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SENSORY SYSTEMS

Connecting olfaction

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The mammalian olfactory bulb (OB) contains parvalbumin-expressing (PV+) GABAergic interneurons, but their functional role in this structure is poorly understood. Two new studies reveal that these interneurons form extensive connections with mitral cells and tufted cells — the major output neurons of the OB — and have a role in odour processing.

To assess neural connectivity in the OB, Miyamichi, Shlomai-Fuchs *et al.* used a rabies virus-mediated monosynaptic tracing system, in which the expression of virus-encoded green fluorescent protein (GFP) is used to determine presynaptic connections. Following infection of mitral cells and tufted cells, they identified a large population of broadly distributed GFP-expressing cells in the external plexiform layer (EPL) of the OB. These cells had star-like morphologies that resembled interneurons and expressed PV, suggesting that PV+ interneurons are the main presynaptic partners of mitral and tufted cells in the EPL. Conversely, application of the tracing method to the PV+ interneurons revealed broadly distributed mitral cells as the main presynaptic partners of these interneurons.

Kato *et al.* used transgenic mice in which PV+ interneurons expressed the fluorescent reporter tdTomato to examine PV+ interneuron circuitry in the OB. They showed that tdTomato expression in the OB was mainly localized to the EPL, specifically in cells that had multipolar dendrites, and current-clamp recordings in slices revealed that these cells had electrophysiological properties resembling those of fast-spiking cortical PV+ interneurons. Furthermore, paired recordings of mitral cells and PV+ interneurons in the OB showed that action potentials generated in mitral cells elicited fast excitatory postsynaptic currents in PV+ interneurons, whereas action potentials generated in many PV+ interneurons induced inhibitory postsynaptic currents in mitral cells. Thus, together with the findings of Miyamichi, Shlomai-Fuchs *et al.*, these data reveal the high reciprocal connectivity between the two cell types and that PV+ interneurons are a major source of inhibition of mitral cells.

To examine the responsiveness of PV+ interneurons to odours, Miyamichi, Shlomai-Fuchs *et al.* also used mice expressing tdTomato in PV+ interneurons. They exposed anaesthetized animals to five different monomolecular odours and found that many PV+ interneurons in the OB were activated by three or more of the odours. Kato *et al.* also examined odour responses in OB PV+ interneurons, this time in awake mice, through the expression of GCaMP5G (a genetically encoded calcium indicator) in these cells and two-photon calcium imaging. PV+ interneurons showed robust increases in the level of calcium after the presentation of any one of seven tested odours. Together, these findings show that PV+ interneurons in the OB are broadly tuned to odours.

Interestingly, Kato *et al.* found that inactivation of PV+ interneurons enhanced the magnitude of odour-evoked responses in mitral cells in a linear fashion, although the tuning of mitral cells to specific odours remained largely unchanged after such inactivation. This finding led these authors to propose that PV+ interneurons exert a gain control function on mitral cell output.

Together, these studies show that PV+ interneurons are major regulators of excitatory cell output and hence sensory processing in the OB.

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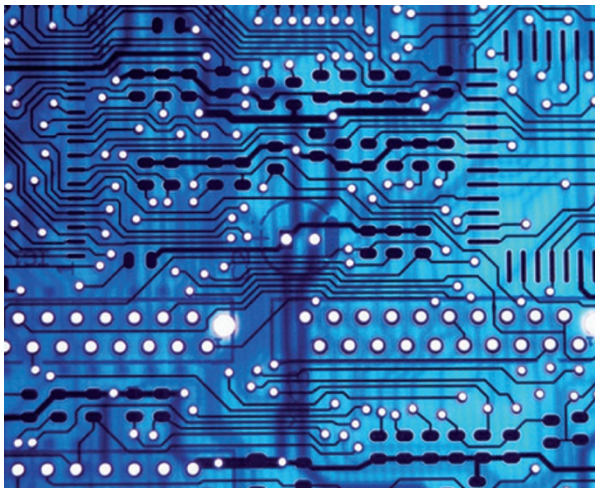

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ORIGINAL RESEARCH PAPERS Miyamichi, K. *et al.* Dissecting local circuits: parvalbumin interneurons underlie broad feedback control of olfactory bulb output. *Neuron* http://dx.doi.org/10.1016/j.neuron.2013.08.027 (2013) | Kato, H. K. *et al.* Parvalbumin-expressing interneurons linearly control olfactory bulb output. *Neuron* http://dx.doi.org/10.1016/j.neuron.2013.08.036 (2013)