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Imaging of the Human Vomeronasal Duct

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Abstract

The human vomeronasal duct (VND) is described as a tubular or pouch-like mucosal invagination of the anterior nasal septum. This study investigated shape, size and orientation of the VND using magnetic resonance imaging (MRI). Fifteen subjects participated (eight women, seven men; mean age 39 years, age range 18–66 years); they had been pre-selected with regard to the presence of a VND opening of 1 mm. MRI was performed before and after application of diluted gadolinium-diethylene-triamino-penta-acetic actetate (Gd-DTPA) into the left or right VND. A tubular structure was found in 12 subjects with a median length of 7 mm (range 3–22 mm; one VND with a length 47 mm). In three subjects a nearly circular, pouch-like structure was observed. Seven of the tubular VNDs were slightly bent upwards, the other five VNDs ran parallel to the floor of the nasal cavity. There was no significant gender-related difference in the length of VNDs. These data indicate considerable variability of shape, size and orientation of the human VND.

Introduction

The vomeronasal organ (VNO) was first mentioned by Ruysch in 1703 (Ruysch, 1703) and re-discovered at the beginning of the nineteenth century by Jacobson (Cuvier, 1811); since then, anatomy and function of this chemosensory organ have been thoroughly investigated in different species (Halpern and Frumin, 1979; Wysocki and Meredith, 1991; Trotier and Døving, 1998). Vomeronasal activation has been shown, for example, in hamsters and/or mice to influence aggression, female cyclicity, mating behavior, or onset of puberty [for a review see Wysocki and Meredith (Wysocki and Meredith, 1991)]. In contrast, function of the human VNO is far from clear. Histological studies of the VNO indicate the presence of sensory epithelium in human embryos (Ortmann, 1989). One investigation (Takami *et al.*, 1993) also finds that the adult human vomeronasal epithelium contains cells expressing markers characteristic of neurons (NSE, PGP9.5) [for a discussion see also Witt *et al*. (Witt *et al.*, 2000)]. Few publications relate to functional aspects (Boehm and Gasser, 1993; Monti-Bloch *et al.*, 1994; Berliner *et al.*, 1996; Lundstrom *et al.*, 2000). It has been reported that application of odorless 'vomeropherins' may result in gender-specific behavioral changes, modulation of autonomic nervous system function, or release of gonadotropins (Monti-Bloch *et al.*, 1998).

An opening of the vomeronasal duct (VND) appears not to be detectable in all humans. Its detectability ranges from 25 to >90% (Potiquet, 1891; Johnson *et al.*, 1985; Garcia-Velasco and Mondragon, 1991; Eloit *et al.*, 1998; Gaafar *et al.*, 1998; Knecht *et al.*, 1999). Corresponding to the few and contradictory studies on its presence in humans, there are only few reports regarding the VND's shape and orientation. Kölliker (Kölliker, 1877) found the length of the vomeronasal duct to range from 2 to 7 mm. Anton (Anton, 1895) described a tubular structure located symmetrically on both sides of the septum with a length of up to 8.4 mm. Mangakis (Mangakis, 1902) observed a VND with a length of 62 mm. Smith *et al.* (Smith *et al.*, 1998) reported a length between 3.5 and 11.8 mm. And, finally, Eloit *et al.* (Eloit *et al.*, 1998) found its length to be between 2 and 5 mm. Thus, the present study was undertaken to investigate the shape, size and orientation of the human VND using magnetic resonance imaging (MRI). Due to both high soft-tissue contrast and high in-plane-resolution, this study was expected to yield more detailed and precise information than previously possible.

Materials and methods

Fifteen healthy volunteers participated (eight women, seven men; mean age 39 years, range 18–66 years). All subjects were in excellent health and none of them reported a major nasal trauma or surgery of the nasal septum. The study was conducted according to the Declaration of Helsinki (Sommerset West amendment); it was approved by the

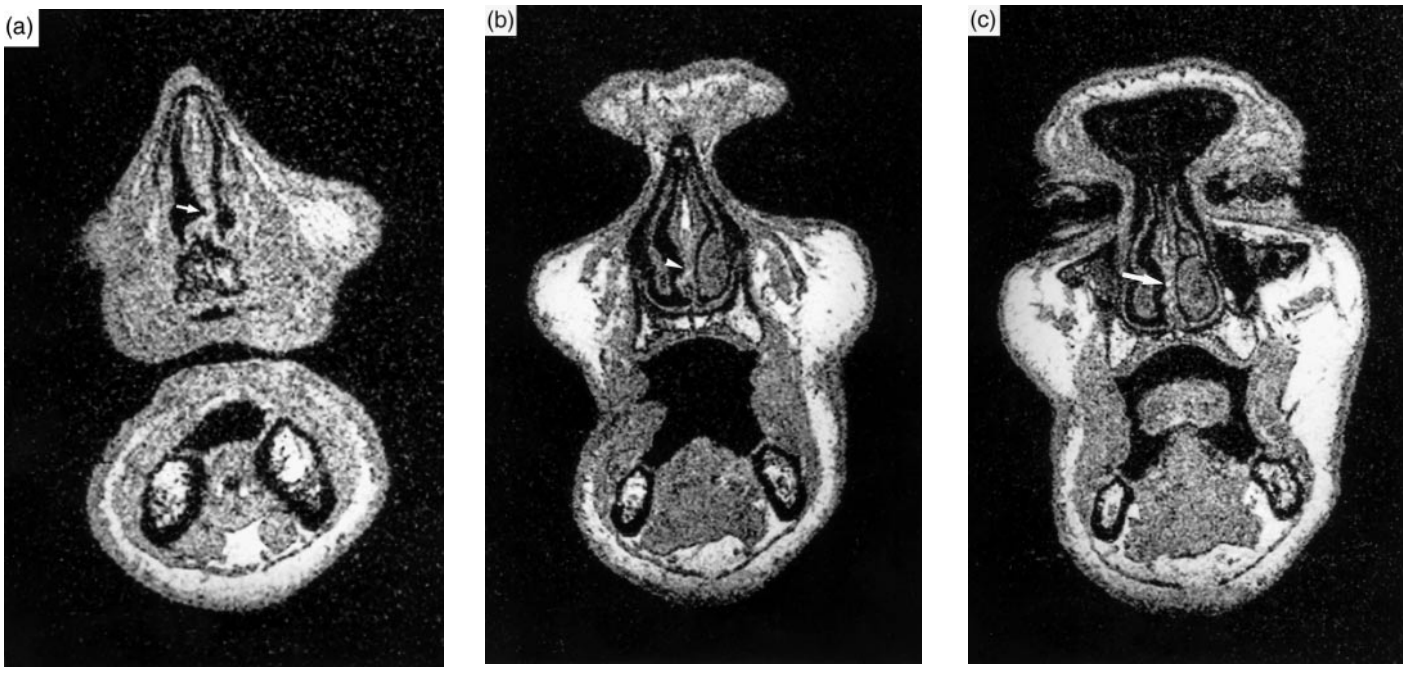

Figure 1 **(a–c)** Coronal reformats of a FLASH-3D of one subject with a tubular VND (TE = 6 ms, TR = 20 ms, $\alpha = 30°$, 512^2 matrix). The ventral opening (small white arrow) is not filled with CA. More dorsally, a very small lumen filled with CA can be seen (white arrowhead); the VND ends 12 mm behind the opening (large white arrow).

University of Dresden Medical Ethics Review Committee. All subjects gave written consent.

The presence of a vomeronasal lumen was verified endoscopically by an experienced otorhinolaryngologist. Criteria for detection were a mucosal invagination on the anterior portion of the septum (up to 2.5 cm above the floor of the nasal cavity, and up to 4.5 cm distant from the naris) that looked different than other humps and invaginations that are occasionally found on the respiratory epithelium. Subjects were pre-selected according to an opening of the lumen of at least 1 mm in diameter. The population presently studied was in part a subset of a population of 173 subjects investigated previously using endoscopical techniques (Knecht *et al.*, 1999). In these subjects a mucosal, 'VNO-like' invagination in the anterior portion of the nasal septum was detected in ~60% of the subjects; in ~25 % of these subjects the opening was ≥1 mm.

The anatomical position of the VND was measured in relation to the columella and the floor of the nasal cavity using custom-built, hook-like rulers with 1 mm graduation marks. Minute amounts (~0.2 ml) of diluted contrast agent [CA = gadolinium-diethylene-triamine-penta-acetic-acic (Gd-DTPA), dilution 1:100; Magnevist®, Schering, Germany] were gently placed into the VND opening until CA reflux was visible; CA instillation was done without exerting any pressure. For this maneuver a flexible Teflon catheter was used (outer diameter 0.8 mm). Only one VND was investigated in each subject. The side of investigation was selected according to the VND's accessibility to endoscope and catheter. To control the possible spill of CA, small pieces of cellulose were placed around the VND opening prior to application. In addition, after CA application the surface of the epithelium was very gently dabbed with cotton swabs. This procedure was performed under endoscopical control in the sitting subjects. MR scans started ~3 min after CA application; they lasted ~20 min.

MRI was performed with a 1.5 Tesla system (Magnetom Vision®, Siemens, Germany) using a standard quadrature head-coil. We used both T1-weighted turbo spin echo (TSE) sequences (TR = 550 ms, TE = 20 ms, 2 Nex; 512^2 matrix, slice thickness 3–4 mm) and T1-weighted volume-sequences (FLASH-3D, TE = 6 ms, TR = 20 ms, $\alpha = 30°$, 512^2 matrix) with a voxel size of 1 × 0.59 × 0.59 mm; in one subject a T1-weighted MP-RAGE with isometric voxels (1 × 1 × 1 mm) was used. With these 3D-datasets, multiplanar reconstruction was performed. To identify the presence of fatty tissue within the nasal septum, MRI was also performed before CA application. In addition, the volume of the VND was calculated including occasional bubbles of air inside the VND. Measurements of both length and position of the VNO were performed by two independent observers. In case of differences between these measurements another experienced radiologist was employed.

Results

The VND's opening was found at a mean distance of 24.6 mm from the columella (range 10–34 mm) and 8.9 mm above the floor of the nasal cavity (range 5–18 mm). None

Table 1 Characteristics of investigated VNDs

Subject gender	Subject age (years)	VND type	Distance of opening from columella (mm)	Distance of opening from nasal floor (mm)	Distance of posterior portion from nasal floor (mm)	Length (mm)	Volume (mm^3)
Female	21	Pouch	28	15	15	4	25
Female	18	Pouch	20	9	9	10	126
Female	41	Tubular	20	5	8	19	66
Female	44	Tubular	25	18	18	3	10
Female	21	Tubular	20	5	5	4	6
Female	52	Tubular	25	6	10	5	5
Female	22	Tubular	28	10	12	6	10
Female	22	Tubular	30	10	12	8	10
Male	73	Pouch	32	10	13	20	114
Male	58	Tubular	34	6	7	5	8
Male	63	Tubular	32	11	11	5	7
Male	57	Tubular	22	6	8	9	26
Male	66	Tubular	16	10	10	12	23
Male	45	Tubular	10	5	7	22	66
Male	31	Tubular	27	7	16	47	77

of the subjects reported painful sensations in response to CA application. MRI of the VND was possible in all investigated cases (examples are shown in Figures 1 and 3).

MRI indicated high variability of both shape and size of the VND. In three subjects pouch-like VNDs were observed (length 4–20 mm, volume 25–126 mm^3). CA was found in close contact to the VND's opening. The remaining 12 subjects had tubular VNDs (median length 7 mm, range 3–47 mm, volume 5–77 mm^3; Table 1, Figure 2).

Three subjects exhibited VNDs which differed significantly from others. Subject A had a large pouch-like VND which extended from the application site into a bulge in the nasal septum without cross-over to the contralateral side. In subject B the VND had a volume of 26 mm^3 and a length of 9 mm. After CA application on the left side of the nasal septum, the agent was found to cross over the septum to the right side 6 mm dorsal to the opening (Figure 3). In subject C the VND opening was found 27 mm dorsal to the columella connected to a tubular structure of 9 mm length. From here on no CA was seen for a length of 32 mm until a pouch-like structure (diameter 6 mm) appeared which, again, was filled with CA (volume 76.5 mm^3).

VNDs tended to be slightly longer in men (median = 12 mm, mean = 17.4 mm, SD = 14.7) compared to women (median = 5.5 mm, mean = 7.4 mm, SD = 5.2) (*t*-test, $P = 0.10$); however, the position of the VND's opening was almost identical for men and women (Figure 2).

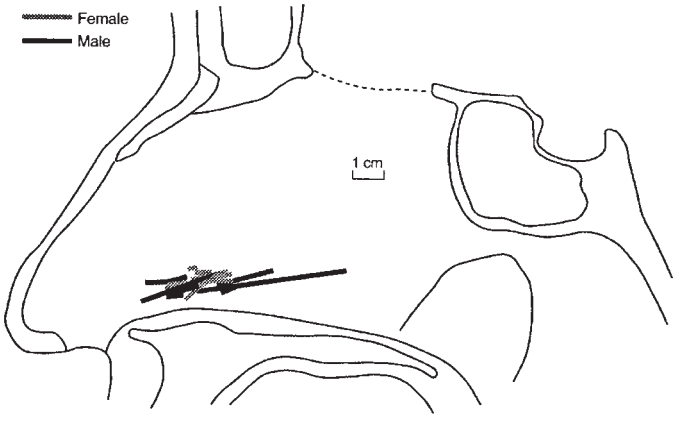

Figure 2 Schematic diagram of the investigated VNDs in the midsagittal plane of the nasal septum. Position, orientation and length of the VNDs are shown separately for men ($n = 7$, black lines) and women ($n = 8$, gray lines), irrespective of the individual volume of the nasal cavity. All investigated VNDs originated from the anterior portion of the nasal septum.

Discussion

The present study produced three major results. It indicated that the VND (i) has a median length of 7 mm; (ii) exhibits large variation in shape; and (iii) may cross over to the contralateral side. To our knowledge, this was the first time that the VND has been investigated using MRI.

Most previous studies indicated that the VND's length ranges between 2–12 mm (Kölliker 1877; Anton 1895; Stensaas *et al.*, 1991; Moran *et al.*, 1995; Jahnke and Merker 1998). While this corresponds with present observations, we had one subject where the VND was found to have a length of 47 mm. To our knowledge, there is only one anecdotal report from Mangakis (Mangakis, 1902) where a bilateral VND of 62 mm length was found. Similar to findings in the present study, Mangakis also reported that these tubular structures were connected to each other through the septum. Other than all previous findings, however, Mangakis

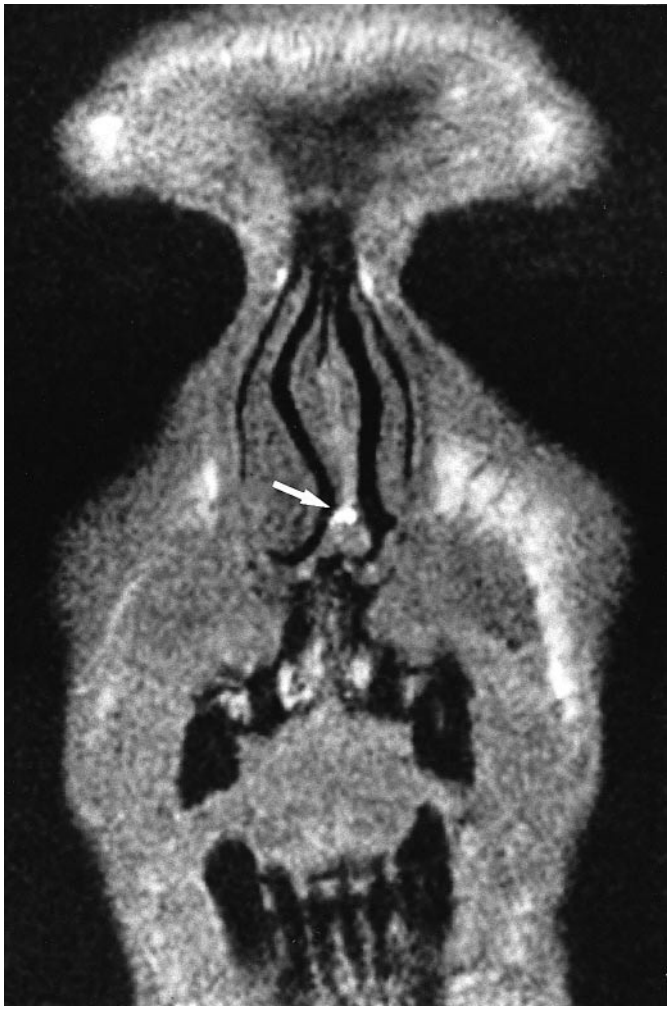

Figure 3 Coronal reformats of a FLASH-3D (TE = 6 ms, TR = 20 ms, α = 30°, 512^2 matrix). After local application of CA on the left side (!) parts of the right-sided VND are filled with CA (white arrow).

reported that these symmetrical ducts did not end blindly but had a posterior opening. Thus, the present study confirms this previous report as one VND was found to have a length of at least 47 mm. It remains a question, however, as to how this extremely long duct relates to the much shorter mucosal ducts found in the anterior portion of the septum, or whether these long ducts represent a different anatomical entity unrelated to the VND.

As the CA was poured into the VND's opening without any pressure, the actual length of the VND may have been underestimated. Specifically, the VND's lumen may not always have been filled completely with CA. On the other hand, regardless of whether the filling was complete or not, the fact that CA was found in the VND points at the possibility that in humans a similar pumping mechanism may exist as it is thought to exist in animals (Meredith and O'Connell, 1979; Eccles, 1982). There, it is possible that the constriction of blood vessels may create a vacuum which draws stimulus-laden air and/or mucus into the VND's lumen. Whether such pump-like mechanisms exist in humans or not might be explored in cadavers. However, when running such experiments it would be mandatory to use absolutely fresh material in order to avoid potentially disturbing effects of dehydration of the mucosa on the interaction with hydrophilic contrast agents.

In addition to variation in length, the investigated VNDs also exhibited variation in size—which to some extent may be due to septal deviations. Three subjects exhibited pouch-like VNDs, while the other subjects had tubular ones. A similar variability in shape has been reported more than 100 years ago. Anton (Anton, 1895) found one specimen to be pouch-like, with a diameter of 2.2 mm; he described an additional six VNDs which had a tubular shape.

Finally, the present study revealed that VNDs may cross over to the contralateral side. Provided that the human VND subserves chemosensory functions, this may have consequences in terms of septal surgery. It seems possible that the surgeon may unknowingly destroy the VND on one side where no opening can be detected. As a consequence, it must be discussed whether investigations, similar to the one we have performed, should become standard procedure before septal surgery. Alternatively, until the question of the VND's function in humans has been answered convincingly, the subperiostal approach for nasal septum surgery should be preferred whenever possible.

In conclusion, the present paper indicated large variability in the shape and size of the human VND. In addition, it provided data which are in favor of a careful, subperiostal approach in septal surgery, even when no ipsilateral opening is detectable.

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