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Dependence of the transmitter effect on the physiological status of the postsynaptic cells

Neurons communicate with each other via chemical synapses. The firing of an action potential opens the voltage-gated calcium channels what triggers the neurotransmitter filled vesicles to get out from the presynaptic cell by exocytosis. The neurotransmitters bind to the receptors which are located at the postsynaptic cells’ membrane. Ions flowing through the channels generate postsynaptic current, which in turns changes the membrane potential to produce a postsynaptic potential(PSP).

Excitatory postsynaptic potential (EPSP) increases the likelihood of an action potential occurring while Inhibitory postsynaptic potential (IPSP) decreases the probability. One neuron receives inputs from both types, The summation(in space and time) of PSPs determines whether a postsynaptic cell will fire an action potential, what happens when the depolarization reaches the threshold. GABA and glycine are the major inhibitory neurotransmitters and glutamate and acetylcholine are excitatory neurotransmitters.

The change of the membrane potential due to the receptor bindings what triggers the ion channels to open or close, therefore the transmitter effect heavily depends on the receptor’s attributes. There are two types of postsynaptic receptors: ionotropic(ligand gated ion channels) receptors which ones are linked directly to ion channels and metabotropic (G-protein-coupled )receptors. They affect channels by the activation of intermediate molecules called G-proteins. G proteins dissociate from the receptors and directly triggers ion channels to open or close. Ionotropic receptors generate short lasting PSPs while metabotropic receptors typically produce much slower potentials (even minutes long) due to the ordered (and complex) mechanism to open or close ion channels. One synapse can have both types of receptors which binds with one kind of neurotransmitter to generate short and long term potentials.

Different neurotoxins can change the transmitter effect by targeting neurotransmitter receptors. For example the banded krait’s venom contains alpha-bungarotoxin what blocks the transmission at neuromuscural junctions by blocking irreversibly the nicotine ACh receptors preventing neurotransmitter binding. Paralysis happens because motor neurons no longer can be activated by ACh. Some neurotoxins can target inhibitory synapses eg. strychnine blocks inhibitory glycinergic receptors causing overactivity in the brain stem and the spinal cord what can lead to seizures.

The change in the duration of the neurotransmitter termination can also affect the transmitter effect of the postsynaptic cell. ACh is terminated by an enzyme called acetylcholinesterase (AChe) which hydrolises the ACh. Organophosphates accumulate ACh at the postsynaptic synapses by inhibiting AChE which can cause paralysis and temporary vision problems.

The number and the lifespan of the receptors are regulated by the cell. Long exposure of a neurotransmitter at certain receptors can lead to a decrease in the number of receptors. That’s why certain drugs can lose their effect after long-term use. The name of this mechanism is down-regulation. Similarly a lack of certain neurotransmitters can motivate neurons to produce more receptors making the PS neuron hypersensitive. This mechanism is called up-regulation.

Some unconventional neurotransmitters (e.g. anandamide and nitric oxide) can also change the synaptic transmission, signalling from the postsynaptic cell to the presynaptic cell via retrograde synaptic mechanism. Endocannabinoids regulate GABA release at certain inhibitory synapses by binding to CB1 receptors located in the presynaptic membrane.

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