off food. Interestingly, the authors found that serotonin is important under both conditions, although different signalling pathways might be activated depending on feeding status. In the absence of food, serotonin induces avoidance behaviours and requires the postsynaptic glutamate receptor GLR-1. Neither GLR-1 nor GPA-11 is involved in detecting undiluted octanol on food, and Chao and colleagues are still trying to identify the signalling components that are activated by serotonin under this condition.

It is intriguing that worms use different strategies to detect noxious stimuli depending on the strength of the signals and their feeding status. Whether this finding can help to explain serotonin-mediated behaviours in vertebrates remains to be seen.

Jane Qiu

References and links

ORIGINAL RESEARCH PAPER Chao, M. Y. *et al.* Feeding status and serotonin rapidly and reversibly modulate a *Caenorhabditis elegans* chemosensory circuit. *Proc. Natl Acad. Sci. USA* **101**, 15512–15517 (2004)

DEVELOPMENT

Dividing the diencephalon

Despite repeated attempts to define the embryonic forebrain as a segmented structure, only two true cell-lineage-restriction boundaries have been identified — the mesencephalic/synencephalic boundary and the zona limitans intrathalamica (ZLI). Reporting in *Nature Neuroscience*, Kiecker and Lumsden show that, as well as physically segregating the prethalamic and thalamic primordia in the diencephalon (the posterior subdivision of the forebrain), the ZLI provides a crucial signal that regulates regional cell identity.

In the early chick brain, the ZLI initially manifests itself as a wedge-shaped gap in the expression domain of the *lunatic fringe* gene. This wedge subsequently collapses into a narrow strip and begins to express the signalling molecule sonic hedgehog (SHH). Kiecker and Lumsden found that SHH-signal transducers and downstream targets of SHH are expressed on either side of the ZLI, confirming that SHH signalling is operational in this area.

Because of the pivotal role of SHH in embryonic development, global *Shh* knockouts in mice have not been informative about its specific role at the ZLI. Therefore, the authors used *in ovo* electroporation to manipulate SHH signalling activity in a spatiotemporally restricted manner in chick embryos, and they examined the effects of SHH gain and loss of function on the expression of various homeobox genes in the diencephalon.

Normally, the thalamus expresses *GBX2*, and is also characterized by the absence of *PAX6* expression, whereas the prethalamus expresses *DLX2* and *PAX6*. Overexpression of SHH in the diencephalon caused an expansion of the *GBX2* domain in the thalamic region and the *DLX2* domain in the prethalamic region. Moreover, *PAX6* was downregulated prematurely in the thalamus, but its expression was unaffected in the prethalamus.

To make diencephalic cells unresponsive to SHH signalling, the authors transfected the diencephalon with a DNA construct that expressed *Ptc^{Δloop2}*, a mutant form of the SHH receptor Patched. In the transfected embryos, SHH signalling was inhibited in a mosaic fashion, and there were patches of thalamic cells that did not express *GBX2* and patches of prethalamic cells that did not express *DLX2*. Most strikingly, the thalamic cells that expressed *Ptc^{Δloop2}* failed to downregulate *PAX6*, although this gene was downregulated in *Ptc^{Δloop2}*-expressing prethalamic cells. Therefore, SHH seems to have opposing effects on the thalamus and prethalamus with regard to *PAX6* expression.

The prethalamus and thalamus both seem to need SHH signalling to acquire their distinctive gene-expression profiles, but how can this single signal elicit different responses on either side of its source? Part of the answer might lie with the prepatterning gene *IRX3*, which has its anterior expression boundary at the ZLI. Ectopic expression of *IRX3* in the prethalamic region caused upregulation of thalamus-specific markers, including *GBX2*, and downregulation of *DLX2*. These effects could be rescued by expressing *Ptc^{Δloop2}* in conjunction with *IRX3*. Therefore, *IRX3* seems to make diencephalic tissue competent to acquire a thalamic identity in response to SHH.

These findings provide intriguing new insights into patterning mechanisms in the diencephalon, and the ZLI can now be added to the growing list of local signalling centres in the developing CNS.

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References and links

ORIGINAL RESEARCH PAPER Kiecker, C. & Lumsden, A. Hedgehog signaling from the ZLI regulates diencephalic regional identity. *Nature Neurosci.* **7**, 1242–1249 (2004)

FURTHER READING Puellas, L. & Rubenstein, J. L. Forebrain gene expression domains and the evolving prosomeric model. *Trends Neurosci.* **26**, 469–476 (2003) | Gómez-Skarmeta *et al.* Half a century of neuronal prepatterning: the story of a few bristles and many genes. *Nature Rev. Neurosci.* **4**, 587–598 (2003)