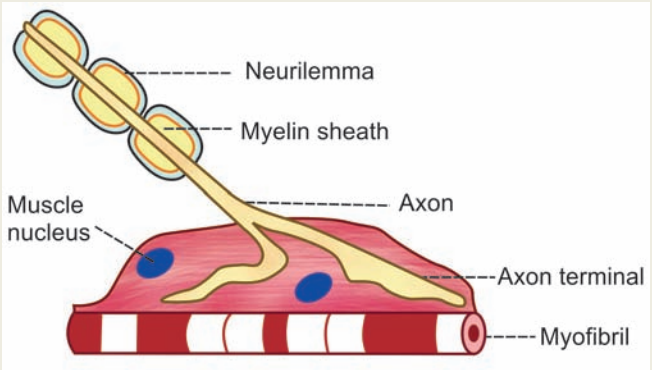

FIGURE 32.1: Longitudinal section of neuromuscular junction

substance, acetylcholine (Ach). The Ach is synthesized by mitochondria present in the axon terminal and stored in the vesicles. Mitochondria contain ATP, which is the source of energy for the synthesis of acetylcholine.

Synaptic Trough or Gutter

Motor endplate invaginates inside the muscle fiber and forms a depression, which is known as **synaptic trough** or **synaptic gutter.** The membrane of the muscle fiber below the motor endplate is thickened.

Synaptic Cleft

Membrane of the nerve ending is called the **presynaptic membrane.** Membrane of the muscle fiber is called **postsynaptic membrane.** Space between these two membranes is called **synaptic cleft.**

Synaptic cleft contains **basal lamina.** It is a thin layer of spongy reticular matrix through which, the extracellular fluid diffuses. An enzyme called acetylcholinesterase (AchE) is attached to the matrix of basal lamina, in large quantities.

Subneural Clefts

Postsynaptic membrane is the membrane of the muscle fiber. It is thrown into numerous folds called **subneural clefts.** Postsynaptic membrane contains the receptors called nicotinic **acetylcholine receptors** (Fig. 32.2).

■ NEUROMUSCULAR TRANSMISSION

Definition

Neuromuscular transmission is defined as the transfer of information from motor nerve ending to the muscle fiber through neuromuscular junction. It is the mechanism by which the motor nerve impulses initiate muscle contraction.

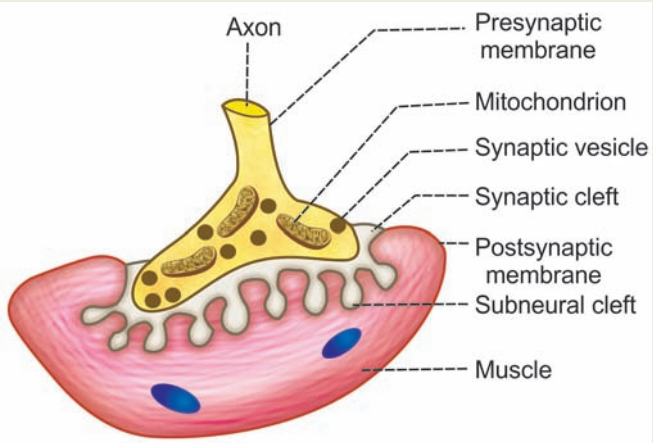

FIGURE 32.2: Structure of neuromuscular junction

Events of Neuromuscular Transmission

A series of events take place in the neuromuscular junction during this process (Fig. 32.3). The events are:

1. Release of acetylcholine
2. Action of acetylcholine
3. Development of endplate potential
4. Development of miniature endplate potential
5. Destruction of acetylcholine.

■ 1. RELEASE OF ACETYLCHOLINE

When action potential reaches axon terminal, it opens the voltage-gated calcium channels in the membrane of axon terminal. Calcium ions from extracellular fluid (ECF) enter the axon terminal. These cause bursting of the vesicles by forcing the synaptic vesicles move and fuse with presynaptic membrane. Now, acetylcholine is released from the ruptured vesicles. By **exocytosis,** acetylcholine diffuses through the presynaptic membrane and enters the synaptic cleft.

Each vesicle contains about 10,000 acetylcholine molecules. And, at a time, about 300 vesicles open and release acetylcholine.

■ 2. ACTION OF ACETYLCHOLINE

After entering the synaptic cleft, acetylcholine molecules bind with nicotinic receptors present in the postsynaptic membrane and form acetylcholine-receptor complex. It increases the permeability of postsynaptic membrane for sodium by opening the ligand-gated sodium channels. Now, sodium ions from ECF enter the neuromuscular junction through these channels. And there, sodium ions alter the resting membrane potential and develops the electrical potential called the endplate potential.

■ 3. DEVELOPMENT OF ENDPLATE POTENTIAL

Endplate potential is the change in resting membrane potential when an impulse reaches the neuromuscular junction. Resting membrane potential at neuromuscular junction is –90 mV. When sodium ions enter inside, slight depolarization occurs up to –60 mV, which is called endplate potential.

Properties of Endplate Potential

Endplate potential is a graded potential (Chapter 31) and it is not action potential. Refer Table 31.1 for the properties of graded potential.

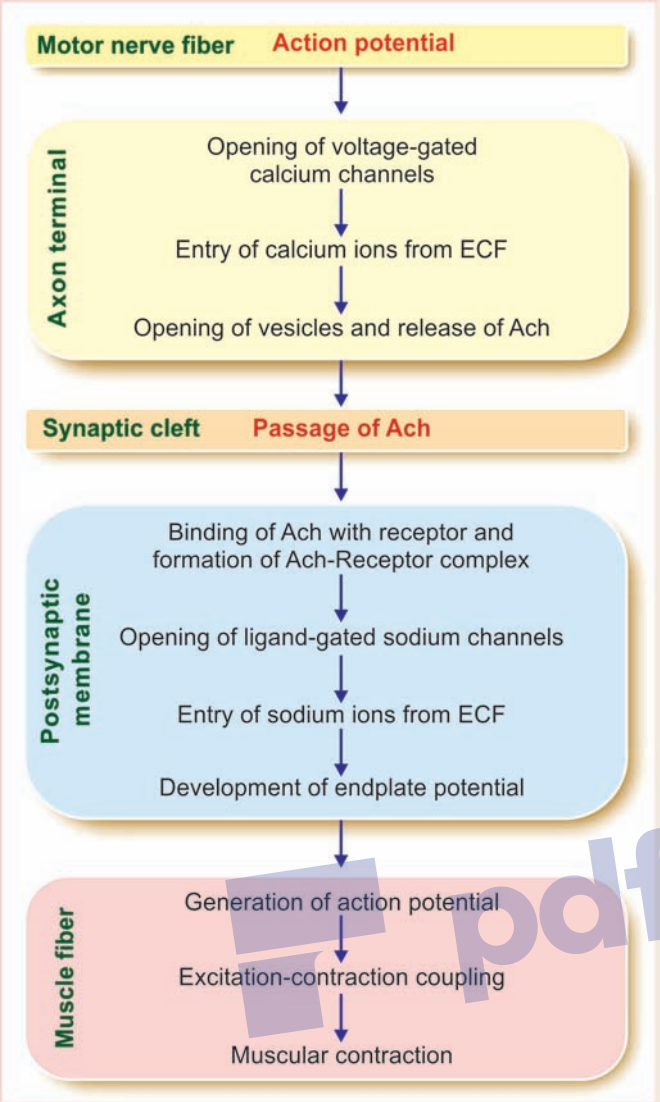

FIGURE 32.3: Sequence of events during neuromuscular transmission. Ach = Acetylcholine, ECF = Extracellular fluid.

Significance of Endplate Potential

Endplate potential is non-propagative. But it causes the development of action potential in the muscle fiber.

■ 4. DEVELOPMENT OF MINIATURE ENDPLATE POTENTIAL

Miniature endplate potential is a weak endplate potential in neuromuscular junction that is developed by the release of a small quantity of acetylcholine from axon terminal. And, each quantum of this neurotransmitter produces a weak miniature endplate potential. The amplitude of this potential is only up to 0.5 mV.

Miniature endplate potential cannot produce action potential in the muscle. When more and more quanta of acetylcholine are released continuously, the miniature endplate potentials are added together and finally produce endplate potential resulting in action potential in the muscle.

■ 5. DESTRUCTION OF ACETYLCHOLINE

Acetylcholine released into the synaptic cleft is destroyed very quickly, within one millisecond by the enzyme, acetylcholinesterase. However, the acetylcholine is so potent, that even this short duration of 1 millisecond is sufficient to excite the muscle fiber. Rapid destruction of acetylcholine has got some important functional significance. It prevents the repeated excitation of the muscle fiber and allows the muscle to relax.

Reuptake Process

Reuptake is a process in neuromuscular junction, by which a degraded product of neurotransmitter re-enters the presynaptic axon terminal where it is reused. Acetylcholinesterase splits (degrades) acetylcholine into inactive choline and acetate. Choline is taken back into axon terminal from synaptic cleft by reuptake process. There, it is reused in synaptic vesicle to form new acetylcholine molecule.

■ NEUROMUSCULAR BLOCKERS

Neuromuscular blockers are the drugs, which prevent transmission of impulses from nerve fiber to the muscle fiber through the neuromuscular junctions. These drugs are used widely during surgery and trauma care. Neuromuscular blockers used during anesthesia relax the skeletal muscles and induce paralysis so that surgery can be conducted with less complication.

Following are important neuromuscular blockers, which are commonly used in clinics and research.

1. *Curare*

Curare prevents the neuromuscular transmission by combining with acetylcholine receptors. So, the acetylcholine cannot combine with the receptors. And, the endplate potential cannot develop. Since curare blocks the neuromuscular transmission by acting on the acetylcholine receptors, it is called receptor blocker.

2. *Bungarotoxin*

Bungarotoxin is a toxin from the venom of deadly snakes. It affects the neuromuscular transmission by blocking the acetylcholine receptors.

3. *Succinylcholine and Carbamylcholine*

These drugs block the neuromuscular transmission by acting like acetylcholine and keeping the muscle in a depolarized state. But, these drugs are not destroyed by cholinesterase. So, the muscle remains in a depolarized state for a long time.

4. *Botulinum Toxin*

Botulinum toxin is derived from the bacteria *Clostridium botulinum*. It prevents release of acetylcholine from axon terminal into the neuromuscular junction.

■ DRUGS STIMULATING NEUROMUSCULAR JUNCTION

Neuromuscular junction can be stimulated by some drugs like neostigmine, physostigmine and diisopropyl fluorophosphate. These drugs inactivate the enzyme, acetylcholinesterase. So, the acetylcholine is not hydrolyzed. It leads to repeated stimulation and continuous contraction of the muscle.

■ MOTOR UNIT

■ DEFINITION

Single motor neuron, its axon terminals and the muscle fibers innervated by it are together called motor unit. Each motor neuron activates a group of muscle fibers through the axon terminals. Stimulation of a motor neuron causes contraction of all the muscle fibers innervated by that neuron.

■ NUMBER OF MUSCLE FIBERS IN MOTOR UNIT

Number of muscle fiber in each motor unit varies. The motor units of the muscles concerned with fine, graded and precise movements have smaller number of muscle fibers.

For example,

Laryngeal muscles : 2 to 3 muscle fibers per motor unit
Pharyngeal muscles : 2 to 6 muscle fibers per motor unit
Ocular muscles : 3 to 6 muscle fibers per motor unit

Muscles concerned with crude or coarse movements have motor units with large number of muscle fibers. There are about 120 to 165 muscle fibers in each motor unit in these muscles. Examples are the muscles of leg and back.

■ RECRUITMENT OF MOTOR UNITS

While stimulating the muscle with weak strength, only a few motor units are involved. When the strength of stimulus is increased, many motor units are put into action. So, the force of contraction increases. The process by which more and more motor units are put into action is called recruitment of motor unit. Thus, the graded response in the muscle is directly proportional to the number of motor units activated.

Activation of motor units can be studied by electromyography.

■ APPLIED PHYSIOLOGY – DISORDERS OF NEUROMUSCULAR JUNCTION

■ MYASTHENIA GRAVIS

Myasthenia gravis is an autoimmune disorder of neuromuscular junction caused by antibodies to cholinergic receptors. Refer Chapter 34 for details.

■ EATON-LAMBERT SYNDROME

Eaton-Lambert syndrome is also an autoimmune disorder of neuromuscular junction. It is caused by antibodies to calcium channels in axon terminal. Refer Chapter 34 for details.