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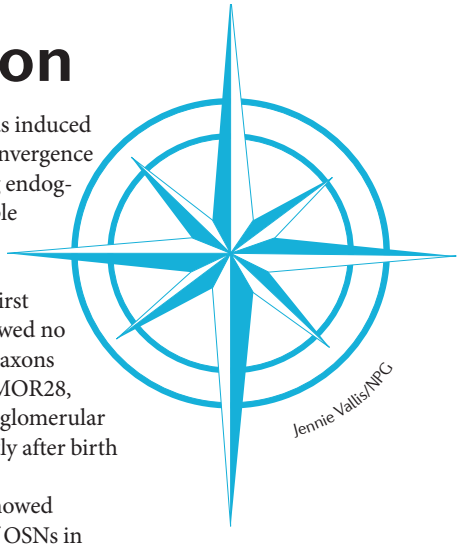
OLFACTION

Critical timing in mapping olfaction



Whether there are critical periods — phases of heightened plasticity in response to stimuli — in the development of the mammalian olfactory system has been unclear, not least because this sensory system exhibits a high level of plasticity throughout an animal's lifespan. However, two new studies reveal a critical period in olfactory bulb development during which the glomerular map is established.

The axons of mammalian olfactory sensory neurons (OSNs) project from the nasal cavity to structures in the olfactory bulb, termed glomeruli. OSNs each express one type of olfactory receptor, and axons of OSNs expressing the same olfactory receptor type project to the same glomerulus. Thus, OSNs form a sensory map — the glomerular map — whereby odours can be characterized by the glomeruli that they activate. In mice, this map appears during the perinatal period.

To investigate whether there is a critical period in glomerular map formation, Ma and colleagues followed the expression of three different olfactory receptors in a transgenic mouse line in which OSNs ectopically expressed inward rectifier K^+ channel Kir2.1 in the absence of doxycycline. Ectopic Kir2.1 expression suppressed OSN activity and disrupted the targeting of OSNs expressing the same type of olfactory receptor to the same glomerulus. Mice that were fed doxycycline to suppress ectopic OSN Kir2.1 expression from birth developed normal glomerular maps. However, suppression of such expression after postnatal day 7 (P7) was associated with abnormal glomerular map formation.

These findings suggested that glomerular map formation is sensitive to disturbance of OSN neural activity between birth and P7. However, the authors found that mice in which lamin B receptor (LBR) was ectopically expressed in OSNs, leading to abnormal olfactory receptor gene expression, also showed abnormal glomeruli innervation and that suppressing LBR expression before but not after P7 enabled largely normal glomerular map formation. Thus, disruption of a developmental programme in OSNs — rather than suppression of neural activity per se — during this time window disrupts glomerular map formation.

Tsai and Barnea investigated the existence of olfactory system critical periods by inducing the expression of a transgenic copy of the gene encoding the olfactory receptor MOR28 in a small proportion of OSNs and assessing the effects of such expression on OSNs that expressed this receptor endogenously. They showed that mice in which ectopic expression of transgenic MOR28 was induced before birth exhibited convergence of OSN axons expressing endogenous MOR28 on multiple glomeruli. By contrast, animals in which transgenic MOR28 was first expressed after birth showed no such misrouting of OSN axons expressing endogenous MOR28, again indicating that the glomerular map stabilizes at or shortly after birth in mice.

Finally, the authors showed that chemical ablation of OSNs in 2-month-old mice that expressed transgenic MOR28 from birth, but in which such expression was prevented thereafter, still led to misrouting of OSNs expressing endogenous MOR28, as the OSNs regenerated. This finding supports the idea that markers for OSN routing are put in place only during glomerular map formation.

The findings of these two studies thus provide evidence for a critical period in the development of the olfactory system in mice.

Darran Yates

ORIGINAL RESEARCH PAPERS Ma, L. *et al.* A developmental switch of axon targeting in the continuously regenerating mouse olfactory system. *Science* **344**, 194–197 (2014) | Tsai, L. & Barnea, G. A critical period defined by axon-targeting mechanisms in the murine olfactory bulb. *Science* **344**, 197–200 (2014)

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