**5/7 – Peptide transmitters target metabotropic receptors**

Neurotransmitters are classified into two major categories: amine, and peptide transmitters.

Peptide transmitters are built from amino acids, their precursors and the enzymes that activate the precursors are synthesized at the cell body and get to the axon terminal by vesicular transport. There the enzymes modify the precursors and produce transmitters. After the synaptic vesicles release the transmitters to the synaptic cleft, the presynaptic cell does not take them back, they diffuse away, and proteolytic enzymes degrade them, thus peptide transmitters are for one use. Peptide transmitters are also called neuropeptides and they are related to neuropeptide hormones because of the similarities in their function. Some widely known example for neuropeptides are endorphin, insulin, oxytocin or vasopressin.

Neurotransmitter receptors have two main types too: the ionotropic and the metabotropic receptors. Ionotropic receptors are ligand-gated ion channels, metabotropic receptors are G-protein coupled receptors.

In the case of ionotropic receptors, ligand binding causes the opening of the channel directly and relatively fast.

In contrast, in the case of metabotropic receptors, the ligand has an indirect, slower effect, through many metabolic steps. These receptors are transmembrane peptides usually have seven transmembrane region what have alpha-helical structure. The extracellular domain can bind the ligand, and on the cytoplasmic surface, the receptor is associated with GDP/GTP-binding and hydrolyzing protein, called G-proteins. These proteins can be heterotrimeric and have alpha, beta and gamma subunits, or monomeric, like Ras-proteins. When a membrane-localized G-protein binds to the receptor, the alpha subunit and the monomeric G-protein binds GDP, but if ligand binds to metabotropic receptor, GDP exchanges with GTP and the active alpha subunit or G-protein indicate numbers of metabotropic process, through second messenger pathways. The most important second messengers are cAMP, Ca2+, IP3, and DAG.

In the cAMP-mediated path, the activated subunit activates the adenylyl-cyclase, it produces cAMP what activates PKA.

Or in an IP3 and DAG mediated path, G-protein activates PLC, which activates IP3 pathway, which leads to Ca2+ release and DAG pathway, where DAG activates PKC.

At the end of the metabotropic processes, the effect can be increase or decrease of peptide phosphorylation, indirect activation of ion channels, or the manipulation of transcription factors.

Because of the many steps, this kind of signal transduction is relatively slow, but gives an opportunity to high-level amplification, diversity, and sometimes, to long term changes.

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