performance much sooner than wild-type mice following administration of intravenous etomidate. The reason for this was revealed by analysis of EEG patterns, which showed that slow-wave sleep was prolonged in wild-type mice during recovery from anaesthesia, whereas mutant mice had normal sleep rhythms.

Taken together, these data indicate that β2-containing $GABA_A$ receptors mediate the sedative properties of etomidate, while its anaesthetic effects are exerted through β3 subunits. This insight could lead to the development of effective anaesthetics that do not induce the 'hypnotic hangover' with which so many of us are familiar.

Suzanne Farley

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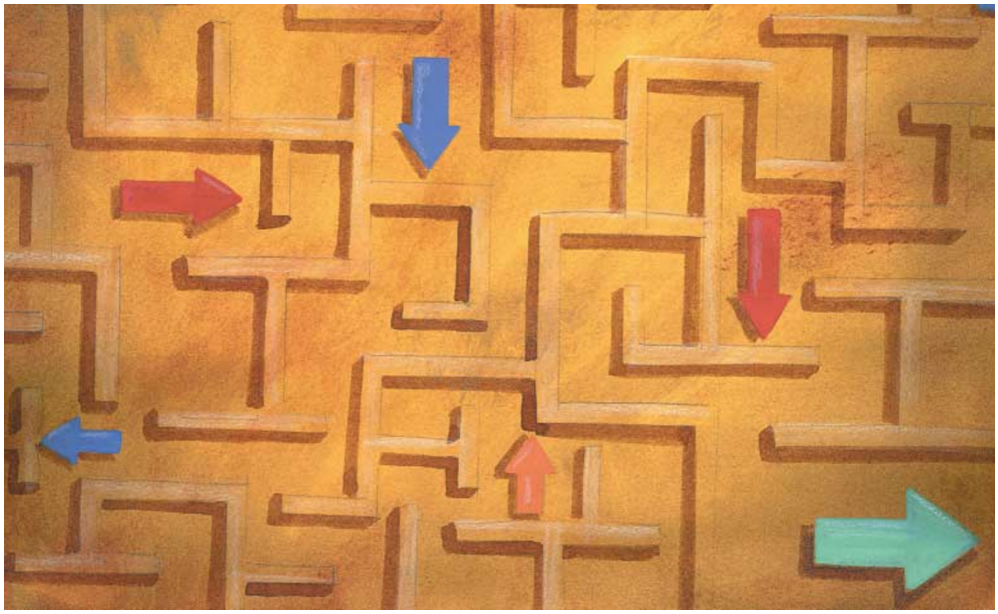
Anaesthesia: modern approaches



DEVELOPMENT

Finding the way

In the mouse visual system, most axons of retinal ganglion cells cross at the optic chiasm to project to the contralateral side of the brain. But a small proportion — about 3% — project ipsilaterally instead, allowing the development of binocular vision. In humans, the ipsilateral projection is larger, but the problem is the same. What controls this divergence of growing axons? A new study provides evidence that the ephrins and Eph receptors are involved.

Previous evidence has implicated the Eph receptors in retinal axon guidance. The two classes of Eph receptor are expressed in gradients across the retina, with EphAs being highest in the temporal retina and EphBs in the ventral retina. In addition, dorsal retinal axons that express ephrin-Bs can use EphBs as a guidance cue. But Williams *et al.* have uncovered more details of the role of Eph receptors and ephrins in retinal axon guidance.

The ganglion cells whose axons fail to cross at the midline are found in the most ventrotemporal part of the retina. Williams and colleagues found that these cells specifically express a particular Eph receptor, EphB1. They also showed that ephrin-B2, a ligand for EphB1, is expressed at the optic chiasm, and that although ephrin-B2 inhibits axon outgrowth from all ventral retinal ganglion cells *in vitro*, it is most inhibitory to the axons of cells from the ventrotemporal retina. These findings tie in with previous findings in the *Xenopus* retina, indicating that the system might be conserved.

When the researchers blocked ephrin-B2 in a coculture of retinal ganglion cells and optic chiasm cells, or in a semi-intact preparation, the treatment abolished the ability of chiasm cells to inhibit outgrowth from ventrotemporal ganglion cells. And in mice lacking the EphB1 receptor, the ipsilateral projection from the retina was greatly reduced, with more axons crossing the midline instead of being repelled by the chiasm.

These results strongly support the idea that a subset of retinal ganglion cells — those that are destined to project ipsilaterally — expresses a specific Eph receptor, EphB1, and that this receptor interacts with ephrin-B2 at the optic chiasm to prevent the axons from crossing. But the fact that the ipsilateral projection in EphB1-null mice was reduced rather than abolished indicates that other signals are also involved.

In a related study, Herrera *et al.* found that the transcription factor Zic2 is selectively expressed in the ventrotemporal subset of retinal ganglion cells that project ipsilaterally. Mice with reduced levels of Zic2 had smaller than normal ipsilateral projections, and ectopic expression of Zic2 in dorsal retinal ganglion cells *in vitro* caused the axons of those cells to become abnormally sensitive to inhibition by chiasm cells. These results raise the tantalizing possibility that Zic2 might regulate the expression of EphB1 in ventrotemporal retinal ganglion cells, and so mediate the formation of the ipsilateral visual projection.

Rachel Jones

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