Differences Between Orthonasal and Retronasal Olfactory Functions in Patients With Loss of the Sense of Smell

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Objective: To investigate differences between orthonasal and retronasal olfaction in patients with loss of the sense of smell without taste complaints.

Design: Electrophysiological and psychophysical testing of orthonasal and retronasal olfactory functions.

Setting: Outpatient clinics.

Patients: A series of 18 patients who had olfactory loss due to various reasons but no “taste” complaints.

Main Outcome Measures: Orthonasal and retronasal olfactory functions assessed by olfactory event-related potentials and psychophysical smell tests.

Results: Psychophysical testing revealed retronasal olfaction to be normal or slightly altered, whereas orthonasal olfaction was either absent or severely compromised. Findings from nasal endoscopic examinations and computed tomographic scans were within the reference range in all subjects. In response to orthonasal stimulation there were neither detectable olfactory event–related potentials nor any with small amplitudes, whereas olfactory event–related potentials in response to retronasal stimulation were clearly present in some patients.

Conclusion: These clinical observations, together with the psychophysical and electrophysiological findings, suggest that orthonasal and retronasal olfaction might be processed differently.


R E T R O N A S A L  O L F A C T I O N  I S  T H E  p e r c e p t i o n  o f  o d o r s  e m a n a t i n g  f r o m  t h e  o r a l  c a v i t y  d u r i n g  e a t i n g  a n d  d r i n k i n g ,  a s  o p p o s e d  t o  o r t h o n a s a l  o l f a c t i o n ,  w h i c h  o c c u r s  d u r i n g  s n i f f i n g .  T h e  r e t r o n a s a l  o l f a c t o r y  p a t h w a y ,  w h i c h  c o n t r i b u t e s  t o  t h e  f l a v o r  o f  f o o d s  o r  d r i n k s ,  i s  c o m m o n l y  a s s o c i a t e d  w i t h  t h e  s e n s e  o f  t a s t e .  T h e s e  g u s t a t o r y  a n d  o l f a c t o r y  s e n s a t i o n s  h a v e  b e e n  m i s i d e n t i f i e d  s i n c e  t h e  v e r y  f i r s t  r e p o r t s  o n  o l f a c t o r y  d i s o r d e r s ,  Z w a a r d e m a k e r ,  a  p i o n e e r  i n  o l f a c t o r y  r e s e a r c h ,  n a m e d  i t  “ g u s t a t o r y  o l f a c t i o n . ”  D u r i n g  t h e  1 9 5 0 s ,  “ h e m a t o g e n i c a l l y ”  i n d u c e d  o d o r o u s  s e n s a t i o n s  h a v e  a l s o  b e e n  i d e n t i f i e d  a s  a  f o r m  o f  r e t r o n a s a l  o l f a c t i o n .  U n t i l  r e c e n t l y ,  r e t r o n a s a l  o l f a c t i o n  w a s  o f  i n t e r e s t  o n l y  i n  f o o d - r e l a t e d  q u e s t i o n s ,  a n d  i t s  c l i n i c a l  s i g n i f i c a n c e  w a s  r e d u c e d  t o  a  m e a n s  f o r  d e t e c t i n g  m a l i n g e r e r s  i n  a  m e d i c o l e g a l  c o n t e x t ( H u m m e l  e t  a l . ) .  P e r h a p s  b e c a u s e  o f  t h e  l a c k  o f  s t a n d a r d i z e d  t e s t s ,  r e t r o n a s a l  o l f a c t o r y  t e s t i n g  h a s  n o t  y e t  b e c o m e  p a r t  o f  t h e  r o u t i n e  c l i n i c a l  a s s e s s m e n t  o f  t h e  s e n s e  o f  s m e l l .  H o w e v e r ,  r e c e n t  a t t e m p t s  t o  r e m e d y  t h i s  s i t u a t i o n  h a v e  p r o d u c e d  s i m p l e  a n d  r e l i a b l e  t e s t s  o f  r e t r o n a s a l  o l f a c t o r y  f u n c t i o n  b a s e d  o n  o d o r  i d e n t i f i c a t i o n  t a s k s .  F r o m  a  c l i n i c a l  p o i n t  o f  v i e w ,  t h e  t e s t i n g  o f  r e t r o n a s a l  o l f a c t o r y  f u n c t i o n  s e e m s  t o  p r o v i d e  r e d u n d a n t  i n f o r m a t i o n  c o m p a r e d  w i t h  o r t h o n a s a l  t e s t s .  H o w e v e r ,  r e t r o n a s a l  p e r c e p t i o n  i s  c l e a r l y  d i f f e r e n t  f r o m  o r t h o n a s a l  o l f a c t i o n  ( e g ,  t h e  u n p l e a s a n t  s m e l l  o f  a  c e r t a i n  c h e e s e  b e c o m e s  v e r y  p l e a s a n t  w h e n  s m e l l e d  r e t r o n a s a l l y ) ,  a n d  b o t h  e l e c t r o p h y s i o l o g i c a l  a n d  m a g n e t i c  r e s o n a n c e  i m a g i n g  d a t a  s u g g e s t  t h e  p r o c e s s i n g  o f  o r t h o n a s a l  a n d  r e t r o n a s a l  i n f o r m a t i o n  t o  b e  d i f f e r e n t .  M o s t  p a t i e n t s  w i t h  o l f a c t o r y  d i s f u n c t i o n  h a v e  l o s e  t h e  s e n s e s  o f  s m e l l  a n d  t a s t e .  F u r t h e r m o r e ,  t h i s  l o s s  h a s  b e e n  r e p o r t e d  t o  a f f e c t  t h e  q u a l i t y  o f  l i f e  o f  m o s t  p a t i e n t s  w i t h  o l f a c t o r y  d i s o r d e r s  ( H u m m e l  a n d  N o r d i n ) .  A l t h o u g h  t h i s  c l a i m  i s  a  c o m m o n  c l i n i c a l  p r e s e n t a t i o n ,  o u r  r e c e n t  r e p o r t ,  b a s e d  o n  p s y c h o p h y s i c a l  t e c h n i q u e s ,  d e s c r i b e d  a n  n u m b e r  o f  p a t i e n t s  w i t h  c o m p l e t e  l o s s  o f  t h e  s e n s e  o f  s m e l l  w i t h o u t  a n y  t a s t e  c o m p l a i n t s .  W e  f o u n d  t h a t  m o s t  o f  t h e s e  p a t i e n t s  h a d  n a s a l  p o l y p s ,  s o  t h i s  p a t t e r n  i s  h i g h l y  s u g g e s t i v e  o f  n a s a l  p o l y p o s i s .  H o w e v e r ,  w e  v e r y  r e a r l y  e n c o u n t e r  p a t i e n t s  w i t h  o l f a c t o r y  l o s s  w i t h o u t  a l t e r e d  f l a v o r  p e r c e p t i o n — a n d  t h e n  a l s o  i n  t h e  a b s e n c e  o f  n a s a l  p o l y p o s i s .  O u r  o b j e c t i v e  w a s  t o  i n v e s t i g a t e  t h i s  p e c u l i a r  c l i n i c a l  p r e s e n t a t i o n  b y  u s i n g  a  p s y c h o p h y s i o l o g i c a l  a p p r o a c h  a n d ,  m o s t  i m p o r t a n t ,  t o a d d r e s s  t h i s  p h e n o m e n o n  w i t h  e l e c t r o p h y s i o l o g i c a l  t e c h n i q u e s .
METHODS

PATIENTS

Nineteen patients (6 men and 13 women; mean ± SD age, 47 ± 3.8 years) who were treated at the smell and taste outpatient clinics in Dresden, Germany, and Geneva, Switzerland, were identified as having loss of orthonasal olfactory function, but their sense of taste was virtually unaffected. When questioned in detail, these patients confirmed that they still enjoyed the pleasures of different tastes while eating and drinking. All of these patients exhibited low orthonasal test scores, whereas retronasal testing results indicated olfactory function in the reference range.

The patients underwent a structured interview and extensive otorhinolaryngological examinations that included endoscopic and radiological investigations (magnetic resonance imaging or computed tomographic scan) to exclude the presence of nasal polyps and to ascertain an open olfactory cleft. In cases in which the cause of the olfactory disorder remained unclear, supplementary investigations (eg, neurological examinations) were performed. All patients received psychophysical tests of their olfactory function. In addition, for most of the patients, olfactory event–related potentials (OERPs) were recorded.

PSYCHOPHYSICAL OLFACTORY TESTING

Olfactory testing was performed by means of Sniffin’ Sticks (Burghart Instruments, Wedel, Germany),17 a validated instrument containing separate tests for odor thresholds, odor discrimination, and odor identification. To represent general olfactory function, results of the individual tests are added to a threshold, discrimination, and identification score (for details, see Kobal et al17 and Wolfensberger et al18), which allows the differentiation of quantitative olfactory loss.

We performed retronasal olfactory testing by using odorized powders presented to the oral cavity, as described and standardized previously.10,11 We applied the substances by using squeezable plastic vials with 6-cm-long spouts. The retronasal test consisted of grocery store condiments and food items that were available in powder form or odorized powders used in the food industry (Givaudan SA, Dübendorf, Switzerland). The substances were applied on the middle of the tongue inside the oral cavity. Before application, subjects had to block their noses; they were allowed to unblock their noses after the powder was placed in the oral cavity with the mouth closed. Using a forced multiple-choice paradigm after presentation of each item, subjects had to select 1 of 4 verbal choices to describe the powder’s odor. After each trial, subjects rinsed their mouths with tap water. We obtained scores by adding the number of correct identifications. The test for retronasal function is similar to the orthonasal test in that it allows for the quantification of olfactory loss.

OLFACTORY EVENT–RELATED POTENTIALS

We performed chemoosensory nasal stimulation by using the Olfactometer (model OM2; Burghart Instruments).19 Hydrogen sulfide (4 ppm; the smell of rotten eggs) was used for specific olfactory stimulation (stimulus duration, 200 microseconds; interstimulus interval, 40 seconds).20 During each session, 32 stimuli were administered in blocks of 8 stimuli each, in alternating orthonasal or retronasal applications.13 An electroencephalogram was recorded from 5 positions (Cz, C3, C4, Fz, and Pz) of the international 10/20 system referenced to linked
earlobes (Figure 1). Following artifact rejection and averaging of the stimulus-linked electroencephalogram segments (bandpass, 0.2-30 Hz; sampling frequency, 250 Hz), averages were inspected for absence or presence of a response.21,22

STATISTICAL ANALYSES

Results were analyzed using the statistical software SPSS 11.0 for Windows (SPSS Inc, Chicago, Ill). Descriptive statistics of the orthonasal and retronasal test scores within the body of text are expressed as mean ± SEM of the percentage of correctly identified items. Comparisons between orthonasal and retronasal scores were analyzed using the Wilcoxon matched pairs test. The α level was set at .05.

RESULTS

PATIENTS

Causes of olfactory impairment were diverse (Table). Most patients had idiopathic olfactory loss (n=9); 6 patients had olfactory loss following upper respiratory tract infections; other patients had smell loss after trauma (n=1) or myocardial infarction (n=1) or had congenital olfactory dysfunction (n=1). Before we reached a definitive diagnosis, all subjects received systemic corticosteroids for at least 7 days; they were tested before and after the course of corticosteroids. Only 1 patient had improved when retested (patient 6; the threshold, discrimination, and identification score changed from 9 to 17), which indicated the presence of sinus or nasal olfactory dysfunction; this patient was excluded from further study. Thus, any major inflammatory component in the olfactory disorder of the remaining patients could be excluded.23 In 2 patients whose olfactory loss was of idiopathic origin, the computed tomographic scan showed an isolated, partial congestion in the olfactory cleft (Figure 2). However, these patients neither responded to systemic corticosteroids nor exhibited nasal symptoms such as obstruction or rhinorrhea.

PSYCHOPHYSICAL OLFACTORY TESTING

With 4 exceptions, all subjects exhibited threshold, discrimination, and identification scores compatible with a diagnosis of functional anosmia.17 The mean score was 12.5±1.8 (25.8%±3.7% of the maximum possible score). The percentage of correctly identified orthonasal items was 36.1%±5.4%; for retronasal items, the percentage correctly identified was 54.7%±5.7% (Figure 3). A significant difference existed between correct orthonasal and retronasal odor identification (P=.009).

OLFACTORY EVENT–RELATED POTENTIALS

Thirteen patients underwent OERP investigations. There were either no OERPs or OERPs with very small amplitude in response to orthonasal stimulation in these patients. However, in 4 of these 13 patients, the clinical and psychophysical findings of orthonasal anosmia/hyposmia and retronasal normosmia/hyposmia could be corroborated through electrophysiological recordings. These patients exhibited clearly detectable retronasal OERPs, but no orthonasal OERP was recorded. The OERP of 1 patient, a 54-year-old woman with post–upper respiratory tract infection olfactory loss, is shown in Figure 1.

COMMENT

The most important result of the present study was the electrophysiological confirmation of a psychophysical observation. The clinical observations of patients complain-

Table. Characteristics of Patients Identified Over a 4-Year Period as Having Olfactory Loss With Intact Perception of Flavors and No Nasal Polyposis

<table>
<thead>
<tr>
<th>Patient/ Sex/Age, y</th>
<th>TDI Score</th>
<th>Orthonasal Identification Test Results, %</th>
<th>Retronasal Identification Test Results, %</th>
<th>OERP Pattern*</th>
<th>Diagnosis</th>
<th>Remarks</th>
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<tr>
<td>1/F/63</td>
<td>7</td>
<td>6</td>
<td>75</td>
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<td>Phantosmia</td>
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<td>2/F/58</td>
<td>15.25</td>
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<td>Post-URTI</td>
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<td>3/F/64</td>
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<td>44</td>
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<td>Post-URTI</td>
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<td>5/M/89</td>
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<td>20.25</td>
<td>62</td>
<td>35</td>
<td>No</td>
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</table>

Abbreviations: OERP, olfactory event–related potential; TDI, threshold, discrimination, and identification; URTI, upper respiratory tract infection.

*No orthonasal OERP but retronasal OERP present.
ing of olfactory loss but having intact perception of flavors was reported in early descriptions of olfactory disorders. Ogle wrote in 1870,

These simple tastes (acid, salt, sweet and bitter) compounded with smells form flavours. Various cases are then considered which seem in contradiction with this opinion—cases, namely, in which smell is apparently lost, and yet the perception of flavours remains.

Although numerous clinicians may have made similar observations, to our knowledge, no systematic study has been conducted to further investigate this phenomenon.

Differences between retronasal and orthonasal olfactory functions have recently been shown to characterize olfactory disorders related to the presence of nasal polyps. However, although many patients with olfactory loss and intact sense of taste present with nasal polyps, here we observed a series of patients in whom no polyps could be found even after endoscopic and radiological examinations. Thus, the present data confirm on psychophysical and electrophysiological levels that differences exist between orthonasal and retronasal olfaction, even in the absence of sinus or nasal disease.

In patients with nasal polyposis, the differences between orthonasal and retronasal function may be related to the growth pattern of the polyps, which changes the orthonasal access of odorants to the olfactory cleft. In contrast, the patients described herein had no major obstruction of their olfactory clefts. Most patients were diagnosed as having idiopathic olfactory loss. Patients with post–upper respiratory tract infection olfactory loss constituted the second largest group. Finally, other causes for olfactory loss existed, such as congenital and posttraumatic olfactory loss and olfactory loss following myocardial infarction. It may be hypothesized that as a common mechanism in the diverse cases presented herein, the anterior portions of the olfactory epithelium (OE) lose their function, whereas those in the posterior area of the OE retain their function.

Orthonasal and retronasal olfactory information has been shown to be differently processed on a cerebral level. This seems to suggest that the structures responsible for orthonasal and retronasal olfaction are functionally different but may also be structurally different at the OE or olfactory bulb levels, or even at cerebral levels. A possible cause of intact retronasal perception in the absence of orthonasal olfactory function could be the difference in vulnerability between the anterior and posterior OE. Thus, the cause of diminished orthonasal function would partially spare retronasal function. Another hypothesis is that the

Figure 2. Example of a patient with idiopathic olfactory loss (TDI [threshold, discrimination, and identification] score 4; orthonasal and retronasal scores were both poor, with 6% and 5% identified, respectively), who showed an opacity of the olfactory cleft (A, transversal computed tomographic [CT] slice; B, coronal CT slice). Otherwise, the CT scan shows healthy nasal cavities. The patient had no sinus or nasal complaints such as chronic rhinorrhea or nasal obstruction. A diagnostic trial with systemic corticosteroids did not change olfactory function either subjectively or on psychophysical testing.

Figure 3. Correctly identified items for retronasal and orthonasal olfactory identification (mean±SEM). There was a significant difference in results of tests for retronasal olfaction.

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process of neuronal regeneration is different for the orthonasal and retronasal areas of the OE and that the retronasal OE region seems to be better protected from environmental irritants than the anterior portions of the OE. On a clinical level, this hypothesis of a differential damage to anterior or posterior portions of the OE is confirmed by studies of morphologic traits. Olfactory receptor neurons are most likely to be found in dorsoposterior regions of the nasal septum and the superior turbinate rather than in anterior portions of the septum or the middle turbinate. 25

The case of patient 5, who had a history of cardiovascular disease, raises the question of the extent to which vascular diseases could be involved. It is known that numerous internal diseases lead to olfactory disorders, 26 and the blood supply of the olfactory bulb and epithelium has been poorly studied. According to an anatomical study 27 in humans, the olfactory artery, which represents the main blood supply of the bulb, shows considerable variations among individuals, especially in its distal ramification. It is conceivable that arteriosclerosis could lead to ischemia within peripheral olfactory structures. The consecutive damage would mostly affect anterior portions of the OE and, thus, orthonasal olfactory function.

In the computed tomographic scans of 2 patients, we also found isolated areas of congestion in the olfactory cleft (Figure 2), although they had no accompanying sinus or nasal symptoms such as obstruction or rhinorrhea. Like the rest of the patients, they showed no improvement in symptoms in response to a course of systemic corticosteroids. These computed tomographic scans are reminiscent of an image in a recent report 28 of so-called olfactory cleft disease, a presentation of anosmia of unknown origin documented in 13 cases. Unfortunately, the authors neither tested retronasal olfaction nor documented flavor perception in their patients, which makes it difficult to draw any conclusions parallel to the cases described herein.

In conclusion, the present data, obtained by using electrophysiological and psychophysical techniques, confirm the clinical observation of patients with olfactory loss yet intact perception of flavor. This clinical observation is made in patients without any sinus, nasal, or congestive nasal disease, which makes changes of intranasal flow patterns unlikely to be the reason for the observed differences between olfactory and retronasal olfactory function. Although this clinical observation seems to be a rare finding, it should encourage physicians to test retronasal olfactory function in their patients. Because the underlying pathophysiological mechanisms remain unclear, physicians should be especially cautious in interpreting differences in the perception of orthonasal and retronasal olfaction as a clear indicator of malingering in a medicolegal context. 8

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REFERENCES