Chem. Senses 33: 107–118, 2008
doi:10.1093/chemse/bjm069
Advance Access publication October 24, 2007

Retronasal but Not Oral-Cavity-Only Identification of ''Purely Olfactory'' Odorants

Veronica Chen[1,3] and Bruce P. Halpern[1,2]

Departments of [1]Neurobiology and Behavior and [2]Psychology, Cornell University, Ithaca, NY 14853, USA
[3]Present address: 2023 Foothill Drive, Fullerton, CA 92833, USA

Correspondence to be sent to: Bruce P. Halpern, Departments of Psychology and Neurobiology and Behavior, Uris Hall, Cornell University, Ithaca, NY 14853-7601, USA. e-mail: bph1@cornell.edu

Abstract

Identifications of 5 odorants selected to be nontrigeminal stimuli were compared using retronasal and oral-cavity-only (OCO) air-phase presentations, with OCO produced by both exhalation through the mouth and a nose clip that closed the nostrils. Nine identifiers were available on each trial; 1 or 2 were correct for each odorant. Correct retronasal identifications were more common than OCO identifications and exceeded chance across subjects and for each subject; OCO correct identifications did not exceed chance. Retronasal reaction times were briefer than OCO reaction times. Correct retronasal identifications for vanillin, octanoic acid, phenylethyl alcohol, coumarin, and octane were 88%, 73%, 87%, 70%, and 85%, respectively; correct OCO identifications were, respectively, 10%, 12%, 18%, 35%, and 33%. Identifiers selected for retronasally presented odorants differed from those for other retronasally presented odorants, but identifiers for OCO-presented odorants did not differ between odorants. Overall, the retronasal identifications of nontrigeminal odorants both depended upon the odorant that was presented and corresponded to previous reported orthonasal identifications. In contrast, the OCO identifications, characterized by low percentages of correct identifications and an absence of differences between odorants in selected identifiers, suggested that OCO responses to nontrigeminal, purely olfactory odorants lack sufficient sensory information for either correct or differential identification.

Key words: human psychophysics, olfaction, oral cavity, smell, trigeminal

Introduction

Odorants may be categorized in many ways. One approach is chemical, including the general molecular structure (e.g., alkanes, alkenes, esters, and terpenes) or the presence of particular groups (e.g., alcohols, aldehydes, and amines) (e.g., Cain 1988; Leffingwell 2001). Another approach is functional, which can emphasize genetic, perceptual, or neuroanatomical aspects. A functional genetic categorization of odorants can include relevant genes and their associated receptors (see Malnic et al. 1999; Mombaerts 2004; Pernollet et al. 2006). A perception-based approach can address categories to which humans assign odorants (e.g., citrus, floral, grassy, and woody [see Moncrieff 1967; Cain 1978, 1988; Lawless 1989, 1997; Jellinek 1992; Wise et al. 2000]) or, instead, specific identifications (e.g., almond, gasoline, and ''vanilla''). A third functional approach focuses on the cranial nerve or nerves involved in behavioral responses to vapor-phase stimuli (e.g., olfactory and/or trigeminal nerves [see Silver and Finger 1991; Rawson 2000; Doty and Cometto-Muñiz 2003]). Categorization as a vapor-phase trigeminal stimulus (aka trigeminal odorant) is often based upon the extent to which individuals who lack a functional olfactory system, that is, anosmics, can detect or describe the stimulus and the degree of nasal pungency (e.g., Doty et al. 1978; Kobal and Hummel 1992; Cometto-Muñiz et al. 1998, 2005). Another measure of the responsiveness of the human trigeminal system to odorants (i.e., nasal chemesthesis [see Shusterman 2002; Cain et al. 2005]) has been the degree to which odorants could be lateralized to one nostril or the other (e.g., Kobal et al. 1989; Kobal and Hummel 1992; Radil and Wysocki 1998; Savic and Berglund 2000; Wysocki et al. 2003; Wysocki and Wise 2004; Cometto-Muñiz et al. 2005; Frasnelli and Hummel 2005; Cain et al. 2006) (but see Mainland and Sobel 2006).

An odorant consisting of a single pure chemical that is rarely detected or not reliably described by anosmics, or is not readily lateralized, has been designated as ''lacking nasal chemesthetic impact,'' ''nontrigeminal,'' ''odor-only,'' or as a ''pure'' olfactory odorant (e.g., Cometto-Muñiz et al.

2005). In general, these nontrigeminal, purely olfactory odorants have been tested by presenting them to the nostrils (anterior nares) for smelling. That is, an orthonasal presentation was used in which odorants are normally inhaled into and through a nasal cavity. Nonetheless, air-phase nontrigeminal chemical odorants such as vanillin and phenylethyl alcohol (PEA) (see Doty et al. 1978; Cometto-Muñiz et al. 2005) have also been presented via a retronasal route (see Halpern 2004a, 2004b; Shepherd 2004) and found effective (e.g., Voirol and Daget 1986; Heilmann and Hummel 2004). More specifically, both these purely olfactory odorants could be discriminated and could be assigned intensities when delivered by a retronasal route (identifications were not measured). In contrast, if such nontrigeminal pure chemical odorants were restricted to a region that had trigeminal but no olfactory innervation, such as the oral cavity, it would be expected that they would not be effective stimuli.

Odorants that are present in the oral cavity at concentrations which are effective for retronasal smelling may fail to initiate reliable judgments during respiration if access to the nasal cavities is prevented (e.g., Dragich and Halpern forthcoming). For oral-cavity-only (OCO) stimulation, closure of the nostrils together with exhalation from the mouth is the usual approach (e.g., Murphy et al. 1977; Pierce and Halpern 1996; Mojet et al. 2003; Lim and Lawless 2005; Sun and Halpern 2005). Such restriction of odorants to the oral cavity while respiration continues is often done to allow a comparison of OCO and retronasal stimulation. However, it should be noted that in some instances, the intention has been to permit controlled delivery of odorants to a nasal cavity independently of respiration. In this instance, odorants are delivered directly into the nasal cavity, and the velum is elevated to isolate the nasal cavities from the oral cavity (e.g., Kobal and Hummel 1991, 1992).

A velopharyngeal closure produced by sufficient elevation of the velum provides a mechanical barrier between the oral and the nasal cavities (see Buettner and Schieberle 2000; Halpern 2004a, 2004b). If complete, a velopharyngeal closure would isolate the oral cavity and the oropharynx from the nasal cavity, thus preventing any movement of odorants from the oral cavity to the nasal cavities. Respiration through the nostrils would also be prevented. In contrast, nostril closure, often done using a nose clip, prevents respiration through the nostrils and therefore precludes respiratory movement of odorants into the nasal cavities from the oral cavity. However, in principle, given sufficient time, diffusion of odorants from the oral cavity to the nasal cavities might occur. Because this diffusion would be relatively slow, any identification based upon diffusion from the oral cavity would be expected to yield a positive relationship between reaction times and correct identifications. Consequently, measuring the reaction time of OCO identifications could provide an indication of the possibility that they were diffusion based.

The present research had 2 goals. These goals were to examine retronasal identifications of orthonasally characterized purely olfactory odorants and to compare retronasal and OCO identifications of these odorants. The hypotheses were that retronasal identifications would be predicted by previously measured orthonasal identifications and that identifications during OCO presentations would differ from retronasal identifications and might be unrelated to the odorant presented. Confirmation of the first hypothesis would indicate that despite potential retronasal versus orthonasal differences in airflow patterns, odorant conduction, and central nervous system processing, purely olfactory single odorants nonetheless received similar qualitative characterizations. The second hypothesis would evaluate the degree to which retronasal identifications of the tested purely olfactory odorants were based only upon stimulation within the nasal cavities. A brief report of these data has been made (Chen and Halpern 2006).

Materials and methods

Subjects

Subjects were 20 paid volunteers, 14 females and 6 males (mean age = 22 years), ranging from 18 to 49 years of age. They were nonsmoking, nonpregnant, and nonlactating individuals associated with Cornell University, over the age of 18, who could communicate in American English, recruited using posters and an online Web site (http://susan.psych.cornell.edu/). No chemosensory screening of subjects was done. The protocol was reviewed and approved by the Cornell University Committee on Human Subjects (UCHS). Each potential subject read and signed an Informed Consent Form approved by the UCHS before participating in the experiment. Subjects were asked not to eat and drink anything except water for 1 h before a scheduled session. They were informed that the experiment would compare 2 different methods of sensing odors, retronasal and trigeminal, that is, OCO. For the purposes of this study, retronasal smelling was described as inhaling through the mouth and exhaling through the nose; OCO perception, both inhaling and exhaling through the mouth.

Odorants

The 5 odorants were 1) high performance liquid chromatography ≥ 99% coumarin, 2) 98% reagent grade octane, 3) ≥98% octanoic acid, 4) high performance liquid chromatography ≥99% coumarin, Food Chemicals Codex PEA, and 5) 99% ReagentPlus vanillin, all from Sigma-Aldrich, Inc. (St Louis, MO). These 5 chemicals were selected as nontrigeminal odorants on the basis of previous data indicating little or no detection by anosmics upon orthonasal presentation and a general lack of nasal lateralization (Doty et al. 1978, Radil and Wysocki 1998; Wysocki and Wise 2004; Cometto-Muñiz et al. 2005). However, it should be noted that Kobal and Hummel (1992) found some orthonasal lateralization with PEA, and Savic and Berglund (2000) reported lateralization of octane.

The correct identifications (IDs) of the odorants (Table 1) were based upon previous reports (coumarin: cinnamon [Buttery et al. 1978]; octane: gasoline [Moncrieff 1967; Haz-map Octane 2007; MSDS Octane 2007]; octanoic acid: rancid [Moncrieff 1967; O'Neil 2006]; PEA: floral, rose [Moncrieff 1967; Livermore and Laing 1998; O'Neil 2006]; vanillin: vanilla [O'Neil 2006]); and preliminary experiments. Odorants were presented at room temperature, 21 ± 1 °C.

Each presentation of an odorant in an odorant delivery container (ODC) (see Odorant delivery containers) had a total of 5 ml of the liquid odorant including diluent. The solvents used for dilution were United States Pharmacopeia-Food Chemicals Codex glycerin for coumarin, octanoic acid, PEA, and vanillin; sunflower oil (Wesson brand) for octane. Concentrations of the presented odorants (Table 1) are given in reference to the undiluted odorant, which would be 100% (i.e., neat). The concentrations that were used were based upon previous studies (PEA [Kobal and Hummel 1992; Radil and Wysocki 1998; Ferreira et al. 2000; Dalton et al. 2003]; octanoic acid [Laska and Teubner 1998; Ferreira et al. 2001; Acree and Heinrich 2004]; vanillin [Eccles et al. 1989; Kobal and Hummel 1992; Snyder and Drummond 1997; Radil and Wysocki 1998; Savic and Berglund 2000; Glasser 2002; Sulmont et al. 2002]; coumarin [Rychlik et al. 1998; Acree and Heinrich 2004]; octane [Laing 1988; Sobel et al. 1999]), and preliminary experiments that confirmed that the concentrations were sufficient to consistently evoke retronasal judgments. The goal was to obtain concentrations that were suprathreshold for retronasal smelling. Fresh dilutions were made every 2 days.

Odorant delivery containers

Odorants were presented for both retronasal and OCO conditions using an ODC (Figure 1). They were clean, odorless, 0.4-mm wall thickness, black homopolymer polypropylene, 118 ml volume, 5.1 cm high, tapered elliptical containers (Ellipso Portion Cups, Newspring Packaging, Kearny, NJ, http://www.Instawares.com). The upper major axis was 7.8 cm; upper minor axis, 4.9 cm. The lower major axis was 5.4 cm; lower minor axis, 2.7 cm. The 5 ml total volume of a diluted odorant just covered the bottom of the ODC, providing an odorant surface area of 11.45 cm^2. In the tight-fitting, transparent homopolymer polypropylene elliptical lids for the containers, two 5-mm diameter holes were made, centered on the major axis, 1.8-cm apart, and 3.5 cm from the ends of the lid. In one of the holes, a 6.5-cm long, 5-mm outer diameter, 4.8-mm inner diameter, homopolymer polypropylene straw (Jetware Unwrapped Plastic drinking straw, Jet Plastica Industries, Inc., Hatfield, PA) was inserted perpendicular to the lid, such that 3.25 cm of the straw was inside the container, and was fixed in position. This allowed each straw to sample the headspace over a liquid odorant but precluded contact with the liquid odorant. Aluminum foil rectangles, with holes corresponding to the 2 holes in the lids, were positioned over the lids in order to prevent visual observation by subjects of the diluted odorants (Figure 1). Each ODC, including lid and straw, was used for 1 odorant and was discarded after use with 1 subject.

Table 1 Concentrations, solvents, and correct identification for odorants

Odorant	Concentration %	Solvent	Correct identification (letter association)
Octanoic acid	10	Glycerin	Rancid (r), sweat (s)
PEA	10	Glycerin	Floral (f), rose (o)
Coumarin	10	Glycerin	Almond (a), cinnamon (n)
Vanillin	10	Glycerin	Vanilla (v)
Octane	67	Sunflower oil	Cleaner (c), gasoline (g)

Nose clip

All odorant presentation procedures began with the subject putting on a nose clip (Spirometrics Nose Clip #2104, Spirometrics, Gray, ME; 207-657-6700) prior to receiving an ODC containing an odorant. Each nose clip was used for 1 subject and then discarded. The nose clip was removed at the beginning of each retronasal odorant flow from the oral cavity but remained in place for OCO odorant presentations (see Odorant ID).

Training

Empty ODC

Subjects were presented with an empty ODC, whereas an experimenter used another empty ODC to demonstrate its use. Subjects were taught to hold the ODC such that the larger surface was on top and horizontal, with the straw upright.

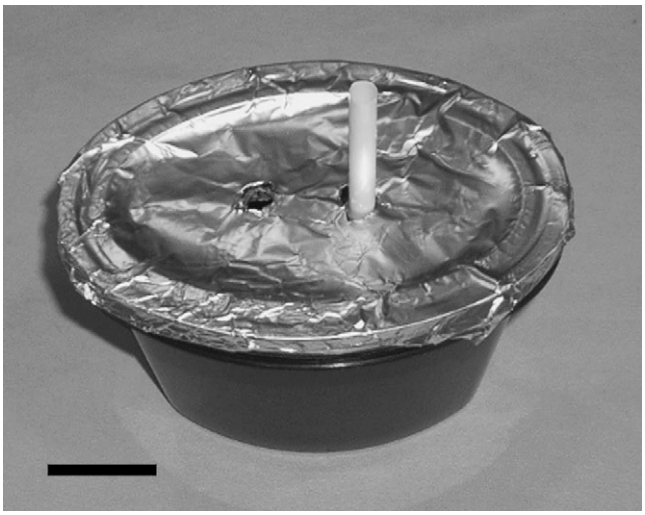

Figure 1 Photograph of the ODC, with straw in place in 1 of the 2 holes in the tight-fitting lid, which was covered with aluminum foil. The ODC had a total volume of 118 ml. During identification trials it contained 5 ml of odorant, which just covered the bottom. The horizontal calibration line represents 3 cm.

For both retronasal and OCO presentations, the first training instruction was 1) ''Put on the nose clip.'' Subjects were guided through the subsequent steps of the procedures. For retronasal presentations, subsequent training instructions were 2) ''Exhale deeply through your mouth''; 3) ''Place your mouth over the straw, close your lips, and inhale deeply through your mouth''; 4) ''Keeping your lips closed, remove the straw from your mouth''; 5) ''As the experimenter removes the nose clip, exhale deeply through your nose.'' The subject was told that if this were an identification trial on the computer, they would press the space bar on the computer as the experimenter removed the nose clip, 6) ''If there were an odorant present, you would now identify it as quickly as possible.'' The procedures for identification are presented below, after training for OCO presentations is described.

For the OCO presentations, the first training instruction was 1) ''Put on the nose clip.'' However, in contrast to retronasal trials, the nose clip remained in place throughout the trial. The OCO training instructions with an empty ODC after the nose clip was put on were 2) ''Place your mouth over the straw, close your lips, and inhale deeply through your mouth''; 3) ''Exhale slowly.'' Subjects were told that if this were an identification trial on the computer, they would press the space bar on the computer as they began to exhale, 4) ''If there were an odorant present, you would now identify it as quickly as possible.'' The procedures for identification are presented below.

ID list

After training with the empty ODC, subjects were given a printed list of the 9 available identifiers (IDs) and the single letters associated with each (Table 1). These letters would subsequently be entered by subjects on the computer keyboard to provide identification of odorants.

Odorant ID learning

Next, in a fixed random order, subjects were given the 5 odorants, each in a separate ODC, and asked to identify each odorant using the printed list of 9 IDs (Table 1), first with the retronasal procedure and then with the OCO procedure, as described above. However, because each ODC now contained an odorant, when the subject inhaled deeply through the ODC's straw, they obtained an air-phase odorant. Presentations of odorants were separated from a preceding identification by at least 10 s. Selection of a correct identifier was confirmed and the next odorant presented; incorrect ID was corrected and the odorant sampled again. Subjects were told that they would be asked to identify the odorants again later and were encouraged to become familiar with the ID of each odorant. An ID was required for each presentation.

Computer ID practice

Next, so that subjects could become facile with entering IDs for the odorants using the computer keyboard, the list of 9 IDs and their associated letters (see Table 1) were presented on a computer display. Subjects were told that the odorants which they were going to identify retronasally and OCO were the same ones for which they had just learned IDs, were reminded to press the space bar when they began to exhale after sampling the odorant from the ODC, and were told that the letter associated with an ID was to be typed on the computer keyboard as quickly as possible after exhalation began. The 5 odorants were presented, following both retronasal and OCO procedures, using a fixed random order different from that used for the odorant ID learning. An ID was required for each presentation.

Odorant ID

The complete sequence of instructions for retronasal presentations, and subsequently for OCO presentations, were provided on a computer display. Subjects had as much time as they wished to read the instructions. Each odorant was presented 3 times, in blocks of 5, in a fixed random order different from those used for odorant ID learning and computer ID practice, first retronasally and then OCO. At least 10 s elapsed between the time that the subject pressed a key on the computer keyboard to indicate an ID and presentation of the next odorant-containing ODC. Retronasal odorant ID trials consisted of 8 steps, with odorant flow from the oral cavity starting on step 7: The retronasal trials sequence was 1) the subject put on their nose clip, 2) the subject exhaled through their mouth, 3) the subject placed their mouth over the ODC's straw, 4) the subject inhaled through the ODC's straw, 5) The subject removed the straw from their mouth while keeping their lips closed, 6) The experimenter said ''ready, set, go,'' removing the subject's nose clip on ''go'', 7) the subject then immediately pressed the computer's space bar, simultaneously deeply exhaling through the nose, and 8) the subject typed the letter that best identified the odorant as quickly as possible. Pressing the space bar began the timing for each trial, which ended when a key was pressed indicating the odorant's ID. The resultant time interval was the reaction time for that trial.

For OCO presentations, the nose clip remained in place. After the subject inhaled deeply through the ODC's straw, the subject maintained closed lips until she/he began to exhale slowly from the mouth and simultaneously pressed the space bar. Here too, pressing the space bar began timing for a trial, which ended when a key was pressed indicating the odorant's ID. An ID was required for each presentation.

Statistical analyses

Overall percent correct identification for each odorant was calculated using all 60 identifications (20 subjects and 3 judgments each, see Figure 2) for each of the 2 presentation conditions. This provided an overall indication of the degree of correct identifications for the retronasal and OCO presentation conditions across all subjects and trials for each odorant

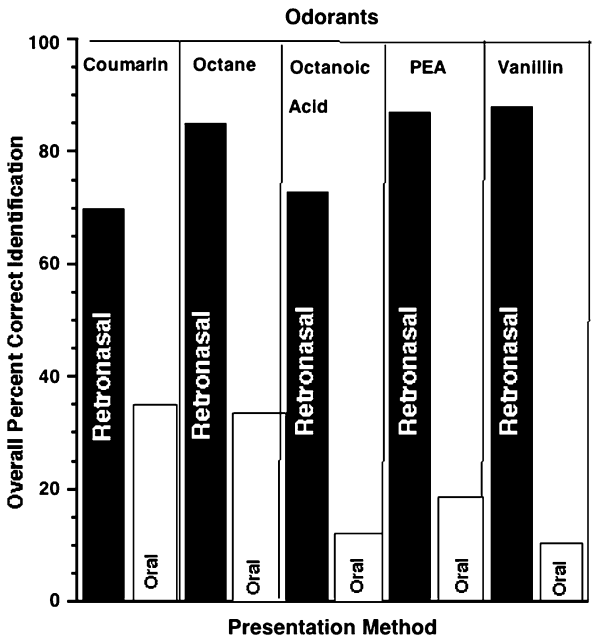

Figure 2 Overall percent correct identifications by 20 subjects presented each of 5 air-phase odorants 3 times, randomized in blocks of 5, either retronasally or OCO (oral).

under each presentation condition. Central tendencies and variability of correct identifications were obtained by calculating median and semi-interquartile range (SIR) percent correct identifications for each odorant for each of the presentation conditions, using the percentage of correct identification of each of the 20 subjects (Table 2). This required first calculating, for each subject, each odorant, and each presentation condition, the percentage of correct identification. The percentage of correct identification could range from 0% to 100%, based upon 3 identifications by that subject. For example, for 1 subject and 1 odorant, no correct identifications would be 0%; 1 correct, 33%; 2 correct, 67%; 3 correct, 100%, for each of the 2 presentation conditions, with percentages rounded to closest integer (Table 2). In order to provide specific information on the extent to which each of the IDs was selected across odorants and presentation conditions, the percent of identifications selected for each of 9 IDs (plus no response) by the 20 subjects was calculated for retronasal and OCO presentations (Table 3). The identifications that are summarized in Table 3 permitted evaluation of the extent to which the IDs that were selected for retronasal or OCO presentations of each odorant differed from the IDs selected for the other odorants. In addition, because the percentages for both the correct identifications and for all other identifications are provided, Table 3 constitutes a confusion matrix, indicating the extent to which odorants were misidentified as well as correctly identified.

The 3 reaction times of a subject's 3 IDs for each odorant for each of the 2 presentation conditions were used to calculate a median reaction time for that odorant, subject, and presentation condition. These 20 median reaction times for each subject, odorant, and presentation condition were used to calculate median and SIR reaction times for odorants and presentation conditions (Table 4).

For inferential statistics, because of the relatively small sample size and in order to avoid unnecessary assumptions, nonparametric statistics were used whenever possible, with $P \leq 0.05$ taken as an indication of statistical significance. Friedman nonparametric analysis of variance (ANOVA), Wilcoxon signed-rank tests, Kendall's rank correlation, and factorial ANOVA were used.

Results

Identifications

There was a significant difference in the number of correct identifications for retronasal and OCO conditions across the 5 odorants $P < 0.0001$ (Friedman nonparametric ANOVA, degrees of freedom [df] = 9, $\chi^2 = 113.14$). This Friedman ANOVA outcome indicated that one or more differences in the numbers of correct identifications existed between presentation conditions and that pairwise comparisons between conditions were justified. Pairwise comparisons for each odorant delivered retronasally versus OCO found that the number of correct identifications was significantly greater for all odorants when presented retronasally ($P \leq 0.004$, $Z < -2.92$, Wilcoxon signed-rank test). This outcome showed that the 2 odorant presentation conditions, retronasal versus OCO, produced differences for all tested odorants in the number of correct identifications. A factorial ANOVA confirmed this outcome. In this case, interactions between odorant and presentation condition (retronasal or OCO) for the number of correct identifications for each of the 5 odorants were significant, $P < 0.0001$ (factorial ANOVA, df = 4, sums of squares > 15, $F > 9.7$).

The degree to which the odorants had comparable or dissimilar effects on the number of correct identifications within each presentation condition was tested using the Friedman ANOVA. Across odorants presented retronasally, there was not a significant difference in the number of correct identifications ($P = 0.16$, df = 4, $\chi^2 = 6.577$), but across odorants presented OCO, there was a significant difference in the number of correct identifications ($P = 0.02$, df = 4, $\chi^2 = 11.28$), Friedman nonparametric ANOVA. This outcome showed that, for retronasal presentations, the 5 odorants did not differ in the number of correct identifications produced. In contrast, for the OCO method, the number of correct identifications produced was not comparable across the 5 odorants.

For all odorants, the overall percentages of correct identifications for retronasal smelling exceeded the overall percentages of correct identifications for OCO identifications (Figure 2). For retronasal smelling, the overall percentages of correct identifications ranged from 70% to 88%; for OCO, from 10% to 35%. The median percent correct identifications

Table 2 Percent correct identifications by each of 20 subjects for 3 trials of 5 air-phase odorants, randomized in blocks of 5, presented retronasally (retronasal) and OCO (oral cavity), and median percent correct identification and SIR for each odorant and presentation condition

Subject	Odorants									
	Coumarin		Octane		Octanoic acid		PEA		Vanillin	
	Retronasal	Oral cavity	Retronasal	Oral cavity	Retronasal	Oral cavity	Retronasal	Oral cavity	Retronasal	Oral cavity
1	67	0	**100**	67	33	0	**100**	0	**100**	0
2	67	33	67	**100**	33	0	**100**	33	**100**	33
3	**100**	0	**100**	33	67	0	33	0	**100**	0
4	67	33	67	67	**100**	33	**100**	0	**100**	67
5	**100**	**100**	**100**	0	**100**	33	67	0	67	0
6	**100**	0	**100**	67	0	0	67	33	**100**	0
7	**100**	0	**100**	0	33	0	**100**	33	**100**	0
8	**100**	0	**100**	33	**100**	0	**100**	33	**100**	0
9	**100**	67	67	33	**100**	33	67	0	**100**	0
10	67	33	33	0	33	33	67	33	67	0
11	33	67	**100**	0	**100**	33	**100**	0	33	0
12	33	0	**100**	67	**100**	33	**100**	33	**100**	33
13	67	67	67	67	**100**	0	67	33	**100**	0
14	67	33	**100**	0	**100**	0	**100**	33	**100**	33
15	33	33	**100**	0	**100**	0	**100**	33	33	0
16	67	67	**100**	33	**100**	0	**100**	0	**100**	0
17	33	0	**100**	0	33	33	**100**	33	**100**	33
18	67	**100**	**100**	67	33	0	67	0	67	0
19	**100**	33	67	33	**100**	0	**100**	33	**100**	0
20	33	33	33	0	**100**	67	**100**	0	**100**	0
Median	67	33	**100**	33	**100**	0	**100**	33	**100**	0
SIR	21	34	17	34	34	17	17	17	4	4

100% correct identifications are in boldface; 67% correct identifications are underlined. Percents are rounded to nearest integer.

with retronasal smelling ranged from 100% for 4 of the odorants (SIR = 4–34%) to 67% for coumarin (SIR = 21%) (Table 2). In contrast, with OCO presentations, median percent correct identifications ranged from 0% correct for vanillin and octanoic acid (SIR < 18%) to 33% for the 3 other odorants (SIR = 17–34%) (Table 2).

For each odorant, within each presentation condition (OCO or retronasal), the percentages of correct identifications (see Table 2) were compared with the percentages of correct identifications predicted by chance, both across subjects and for each subjects. A correct identification by chance across the 9 IDs would occur on 11% of trials for those odorants with 1 correct ID (1/9 = 0.11) and on 22% of trials for odorants with 2 correct IDs. Across subjects, for each retronasally presented odorant, the percent correct identifications were significantly different from chance ($P \leq 0.0002$, Bonferroni corrected, $Z \geq -3.765 < -4.129$, Wilcoxon signed-rank test). Within subjects, for each presentation condition, each subject made 3 identifications of an odorant; therefore, 1 correct ID would be 33% correct. It was found that the retronasal percent correct identifications for all 20 subjects were greater than chance for coumarin, octane, PEA, and vanillin and for 19 of the 20 subjects for octanoic acid. That is, every subject made at least 1 retronasal correct identification for coumarin, octane, PEA, and vanillin, and all but 1 subject made at least 1 retronasal correct identification for octanoic acid (Table 2). Furthermore, 13 of the 20 subjects made more than 1 correct retronasal identification for octanoic acid (i.e., at least 67% correct), 15 of the 20 subjects made more than 1 correct retronasal identification for coumarin, 18 of the 20 subjects for octane and vanillin, and 19 of the 20 subjects for PEA (underlined or boldfaced

Table 3 Percent of identifications (IDs) selected for each of 9 IDs (plus no response) by 20 subjects presented each of 5 air-phase odorants 3 times, randomized in blocks of 5, retronasally or OCO

Odorant	Percent of each ID selected for each odorant and presentation condition									
	No response (%)	Almond (%)	Cleaner (%)	Gasoline (%)	Rancid (%)	Sweat (%)	Cinnamon (%)	Floral (%)	Rose (%)	Vanilla (%)
Coumarin					Retronasal					
	0	**58**	5	0	2	0	**12**	0	2	22
					OCO					
	0	**30**	12	2	2	10	**5**	10	7	23
Octane					Retronasal					
	0	0	**72**	**13**	7	5	0	2	2	0
					OCO					
	2	12	**25**	**8**	8	8	3	3	8	22
Octanoic acid					Retronasal					
	3	2	17	2	**37**	**37**	0	0	2	2
					OCO					
	0	12	25	2	**5**	**7**	3	10	12	25
PEA					Retronasal					
	0	2	3	0	2	5	0	**33**	**53**	2
					OCO					
	2	10	12	2	17	20	2	**7**	**12**	18
Vanillin					Retronasal					
	0	8	2	0	0	2	0	0	0	**88**
					OCO					
	0	12	20	3	8	13	3	15	15	**10**

Boldface percents are correct identifications for each odorant. Percents are rounded to nearest integer.

values of Table 2). These outcomes showed that not only were correct retronasal identifications the general finding for all odorants tested but also that the pattern of correct retronasal identifications was observed for essentially all subjects.

Quite different results occurred with OCO presentations (Table 2). Across subjects, the percent correct identifications for OCO-presented coumarin, octane, PEA, and vanillin did not differ significantly from chance ($P \geq 0.453$, Bonferroni corrected, $Z > -0.589 < 1.51$) and were less than chance for OCO-presented octanoic acid ($P = 0.014$, Bonferroni corrected, $Z = -2.986$, Wilcoxon signed-rank test). Within subjects, the OCO percent correct identifications differed from chance for only about half the subjects or less (Table 2). Specifically, for OCO-presented odorants, subject's percent correct identifications were greater than chance for 5 of the 20 subjects for vanillin, greater than chance for 7 of the 20 subjects for OCO-presented octanoic acid, for 11 of the 20 subjects for PEA, and 12 of the 20 subjects for coumarin and octane (Table 2). These comparisons of OCO correct identifications with identifications based upon chance extended the direct comparisons between retronasal and OCO correct identifications: not only were frequencies of OCO correct identifications different from and less than retronasal correct identifications but also OCO correct identification frequencies were at chance rates.

Overall identification percentages for all 9 IDs, for retronasal and OCO presentations, are shown in Table 3. For retronasal presentations, analysis across the 5 odorants of the IDs selected by the 20 subjects for the 3 trials of each odorant showed that there were 1 or more differences between the 5 odorants in the identifications selected, $P < 0.0001$ (df = 4, $\chi^2 = 174.921$, Friedman nonparametric ANOVA). Pairwise comparisons showed that the IDs selected for each of the retronasally presented odorants were significantly different from the IDs selected for the other retronasally presented odorants, $P < 0.0004$, Bonferroni corrected ($Z < -3.527$, Wilcoxon signed-rank test).

The identifier-selection outcomes for OCO presentations were quite different. For OCO presentations, although analysis across the 5 odorants of the IDs selected by the 20 subjects

Table 4 Overall median identification reaction times, and SIR, in seconds, for 5 odorants presented 3 times each, randomized in blocks of 5, to 20 subjects, both retronasally and OCO

Odorant	Presentation condition	Reaction time	
		Median	SIR
Vanillin	Retronasal	1.96	0.62
	OCO	4.04	1.48
PEA	Retronasal	2.18	0.82
	OCO	4.04	1.47
Coumarin	Retronasal	2.43	0.96
	OCO	3.96	1.36
Octane	Retronasal	1.62	0.33
	OCO	3.05	1.06
Octanoic acid	Retronasal	2.09	0.67
	OCO	4.11	1.53

SIR, Semi-interquartile range, that is, the difference resulting from the first quartile (Q1) subtracted from the third quartile, (Q3), divided by 2 [(Q3 − Q1)/2].

for the 3 trials of each odorant also showed that there were 1 or more differences between the 5 odorants in the identifications selected, the probability that the difference was due to chance was much higher than had been the case for retronasal presentations ($P = 0.02$, df = 4, $\chi^2 = 12.107$, Friedman nonarametric ANOVA). Pairwise comparisons showed that none of the IDs selected for each of the OCO-presented odorants differed significantly from the IDs selected for the other OCO-presented odorants, $P > 0.08$, Bonferroni corrected ($Z < -0.365 > -2.611$, Wilcoxon signed-rank tests). Without the Bonferroni corrections for multiple analyses, 3 comparisons, between the IDs selected for OCO-presented vanillin versus coumarin and octane, and between octane versus PEA IDs, would have been significant, $P < 0.05$ ($Z < -1.978 > -2.610$ Wilcoxon signed-rank tests). None of the other comparisons of the IDs selected for OCO presentation of odorants would have been significant if Bonferroni corrections had not been applied ($P > 0.05$, $Z < -0.365 > -1.949$, Wilcoxon signed-rank tests). These analyses indicated that subjects selected a unique set of IDs from the available array for each of the retronasally presented odorants but failed to select different IDs for each odorant when the same odorants were presented OCO. If a less demanding statistical approach is applied, a few differences between the IDs selected for OCO odorants are indicated, with the IDs for most oral cavity odorants still not significantly different.

Viewed as a confusion matrix (See Wright 1987; Kurtz et al. 2001; Sun and Halpern 2005), Table 3 indicated that vanilla was often an incorrect OCO ID, accounting for 22% of the incorrect OCO ID choices overall. Frequent selection of vanilla as an incorrect OCO ID included the odorants octane, octanoic acid, and PEA (27% of incorrect ID). In contrast, when presented retronasally, these 3 odorants were either never (octane) or very rarely (2% of trials) identified as vanilla. Across all odorants, 4 IDs, vanilla, "cleaner," rancid, and sweat, were 47% of all incorrect OCO IDs. For the odorant vanillin, which was rarely (2% of trials) identified as cleaner retronasally, cleaner was the most numerous incorrect ID for OCO stimulation, 22% of incorrect vanillin OCO IDs.

Reaction time

There was a significant difference in identification reaction times for retronasal and OCO smelling across the 5 odorants $P < 0.0001$ (Friedman nonparametric ANOVA df = 9, $\chi^2 = 83.542$). This Friedman ANOVA outcome indicated that 1 or more differences in identification reaction times existed between conditions or odorants and that additional comparisons were justified. Within presentation conditions (retronasal or OCO), there were no significant differences in identification reaction times, $P > 0.33$ (df = 4, $\chi^2 > 0.82 < 1.6$, Friedman nonparametric ANOVA). However, for each odorant, there was a significant difference between retronasal and OCO identification reaction times ($P < 0.0007$, $Z < -3.435 > 3.845$, Wilcoxon signed-rank test). Median OCO identification reaction times were longer than the median retronasal reaction times for all odorants (Table 4). On the other hand, there were no significant correlations between the number of correct identifications and reaction times for any of the odorants for either retronasal ($P > 0.093$, Tau $< -0.038 > -0.203$) or OCO ($P > 0.158$, Tau $< 0.154 > -0.22$) presentations (Kendall's rank correlation).

Discussion

By definition, purely olfactory odorants must reach an array of olfactory receptor neurons if olfactory responses are to occur (e.g., Sobel et al. 1999). In humans, the olfactory receptor neurons are located only on limited regions of nasal cavity turbinates (see Rawson 2000; Hornung 2006). Retronasal smelling can afford access to these regions. Under normal circumstances, odorants that are smelled retronasally originate in the oral cavity, are carried into the nasal cavities during exhalations, and exit through the nostrils. In the present study, retronasal smelling of the 5 odorants produced consistent identifications, with percent correct identifications ranging from 70% to 88%. Given these high percent correct retronasal identifications, other finding follow logically: the retronasal correct identifications differed from chance, and the IDs selected for each retronasally presented odorant were significantly different from the IDs selected for the other retronasally presented odorants. Thus, using several measures, correct retronasal identifications of the odorants were not only accurate but also highly consistent.

The identifications categorized as correct had been largely based upon identifications previously found during orthonasal smelling. Thus, the first hypothesis, that retronasal

identification of purely olfactory odorants would be predicted by previously measured orthonasal identifications, is confirmed. It might seem that this qualitative correspondence between orthonasal and retronasal identifications is not surprising because previous reports indicated that orthonasal and retronasal identification of complex, multicomponent odorants were often qualitatively comparable (e.g., Pierce and Halpern 1996; Sun and Halpern 2005). However, the use of single pure chemicals that were considered to be purely olfactory stimuli, all at concentrations not adjusted for differences between retronasal versus orthonasal sensitivity, provided a more demanding test than prior studies. The prior studies had used common substances or natural extracts that might have offered more familiar stimulus patterns for retronasal identification. In addition, one of those prior studies (Sun and Halpern 2005) required each subject to separately choose retronasal and orthonasal concentrations that matched, for each subject, the perceived intensity of a common standard. Based on the present outcome, together with earlier reports, it can be proposed that for a wide variety of air-phase suprathreshold concentration odorants that have relatively familiar orthonasally derived linguistic labels, the same labels will be chosen when suprathreshold retronasal presentations are done. It follows that comparable cognitive categorizations and linguistic connections occur for responses to the 2 odorant presentation methods. This could be unexpected given the known differences between responses to orthonasal and retronasal odorant presentations in detection threshold sensitivity (Voirol and Daget 1986; Heilmann and Hummel 2004), identification accuracy (Sun and Halpern 2005), airflow patterns and odorant conduction within the nasal cavities (Zhao et al. 2004), and central nervous system processing (Small et al. 2005).

The second hypothesis was that identifications during OCO presentations would differ from retronasal identifications and might be unrelated to the odorant presented. It was found that the number of correct identifications produced by OCO smelling were significantly different from those occurring during retronasal smelling. Correct identifications for OCO presentations ranged from 10% to 35%, whereas correct retronasal identifications ranged from 70% to 88%. Differences in median percent correct identifications were even more striking, being 100% correct for 4 of the 5 odorants presented retronasally, compared with a median of 0% correct for 2 of the same odorants presented OCO and medians of 33% correct identifications for the other OCO presentations. At the level of individual subjects, every subject made at least 1 correct retronasal identification for coumarin, octane, PEA, and vanillin (1 subject made no correct retronasal identifications for octanoic acid). Seventy percent of the subjects made correct retronasal identifications on at least 2 of their 3 trials for all odorants. In contrast, at least 60% of the subjects made no correct OCO identifications for octanoic acid, PEA, and vanillin; the remaining subjects made only 1 correct identification for octanoic acid and PEA. The statistically significant differences, as well as the numerically large and disparate overall and median percent correct identification differences, together with the correct identification differences at the level of individual subjects, all confirm the "difference between OCO and retronasal correct identifications" part of the second hypothesis.

However, the differences between numbers of correct OCO and retronasal identifications could indicate either that identification during OCO presentations simply did not correspond to retronasal identifications or, in full conformity with the second hypothesis, that the identifications reported during OCO presentations were not determined by the odorants presented. The latter possibility is supported by the observation that the IDs selected for each of the OCO-presented odorants did not differ significantly from the IDs selected for any of the other OCO-presented odorants. This outcome is perhaps equivocal in that if Bonferroni corrections for multiple comparisons are not applied, 3 of the 9 possible OCO ID comparisons would be significantly different: the IDs selected for OCO vanillin would differ significantly from those for coumarin and octane, and the IDs for PEA would also differ from those for octane. Although there have been arguments that Bonferroni corrections are too conservative and should not be applied (see Nakagawa 2004), use of these corrections for the retronasal ID data had allowed strong conclusions to be reached concerning the unique status of the IDs selected for each retronasal odorant. It does not seem appropriate to abandon Bonferroni corrections in order to find a few ID differences within OCO-presented odorants.

If the OCO-presented odorants provided minimal or perhaps no differential sensory information, selection of IDs would be very difficult and, presumably, slow. Compatible with this idea were the observations that the median identification reaction times for OCO odorants were 1 or 2 s longer than retronasal identification reaction times (Table 4) and that OCO identification reaction times for all odorants were significantly different from reaction times for retronasal identifications.

Examination of the IDs selected for OCO-presented odorants reveals a relatively high incidence of vanilla for several of the odorants (Table 3). It is tempting to suggest that, under the OCO condition, vanilla was often chosen when subjects knew that some odorant must be present but had no sensory information upon which to base a choice. This suggestion would be compatible with the observed absence of significant differences between the IDs selected for OCO odorants. However, vanilla as a default identification does not fit the outcome for OCO vanillin, for which 5 other IDs were more common than vanilla, with cleaner the most numerous. Vanillin never was identified as cleaner on any retronasal identification trial.

Some correct identifications were selected in the OCO condition. Because this presentation condition was produced by the presence of a nose clip that prevented exhalation through

the nostrils, it is possible that diffusion from the oral cavity to the nasal cavities permitted very slow access to the olfactory receptor neurons during OCO presentations. The absence of significant correlations between reaction times and the number of correct identifications during OCO presentations fails to support this possibility. Consequently, it appears that the use of a nose clip is an adequate method to restrict odorants to the oral cavity. However, it should be noted that odorant conduction both to and within the nasal cavity is complex and can change with not only alterations in the diameter of the nasal valve, the olfactory cleft, and other regions but also with the sorptive characteristics of odorants (see Sobel et al. 1999; Kurtz et al. 2004; Zhao et al. 2004, 2006; Ishikawa et al. 2006). Consequently, although diffusion from the oral cavity to the nasal cavities during the observed OCO reaction times appears unlikely, direct measurements or appropriate modeling are needed to permit definitive conclusions.

Previous studies found that octanoic acid, PEA, and vanillin were rare if ever detected by anosmics (Doty et al. 1978; Cometto-Muñiz et al. 2005) and could not be lateralized during quiet breathing (Radil and Wysocki 1998; Wysocki and Wise 2004), although Kobal and Hummel (1992) found some orthonasal lateralization with PEA. Most of these observations indicated that octanoic acid, PEA, and vanillin were not trigeminal stimuli, at least when presented by an orthonasal route. In agreement with this prior characterization of certain odorants as purely olfactory odorant, that is, nontrigeminal stimuli, in the present study these 3 odorants had the lowest overall percentages of correct identifications during OCO presentations, 10–18%. Octanoic acid, PEA, and vanillin also had 0% median correct identifications for OCO presentations, correct identifications across subjects at chance levels, and ID selections that did not differ significantly between these 3 odorants for OCO presentations.

Coumarin and octane had the highest percentages of correct ID during OCO, 35% and 33% (median percentages of correct ID of 33%). The significant difference across odorants in the number of correct ID for the OCO condition suggested that the 5 odorants were not comparable as OCO stimuli. A previous study found that octane was detected by 30% of anosmics at 23 °C; by 70% at 37 °C (Cometto-Muñiz et al. 2005). Another study reported that octane could be lateralized, implicating trigeminal stimulation (Savic and Berglund 2000). These prior reports indicated that octane probably can be a trigeminal stimulus, with its effectiveness increasing sharply with vapor-phase concentration. The present data may imply that differential octane elicited–OCO responses may occur in some subjects. For example, 12 of the 20 subjects provided correct ID with a frequency greater than chance, although across subjects, correct OCO ID for octane did not differ from chance. In addition, if ID selections were evaluated using a lower statistical criterion, employing non-Bonferroni–corrected probability values, the IDs selected for OCO octane would differ from those for OCO vanillin and PEA. Overall, in agreement with prior findings, octane may have been an effective trigeminal stimulus for some subjects.

The concentrations of the odorant were all intended to be not only suprathreshold for retronasal smelling but also comparable for a relevant retronasal psychophysical measure. The median percent correct retronasal identifications of 100% for 4 of the 5 odorants, and 67% correct for the fifth, indicate that the concentrations were clearly suprathreshold. This was confirmed by the findings that the median percent correct identifications for all retronasally presented odorants were significantly different from chance across subjects, that every subject's percent correct IDs were greater than chance for 4 of the odorants, and for 19 of the 20 subjects for octanoic acid. The absence of a significant difference in retronasal reaction times denotes comparable retronasal psychophysical efficacy.

Several aspects of the findings of this study are noteworthy. The observation that orthonasally derived identifications of pure chemicals were correctly used during retronasal smelling indicates that both orthonasal and retronasal smelling provide sensory input that can utilize a common set of linguistic categories or labels. This connotes significant shared attributes of these 2 smell systems, as had been noted in a previous study (Pierce and Halpern 1996). Thus, the spatial–temporal distinctions between retronasal and orthonasal pathways and odorant conduction (Zhao et al. 2004; Halpern 2004a, 2008), as well as central nervous system differences (e.g., Small et al. 2005), do not necessarily prevent shared identifications.

A second important observation is the lack of oral cavity–derived differential identifications when presented with the purely olfactory vapor-phase odorants that were so effective retronasally. This demonstrates a limitation of the trigeminal receptor neurons located in the oral cavity. If nasal cavity trigeminal receptor neurons have response characteristics that are similar to those of the oral cavity, the observed retronasal identifications occurred only because of olfactory receptor neuron's responses. However, questions remain for octane and coumarin, at least for some subjects. In addition, the lack of successful identifications does not preclude differential responses to some odorants from oral cavity stimulation. For example, vapor-phase peppermint and dl-menthol were correctly identified when restricted to the oral cavity (Dragich and Halpern forthcoming; Parikh et al. 2007).

At a more technical level, the 2 outcomes noted above, that is, correct retronasal identifications and the lack of correct OCO identifications, demonstrate that the OCO procedures (a nose clip and oral breathing) successfully prevented retronasal smelling. This is important because it provides, using a set of frequently studied pure chemicals, validation of a simple and often-used technique designed to limit odorants to the oral cavity.

In conclusion, correct retronasal identifications for the studied nontrigeminal odorants were qualitatively comparable to

orthonasal identifications and were both much more frequent and faster than identifications for OCO presentations. Identifiers selected for retronasal but not OCO presentations differed between odorants, indicating a lack of differential sensory responses from the trigeminally innervated oral cavity. Although use of a nose clip to prevent retronasal airflow does not preclude eventual diffusion from the oral cavity to the nasal cavities, for the trial durations of the present study, typically less than 10 s, diffusion from the oral cavity to the nasal cavities was probably not a factor in those correct OCO identifications that did occur.

Funding

United States Department of Agriculture Hatch (NYC-191403).

Acknowledgements

We thank Harry T. Lawless, Christiane Linster, Robert E. Johnston, Jennifer Lee, and the anonymous referees for comments on previous versions of the manuscript.

References

Acree T, Heinrich A. 2004. Flavornet and human odor space. Available from: http://www.flavornet.org/index.html. Accessed 13 May 2007.

Buettner A, Schieberle P. 2000. Exhaled odorant measurement (EXOM)—a new approach to quantify the degree of in-mouth release of food aroma compounds. Lebensm WissTechnol. 33:553–559.

Buttery RG, Ling LC, Bean MM. 1978. Coumarin off-odor in wheat flour. J Agric Food Chem. 26:179–180.

Cain WS. 1978. History of research on smell. In: Carterette EC, Friedman MP, editors. Handbook of perception. Vol. VIA: Tasting and smelling. New York: Academic Press. p. 197–229.

Cain WS. 1988. Olfaction. In: Atkinson RC, Herrnstein RJ, Lindzey G, Luce RD, editors. Stevens' handbook of experimental psychology. 2nd ed. Vol. 1: Perception and motivation. New York: Wiley. p. 409–459.

Cain WS, Lee N-S, Wise PM, Schmidt R, Ahn B-H, Cometto-Muñiz JE, Abraham MH. 2006. Chemesthesis from volatile organic compounds: psychophysical and neural responses. Physiol Behav. 88:317–324.

Cain WS, Wijk RA, Jalowayski AA, Pilla Caminha G, Schmidt R. 2005. Odor and chemesthesis from brief exposures to TXIB. Indoor Air. 15:445–457.

Chen V, Halpern BP. 2006. Retronasal but not oral-cavity identifications of non-trigeminal odorants. Chem Senses. 31:479 [abstract].

Cometto-Muñiz JE, Cain WS, Abraham MH. 1998. Nasal pungency and odor of homologous aldehydes and carboxylic acids. Exp Brain Res. 118:180–188.

Cometto-Muñiz JE, Cain WS, Abraham MH. 2005. Determinants for nasal trigeminal detection of volatile organic compounds. Chem Senses. 30: 627–642.

Dalton P, Cowart B, Dilks D, Gould M, Lees PSJ, Stefaniak A, Emmett E. 2003. Olfactory function in workers exposed to styrene in the reinforced plastic industry. Am J Indust Med. 44:1–11.

Doty RL, Cometto-Muñiz JE. 2003. Trigeminal chemoreception. In: Doty RL, editor. Handbook of olfaction and gustation. 2nd ed. New York: Marcel Dekker. p. 981–999.

Doty RL, Cometto-Muñiz JE, Brugger WE, Jurs PC, Orndorff MA, Snyder PJ, Lowry LD. 1978. Intranasal trigeminal stimulation from odorous volatiles: psychometric responses from anosmic and normal humans. Physiol Behav. 20:175–185.

Dragich AM, Halpern BP. Forthcoming. Retronasal smelling: an oral cavity component. Physiol. Behav.

Eccles R, Jawad MS, Morris S. 1989. Olfactory and trigeminal thresholds and nasal resistance to airflow. Acta Otolaryngol. 108:268–273.

Ferreira V, Aznar, M, López, R, Cacho JF. 2001. Quantitative gaschromatography-olfactometry carried out at different dilutions of an extract—key differences in the odor profiles of four high-quality spanish aged red wines. J Agric Food Sci. 49:4818–4824.

Ferreira V, López R, Cacho JF. 2000. Quantitative determination of the odorants of young red wines from different grape varieties. J Sci Food Agric. 80:1659–1667.

Frasnelli J, Hummel T. 2005. Intranasal trigeminal thresholds in healthy subjects. Environ Toxicol Pharmacol. 19:575–580.

Glasser D. 2002. Experimental studies of primate sensory capacities. Evol Anthropol. 11(Suppl 1):136–139.

Halpern BP. 2004a. Retronasal and orthonasal smelling. Chem Sense. 6:1–7.

Halpern BP. 2004b. When are oral cavity odorants available for retronasal olfaction? In: Deibler KD, Delwiche J, editors. Handbook of flavor characterization: sensory, analysis, chemistry, and physiology. New York: Marcel Dekker. p. 51–63.

Halpern BP. Forthcoming 2008. Food and fragrances: retronasal olfaction. In: Squire L, editor. Encyclopedia of neuroscience. New York: Elsevier.

Haz-map Octane. 2007. [Internet]. [cited 2007 Oct 11]. Available from: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=106.

Heilmann S, Hummel T. 2004. A new method for comparing orthonasal and retronasal olfaction. Behav Neurosci. 118:412–419.

Hornung DE. 2006. Nasal anatomy and the sense of smell. In: Hummel T, Welge-Lssen A, editors. Taste and smell: an update. Vol. 63. Basel (Switzerland): Karger. p. 1–22.

Ishikawa S, Nakayama T, Watanabe M, Matsuzawa T. 2006. Visualization of flow resistance in physiological nasal respiration: analysis of velocity and vorticities using numerical simulation. Arch Otolaryngol Head Neck Surg. 132:1203–1209.

Jellinek JS. 1992. Perfume classification: a new approach. In: Van Toller S, Dodd GH, editors. Fragrance: the psychology and biology of perfume. London: Elsevier Applied Science. p. 229–242.

Kobal G, Hummel T. 1991. Olfactory evoked potentials in humans. In: Getchell TV, Doty RL, Bartoshuk LM, Snow JB Jr, editors. Smell and taste in health and disease. New York: Raven Press. p. 255–275.

Kobal G, Hummel T. 1992. Olfactory evoked potential activity and hedonics. In: Van Toller S, Dodd GH, editors. Fragrance: the psychology and biology of perfume. London: Elsevier Applied Science. p. 175–194.

Kobal G, Van Toller S, Hummel T. 1989. Is there directional smelling? Cell Mol Life Sci. 45:130–132.

Kurtz DB, White TL, Sheehe PR, Hornung DE, Kent PF. 2001. Odorant confusion matrix: the influence of patient history on patterns of odorant identification and misidentification in hyposmia. Physiol Behav. 72: 595–602.

Kurtz DB, Zhao K, Hornung DE, Scherer PW. 2004. Experimental and numerical determination of odorant solubility in nasal and olfactory mucosa. Chem Senses. 29:763–773.

Laing DG. 1988. Relationship between the differential adsorption of odorants to the olfactory mucosa and their perception in mixtures. Chem Senses. 13:463–471.

Laska M, Teubner P. 1998. Odor structure-activity relationships of carboxylic acids correspond between squirrel monkeys and humans. Am J Physiol. 274:R1639–R1645.

Lawless HT. 1989. Exploration of fragrance categories and ambiguous odors using multidimentional scaling and cluster analysis. Chem Senses. 14:349–360.

Lawless HT. 1997. Olfactory psychophysics. In: Beauchamp GK, Bartoshuk L, editors. Tasting and smelling. New York: Academic Press. p. 125–174.

Leffingwell JC. 2001. Olfaction. Available from: http://www.leffingwell.com/olfaction.htm. Accessed 13 May 2007.

Lim J, Lawless HT. 2005. Qualitative differences of divalent salts: multidimensional scaling and cluster analysis. Chem Senses. 30:719–726.

Livermore A, Laing DG. 1998. The influence of odor type on the discrimination and identification of odorants in multicomponent odor mixtures. Physiol Behav. 65:311–320.

Mainland J, Sobel N. 2006. The sniff is part of the olfactory percept. Chem Senses. 31:181–196.

Malnic B, Hirono J, Sato T, Buck LB. 1999. Combinatorial receptor codes for odors. Cell. 96:713–723.

Mojet J, Heidema V, Christ-Hazelhof E. 2003. Taste perception with age: generic or specific losses in supra-threshold intensities of five taste qualities? Chem Senses. 28:397–413.

Mombaerts P. 2004. Odorant receptor gene choice in olfactory sensory neurons: the one receptor-one neuron hypothesis revisited. Curr Opin Neurobiol. 14:1–6.

Moncrieff RW. 1967. The chemical senses. Cleveland (OH): CRC Press.

MSDS Octane. 2007. [Internet]. [cited 2007 Oct 11]. Available from: http://www.jtbaker.com/msds/englishhtml/o1694.htm.

Murphy C, Cain WS, Bartoshuk LM. 1977. Mutual action of taste and olfaction. Sens Process. 1:204–211.

Nakagawa S. 2004. A farewell to Bonferroni: the problem of low statistical power and publication bias. Behav Ecol. 15:1044–1045.

O'Neil MJ. 2006. The Merck index. 14th ed. Whitehouse Station (NJ): Merck.

Parikh V, Lee-Lim AP, Halpern, BP. 2007. Retronasal and oral-cavity identifications of trigeminal odorants. Chem Senses. 32: A47 [abstract].

Pernollet J-C, Sanz G, Briand L. 2006. Les récepteurs des molecules odorantes et le codage olfactif. C R Biologies. 329:679–690.

Pierce J, Halpern BP. 1996. Orthonasal and retronasal identification based upon vapor phase input from common substances. Chem Senses. 21: 529–543.

Radil T, Wysocki CJ. 1998. Spatiotemporal masking in pure olfaction. Proc Natl Acad Sci USA. 855:641–644.

Rawson NE. 2000. Human olfaction. In: Finger TF, Silver WI, Restrepo D, editors. The neurobiology of taste and smell. New York: Wiley-Liss. p. 257–284.

Rychlik M, Schieberle P, Grosch W. 1998. Compilation of odor thresholds, odor qualities and retention indices of key food odorants. Garching (Germany): Institut für Lebensmittelchemie der Technischen Universität München und Deutsche Forschungsanstalt für Lebensmittelchemie.

Savic I, Berglund H. 2000. Right-nostril dominance in discrimination of unfamiliar, but not familiar, odours. Chem Senses. 25:517–523.

Shepherd G. 2004. The human sense of smell: are we better than we think? PloS Biol. 2:0572–0575.

Shusterman D. 2002. Individual factors in nasal chemesthesis. Chem Senses. 27:551–564.

Silver WL, Finger TE. 1991. The trigeminal system. In: Getchell TV, Doty RL, Bartoshuk LM, Snow JB Jr, editors. Smell and taste in health and disease. New York: Raven Press. p. 97–108.

Small DM, Gerber JC, Erica YE, Hummel T. 2005. Differential neural responses evoked by orthonasal versus retronasal odorant perception in humans. Neuron. 47:593–605.

Snyder RD, Drummond PD. 1997. Olfaction in migraine. Cephalalgia. 17: 729–732.

Sobel N, Khan RM, Saltma A, Sullivan EV, Gabriel JDE. 1999. Olfaction: the world smells different to each nostril. Nature. 402:35.

Sulmont C, Issanchou S, Köster EP. 2002. Selection of odorants for memory tests on the basis of familiarity, perceived complexity, similarity, pleasantness and identification. Chem Senses. 27:307–317.

Sun BC, Halpern BP. 2005. Identification of air-phase retronasal and orthonasal odorant pairs. Chem Senses. 30:1–14.

Voirol E, Daget N. 1986. Comparative study of nasal and retronasal olfactory perception. Food Sci Technol. 19:316–319.

Wise PM, Olsson MJ, Cain WS. 2000. Quantification of odor quality. Chem Senses. 25:429–443.

Wright HN. 1987. Characterization of olfactory dysfunction. Arch Otolaryngol. 113:163–168.

Wysocki CJ, Cowart BJ, Radil T. 2003. Nasal trigeminal chemosensitivity across the adult life span. Percept Psychophys. 65:115–122.

Wysocki CJ, Wise P. 2004. Methods, approaches, and caveats for functionally evaluating olfaction and chemesthesis. In: Deibler KD, Delwiche J, editors. Handbook of flavor characterization. Sensory analysis, chemistry, and physiology. New York: Marcel Dekker. p. 1–40.

Zhao K, Dalton P, Yang GC, Scherer PW. 2006. Numerical modeling of turbulent and laminar airflow and odorant transport during sniffing in the human and rat nose. Chem Senses. 31:107–118.

Zhao K, Scherer PW, Hajiloo SA, Dalton P. 2004. Effect of anatomy on human nasal airflow and odorant transport patterns: implications for olfaction. Chem Senses. 29:365–379.

Accepted September 19, 2007