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Physiology 300level

Synthesis of Neurotransmitters

Acetylcholine is classified under amine group,it is synthesized from acetyl coenzyme A and choline by the enzyme choline acetyltransferase. In the nervous system, this enzyme is thought to exist primarily in the nerve terminal cytoplasm. Coenzyme A is synthesized in mitochondria and accesses choline acetyltransferase following transport across the mitochondrial membrane into the cytoplasm. In addition to its synthesis in the liver, choline employed in acetylcholine production is derived from dietary sources. There is a carrier system in capillary endothelial cells that is responsible for transport of choline, in its free and phospholipid forms, into the brain. Hydrolysis of choline-containing phospholipids may also liberate choline that is used in acetylcholine synthesis. As choline acetyltransferase is not saturated by concentrations of acetyl coenzyme A and choline that are estimated to be present in the nerve terminal, it appears that the rate of acetylcholine synthesis is dependent on precursor availability. Enzyme activity is also regulated by product inhibition; by binding at an allosteric site on choline acetyltransferase, acetylcholine inhibits its activity. In addition, mass action and neuronal activity influence the rate of acetylcholine formation. Short-term regulation of enzyme activity is partly achieved by phosphorylation induced by protein kinases. There are no very specific and potent inhibitors of the enzyme and it should be noted that pharmacological blockade of this step (e.g. with naphthylvinylpyridine) in the life-cycle of acetylcholine produces a less profound effect on the transmitter than does inhibition of choline transport.

Glutamate is classified under amino acid, Glutamate synthesis and cycling between neurons and glia. The action of glutamate released into the synaptic cleft is terminated by uptake into neurons and surrounding glial cells via specific transporters. Within the nerve terminal, the glutamine released by glial cells and taken up by neurons is converted back to glutamate. Following its packaging into synaptic vesicles by a Mg2+/ATP-dependent transport process, glutamate-filled vesicles are ready to dock and be released from presynaptic sites. Glutamate is removed from the synaptic cleft by several high-affinity glutamate transporters present in both glial cells and presynaptic terminals. Glial cells contain the enzyme glutamine synthetase, which converts glutamate into glutamine; glutamine is then transported out of the glial cells and into nerve terminals. In this way, synaptic terminals cooperate with glial cells to maintain an adequate supply of the neurotransmitter. This overall sequence of events is referred to as the glutamate-glutamine cycle.