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SENSORY DETECTION OF VOCs SINGLY AND IN MIXTURES: ODOR AND SENSORY IRRITATION

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ABSTRACT

To increase our understanding of the olfactory and trigeminal (i.e., sensory irritation) impact of chemical mixtures we have studied the binary mixture butyl acetate/toluene. First, we measured complete concentration-response (i.e., psychometric) functions for the odor, nasal pungency, and eye irritation detectability of the single chemicals. Second, we selected fixed detectability levels between chance ($p=0.0$) and perfect ($p=1.0$) detection (e.g., $p=0.6$). Finally, we compared the detection of the single chemicals at the concentration producing these selected levels with the detection of binary mixtures at proportions that, if a rule of dose additivity were to hold, should be as detectable as the single chemicals. The outcome revealed that the degree of dose additivity is larger for the irritation modalities than for the odor modality.

INDEX TERMS

Odor, Nasal Pungency, Eye Irritation, VOC Mixtures, Psychometric Functions.

INTRODUCTION

Among the most often cited complaints expressed by occupants of spaces with poor indoor air quality we find sensory irritation of eyes, nose, and throat (Apter et al., 1994; Cometto-Muñiz and Cain, 1992). Volatile organic compounds (VOCs) constitute the principal culprits for the appearance of these irritative symptoms (Kostiainen, 1995; Rothweiler and Schlatter, 1993). The scarce understanding of the physicochemical basis for any given VOC to be a potent or weak odorant and/or irritant hampers the interpretation of chemical measurements in indoor environments in terms of actual sensory impact. Over the last decade, systematic studies of chemosensory thresholds for individual members of homologous and other structurally-related chemical series (Cometto-Muñiz, 2001), in combination with a solvation model (Abraham, 1993a, b), have allowed development of quantitative structure-activity relationships (QSARs) that account for the nasal pungency (i.e., irritation) (Abraham et al., 1998a), eye irritation (Abraham et al., 1998b), and odor (Abraham et al., 2001) potency of VOCs. One crucial aspect that remains to be investigated further relates to the sensory impact of chemical mixtures. In particular, the rules of sensory agonism or antagonism among the chemical components of the mixtures that determine detection need to be understood better. Since environmental exposures almost invariably involve many chemicals, the issue is of considerable practical significance.

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Much of the work on chemosensory responses to mixtures has focused on olfaction, and on the suprathreshold range (e.g., Berglund and Olsson, 1993) or on odor identification of the components within mixtures (e.g., Jinks and Laing, 2001). Fewer studies have focused on perithreshold levels, and most of them have dealt only with olfaction (e.g., Laska and Hudson, 1991; Patterson et al., 1993). The development of techniques to separate olfactory from trigeminal (i.e., sensory irritation) input (Cometto-Muñiz and Cain, 1998) has provided the tools to study the latter responses, at threshold levels, in bias-controlled experiments involving both single chemicals and mixtures. An investigation of the detection of odor, nasal pungency, and eye irritation from mixtures of up to nine components found various degrees of sensory agonism which increased with number of components and lipophilicity of the components (Cometto-Muñiz et al., 1997). The present study continues the work with mixtures but includes two additional features: 1) measurement of complete concentration-response (i.e., psychometric or detectability) functions for each chemical (Cometto-Muñiz et al., 1999) and 2) an experimental design allowing an analysis of chemosensory agonism along various peri-threshold levels of sensory detectability, i.e., from slightly above chance detection to slightly below perfect detection (Cometto-Muñiz et al., 2001).

MATERIALS AND METHODS

Stimuli. Butyl acetate (99+%) and toluene (99.8%) served as stimuli, and mineral oil (light, Food Chemical Codex quality) served as solvent and blank. The chemicals were prepared, stored, and delivered from 1,900 ml glass vessels containing 200 ml of solution and adapted with nosepieces (Cometto-Muñiz et al., 2000) or eyepieces (Cometto-Muñiz et al., 2001). For single chemicals, the different concentrations were achieved by serial dilution of the neat compound. For the binary mixtures in various proportions, concentration of the components were chosen based on the detectability of the individual constituents in a way that, if a rule of dose additivity were to hold, the mixtures should be nearly as detectable as a reference concentration of each of the single chemicals. In all cases, concentrations of the stimuli were measured in the vapor headspace of each glass vessel (i.e., above the liquid solution) by gas chromatography (GC) with a flame ionization detector. GC measurements were typically done weekly to confirm stability.

Subjects. For experiments on odor and eye irritation detection, only data from subjects with a normal sense of smell (i.e., normosmics) (Cain, 1989) are included here. For odor, depending on the experiment, we tested a group of 10 to 20 normosmics, about half of them females, ranging from 18 to 56 years of age. For eye irritation, depending on the experiment, we tested a group of 7 to 12 normosmics, about half of them females, ranging from 19 to 51 years of age. For experiments on nasal pungency detection, we tested a group of 5 to 6 anosmics (i.e., subjects with no sense of smell), about half of them females, ranging from 36 to 74 years of age.

Procedure. We employed either a two- or a three-alternative forced-choice procedure (2AFC or 3AFC) against blanks (i.e., mineral oil) to build the detectability function for each chemical and sensory response, and to compare the detectability of the mixtures vis-à-vis that of the single chemicals.

Data analysis. Plots of detection probability as a function of either stimulus concentration (in ppm by volume) or stimulus composition (proportion of each component in a mixture) summarize the outcomes. Detection probability was corrected for chance (Macmillan and Creelman, 1991) and ranges from 0.0, that is, chance detection, to 1.0, that is, perfect

detection. Analyses of variance (ANOVAs) were performed on the results of the experiments directly comparing detectability of single chemicals and mixtures within the same subjects.

RESULTS

1) Detectability of the Single Chemicals

Figure 1 shows the detectability (i.e., psychometric) functions for the odor, eye irritation, and nasal pungency evoked by butyl acetate and toluene presented singly. The functions showed the typical ogival shape with a close-to-linear relationship in the middle of the range (shown here). Consistent with previous work, the following features are evident: 1) odor functions lie at concentrations orders of magnitude lower than sensory irritation functions and depict slopes less steep than those for sensory irritation (cf. Cometto-Muñiz et al., 1999); 2) odor functions for butyl acetate and toluene show similar slopes (around 0.13) but sensory irritation functions for butyl acetate are about three times less steep than those for toluene (0.48 vs. 1.63 for the eye, and 1.04 vs. 2.84 for the nose) (cf. Cometto-Muñiz et al., 2002).

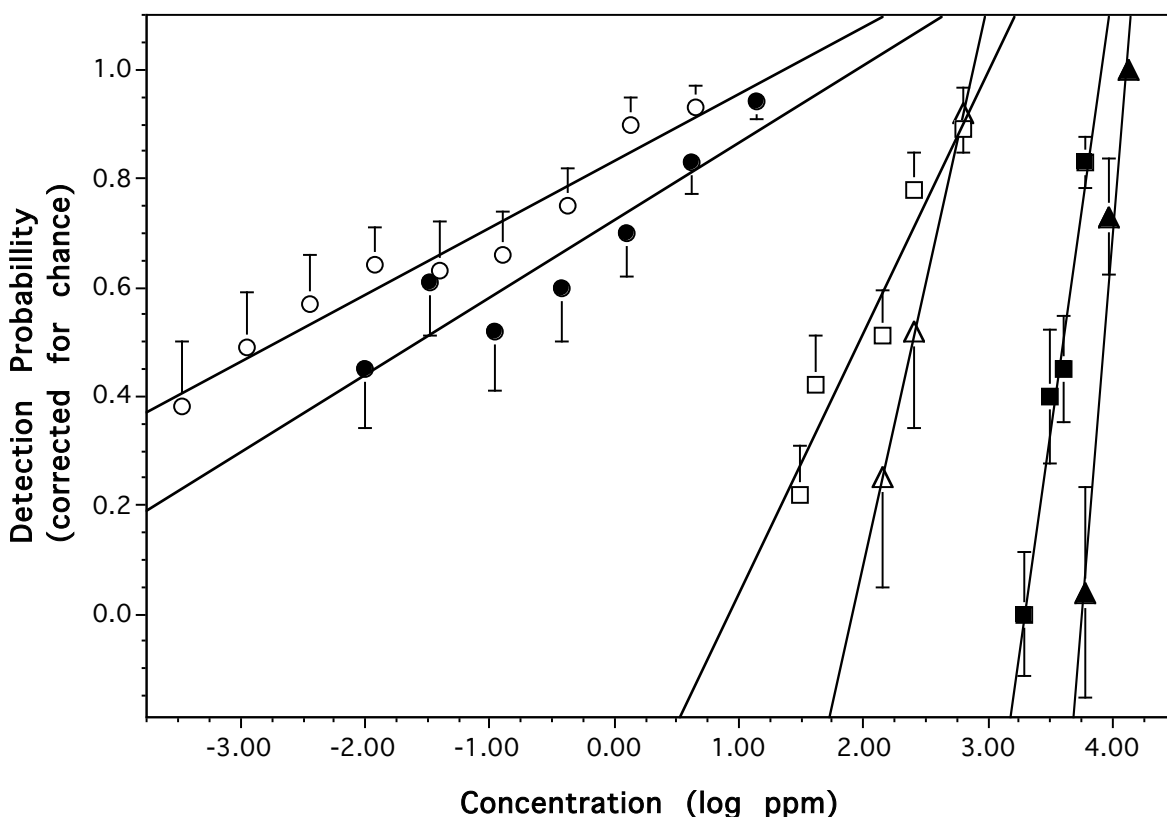


Figure 1. Detectability functions for the odor (circles), eye irritation (squares), and nasal pungency (triangles) of butyl acetate (empty symbols) and toluene (filled symbols), presented singly. Bars indicate standard errors.

2) Detectability of the Binary Mixtures

Once the detectability function for each individual chemical and sensory endpoint was obtained, this information was used to create, for each sensory endpoint, various sets of five stimuli. Each set comprised two stimuli that were actually single chemicals (one butyl acetate and the other toluene) and three stimuli that were mixtures of the two chemicals in the proportions 3/4 butyl acetate + 1/4 toluene, 1/2 butyl acetate + 1/2 toluene, and 1/4 butyl acetate + 3/4 toluene. The concentrations within each set of five stimuli were calculated from

the functions shown in Figure 1 in such a way that, if a rule of complete dose additivity were to hold, all five stimuli on the set would be roughly comparably detectable for that particular sensory endpoint. It should be mentioned that the five stimuli in a set are tested within the same experiment and in the same group of subjects.

Figure 2 depicts the detectability in terms of odor, eye irritation, and nasal pungency for two such sets of five stimuli: On the upper row the detectability of the single chemicals (stimuli 1 and 5) across the three modalities ranges between 0.6 and 0.9; on the lower row, it ranges between 0.55 and 0.65. The loss in detectability of the mixtures, indicating departure from dose additivity, is more pronounced for odor than for irritation, particularly when odor is compared with nasal pungency. Eye irritation follows rules of additivity (or agonism) between those for odor and nasal pungency.

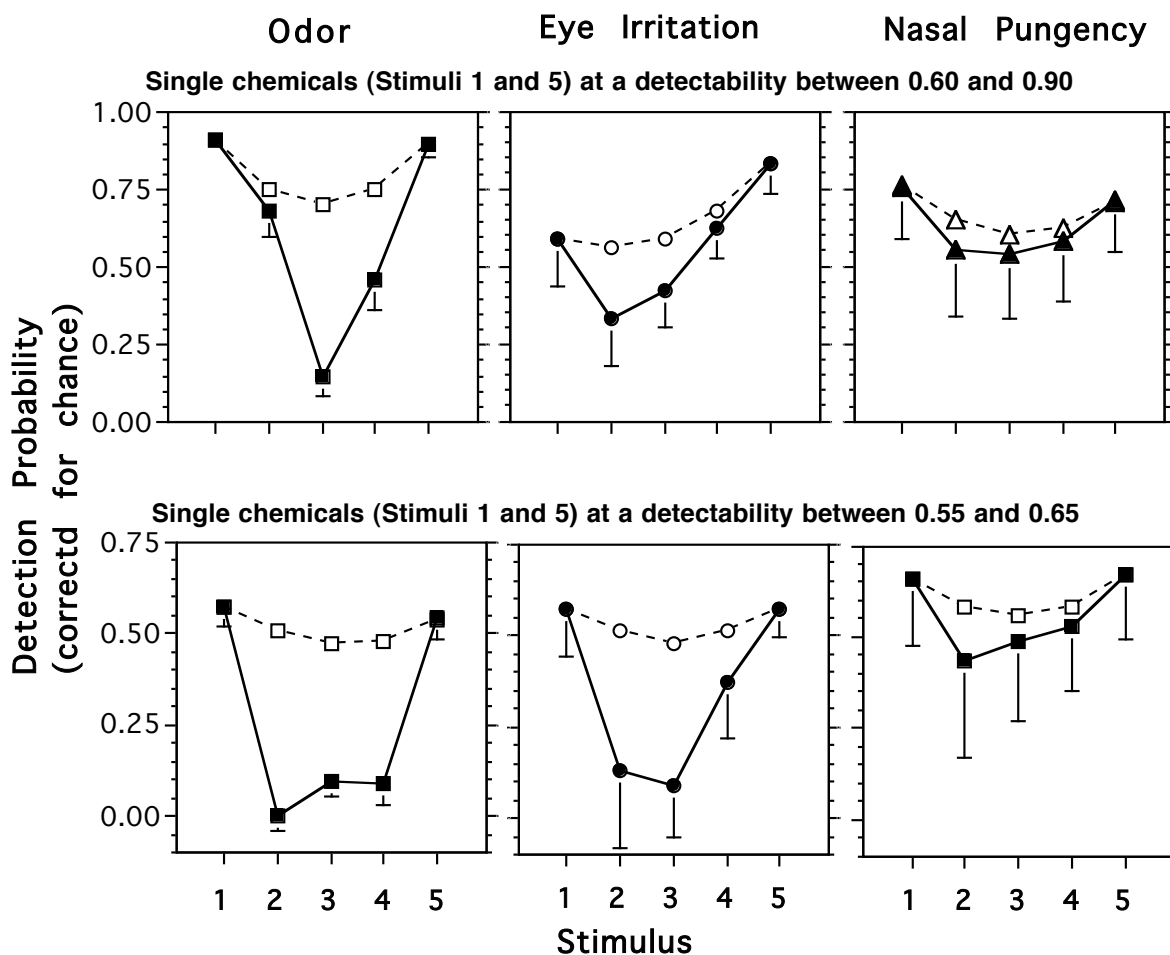


Figure 2. Upper row. Detectability of odor, eye irritation, and nasal pungency for sets of five stimuli where stimuli 1 and 5 consist of the single chemicals butyl acetate and toluene, respectively, and stimuli 2, 3, and 4 consist of their binary mixture in the proportions 3/4-1/4, 1/2-1/2, and 1/4-3/4, respectively. If dose additivity were to hold perfectly, detectability of all stimuli would fall along the dotted line. Detectability of the single chemicals across the three modalities brackets the range 0.60 - 0.90. Lower row. Same as above but, here, detectability of the single chemicals across the three modalities brackets a lower range 0.55 - 0.65. In both rows, bars indicate standard errors.

DISCUSSION

The present results indicate that trigeminal chemosensory responses (i.e., nasal pungency and eye irritation) depict a higher degree of agonism, in the sense of dose additivity, than olfactory responses (i.e., odor). This outcome agrees with the trend seen for more complex mixtures of up to nine components (Cometto-Muñiz et al., 1997), but where the sensory endpoint measured did not include complete psychometric functions due to the high number of chemicals tested. A recent study of another binary mixture: 1-butanol and 2-heptanone had also relied on complete psychometric functions and found support, as a first approximation, to the notion of dose additivity for trigeminal and olfactory responses (Cometto-Muñiz et al., 1999). Nevertheless, that study analyzed the outcome in terms of overall detection trends from chance to perfect detection and had not focused, like this study, on a detailed testing of dose additivity at fixed levels of detectability (e.g., $p=0.60$). We cannot rule out the possibility that the greater difference in chemical structure between the present pair of chemicals, compared to the previous one, had played a role in the lower agonism observed here. A long range goal of our studies is, precisely, to begin to clarify how structural and physicochemical similarities/dissimilarities influence sensory agonism among chemicals (Cometto-Muñiz et al., 2001).

CONCLUSION AND IMPLICATIONS

The degree of sensory agonism, in the sense of dose additivity, within chemical mixtures of butyl acetate and toluene, presented at perithreshold levels, tends to be higher for responses involving irritation (of nose and eyes) than for those involving odor. Further experiments with these compounds at lower levels of detectability (e.g., 0.40 or 0.20) should determine if detectability level plays a systematic role in degree of dose additivity observed for odor as seems to be the case for irritation (Cometto-Muñiz et al., 2001). Ultimately, the generality of these results beyond the particular VOCs selected needs to be established. One important step towards that goal is to determine whether the use of physicochemical descriptors proven useful to describe and predict the sensory impact of single VOCs (Abraham et al., 2001; Abraham et al., 1998a, b) hold clues to describe and predict the impact of mixtures of VOCs.

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