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Review

Construction of functional neuronal circuitry in the olfactory bulb

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ABSTRACT

Recent studies using molecular genetics, electrophysiology, in vivo imaging, and behavioral analyses have elucidated detailed connectivity and function of the mammalian olfactory circuits. The olfactory bulb is the first relay station of olfactory perception in the brain, but it is more than a simple relay: olfactory information is dynamically tuned by local olfactory bulb circuits and converted to spatiotemporal neural code for higher-order information processing. Because the olfactory bulb processes ~1000 discrete input channels from different odorant receptors, it serves as a good model to study neuronal wiring specificity, from both functional and developmental aspects. This review summarizes our current understanding of the olfactory bulb circuitry from functional standpoint and discusses important future studies with particular focus on its development and plasticity.

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Abbreviations: AONpE, anterior olfactory nucleus pars externa; EPL, external plexiform layer; HDB, the horizontal limb of the diagonal band of Broca; OB, olfactory bulb; OR, odorant receptor; OSN, olfactory sensory neurons; PV, parvalbumin; SVZ, subventricular zone.

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1. Introduction

Studies of the olfactory bulb (OB) have a long history. Over a hundred years ago, Camillo Golgi and Ramon y Cajal used the Golgi staining method to study OB circuits in various species, and proposed information flow in the OB, for both sensory inputs and centrifugal feedback [1]. However, our clear-cut understanding of the OB circuitry came relatively recently, after the molecular cloning of odorant receptors (ORs) [2].

In the mammalian olfactory system, odorants are detected by ~1000 types of ORs expressed by olfactory sensory neurons (OSNs). Each olfactory sensory neuron expresses a single type of OR out of ~1000, and OSNs expressing the same type of OR converge their axons to a spherical structure in the OB, called glomerulus [3]. Thus, a glomerulus is a functional unit in the OB representing sensory inputs from a single type of OR. Within a glomerulus, odor information is relayed to the second-order neurons, mitral and tufted cells. However, the OB is not just a relay station: mitral/tufted cells are heavily modulated by intrabulbar circuits and centrifugal inputs. Such modulations shape and produce a unique odor code by these neurons. Recent studies incorporating molecular genetics, electrophysiology, in vivo imaging, and behavioral analyses have begun to reveal how odor information is encoded in the OB and how distinct circuits mediate various aspects of olfactory information processing.

These studies also raised intriguing questions in circuit formation. Because the OB is composed of ~1000 different parallel channels from different ORs, the OB has to face a challenging task in its wiring process. Thus, the OB would be an ideal model system, not only to understand sensory information processing, but also to investigate the origin of neuronal wiring specificity in the brain. This review describes our current understanding of OB circuit function and discusses the development of wiring specificity in the OB. Due to space limitation, this review will only focus on OB circuitry and does not mention mechanisms of olfactory map formation by OSNs, which has been discussed previously [4–6]. For introduction to olfactory cortical circuitry, please see the following recent excellent reviews [7,8].

2. Odor information processing in a glomerulus

2.1. Synaptic transmission in a glomerulus

Odor information detected by OSNs is first processed in glomeruli of the OB (Fig. 1A). OSNs expressing a given type of an OR typically project their axons to two glomeruli in an OB, one in medial and the other in lateral side. Each glomerulus receives axons from a single type of OSNs expressing a common OR. In mice, a typical glomerulus receives ~1,000 OSN axons. OSN axon terminals release glutamate to post-synaptic neurons. Post-synaptic neurons include two major types of glutamatergic neurons, mitral cells and tufted cells. In addition, GABAergic periglomerular cells and short axon cells located in a juxtaglomerular area also receive direct inputs from OSN axons.

A typical glomerulus is innervated by primary dendrites of 20–50 mitral/tufted cells, among which 5–20 are mitral cells [9,10]. Each of these neurons extends a single apical dendrite to a single glomerulus, where their tufts ramify within the glomerulus. They also extend long lateral dendrites (up to 1 mm long) within the external plexiform layer, where they synapse with GABAergic interneurons.

OB interneurons are diverse in terms of molecular markers. However, a typical periglomerular cell exclusively ramifies their dendrites within a single glomerulus. Periglomerular cells can be classified into calretinin-positive and calbindin-positive neurons, although their functional distinctions remain elusive. Periglomerular cells are activated by OSN, tufted cells, and mitral cells, and in turn send GABAergic inhibition back to all of them, as well as for neighboring periglomerular cells [11]. Many of these inhibitory synapses are known to be reciprocal synapses where pre- and post-synapses are closely located, and GABA release is controlled by dendritic Ca^{2+} spikes rather than action potentials.

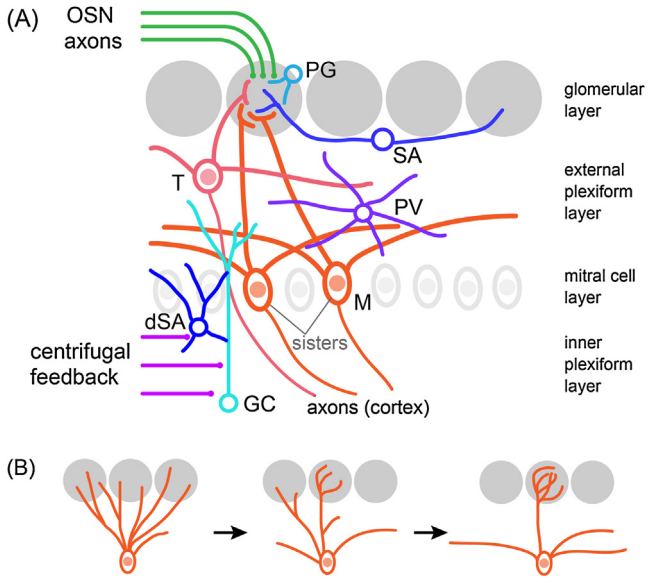

Fig. 1. OB circuitry. (A) Organization of a glomerular circuitry. Each glomerulus receives convergent axonal inputs from OSNs expressing a given OR. OSNs release glutamate to tufted, mitral, periglomerular, and short axon cells. Periglomerular cells send GABAergic inhibition to other neurons as well as to OSN axon termini. Short axon cells are GABAergic and dopaminergic and mediate lateral inhibition among glomeruli. PV neurons form dense connections with numerous mitral/tufted cell dendrites and control global gain. Granule cells and deep short axon cells receive centrifugal feedback from olfactory cortex, leading to inhibition or disinhibition of mitral/tufted cells. Mitral/tufted cells associated with a common glomerulus are called 'sister' cells. (B) Dendrite pruning of mitral/tufted cells. Mitral/tufted cells initially extend multiple dendrites to multiple glomeruli (left). During early postnatal period, they prune all but one primary dendrite and eventually establish a single primary dendrite [44]. A mature mitral/tufted cell typically possesses a single primary dendrite and several lateral dendrites (right). OSN, olfactory sensory neuron; PG, periglomerular cell; SA, short axon cell; PV, parvalbumin-expressing interneuron; T, tufted cell; M, mitral cell; dSA, deep short axon cell; GC, granule cell.