NEUROBIOLOGY

Glia and neurons in dialogue

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NEURONS are the computational elements in the brain, their function being to modify signals and transmit them to other neurons. The numerically superior glial cells merely support neuronal function by controlling the concentrations of neurotransmitters and ions outside the neurons. In a nutshell, these are the tenets that dominate current views of information processing in the brain.

Two papers, one by Parpura *et al.* on page 744 of this issue[1] and one by Nedergaard in *Science*[2], challenge this dogma by showing that rises of the calcium concentration, $[Ca^{2+}]_i$, in glial cells (astrocytes) can cause $[Ca^{2+}]_i$ rises in surrounding neurons. The implication is that glia may well be involved in information processing. But although both papers report the same basic observation, they provide contradictory data on the mechanisms by which calcium signals pass from glia to neurons.

Parpura and colleagues report that a $[Ca^{2+}]_i$ rise in cultured astrocytes, produced with bradykinin, mechanical stimulation or strong illumination, leads both to the release of the excitatory neurotransmitter glutamate from the astrocytes and to a rise in $[Ca^{2+}]_i$ in adjacent neurons. The rise in neuronal $[Ca^{2+}]_i$ could be blocked with the glutamate analogue D-2-amino-5-phosphonopentanoic acid, which suggests that it is generated by the released glutamate activating *N*-methyl-D-aspartate (NMDA) receptor channels — a type of glutamate-gated membrane ion channel which is known to have a high permeability to calcium.

Conventionally it is neurons that release glutamate in the nervous system. How might astrocytes do this? There are three well-known mechanisms of glutamate release: calcium-dependent exocytosis of glutamate stored in vesicles[3]; reversed operation of sodium-dependent uptake carriers[4], which normally remove glutamate from the extracellular space to terminate synaptic transmission; and release through a furosemide-sensitive anion channel or carrier which can be activated by astrocyte swelling[5]. Despite its calcium dependence, the glutamate release reported by Parpura *et al.* is unlikely to be by exocytosis; this is because the astrocytes studied expressed no synaptotagmin, a vesicular protein involved in calcium-dependent exocytosis[3]. Glutamate release is also unlikely to be by reversed uptake, because this process does not require a rise in $[Ca^{2+}]_i$ and because blockers of the operation of glutamate-uptake carriers did not affect glutamate release from astrocytes[1].

Finally, although Parpura *et al.* found that the bradykinin-induced glutamate release from astrocytes was blocked by furosemide, it was also blocked by removing external calcium; yet the swelling-activated, furosemide-sensitive mechanism of glutamate release studied previously[5] is unaffected by removal of calcium[6]. So unless a rise in $[Ca^{2+}]_i$ and cell swelling can independently activate glutamate release by a common mechanism, the mode of release in the latest experiments[1] remains unclear.

In contrast to the results of Parpura *et al.*, Nedergaard found that the rise in neuronal $[Ca^{2+}]_i$ evoked by a rise in glial $[Ca^{2+}]_i$ was unaffected by blocking NMDA receptors and by calcium removal, but was inhibited by agents that block gap junctions. Nedergaard therefore attributed the $[Ca^{2+}]_i$ signal to calcium release from intracellular stores, and postulated that it spread through gap junctions between astrocytes and neurons. There is no easy way to reconcile the two sets of data[1,2]: perhaps there are two independent mechanisms for transmission of calcium signals from glia to neurons.

VISION

Driven around the bend in Scotland

VEHICLE manufacturers around the world are investing a great deal in attempts to develop intelligent guidance systems. But how do human drivers use visual information from the road ahead to steer their cars? On page 742 of this issue M. F. Land and D. N. Lee address one aspect of the question — that of where drivers fixate their gaze. Using an instrumented car equipped with a computerized video monitor, the authors recorded the directions of eye and head movements as drivers negotiated a winding road. By choosing a one-way street (around Arthur's Seat, a large hill in the centre of Edinburgh), they eliminated the problem of oncoming traffic. Once stripped to its essentials, the answer turned out to be surprisingly simple: as they come around the curves, drivers show a strong tendency to fixate along a tangent from the car to the inside edge of the road (picture on the left, above). The direction of gaze is highly correlated with the direction of steering, and the authors suggest that the angle between the line of gaze and the direction of movement may be used as a simple predictor of the sharpness of the bend ahead, and hence of how the steering wheel should be positioned. Of course, human drivers are sometimes distracted (in the instance shown here, by a jogger of the opposite sex: right, above), and some are more easily distracted than others (see Fig. 1 of the paper). Nevertheless, their gaze consistently returns to the edge of the road. Besides offering the prospect of a somewhat Orwellian way of investigating our inner thoughts, these results will no doubt stimulate new approaches to the design of intelligent vehicles. It seems likely that they will also prompt further investigation into how people select visual information during the performance of other complex tasks. Charles Jennings

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