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SENSORY DETECTION OF VOCs SINGLY AND IN BINARY MIXTURE VIA ODOR, NASAL PUNGENCY, AND EYE IRRITATION

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ABSTRACT

Using 1-butanol and 2-heptanone, representatives of VOCs found in indoor air, we investigated the rules for sensory detection of binary mixtures relative to the detection of the single components. Stimuli were measured via gas chromatography, and sensory responses via a two-alternative forced-choice procedure, with presentation of ascending concentrations. Results for individual chemicals and mixtures were expressed as stimulus-response detectability functions (i.e., psychometric functions). The rate of increase of detectability was similar for butanol and heptanone and was larger for the trigeminal responses (nasal pungency and eye irritation) than for the olfactory response (odor). For all three sensory endpoints, the mixtures became more detectable with increasing amounts of the components mixed. The increase followed a model of agonism whereby introduction of a second component can be seen as introduction of more of the first component. Further work will address the roles of number and chemical identity of components in the sensory detection of mixtures.

INTRODUCTION

One of the most common adverse responses produced in situations of indoor air quality problems is that of unwanted sensory reactions, in particular irritation of nose, eyes, and throat, but also odor [1-3]. In addition, these sensory responses can be evoked, quantified, and studied in the laboratory using human subjects [4]. Due to their scientific accessibility and relevance to indoor air issues, sensory irritation and odor constitute important topics of study.

Odor and nasal pungency (i.e., piquancy, tingling, irritation, burning, freshness, prickling, stinging, and the like) result from the activation of the olfactory nerve (cranial nerve I) and the trigeminal nerve (cranial nerve V), respectively. Since virtually all chemical stimuli that evoke an odor can also, at high enough concentration, evoke pungency, it is difficult to study one sensory channel devoid of the influence of the other. To achieve such functional separation we have resorted to study nasal detection of volatile organic compounds (VOCs) in participants lacking olfaction (anosmics) for whom odors would not interfere [5]. More recently, we have also included the alternative of measuring nasal localization (i.e., lateralization) thresholds that, even in subjects with normal olfaction (normosmics), rest on trigeminal nerve activation [6]. To facilitate the search for the physicochemical basis of odor and pungency potency of VOCs we have studied families of related compounds, typically homologous chemical series [7, 8], but also other groups of structurally-related substances [9]. Using a quantitative structure-activity relationship (QSAR) based on a solvation model [10, 11] we have successfully described and predicted nasal pungency [8, 12, 13] and eye irritation

thresholds [14]. Odor thresholds have proven more difficult to model though the solvation approach has done no worse than any other model [15].

In indoor environments, occupants are exposed to dozens, perhaps hundreds, of VOCs. The study of sensory responses to chemical mixtures carries, then, particular significance. In the present investigation we have looked in detail at one example of the simplest mixture case, the binary one, in an attempt to begin to unveil the rules governing the sensory impact of mixtures. The compounds employed were 1-butanol and 2-heptanone — representatives of compounds found in indoor air — and the sensory responses explored included odor, nasal pungency and eye irritation. In our previous studies we had measured sensory thresholds according to a fixed criterion of performance. Here we have measured stimulus-response detectability (i.e., psychometric) functions covering the range from chance detection to virtually perfect detection.

METHODS

Stimuli. The chemicals 1-butanol (99.8% purity) and 2-heptanone (98% purity) served as stimuli; mineral oil (light, Food Chemical Codex quality) served as solvent and sensory blanks. To measure detectability functions for the single substances we prepared two-fold dilution series starting with the undiluted chemical (100% v/v, dilution step 0). This produced solutions of 50, 25, 12.5, 6.25, etc. % v/v, labeled dilution steps 1, 2, 3, 4, etc., respectively. Once the detectability functions were experimentally measured for each chemical and sensory endpoint, we interpolated the four concentrations of butanol and the four of heptanone that produced detection probabilities (corrected for chance) of 0.2, 0.4, 0.6, and 0.8 on a scale where 0.0 equals chance detection and 1.0 equals perfect detection. The two sets of four concentrations were combined to create a matrix of 16 (4 X 4) binary mixtures. These 16 binary mixtures, along with five concentrations of butanol alone and five of heptanone alone (those producing detection probabilities of 0.0, 0.2, 0.4, 0.6, and 0.8) were all tested for detection within the same experiment and using the same subjects. (Inclusion of the single stimuli among the mixtures within the same experiment aimed at increasing their relative comparability, and so did the testing of the same subjects).

Stimuli were presented from 270-ml high density polyethylene (HDPE) squeeze bottles [16]. The vapor-phase concentration in the headspace of every bottle was measured by gas chromatography (flame ionization detection) via a gas sampling valve (1 ml sampling loop). The bottles were checked periodically to assure stability of single and mixed stimuli. Vapor concentrations in all bottles were calibrated with reference to the concentration of vapor saturation at room temperature (23°C) for each chemical (that is, the vapor concentration of the bottle containing the undiluted chemical).

Subjects. A group of 4 anosmics provided data on nasal pungency and eye irritation detection. They included one male, 59 years old, and three females, 28, 32, and 40 years old. The 32 year-old female became unavailable after being tested with the single chemicals and was replaced by a 43 year-old anosmic female. All these participants were congenital anosmics. A group of 4 normosmics provided data on odor and eye irritation detection. They included one male, 54 years old, and three females, 24, 28, and 37 years old. All subjects were screened before participation for anosmic or normosmic status via a standardized olfactory test [16].

Procedure. The first part of the study entailed measurement of detectability functions for odor, nasal pungency and eye irritation from the single substances. A two-alternative, force-choice

procedure, with presentation of ascending concentrations, served to measure such functions. In the second part of the study, based on the data for the single compounds, we prepared a series of 16 binary mixtures, as described under "Stimuli", where the components varied systematically in their individual detectabilities. Then, the detectability of the mixtures and of the single compounds was tested within the same experiment and employing the same subjects, again using a two-alternative, force-choice procedure.

Data analysis. The outcome was summarized in plots of detection probability (ranging from 0.0, i.e., chance detection, to 1.0, i.e., perfect detection) as a function of concentration (in ppm by volume). Statistical comparison of detectability functions for single chemicals and for the mixtures was performed by analysis of variance (ANOVA) with reported p values corrected (Huynh-Feldt correction).

RESULTS

Figure 1 shows the detectability functions for odor, nasal pungency and eye irritation of each single chemical. Eye irritation detectability did not differ between anosmics and normosmics so the combined data from the two groups is presented in Figure 1. All detectability functions have a sigmoidal shape with an approximately linear portion in the middle of the range of detection probabilities, approximately between 0.20 and 0.95. For both substances, odor functions lay at concentrations about three orders of magnitude lower than nasal pungency and eye irritation functions. Both trigeminal functions fell into register for each chemical, particularly in the case of 1-butanol. Along their linear range, both odor functions have a slope of 0.5 whereas the trigeminal functions have higher slopes, between 0.7 and 0.8.

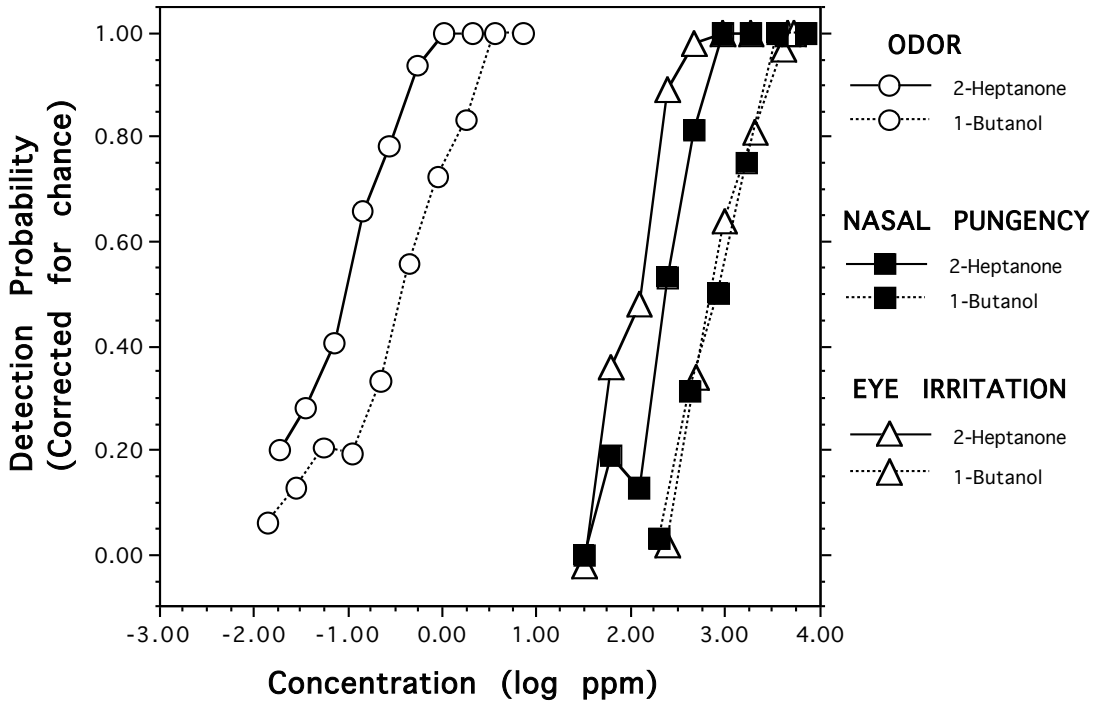

Figure 1. Detectability of the odor, nasal pungency, and eye irritation of 2-heptanone and 1-butanol as a function of vapor-phase concentration. For odor and nasal pungency, each point represents the average of 64 trials from 4 subjects. For eye irritation, each point represents the average of 128 trials made by 8 subjects.

As described under "Methods", the detectability functions measured for the single chemicals in the first part of the study were used to prepare the specific 16 binary mixtures for each sensory endpoint. These mixtures were tested interspersed with stimuli comprising only butanol and only heptanone. Thus, in this second part of the study, mixed and single stimuli where tested together within the same experiment for each sensory endpoint. Figure 2 shows detectability functions for odor, nasal pungency, and eye irritation of mixed and selected single stimuli. All plots are presented as a function of concentration of heptanone (*x* axis) with the five levels of butanol (including 0) as the parameter. (The outcome is similar if plotted as a function of concentration of butanol with heptanone as the parameter.) An ANOVA performed on the odor data of Figure 2 revealed significant effects for the factors heptanone ($F[3,9]=5.96$, $p<0.05$) and butanol ($F[4,12]=5.17$, $p<0.05$) concentrations but not for their interaction. An ANOVA performed on the nasal pungency data of Figure 2 also revealed significant effects for the factors heptanone ($F[3,15]=8.92$, $p<0.005$) and butanol ($F[4,20]=21.34$, $p=0.0001$) concentrations but not for their interaction. Finally, an ANOVA performed on the eye irritation data of Figure 2 revealed significant effects for the factors heptanone ($F[3,21]=34.38$, $p=0.0001$) and butanol ($F[4,28]=41.51$, $p=0.0001$) concentrations as well as for their interaction ($F[12,84]=3.26$, $p<0.005$).

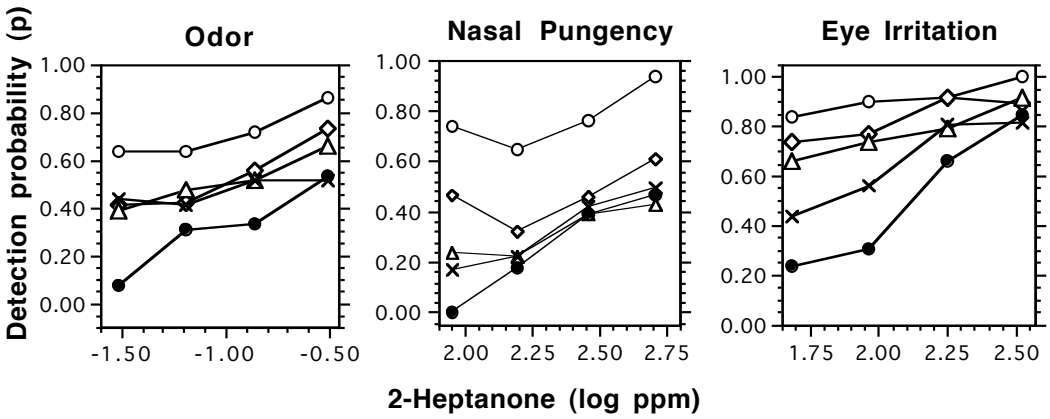

Figure 2. Detectability functions for the odor, nasal pungency, and eye irritation of four concentrations of heptanone alone (filled circles), and mixed with four increasing concentrations of butanol (crosses, triangles, diamonds, and empty circles, respectively, in increasing order).

DISCUSSION

A previous investigation had explored detection of VOCs through these three chemosensory modalities comparing concentration thresholds obtained with single chemicals with those obtained in mixtures containing 3, 6, and 9 components [17]. The study revealed that the degree of agonism seen in the mixtures increased with the number and the lipophilicity of the components, confirming the important role that physicochemical properties play in the determination of chemosensitivity to both single substances and mixtures. The present investigation focuses on an example of the simplest type of mixture, the binary case, but where the two components vary widely and systematically in their relative proportions in the mixture and where the sensory outcome is measured as complete detectability functions, not simply as a single threshold value.

The results clearly show the existence of sensory agonism between 1-butanol and 2-heptanone to produce detection by odor, nasal pungency, and eye irritation. For odor and nasal pungency, visual inspection and statistical analysis of the detectability functions shown in Figure 2 suggest the existence of uniform dose agonism between the two compounds across the detection range. For eye irritation, visual inspection of Figure 2 and the significance of the ANOVA interaction term indicate that the functions tend to converge at high concentrations. This could be seen as a larger degree of agonism for eye irritation at relatively low detectability levels than at higher detectability levels. Additional binary mixtures need to be studied to probe into the generality of the results.

The present study is the beginning of a systematic investigation of the rules of sensory agonism in chemical mixtures. The level of detail in the approach taken: measurement of detectability functions and test of the same components at orderly varying proportions, precludes, for now, the use of mixtures of more than three or four components. We hope that, starting with binary mixtures, we will begin to unravel these rules with a bottom-up approach. Our first goal will be to explore how applicable the present results are in the case of components that differ more radically in chemical structure than butanol and heptanone do. One example could be toluene and butyl acetate. Once we have a sense of the role played by differences in chemical structure (with the underlying differences in physicochemical properties) we will move to another key factor: number of components, addressing the study of ternary and quaternary mixtures. Of course, as the number of components increases, we will need to reduce the number of different proportions in which the same components are presented in order to keep the total number of stimuli manageable. In order to speed-up progress we will apply the solvation equation that has worked so well for individual substances, at least regarding trigeminal responses, to model and predict the sensory impact of both relatively simple and more complex chemical mixtures. Even when it is true that in indoor environments there are dozens, even hundreds, of VOCs, knowledge of their relative sensory impact — referenced to their actual concentration and chemical identity — would allow selection of the, perhaps, 6 to 12 most relevant ones for the solvation model to make predictions about their combined sensory effects.

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