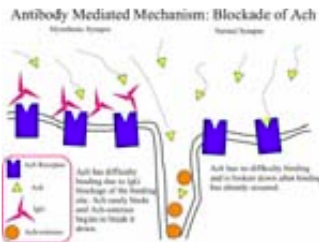


Cholinergic Aspects

Myasthenia Gravis and Acetylcholine

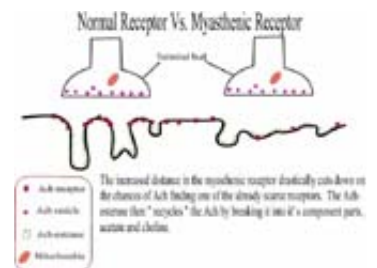
The muscular weakness and fatigability associated with myasthenia gravis are caused by an autoimmune attack on the [acetylcholine receptor](#) at the [neuromuscular junction](#). Antibodies have been shown to decrease the usefulness of acetylcholine receptors through accelerated endocytosis and blockade of the receptor. Endocytosis is the process of extracellular substances being incorporated into the cell by vesicles forming inward through budding of the plasma membrane. Researchers have been able to demonstrate the effect of antibodies on acetylcholine receptor degradation by using radioactively labeled alpha bungarotoxin, a snake poison, to follow the rate of degradation. Antibodies from patients with MG cause a two to three fold increase in the rate of degradation of acetylcholine receptors. The myasthenic antibodies cause a cross linking between the acetylcholine receptors, causing the linked receptors to be drawn together into clusters and rapidly endocytosed.



Blockade of acetylcholine receptors is another form of autoimmune attack. Antibodies from patients with MG have been shown to block the acetylcholine binding sites, which prevents acetylcholine from binding to its receptor and opening the ion channel. It is probable that the antibodies bind near the acetylcholine binding site rather than directly on it, because the acetylcholine binding site is so small. In this case the antibodies

would prevent acetylcholine from binding at the receptor by "getting in the way" of the acetylcholine molecule as it moves towards its receptor; this effect is known as [steric hindrance](#).

In myasthenic patients the neuromuscular junction has decreased numbers of acetylcholine receptors, a wider synaptic cleft, and simplified synaptic folds. These changes account for the clinical features of myasthenia gravis. Decreased numbers of acetylcholine receptors result in fewer interactions between acetylcholine and its receptors, leading to decreased activation of action potentials. When the transmission of action potentials decreases, the power of the muscle's contraction is reduced, causing weakness. During repeated nerve stimulation the amount of acetylcholine normally declines, or runs down. In myasthenia gravis, this run down occurs more rapidly due to a decrease of receptors in myasthenic junctions, causing muscular



fatigability. The wider synaptic cleft and simplified synaptic folds also work to decrease the number of interactions between acetylcholine and acetylcholine receptors.

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