Distorted Odorant Perception

Analysis of a Series of 56 Patients With Parosmia

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Objective: To characterize the self-reported olfactory and gustatory symptoms, olfactory function, and causes in parosmia.

Design: Assessment of olfactory symptoms and function in patients with a chief complaint of parosmia.

Setting: A university hospital clinic and research facility.

Patients: Fifty-six consecutive patients presented to the ORL Clinic, European Hospital Georges Pompidou, with a chief complaint of parosmia between October 2001 and November 2003.

Main Outcome Measures: Subjective olfactory symptom analysis and olfactory function test results.

Results: The mean duration of parosmia was 63.0 months. Forty patients (71.4%) reported associated hyposmia and 16 (28.6%) reported anosmia. Olfactory testing revealed moderate to severe olfactory loss in all patients. Quantitative and qualitative alterations occurred simultaneously in 32 patients (57.1%); parosmia onset occurred within 3 months after quantitative dysosmia in 19 patients (33.9%) and after 3 months in 5 patients (8.9%). The sensation of parosmia was always unpleasant. The main odorant triggers eliciting parosmia are described. The mean severity of flavor dysfunction of the population, evaluated using a 10-cm visual analog scale, was 6.4. Thirty-one patients (55.4%) viewed their olfactory alteration as severely affecting their quality of life. The main clinical association of parosmia was upper respiratory tract infection, found in 42.8% of the patients. Others clinical associations are described.

Conclusion: The series of patients with parosmia presented herein, the largest in the literature, permits a clinical description of this rare olfactory abnormality.

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CHEMOSENSORY DYSFUNCTION is common. Smell and taste alterations result in more than 200 000 visits to physicians annually in the United States.[1] The chemical senses play an important role in determining the flavor of beverages and food. The sense of smell is an important early warning system for detecting such threats as dangerous fumes, spoiled foods, and fires. Moreover, chemosensory dysfunction can be of considerable practical consequence to individuals whose livelihood depends on the normal functioning of their olfactory sense (eg, professional beverage or food tasters, cooks, and firefighters). Furthermore, alterations in the pleasure of these chemosensory sensations have serious effects on the quality of life.

Complaints of olfactory dysfunction can be quantitative (mainly, a decrease in sensitivity) or qualitative (an inappropriate or unpleasant quality). Quantitative alteration of smell may be subdivided as follows: (1) *anosmia* is the inability to detect any olfactory sensation and (2) *hyposmia* is a decreased sensitivity to odorants. The term *dysosmia* can be used to describe any qualitative distortion of the sense of smell. Dysosmia may be subdivided as follows: (1) *cacosmia* is the presence of an unpleasant and real odorant due to nasosinusal or pharyngeal infections; (2) *parosmia* is the perception of an unpleasant olfactory experience when an odorant is being presented; and (3) *phantosmia*, or *olfactory hallucination*, is the perception of an odor that occurs in the absence of an odorant in the environment.[2,3]

Clinical descriptions of large series of patients with parosmia are rare. Most publications are case reports or reviews.[2,4-8] In this study, demographic, medical, and che-

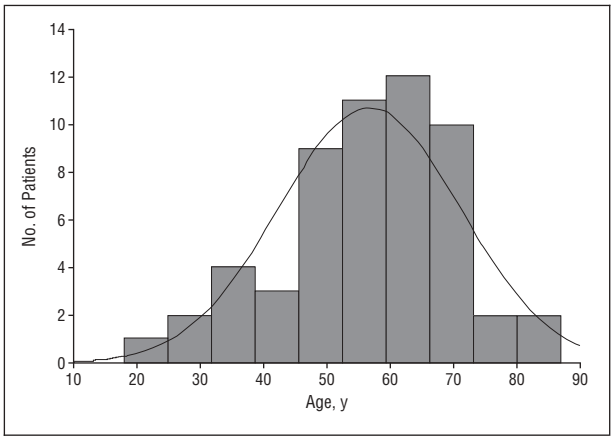

Figure 1. Histogram of age range among the 56 patients.

mosensory results from 56 consecutive patients with a chief complaint of parosmia are presented.

METHODS

Fifty-six consecutive patients (29 women and 27 men) presented to the ENT Clinic, European Hospital Georges Pompidou, with a chief complaint of parosmia between October 2001 and November 2003. Fewer than 5 olfactory centers exist in France for 60 million inhabitants. The mean±SE age of the study population was 56.7±1.9 years (**Figure 1**). The same physician (P.B.) examined all patients for the entire duration of the study. Medical information included a history and routine examination and, when required, imaging and other specialized tests (computed tomographic scans for patients with nasosinusal infections and cerebral magnetic resonance imaging for patients with neurological symptoms). Routine evaluations included otorhinolaryngological, neurological, and physical examinations and evaluation of smell. Detailed information regarding each patient's medical history, chemosensory complaints (quantitative or qualitative olfactory and gustatory dysfunction, as well as signs of dysosmia), and nasal symptoms was obtained during patient interviews and medical examination. Based on data from the medical histories and examinations, each patient was noted as having a specific clinical association of dysosmia (eg, nasal or paranasal sinus disease, upper respiratory tract infection [URTI], head trauma, neurological disorder, exposure to toxic chemicals, psychiatric association, nasal operation, aging, or idiopathic association).[9] Quality of life was considered as altered if the patient reported a decrease in his or her appetite or body weight or a change in psychological well-being or daily living.

OLFACTORY SYMPTOM EVALUATION

Two evaluations of the severity of olfactory dysfunction (ie, quantitative and qualitative) were performed. All tests were done in both nostrils. First, patients were assessed using a scale that included the categories "normal olfaction," "mild alteration of olfaction," "moderate alteration of olfaction," and "severe alteration of olfaction." Second, patients used a 10-cm visual analog scale (VAS) to grade the olfactory alteration severity. Patients also used a VAS to grade gustatory alteration severity. A comparison between these 3 methods was done using nonparametric Kruskal-Wallis test.

OLFACTORY FUNCTION TEST

An assessment of olfactory function was performed using a Biolfa (Amplifon CCA Biodigital, Paris, France) olfactory test. This test was described in a previous article.[10] The Biolfa test includes 2 series of 30-mL glass bottles containing chemical substances with different smells.

The first series measured olfactory thresholds for 3 different substances (eugenol, phenylethyl alcohol [PEA], and aldehyde C14). These 3 agents are useful in human olfactory investigation, as they allow psychophysical investigation of the first cranial nerve without potential confounding effects from the trigeminal nerve (fifth cranial nerve).[11] The lowest concentration for which the faint presence of an odor is noted is termed the *detection threshold*. We used a 2-alternative, forced-choice, single-staircase, detection threshold procedure. In each test, we presented two 30-mL glass sniff bottles to the patient (an odorant and a blank). We asked the subject to indicate which of 2 stimuli, presented sequentially and in random order, smelled the stronger.[10] Some patients with anosmia cannot detect any odorant during the test. To analyze the olfactory function in such patients, a test score was calculated for each odorant. The eugenol, PEA, and aldehyde C14 scores were the values (1/eugenol threshold), [(1/PEA threshold)×100], and (1/aldehyde C14 threshold), respectively. In patients who cannot detect any odorant, the olfactory threshold tends to infinity, and the test score tends to zero and was therefore estimated as zero. The results of the autoevaluation using the VAS to grade the olfactory alteration severity and the eugenol, PEA, and aldehyde C14 (Biolfa) scores were compared using Pearson product moment correlation.

The second series was an identification test. Regardless of geographic origin, existing differences in cultural patterns may be expected to affect odor perception. Therefore, an olfactory test for the specific population of southern Europe has been developed. This test used 8 components dissolved in dipropylene glycol, including citronella (odor of citronella), *cis*-3-hexenol (grass), aldehyde C14 (peach), L-carvone (mint), eugenol (clove), 1-octene-3-ol (mushroom), vanillin (vanilla), and para-cresyl acetate (horse dung). For each odorant, 4 dilutions were used, ranging from level 1 (low concentration) to level 4 (high concentration). For each component, a global test score was determined as the number of olfactory items correctly identified out of a total of 8. The duration of the test never exceeded 30 minutes.

RESULTS

CHEMOSENSORY COMPLAINTS

All patients presented to the ENT Clinic with a chief complaint of parosmia (ie, the perception of an unpleasant olfactory experience, such as a burn odor or feces odor, when a normal odor is being presented). Patients reported that parosmia was associated with a specific odorant. The duration of parosmia among the 56 subjects ranged from 3 months to 22 years (mean±SE, 63.0±7.6 months) (**Figure 2**). Parosmia was bilaterally perceived for all patients except 1 who perceived only a right but severe parosmia of unknown cause. The patients indicated whether parosmia was bilateral by their answer to a simple yes or no question. The percentage of smokers in the population was 7.1% (n=4).

All patients noted that quantitative olfactory dysfunction was associated with parosmia, including 40 patients (71.4%) who reported hyposmia and 16 (28.6%) who re-

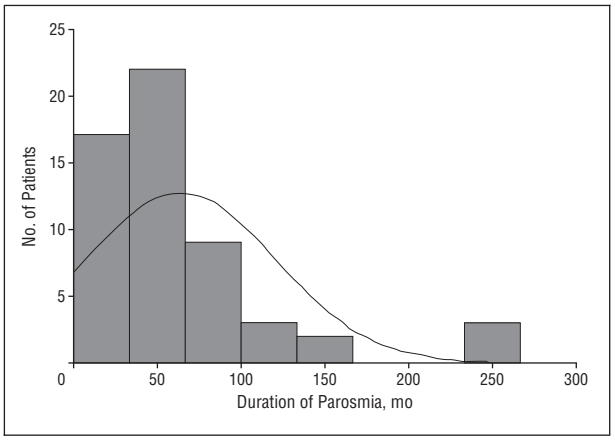

Figure 2. Histogram of duration of parosmia among the 56 patients.

ported anosmia. Quantitative and qualitative (parosmia) alterations occurred simultaneously in 32 patients (57.1%). In contrast, parosmia onset occurred within 3 months after quantitative olfactory dysfunction in 19 patients (33.9%) and after 3 months in 5 patients (8.9%). The mean±SE time of onset in these 24 patients was 1.5±0.3 months after quantitative olfactory dysfunction.

In all patients, the sensation of parosmia was unpleasant and was typically described as a "foul," "rotten," "sewage," or "burn" smell. Different odors triggered parosmia. Patients reported stimulant-unidentifiable parosmia (ie, the odorant eliciting parosmia was not identified by the patient) (10 patients [17.9%]) or stimulant-identifiable parosmia (46 patients [82.1%]). In these patients, the main odorant stimuli eliciting parosmia were gasoline (30.4%), tobacco (28.3%), coffee (28.3%), perfumes (21.7%), fruits (15.2%, mainly citrus fruits and melon), and chocolate (13.0%).

All the complaints concerned olfactory alterations, alone (4 patients [7.1%]) or in combination with flavor dysfunction (49 patients [87.5%]). The mean±SE flavor dysfunction severity of the population, evaluated using a VAS, was 6.4±0.3. Flavor perception is largely an olfactory function and mainly involved parageusia, with meals having the aroma of burned food, feces, or garbage. No burning mouth syndrome was observed. Thirty-one patients (55.4%) viewed their olfactory alteration as severely affecting their quality of life.[9]

CLINICAL ASSOCIATIONS OF PAROSMIA

Different clinical conditions were associated with parosmia. The most common etiology of parosmia was URTI, which accounted for approximately 42.8% of patients. Other possible etiologies were nasal and paranasal sinus disease (8 patients), toxic chemical exposure (4 patients), neurological abnormalities (3 patients), head trauma (2 patients), nasal surgery (2 patients), aging (1 patient), and idiopathic causes (12 patients).

DYSOSMIA SEVERITY

It was difficult to separate the severity of quantitative olfactory dysfunction and the severity of parosmia. Therefore, the severity of olfactory dysfunction was evaluated based on quantitative and qualitative alterations (**Figure 3**). First, patients were assessed using a category scale; no patient considered his or her olfaction as normal. Only 25.0% (14/56) of the population considered themselves as having mild or moderate olfactory dysfunction. Forty-two (75.0%) of the 56 patients considered their olfactory dysfunction as severe. Second, patients used a VAS to grade olfactory dysfunction severity. Ten (17.9%) of the 56 patients scored their olfaction as 5 or lower and 46 (82.1%) as 8 or higher. The mean±SE severity of olfactory loss among the 56 patients was 7.5±0.3. Kruskal-Wallis test comparing the 2 ranking methods showed a high correlation ($P<.001$).

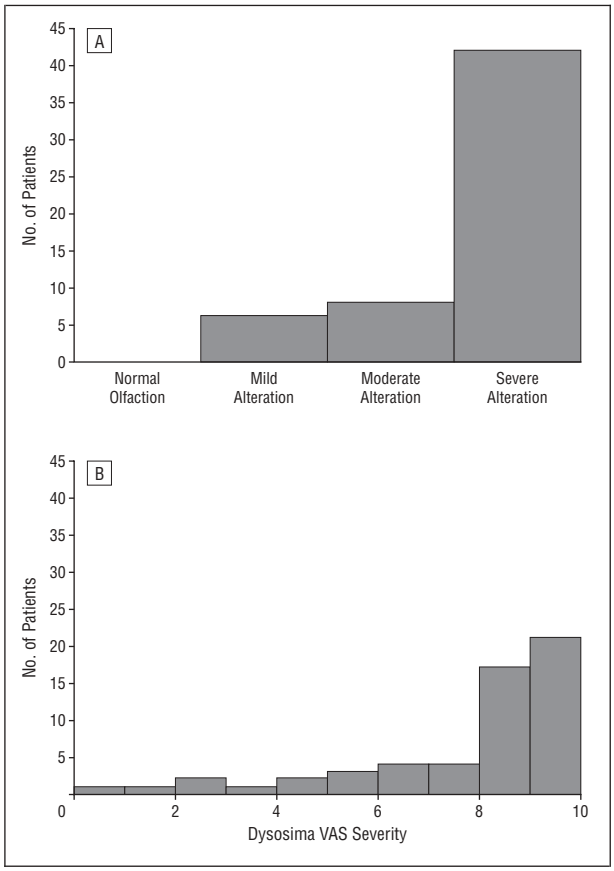

Figure 3. Severity of olfactory complaints. A, Patients used a category scale that included 4 categories. B, Patients also used a 10-cm visual analog scale (VAS).

OLFACTORY ASSESSMENT

The mean±SE scores among the 56 patients for eugenol, PEA, and aldehyde C14 were 0.95±0.34, 3.58±0.63, and 1.92±0.64, respectively. **Figure 4** shows the score distribution for the 56 patients. The results of the autoevaluation using the VAS to grade olfactory alteration severity and the scores for eugenol, PEA, and aldehyde C14 were compared using Pearson product moment correlation. Highly significant correlation was found relating the 2 methods ($P<.001$ for all 3 substances; and $r=0.36$, $r=0.51$, and $r=0.45$ for eugenol, PEA, and aldehyde C14, respectively). Among the 56 patients, the

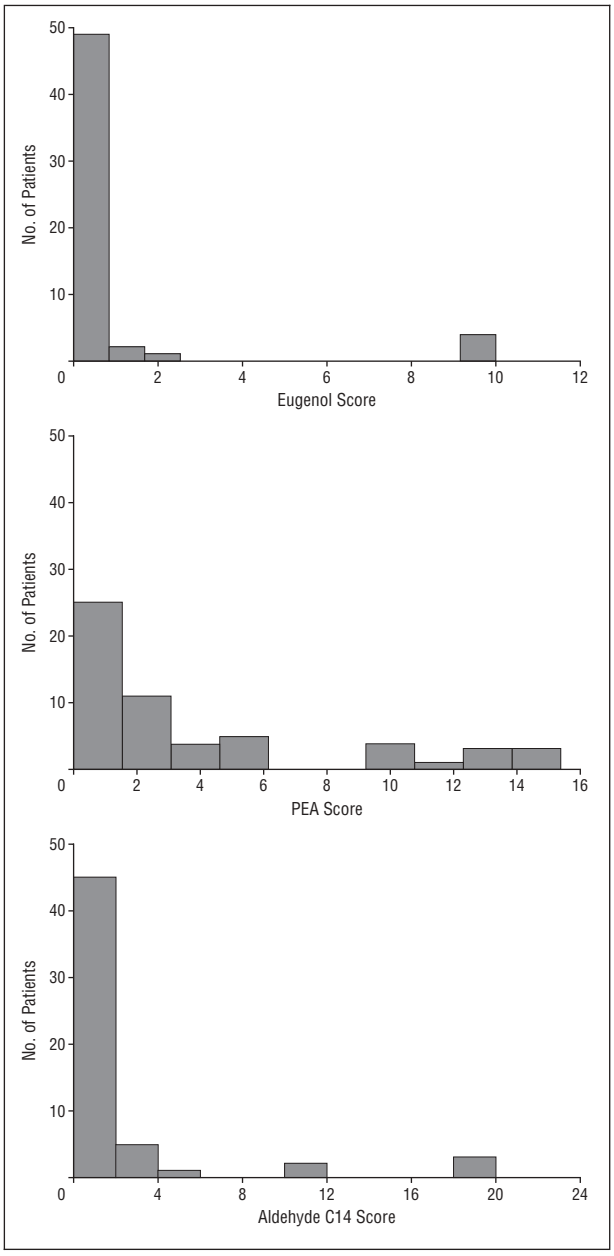

Figure 4. Eugenol, phenylethyl alcohol (PEA), and aldehyde C14 score distribution among the 56 patients.

mean±SE global test scores for the concentration levels were 0.64±0.21, 0.93±0.25, 1.02±0.26, and 2.29±0.28 for level 1, level 2, level 3, and level 4, respectively. **Figure 5** shows the global test score distribution for each level of concentration.

COMMENT

As suggested by Leopold,[2] one of the most important problems in the analysis of olfactory dysfunction has been the terms used to describe olfactory distortions. Parosmia describes a perceived distortion when there is an odorant stimulus present. Parosmia must be differentiated from phantosmia, or olfactory hallucination, which is the perception of an odor without any odorant stimulation. Zilstorff and Herbild[4] published one of the first articles, to our knowledge, on parosmia in 1979. However, only 2 patients were described, and their symptoms are more indicative of phantosmia than parosmia. The first patient was a 66-year-old woman who complained of parosmia after severe head trauma, and the second was a 30-year-old woman who had parosmia of unknown cause for 8 years. Since 1979, a limited number of publications[7,8] report some isolated cases of parosmia. This article presents the first large series in the literature concerning patients with a chief complaint of parosmia.

The main objective of this study was to present the clinical evaluation of a large series of 56 patients with a chief complaint of parosmia. Quantitative olfactory loss was not the chief complaint and was not a problem for most of the patients. The duration of parosmia was long, ranging from 3 months to 22 years (mean±SE, 63.0±7.6 months) (Figure 2). It is unknown whether parosmia decreased spontaneously. The global assessment of olfactory dysfunction (ie, parosmia and decreased olfactory sensitivity) was evaluated by a category scale or by a VAS (Figure 3). Forty-two (75.0%) of the 56 patients considered that their olfactory dysfunction was severe. The mean±SE severity of olfactory dysfunction among the 56 patients on the VAS was 7.5±0.3. There was a high correlation between the category scale and VAS methods of evaluation. Moreover, all but 4 patients with parosmia (52 patients [92.8%]) also complained of flavor dysfunction. Flavor perception is largely an olfactory function. The mean±SE severity of flavor dysfunction, evaluated with the VAS, was 6.4±0.3. Flavor dysfunction was noted by the patients as a perception of burned food, feces, or garbage. These olfactory and flavor dysfunctions could explain why 31 (55.4%) of the patients viewed their chemosensory alteration as severely affecting their quality of life.

Quantitative olfactory dysfunction was not the main complaint of these patients but was observed in all them, including 40 patients (71.4%) with hyposmia and 16 (28.6%) with anosmia. These quantitative alterations were confirmed by the Biolfa test results (Figure 4 and Figure 5).[10] Most of the patients with a chief complaint of parosmia had moderate to severe hyposmia, but this quantitative olfactory alteration was not the principal complaint. A highly significant correlation was found between the VAS results and the Biolfa results ($P<.001$). The low r value (eg, only 26% of the variance explained by the correlation for PEA) could be because of the differences in the 2 methods of evaluation. The VAS grades the severity of olfactory dysfunction (ie, quantitative and qualitative). Biolfa tests only explore quantitative alterations of olfaction.

The daily perception of parosmia was unpleasant for all patients and was typically described as a foul, rotten, sewage, or burn smell. Forty-six (82.1%) of the patients could identify the stimuli eliciting parosmia. A large variety of extrinsic stimuli can trigger parosmia. The main odorant triggers were gasoline (30.4%), tobacco (28.3%), coffee (28.3%), perfumes (21.7%), fruits (15.2%, mainly citrus fruits and melon), and chocolate (13.0%). Such descriptions were not observed in the literature.

Antecedent events that precede parosmia have been described in the literature. The main categories of olfac-

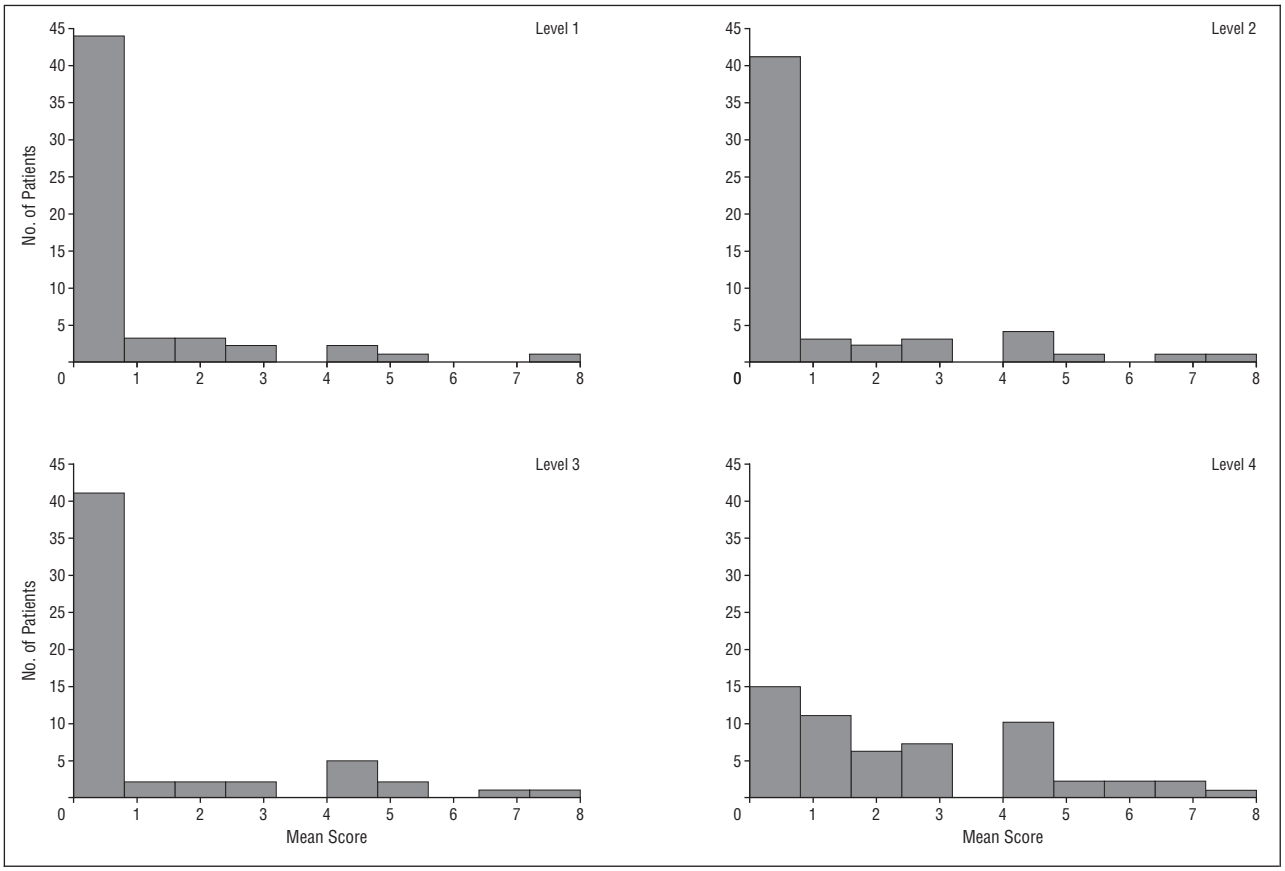

Figure 5. Global test score distribution for each level of concentration.

tory loss are URTI, head trauma, and nasal and paranasal sinus disease (ie, allergic rhinitis or chronic rhinosinusitis), with a predominance of URTI.[2,12-17] In our series, based on data from the medical histories and examinations, a probable etiology of parosmia was assigned for each patient. The main clinical association of parosmia was URTI, accounting for approximately 42.8% of patients. Other possible etiologies were nasal and paranasal sinus disease (8 patients), toxic chemical exposure (4 patients), neurological abnormalities (3 patients), head trauma (2 patients), nasal surgery (2 patients), aging (1 patient), and idiopathic causes (12 patients). Parosmia is not caused by conditions that destroy the sense of smell. Rather, it occurs in people who have lost their sense of smell, and perhaps this is the general common denominator for this condition.

The temporal relationship between quantitative olfactory dysfunction and parosmia is not simple. Quantitative and qualitative (parosmia) loss occurred simultaneously in 32 patients (57.1%). Parosmia never occurred before quantitative olfactory alteration, but parosmia occurred after quantitative olfactory loss in 24 patients (42.9%). In these patients, parosmia onset occurred within 3 months after quantitative olfactory decrease in 19 patients (33.9%) and after 3 months in 5 patients (8.9%). The mean±SE time of onset in the 24 patients was 1.5±0.3 months after quantitative olfactory decrease. The physiopathological basis of these 2 phenomena cannot be explained by the same mechanisms. The cause of parosmia is not clear. Two main physiopathological hypotheses include a *peripheral theory* and a *central theory*. The *peripheral theory* is based on the inability of abnormal olfactory neurons to form a complete picture of the odorant.[2,12] This hypothesis is in agreement with our findings that all individuals with parosmia have an intensity loss along with parosmia. Recently, Leopold et al[13] described a series of 8 patients surgically treated for phantosmia. The excised olfactory mucosa generally showed a decreased number of olfactory neurons, a greater ratio of immature to mature neurons, and disordered growth of axons with some intraepithelial neuromas. Among 24 patients in the present study with parosmia onset occurring within weeks after quantitative olfactory dysfunction, parosmia may have arisen because neurons located near intraepithelial neuromas have an altered response to odorants (ie, activity may be modulated by ionic shifts occasioned by a large mass of activated axons).[12] For patients with immediate parosmia, ephaptic transmission between axons that are disconnected and others that innervate the bulb might result in disordered signaling in response to an odorant.[12] However, these observations cannot exclude a *central theory* that the integrative or interpretive centers in the brain form parosmia.[2] Some positron emission tomographic scan results are also consistent with the central theory.[12]

Only a few publications[4,7,8] on parosmia can be found in the literature. Research on humans with parosmia is practically nonexistent.[2] The terms used to describe olfactory distortion are often confusing, and the physiopathological basis of this symptom remains unknown.

The patients with parosmia presented herein represent the first large series in the literature, to our knowledge, and permit a clinical description of this rare olfactory abnormality.

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