3. Periglomerular cells (inhibitory interneurons)

- Spherical structures where ORNs synapse with:

Olfactory bulb

In most vertebrates, the olfactory bulb is the brain's most rostral (forward) part. In humans, however, the olfactory bulb is on the brain's inferior (bottom) side. The olfactory bulb is supported and protected by the cribriform plate of the ethmoid bone, which in mammals separates it from the olfactory epithelium, and which is perforated by olfactory nerve axons. The bulb is divided into two distinct structures: the main olfactory bulb and the accessory olfactory bulb.

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Neurobiology

The **olfactory bulb** is a critical brain structure involved in the **processing of smell (olfaction)**. It plays an essential role in the detection, discrimination, and perception of odors.

Anatomy of the Olfactory Bulb

- **Location**: Just above the nasal cavity and beneath the frontal lobes. - **Structure**: Bilateral, with each bulb connected to one nasal passage. - **Layers**: Organized in distinct layers, from outer to inner: 1. **Olfactory nerve layer** – axons from olfactory receptor neurons (ORNs).

- 2. Glomerular layer initial synapse site.
- 3. External plexiform layer dendrites of mitral and tufted cells.
- 4. Mitral cell layer large principal output neurons.
- 5. Internal plexiform layer
- 6. **Granule cell layer** interneurons for lateral inhibition.

Functional Circuitry

Olfactory receptor neurons (ORNs)

- Located in the **olfactory epithelium** of the nasal cavity. - Each ORN expresses **one type of odorant receptor** and projects to a specific **glomerulus** in the olfactory bulb.

Glomeruli

1. Mitral cells



- **Each glomerulus receives input from ORNs expressing the same receptor**, creating a spatial map of odors.

Mitral and Tufted cells

- Principal output neurons of the olfactory bulb. - Send signals to:

- 1. Olfactory cortex
- 2. Amygdala
- 3. Entorhinal cortex

- Receive modulation from granule cells via dendrodendritic synapses (inhibitory).

Granule cells

- Inhibitory interneurons (GABAergic). - Enable **lateral inhibition**—sharpens odor representations by dampening neighboring mitral cell activity.

Neurotransmitters Involved

- **Glutamate**: excitatory output from mitral/tufted cells. - **GABA**: inhibition from periglomerular and granule cells. - **Dopamine, norepinephrine, acetylcholine**: modulatory inputs from other brain regions (e.g., locus coeruleus, basal forebrain).

Functional Highlights

- **Pattern recognition**: The olfactory bulb transforms chemical odor signals into spatial and temporal neural codes. - **Plasticity**: The bulb exhibits **experience-dependent plasticity**, e.g., during learning of new odors. - **Neurogenesis**: One of the few brain areas where **adult neurogenesis** occurs—new granule and periglomerular cells from the subventricular zone.

Projection Targets

- **Piriform cortex** (primary olfactory cortex) - **Amygdala** (emotional response to odors) - **Entorhinal cortex** (link to memory) - **Orbitofrontal cortex** (conscious perception of smell via thalamus)

Important role in neurosurgery

The **olfactory bulb** plays a nuanced but important role in neurosurgery, especially in skull base and anterior cranial fossa procedures. Here's a breakdown of its **clinical and surgical relevance**:

[] What is the Olfactory Bulb? - A paired structure located on the inferior surface of the frontal lobe. - First relay station in the **olfactory pathway**, receiving input from the olfactory nerves (CN I) and transmitting signals to the olfactory cortex.

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[] Surgical Importance 1. Skull Base Surgery

- 1. In **anterior cranial fossa meningiomas** (e.g., olfactory groove meningiomas), the olfactory bulbs are often compressed, displaced, or sacrificed for tumor access.
- 2. Surgeons must balance oncological resection with preservation of olfaction, especially in **unilateral lesions**.

2. Endoscopic Endonasal Approach (EEA)

- 1. Used for accessing lesions at the planum sphenoidale, tuberculum sellae, and crista galli.
- 2. These procedures risk damaging the olfactory bulb and tract, potentially leading to **anosmia**.

3. Trauma and CSF Leak Repair

- 1. In patients with **cribriform plate fractures** or **CSF rhinorrhea**, the olfactory bulb may be exposed or damaged.
- 2. During surgical repair, the bulb may need to be handled carefully or even resected, depending on the context.

4. Epilepsy Surgery

- 1. Rarely, the olfactory bulb/tract may be involved in seizure propagation or aura (olfactory hallucinations).
- 2. Not a typical target, but important in presurgical mapping.

[] Functional & Psychological Implications - Anosmia is often dismissed but can significantly impact quality of life, nutrition, and even safety (e.g., detecting gas leaks). - Postoperative olfactory dysfunction can contribute to **depression**, especially if bilateral. - In **neurodegenerative diseases** (e.g., Parkinson's, Alzheimer's), early olfactory bulb changes may offer a diagnostic clue.

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[] Key Points for Neurosurgeons - Always assess baseline olfaction in anterior skull base surgeries. - Consider olfactory preservation in surgical planning when feasible. - Inform patients of the risk of postoperative anosmia, especially if bilateral approaches are planned. - Intraoperative neuronavigation and endoscopy help minimize collateral damage.

Let me know if you want an illustrated diagram or a slide for teaching purposes.

Research studies

In the olfactory bulb (OB), odorant receptor-specific input converges into glomeruli. Subsequently, the coding of odor information is fine-tuned by local synaptic circuits within the glomeruli and the deeper external plexiform layer (EPL) in the OB. Deciphering the organization of inhibitory granule cells (GCs) in the EPL relative to the secondary dendrites of projection neurons is pivotal for understanding odor processing. Liberia et al. conducted a detailed investigation of GCs, focusing on the timing of neurogenesis, laminar distribution, and synaptogenesis between GCs and projection neurons. In summary, GCs develop following a developmental continuum with an outside-in maturation pattern from embryogenesis to adulthood. GCs born 1 week after birth display a unique sublayer-specific distribution pattern, marking a transition between embryonic or neonatal and adult stages. Integration into reciprocal synaptic circuits occurred 10 days post-neurogenesis. They conclude that the timing of neurogenesis dictates the anatomical configuration of GCs within the OB, which, in turn, regulates preferential synaptic integration with either mitral cell or tufted cell secondary dendrites ¹⁾.

This study by Liberia et al. makes a significant contribution to the developmental neurobiology of the olfactory bulb by establishing a link between the timing of neurogenesis and the microanatomical organization of granule cells. The findings support the idea that temporal patterning is a crucial determinant of inhibitory circuit architecture and suggest a functional subdivision of GCs based on birthdate.

For future research, incorporating functional imaging, electrophysiological validation, and behavioral correlates would elevate these findings from anatomical mapping to a more comprehensive understanding of OB circuit function. Additionally, examining whether similar principles apply in neurogenic zones of other brain regions (e.g., hippocampus) could generalize this framework across sensory and cognitive systems.

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Liberia T, Han K, Spence NJ, Meller SJ, Martin-Lopez E, Greer CA. Timing Matters: Lessons From Perinatal Neurogenesis in the Olfactory Bulb. J Comp Neurol. 2025 Apr;533(4):e70045. doi: 10.1002/cne.70045. PMID: 40128105.

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