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Assembly of ligand-gated ion channel receptors – how individual subunits contribute to receptor function

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Ligand-gated ion channels mediate rapid signalling at synapses and the neuromuscular junction. The strychnine-sensitive glycine receptor is the predominant mediator of inhibitory transmission in the mammalian spinal cord and brainstem. Glycine receptor defects underlie the human motor disorder, hyperekplexia (startle disease, stiff baby syndrome).

Signalling responses of ligand-gated ion channels are fine-tuned by a number of different mechanisms, such as phosphorylation, the effects of modulatory ligands, ions, and intracellular binding partners and proteins. Another source of receptor variety comes from the existence of different receptor subunits, with specific functional characteristics and pharmacological profiles.

Native ligand-gated ion channels are composed of five (acetylcholine-receptor type) or four (currently assumed for ionotropic glutamate receptors) subunits, who may each contribute to receptor function.

Here, glycine receptors subunits with different current kinetics were co-expressed in a recombinant system and their current responses analysed using rapid kinetic techniques in combination with electrophysiological recording methods. Comparison of experimental data and modeling of kinetic properties showed that subunits assemble statistically, with each subunit contributing to conductance and opening kinetics of the mixed channels. The technique may be useful to quantify the effects of subunit composition, and the extent to which mutations may affect the properties of an ion-channel receptor.