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Sniff Magnitude Test: Relationship to Odor Identification, Detection, and Memory Tests in a Clinic Population

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Abstract

Recently a novel measure of olfactory function, the Sniff Magnitude Test (SMT), was developed that relies on changes in inhalation in response to an odor. The relationship of this unique test to that of other olfactory tests has received little investigation. In this study, we assessed, in 132 patients presenting to a chemosensory disorders clinic, the relationship of SMT scores to those from 3 standardized psychophysical tests: the University of Pennsylvania Smell Identification Test (UPSIT), a phenyl ethyl alcohol odor detection threshold test, and a short-term odor memory/discrimination test. SMT scores were roughly related to olfactory dysfunction categories defined for the UPSIT and correlated moderately with the other tests. Malodors (1% and 3% methylthiobutyrate [MTB], 1% ethyl 3-mercaptoproprionate) exhibited stronger correlations than nonmalodors (3% phenyl ethyl alcohol [PEA], 3% amyl acetate, 3% *n*-butanol) and elicited greater sniff suppression. In a principal component analysis, the SMT measures loaded on components different from those of the other tests, which loaded on a separate component. Anticipatory responses (i.e., smaller sniffs) occurred across trials for the first malodor (1% MTB), but not for the first nonmalodor (3% PEA), that was encountered. These results, along with those of an earlier factor analysis, suggest that sniff magnitude is influenced by odorant quality and intensity, as well as by cognitive factors.

Key words: factor analysis, odor identification, odor memory, odor threshold, sniff magnitude, UPSIT

Introduction

Numerous clinical olfactory tests have been described in the literature, including ones incorporating psychophysical, electrophysiological, and psychophysiological methods (for reviews, see Doty and Laing 2003; Kobal 2003). Such tests range from simple single-item odor identification screening tests to complex electrophysiological tests employing sophisticated olfactometers. Most olfactory psychophysical tests are positively correlated with one another and measure common attributes (Doty, Shaman, and Dann 1984; Yoshida 1984; Doty et al. 1985, 1995; Cain and Rabin 1989; Hummel et al. 1997; Frank et al. 2003), although intensity and pleasantness ratings have been found to be somewhat independent of measures of detection, identification, and memory (Doty et al. 1994).

Recently a novel test of olfactory function, the Sniff Magnitude Test (SMT), has been developed (Frank et al. 2003). Rather than relying on verbal responses, this test establishes the ratio of the magnitude of sniffs given to odorants to the magnitude of sniffs given to nonodorized air (the sniff magnitude ratio). The standard odors used in this test are "malodors," that is, 1% and 3% methylthiobutyrate (MTB) and 1% ethyl 3-mercaptoproprionate (EMP). According to Frank et al. (2003), the SMT relies on a "reflex-like" reduction in inhalation upon encountering an odorant and is relatively unaffected by memory, attention, linguistic skills, and other nonolfactory cognitive processes, making it useful in testing very young persons, patients with dementia, and aphasics. Despite such assertions, however, the degree to which cognitive processes are involved is debatable. For example, it is well established that humans tend to sample unpleasant or strong odorants using small or moderate sniffs and pleasant or weak ones with larger sniffs, suggesting that such sampling is modulated by judgment and prior experience (Laing 1983; Warren et al. 1994; Johnson et al. 2003; Mainland and Sobel 2006).

Frank et al. (2006) have recently shown an inverse association between the sniff magnitude ratio and University of Pennsylvania Smell Identification Test (UPSIT) olfactory function categories (i.e., anosmia, severe microsmia, moderate microsmia, mild microsmia, and normosmia). Thus, as

the sniff magnitude ratio increased (indicating less odor-induced sniff suppression and poorer olfactory ability), scores on the UPSIT decreased. It is unknown if this relationship holds for nonaversive odorants or for sniff magnitude alone, that is, the magnitude of a sniff directed to an odorant without comparison to nonodorized air. Although it has been assumed that the sniff magnitude ratio provides a more sensitive measure than sniff magnitude by controlling for individual differences in the size of sniffs, this has not been empirically assessed.

The present study determined, in a clinic population, the relationship of SMT scores to those from 3 standardized tests of odor identification, detection, and memory/discrimination. We sought to establish whether such associations are influenced by odorant type, whether they differ for sniff magnitude ratio than for sniff magnitude, and how these measures relate to UPSIT function categories. To establish if expectation influences the sniff magnitude measures, we determined whether the inhalation responses decreased over 3 successive repeated trials for an aversive malodor and a nonaversive nonmalodor, each of which was encountered before confounding exposures to other odors had occurred. We also established whether anosmic patients exhibited suppression to the odors and, if so, whether such odor-induced sniff suppression differed between the malodors and nonmalodors.

Methods

Subjects

The subjects were 132 patients (51 males, 81 females) presenting to the Smell and Taste Center's clinic with complaints of taste or smell dysfunction. The complaints stemmed from a variety of causes [i.e., carcinoma, $n = 1$; chronic rhinosinusitis, $n = 8$; congenital anosmia, $n = 2$; head trauma, $n = 15$; iatrogenesis (including medication induced), $n = 14$; idiopathy, $n = 34$; Sjögren's syndrome, $n = 1$; toxic exposure, $n = 1$; and upper respiratory infections, $n = 56$). The subjects ranged in age from 13 to 84 years (mean [SD] = 54.74 [15.6]). Most were paid $20.00 for taking the SMT, which was a test not administered in our routine clinical assessment. Informed written consent was obtained in accord with the requirements of the University's Office of Regulatory Affairs.

Test instruments

Sniff Magnitude Test

The SMT is a computerized device in which stimulus canisters are presented, one at a time, to the subject for sniffing (Frank et al. 2003, 2004, 2006). Within milliseconds of sniffing the surface of a canister, its top opens and either an odorant or nonodorized air is released. A piezoelectric pressure transducer senses the negative pressure induced by the subject's sniff via a nasal cannula, sending a digitized signal to a laptop computer. The sniff pressure measurements are calculated every 10 ms once a sniff is detected, and recording continues until a return to ambient air pressure occurs. "Sniff magnitude" is computed as the sum of the 10-ms negative pressure values generated across the sniff epoch and is proportional to the area under the sniff pressure–time curve. "The sniff magnitude ratio" is the ratio of sniff magnitude value given to an odorant to that given to nonodorized air. When suppression occurs more to an odorant than to a nonodorant, then this ratio is less than one. In the present study, the mean of the sniff magnitude values of 3 odor trials was divided by the mean of the sniff magnitude values of 3 nonodor trials to achieve this ratio (see Procedures).

Six different stimuli and an air blank were employed in this study. The odorants were embedded in polypropylene absorbent pads contained within each sniff canister (5 ml/pad). The 6 stimuli and their v/v concentrations in light mineral oil (0121-4, Fisher Scientific, Pittsburgh, PA) were as follows: 1% MTB, 3% MTB, 1% EMP, 3% phenyl ethyl alcohol (PEA), 3% amyl (pentyl) acetate (AA), and 3% *n*-butanol (NBUT). The odors generated in the headspace of the canister for these stimuli were above threshold and easily detected by a person with a normal sense of smell. The MTB and EMP stimuli, which are the standard stimuli employed by the test's developers, are described as having a fecal, ripe cheese odor and a burnt, skunky odor, respectively, at the concentrations used in the test (Frank et al. 2006). According to Frank et al. (2006), MTB and EMP produce no nasal irritation, as demonstrated by the inability of subjects to localize them in a 2-nostril localization test. The AA, NBUT, and PEA concentrations were selected to provide clearly discernable nonaversive odors while minimizing potential trigeminal stimulation. No attempt was made to equate the stimuli on intensity. For the purposes of analysis, we classified MTB 1%, MTB 3%, and EMP as malodors (in accord with the classification of Frank et al. 2003) and AA, NBUT, and PEA as nonmalodors. Preliminary tests indicated that 2 of the latter 3 odorants (AA, PEA) were perceived as pleasant by 12 of 12 subjects, whereas NBUT was generally perceived as neutral.

University of Pennsylvania Smell Identification Test

This forced-choice olfactory test is based upon basic psychological test measurement theory and focuses on the comparative ability of subjects to identify odorants at the suprathreshold level (Doty, Shaman, Applebaum, et al. 1984; Doty, Shaman, and Dann 1984). Physically, the test consists of 4 envelope-sized booklets, each containing 10 "scratch and sniff" odorants embedded in 10- to 50-μm microcapsules positioned on brown strips at the bottom of the pages of the booklets. The odorants comprised multi-odorant compounds that realistically mimic odorants experienced in everyday life. The stimuli are released by scratching microencapsulated odorant strips with a pencil tip in a standardized manner. Above each odorant strip is a multiple-choice question with 4 alternative responses. The subject's task is to smell each odor and pick the one

descriptor that best corresponds to the odor. The subject must provide a response even if no odor is perceived (i.e., the test is forced choice). The specifics and criteria for item selection and standardization are described in detail elsewhere (Doty, Shaman, Applebaum, et al. 1984). The internal consistency and test–retest reliability coefficients of this instrument are greater than 0.90 (Doty, Shaman, and Dann 1984; Doty et al. 1989).

Phenyl ethyl alcohol detection threshold test

The phenyl ethyl alcohol test (PEA-T) measures detection threshold sensitivity (Doty et al. 1986, 1995; Deems and Doty 1987; Betchen and Doty 1998). The odorant concentrations are presented by polypropylene squeeze bottles. A staircase psychophysical procedure is used. The staircase begins at the −6.00 log concentration step of a half-log step (v/v) dilution series extending from −10.00 log concentration to −2.00 log concentration. The odorant concentration is increased in full-log steps until correct detection occurs on 5 sets of consecutive trials at a given concentration. A trial consists of the presentation of a diluent and odorant, one after the other. The subject's task is to indicate which of the 2 stimuli seems stronger. If no difference is perceived, the subject must still report an answer, that is, the test is forced-choice. If an incorrect response occurs on any trial, the staircase is moved upward one full-log step. When a correct response is made on all 5 trials, the staircase is reversed and subsequently moved up or down in 0.50 log increments or decrements, depending upon the subject's performance on 2 pairs of trials at each concentration step. The geometric mean of the last 4 of 7 staircase reversal points serves as the threshold measure.

Odor memory test

The odor memory test (OMT) is a 12-item test of short-term odor memory and discrimination that employs 10-, 30-, and 60-s delay intervals between the presentation of a target odorant and a set of odors from which the target is to be selected (Choudhury et al. 2003). The target odorant is initially released by scratching an odorized label that is then presented to the subject for sampling. After a given delay interval, the 4 subsequent odorants (the target and 3 foils) are similarly released and presented at approximately 5-s intervals. The subject's task is to report which odor in the odor response set is the same as the target stimulus. During the delay interval, the subject counts aloud backward by 3 from 280 to minimize verbal rehearsal. The presentation order of the stimuli is counterbalanced such that 1) all target odorants occur an equal number of times at each delay interval, 2) each target odorant is represented at a given delay interval once in each of the 4 possible response positions (i.e., a, b, c, and d), and 3) all 4 odorants are presented in the first, second, and third segments of the test. The test–retest reliability of the OMT is above 0.70 (Doty et al. 1995).

Procedures

A given patient received all the olfactory tests on the same clinic day. The OMT was always administered before the UPSIT to minimize potential confounding of the memory test items by semantic cues from the written UPSIT response alternatives. The SMT was always the last sensory test administered. The tests were administered in accord with the instructions of the manufacturers.

On a given SMT trial, the test administrator placed the target odorant canister approximately 2.0 cm beneath the patient's nose, and once in position, the patient was instructed, as indicated by the test developers, to "sniff until you smell something." Each test started with 3 trials using the nonodorized blank air canister to establish a no-odor sniffing baseline. The subjects received the following odor sequences, with half of the subjects receiving one sequence first and the other half the other sequence first—"malodor sequence": blank (3 trials), MTB 1% (3 trials), MTB 3% (3 trials), EMP (3 trials); "nonmalodor sequence": blank (3 trials), PEA (3 trials), AA (3 trials), NBUT (3 trials).

Statistical analyses

We first computed Spearman correlations among the test scores to examine the relationships among the tests. Differences among the correlation coefficients obtained for the sniff magnitudes and the sniff magnitude ratios were tested for significance using the correlation comparison statistics found in the MedCalc statistical package (Schoonjans 2006). The correlation matrix was then subjected to a principal component factor analysis with orthogonal (varimax) and nonorthogonal (oblimin) rotations (Wilkinson 1990). The use of the 2 rotations was made to determine whether the same general factor solution would occur when both constrained and nonconstrained (i.e., correlated and noncorrelated) factor solutions were applied.

Analysis of covariance (ANCOVA) was used to assess associations between the SMT test measures and such factors as age, sex, and degree of olfactory dysfunction, as measured by well-established UPSIT function categories based upon normative samples (Doty 1995). Post hoc comparisons were made using 2-tailed t tests with Holm's (1979) α correction for multiple assessments. Because preliminary analyses found no effects of sex or interactions with sex on any of the SMT measures, this variable was dropped in subsequent analyses. The UPSIT diagnostic categories were normosmia, 34–40; mild microsmia, 30–33; moderate microsmia, 26–29; severe microsmia, 19–25; and anosmia, 1–18.

Results

Relationship of SMT scores to other test measures

The Spearman correlations among the measures are shown in Table 1, where the SMT data are based upon sniff magnitude, and Table 2, where they are based upon the sniff

Table 1 Spearman correlations among tests, with sniff magnitude (SM) as the SMT measure

	UPSIT	PEA-T	OMT	MTB1-SM	MTB3-SM	EMP-SM	PEA-SM	AA-SM	NBUT-SM
UPSIT	1.0								
PEA-T	**−0.84**	1.0							
OMT	**0.67**	**0.64**	1.0						
MTB1-SM	**−0.49**	**−0.47**	**−0.33**	1.0					
MTB3-SM	**−0.53**	**−0.50**	**−0.36**	**0.92**	1.0				
EMP-SM	**−0.57**	**−0.54**	**−0.42**	**0.88**	**0.92**	1.0			
PEA-SM	**−0.37**	**−0.38**	−0.21	**0.75**	**0.73**	**0.76**	1.0		
AA-SM	**−0.42**	**−0.41**	**−0.27**	**0.77**	**0.78**	**0.80**	**0.91**	1.0	
NBUT-SM	**−0.33**	**−0.37**	−0.15	**0.76**	**0.76**	**0.78**	**0.89**	**0.90**	1.0

MTB1, 1% MTB; MTB3, 3% MTB; EMP, 1% EMP; PEA, 3% PEA; AA, 3% AA; and NBUT, 3% NBUT. Correlation coefficients that are significant at ≤0.01 are shown in bold. *P* values corrected using Holm's (1979) method for multiple comparisons.

Table 2 Spearman correlations among tests, with sniff magnitude ratio (SMR) as the SMT measure

	UPSIT	PEA-T	OMT	MTB1-SMR	MTB3-SMR	EMP-SMR	PEA-SMR	AA-SMR	NBUT-SMR
UPSIT	1.0								
PEA-T	**−0.84**	1.0							
OMT	**0.67**	**0.64**	1.0						
MTB1-SMR	**−0.48**	**−0.38**	**−0.46**	1.0					
MTB3-SMR	**−0.55**	**−0.47**	**−0.52**	**0.86**	1.0				
EMP-SMR	**−0.57**	**−0.48**	**−0.57**	**0.79**	**0.88**	1.0			
PEA-SMR	**−0.29**	−0.22	**−0.34**	**0.38**	**0.42**	**0.40**	1.0		
AA-SMR	**−0.34**	−0.25	**−0.37**	**0.48**	**0.51**	**0.53**	**0.80**	1.0	
NBUT-SMR	−0.14	−0.08	−0.15	0.19	0.21	0.24	**0.54**	**0.69**	1.0

For explanation of test abbreviations, see Table 1 footnote. Correlation coefficients that are significant at ≤0.01 are shown in bold. *P* values corrected using Holm's (1979) method for multiple comparisons.

magnitude ratio. It is apparent from both of these tables that, in nearly all instances, the SMT measures correlated moderately and significantly with the other 3 measures (left 3 columns of each table). Although, in general, sniff magnitudes correlated more strongly than sniff magnitude ratios with the UPSIT and PEA threshold measures (10 of 12 coefficients; binomial $P = 0.016$), the reverse was the case for the OMT measure (5 of 6 coefficients; binomial $P = 0.09$). However, statistical analysis of the differences between the respective correlation coefficients for the sniff magnitude and sniff magnitude ratios for these tests found no significant differences, with the exception of the difference between the correlations between the NBUT SMT measure and the PEA threshold measure ($P = 0.01$).

It is also apparent from Tables 1 and 2 that the correlations among the 6 different stimuli of the SMT tests were larger for the sniff magnitudes than for the sniff magnitude ratios (columns 4–8). Thus, all 15 of these correlation coefficients were larger for the sniff magnitudes (binomial $P < 0.001$), and in all but one case (3% MTB, EMP; $P = 0.087$), the respective correlation coefficients differed significantly from one another (in 11 cases, $P < 0.0001$; in the remaining 3 cases, P's = 0.0006, 0.018, and 0.015).

Principal component analyses

The principal component loadings, following varimax rotations, are shown for the sniff magnitude and sniff magnitude ratio data in Tables 3 and 4, respectively. The same pattern of loadings was present for the oblimin rotations and is not presented here. Two meaningful principal components (i.e., eigenvalues ≥ 1) emerged when sniff magnitude was employed and 3 meaningful components when the sniff magnitude ratio was employed. The extracted SMT components were clearly separate from the component that received major loadings from the identification, detection, and

Table 3 Varimax rotated principle components analysis of sniff magnitude (SM)

	1	2
UPSIT	−0.29	**−0.88**
PEA-T	−0.22	**−0.87**
OMT	−0.08	**−0.86**
MTB1-SM	**−0.91**	−0.24
MTB3-SM	**−0.90**	−0.27
EMP-SM	**−0.90**	−0.22
PEA-SM	**−0.92**	−0.15
AA-SM	**−0.91**	0.21
NBUT-SM	**−0.94**	0.11
Total variance explained	57.04%	28.09%

For explanation of test abbreviations, see Table 1 footnote. Component loadings significant at ≤0.01 are shown in bold.

Table 4 Varimax rotated principle components analysis of sniff magnitude ratios (SMRs)

	1	2	3
UPSIT	−0.25	−0.15	**−0.88**
PEA-T	−0.15	−0.04	**−0.91**
OMT	−0.29	−0.17	**−0.77**
MTB1-SMR	**0.89**	0.16	0.17
MTB3-SMR	**0.88**	0.20	0.30
EMP-SMR	**0.89**	0.12	0.24
PEA-SMR	0.15	**0.87**	0.15
AA-SMR	0.26	**0.88**	0.13
NBUT-SMR	0.05	**0.89**	0.05
Total variance explained	28.90%	27.31%	26.85%

For explanation of test abbreviations, see Table 1 footnote. Component loadings significant at ≤0.01 are shown in bold.

memory measures. In the case of the sniff magnitude ratio, one component received loadings from the 3 malodors and the other component from the 3 nonmalodors. The factor solutions were nearly equivalent for each sex.

In light of an earlier factor analysis study by Frank et al. (2003) that found the SMT (1% MTB), the UPSIT, an NBUT threshold test, and the alcohol sniff test loaded on a single factor, we reduced the number of variables in our analysis to 4, to see if a similar solution occurred. We employed the same SMT odorant (1% MTB), the UPSIT, the PEA-T, and the OMT. As in the case of Frank et al. (2003), we also found that one principle component emerged, accounting for 66% of the variance. This solution remained stable after varimax and oblimin rotations. We then introduced a second SMT measure (MTB 3%), which resulted in a 2-component solution both before and following rotation. Before rotation, one component accounted for 64% of the variance and still received major loadings from all 5 test measures. The second component, which accounted for 21% of the variance, loaded most heavily with MTB 1% and MTB 3%, although the loadings for these variables were still stronger on the first factor. After varimax rotation, these 2 SMT measures strongly loaded on a principal component separate from the other 3 measures. This component accounted for 37% of the variance, whereas the component receiving loadings from the UPSIT, the PEA-T, and the OMT accounted for 47% of the variance. A similar solution was found with the oblimin rotation.

Relationship of SMT scores to UPSIT function categories

For sniff magnitude, an UPSIT function category (normosmia, mild microsmia, moderate microsmia, severe microsmia, anosmia) × odorant type (malodor, nonmalodor) × age ANCOVA, with age as a covariate and odorant type as a repeated measures factor, revealed significant effects of UPSIT function category ($F(4, 126) = 7.94$, $P \leq 0.001$), odorant type ($F(1, 126) = 12.17$, $P \leq 0.001$), and an odorant type × age interaction ($F(1, 126) = 7.23$, $P = 0.008$). Univariate F tests revealed that the age effect was present for the malodors ($F(1, 126) = 4.72$, $P = 0.032$) but not for the nonmalodors ($F(1, 126) = 0.15$, $P = 0.70$), reflecting the tendency for younger persons to exhibit more suppression than older ones to malodors. Overall, smaller sniffs were directed toward malodors than nonmalodors (mean [SEM] sniff magnitudes = 50.65 [4.58] and 60.05 [5.06]). The relationship between sniff magnitude and UPSIT dysfunction categories is depicted in Figure 1. The only significant differences among the means were those between the anosmic patients and the patients with either mild microsmia or normosmia (P's < 0.001).

The same analysis performed on the sniff magnitude ratios revealed a significant UPSIT function category ($F(4, 126) = 8.85$, $P < 0.001$), as well as a significant odorant type UPSIT function category interaction ($F(4, 126) = 2.43$, $P = 0.05$). In contrast to the sniff magnitudes, neither the odorant type nor the odorant type × age interaction was significant (P's > 0.70). The odorant type × UPSIT function category interaction reflected the fact that sniff magnitude ratios for malodors, but not nonmalodors, significantly changed across UPSIT function categories (Figure 2). Patients with normosmia and mild microsmia exhibited significantly smaller sniff magnitude ratios for malodors than for nonmalodors (P's < 0.05). As with sniff magnitude, the only significant differences among the means for the malodors were between those of the patients with anosmia and either mild microsmia or normosmia (P's < 0.001).

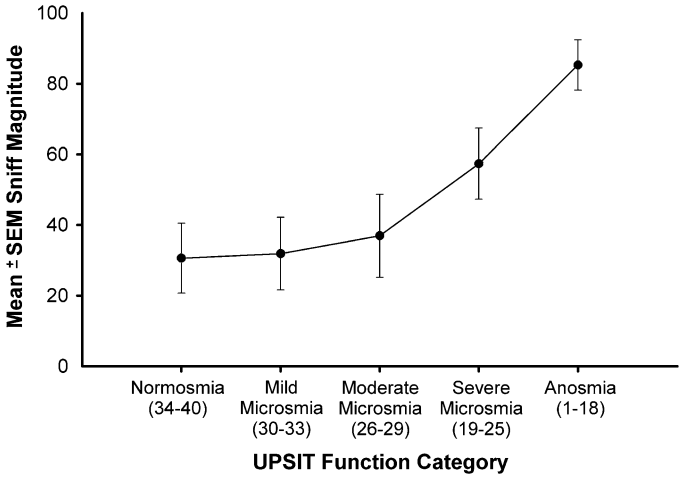

Figure 1 Mean sniff magnitude estimates as a factor of UPSIT function category. Means represent average responses across 3 trials each of 6 stimuli: 1% MTB, 3% MTB, 1% EMP (malodors), 3% PEA, 3% AA, and 3% NBUT (nonmalodors). Sample sizes are as follows: normosmia (n = 24), mild microsmia (n = 22), moderate microsmia (n = 17), severe microsmia (n = 23), anosmia (n = 46).

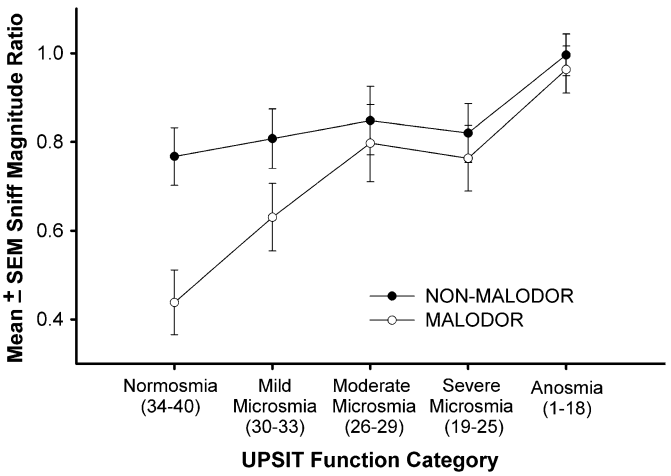

Figure 2 Mean sniff magnitude ratio estimates of the 3 malodors and the 3 nonmalodors (see figure caption 1). Sample sizes are as follows: normosmia (n = 24), mild microsmia (n = 22), moderate microsmia (n = 17), severe microsmia (n = 23), anosmia (n = 46).

Sniff suppression across trials

To establish whether the SMT measures changed over successive trials after first being encountered and, if so, whether such change differed as a function of odorant type (i.e., malodor vs. nonmalodor), we subjected the sniff magnitude and the sniff magnitude ratios to separate ANCOVAs with UPSIT function category (5 levels) as a between-groups factor, trial (3 levels) as a within-groups factor, and age as a covariate. The 2 stimuli for which these analyses were possible, that is, for which no previous encounters with other stimuli had occurred, were MTB (1%) (malodor) and PEA

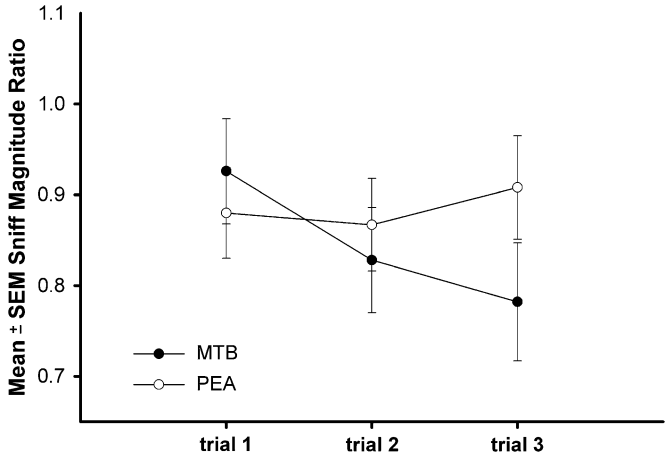

Figure 3 Mean sniff magnitude ratio estimates across the 3 trials for 1% MTB and 3% PEA.

(3%) (nonmalodor). In the case of the sniff magnitude ratio, a significant decrease occurred across trials for MTB (F (2, 124) = 4.04, P = 0.020) but not for PEA (F (2, 116) = 0.075, P = 0.927) (Figure 3). In the case of sniff magnitude, a nonsignificant decrease occurred across trials for MTB (F (2, 124) = 2.41, P = 0.094) but not for PEA (F (2, 116) = 0.67, P = 0.514). Analogous to the data shown in Figure 1, sniff magnitudes decreased as smell ability increased for both PEA and MTB, as indicated by significant UPSIT group effects (PEA F (4, 58) = 2.96, P = 0.027; MTB F (4, 62) = 2.83, P = 0.032). Sniff magnitude ratios for MTB, but not PEA, also exhibited this effect (MTB F (4, 62) = 2.51, P = 0.051; PEA F (4, 58) = 0.95, P = 0.442].

Sniff suppression in anosmics

We examined the means and medians of the sniff magnitude ratios of the 31 anosmic subjects (i.e., individuals with PEA values > −2.00 log v/v and UPSIT scores ≤ 16) to establish whether the responses to SMT were potentially being mediated by non-cranial nerve 1 afferents. The mean and median ratios were very close to 1 for both the malodors (mean [SD] = 1.05 [0.25]; median [range] = 0.99 [0.55–2.04]) and nonmalodors (mean [SD] = 1.06 [0.33]; median [range] = 1.04 [0.58–1.54]), implying that non-CN I afferents were unlikely influencing the SMT responses.

Discussion

A major finding of the present study is that the SMT appears to measure, to a significant degree, elements of variance different from those of the UPSIT, the OMT, and the PEA threshold test. These elements seemingly reflect, in large part, a hedonic dimension because the malodors and nonmalodors loaded, in the case of the sniff magnitude ratio, on separate principal components. This hypothesis is supported by the fact that the sniff magnitude ratio decreased across trials for MTB, a malodorant, but not for PEA, a nonmalodorant,

implying expectancy based upon hedonics. Additional support for this hypothesis comes from our finding of greater suppression for malodors than for nonmalodors, as well as from an earlier factor analysis study in which the UPSIT, the PEA threshold test, and an OMT all loaded on a common factor, whereas ratings of odorant pleasantness/unpleasantness loaded on a separate factor (Doty et al. 1994).

That being said, one cannot exclude the possibility that odorant intensity is also involved in producing some of our findings, particularly because 1) the malodors of the present study appeared to be stronger than the nonmalodors, 2) the Doty et al. (1994) factor analysis study found odor intensity ratings, like odor hedonic ratings, to account for a significant amount of variance independent of the other measures, and 3) sniff magnitude ratios can be influenced by stimulus intensity (Bailie 2006). Koskinen et al. (2004) also found, in a factor analysis study, that intensity ratings loaded on a factor separate from odor identification and threshold measures. Unfortunately, perceived odor intensity and pleasantness/unpleasantness are often related in complex ways and are difficult to disentangle. In some cases, this relationship is not linear or even monotonic, although odor intensity and pleasantness are typically negatively (i.e., inversely) related for stimuli perceived as unpleasant and positively related for ones perceived as pleasant (Doty 1975). Although there is evidence that odor intensity and hedonics are encoded in parallel (Savic et al. 2000), it has been suggested that odor intensity may be encoded in brain structures, such as the amygdala, "early in the olfactory processing stream," whereas odor hedonicity occurs "further down the stream," for example, in the orbitofrontal cortex (Johnson et al. 2003). If this is the case, then intensity may, in fact, be a more salient determinant of sniff magnitude than hedonics. Clearly, an elucidation of the relative roles of odor quality, hedonics, and intensity require additional study.

Although relationships were found between the SMT measures and the tests of odor identification, detection, and discrimination, they were not strong. This likely explains, in part, why neither sniff magnitudes nor sniff magnitude ratios significantly discriminated between patients classified as normal by the UPSIT and those classified as having mild, moderate, or even severe microsmia (Figure 1) and why these measures did not differentiate among adjacent UPSIT dysfunction categories. Our findings contrast somewhat from those of the study of Frank et al. (2006), which found significant sniff magnitude ratio differences between normosmics and moderate and severe microsmics. The basis of this discrepancy is not clear, although it is conceivable that having the same subjects perform both malodor and nonmalodor trials dilutes the effects of malodors on the dependent measures. Other procedural differences may also be involved. For example, following the presentation of 3 blanks, Frank et al. presented three 1% MTB trials. If the subject evidenced suppression to these trials relative to the blanks (i.e., a sniff magnitude ratio of 0.75 or less), only then did they continue with 6 additional trials, the first 3 employing 3.0% MTB and the second three 1% EMP. In our study, we administered this entire sequence of trials to all subjects, regardless of whether they exhibited initial suppression to MTB.

The present study is the first to assess sniff magnitude in addition to the sniff magnitude ratio. We examined this because one could argue that sniff magnitude, per se, is a more fundamental measure of the sniff response to an odorant than the sniff magnitude ratio as its score does not depend upon an individual's sniffing behavior to nonodorized air. It is conceivable that a person with normal smell function could quickly recognize that no odor is present and would discontinue sniffing the blank canister. If the magnitude of the sniff directed to the blank is similar to the magnitude of the sniff directed to the odorant, the resulting sniff magnitude ratio would indicate a score suggestive of anosmia. In fact, we found that 5/24 (21%) of patients scoring in the normal range on the UPSIT had a sniff magnitude ratio greater than one for nonmalodors, an effect that did not occur for malodors. Interestingly, 10/24 (42%) of those normosmic patients had a nonmalodor sniff magnitude ratio greater than 0.80, a value considered abnormal according to SMT norms. Our findings suggest that sniff magnitudes generally correlated more strongly with the other test measures, save the OMT. Whereas sniff magnitudes were somewhat more sensitive, overall, to odorant type (malodor, nonmalodor), sniff magnitude ratios tended to exhibit less variance and to better define the association between odor type and smell dysfunction, as indexed by UPSIT function categories and the emergence of malodor and nonmalodor principal components. When sniff magnitude was employed, 2 principal components emerged, whereas when the sniff magnitude ratio was employed, 3 principal components emerged. Such findings make it difficult to determine what specific elements of olfactory function are being differentially sampled by these 2 measures.

In this study, we compared, for the first time, SMT responses to nonaversive odorants to those of aversive odors typically employed in the SMT. We found that suppression occurs better for malodors than for nonmalodors. Thus, smaller sniffs were directed, overall, toward malodors (mean [SEM] sniff magnitudes = 50.65 [4.58] vs. 60.05 [5.06]), and patients with normosmia and mild microsmia exhibited significantly smaller sniff magnitude ratios for malodors than for nonmalodors (P's < 0.05). In accord with the data of Frank et al. (2006), we found that sniff magnitude ratios to malodors were larger in older than in younger persons, as would be expected if this measure is sensitive to age-related olfactory deficits. However, the age effect was not present for nonmalodors. The latter finding is somewhat counterintuitive because one might assume that nonmalodors would be more poorly detected by older than by younger persons as they are seemingly less salient—and hence more likely to be influenced by age—than malodors. Presumably this phenomenon is related to the fact that malodors elicit stronger and less variable sniff suppression than nonmalodors.

By examining only those trials on which the first SMT-related odor experiences had occurred, we were able to establish whether the inhalation responses were altered by repeated exposure. A systematic decrease in the sniff magnitude ratio (i.e., increased suppression) occurred across trials for the malodor (MTB 1%) but not for the nonmalodor (PEA). Although a similar increase in suppression across repeated trials was also noted in the sniff magnitude measure, it was not significant at the 0.05 α level ($P = 0.094$). These observations suggest that the sniff magnitude ratio is influenced by expectation and that sniff suppression is modified by learning, depending upon the nature of the stimulus employed.

Our finding that the sniff magnitude ratios of the 31 anosmic subjects were close to one for both the malodors and the nonmalodors suggests that nonolfactory afferents, such as from CN V, are unlikely responsible for the inhalation suppression observed in this study. This observation is in accord with the indication of Frank et al. (2006) that MTB and EMP, at the concentrations used in this study, are unable to be localized in a 2-nostril lateralization test.

In summary, the present study clearly demonstrates that sniff magnitude measures are altered by a number of factors, including the type of odorant employed in testing. Importantly, this work suggests that the SMT assesses components of olfactory function distinct from those measured by odor identification, detection, and short-term memory and probably is assessing suprathreshold hedonics and/or intensity. This would explain the SMT's lesser sensitivity to clinically meaningful alterations in smell function because, in general, suprathreshold scaling of odor intensity and pleasantness is less sensitive to olfactory deficits than measures of threshold and identification (Doty and Laing 2003). Whereas the SMT has been reported as reflecting ''reflex-like'' responses to odorants, the present study suggests that SMT measures are influenced by prior experience and cognitive factors, including the ability to rapidly recognize odorant quality. Given that subjects must still understand and follow the instructions (sniff until you smell something) and the considerable variability in the SMT measures, additional research is needed to determine whether the SMT has significant advantages over other tests in assessing the olfactory function of patients less amenable to traditional testing, such as aphasics and cognitively compromised or demented ones.

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References

Bailie JM. 2006. Clarifying the nature of the olfactory impairment found in patients with Parkinson's disease [dissertation]. University of Cincinnati, Cincinnati, OH.

Betchen SA, Doty RL. 1998. Bilateral detection thresholds in dextrals and sinistrals reflect the more sensitive side of the nose, which is not lateralized. Chem Senses. 23:453–457.

Cain WS, Rabin RD. 1989. Comparability of two tests of olfactory function. Chem Senses. 14:479–485.

Choudhury ES, Moberg P, Doty RL. 2003. Influences of age and sex on a microencapsulated odor memory test. Chem Senses. 28:799–805.

Deems DA, Doty RL. 1987. Age-related changes in the phenyl ethyl alcohol odor detection threshold. Trans Pa Acad Ophthalmol Otolaryngol. 39: 646–650.

Doty RL. 1975. An examination of relationships between the pleasantness, intensity, and concentration of 10 odorous stimuli. Percept Psychophys. 17:492–496.

Doty RL. 1995. The Smell Identification Test™ Administration Manual. 3rd ed. Haddon Hts (NJ): Sensonics, Inc. p. 57.

Doty RL, Frye RE, Agrawal U. 1989. Internal consistency reliability of the fractionated and whole University of Pennsylvania Smell Identification Test. Percept Psychophys. 45:381–384.

Doty RL, Gregor TP, Settle RG. 1986. Influence of intertrial interval and sniff-bottle volume on phenyl ethyl alcohol odor detection thresholds. Chem Senses. 11:259–264.

Doty RL, Laing DG. 2003. Psychophysical measurement of olfactory function, including odorant mixture assessment. In: Doty RL, editor. Handbook of olfaction and gustation. New York: Marcel Dekker. p. 203–228.

Doty RL, McKeown DA, Lee WW, Shaman P. 1995. A study of the test-retest reliability of ten olfactory tests. Chem Senses. 20:645–656.

Doty RL, Newhouse MG, Azzalina JD. 1985. Internal consistency and short-term test-retest reliability of the University of Pennsylvania Smell Identification Test. Chem Senses. 10:297–300.

Doty RL, Shaman P, Applebaum SL, Giberson R, Siksorski L, Rosenberg L. 1984. Smell identification ability: changes with age. Science. 226: 1441–1443.

Doty RL, Shaman P, Dann M. 1984. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. Physiol Behav. 32:489–502.

Doty RL, Smith R, McKeown DA, Raj J. 1994. Tests of human olfactory function: principal components analysis suggests that most measure a common source of variance. Percept Psychophys. 56:701–707.

Frank RA, Dulay MF, Gesteland RC. 2003. Assessment of the Sniff Magnitude Test as a clinical test of olfactory function. Physiol Behav. 78:195–204.

Frank RA, Dulay MF, Niergarth KA, Gesteland RC. 2004. A comparison of the sniff magnitude test and the University of Pennsylvania Smell Identification Test in children and nonnative English speakers. Physiol Behav. 81:475–480.

Frank RA, Gesteland RC, Bailie J, Rybalsky K, Seiden A, Dulay MF. 2006. Characterization of the sniff magnitude test. Arch Otolaryngol Head Neck Surg. 132:532–536.

Holm S. 1979. A simple sequentially rejective multiple test procedure. Scand J Stat. 6:65–70.

Hummel T, Sekinger B, Wolf SR, Pauli E, Kobal G. 1997. 'Sniffin' sticks': olfactory performance assessed by the combined testing of

odor identification, odor discrimination and olfactory threshold. Chem Senses. 22:39–52.

Johnson BN, Mainland JD, Sobel N. 2003. Rapid olfactory processing implicates subcortical control of an olfactomotor system. J Neurophysiol. 90:1084–1094.

Kobal G. 2003. Electrophysiological measure of olfactory function. In: Doty RL, editor. Handbook of olfaction and gustation. New York: Marcel Dekker. p. 229–249.

Koskinen S, Vento S, Malmberg H, Tuorlla H. 2004. Correspondence between three olfactory tests and suprathreshold odor intensity ratings. Acta Oto-Laryngolog. 124(9):1072–1077.

Laing DG. 1983. Natural sniffing gives optimum odour perception for humans. Perception. 12:99–117.

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

Savic I, Gulyas B, Larsson M, Roland P. 2000. Olfactory functions are mediated by parallel and hierarchical processing. Neuron. 26:735–745.

Schoonjans F. 2006. MedCalc (version 9.0) [Computer Software]. MedCalc Software, Mariakerke, Belgium.

Warren DW, Walker JC, Drake AF, Lutz RW. 1994. Effects of odorants and irritants on respiratory behavior. Laryngoscope. 104:623–626.

Wilkinson L. 1990. SYSTAT: the system for statistics. Evanston (IL): SYSTAT, Inc.

Yoshida M. 1984. Correlation analysis of detection threshold data for "standard test" odors. Bull Fac Sci Eng Cho Univ. 27:343–353.

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