Anterior Olfactory Nucleus

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Synonyms

Anterior olfactory cortex

Definition

The primary component of the region of the telencephalon located between the olfactory bulb and the ►piriform cortex.

Characteristics

The olfactory system is highly developed in vertebrates, particularly in "macrosmic" mammals (such as many rodents) where olfaction is the primary sensory system used to navigate in the world. As olfactory ability has evolved, there has been a concurrent increase in the size and complexity of cortical structures dedicated to encoding and deciphering olfactory information (►cortical circuitry). Below is an overview of one of these cortical regions, the ►anterior olfactory nucleus (AON), which plays a central, though largely uncharted role in olfactory information processing.

In vertebrates, odor information is transduced by olfactory receptor neurons that line the nasal cavity (or olfactory rosette in fishes). The information is sent via the olfactory nerve (Cranial Nerve I) to the olfactory bulb, an evagination of the ventral forebrain that is the rostral-most portion of the telencephalon and is commonly found just behind (or above) the nasal cavity. The general circuitry of the olfactory bulb is similar to that of the retina in that a) incoming sensory information is parsed into separate data streams, and b) it contains two layers of inhibitory interactions to reinforce the differences between these data channels. Axons of the two major output neurons, the mitral and tufted cells, travel caudally and ventrally in the bulb, coalescing to form the lateral olfactory tract (LOT) that courses along the ventrolateral surface of the forebrain.

The area directly behind the olfactory bulb is often referred to as the ►olfactory peduncle (or retrobulbar area, Fig. 1). The peduncle contains the anterior olfactory nucleus (AON) as well as two other much smaller regions, the *tenia tecta* (or dorsal hippocampal rudiment) and the dorsal penduncular cortex. The olfactory peduncle merges caudally with the ►olfactory tubercle on the medial side and with the piriform cortex laterally. The core of the peduncle is formed by a subependymal layer that is continuous with the rostral extension of the lateral ventricle, and comprises the "rostral migratory stream" that provides new interneurons to the olfactory bulb throughout life. Overlying the rostral migratory stream is the anterior or olfactory limb of the anterior commissure, the source of centrifugal fibers, including some from the medial forebrain bundle, to the region.

The Anterior Olfactory Nucleus is Comprised of two Separate Structures

The first is a thin ring of cells encircling the rostral end of the olfactory peduncle known as "*pars externa.*" *Pars externa* contains large cells with apical dendrites that have long and thin dendritic spines. Evidence gathered from injections of neuronal tracers suggests that there are topographical projections from the olfactory bulb to *pars externa*: cells in the lateral and medial portions of the bulb project to corresponding regions in *pars externa*. No evidence for patterning in the rostral-caudal dimension has been reported. Axons from *pars externa* travel via the anterior commissure to the contralateral olfactory bulb where they synapse in the internal plexiform layer.

The second and largest region, "*pars principalis,*" appears as a two-layered structure in coronal sections from rodents (Fig. 1). The deepest (Layer II) is a thick ring of cell bodies surrounding the anterior limb of the anterior commissure. Many of the resident neurons are similar to neocortical pyramidal cells with a thick apical dendrite, several basal dendrites, and dense dendritic spines. The outer layer has been subdivided into a superficial zone (Layer Ia, which contains the output axons from the olfactory bulb) and a deeper area (Layer Ib) where these axons synapse with the dendrites of Layer II neurons. The subdivisions of Layer I are easily discernable in Nissl-stained sections based on patterns of glial staining.

Since the only landmark in *pars principalis* is a small, cell-free gap in the ventromedial region of Layer II

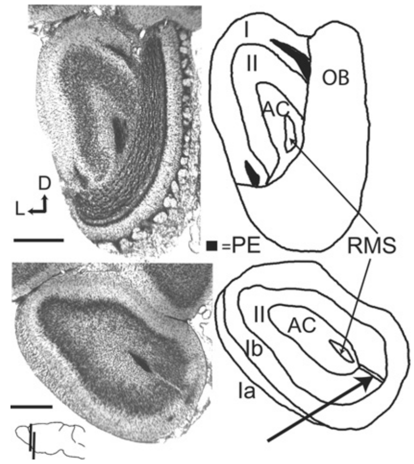
(Fig. 1), most studies divide the region on the basis of the "compass points," yielding *pars dorsalis*, *pars ventralis*, *pars medialis*, *pars lateralis*, and *pars posterioralis* (often combined with *pars ventralis* to form *"pars ventroposterioralis"*). However, since there are few obvious ways to make these subdivisions, the boundaries employed are often arbitrary and exhibit wide variations, leading to considerable confusion.

Pars lateralis is often defined as the area that lies directly under the major portion of the lateral olfactory tract. Caudally, *pars lateralis* merges with the piriform cortex. The transition occurs with the emergence of a deep polymorphic cell layer (Layer III, the "polymorphic cell zone" of the piriform cortex), and the emergence of the pre-endopiriform and endopiriform nuclei.

Pars medialis appears in anterior regions caudal to the remnant of the granule cell layer of the olfactory bulb. In posterior regions the structure is replaced by the ventral tenia tecta. The ventral border of the subregion is the cell-free notch in Layer II, while the dorsal border can be difficult to delineate and is often determined by examining variations in cell size and density.

Pars dorsalis is typically defined by exclusion: it is found between *pars lateralis* and *pars medialis* on the dorsal aspect of the AON. The superficial plexiform layer overlying both *pars dorsalis* and *pars medialis* has few myelinated fibers except in the area of transition with *pars lateralis*, reflecting a relatively small innervation by the olfactory bulb. The caudal border of *pars dorsalis* occurs with the emergence of the dorsal peduncular cortex and the transition zone between the AON and the frontal neocortex.

Pars ventralis can also be defined by exclusion as the area between *pars lateralis* and *pars medialis* on the ventral surface. It is relatively small, often only slightly larger than *pars medialis* in coronal sections. In caudal areas, *pars ventralis* merges with *pars posterioralis*. In posterior regions this area forms the caudomedial boundary of the AON with the olfactory tubercle.



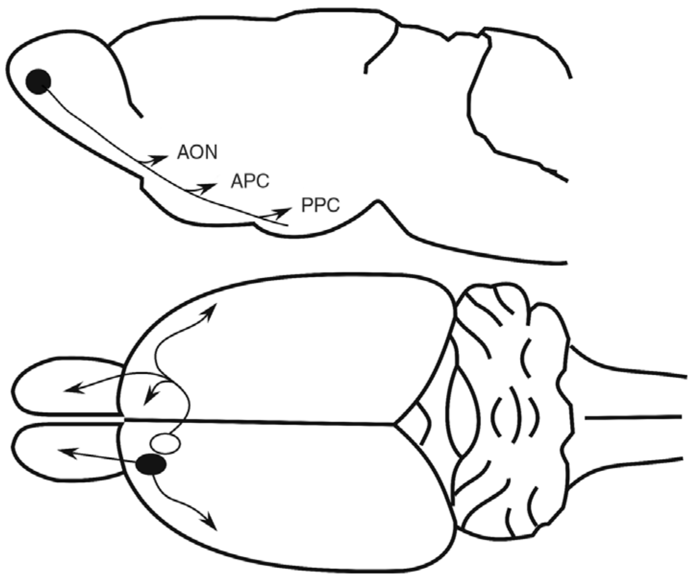
Anterior Olfactory Nucleus. Figure 1 *Left panels*: Photomicrographs of coronal Nissl-stained sections at two levels of the rat olfactory peduncle (Small panel on bottom left shows the approximate location of these two sections). *Right panels*: diagrams of cytoarchitectural features in the left panels. The two top panels show an anterior section that includes *pars externa* (PE). The bottom panels depict a section approximately 600 μm more caudal, where *pars principalis* predominates. Abbreviations: *I* = Layer I of the AON; *Ia, Ib* = sublaminae within Layer I; *II* = Layer II of *pars principalis*; *LOT* = Lateral olfactory tract; *RMS* = Rostral migratory stream; *AC* = Anterior limb of the anterior commissure; *OB* = Olfactory bulb; *D*, *L* = dorsal and lateral. Scale bars = 150 μm.

Role in the Olfactory Information Processing

The position of the AON in the olfactory circuit suggests that it plays a crucial role in olfactory information flow (Fig. 2). The fact that the region receives a substantial input from the olfactory bulb has been known for a century; indeed, Ramon y Cajal formed his "law of dynamic polarization" (information flows from the axon of one cell to the dendrites of the next) partly by observing the projection of mitral and tufted cell axons onto the dendrites of AON cells. There is a broadly topographical organization in the anterior olfactory peduncle and LOT, with fibers from the dorsal olfactory bulb contacting the dorsal AON, ventral bulb to ventral AON, etc. The LOT continues through the olfactory peduncle to innervate the piriform cortex. The projection appears to be organized in that deep relay cells in the bulb (e.g., mitral cells and the deep tufted cells) send axons all the way to the entorhinal cortex while more superficial tufted cells rarely project caudal to the AON and rostral piriform cortex. Evidence for more specific topographical patterns is difficult to find, indeed, it appears that individual projection neurons innervate broad regions in both the AON and PC.

The AON sends a substantial reciprocal input back to the olfactory bulb. The connections are so widespread that the AON is capable of interacting at nearly every synaptic step in bulb processing. Significant regional differences have been observed these projections. Converging evidence indicates that *pars medialis* fibers are heaviest in the deep granule cell layer of the ipsilateral bulb, while *pars externa* predominately innervates the contralateral internal plexiform layer. The remaining regions have bilateral projections to broader regions.

The AON projects predominantly to the ventromedial portion of anterior piriform cortex (APC), primarily to the region deep to the LOT and extending from the olfactory tubercle laterally to just beyond the border of the LOT. Axons run primarily in deep Layer Ib, adjacent to the compact cell body layer. A broad topography exists, with the heaviest projections from *pars dorsalis*, *pars lateralis* and *pars ventroposterioralis* going to the



Anterior Olfactory Nucleus. Figure 2 Schematic view of a mouse or rat brain from the lateral (*top*) and dorsal (*bottom*) sides. Top panel depicts the trajectory of the lateral olfactory tract, leaving the olfactory bulb (*on left*) and distributing information to the anterior olfactory nucleus *AON*, anterior piriform cortex *APC* and posterior piriform cortex *PPC*. Bottom panel shows the ipsilateral (*bottom*) projections of the AON (to the olfactory bulb and anterior piriform cortex) and contralateral (*top*) projections (to opposite AON, olfactory bulb, and APC).

dorsolateral, central, and ventromedial APC respectively. There is an abrupt decrease in labeled fibers at the boundary with the posterior piriform cortex.

Back-projections from the piriform cortex to the AON are also complex. The APC projects primarily to *pars lateralis*, with a smaller projection to both *pars dorsalis* and *pars ventroposterioralis*, and maintains the broad medial-to-lateral topography displayed in the projections from AON. Interestingly, connections from PPC to the AON are apparently plentiful to all parts of the AON except for *pars externa*.

While much remains to be learned about the precise nature of the projections into and out of the AON, it is obvious that the region is involved in the feedforward regulation of information passing from the bulb to the anterior piriform cortex, and in the feedback regulation of the return circuit. Further, it regulates information flow between the left and right olfactory bulbs via the anterior commissure, and it serves a similar role in distributing information to the left and right piriform cortices.

Development

AON neurons in the rat are generated during the last week of embryonic development in two distinct patterns. All divisions exhibit a caudal-to-rostral gradient of neurogenesis similar to that seen in the PC. A second superficial-to-deep gradient is also observed which contrasts with the "inside-out" sequence typical of cortical areas. Patterns of axonal ingrowth from the bulb follow the sequence of cell proliferation. Axonal projections from *pars externa* develop sooner than those from other, deeper AON regions. Similarly, the earliest contralateral projections of *pars lateralis* arise from its caudal- and superficial-most regions, while more rostral, deeper cells send projections 2–3 days later. Finally, three different patterns in the postnatal growth of the subregions of the AON have been reported: a) relatively little expansion (*pars lateralis*), b) moderate growth with overshooting of size and subsequent reduction (*pars medialis*), and c) exuberant growth with subsequent size reduction (*pars dorsalis* and *pars ventroposterior*). Such independent development of the various subregions is compelling evidence that they may serve different functions.

Anterior Olfactory Nucleus or Anterior Olfactory Cortex?

Several have suggested that the AON would more properly be labeled the anterior ►olfactory cortex. Arguments include the fact that the area is rigidly laminated and populated by pyramidal-shaped cells characteristic of the cerebral cortex, and that it gradually merges with the three-layered piriform cortex. An argument based on functional attributes has been made by Haberly, who suggested that the AON shares features with the primary sensory cortices of other sensory modalities. Haberly split the traditional AON into two functionally distinct areas (the "anterior" and "medial" olfactory cortices), opening the door for further research examining regional differences within the structure. In light of its substantial connections with both the olfactory bulb and the piriform cortex, the AON is likely to play a central role in olfactory information processing; understanding this role will lead to a more complete understanding of vertebrate olfaction.

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References

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