REVIEW *Anatomy*

Phylogenic Outline of the Olfactory System in Vertebrates

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(Received 27 July 2010/Accepted 8 September 2010/Published online in J-STAGE 22 September 2010)

ABSTRACT. Phylogenic outline of the vertebrate olfactory system is summarized in the present review. In the fish and the birds, the olfactory system consists only of the olfactory epithelium (OE) and the olfactory bulb (B). In the amphibians, reptiles and mammals, the olfactory system is subdivided into the main olfactory and the vomeronasal olfactory systems, and the former consists of the OE and the main olfactory bulb (MOB), while the latter the vomeronasal organ (VNO) and the accessory olfactory bulb (AOB). The subdivision of the olfactory system into the main and the vomeronasal olfactory systems may partly be induced by the difference between paraphyletic groups and monophyletic groups in the phylogeny of vertebrates.

KEY WORDS: monophyletic, olfactory system, paraphyletic, phylogeny, vomeronasal system.

J. Vet. Med. Sci. 73(2): 139–147, 2011

Olfaction is one of special senses of vertebrates, appears earliest among special senses in phylogeny, and remarkably contributes to the development of the neocortex in mammals [42, 43, 76]. In this context, studies on the phylogeny of olfaction in vertebrates are essential for the understanding of the evolution of the nervous system in mammals. On the other hand, although the large amount of data are accumulated on the morphology and function of the olfactory system in vertebrates, only a limited number of studies are published on the phylogeny of the olfactory system from a comparative anatomical point of view [7, 33, 34, 41, 48, 88]. In the present review, therefore, we tried to describe our interpretation of the phylogeny of the olfactory system mainly on the basis of our morphological findings [44, 60–63, 65–67, 72–75, 79, 82–92, 100, 101] and generally accepted paleontological data [36, 37, 43, 76].

COMPONENTS AND FUNCTIONS OF THE OLFACTORY SYSTEM

The olfactory system consists of the olfactory receptor organs and the primary and higher olfactory centers [30, 43]. In the present review, the olfactory system must refer to the primary olfactory system consisting of the olfactory receptor organs and the primary olfactory center. The olfactory receptor organs are frequently represented by the olfactory epithelium (OE) and the vomeronasal organ (VNO) [11, 15, 23, 24, 33, 50, 60, 89–92, 96], although the VNO is not an anatomically distinct structure in lower vertebrates and called as the vomeronasal sensory epithelium (VSE). It is generally accepted that the OE perceives the ordinary smells (odors) and the VNO the pheromones. By the way, the primary olfactory center is the olfactory bulb (OB). The OB is subdivided into the main olfactory bulb (MOB) and the accessory olfactory bulb (AOB) in several species [58, 61, 87]. In this case, the MOB receives projections from the OE, and the AOB from the VNO [4, 5, 32, 62, 79, 87, 97]. The OE and MOB constitute the main olfactory system, and the VNO and AOB the vomeronasal (accessory) olfactory system. The olfactory receptor organs and the primary olfactory center underwent diverse changes during phylogeny. The presence or absence of the VNO is briefly described in Fig. 1 as the phylogenic tree.

FISH OLFACTORY SYSTEM

Fossil data suggest that the archaic fishes appeared in the Silurian period about 450 million years ago, and radiated to become dominant creatures in the Devonian period about 400 million years ago [43, 76]. The olfactory system seems to be equipped even with the archaic fishes.

The olfactory receptor organ is solely represented by the OE in the fish. It covers the olfactory lamellae (Fig. 2) and occasionally takes the form of rosette in several species. It is characteristic that the OE is divided into several grooves by ridges of non-sensory epithelia in the fish. Although the OE exists ubiquitously throughout all classes of vertebrates, it underwent modifications in cellular components along the course of phylogenetic development. In the fish, the OE generally consisted of the ciliated receptor cells, microvillous receptor cells, ciliated supporting cells, microvillous supporting cells, and basal cells [75, 100, 101]. In addition, the crypt cells are occasionally encountered in several species. They are one of the receptor cells equipped with cilia and microvilli, and project their axons to the OB [63]. Their functional roles in the fish olfactory system are still unknown. On the other hand, increasing data suggest that the ciliated and microvillous receptor cells perceive ordi-

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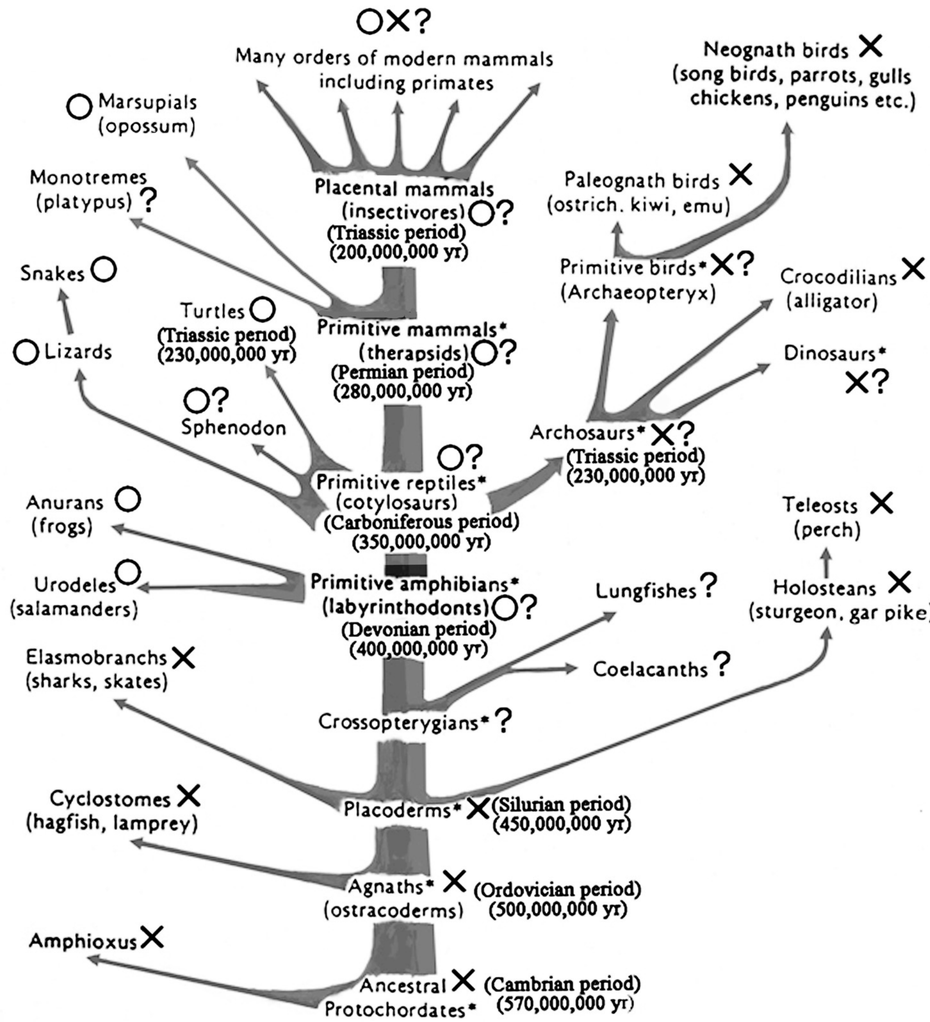

Fig. 1. Schematic drawings of the phylogenic tree of the vertebrates showing the presence or absence of the vomeronasal organ.

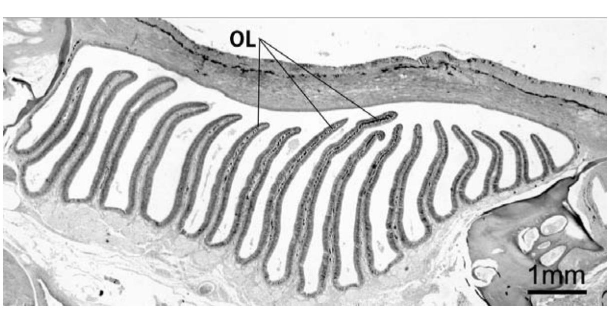

Fig. 2. Sagittal section of the nasal pit of a flatfish, barfin flounder (*Verasper moseri*), showing many olfactory lamellae (OL).

nary smells and pheromones, respectively [62]. Since the perception of ordinary smells and pheromones is achieved equally by the OE in the fish, the fish OE seems to represent the primitive form of the vertebrate OE.

The primary olfactory center of the fish is the OB. Its cytoarchitecture is rather primitive, and shows a small kind of output neurons, interneurons and glial components [62]. Its output neurons are named mitral/tufted cells, because mitral and tufted cells are not distinguished in the fish OB. Similarly, the MOB and AOB are not distinguished in the fish OB. As interneurons, periglomerular cells are distinguished in the OB. Because periglomerular cells are small in number, the formation of the olfactory glomeruli is still incomplete to demarcate among them [62]. Projection patterns of ciliated or microvillous receptor cells to individual olfactory glomeruli are still obscure, but our lectin histochemical data suggest that a region of the OB receives projections from the microvillous, or pheromone receptor cells [62].

There is one question. Is the OE really the sole olfactory receptor organ in the fish? That is, is the VNO lacking in the fish? Since there are tens of thousands of the fish species,

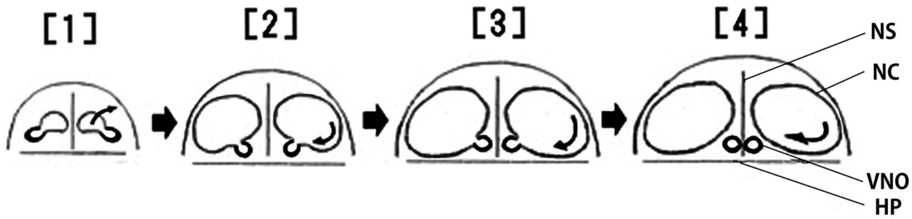

Fig. 3. Schematic drawings of the changes in the location of the vomeronasal organ during the phylogenic development. HP: hard palate, NC: nasal cavity, NS: nasal septum, VNO: vomeronasal organ.

about ten times of those of mammals, and only a few of them have been examined, our knowledge on the fish olfactory system is very limited. If we extend our observations to all species of fish, we might discover primordial VNO.

AMPHIBIAN OLFACTORY SYSTEM

Although the amphibians are thought to be derived from the crossopterygians, their true origin is still obscure. In taxonomy, there are 3 living orders in the amphibian: anurans, urodeles, and apodans. The urodeles are said to branch off from the primitive amphibian, caudates, in the Triassic period (about 230 million years ago), while the anurans from the protoanurans, another type of the primitive amphibian, in the Jurassic period (about 180 million years ago) [43, 76]. Among them, the apodans are rather retrogressive and lacking limbs, very small in number of species, and live in very restricted areas on earth. In addition, there have been no reports on the olfactory system in the apodans in our best knowledge. Therefore, we adopt the urodeles and anurans as the representatives of living amphibians in the present review.

The second olfactory receptor organ, the VNO, first appears phylogenically in the amphibians as shown in Fig. 1. In the urodeles, the nasal cavity consists of the main nasal chamber and the lateral diverticulum. The main chamber occupies most of the nasal chamber and is lined with the OE [72, 79]. The OE in the urodeles is divided into several grooves by ridges of non-sensory epithelia as in the fish [72]. The lateral diverticulum is lined with the VSE. It is a series of the sensory epithelium not interrupted by non-sensory epithelia as in the OE in the fish and urodeles. Although it is literally located on the lateral wall of the nasal cavity in the urodeles, it changes its location from lateral to medial in the nasal cavity in the anurans. This change in its location seems to be caused by the enlargement of the nasal cavity toward the dorsolateral direction to shift the VNO to the ventromedial side of the nasal cavity (Fig. 3). The VNO becomes to be situated at the base of the nasal septum as a tubular structure independent from or with only a slight communication with the nasal cavity in snakes and mammals.

In the anurans, the nasal cavity is divided into three chambers communicating with each other, i.e., principal, middle and inferior chambers [25, 67]. These chambers are generally lined with different types of epithelia. The principal chamber is lined with the OE, the middle chamber the non-sensory respiratory epithelium, and the inferior chamber the VSE [25]. The OE and the VSE are respectively a series of the sensory epithelium not interrupted by non-sensory epithelia. The projecting patterns of the axons from the OE and the VNO to the MOB and the AOB are illustrated in Fig. 4. In a few anuran species such as *Xenopus laevis*, however, the middle chamber is lined with a third type of sensory epithelium, arbitrarily called as the middle chamber epithelium (MCE) [67]. The MCE is also a series of the sensory epithelium not interrupted by non-sensory epithelia.

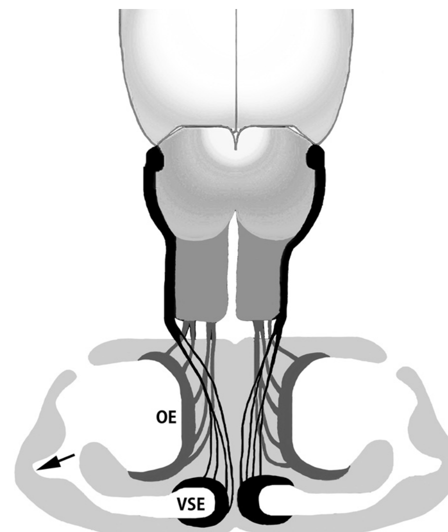

Fig. 4. Schematic drawings of the projection patterns of the main and accessory olfactory system in the ordinary anuran species. OE: olfactory epithelium, VSE: vomeronasal sensory epithelium. An arrow indicates the middle chamber.

Cellular components of the olfactory sensory epithelia in the amphibians are different among the OE, VSE and MCE. The OE consists of ciliated olfactory cells, microvillous supporting cells and basal cells, while the VSE microvillous sensory cells, ciliated supporting cells and basal cells, and the MCE ciliated sensory cells, microvillous sensory cells, ciliated supporting cells, microvillous supporting cells and basal cells. Judging from the characteristics of cellular components, the MCE is similar to the primitive olfactory epithelium in the fish. Functionally, the OE is supposed to detect airborne odoriferous molecules, the MCE water-soluble odoriferous molecules and the VSE the pheromones. This supposition is partly supported by the facts that the OE and the VSE are equipped with the associated glands, but not the MCE.

The OB is subdivided into the MOB and AOB in amphibians. Cellular components are similar between MOB and AOB, although the mitral cells and tufted cells in the MOB are not distinguished in the AOB and grouped as the mitral/tufted cells. In *Xenopus laevis*, the MOB is further subdivided into the dorsal (D-MOB) and ventral (V-MOB) regions. The OE, MCE and VSE project their axons to the D-MOB, V-MOB and AOB, respectively, and show the different binding patterns of lectins among the D-MOB, V-MOB and AOB [74]. Despite the difference in the binding patterns of lectins between D-MOB and V-MOB, there is no difference in the cellular components of the D-MOB and V-MOB.

REPTILIAN OLFACTORY SYSTEM

Primitive reptiles are thought to be derived from their ancestral amphibians in the Carboniferous period about 350 million years ago [43, 76]. In reptiles, the nasal cavity is separated from the oral cavity by the formation of the secondary palate, which is the big event in the course of the phylogenic development. The formation of the secondary palate makes the reptiles and mammals possible to possess the VNO independent from or with only a slight communication with the nasal cavity.

By the way, there is a serious problem to consider the phylogeny of the olfactory system in the reptiles, because the reptiles are not thought to be derived from a single ancient animal, but from a taxonomical variety of animals. Therefore, the reptiles are considered to be the assembly of paraphyletic groups at present.

The paraphyleticity of the reptiles affects some influences on the phylogeny of the olfactory system in the reptiles. For example, the majority of reptiles derived from the primitive reptiles possess both the OE and the VNO. In contrast, reptiles derived from the archosaurs, a branch of the primitive reptiles, do not possess the VNO but possess only the OE. In other words, although the living reptiles such as snakes, lizards and turtles possess the OE and VNO as the olfactory receptor organs, certain types of reptiles, such as crocodiles and alligators, lack the VNO and possess only the OE. Crocodiles and alligators are descendants of the archosaurs and branched off from the primitive reptiles in the Triassic period about 230 million years ago. In addition, although turtles and tortoises are directly derived from the primitive reptiles, some of their families lack the VNO. As the results, the organization of the olfactory system differs greatly among reptilian species as described below.

Among the reptilian species, the animals belonging to the order squamates possess the well-developed vomeronasal olfactory system, although the paraphyleticity of the reptiles also affects some influences on the phylogeny of the olfactory system in the squamates to result in the conspicuous differences in the morphology of the VNO [33]. For example, the VNO in the snakes is the tubular structure completely separated from the nasal cavity, and communicates with the oral cavity via a short canal. The tubular VNO contains a crescent-shaped lumen, whose medial wall is lined with the thick sensory epithelium (VSE) and lateral wall with the non-sensory epithelium. On the other hand, although the VNO in the lizards is also the tubular structure, it communicates with the nasal cavity by the small orifices at the anterior tip of the VNO. Histological features of the VSE are also different. The VSE in the snakes consists of numbers of columnar structures surrounded by satellite cells and separated by the invading connective tissue, while the VSE in the lizards is the series of the sensory epithelium not interrupted by the connective tissue [44, 73]. Morphological and histochemical characteristics in the squamates are well-documented by our recent studies [44]. The projection patterns of their olfactory axons are common to those in the amphibians, i.e., from the OE to the MOB, and from the VSE to the AOB. The features of the MOB and AOB are almost the same as in those in the amphibians.

The olfactory system in the turtle is completely different from that in the squamates. Its nasal cavity is separated into the upper and lower chambers whose sizes are almost the same. Although the lower chamber is considered to correspond to the VNO, it is not a mere diverticulum of the nasal cavity and does not take a form of tubular structure [25, 33]. In addition, the organization of the OB is unique in turtles. It is divided into two halves whose sizes are almost the same as in the nasal cavity in this species. Although their cytoarchitectures are almost the same, the upper half is considered to be the AOB and the lower half to be the MOB, since the former and the latter receive projections from the lower and upper chambers, respectively. We are now wondering whether the lower chamber really corresponds to the VNO. There is a possibility that the olfactory system of the turtle consists of the combinations of the upper chamber of the nasal cavity and the lower half of the OE, and the lower chamber of the nasal cavity and the upper half of the OB, and none of them constitutes the vomeronasal olfactory system.

AVIAN OLFACTORY SYSTEM

It is frequently neglected that the birds are very close in taxonomy to the reptiles. The most primitive bird, *Archaeopteryx*, appeared in the Jurassic period about 180 million years ago [76]. This bird possesses teeth in the mouth, fingers with claw in the forelimb and the bony structure in the tail, and closely resembles to the reptiles [43]. Indeed, even the living birds possess scales on the foot as an evidence of its origin from the reptiles. Huxley proposed a new taxonomical category "Sauropsida" composed of reptiles and birds and regarded the birds as a group of reptiles with feathers [37].

The avian olfactory system consists of the OB and the OE and completely lacks the components of the vomeronasal olfactory system. This may be derived from the fact that the primitive birds are derived from the archosaurs, the same ancestor as for crocodiles which do not possess the VNO. At all rates, the birds depend heavily on the vision rather than olfaction probably because of their flying behavior.

Cellular components and cytological features of the avian OE are almost the same as in the reptiles, although the avian OE is frequently thin and organized by small numbers of cellular components. It is characteristic that the olfactory receptor cells in the avian OE frequently possess cilia and microvilli in one same cell [31, 39, 57]. Although the functional significance of the presence of cilia and microvilli in the same cell is not evidently elucidated, it may compensate the olfactory function of the avian OE organized by small numbers of cellular components.

Cytoarchitecture of the avian OB is also almost the same as in the reptiles. The avian OB consists of mitral cells, tufted cells, interneurons and glial components as in the reptilian MOB and mammalian MOB [6]. Since the birds lack the VNO and AOB, the avian OB corresponds to the MOB in the other animals. It is unique that the right and left halves of the OB frequently fuse to form a single mass [102, 103]. By the way, the organization of the olfactory system is strictly unilateral in all vertebrates, that is, the OE in the right nasal cavity projects the axons to the right half of the OB, and the OE in the left nasal cavity to the left half of the OB. The unilateral organization of the olfactory system is highly efficient to detect the hostile others, preys or fellows in the vicinity of individual animals. In this context, the fusion of the right and left halves of the OB in the birds seems to abandon the effectiveness of the olfactory function in their struggle for existence. The fused OB in the birds may be interpreted as the results that the merit of the olfactory orientation gradually declines in the birds in the course of their development of the flying ability.

MAMMALIAN OLFACTORY SYSTEM

The archaic mammals already appeared in the Jurassic period about 180 million years ago. Most of them extinguished in the Mesozoic era, but one group, the pantotheria, survived to the Cenozoic era and branched off to diverse species in the Tertiary period about 65 million years ago [43, 76]. Since all the living mammals are derived from the pantotheria, the mammals are defined as the monophyletic group [43]. There are over four thousand species in the mammals.

In spite of their taxonomical status as a monophyletic group, the mammalian olfactory systems are different among "family" levels, that is, some mammalian groups lack the vomeronasal olfactory system, and possess only the main olfactory system consisting of the OE and the MOB. For example, the marine animals such as whales and dugongs lack the VNO. In the chiropteran, some bats possess the VNO, but the others do not [8, 13]. Even in the groups possessing the vomeronasal system, the degree of the development of the VNO varies among species. Histological, ultrastructural and histochemical findings on the VNO and the AOB in various mammalian species are well-documented in many reports including ourselves [1, 3, 11, 12, 16–18, 22, 35, 38, 45, 49, 54, 55, 59, 66, 69, 83–86, 93, 97, 98]. Histological, ultrastructural and histochemical findings on the OE and the MOB in various mammalian species are also well-documented in many reports including ourselves [11, 14, 15, 19, 26, 28, 68, 78]. When present, the VNO and the AOB are similar to those in the lizards. Although the VNO is situated at the base of the nasal septum, its opening is diverse among species; it opens into the nasal cavity via a small pore at its apical end, it meets the incisive duct and communicates with the nasal and oral cavities, or it independently opens into the oral cavity with its own duct.

In the human, the presence of the VNO is controversial. It has long been considered that the VNO is absent in the human as in the other higher primates, and only temporarily appeared as a primordium in the early fetal stages [63]. On the other hand, several authors reported the presence of the VNO in the human since the 1980s [40, 56, 79]. They reported that the human VNO has a small pore opening to the lateral wall of the nasal septum and that the human VNO is the same in its fine structure as that of other mammals. Some authors declared that almost all humans possess the VNO, whereas the other authors proposed that only a certain percentage of humans possess the VNO.

Our personal opinion about this problem is that there is no VNO in the human, because there is no report on the presence of the AOB in the human. In this context, it is reported in the chiropteran that the bat without the VNO lacks the AOB. In addition, according to our personal communications, the removal of the VNO in mice resulted in the gradual degeneration of the AOB to lead to its complete disappearance after several months of the VNO removal. These findings make us conclude that the VNO is absent in the human.

By the way, if the VNO is the pheromone receptor organ, the human lacking the VNO do not perceive pheromones? In this instance, we remind the phenomenon called the dormitory effect. This phenomenon is known since early times among groups of nuns; when they are isolated to live together in a group, their menstrual periods gradually become synchronized. This phenomenon is frequently adopted as the evidence that the human can perceive pheromones. Since pheromones are not necessarily perceived by the VNO alone, the dormitory effect suggests that the human maintain the ability to perceive pheromones. Although the fish and the birds lack the VNO, they are said to perceive pheromones with the OE. This interpretation strongly suggests that the human OE can perceive pheromones.

MAMMALIAN OLFACTORY SUBSYSTEMS

Most mammalian species have evolved multiple olfactory systems to detect general odors as well as social cues.

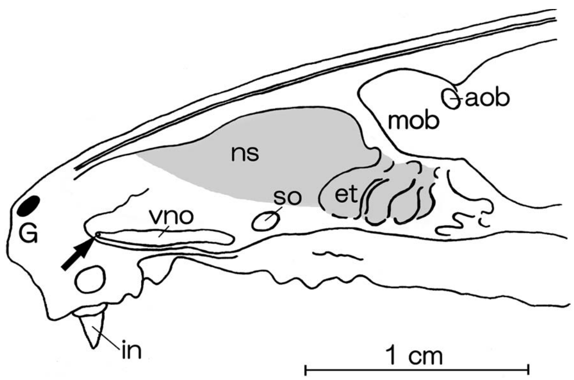

Fig. 5. Schematic drawings of the sagittal section of the rat nasal cavity to show the location of olfactory receptor organs and their primary centers. aob: accessory olfactory bulb, et: endoturbinates, G: Grueneberg ganglion, in: incisor, mob: main olfactory bulb, ns: nasal septum, so: septal olfactory organ of Masera. An arrow indicates the opening of the vomeronasal organ to the nasal cavity.

These systems make the mammals possible to detect all essential elements for survival, such as food, danger and mates. There are two olfactory receptors other than the OE and the VNO, that is, the septal olfactory organ of Masera (SO) [2, 10, 29, 46, 53, 64, 70, 76, 80, 81, 93, 94] and the Grueneberg ganglion (GG) [9, 20, 21, 27, 47, 51, 52, 69]. They play some roles as olfactory subsystems in the mammals.

The SO is a small patch of the sensory epithelium isolated from the OE in the nasal cavity and surrounded by the respiratory epithelium. The histological features are very similar to those of the OE, although the SO is rather low in height in comparison with the OE. Since the SO is present in the restricted number of mammalian species, it may exist only in species where the nasopalatine duct does not open into the VNO. Although its function is still unknown, it seems to serve as a separate accessory olfactory organ with properties different from both OE and VNO.

The GG is a newly appreciated olfactory subsystem with neural connections with the OB. Although the cells of the GG lack the direct contact with the lumen of the nasal cavity, they possess several features as the olfactory neurons such as the olfactory marker protein and the distinctive olfactory receptor proteins. Although the functional significance of the GG is still unknown, the increasing data suggest that the GG at least partly function as thermo-sensors.

The locations of the olfactory receptor organs including those in the olfactory subsystems in the mammals are schematically described in Fig. 5.

DISCUSSION AND CONCLUSION

The recent findings and our interpretation on the phylogeny of the olfactory system are summarized in this review. In the fish, the olfactory system is simple and consists only of the OE and the OB. In the amphibians, the olfactory system is subdivided into the main olfactory and the vomeronasal olfactory systems, and the former consists of the OE and the MOB, while the latter the VNO and the AOB. The third olfactory receptor organ, the MCE, is encountered in some species. In the reptiles, the organization of the olfactory system is diverse among reptilian species, and some are equipped with the main olfactory and vomeronasal olfactory systems, while the other lack the vomeronasal olfactory system. These situations may be induced by the fact that the reptiles are the assembly of paraphyletic groups. In the birds, the olfactory system lacks the vomeronasal system and merely consists of the OE and the OB. This may be induced by the origin of the birds as the descendant archosaurs probably lacking the VNO. In the mammals, the olfactory system shows diverse modifications in spite of their origin as the monophyletic group. The organization of the olfactory system in vertebrates is partly affected by their origin as the paraphyletic group or monophyletic group, but cannot be elucidated from this point of view in the mammals.

REFERENCES

1. Adams, D. R. 1986. The bovine vomeronasal organ. *Arch. Histol. Jpn.* **49**: 211–225.
2. Adams, D. R. and McFarland, L. Z. 1971. Septal olfactory organ in *Peromyscus*. *Comp. Biochem. Physiol.* **40A**: 971–974.
3. Adams, D. R. and Wiekamp, M. D. 1984. The canine vomeronasal organ. *J. Anat.* **138**: 771–790.
4. Barber, P. C. and Raisman, G. 1974. An autoradiographic investigation of the projection of the vomeronasal organ to the accessory olfactory bulb in the house mouse. *Brain Res.* **81**: 21–30.
5. Beauchamp, G. K., Magnus, J. G., Shmunes, N. T. and Durham, T. 1977. Effects of olfactory bulbectomy on social behavior of male guinea pigs (*Cavia porcellus*). *J. Comp. Physiol. Psych.* **91**: 336–346.
6. Bedini, C., Fiaschi, V. and Lanfranchi, A. 1976. Olfactory nerve reconstitution in the homing pigeon after resection: ultrastructural and electrophysiological data. *Arch. Ital. Biol.* **114**: 1–22.
7. Bertmar, G. 1981. Evolution of vomeronasal organs in vertebrates. *Evolution* **35**: 359–366.
8. Bhatnagar, K. P., Matulionis, D. and Breipohl, W. 1982. Fine structure of the vomeronasal neuroepithelium of bats. A comparative study. *Acta Anat.* **112**: 158–177.
9. Brechbühl, J., Klaey, M. and Broillet, M. C. 2008. Grueneberg ganglion cells mediate alarm pheromone detection in mice. *Science* **321**: 1092–1095.
10. Breipohl, W., Naguro, T. and Walker, D. G. 1989. The postnatal development of Masera's organ in the rat. *Chem. Senses* **14**: 649–662.
11. Ciges, M., Labella, T., Gayoso, M. and Sanchez, G. 1977. Ultrastructure of the organ of Jacobson and comparative study with olfactory mucosa. *Acta Otolaryngol. (Stockh.)* **83**: 47–58.
12. Clancy, A. N., Coquelin, A., Macrides, F., Gorski, R. A. and Noble, E. P. 1984. Sexual behavior and aggression in male mice: involvement of the vomeronasal system. *J. Neurosci.* **4**: 2222–2229.
13. Cooper, J. G. and Bhatnagar, K. P. 1976. Comparative anatomy of the vomeronasal organ complex in bats. *J. Anat.* **122**:

571–601.
14. Costanzo, R. M. and Morrison, E. E. 1989. Three-dimensional scanning electron microscopic study of the normal hamster olfactory epithelium. *J. Neurocytol.* **18**: 381–391.
15. Cushieri, A. 1974. Enzyme histochemistry of the olfactory mucosa and vomeronasal organ in the mouse. *J. Anat.* **118**: 477–490.
16. Eisthen, H. L., Wysocki, C. J. and Beauchamp, G. K. 1987. Behavioral responses of male guinea pigs to conspecific chemical signals following neonatal vomeronasal organ removal. *Physiol. Behav.* **41**: 445–449.
17. Eloff, F. C. 1951. On the organ of Jacobson and the nasal floor cartilage in the chondrocranium of *Galago senegalensis*. *Proc. Zool. Soc. Lond.* **121**: 651–655.
18. Estes, R. D. 1972. The role of the vomeronasal organ in mammalian reproduction. *Mammalia* **36**: 315–341.
19. Farbman, A. and Margolis, F. 1980. Olfactory marker protein during ontogeny: immunohistochemical localization. *Dev. Biol.* **74**: 205–215.
20. Fleischer, J., Schwarzenbacher, K., Besser, S., Hass, N. and Breer, H. 2006. Olfactory receptors and signalling elements in the Grueneberg ganglion. *J. Neurochem.* **98**: 543–554.
21. Fleischer, J. and Breer, H. 2010. The Grueneberg ganglion: a novel sensory system in the nose. *Histol. Histopathol.* **25**: 909–915.
22. Fleming, A., Vaccarino, F., Tambossee, L. and Chee, P. 1979. Vomeronasal and olfactory modulation of maternal behavior in the rat. *Science* **203**: 372–374.
23. Franceschini, V., Lazzari, M., Revoltella, R. P. and Ciani, F. 1994. Histochemical study by lectin binding of surface glycoconjugates in the developing olfactory system of rat. *Int. J. Devl. Neurosci.* **12**: 197–206.
24. Freitag, J., Krieger, J., Strotmann, J. and Breer, H. 1995. Two classes of olfactory receptors in Xenopus laevis. *Neuron* **15**: 1383–1392.
25. Freitag, J., Ludwig, G., Andreini, I., Rössler, P. and Breer, H. 1998. Olfactory receptors in aquatic and terrestrial vertebrates. *J. Comp. Physiol. A* **183**: 645–650.
26. Frisch, D. 1967. Ultrastructure of the mouse olfactory mucosa. *Am. J. Anat.* **121**: 87–120.
27. Fuss, S. H., Omura, M. and Mombaerts, P. 2005. The Grueneberg ganglion of the mouse projects axons to glomeruli in the olfactory bulb. *Eur. J. Neurosci.* **22**: 2649–2654.
28. Getchell, M. L. and Getchell, T. V. 1992. Fine structural aspects of secretion and extrinsic innervation in the olfactory mucosa. *Microsc. Res. Tech.* **23**: 111–127.
29. Giannetti, N., Pellier, V., Oestreicher, A. B. and Astic, L. 1995. Immunocytochemical study of the differentiation process of the septal organ of Masera in developing rat. *Dev. Brain Res.* **84**: 287–293.
30. Gomez, G. and Celii, A. 2008. The peripheral olfactory system of the domestic chicken: physiology and development. *Brain Res. Bull.* **76**: 208–216.
31. Graziadei, P. P. and Bannister, L. H. 1967. Some observations on the fine structure of the olfactory epithelium in the domestic duck. *Z. Zellforsch. Mikrosk. Anat.* **80**: 220–228.
32. Graziadei, P. P. and Okano, M. 1979. Neuronal degeneration and regeneration in the olfactory epithelium of pigeon following transection of the first cranial nerve. *Acta Anat. (Basel)* **104**: 220–236.
33. Halpern, M. 1987. The organization and function of the vomeronasal system. *Ann. Rev. Neurosci.* **10**: 325–362.
34. Harrison, D. 1987. Preliminary thoughts on the incidence, structure and function of the mammalian vomeronasal organ. *Acta Otolaryngol. (Stockh.)* **103**: 489–495.
35. Hunter, A. J., Fleming, D. and Dixson, A. F. 1984. The structure of the vomeronasal organ and nasopalatine ducts in *Aotus trivirgatus* and some other primate species. *J. Anat.* **138**: 217–226.
36. Huxley, J. S. 1923. Time relations in amphibian metamorphosis, with some general considerations. *Sci. Prog.* **17**: 606–618
37. Huxley, J. S. 1942. Evolution: The Modern Synthesis, Allen and Unwin, London.
38. Jacobson, L. 1811. Fait à l'Institut, sur un mémoire de M. Jacobson, intitulé: description anatomique d'un organe observé dans les mammifères. Rapport par M. Cuvier. *Ann. Mus. Hist. Nat. Paris* **18**: 412–424 (in French).
39. Jin, E. H., Peng, K. M., Wang, J. A., Du, A. N., Tang, L., Wei, L., Wang, Y., Li, S. H. and Song, H. 2008. Study of the morphology of the olfactory organ of African ostrich chick. *Anat. Histol. Embryol.* **37**: 161–165.
40. Johnson, A., Josephson, R. and Hawke, M. 1985. Clinical and histological evidence for the presence of the vomeronasal (Jacobson's) organ in adult humans. *J. Otolaryngol.* **14**: 71–79.
41. Jordan, J. 1972. The vomeronasal organ (of Jacobson) in primates. *Folia Morphol.* **31**: 418–432.
42. Kaslin, J., Ganz, J. and Brand, M. 2008. Proliferation, neurogenesis and regeneration in the non-mammalian vertebrate brain. *Philos Trans. R. Soc. Lond. B. Biol. Sci.* **363**: 101–122.
43. Kent, G. C. and Carr, R. K. 2001. Comparative Anatomy of the Vertebrates, 9th ed., McGraw-Hill, New York.
44. Kondoh, D., Yamamoto, Y., Nakamuta, N., Taniguchi, K. and Taniguchi, K. 2010. Lectin histochemical studies on the olfactory epithelium and vomeronasal organ in the Japanese striped snake, *Elaphe quadrivirgata*. *J. Morphol.* **271**: 1197–1203.
45. Kratzing, J. E. 1970. The structure of the vomeronasal organ in the sheep. *J. Anat.* **108**: 247–260.
46. Kratzing, J. E. 1978. The olfactory apparatus of the bandicoot (*Isoodon macrourus*): fine structure and presence of a septal olfactory organ. *J. Anat.* **125**: 601–613.
47. Liu, C. Y., Fraser, S. E. and Koos, D. S. 2009. Grueneberg ganglion olfactory subsystem employs a cGMP signaling pathway. *J. Comp. Neurol.* **516**: 36–48.
48. Loo, S. K. 1977. Fine structure of the olfactory epithelium in some primates. *J. Anat.* **123**: 135–145.
49. Loo, S. K. and Kanagasuntheram, R. 1972. The vomeronasal organ in tree shrew and slow loris. *J. Anat.* **112**: 165–172.
50. Lundh, B., Brockstedt, U. and Kristensson, K. 1989. Lectin-binding pattern of neuroepithelial and respiratory epithelial cells in the mouse nasal cavity. *Histochem. J.* **21**: 33–43.
51. Ma, M. 2007. Encoding olfactory signals via multiple chemosensory systems. *Crit. Rev. Biochem. Mol. Biol.* **42**: 463–480.
52. Mamasuew, K., Breer, H. and Fleischer, J. 2008. Grueneberg ganglion neurons respond to cool ambient temperatures. *Eur. J. Neurosci.* **28**: 1775–1785.
53. Marshall, D. A. and Maruniak, J. A. 1986. Masera's organ responds to odorants. *Brain Res.* **366**: 329–332.
54. Mendoza, A. S. 1986. The mouse vomeronasal glands: a light and electron microscopical study. *Chem. Senses* **11**: 541–555.
55. Mora, O. A. and Criado, J. E. S. 1980. A pheromonal chemoreceptor in the rat: the vomeronasal organ. *Phronesis* **1**: 305–312.
56. Moran, D. T., Jafek, B. W. and Rowley, J. C. III. 1991. The vomeronasal (Jacobson's) organ in man: ultrastructure and frequency of occurrence. *J. Steroid Biochem. Mol. Biol.* **39**: 545–552.

57. Müller, H., Drenckhahn, D. and Haase, E. 1979. Comparative and quantitative ultrastructural study of the olfactory organs of four strains of domestic pigeons. *Z. Mikrosk. Anat. Forsch.* **93**: 888–900.
58. Murphy, M. R. and Schneider, G. E. 1970. Olfactory bulb removal eliminates mating behavior in the male golden hamster. *Science* **167**: 302–304.
59. Naguro, T. and Breipohl, W. 1982. The vomeronasal epithelia of NMRI mouse. A scanning electron microscopic study. *Cell Tissue Res.* **227**: 519–534.
60. Nakajima, T., Shiratori, K., Ogawa, K., Tanioka, Y. and Taniguchi, K. 1998. Lectin-binding patterns in the olfactory epithelium and vomeronasal organ of the common marmoset. *J. Vet. Med. Sci.* **60**: 1005–1011.
61. Nakajima, T., Sakaue, M., Kato, M., Ogawa, K. and Taniguchi, K. 1998. Immunohistochemical and enzyme-histochemical study on the accessory olfactory bulb of the dog. *Anat. Rec.* **252**: 393–402.
62. Nakamuta, N., Yokoyama, N., Yamamoto, Y., Taniguchi, K. and Taniguchi, K. 2009. Lectin histochemical analysis of the olfactory bulbs in the barfin flounder (*Verasper moseri*). *Anat. Histol. Embryol.* **39**: 67–73.
63. Nakamuta, S., Nakamuta, N. and Taniguchi, K. 2010. Ultrastructure of the olfactory epithelium in a flatfish, barfin flounder (*Verasper moseri*). *J. Vet. Med. Sci.* **72**: 801–804.
64. Nakashima, T., Kimmelman, C. P. and Snow, J. B. Jr. 1984. Structure of human fetal and adult olfactory neuroepithelium. *Arch. Otolaryngol.* **110**: 641–646.
65. Oikawa, T., Saito, H., Taniguchi, K. and Taniguchi, K. 2001. Immunohistochemical studies on the differential maturation of three types of olfactory organs in the rats. *J. Vet. Med. Sci.* **63**: 759–765.
66. Oikawa, T., Shimamura, K., Saito, T. R. and Taniguchi, K. 1994. Fine structure of the vomeronasal organ in the chinchilla (*Chinchilla laniger*). *Exp. Anim.* **43**: 487–497.
67. Oikawa, T., Suzuki, K., Saito, T. R., Takahashi, K. W. and Taniguchi, K. 1998. Fine structure of three types of olfactory organs in *Xenopus laevis*. *Anat. Rec.* **252**: 301–310.
68. Polyzonis, B. M., Kafandaris, P. M., Gigis, P. I. and Demetriou, T. 1979. An electron microscopic study of human olfactory mucosa. *J. Anat.* **128**: 77–83.
69. Powers, J. B. and Winans, S. S. 1975. Vomeronasal organ: critical role in mediating sexual behavior of the male hamster. *Science* **187**: 961–963.
70. Pyrski, M., Koo, J. H., Polumuri, S. K., Ruknudin, A. M., Margolis, J. W., Schulze, D. H. and Margolis, F. L. 2007. Sodium/calcium exchanger expression in the mouse and rat olfactory systems. *J. Comp. Neurol.* **501**: 944–958.
71. Rodolfo-Masera, T. 1943. Su l'esistenza di un particolare organo olfattivo nel setto nasale della cavia e di altri roditori. *Arch. Ital. Anat. Embriol.* **48**: 157–213 (in Italian).
72. Saito, S., Matsui, T., Kobayashi, N., Wakisaka, H., Mominoki, K., Matsuda, S. and Taniguchi, K. 2003. Lectin histochemical study on the olfactory organ of the newt, *Cynopus pyrrhogaster*, revealed heterogenous mucous environments in a single nasal cavity. *Anat. Embryol. (Berl.)* **206**: 349–356.
73. Saito, S., Oikawa, T., Taniguchi, K. and Taniguchi, K. 2010. Fine structure of the vomeronasal organ in the grass lizard, *Takydromus tachydromoides*. *Tissue Cell* **42**: 322–327.
74. Saito, S. and Taniguchi, K. 2000. Expression patterns of glycoconjugates in the three distinctive olfactory pathways of the clawed frog, *Xenopus laevis*. *J. Vet. Med. Sci.* **62**: 153–159.
75. Saito, S., Yamamoto, Y., Mori, M., Amano, M., Yamanome, T., Taniguchi, K., Yamamori, K. and Taniguchi, K. 2004. Variety in histochemical characteristics of the olfactory receptor cells in a flatfish, barfin flounder (*Verasper moseri*). *J. Vet. Med. Sci.* **66**: 1409–1412.
76. Sarnat, H. B. and Netsky, M. G. 1974. Evolution of the Nervous System, Oxford University Press, New York.
77. Schmid, A., Pyrski, M., Biel, M., Leinders-Zufall, T. and Zufall, F. 2010. Grueneberg ganglion neurons are finely tuned cold sensors. *J. Neurosci.* **30**: 7563–7568.
78. Shantha, T. R. and Nakajima, Y. 1970. Histological and histochemical studies on the rhesus monkey (*Macaca mulatta*) olfactory mucosa. *Z. Zellforsch.* **103**: 291–319.
79. Soeta, S., Izu, Y., Saito, T. R., Yamano, S. and Taniguchi, K. 2005. Differential expression of neurofilament 200-like immunoreactivity in the main olfactory and vomeronasal systems of the Japanese newt, *Cynopus pyrrhogaster*. *J. Vet. Med. Sci.* **67**: 701–706.
80. Stensaas, L. J., Lavker, R. M., Monti-Broch, L., Grosser, B. I. and Berlinger, D. L. 1991. Ultrastructure of the human vomeronasal organ. *J. Steroid Biochem. Mol. Biol.* **39**: 553–560.
81. Takami, S., Getchell, M. L. and Getchell, T. V. 1994. Lectin histochemical localization of galactose, N-acetylgalactosamine, and N-acetylglucosamine in glycoconjugates of the rat vomeronasal organ, with comparison to the olfactory and septal mucosae. *Cell Tissue Res.* **277**: 211–230.
82. Taniguchi, K., Arai, T. and Ogawa, K. 1993. Fine structure of the septal olfactory organ of Masera and its associated gland in the golden hamster. *J. Vet. Med. Sci.* **55**: 107–116.
83. Taniguchi, K., Matsusaki, Y., Ogawa, K. and Saito, T. R. 1992. Fine structure of the vomeronasal organ in the common marmoset (*Callithrix jacchus*). *Folia Primatol.* **59**: 169–176.
84. Taniguchi, K. and Mikami, S. 1985. Fine structure of the epithelia of the vomeronasal organ of horse and cattle. A comparative study. *Cell Tissue Res.* **240**: 41–48.
85. Taniguchi, K. and Mochizuki, K. 1982. Morphological studies on the vomeronasal organ in the golden hamster. *Jpn. J. Vet. Sci.* **44**: 419–426.
86. Taniguchi, K. and Mochizuki, K. 1983. Comparative morphological studies on the vomeronasal organ in rats, mice and rabbits. *Jpn. J. Vet. Sci.* **45**: 67–76.
87. Taniguchi, K., Saito, H., Okamura, M. and Ogawa, K. 1993. Immunohistochemical demonstration of protein gene product 9.5 (PGP 9.5) in the primary olfactory system of the rat. *Neurosci. Lett.* **156**: 24–26.
88. Taniguchi, K., Saito, S., Oikawa, T. and Taniguchi, K. 2008. Phylogenic aspects of the amphibian dual olfactory system. *J. Vet. Med. Sci.* **70**: 1–9.
89. Taniguchi, K. and Taniguchi, K. 2008. Embryonic and postnatal differentiation of olfactory epithelium and vomeronasal organ in the Syrian hamster. *J. Vet. Med. Sci.* **70**: 57–64.
90. Taniguchi, K., Taniguchi, K. and Mochizuki, K. 1982. Comparative developmental studies on the fine structure of the vomeronasal sensory and the olfactory epithelia in the golden hamster. *Jpn. J. Vet. Sci.* **44**: 881–890.
91. Taniguchi, K., Toshima, Y., Saito, T. R. and Taniguchi, K. 1996. Development of the olfactory epithelium and vomeronasal organ in the Japanese reddish frog, *Rana japonica*. *J. Vet. Med. Sci.* **58**: 7–15.
92. Taniguchi, K., Toshima, Y., Saito, T. R. and Taniguchi, K. 1996. Development of the Bowman's and Jacobson's glands in the Japanese reddish frog, *Rana japonica*. *J. Vet. Med. Sci.* **58**: 17–22.
93. Vaccarezza, O. L., Sepich, L. N. and Tramezzani, J. H. 1981.

The vomeronasal organ of the rat. *J. Anat.* **132**: 167–185.
94. Weiler, E. and Farbman, A. I. 2003. The septal organ of the rat during postnatal development. *Chem. Senses* **28**: 581–593.
95. Weiler, E. and Benali, A. 2005. Olfactory epithelia differentially express neuronal markers. *J. Neurocytol.* **34**: 217–240.
96. Winans, S. S. and Powers, L. B. 1977. Olfactory and vomeronasal deafferentation of male hamsters: histological and behavioral analysis. *Brain Res.* **126**: 325–344.
97. Wysocki, C. J. 1979. Neurobehavioral evidence for the involvement of the vomeronasal system in mammalian reproduction. *Neurosci. Biobehav. Rev.* **3**: 301–341.
98. Wysocki, C. J., Nyby, J., Whitney, G., Beauchamp, G. K. and Katz, Y. 1982. The vomeronasal organ: primary role in mouse chemosensory gender recognition. *Physiol. Behav.* **29**: 315–327.
99. Wysocki, C. J., Wellington, J. L. and Beauchamp, G. K. 1980. Access of urinary nonvolatiles to the mammalian vomeronasal organ. *Science* **207**: 781–783.
100. Yamamoto, Y., Mori, M., Amano, M., Yamanome, T., Saito, S., Taniguchi, K., Yamamori, K. and Taniguchi, K. 2004. Morphogenesis of the olfactory pit in a flatfish, barfin flounder (*Verasper moseri*). *J. Vet. Med. Sci.* **66**: 1275–1278.
101. Yamamoto, Y., Mori, M., Saito, S., Amano, M., Yamanome, T., Taniguchi, K., Oikawa, T., Yamamori, K. and Taniguchi, K. 2004. Differential expression of histochemical characteristics in the developing olfactory receptor cells in a flatfish, barfin flounder (*Verasper moseri*). *J. Vet. Med. Sci.* **66**: 1609–1611.
102. Yokosuka, M., Hagiwara, A., Saito, T. R., Aoyama, M., Ichikawa, M. and Sugita, S. 2009. Morphological and histochemical study of the nasal cavity and fused olfactory bulb of the brown-eared bulbul, *Hysipetes amaurotis*. *Zoolog. Sci.* **26**: 713–721.
103. Yokosuka, M., Hagiwara, A., Saito, T. R., Tsukahara, N., Aoyama, M., Wakabayashi, Y., Sugita, S. and Ichikawa, M. 2009. Histological properties of the nasal cavity and olfactory bulb of the Japanese jungle crow *Corvus macrorhynchos*. *Chem. Senses* **34**: 581–593.