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Identification of Air Phase Retronasal and Orthonasal Odorant Pairs

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Abstract

Identifications (IDs) of paired retronasal and orthonasal odorants were studied, with stimuli limited to air phase. Odorants were liquid extracts of plant materials, sold as food flavorings, matched by each subject both for retronasal-only and orthonasal-only air phase intensities and then learned to 100% correct veridical name retronasal-only and orthonasal-only IDs. Subjects were tested for ID of (a) retronasal-only and orthonasal-only odorants, (b) homogeneously paired odorant (the same odorant in retronasal and orthonasal locations), and (c) heterogeneously paired odorants (different odorants in retronasal and orthonasal locations). Paired odorants were presented in two different sequences: retronasal location odorant smelled first or orthonasal location odorant smelled first. IDs were reported after odorants were removed. Results were as follows: (a) no significant differences between correct ID of odorants when in retronasal-only versus orthonasal-only locations, although percent correct IDs were lower for half the retronasal-only location odorants; (b) correct ID of a homogeneously paired odorant equaled or exceeded its unpaired ID, with two successive, identical IDs reported on the majority of its trials; (c) with heterogeneous pairs, for all odorants when in the orthonasal location of a pair, correct ID occurred less often than when these odorants were presented orthonasal-only, but for odorants in the retronasal location, correct ID equaled or exceeded retronasal-only correct ID; and (d) perceived order of presentation of heterogeneous pairs was the reverse of the physically presented sequence for both retronasal-first and orthonasal-first conditions. The heterogeneous odorant ID outcome supports the concept that processing of retronasal and orthonasal odorants differ, and the perceived reversal of the presented sequence is in agreement with the importance of recency in odorant memory.

Key words: gas chromatograph model, human, memory, nasal, olfaction, smell

Introduction

In mammalian responses to odorants, there are two distinct pathways by which air phase (i.e., vapor phase) stimuli can reach the olfactory and trigeminal (i.e., respiratory; Menco and Morrison, 2003) epithelia: the orthonasal pathway and the retronasal pathway (Rozin, 1982, 1996; Stevens and Cain, 1986; Voirol and Daget, 1986; Kuo *et al*., 1993; Lawless, 1997; Rawson, 2000; Cerf-Ducastel and Murphy, 2001; Halpern, 2004a,b). The orthonasal pathway involves odorants that travel inward from the external environment via the anterior nares (nostrils) through the nasal cavity, crossing trigeminal mucosa, and moving towards the olfactory mucosa. This is the route that is most often thought of (and studied) in research on olfactory (Dalton, 2002) or trigeminal (Bryant and Silver, 2000; Doty and Commetto-Muñiz, 2003; Wysocki and Wise, 2004) responses. The retronasal pathway involves odorants that normally originate in the oral cavity, ascend through the posterior nares of the nasopharynx towards the olfactory mucosa, traverse trigeminal epithelium, and exit via the nostrils (Burdach and Doty, 1987; Duffy *et al*., 1999).

An appreciable difference between orthonasal and retronasal judgments had been predicted (Rozin, 1982). In agreement with this prediction, studies using only air phase odorants presented by orthonasal versus retronasal routes (orthonasal and retronasal smelling) have indicated that these sensory systems differ in both threshold and suprathreshold properties. More specifically, orthonasal thresholds to air phase odorants were lower than retronasal thresholds, and judged intensity of some odorants was greater when those odorants arrived from an orthonasal location (Voirol and Daget, 1986; Heilmann and Hummel, 2004). Comparisons of identification (ID) when odorants were presented by retronasal or orthonasal routes also showed differences. During natural breathing, accuracy of ID of some air phase odorants was better when the odorants were smelled via the orthonasal route (Pierce and Halpern, 1996; Halpern *et al*., 2000; Puttanniah and Halpern, 2001; Halpern, 2004b).

One possible mechanism for the different responses to orthonasal or retronasal odorants may derive from the

observation that for some odorants not only will contrary patterns of sorption necessarily occur when these odorants flow in opposite directions across the nasal mucosae but also that these opposite patterns can in turn produce mirror-image neural response patterns (Mozell, 1970, 1971; Hornung *et al*., 1980; Hornung and Mozell, 1985). Distinctive input to the olfactory central nervous system from retronasal versus orthonasal odorant flow could be further enhanced by the regional selectivity of olfactory receptor neurons (e.g., Laurent, 1999; Mori *et al*., 1999; Ma and Shepherd, 2000; Paysan and Breer, 2001; Friedrich, 2002; Spors and Grinvald, 2002). Although these biophysical and receptor-sensitivity aspects of interactions between odorants, respiratory flow direction, and nasal mucosae describe nonhuman structures and functions, many similarities to humans as well as some important differences have been noted (e.g., Rawson and Gomez, 2002).

Additional physical factors underlying retronasal versus orthonasal smelling during normal breathing are flow patterns and odorant distributions in humans. The state of the nasal valve can have different effects during exhalation versus inhalation on airflow patterns and the distribution of odorants within the nasal cavity (Zhao *et al*., 2004). This differential consequence for orthonasal versus retronasal flow was proposed as a possible explanation for observations that retronasal (Cowart *et al*., 1999, 2003) or oral (Duffy *et al*., 1999) smelling deficits could be found in individuals who were normosmic for orthonasal smelling. It was also noted that these effects of regional flow patterns within the nasal cavity might interact with the physical properties of odorants and that small intranasal anatomical differences could result in sizeable alterations in sensitivity (Zhao *et al*., 2004).

Under typical eating conditions, odorant delivery via an orthonasal route and stimulation from the oral cavity may occur successively (e.g., Frank and Byram, 1988). Consequently, potential effects on judged odorant intensity or detectability of interactions between stimulation by orthonasal odorants and intraoral tastants or odorants that are in direct contact with the tongue and other oral tissues have been of interest. One finding has been that the intensity of orthonasal odorants decreased in the presence of intraoral tastants compared to only the water solvent in the oral cavity (e.g., Gillan, 1983; Burdach *et al*., 1984). The presence of intraoral water with no added tastants was also reported to reduce orthonasal smell intensity (e.g., Enns and Hornung, 1985). However, when both an odorant and a tastant were presented within an intraoral liquid, odor intensity was not affected by the concentration of tastants in the mixtures, although judged total intensity showed less than complete additivity (Murphy *et al*., 1977; Murphy and Cain, 1980).

The previous investigations of interactions between orthonasal odorants and stimuli from the oral cavity have measured changes in judged intensity, have used liquid stimuli in the oral cavity, and have noted diminished orthonasal intensity in some reports but no interactions when both the odorant and the tastant were in the oral cavity. However, neither the degree of retronasal–orthonasal interaction for judgments of odorant ID nor the outcome when only successive orthonasal and retronasal smelling occurs, with no accompanying potential for gustatory or changing chemesthetic stimulation, is known.

Memory has an important role in responses to odorants. Successful ID of odorants must be accompanied by odorant discrimination and is necessarily dependent on both odorant and semantic memory. If the IDs are to be reported after the odorants have been removed, as was the case in the present study, the nature of memory for odorants may shape the reports. Odorant memory and its role in odorant perception have received extensive study for odorants delivered via an orthonasal route (e.g., Engen, 1982; Cain, 1988; Cain and Potts, 1996; Lehrner *et al*., 1999; Dalton, 2002; Stevenson and Boakes, 2003; Wilson and Stevenson, 2003a,b). Models derived from these studies can permit predictions or explanations of observed odorant ID. For example, it would be expected that correct ID would be consistently obtained for odorants for which ID had previously been thoroughly learned. Consequently, if retronasal ID did not meet this orthonasal-based expectation, a difference in processing from orthonasal odorants might be suggested. With regard to short-term odorant memory, *per se*, because serial position of odorants appears to not be readily encoded but a recency effect has been observed for odorant recall, it could be predicted that the odorant smelled more recently of a pair of successive odorants would be reported to be the odorant smelled first (e.g., Herz and Engen, 1996; White and Treisman, 1997; White, 1998).

The purpose of this study was to investigate possible interactions between ID of air phase odorants smelled via retronasal and orthonasal routes. The hypotheses were that (a) paired odorant ID resulting from successive orthonasal and retronasal simulations with two different odorants during the inhalations and exhalations of the natural breathing cycle would be less accurate than unpaired ID (orthonasal-only and retronasal-only) and (b) order of ID reports would be determined by the odorant pathway that was stimulated first. Brief reports of some of these data have been made (Sun and Halpern, 2001, 2002).

Materials and Methods

General

Subjects

The research was approved by the Cornell University Committee on Human Subjects. All subjects were nonsmoking, nonpregnant, nonlactating, colloquial English-speaking paid volunteers associated with the Cornell University who participated with informed consent. No chemosensory

screening of subjects was done. Subjects were asked to not eat for 1 h before their scheduled experimental session.

Odorants

Some degree of ecological validity was obtained by choosing as odorants alcohol-free flavors prepared and sold for incorporation in human food and beverages. The six odorants were food-grade liquid extracts of plant materials, produced by Frontier Natural Products Co-op (Norway, IA). The names of these extracts, as specified by the manufacturer on the labels, were anise (A), cinnamon (Ci), coffee (Co), orange (O), peppermint (P), and strawberry (S). Subjects used these names for ID, except that the name "licorice" was also used and accepted for the anise odorant (see Preliminary Experiments). These natural odorants were a subset of the odorants used in previous studies (e.g., Cain and Krause, 1979; Wright, 1987; Cain *et al*., 1988; Lehrner *et al*., 1999; Dalton *et al*., 2003). Odorants were presented at room temperature 21 ± 1°C. Analytical data on the chemical composition of the odorants are not available. However, the peppermint odorant probably contained a substantial amount of menthol, cinnamon probably was primarily cinnamaldehyde, and orange was likely to contain D-limonene (Moncrieff, 1967).

Each presentation of an odorant in an odorant presentation container (OPC) (see Odorant Presentation Containers) had a total volume of 300 μl of the liquid odorant including diluent. Dilutions were made with the sole or principal solvent of each odorant, as specified on its label. The solvents used for dilution were either food-grade canola oil (for the A, Ci, O, and P odorants) (Tops Pure Canola Oil, Tops Markets, Inc., Buffalo, NY) or United States Pharmacopeia glycerin (for the Co and S odorants). Concentrations of presented odorants are given in reference to the undiluted odorant, which would be 100% (i.e., neat).

Odorant presentation containers

Odorants were presented in both orthonasal and retronasal locations using OPCs (Pierce and Halpern 1996; Halpern, 2004a). They were clean, odorless, low-density polyethylene, concentric open cylinders, closed at the bottom with a common base. The outer cylinder was 5.4 mm high with a 3.7-cm diameter and 1.3 mm wall thickness. The inner cylinder, within which odorants were placed, was 6.1 mm high with a 2.9-cm diameter and a 0.6 mm wall thickness; both cylinders had a 1.0-mm thick bottom. Each OPC was used for only one location (retronasal or orthonasal) and one concentration and was discarded after use with one subject. Disposable US Department of Agriculture–approved plastic gloves were worn by experimenters throughout odorant presentations, replaced if they came in contact with an odorant, and discarded after each subject.

Odorant presentations

To prevent visual ID, subjects were asked to close their eyes during all odorant ID trials. Observation and inquiry during each experiment confirmed that subjects complied with this instruction. All subjects' responses were communicated verbally after the OPC had been removed from the subject and recorded by the experimenters. The experimenters first demonstrated the procedure on themselves. Subjects then practiced and became accustomed to orthonasal and to retronasal placements of OPC before any judgments were made. For orthonasal odorant presentation, an OPC was suspended by hand approximately 3–4 mm below the subject's anterior nares (nostrils), above the upper lip. Subjects were told to breathe normally through their nose, with their mouth closed. Orthonasal sniffing was not permitted. That is, quiet resting breathing was permitted but not sniffing [defined as "To inhale forcibly through the nose" (The American Heritage Electronic Dictionary of the English Language, 1992)]. Subjects who accidentally sniffed were reminded to breathe normally.

For retronasal odorant presentations, an OPC was placed on the subject's extended tongue after the subject put on a Spirometer nose clip (Spirometrics D1060, Spirometrics Medical Equipment, Gray, ME) to prevent orthonasal airflow. Subjects were then told to bring the OPC into the mouth by retracting the tongue. They were then asked to lower their teeth gently toward the edges of the OPC (the wall of the outer cylinder), close their mouth, remove their nose clip, breathe normally, and minimize any tongue or mouth movements. With an OPC in place in the retronasal location and the lips closed, little tongue movement was possible. When retronasal and orthonasal odorant pairs were used, the nose clip was put on before either odorant was placed in position and was removed by the subject before an inhalation or an exhalation (see Main Experiment). The nose clip was replaced by the subject before they protracted their tongue, removed the OPC, and reported their judgment. Each subject had her own nose clip.

Individual sensitivity and concentration effects were minimized by having each subject select, both retronasally and orthonasally, concentrations of five odorants that they judged to match the intensity of a standard odorant (see Intensity matching subsection under Main Experiment).

Preliminary experiments

Appropriate concentration ranges for intensity matching (see Intensity Matching) to the orange odorant standard were determined in preliminary experiments. ID by these preliminary subjects indicated that descriptions of the anise odorant as licorice should be expected. In a subsequent preliminary experiment, intensity matching and odorant ID learning procedures of the main experiment were employed (see Intensity Matching and Odorant ID Learning), followed by the odorant pairs of the main experiment randomized with OPC pairings in which the odorants in the orthonasal location were paired with an empty OPC in the retronasal location. All odorants when paired with an empty OPC

in the retronasal location were correctly identified. This preliminary experiment indicated that having an OPC in the mouth does not interfere with orthonasal odorant ID.

Main experiment

Subjects

Twenty paid volunteers, mean and median age = 20 years (range: 18–22 years), 11 females and 9 males, participated in two sessions. They were informed that the experiment involved study of two pathways of smelling, one through the nose and the other inside the mouth, and that both would be tested.

Sequence

In the first session, subjects first did intensity matching and then odorant ID learning, with orthonasal-only odorant presentations completed for a procedure before retronasal-only presentations were done for that procedure. Veridical retronasal and orthonasal IDs of the six odorants were learned to 100% accuracy. For the retronasal-only presentations, before any judgments, subjects were taught to use the OPC and to exhale first after putting the OPC in position. In the second session, subjects were tested for orthonasal-only and retronasal-only unpaired odorant ID, followed by paired odorant ID using retronasal-first (exhale first) and then orthonasal-first (inhale first) breathing sequences. Sessions were separated by at least 1 day.

First session

Intensity matching. Subjects were presented with five rows of OPCs, six containers in a row. Each row held a single odorant, with concentrations increasing from right to left. The specific concentrations presented to subjects differed between odorants (Table 1) based on responses during the preliminary experiments. All OPCs in the rows were covered except for the OPC in the row from which an intensity match was to be selected. The common name of the odorant in the row under selection was stated and was also available on a printed sheet that was visible to subjects. Subjects were told that each row contained dilutions of one odorant. Each subject chose, one row at a time, the odorant in a row that most closely matched for them the perceived intensity of smell of the standard, which was 67% O. The standard was always available. Subjects were encouraged to refer to it as often as they wished but were required to smell it when beginning each row. Intensity matching started with the lowest concentration in that row and proceeded towards higher concentrations. If the lowest available concentration (Level 6, Table 1) was judged to be too intense, a lower concentration (Level 7, Table 1) was used during the second session for that particular subject, odorant, and odorant location. This never occurred for the A or S odorants but did occur for one subject for Ci in the retronasal location and for another subject for both Co and P in the orthonasal location. When an intensity match was reported, subjects were encouraged to also try the next highest concentration. If the highest available concentration (Level 1, Table 1) was judged to be insufficiently intense to match the O standard odorant, a higher concentration (Level 0, Table 1) was used during the second session for that particular subject, odorant, and odorant location. This never occurred for the Ci, Co, or P odorants but did occur for two subjects for A and for another subject for S in an orthonasal location and for two subjects for A and for another subject for S in a retronasal location. Orthonasal intensity matching and retronasal intensity matching were done separately within the same session.

Odorant ID learning. Initially, the highest available concentrations of the five odorants were presented (Level 1, Table 1), as well as the O standard (67% concentration). Subjects were reminded of the six possible odorant ID and were required to respond with an odorant name whether or not they were confident of the ID. Errors were corrected. Between trials, subjects could view a printed sheet with the six odorant names. Familiar odorants and experimenter-provided veridical odorant labels were employed because of their previously demonstrated effectiveness (Cain and Krause, 1979). This procedure was repeated until all six

Table 1 Odorant concentrations, in percentage of undiluted odorants, for matching to the perceived intensity of the orange odorant standard

Odorants	Odorant concentrations (%)							
	(Level 0)	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6	(Level 7)
Anise	67	50	33	25	20	17	14	NU
Cinnamon	NU	20	11	9	7	5	4.80	4
Coffee	NU	50	33	25	20	17	14	11
Peppermint	NU	25	20	17	14	13	12	7
Strawberry	25	20	14	13	12	9	8	NU

Concentration Levels 1 through 6 were available for intensity matching. The concentrations indicated in Levels 0 and 7 were used for the later unpaired and paired odorant ID sessions if Level 1 or Level 6 were not sufficient to match the standard; NU: not used.

odorants were correctly identified in succession for both orthonasal (inhale-first breathing) and retronasal (exhale-first breathing) location.

Second session

Unpaired odorant ID testing. Each of the six odorants was presented once in the orthonasal location, using a random order that was employed for all subjects, followed by each of the six odorants presented once in the retronasal location, using a different random order. Concentrations of A, Ci, Co, P, and S were, for each subject and each odorant location (orthonasal or retronasal), those selected by that subject as an intensity match for the O standard from the first session. The concentration of O was 67%, the same as the concentration of O that had been used throughout the intensity matching and ID learning. The subject identified each odorant, and errors were corrected.

Paired odorant ID testing. For paired testing, a specified odorant could be in the orthonasal location or the retronasal location (or both). In order to unambiguously denote the orthonasal versus retronasal location of an odorant when heterogeneous odorant pairs (different odorants in retronasal and orthonasal locations) were presented, a convention was adopted such that the first odorant of a named pair was always in the retronasal location and the second always in the orthonasal location. For example, when the peppermint odorant (P) was presented retronasally and the anise odorant (A) orthonasally, the pair was designated P-A. Conversely, when the same two odorants were paired, but A was presented retronasally and P orthonasally, the pair was designated A-P. Note that this convention specified the location of the members of a heterogeneous odorant pair but did not indicate which odorant was smelled first (see Retronasal-first paired testing and Orthonasal-first paired testing).

The concentrations that had been employed for each subject in the unpaired odorant ID testing were used. The 10 odorant pairs were P-Co, A-P, S-O, Ci-A, Co-Ci, Co-Co, P-A, Co-S, O-S, and P-S. The completion of the presentation of one pair including the removal of the OPC from the subject and the subject's ID report was separated from the beginning of the presentation of the next pair by at least 10 s. During presentation of pairs, subjects were asked to replace their nose clip when they could identify the odor. They were told that there might be more than one odorant but that the odorants would be the same ones they had been smelling, that the time interval from removing their nose clip in order to begin smelling the odorant to replacing the nose clip would be measured, and that they should report what they had smelled in the order in which they had smelled it. For example, subjects were told "Give answers such as 'strawberry' if you smelled strawberry or 'orange-strawberry' if you smelled orange and then strawberry." Each OPC was discarded after one use.

Retronasal-first paired testing. First, the 10 pairs of odorants were presented three times each using a random order that was employed for all subjects. Subjects were instructed to inhale, put on their nose clip, place an OPC in the retronasal location, place an OPC in the orthonasal location, remove their nose clip, and then exhale. Normal breathing with the mouth closed continued until the subject replaced their nose clip. This sequence, which represents the retronasal-first (exhale first) procedure, was practiced prior to any judgment until the subject was comfortable with it. The subject's eyes remained closed during the entire OPC placement, nose clip removal, exhalation, quiet breathing, nose clip replacement, and OPC removal sequence. After these 30 exhale-first pairs had been judged, a 2-min rest period followed.

Orthonasal-first paired testing. Second, the 10 orthonasal and retronasal pairs of odorants were presented three times each using a different random order that was employed for all subjects, with subjects instructed to inhale after removing the nose clip. This was accomplished by instructing the subjects to exhale, put on their nose clip, place an OPC in the retronasal location, place an OPC in the orthonasal location, remove their nose clip, and then inhale. Normal breathing with the mouth closed continued until the subject replaced their nose clip. This sequence, which represents the orthonasal-first (inhale first) procedure, was practiced prior to any judgments until the subject was comfortable with it. Subjects' eyes remained closed during the sequence. For both procedures, ID reaction times, that is, time from removing the nose clip to replacing it, were measured with a stopwatch.

Analyses and statistics

A probability level of ≤ 0.05 was taken to indicate statistical significance. When multiple comparisons were done, Bonferroni corrections (Hays, 1981; StatSoft, Inc., 2002) were used.

Because odorants were presented both alone and in pairs, several different comparisons were possible. For the heterogeneous odorant pairs (different odorants in the orthonasal and retronasal locations), one analysis determined the frequency of correct ID of each odorant without regard to the order in which the IDs were made. This was designated reported order–independent correct ID, henceforth called order-independent ID. A second analysis counted the frequency with which members of an odorant pair were correctly identified in the order in which they had been presented (e.g., orthonasal first) or in the reverse of that order (i.e., the odorant that was smelled first reported as being smelled second).

The frequency with which order-independent ID occurred was measured separately for each member of an odorant pair, with responses to retronasal-first and orthonasal-first presentations tallied separately. This was done by counting the number of times each odorant of a pair was correctly identified by a subject. For example, for orthonasal-first

presentations of the odorant pair P-Co (P in the retronasal and Co in the orthonasal location, with Co smelled first), the instances in which the IDs were *x*-P or P-*x*, where *x* is any odorant ID, were summed, yielding the total number of times that P was correctly reported when the P-Co pair was smelled orthonasal first. In a similar fashion, for the same orthonasal-first presentations of the odorant pair P-Co, the instances in which the IDs were Co-*x* or *x*-Co, where *x* is any odorant ID, were summed, yielding the total number of times that Co was correctly reported when the P-Co pair was smelled orthonasal first.

One-sample *t*-tests, applied separately to orthonasal-first and retronasal-first data, were used to obtain the significance of the difference between the number of pairs in which the odorants in the pair were correctly identified in the correct order (fully correct ID) and the number of responses in which the IDs of the odorants in the pair were correct but the reported order was incorrect (reversed order ID). Comparisons were also made between the orthonasal-first and retronasal-first conditions for individual odorant pairs. In order to avoid excessive multiple comparisons, paired *t*-tests were done only when the overall differences between orthonasal-first and retronasal-first in correct but reversed order ID exceeded 10%.

In order to determine effects of the odorant with which an odorant was paired, IDs were compared separately for retronasal-first and orthonasal-first conditions, using paired *t*-tests on the two ID data sets that differed most for each odorant under evaluation. Because more than two data sets could be involved, the resulting *P* values were corrected by multiplying by k', where k' = the overall number of distributions in which the compared odorant occurred multiplied by the number of distributions minus 1, with the product divided by 2. For example, for the comparison of retronasal-first ID of Co in Co-S with Co of Co-Co, Co appeared in three pairs. Therefore, $k' = [3(2)/2] = 3$. For df = 19 and $t = -3.040$, the uncorrected *P* was 0.0067 and $k'(P) = 0.0201$ (Table 3).

Reaction times for ID of paired odorants were analyzed using Systat (SYSTAT, 1992) general linear models. The overall analyses modeled reaction time as a function of subjects, the 10 odorant pairs, and four response types. These response types were as follows: (a) correct description of the odorant pair as presented, (b) correct ID of the members of the pair but in reverse order to that presented, (c) correct ID of the retronasal location member of the pair and incorrect ID for the orthonasal member of the pair, or (d) correct ID of the orthonasal location member of the pair and incorrect ID of the retronasal member of the pair. If an analysis of variance (ANOVA) for these analyses reached significance for odorants or response types, a subsequent analysis was done for only response types "a" (fully correct ID) and "b" (reverse order ID). Finally, if the second ANOVA also yielded significant results, a paired *t*-test was done on the means of reaction times across the 20 subjects.

Results

Intensity matching

The mean isointense concentrations selected for each odorant to match the orange odorant standard across the 20 subjects were similar for retronasal and orthonasal odorant locations (Table 2). There were no significant differences between the concentrations selected for orthonasal and retronasal matches for any odorants, $P > 0.33$ Bonferroni corrected (df = 19, $k = 5$). The largest disparity, found for coffee, was between 25% orthonasal versus 30% retronasal, with $P = 0.332$ ($t = -1.948$, $k = 5$). Disparities between the other odorants were smaller. However, there were large individual disparities as indicated by the sizeable SD, which are all at least 22% of the means and exceed 40% of the mean values for most of the odorants. Individual disparities were also reflected in the range for each odorant.

Unpaired odorant ID

When odorants were presented only in the orthonasal location, IDs were totally or largely correct (94% correct for S and A, 100% for the other four odorants). For odorants presented only in the retronasal location, completely correct IDs were less common: 71% correct for Ci; 82%, Co; 88%, P; and 100% correct for the other three odorants. None of the disparities between orthonasal-only and retronasal-only correct IDs were significant, $P > 0.278$ [df = 16 (data for 4 subjects were not available), $t > -0.6 < 0.9$, $k = 3$]. These data represent a baseline level of ID ability in each location, in the absence of odorant in the other location.

Order-independent ID of paired odorants

Homogeneous pair

The incidence of ID as Co did not differ between unpaired Co and the Co-Co pair. Logically, for the homogeneous pair (Co-Co), orthonasal-first and retronasal-first presentations could not differ in which odorant was smelled first because Co would be smelled first for both locations. However, the location from which the Co odorant initially came did differ between orthonasal first and retronasal first. Consequently, comparisons of order-independent ID for the Co-Co pair versus Co presented only in an orthonasal location or only in a retronasal location were possible. IDs of orthonasal-first order-independent ID for Co-Co (Figure 1) were identical to IDs for orthonasal-only presentations of Co. Although retronasal-first order-independent ID of Co-Co exceeded retronasal-only ID by 18% (Figure 2), the disparity was not significant (df = 16, $t = -1.817$, $P = 0.088$).

Heterogeneous pairs

For all odorants when in the orthonasal location of a heterogeneous pair (clear bars in Figures 1 and 2), their

Table 2 Concentrations of five odorants, in percentage of undiluted odorants, selected by each of the 20 subjects to match the orthonasal or the retronasal intensity of the 67% orange odorant standard and the mean, SD, and range for each odorant and odorant location

Subject	Orthonasal matches					Retronasal matches				
	Anise	Cinnamon	Coffee	Peppermint	Strawberry	Anise	Cinnamon	Coffee	Peppermint	Strawberry
1	20	5	20	14	14	14	11	17	17	13
2	17	20	17	17	8	20	11	50	13	9
3	33	4.8	11	7	14	20	9	33	13	25
4	25	4.8	14	17	20	67	11	33	13	20
5	25	9	33	14	9	33	11	50	14	9
6	33	9	33	25	25	17	5	20	12	8
7	33	7	17	14	8	25	7	33	13	8
8	25	5	20	13	8	14	4	17	12	9
9	25	9	33	13	20	25	7	50	13	9
10	17	11	25	13	13	17	9	20	12	14
11	67	9	14	17	12	20	9	20	14	9
13	50	20	50	12	8	50	11	50	25	14
14	33	4.8	20	12	13	33	7	17	12	9
15	20	5	33	12	20	20	5	33	12	9
16	50	11	17	20	14	50	11	25	25	20
17	33	11	33	25	12	33	9	33	25	12
18	67	9	50	17	14	67	9	33	20	13
19	33	7	17	13	20	33	9	33	12	9
20	20	11	20	17	20	20	9	20	13	14
Mean	33	9	25	15	14	30	9	30	16	12
SD	15	4	11	4	5	16	2	12	5	5
Range	50	15	39	18	17	53	7	33	13	17

order-independent ID fell below ID when these odorants were presented orthonasal-only (clear ellipses in Figures 1 and 2). For orthonasal-first presentations (Figure 1), the disparities in order-independent ID for orthonasal location odorants versus orthonasal-only presentations were large, averaging 27%. Bonferroni-corrected paired *t*-tests revealed that six of the orthonasal location order-independent IDs were significantly different from the corresponding orthonasal-only IDs, $P < 0.05$ (df = 16, $t > -2.82 < -4.82$, $k = 9$) (clear columns marked with an asterisk in Figure 1). Significance was not reached for the other three comparisons, $P > 0.06$ (df = 16, $t > -1.000 < -2.577$, $k = 9$).

Similarly, for retronasal-first presentations (Figure 2), five of the nine disparities between order-independent ID for orthonasal location odorants versus orthonasal-only presentations exceeded 20%, with three greater than 30%. Bonferroni-corrected paired *t*-tests revealed that five of the orthonasal location order-independent IDs were significantly different from the corresponding orthonasal-only IDs, $P \leq 0.01$ (df = 16, $t < -3.68$, $k = 9$) (clear columns marked with an asterisk in Figure 2). Significance was not reached for the other four comparisons, $P > 0.057$ ($t < -1.377 > -2.750$). Overall, in the majority of instances, correct IDs for orthonasal location heterogeneously paired odorants were less frequent than correct IDs for the unpaired odorant.

In contrast, almost no ID differences occurred for retronasal location heterogeneously paired odorants. With heterogeneously paired odorants in the retronasal location (striped bars in Figures 1 and 2), disparities between order-independent ID and ID when these odorants were presented retronasal-only (striped ellipses) were usually small and not unidirectional. Significance was reached in only one instance, odorant A of A-P (striped column marked with an asterisk in Figure 2), $P = 0.015$ (df = 16, $t = 3.771$, $k = 9$). Neither the other retronasal-first comparisons, $P > 0.074$ ($t > -2.95 < 0.52$, $k \leq 8$), nor any of the orthonasal-first retronasal location comparisons were significant, $P > 0.41$ (df = 16, $t > -0.096 < -2.16$, $k = 9$). In general, retronasal

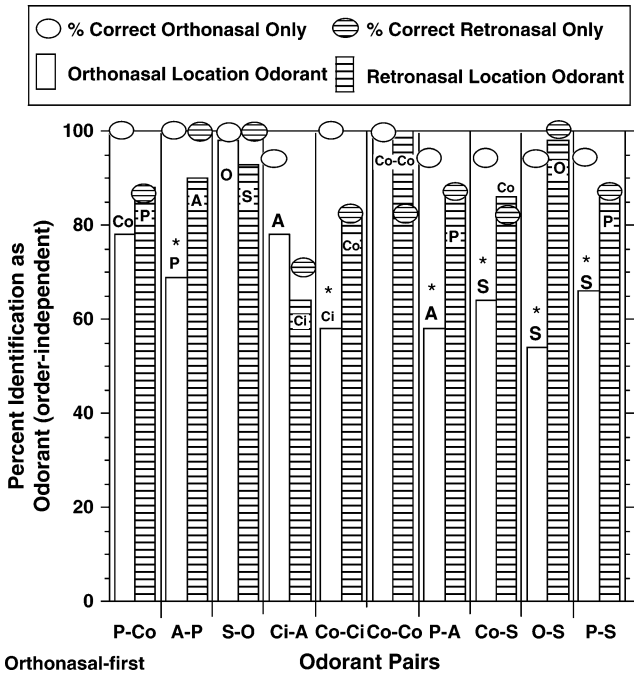

Figure 1 Orthonasal-first order-independent ID of each member of odorant pairs, expressed as percentage of total ID, for 20 subjects. Asterisks denote significant differences between order-independent IDs for an odorant of a pair and IDs for unpaired presentations from the same location. See text for details.

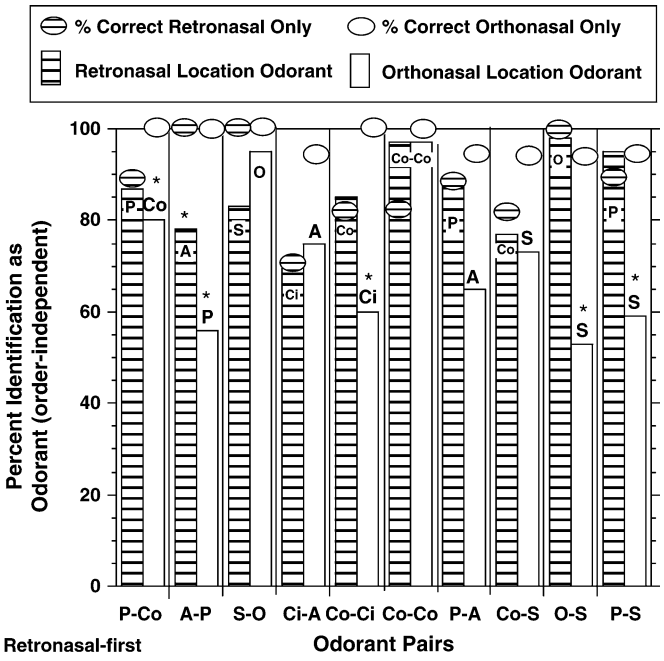

Figure 2 Retronasal-first order-independent ID of each member of odorant pairs, expressed as percentage of total ID, for 20 subjects. Asterisks denote significant differences between order-independent IDs for an odorant of a pair and IDs for unpaired presentations from the same location. See text for details.

location paired odorants showed no change in ID compared with unpaired presentations, but correct ID for orthonasal location heterogeneously paired odorants often decreased.

Specific pairing effects. In addition to the already noted overall consequences of odorant location on correct ID, it was possible that certain pairings of odorants affected ID but others did not. Order-independent IDs were compared for specific odorants in the same locations but paired with different odorants and for specific odorants in opposite locations (Table 3). For both orthonasal-first and retronasal-first presentations, significant effects of odorant location and of the paired odorant occurred. Overall, relationships between S and O were most common, with correct ID of retronasal location S more frequent than orthonasal S when paired with O. On the other hand, no specific effects occurred for ID of Ci or O.

ID frequencies and ID response order

Detailed representations of ID of paired odorants are provided in Tables 4 and 5. These confusion matrices (Wright, 1987; Kurtz *et al.*, 2001) are subsets of the possible complete matrices, which would provide 36 ID columns (six potential paired ID, each in two logical orders, plus possible ID reporting an unpaired odorant). Those potential IDs that were never reported and those with very low frequencies were excluded from the tables. Both tables show that completely correct IDs, which not only correctly indicated the constituent odorants but also the order in which the odorants had been smelled, were uncommon (underlined percentages), always below 30%. For the nine retronasal-first presentations, completely correct ID occurred with a mean of 11% (SD 7%) and for orthonasal-first presentations 7% (SD 4%). In only one instance, the P-Co pair presented retronasal first (Table 5), for which completely correct ID occurred on 27% of the trials, did such ID exceed 17%. The remaining ID often reported smelled odorant order backwards. That is, IDs in which the names of the odorants in the heterogeneous pair were correct but the reported order was the reverse of that in which the odorants had been presented were very common (boldface percentages in Tables 4 and 5). This reversed response ID pattern had a mean of 46% (SD 11%) for retronasal-first presentations and 53% (SD 11%) for orthonasal-first presentations. Across all subjects and odorants pairs, the differences between completely correct ID of pairs and reversed response ID were significant ($P < 0.0001$, df = 19) for both retronasal first ($t = -5.246$) and orthonasal first ($t = -6.640$). Beyond these overall effects, the incidence of reversed response ID could vary with the particular odorant pair between orthonasal-first and retronasal-first conditions. Pairwise comparisons allowed determination of those orthonasal-first pairs versus retronasal-first pairs with significant differences in ID order. Excessive multiple comparisons were avoided by doing paired *t*-tests for an odorant

Table 3 Significant differences in order-independent IDs of odorants across odorant pairs containing that odorant, with the associated correction factor for multiple comparisons, k', and the t value in parentheses

Specific odorants and odorant pairs	Specific odorants and odorant pairs				
	A of P-A	Co of Co-Co	S of S-O	S of O-S	P of P-S
S of O-S			**0.0042**[a] **(6, 4.056)**		
			0.0042[b] (6, 4.046)		
A of Ci-A	**0.0306**[c] **(3, 2.854)**				
Co of Co-Ci		**0.0057**[d] **(1, −3.115)**			
A of A-P	**0.0045**[e] **(3, 3.707)**				
Co of Co-S		0.0201[f] (3, −3.040)			
S of Co-S				0.0459[g] (3, 2.666)	
P of A-P					0.00054[h] (6, 4.945)

Tabled numbers not in parentheses are paired t-test–based corrected probabilities that the difference between two distributions of correct IDs of an odorant was due to chance. Integers in parentheses are k', the correction factor based on the total number of distributions in which the odorant appeared; decimals are the associated t-values. Numbers in boldface are orthonasal first; others are retronasal first.
[a]S of S-O correctly identified more often than S of O-S.
[b]S of S-O identified correctly more often than S of O-S.
[c]A of P-A identified correctly more often than A of Ci-A.
[d]Co of Co-Co identified correctly more often than Co of Co-Ci.
[e]A of P-A correctly identified more often than A of A-P.
[f]Co of Co-Co identified correctly more often than Co of Co-S.
[g]S of Co-S identified correctly more often than S of O-S.
[h]P of P-S identified correctly more often than P of A-P.

Table 4 Percent IDs by 20 subjects of odorant pairs presented orthonasal first; only results for which the percent ID for at least one presented pair exceeded 10% are shown

Odorant pair presented	Odorant IDs													
	P, Co	A, P	S, O	Ci, A	Co, Ci	Co, Co	P, A	Co, S	O, S	P, S	Co, O	O, O	P, Ci	P, O
P-Co	**63**	2				2	3			2	2		5	2
A-P	2	**54**		2			5							
S-O			**75**						17			3		
Ci-A		7		**39**			5							2
Co-Ci				3	**46**	7	2	2			3	2		
Co-Co					8	70		2			7			
P-A	5	5					**41**	2		2			12	8
Co-S	2				3	3	2	**49**			15	3		
O-S			8						**53**			24		
P-S	5			2			2		2	**53**			3	12

For odorant IDs, ID preceding the comma was stated first and that after was stated second. For presented pairs, odorant before dash is in the retronasal location and that after is in the orthonasal location. IDs given in reverse sequence to the order in which the odorants were first smelled are in boldface. IDs corresponding to the order in which the odorants were first smelled are underlined. Odorant identifications that were not >10% for at least one pair are not shown.

pair only when the disparity between orthonasal-first and retronasal-first reversed response IDs exceeded 10%. For the four heterogeneous odorant pairs that met this criterion, two reached significance: P-Co ($t = -2.854$, $P = 0.04$) with orthonasal first exceeding retronasal first and P-A ($t = 2.854$, $P = 0.04$) with retronasal first exceeding orthonasal first (df = 19, $k = 4$). For the other two pairs, A-P and O-S, $P > 0.15$ ($t > -2.238 < -1.1$). In general, completely correct IDs were rare; reversed order IDs were frequent, for both orthonasal-first and retronasal-first presentations.

Table 5 Percent IDs by 20 subjects of odorant pairs presented retronasal first; only results for which the percent ID for at least one presented pair exceeded 10% are shown

Odorant pair presented	Odorant IDs														
	Co, P	P, A	O, S	A, Ci	Ci, Co	Co, Co	A, P	S, Co	S, O	S, P	Ci, A	Co, S	O, O	P, Co	P, P
P-Co	**42**				2	3				7	2			27	7
A-P		**36**	2	2			12	2	2		5			3	3
S-O			**68**					2	10				5		
Ci-A				**33**	2		7				13				
Co-Ci		2		2	**42**	7		2			3			3	
Co-Co	3	2		2	3	50		3				7		3	
P-A				2		5	**58**		3						12
Co-S					2			**43**	3	2	2	12		5	
O-S			8						**42**	2			37		
P-S	2	3							2	**47**				2	14

For odorant IDs, ID preceding the comma was stated first and that after was stated second. For presented pairs, odorant before dash is in the retronasal location and that after is in the orthonasal location. IDs given in reverse sequence to the order in which the odorants were first smelled are in boldface. IDs corresponding to the order in which the odorants were first smelled are underlined. Odorant identifications that were not >10% for at least one pair are not shown.

Reaction times

Reaction times of paired odorant ID responses were analyzed using general linear models. An overall analysis modeled reaction time as a function of subjects, the 10 odorant pairs, and four response types. These response types were as follows: (a) completely correct ID, (b) reversed order ID, (c) correct (order dependent) ID of the retronasal location member of the pair, followed by any ID other than the orthonasal member of the pair, or (d) correct (order dependent) ID of the orthonasal location member of the pair, followed by any ID other than the retronasal member of the pair.

For retronasal-first presentations, effects of odorants (df = 9) on reaction time were not significant ($F = 1.667$, $P = 0.094$), but response types (df = 3) were significant ($F = 9.892$, $P = 0.000003$). For the subsequent model of only response types a and b (response order), both odorants ($F = 1.942$, $P = 0.046$) and response types ($F = 13.059$, $P = 0.0004$) were significant. Mean retronasal-first reaction times were 9.1 s (SD = 5.6) for fully correct IDs and 7.8 s (SD = 4.2) for reverse order IDs; the paired t-test was significant (df = 19, $t = 2.447$, $P = 0.024$), indicating that reversed order IDs were faster than fully correct IDs for retronasal-first presentations.

For the orthonasal-first presentations, effects of odorants on reaction time reached significance ($F = 2.120$, $P = 0.027$) but response types did not ($F = 2.051$, $P = 0.11$). For the subsequent model of completely correct ID versus reversed order ID, again odorants ($F = 2.942$, $P = 0.002$) but not response types reached significance ($F = 2.942$, $P = 0.68$). Mean orthonasal-first reaction times were 9.3 s (SD = 5.3) for completely correct ID and 8.7 s (SD = 5.1) for reverse order ID. Overall, there was a clear distinction in the relationship between ID order and reaction times between orthonasal-first and retronasal-first conditions. For orthonasal-first presentations, no consistent difference in reaction time was found for fully correct ID versus reversed order ID, but for retronasal-first presentations, reversed order IDs were faster.

Discussion

Asymmetrical interactions between orthonasal and retronasal odorants

The finding that decreases in correct ID for an odorant in the orthonasal location occurred, but almost no changes for correct ID of a different odorant in the retronasal location, independent of which location was smelled first, was unexpected. A more general change in correct ID had been anticipated based on the prior reports of perceptual interactions between intraoral liquid stimuli and orthonasally presented odorants (e.g., Rozin, 1982; Burdach *et al.*, 1984; Stevens and Cain, 1986; Burdach and Doty, 1987; Kuo *et al.*, 1993; Aubry *et al.*, 1999; Duffy *et al.*, 1999, 2003; Cerf-Ducastel and Murphy, 2001, 2003, 2004). More specifically, the outcome of smelling the heterogeneous pairs of the present experiment was hypothesized to be mutual masking as had been suggested for orthonasal olfaction (Radil and Wysocki, 1998) and as is often found in other modalities (e.g., Olzak and Thomas, 1986). An outcome considered plausible but less likely was fusion into a unified and perhaps novel perceptual experience (Riggs, 1971; Sekuler and Blake, 1990; Kellogg, 2003). Neither fusion nor mutual masking was found. Instead, separable perceptions of the retronasal and orthonasal components of the exhalations and inhalations of quiet natural breathing were maintained,

but with degradation of ID for heterogeneous odorants in the orthonasal location.

The absence of fusion may be related to the several seconds time gap between natural inhalation and exhalation (Halpern 2004a)—a long delay compared to the 300 ms or briefer interodorant interval needed to prevent orthonasal odorant lateralization (Radil and Wysocki, 1998). Perhaps the condition in the present experiment most favorable for fusion was smelling the same odorant, Co, in both orthonasal and retronasal locations? Here too, reports of Co-Co dominated. These data are compatible with reports that different spatial–temporal patterns are observed in nonhuman olfactory bulbs during inhalation versus exhalation in the presence of orthonasal odorants (see Friedrich, 2002).

The observed asymmetric diminution of ID for the heterogeneous paired odorant in the orthonasal location might imply that retronasal location odorants elicit greater attention ("· · · selecting certain stimuli from among many and focusing cognitive resources on those selected," Kellogg, 2003) than do orthonasal odorants. If so, a major factor in any such differences would seem to begin with the opposite flow directions across the olfactory mucosa and trigeminally innervated respiratory mucosa of retronasal and orthonasal smelling. It is tempting to suggest that the lateral inhibition circuits of the olfactory bulb (Urban, 2002) may contribute to this effect. At cerebral cortical as well as subcortical levels, complex differences between human retronasal and orthonasal olfactions have been observed using functional magnetic resonance imaging (Lèger *et al*., 2003; Small *et al*., 2005).

Adaptive significance of preserving retronasal odorant ID

It has been suggested that orthonasal smelling is an exteroceptive sensory system (aka teleceptive), focusing on events in the external world (Spors and Grinvald, 2002), while retronasal smelling is closer to an interoceptive sensory system (see Shepherd, 1988; Matthews, 2001), pertaining more to events inside the body, or, in this case, to substances that will soon be inside the body if swallowing occurs (Halpern, 2004b). Under natural circumstances, the flavor chemicals released by substances in the mouth into the air phase (Roberts and Acree, 1995, 1996; Roberts *et al*., 2004) and detected by retronasal smelling are both a major source of human enjoyment and important information for rejecting or accepting undesired or desired food or beverages. Perhaps retronasal ID is so important for humans that when only the few seconds of the natural breathing cycle separate retronasal and orthonasal inputs, the retronasal ID has priority. If so, lengthening the time interval should reduce or eliminate the disparity.

Presented versus perceived order of odorant presentation

In this study, when one odorant was in the orthonasal location and another in the retronasal location (a heterogeneous pair), the perceived order of presentation was the reverse of the physically presented sequence for both retronasal-first and orthonasal-first conditions. In addition, reaction times for presented versus perceived odorant order were significantly different for retronasal-first presentations, with mean times for the reversed order ID reports briefer than those for the presented order (fully correct ID). Because the IDs were made several seconds after the odorants were removed, involving short-term odorant memory (Millward, 1971; Herz and Engen, 1996; White and Treisman, 1997; Kellogg, 2003), an odorant smelled second would be more recent than the odorant smelled first. The present data are compatible with the concept that the order of serial odorant recall is dependent on recency (White and Treisman, 1997). However, for orthonasal smelling, correct reporting of the presentation order of heterogeneous purely olfactory odorants presented to one naris and then the other with a time separation of more than 400 ms has been observed (Radil and Wysocki, 1998). A study in which IDs of both successive retronasal-only odorants and odorant pairs were made while the odorants were being smelled could clarify possible differences between retronasal and orthonasal smelling and the role of memory in the observed responses.

Isointense concentrations

From an experimental design perspective, having subjects select isointense concentrations through matching perceived intensities for both orthonasal and retronasal odorants to a standard helped improve upon shortcomings in previous studies by ensuring that odorant concentrations would be appropriate for fair and balanced ID.

The absence of statistical significance between mean matching concentrations for odorants in the retronasal versus orthonasal locations was not expected. Significant differences between air phase orthonasal and retronasal detection thresholds and odorant-dependent suprathreshold intensity judgments have previously been reported (Voirol and Daget, 1986; Heilmann and Hummel, 2004), as well as differences in ability to identify odorants (Pierce and Halpern, 1996; Halpern, 2004b). The high variability associated with these means and underlying disparities between individual may account for the lack of a significant effect.

Unpaired odorant ID

Retronasal IDs of odorants, although not quite as good as orthonasal, were accurate in most subjects with no significant differences between orthonasal-only versus retronasal-only ID. This outcome contrasts with a previous study in which a larger number of odorants, at a fixed 50% dilution for all subjects, produced significantly lower correct ID for the retronasal-only odorants (Puttanniah and Halpern, 2001; Halpern, 2004b) and with other studies in which some individuals could provide normal orthonasal-only ID but made many errors in retronasal-only ID (Cowart *et al*., 1999, 2003). For the present study, perhaps having concentrations

appropriate to each subject facilitated correct ID? Nonetheless, it is interesting that many retronasal-only ID errors were made after error-free learning, compared to error-free or single errors for ID of orthonasal-only odorants. Error-free ID would have been expected under these circumstances (Engen, 1982; Cain, 1988; Cain and Potts, 1996; White and Treisman, 1997; Lehrner *et al*., 1999; Stevenson and Boakes, 2003; Wilson and Stevenson, 2003a,b), possibly suggesting that learning of retronasal-only ID is less well retained or retrieved than orthonasal-only ID.

Neurophysiological effects of odorant flow direction

Electrophysiological measurements reported in 1970 demonstrated that flow of certain odorants in opposite directions across an olfactory mucosa could produce opposite spatial–temporal neurophysiological patterns when responses from distant primary olfactory nerves were compared (Mozell, 1970). These stimulus direction-dependent peripheral neural olfactory responses were considered a function of physical interactions of the odorants with the sorptive characteristics of the olfactory and adjacent mucosa (Mozell, 1971; Mozell and Jagodowicz, 1973; Hornung *et al*., 1980; Hornung and Mozell, 1985). It was hypothesized that the spatial–temporal neural patterns necessarily produced by such sorption could be an important element in differential responses to odorants even if all odorants flowed in the same direction, for example, orthonasal olfaction. This was formalized as the gas chromatographic model of olfaction (Mozell, 1970; Engen, 1982). The proposed differences could be the converse of each other if odorant flow were in opposite directions, that is, retronasal versus orthonasal smelling. Subsequent studies from many laboratories revealed that olfactory receptor neurons differ in their response characteristics even when differential sorption along the olfactory mucosa is precluded (Kauer, 1980, 1987, 1991; Kubie *et al*., 1980) and that there are tendencies for olfactory receptor neurons with similar characteristics to cluster in regions of the olfactory mucosa and to synapse in the same areas (glomeruli) of the olfactory bulb (Laurent, 1999; Mori *et al*., 1999; Ma and Shepherd, 2000; Paysan and Breer, 2001; Friedrich, 2002; Spors and Grinvald, 2002). These latter neurophysiological and anatomical data, which emphasize the heterogeneous but orderly characteristics of the peripheral olfactory system and its initial central nervous system terminations, reinforce the possibility that retronasal odorant presentations will result in neural responses that are quite different from those to orthonasal presentations.

Ecological relevance of orthonasal–retronasal pairs

Under typical conditions of food or beverage consumption, food-derived stimuli are present both within the oral cavity and outside it after the initial sip or bite. Chemical, thermal, and mechanical aspects of the beverage or food may all be relevant inside the oral cavity (Lawless, 1996; Halpern, 1997). Moreover, once inside the mouth, solution, temperature, and mechanical processes can alter the food or beverage (Roberts and Acree, 1995, 1996; Geary *et al*., 2004; Roberts *et al*., 2004). These alterations shape air phase odorants that reach the oral cavity and the nasal cavity from the oral cavity (Halpern, 2004a). Further research that leads to an improved understanding of retronasal olfaction in relation to orthonasal olfaction will make important contributions to both chemosensory science and factors underlying food or beverage selection.

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