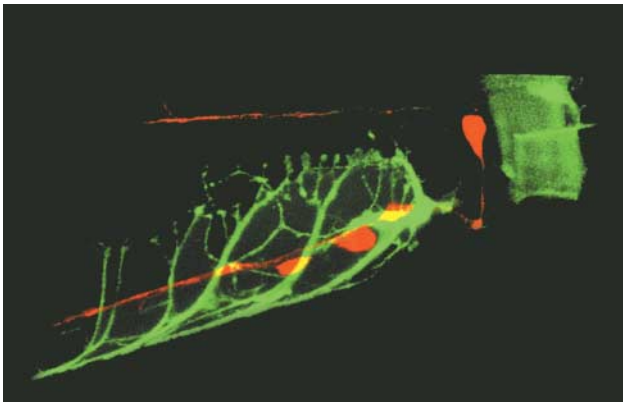

The tail of a *C. elegans* adult. The *exp-1* gene encoding the excitatory GABA receptor is expressed in the intestinal and anal depressor muscles (green, *Pexp-1::GFP*). The motor neuron DVB (right) innervates the enteric muscles and is one of 26 GABA neurons (red, *Punc-47::dsRedII*) in the nematode. Image, courtesy of E. Jorgensen, University of Utah.

ION CHANNELS

An exciting GABA receptor

GABA (γ-aminobutyric acid) is a classical inhibitory neurotransmitter, although it has been suggested that it might mediate excitation in some adult neurons. Beg and Jorgensen, writing in *Nature Neuroscience*, have characterized an unusual GABA receptor that is selective for cations rather than anions, giving it an excitatory effect.

The idea that GABA can be excitatory rather than inhibitory is not new — during development, for example, intracellular chloride levels are so high that activation of GABA receptors causes depolarization when Cl^- ions flow out of the cell. However, in adult nervous systems, depolarization by activation of GABA receptors would require either an effect mediated by bicarbonate efflux, as in some hippocampal neurons, or a cation-selective GABA-gated ion channel. The latter has now been characterized for the first time, in the nematode *Caenorhabditis elegans*.

The enteric muscles in *C. elegans* contract in response to GABA release from a particular pair of motor neurons, indicating that GABA might have an excitatory effect on these muscles. Beg and Jorgensen investigated mutants in which the enteric muscles failed to contract and found one, the *exp-1* mutant, in which the mutated gene was homologous to ligand-gated ion channel subunits. The EXP-1 protein was localized to sites that seemed to be neuromuscular junctions on the enteric muscles.

Further characterization showed that EXP-1 was similar to ionotropic GABA receptors in all domains except for the pore-forming domain, which confers ion specificity on the channel. When EXP-1 was expressed in *Xenopus laevis* oocytes, treatment with GABA evoked current flow with a reversal potential near 0 mV. This reversal potential, and the fact that the current did not depend on the presence of Cl^- ions in the medium, indicated that EXP-1 might be a cation channel.

By testing the current–voltage relationships with different media, the authors determined that EXP-1 is permeable to monovalent cations such as Na^+ and K^+, but not to divalent cations. Receptors like EXP-1 could mediate the excitatory effects of GABA in other invertebrates, which have been suggested to result from the presence of GABA-gated cation channels, although there is less evidence for a similar mechanism in vertebrates.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Beg, A. A. & Jorgensen, E. M. EXP-1 is an excitatory GABA-gated cation channel. *Nature Neurosci.* 12 October 2003 (10.1038/nn1136)
FURTHER READING Ben-Ari, Y. Excitatory actions of GABA during development: the nature of the nurture. *Nature Rev. Neurosci.* **3**, 728–739 (2002)

SYNAPTIC PLASTICITY

How activity shapes spines

Dendritic spines form the postsynaptic point of contact for most excitatory synapses. It is known that long-term changes in synaptic efficacy are accompanied by stabilization of spine morphology, but it is unclear exactly how synaptic activity influences spine stability. Reporting in *Nature Neuroscience*, Ackerman and Matus now propose a mechanism that relies on activity-dependent targeting of a cytoskeletal regulator to spines.

Profilin is a protein that regulates the polymerization of the main cytoskeletal element actin. Ackerman and Matus examined the distribution of profilin in relation to synaptic activity and spine motility. First, they treated hippocampal neurons in culture with glutamate, which activates postsynaptic *N*-methyl-D-aspartate (NMDA) receptors. They found that this led to an accumulation of profilin in the dendritic spines, which was blocked if the cells were treated with NMDA receptor antagonists.

The authors showed that electrical stimulation of the neurons could also cause profilin to be targeted to spines. However, only certain patterns of electrical activity were effective, and interestingly, they were the same patterns that elicit long-term alterations in synaptic efficacy.

Ackerman and Matus also showed that the stabilization of spines depended on the redistribution of profilin. They prevented profilin from accumulating in spines by transfecting neurons with a construct that encoded a cytoplasmic profilin-binding peptide. The dendritic spines on the transfected cells remained in an irregular elongated conformation instead of undergoing maturation and adopting a compact mushroom shape.

These findings indicate a model for spine stabilization, in which synaptic activity causes profilin to be targeted to spines, which in turn promotes actin polymerization. Although profilin and actin do not seem to control synaptic efficacy directly, Ackerman and Matus suggest that they might tag synapses that are destined to undergo long-term changes, thereby providing an important intermediate step in the process of memory consolidation.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Ackermann, M. & Matus, M. Activity-induced targeting of profilin and stabilization of dendritic spine morphology. *Nature Neurosci.* **6**, 1194–1200 (2003)
FURTHER READING Ottersen, O. P. & Helm, P. J. How hardwired is the brain? *Nature* **420**, 751–752 (2002) | Martin, K. C. & Kosik, K. S. Synaptic tagging — who's it? *Nature Rev. Neurosci.* **3**, 813–820 (2002)

Photograph courtesy of C. H. Morgan.