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Individual differences in the quantitative and qualitative responses of human subjects to various odors

Robert J.O'Connell[1], David A.Stevens[2], R.Patrick Akers, David M.Coppola and Alan J.Grant

The Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 and [2]Clark University, Worcester, MA 01610, USA

[1]To whom correspondence should be addressed

Abstract. The diastereoisomeric ketone, *cis*-4-(4'-t-butylcyclohexyl)-4-methyl-2-pentanone (pemenone), shares with 5α-androst-16-en-3-one (androstenone) a pronounced urine-sweaty odor. A specific anosmia for this latter compound has been described. We obtained quantitative and qualitative odor reports from selected human subjects who were presented with various concentrations of these two compounds in order to determine if subjects were likely to rate them in a uniform fashion. We also estimated the generality of these results by evaluating different concentrations of a small number of other compounds for which specific anosmias have been described. Several hundred subjects were screened with a moderate concentration of pemenone (375 μM). Of those screened, 38% reported some odor quality and 47% of those chose an urine-like descriptor. A total of 39 subjects were examined in detail, 54% of these were initially classified as anosmic for the intense urine-sweaty odor of pemenone. The subjects produced magnitude estimates and quality reports for controls and various concentrations of eight different compounds. A principal-components factor analysis of the ranked intensity scores resulted in a four-component solution. The responses to pemenone were significantly correlated with the estimates and reports for androstenone. It was also clear that the odor descriptors for both materials were clustered into several distinct categories for those subjects judged to be anosmic for the urinous note. These data suggest that different processes are activated during the detection of these odors and that a specific anosmia results when one of these processes is reduced or absent.

Introduction

Individuals with specific anosmias are generally defined as those who have a good sense of smell but lack the ability to perceive a particular odorant (Amoore, 1967, 1969; Amoore *et al.*, 1968). In addition to the pronounced shift in threshold which characterizes them, anosmics often provide altered quality judgements when presented with liminal concentrations of the compounds for which they are anosmic. For example, our preliminary experiments with a moderately high concentration (4.2 mM) of the diastereoisomeric ketone *cis*-4-(4'-t-butylcyclohexyl)-4-methyl-2-pentanone (pemenone), which has an intense, particularly unpleasant, urine-sweaty type odor for osmic individuals (Ohloff *et al.*, 1983), indicated that anosmics were likely to report fairly weak but generally pleasant odor perceptions for this material. In some of these individuals, the perceived odor was akin to musk or floral type perfumes and in others to green vegetables. This simple observation, that a single compound can elicit multiple intensity and quality reports from different subjects, suggests that the compound may interact with multiple types of perceptual channels which are unequally distributed within the human population (Beets and Theimer, 1970; Beets, 1974).

There are a large number of different constructs which can explain the quantitative and qualitative differences in odor perception observed across individual osmic and anosmic subjects for a particular odorant. Evaluation of individual differences in quality

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perception have been valuable in other sensory systems (e.g. color vision) to target particular physiological mechanisms for investigation. For example, it may be that quality perception arises from the interaction between a single stimulus compound and several different kinds of primary receptor neurons and the subsequent afferent and cognitive processes that they activate. Thus, anosmics may differ from osmics in that they lack, or are deficient in, some subset of these processes (Polak, 1973; Beets, 1974).

In a preliminary attempt to describe the individual differences that occur in the perception of odor quantity and quality we selected subjects who appeared to have different thresholds for pemenone and then asked them to provide intensity estimates and quality reports for a series of concentrations of eight different compounds. In this set of stimuli were pemenone and other compounds for which specific anosmias were expected. Also included were several odorants that elicit quality reports similar to those produced by the compounds for which specific anosmias have been defined. We hoped that there would be some intrinsic order in the odor reports elicited by this stimulus set and that they would provide clues about the underlying mechanisms of odor perception.

Methods

Subjects

A total of 261 (66% women) college students and staff were screened with a moderate concentration of pemenone (375 μM). They were asked to provide a quality report from an open-ended list of 12 odor descriptors and then to rate both odor strength and pleasantness on individual line scales (153 mm). Of those screened, 100 individuals (65% women) reported some odor quality and 47% of these (64% women) chose a urine-like descriptor. The distribution of intensity ratings provided by these 100 individuals was highly skewed to the right. Subjects with ratings in the first three quartiles of the distribution provided relatively small rankings for the intensity of pemenone (7.6 $\pm$ 7.1 mm; mean $\pm$ 1 SD). Those in the upper quartile (72.6 $\pm$ 27.62 mm) were considered to be osmic for pemenone (64% women). Two groups were formed from this pool of subjects. One included all 25 of the defined osmics and the second (n = 25) was formed from the lower three quartiles of the pool by random assignment constrained by requirements to preserve the sex ratio and average intensity ratings in the selected group relative to the larger pool. A total of 39 paid subjects (69% female) from the selected groups volunteered to be examined in detail; 46% of these (67% women) were initially classified as osmic for the intense urine-sweaty odor of pemenone because of the elevated intensity (73.4 $\pm$ 27.5 mm) and unpleasantness rankings they provided. The remaining 54% of the individuals tested (71% women) provided relatively smaller rankings (4.7 $\pm$ 5.4 mm) for the intensity of the pemenone screen.

Stimuli

A binary dilution series (9 – 15 steps) was prepared in mineral oil for each stimulus. A five-step concentration series for each odorant spanning ~1.5 log units of concentration was selected and matched for intensity by another panel (12 subjects). Stimuli and the concentration range tested (in mM) were: androstenone (0.021 – 1.4), ammonium

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Table I. List of odor descriptors available to the subjects

Almond	Floral	Rancid
Ammonia	Fruity	Smokey
Beer	Garlic	Sulfurous
Bleach	Herbal	Sweaty
Camphor	Minty	Urinous
Fecal	Musk	Vegetable
Fishy	Other	Woody

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hydroxide (0.488 – 31.25), isovaleric acid (0.031 – 1.9), pemenone (0.098 – 6.25), pentadecalactone (1.9 – 125), pepper pyrazine (0.2 – 12.5), phenyl ethyl alcohol (0.122 – 7.8) and pyridine (0.488 – 31.25). The stimuli were presented on cotton swabs, each holding 150 μl, stored in a sterile, single use tube (Falcon Swube no. 2078). A blank tube containing only mineral oil was presented in each concentration series. Within any one concentration series the order of stimulus presentation was randomized and the schedules for individual subjects were arranged so that all possible orders of concentration were employed across the sample. The order of odor presentation was randomized for individual subjects except that pemenone was always the last odor examined. This latter constraint was imposed because an elevated drop-out rate among subjects osmic for pemenone was seen in preliminary experiments when this unpleasant odor was presented early in a test series.

Procedure

Each subject received instruction in magnitude estimation and practiced by lifting and rating a calibrated set of weights (50, 100, 200, 400 g). Then, a selected stimulus swab was sniffed and a magnitude estimate of its odor intensity was produced using the 200-g weight as a modulus with a defined magnitude of 10. An open-ended list of odor descriptors (Table I) was provided to suggest labels for the quality judgements. Both magnitude and quality judgements were obtained for each stimulus swab. The subjects proceeded through the stimulus set at their own sampling rate except for an imposed minimum inter-trial interval of 30 s. There is a tendency for cross-modal magnitude estimates generated in this fashion to underestimate the differences between individuals or groups (Marks *et al.*, 1988). Thus, it is a conservative method for detecting individual differences in odor perception.

Data analysis

Each subjects' magnitude estimates for the two highest concentrations of a particular substance were summed. These values were then ranked across the eight odorants. This ordinal transformation controls for variation between subjects in the absolute magnitude of their quantitative estimates. Normalization by weighted linear transformation was deemed inappropriate because the data suggested that there were individual differences which were likely due to sensory factors as well as cognitive ones. The resulting ranked-data matrix was examined with a prinicipal-component factor analysis (BMDP-4M). The analysis included varimax rotation, Kaiser's normalization and accepted all factors in the solution with eigenvalues > 1.0 (Bieber and Smith, 1986).

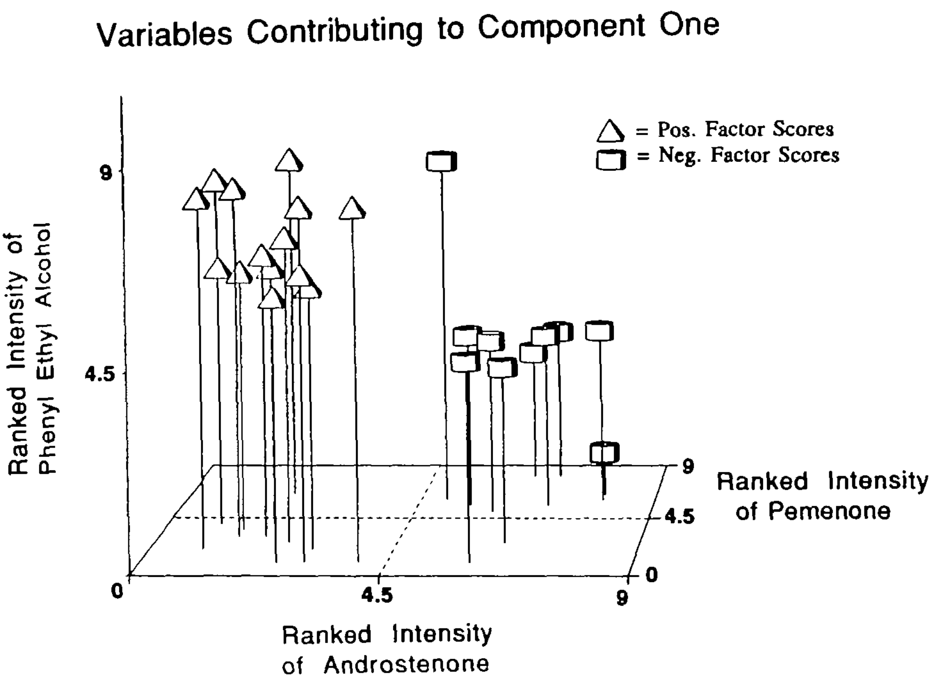

Fig. 1. A plot of individual subjects' ranked estimates of odor intensity for those odors contributing to the first principal component of the factor analysis. Pyramids indicate subjects with large positive factor scores; cylinders indicate subjects with large negative factor scores. For illustrative purposes, the scale of each axis has been drawn to include the ranks of 0 and 9.

Results and discussion

The principal-component factor analysis identified four orthogonal principal components which collectively accounted for 78% of the total variance in the data. The interpretation of these factors typically involves consideration of only those variables with 'large' loadings on a factor even though all of the variables, including those with small loadings, contribute to the solution (Bieber and Smith, 1986). Here we will consider only those variables whose shared variance with the factor is larger than one-third. The shared variance for each variable is computed by squaring the factor loadings in the matrix. For each of the factors in this solution, one or more odorants had rotated factor loadings equal to or larger than the minimum value of $|0.57|$. Thus, pemenone, androstenone and phenyl ethyl alcohol had large loadings on factor 1; isovaleric acid and ammonia were loaded on factor 2; pemenone and pepper pyrazine on factor 3 and pentadecalactone loaded on factor 4.

The ranked intensity scores elicited by each of the odorants with large factor loadings on a particular factor are plotted in Figures 1–4 for each of the subjects who had factor scores $\geq |0.57|$. This loading is just large enough to ensure that all of the subjects load on at least one variable. As before, large individual factor scores indicate those factors which account for a relatively large amount of the subject's variance. With this

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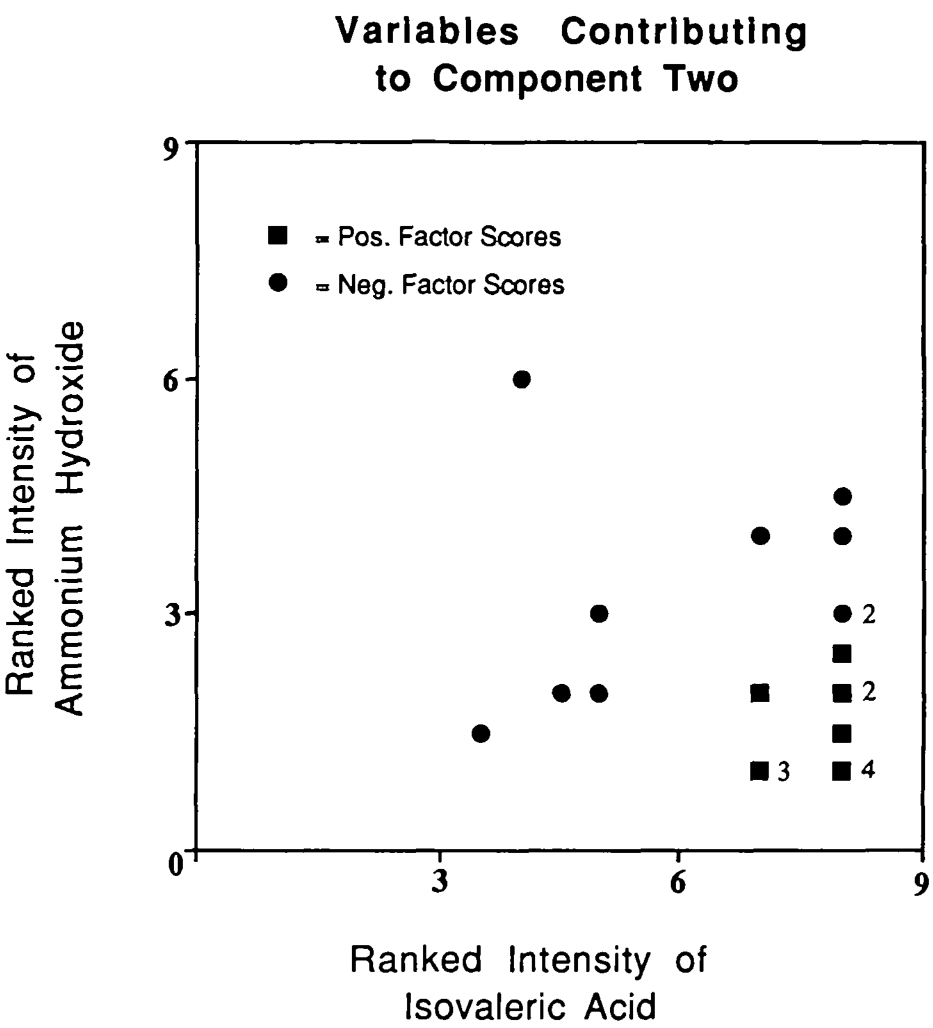

Fig. 2. A plot of individual subjects' ranked estimates of odor intensity for those odors contributing to the second principal component of the factor analysis. The number of subjects with the same rankings are indicated at the appropriate locations on the plot. Filled squares = subjects with positive factor scores; filled circles = subjects with negative factor scores.

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selection criterion most subjects contributed to more than one factor. Five subjects contributed to all four factors, nine contributed to three, 19 contributed to two and only six contributed to a single factor. Subjects with positive factor scores are distinguished from those with negative factor scores in each of the Figures.

The first component (Figure 1) accounted for 29% of the variance in the data set and includes the intensity rankings of three odorants. These are described by a positive relationship between the sensitivities to pemenone and androstenone, and a simultaneous negative relationship with the sensitivity to phenyl ethyl alcohol. It is clear from Figure 1

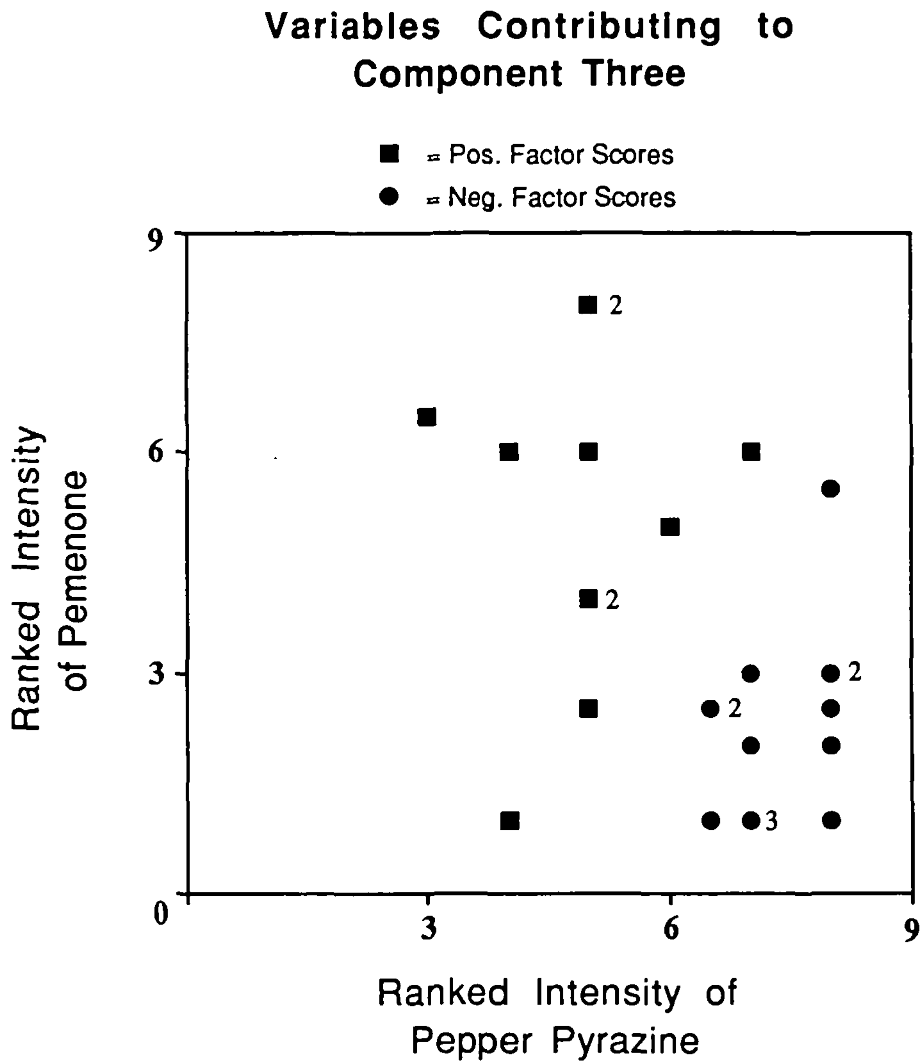

Fig. 3. A plot of individiual subjects' ranked estimates of odor intensity for those odors contributing to the third principal component of the factor analysis. Symbols as in Figure 2.

that most of the subjects with positive factor scores are characterized by relatively lower sensitivity to both pemenone and androstenone than to phenyl ethyl alcohol. In contrast, most of the subjects with negative factor scores for the first component are characterized by relatively higher sensitivity to both pemenone and androstenone than to phenyl ethyl alcohol.

The second component (Figure 2) accounted for an additional 19% of the variance and includes the intensity rankings of two additional odorants. This factor is described in general by a negative relationship between the sensitivity to isovaleric acid and ammonia hydroxide. Those subjects with large positive factor scores clustered tightly

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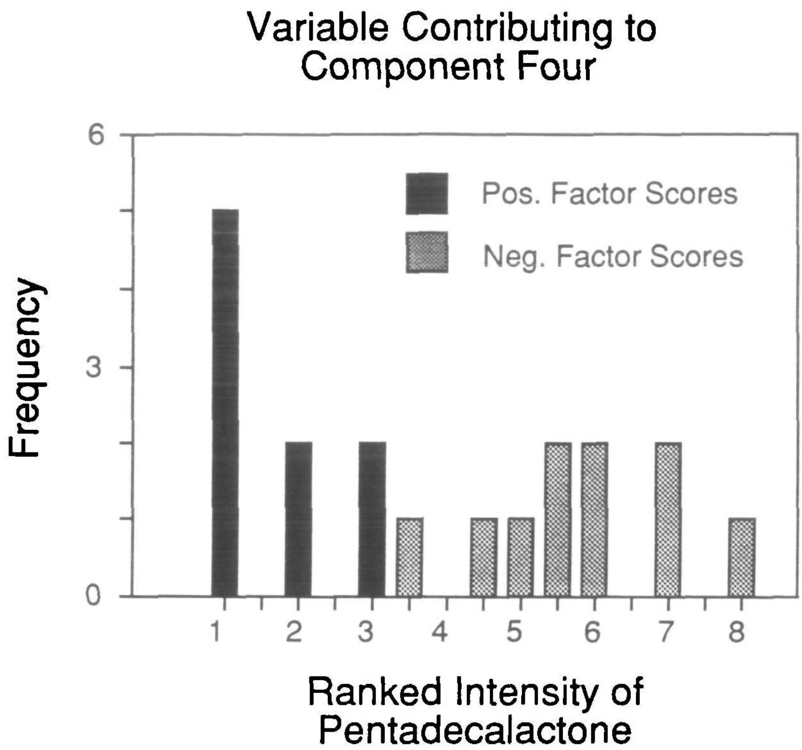

Fig. 4. A plot of the frequency distribution of individual subjects' ranked estimates of odor intensity for the odor which contributes to the fourth principal component of the factor analysis.

in the lower right corner of the plot shown in Figure 2. Those with large negative factor scores were more variable.

The third component (Figure 3) accounted for an additional 16% of the variance in the data set and includes the intensity rankings of pemenone and pepper pyrazine. This factor is described in general by a negative relationship between the sensitivities to these two compounds. There was less variance in sensitivity to those stimuli among the subjects with negative factor scores than for those with positive ones. The intensity rankings produced in response to pemenone contribute to both components 1 and 3. Fifteen of the 34 individual subjects appearing in the two components contributed to both factors. Of these, six subjects had large loadings on only these two components.

The fourth component (Figure 4) accounted for an additional 14% of the variance and describes a range of sensitivities to pentadecalactone. Subjects with large positive factor scores produced low intensity ratings, whereas those with large negative factor scores produced intermediate to high intensity ratings for pentadecalactone.

Since the approach and solution presented here for the magnitude estimates is only one of many, we next sought to obtain an independent verification of the groupings generated by the principal component analysis. Thus, we examined the quality reports generated by the subjects contributing to each of the components. Because the odor-quality descriptor list was open ended it was common for subjects to use alternative

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Table II. Intensity and quality judgements reported by subjects contributing to factor 1

Odorant	Subjects with positive factor scores			Subjects with negative factor scores		
	Intensity	Quality	% reporting	Intensity	Quality	% reporting
Androstenone	low	urine	14	high	urine	90
Pemenone	low	urine	43	high	urine	70
Phenyl ethyl alcohol	high	floral	79	low	floral	50

The frequency of subjects giving appropriate quality descriptors for each odorant is significantly different between subjects ($n = 14$) who provide high intensity ratings and those ($n = 10$) who provide low intensity ratings ($\chi^2 > 14.8$; $P < 0.001$).

quality labels for the different odors they examined (Beets and Theimer, 1970). A set of semantic equivalents was produced by subsuming within a single descriptor (e.g. urine) all of the alternative names that were used to describe a particular target quality by 25%, or more, of the ASTM panel who compiled the *Atlas of Odor Character Profiles* (Dravnieks, 1985). By this criterion, labels judged equivalent to urine were: sweaty, putrid, ammonia and sewer. The quality reports produced by the subjects with large factor loadings on component 1 (Figure 1) were tabulated for the three odors and compared to the intensity judgements produced by the same three odorants (Table II). There is substantial agreement among these subjects as to the predominant odor quality elicited by a compound and its relative intensity. That is, subjects who appear to be osmic for pemenone, because they provide relatively high rankings for its intensity, are also likely to describe its odor quality as urinous. In a like manner, the subjects who appear to be anosmic for pemenone, because they provide relatively low rankings for its intensity, are unlikely to describe its odour quality as urinous. The number of subjects using appropriate quality descriptors, for each of the odorants that contributed to this factor, was significantly different when those providing high intensity ratings were compared to those providing low intensity ratings ($\chi^2 > 14.8$; $P < 0.001$). Similar trends relating the relative magnitude estimates for the odors contributing to a particular factor with the constellation of odor quality reports produced by the subjects with large loadings on that factor were obtained for factors 2–4, but they failed to achieve statistical significance.

Collectively, these data suggest that there is an intrinsic order in the odor quantity and quality reports elicited by these stimuli within this sample of observers. The groupings obtained in the principal component solution suggests that several different sensory or cognitive processes may be activated during the detection and identification of these odors. They also suggest that an apparent anosmia to one odorant (e.g. pemenone) may be coupled to alterations in sensitivity to odorants in the same odor class (androstenone) or to odorants (e.g. phenyl ethyl alcohol and pepper pyrazine) in other quality classes. This suggests that a specific anosmia may result when one or more of the normal processes are reduced or absent. The exact nature of these processes remains undefined.

A common assumption made in the consideration of such data is to postulate the existence of a class of specific 'lock and key' binding sites, one for each odorant, which are distributed in some fashion among individual olfactory receptor neurons (Amoore, 1969; Mason and Morton, 1984). A specific anosmia then merely reflects the absence

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of the binding site class for that particular odor or alternatively a considerable reduction in the number or specificity of its binding sites. In support of this notion is biochemical evidence for the existence of specific binding sites for androstenone in the olfactory mucosa of pigs (Gennings *et al.*, 1977) and sheep (Persaud *et al.*, 1988). There is also psychophysical evidence which demonstrates that an individual's threshold for androstenone has a significant genetic component (Wysocki and Beauchamp, 1984). However, it should also be clear that an anosmia may be evidenced in individuals with normal binding sites and olfactory receptor neurons if they have the appropriate disruptions in sensory or cognitive processing.

The strong association shown here between the subjective reports elicited by pemenone and androstenone indicate that both compounds seem to interact with the same perceptual process, as has been suggested earlier by Beets (1974). The various groupings of stimuli revealed by the principal component factor analysis are also consistent with Polak's multiple profile model of olfaction (Polak, 1973). Here, individual odor molecules are thought to have 'numerous mutually independent or overlapping odor active molecular profiles' which are 'able to interact physically and reversibly with a corresponding receptor site'. In this construct, individual odorant molecules may bind with a variety of different binding sites whose collective effect results in one or more odor quality perceptions. The fact that a single compound like androstenone may elicit widely different quantity and quality reports among individual observers suggests that multiple molecular interactions may well occur (Griffiths and Patterson, 1970). A specific anosmia may result if one or more of these receptor sites is reduced or absent. Similar concepts have been proposed by Beets (1974). The data presented here may be consistent with this hypothesis if individual odors like pemenone and androstenone elicit responses in those judged to be anosmic for their principal odor quality, which fall into a small number of alternate quantity and quality classes. We observed that subjects with positive factor scores on component 1 (Figure 1) described the odors of androstenone and pemenone with labels that could be characterized as floral (40%), urine-sweaty (32%), green vegetables (21%) or other odor qualities (7%). The number of secondary odor qualities elicited by a particular compound, their individual variations among subjects and how they arise are topics for further study.

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