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HIGHLIGHTS

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GLIA

Crystal-clear glia–neuron interactions

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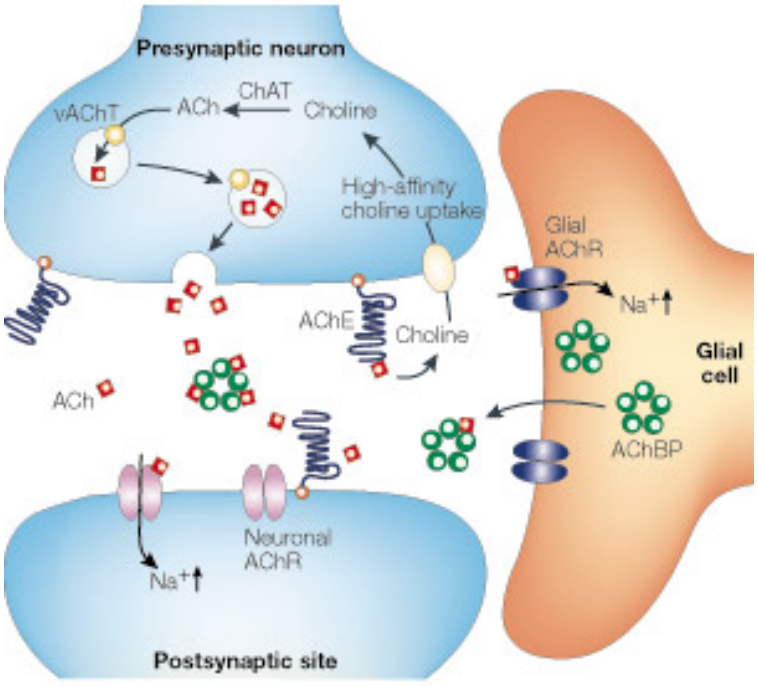
The profound effect that glial cells have on neurotransmission continues to gain notoriety; hardly a month passes without an important breakthrough in this flourishing field. The latest development has come from the study of acetylcholine (ACh)-mediated transmission in the snail *Lymnaea stagnalis*. In this system, Smit et al. have identified an ACh-binding protein (AChBP) released by glia, which can directly modulate the efficacy of synaptic transmission.

The authors observed that if a presynaptic neuron was stimulated repeatedly, the presence of a glial cell around the synapse caused a reduction in the postsynaptic, ACh-dependent response. By analysing this modulation in detail, Smit *et al*. determined that the glial cell responded to ACh and released AChBP, which then acted as a molecular decoy, binding the transmitter and reducing its availability at the synapse.



Nature Reviews | Neuroscience

AChBP shows significant sequence homology to members of the ligand-gated ion-channel (LGIC) family. In particular, AChBP resembles the ligand-binding site of nicotinic ACh receptors. In a companion paper, Brejc *et al*. report that they have solved the crystal structure of AChBP and, indirectly, gained new insights into the atomic structure of the ACh-receptor binding site. As predicted for the ACh receptor, AChBP forms pentamers in which the

ligand-binding site is located at the interface between subunits. The authors identified the residues that form the binding site and noted that they are quite variable among LGICs, reflecting perhaps their different binding properties. By contrast, residues conserved between AChBP and LGICs do not contribute to ligand binding but seem to stabilize the global structure of each subunit.

So, in addition to re-emphasizing the influence of glial cells on neurotransmission, the study of AChBP constitutes a double triumph, providing the first detailed three-dimensional account of the ACh binding site. This information will have a great influence on the structural analysis of other LGICs, comparable only to the impact that the structure of KcsA has had on the study of other voltage-gated ion channels.

References and links

ORIGINAL RESEARCH PAPER

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back to top