NEURONAL MIGRATION

Reelin out the hindbrain nuclei

The extracellular matrix protein reelin (RELN) is best known for regulating the radial migration of neurons in the developing neocortex, and it seems to function similarly in other parts of the brain, including the cerebellum and hippocampus. Reporting in *Development*, Rossel and colleagues show that RELN is also required in the hindbrain, where it controls a specific step in the positioning of certain motor nuclei.

It has previously been shown that reeler mutant mice, which lack RELN function, show disorganization of cells in various hindbrain nuclei. However, until now neuronal migration in the hindbrain had not been investigated in detail. Rossel *et al.* focused on two neuronal populations — the olivocochlear (OC) nucleus and the facial visceral motor (FVM) nucleus. During development, the motor neuron precursors (MNPs) that contribute to these nuclei show similar migration patterns in the neural tube: first, they migrate out laterally from the proliferative zone, then they migrate radially to adopt their final position at the ventral pial surface.

In reeler mutant mouse embryos, the initial lateral phase of migration was unaffected, but the MNPs failed to migrate radially, and they remained in an abnormally dorsal position. Despite their ectopic position, the MNPs expressed the normal range of molecular markers that are associated with motor neuron and OC efferent differentiation, so neuronal specification did not seem to be affected.

The authors found that in wild-type embryos, RELN is expressed in the region of the neural tube where migration of the OC and FVM neurons terminates. The MNPs themselves express disabled homologue 1 (DAB1) — an effector molecule that activates intracellular signalling pathways in response to the binding of RELN to its receptors. *Dab1* mutant mice (also known as scrambler mice) showed the same hindbrain phenotype as the reeler mutants.

Rossel *et al.* conclude that the OC and FVM cell migration pathways can be divided into two discrete steps — a RELN-independent lateral step, and a RELN-dependent radial step. The identity of the receptors that mediate the RELN-dependent step is still unknown: in embryos that lacked the RELN receptors APOER2 (apolipoprotein E receptor 2) and VLDLR (very low-density lipoprotein receptor), the OC and FVM nuclei were normally positioned. Therefore, further work will be required to identify the receptors that mediate the effects of RELN in the hindbrain.

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References and links

ORIGINAL RESEARCH PAPER Rossel, M. *et al.* Reelin signaling is necessary for a specific step in the migration of hindbrain efferent neurons. *Development* **132**, 1175–1185 (2005)

FURTHER READING Tissir, F. & Goffinet, A. M. Reelin and brain development. *Nature Rev. Neurosci.* **4**, 496–505 (2003)