Neuromuscular Transmission

Neuromuscular junctions are specific chemical synapses. The synapses between the axons of motor neurons and skeletal muscle fibers (also known as "motor end-plates") have been the first synapses studied. They possess all common characteristics of the CNS synapses.

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Function

The steps that take place when the action potential is conducted to the muscle fiber are:

1. The depolarization caused by an action potential transiently opens voltage-gated Ca^{2+} channels and increases the calcium conductance. Ca^{2+} flows down its electrochemical potential gradient into the axon terminal at a high rate.
2. The increase of free Ca^{2+} concentration is short-lived, because Ca^{2+}-binding proteins and Ca^{2+} pumps (e.g. Na/Ca anti-porter) rapidly take up and remove the Ca^{2+}, respectively. In this way the terminal is ready to transmit another signal in a very short time.
3. The influx of Ca^{2+} triggers an interaction of contractile proteins (synapsin I = actin-like protein), attached to the presynaptic membrane, with synaptic vesicles. Vesicles fuse with the presynaptic membrane and discharge their contents into the synaptic cleft (exocytosis).
4. The exocytosis is restricted to specialized regions known as **active zones** (or release sites), exactly opposite the receptors on the postsynaptic cell. The membrane of the discharged synaptic vesicles is subsequently retrieved from the presynaptic plasma membrane by endocytosis.
5. An axon terminal at a neuromuscular junction typically releases a few hundred of its many thousands of synaptic vesicles in a response to a single action potential.
6. The time required for calcium channels to open in response to depolarization is the major component of synaptic delay.
7. The conversion of the chemical signal into an electrical signal is achieved by ligand-gated ion channels in the postsynaptic membrane. When transmitter binds to the receptor proteins, they change their conformation – open the ion channel → membrane potential is altered. If the shift of membrane potential is large enough, it causes the voltage-gated channels to open → action potential is triggered.
8.

Unlike voltage-gated ion channels, the ligand-gated ion channels are relatively insensitive to the membrane potential. They cannot by themselves produce an all-or-non, self-amplifying excitation. Instead they produce an electrical change that is graded according to the intensity and duration of the external chemical signal, according to how much transmitter is released into the synaptic cleft and how long it stays there. This feature is important for the integration properties of the signal by neurons.

Postsynaptic ligand-gated channels have enzyme-like specificity for a particular ligand → they respond only to one neurotransmitter (the one released from the presynaptic terminal), with other transmitters having no effect. In their role as channels, they are characterized by different ion selectivity (to K^+, Cl^-, nonselective to cations but exclude anions) → the ion selectivity determines the character of the postsynaptic response.

The channels in the skeletal muscle cell membrane gated by acetylcholine (acetylcholine receptors) have several discrete alternative conformations. Upon binding acetylcholine the channel jumps from closed to an open state and then stays open, with the ligand bound, for a randomly variable length of time (average about 1 ms, depending on temperature and the species). In the open conformation the channel is indiscriminately permeable to small cations including Na^+, K^+, and Ca^{2+}, but impermeable to anions. Since there is little selectivity among these cations, their relative contributions to the current through the channel depend chiefly on their concentrations and on the electrochemical driving forces:

- If the muscle cell membrane is at its resting potential, the net driving force for K^+ is near zero, because the voltage gradient (negative inside) nearly balances the K^+ concentration gradient.
- For Na^+, the voltage gradient and the concentration gradient both act in the same direction to drive Na^+ into the cell. Similarly some Ca^{2+} ions contribute to the total inward current.

In order for the post-synaptic excitation to be accurately controlled by the pattern of signals sent from the presynaptic terminal, it must be switched off very rapidly when the presynaptic cell falls quiet. This is achieved by the removal of the acetylcholine from the synaptic cleft and it takes a few hundred microseconds:

1. Acetylcholine disperses by diffusion.
2. Acetylcholine is hydrolyzed by acetylcholinesterase to acetate and choline.

Links

Related articles

Sources

- Lecture Notes: Prof. MUDr. Jaroslav Pokorný DrSc.

Bibliography

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