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A Bisensory Method for Odor and Irritation Detection of Formaldehyde and Pyridine

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Abstract A bisensory method was developed for determining the psychometric functions and absolute thresholds for odor and sensory irritation of two odorous irritants. Individual and group thresholds for formaldehyde or pyridine were measured for 31 age-matched subjects (18–35 years old). P_{50} absolute thresholds were for formaldehyde odor 110 ppb (range 23–505), for pyridine odor 77 ppb (range 20–613), and for pyridine irritation 620 ppb (range 90–3,656); too few subjects' formaldehyde irritation thresholds were possible to determine (human exposures limited to 1 ppm). In spite of large interindividual differences, all thresholds for irritation were higher than for odor. The average slopes of the 62 psychometric functions for odor and the 32 possible for sensory irritation were highest for formaldehyde odor (83% per log ppb) and equal for pyridine odor and irritation (68% per log ppb). The bisensory method for measuring odor and sensory irritation jointly produced detection functions and absolute thresholds compatible with those earlier published; however, a steeper slope for sensory irritation than odor was expected for pyridine. The bisensory method is intended for measuring odor and sensory irritation to broadband mixtures and dynamic exposures, like indoor air.

Keywords Bisensory method · Odor thresholds · Sensory irritation thresholds · Psychometric functions · Formaldehyde · Pyridine

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Introduction

In their environmental health criteria document on formaldehyde, the World Health Organization (WHO 1989) decided for the first time to include and review critically odor and sensory irritation[1] as adverse health outcomes (Andersen et al. 1975; Ahlström et al. 1986; Cain et al. 1986), in parallel with symptoms (Baird et al. 1990, 1994; Dalton et al. 1997), toxic effects, and cancerogenic and respiratory diseases. Wolkoff and Nielsen (2010) constitute the most recent review. Potent odorous irritants should be banned, not only in occupational but also in nonindustrial indoor environments. Wolkoff et al.

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[1] The perceptual word *sensory irritation* is used in this text because it translates best to the Swedish word 'sensorisk irritation' used in the present experiments. References cited have sometimes used other concepts in their research, for example 'nasal pungency' but 'eye irritation', 'ocular irritation' and 'skin irritation'. Some have replaced 'nasal pungency' with 'nasal irritation'. The authors prefer 'chemesthesis' or 'trigeminal chemosensory system' (supplementary to 'olfaction') to the much broader term 'somatosensory system', which is frequently used, for example, in pain research.

(2006) present another review involving building materials and household products.

Volatile organic compounds (VOCs) in homes and offices are often a factor of 1,000 below the threshold limit values (TLVs) for industrial environments. Still, sensory irritation symptoms are reported (Cain and Murphy 1980; Noma et al. 1988; Baird et al. 1994; Wysocki et al. 1997; Wolkoff et al. 2006). In overviews of sensory effects from airborne contaminants, Engen (1986) and Cometto-Muñiz and Cain (1991) showed that apart from thresholds (Cometto-Muñiz and Cain 1990; Wysocki et al. 1997), there is a need of knowledge on individual psychometric functions for both odor and sensory irritation (Cain et al. (2005) on ethanol; Cain et al. (2007) on glutaraldehyde; Cain and Schmidt (2009) on n-butyl and t-butyl acetate) and on the effects of time of stimulation (Cain et al. 1987; Dalton et al. 1997). Two odorous irritants, formaldehyde and pyridine, continue to be important to control in nonindustrial indoor environments because of their role in building material emissions (Berglund and Nordin 1992; Wolkoff and Nielsen 2010) and smoking (Ahlström et al. 1987; Cain et al. 2010), respectively.

Research indicates that with increasing concentration and/or time of exposure, olfaction and chemesthesis shift in dominance towards ‘background’ odor and ‘forefront’ irritation (Cain 1976; Cain et al. 2005; Zheng 2010). In anosmics and normosmics, Kobal and Hummel (1991) have confirmed such shifts by olfactory and chemosensory evoked potential recordings. For supraliminal hexanal concentrations, the subjects in the study by Zheng (2010) made drawings of each sniff with odor maxima always before sensory irritation maxima and with significantly lower rise times for odor than sensory irritation. Other factors that affect odor thresholds are: large fluctuation of individual thresholds over time (Stevens et al. 1988) and large variation also among individuals (Ahlström et al. 1986: formaldehyde threshold range 1–1000 ppb for 64 subjects). Odor detection thresholds vary with age (for pyridine see Schemper et al. (1981); see also Stevens et al. (1982); Amoore 1991), gender (for example Engen 1987), smoking habits (Dunn et al. 1982; Ahlström et al. 1987; Berglund and Nordin 1992), and physical exposure factors such as air temperature and humidity (for example Grundvig et al. 1967).

The purpose of the present research is threefold: (1) To determine the odor and sensory irritation for each of two odorous irritants common in indoor air (formaldehyde and pyridine). This includes the individual psychometric detection functions, and the absolute thresholds, their interquartile ranges, and the effective thresholds (Berglund 1991); (2) To develop a bisensory version of the method of constant stimulus (e.g. Engen 1971), in which the detection of odor and/or of sensory irritation is measured jointly for each sniff. In this way, it would be guaranteed that all odor and all sensory irritation detections refer to identical stimulus exposures; and (3) To apply the bisensory method in environmental field situations for measuring odor and sensory irritation of indoor air or emissions from materials because it is impossible to measure exposures chemically (Berglund et al. 1988a).

Materials and Method

Participants

Two groups of 31 subjects took part in an experiment with pyridine (17 women, 14 men) or with formaldehyde (15 women, 16 men). The two groups were matched for age (mean 24.5 years old and range 18–35 years). All 62 were healthy volunteers, and a majority were university students. Smokers and oral or nasal snuff users were not allowed (e.g. Ahlström et al. 1987; Berglund and Nordin 1992). Before the start of the experiment, the experimenter checked that the participant fulfilled recruitment requirements: (a) was not wearing perfume, scented cosmetics, skin creams, and lotions, (b) had not eaten spicy food like garlic, and (c) was in good health and without allergies, colds, or any respiratory tract disease. Participants were informed that all hood concentrations were below the Swedish threshold limit value (TLV) for 8-h occupational exposure. Informed consent was obtained from all subjects, who were also paid for their participation.

Research Equipment

The 62 experiments were conducted in an odor laboratory (described by Berglund et al. (1986); hood exposure performance by Berglund et al. (1974)). It consists of three parts: an air-quality controlled and air conditioned waiting room combined with an adjacent clean-air test chamber with an exposure hood in front of the subject’s seat. On the other side of the wall, the hood is connected to a dynamic-flow olfactometer in a chemical laboratory. Stimulus concentrations are created from a high-concentration invariant headspace by injecting steel capillaries of the olfactometer into a main high airflow of clean air (100 l/min), which enters the exposure hood from below, passes, and is evacuated continuously at the top. Natural breathing conditions prevail in the hood and the test chamber. The air of the test chamber and of the hood (and the waiting room) was kept at a temperature of 22 °C (SD=1) and relative air humidity of 40% (SD=3). These two sets of values are based on 1736 or 1756 measures collected during the formaldehyde or pyridine experiments, respectively.

Stimuli

The formaldehyde stimulus consisted of a series of 18 concentrations [range 6.36–1000.0 ppb (vol/vol)]. The formaldehyde concentrations measured in the hood during the 31 experiments were (for measurement precision, see Berglund and Nordin (1992); Shams Esfandabad 1993): 6.36, 10.1, 14.4, 18.1, 23.1, 31.7, 42.4, 57.4, 73.4, 101.4, 134.1, 177.7, 236.7, 316.1, 420.7, 567.0, 755.0, and 1000.0 ppb. The Swedish threshold limit value (TLV) for 8-h occupational exposure was 1,000 ppb. The formaldehyde atmosphere was generated by blowing charcoal filtered air through a solution of paraformaldehyde (analytical grade, Merck, Darmstadt, Germany; pretreated in 105–110 °C for 3 h) in 1 N sodium hydroxide. This atmosphere was in the dynamic-flow olfactometer diluted with charcoal filtered air in two steps: first to 100 ppm (vol/vol) formaldehyde, monitored continuously with infrared analysis (Miran 80), and then to the 18 concentrations with the aid of steel capillaries injected into the main clean airflow (100 l/min) to the exposure hood. Every experimental day, the 18 hood concentrations of formaldehyde (and the blanks) were measured 12 times with a continuous flow analysis instrument (Skalar SA 90000). It is based on the acetyl acetone method and UV detection, with a lowest range setting of 0–50 ppb formaldehyde. No formaldehyde was detected in background clean air of the hood (blanks).

The pyridine stimulus consisted of 15 concentrations in a geometric series (steps 0.2 log ppb), from 7.50 to 4732.5 ppb (vol/vol). During the experiment, the 15 average pyridine exposures were: 7.50, 11.9, 18.8, 29.9, 47.3, 75.0, 118.9, 188.4, 298.6, 473.2, 750.0, 1188.7, 1884.0, 2986.0, and 4732.5 ppb. The concentrations were generated and controlled by the same type of olfactometer, as for formaldehyde, and in a corresponding two-step procedure. First, a headspace was created from a water solution of pyridine (analytical grade, Merck, Darmstadt, Germany) in a glass flask, which was embedded in an oven and kept at 35 °C. By blowing charcoal filtered air through this liquid pyridine, a 190-ppm (vol/vol) base concentration was formed and fed into the dynamic-flow olfactometer. The base concentration was monitored manually (±2%) once per minute from readings of continuous analyses with a photo-ionization instrument (AID Portable Organic Vapor Meter, Model 580). By restricting the gas flow with steel capillaries to be injected into the main clean airflow (100 l/min), the 15 pyridine concentrations were formed in the exposure hood.

In both the formaldehyde and the pyridine experiments, the blanks were 'presented' by pulling electrically two unconnected, empty magnetic valves. The participant would then be exposed solely to the charcoal-filtered clean air of the main airflow in the hood. As a precaution, all capillaries were tested for adequate pressure resistance before and repeatedly during the two experiments. No significant changes were revealed.

Procedure

To become adapted to the clean air of the test chamber, each participant first spent at least 30 min in the waiting room of the laboratory. For formaldehyde, each of 31 participants evaluated 288 hood exposures (12×18 concentrations plus 72 blanks). For pyridine, each of 31 participants evaluated 280 hood exposures (14×15 concentrations and 70 blanks). In both experiments, the blanks constituted 25% of the presentations.

Hood exposures were stable and available during at least 5 s (green signal in hood). The participant took one sniff of less than 3 s in the hood. The face (nose with closed mouth) was then moved inside a teflon-sheet opening of the front of the exposure hood (teflon-coated). During the inter-exposure intervals (in-between sniffs), the subject's head was withdrawn from the hood for her/him to be able to breathe the clean air of the test chamber (red signal in hood). Presentation orders were random with 36 formaldehyde (or 35 pyridine) presentations in each of eight 12-min sessions (3 sniffs per minute). Between sessions there was a 10-min pause, which was prolonged to a 30-min pause between the fourth and fifth sessions. Pauses were spent in the clean-air waiting room. One of the 62 participants took part each day (4 h including pauses).

Oral and written instructions were given. The participant's ability to detect odor and/or sensory irritation and clean air (the blanks) was determined with an adjusted version of the method of constant stimuli (Engen 1971). For every hood presentation (odorous irritant or blanks), the participant evaluated his/her sniff and responded with one of four forced-choice response alternatives (see Table 1): (1) yes-yes: an odor was detected accompanied with a sensory irritation detection, (2) yes-no: an odor was detected but not a sensory irritation, (3) no-yes: an odor was not detected, but a sensory irritation was, and (4) no-no: neither an odor nor a sensory irritation was detected. Participants were told not to worry if they would need to use 'yes' or 'no' quite frequently. They were only to judge each sniff the way they perceived it. Before starting the experiment, each participant was trained in the psychophysical procedure for at least 10 trials of representative low and high formaldehyde concentrations and blanks (or of representative low and high pyridine concentrations and blanks).

Results

The quality of the psychometric functions and detection thresholds for the odorous irritants will depend on the quality of the 25% clean-air presentations, which serve as reference for each subject's 'no odor' and 'no sensory irritation'.

Table 1 The three sensory classes of the four odor-irritation response alternatives used in the formaldehyde and pyridine experiments, blanks included

Sensory class	Formaldehyde/ Pyridine concentrations		Clean air presentations (blanks)	
	Hits	Misses	False alarms	Correct rejection
Overall	Yes-yes	No-no	Yes-yes	No-no
	Yes-no		Yes-no	
	No-yes		No-yes	
Odor	Yes-yes	No-no	Yes-yes	No-no
	Yes-no	No-yes	Yes-no	No-yes
Irritation	Yes-yes	No-no	Yes-yes	No-no
	No-yes	Yes-no	No-yes	Yes-no

The four response alternatives (yes-yes, yes-no, no-yes, no-no) refer to one sniff: the first position is detection or not of odor and the second detection or not of sensory irritation. For the blanks, odor and/or sensory irritation detection is coded as false alarms and non-detections as correct rejections

False Alarms

A false alarm means that a participant detects an odor and/or a sensory irritation upon a clean-air presentation (the blanks). The two columns to the right of Table 1 present the bisensory method's four response alternatives for the blanks: yes-yes, yes-no, no-yes (and no-no). Based on the three positive response alternatives, the three kinds of sensory classes of the false alarms (and correct rejection=no-no) were calculated: odor, sensory irritation, or overall. Table 2 presents the false alarms and correct rejections in the formaldehyde (fourth and fifth columns) and pyridine (eighth and ninth columns) experiments. The false alarms for the response alternatives yes-no (only odor) and no-yes (only sensory irritation) were the same in both experiments. This indicates random response to the blank. The false alarms were more common in the formaldehyde than the pyridine experiment, for odor and sensory irritation 13 vs. 10%, respectively (Table 2).

In the two groups of 31 subjects, the interindividual variation in false alarms (upon blanks) was large. The two distributions are strongly positively skewed for the three sensory classes (Fig. 1; bars: overall, odor, or sensory irritation coded in black, white, or grey, respectively). In the formaldehyde (or pyridine) experiments, only one subject (or four subjects) produced zero false alarms (no-no upon all blanks: 100% correct rejections). The false alarms for overall detection (odor and/or sensory irritation for blanks) for formaldehyde was on average 23.1% (AM; range 0–29.1%; *N*=31) and for pyridine 18.1% (range 0–75.0%; *N*=31). Conversely, the correct rejections upon blanks (no-no) were 76.9% (range 20.9–100%; *N*=31) in the formaldehyde and 81.9% (range 24.3–100%; *N*=31) in the pyridine experiment.

Odor and Irritation Detections of Formaldehyde or Pyridine Concentrations

Figure 2 presents the three kinds of odor and/or sensory irritation detections (yes-yes, yes-no, or no-yes) and the misses (no-no), separately, for the 18 and 15 concentrations of formaldehyde (top left diagram) and pyridine (top right diagram), respectively. The two lower diagrams classify the detection data in their three sensory classes (Table 1): overall, odor, and sensory irritation, and the curves for misses (no-no=cross) are drawn as references. Notably, for the lowest concentration, the misses are very close to the overall correct rejections for the blanks (cross, Fig. 2, left and right), which were 77% for formaldehyde and 82% for pyridine, respectively.

The two upper-diagram curves of Fig. 2 (left: formaldehyde; right: pyridine) convey no redundancy. Conversely, the two lower diagrams have the yes-yes response alternative (open triangle) as its base for the three kinds of psychometric functions for sensory class (Table 1, overall, odor, or sensory irritation) for formaldehyde (left) or for pyridine (right). The overall detection curve (filled triangle) is the inverse of the curve for misses (cross). The concentration at which there is a 50% probability of detecting 'something' (overall) and a

Table 2 Sensory classes: hits, misses, correct rejections, and false alarms given as response percentages in the formaldehyde or pyridine experiments (31 subjects in each)

Sensory class	Formaldehyde concentrations		Clean air presentations		Pyridine concentrations		Clean air presentations	
	Hits	Misses	False alarms	Correct rejection	Hits	Misses	False alarms	Correct rejection
Overall	63	37	23	77	67	33	18	82
Odor	53	47	13	87	62	38	10	90
Irritation	32	68	13	87	37	63	9	91

The total number of determinations in the two experiments, each based on 31 subjects, was for formaldehyde 80,352 (and for pyridine 88,200) and for the blanks 2,232 (and 2,940), respectively

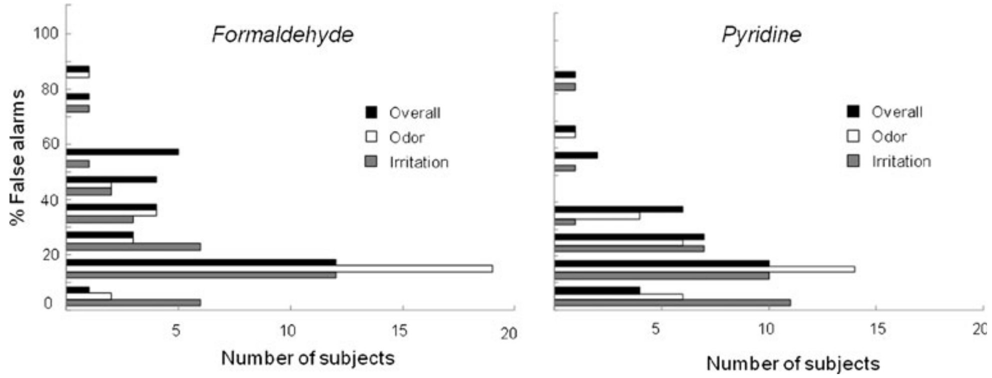


Fig. 1 False alarms upon blanks of the 31 subjects in the formaldehyde (*left*; 2232 blanks) or of the 31 subjects in the pyridine (*right*; 2940 blanks) experiment. The ordinate shows positively skewed distributions of false overall detections (*black bars*: yes-yes, yes-no, and no-yes), false odor detections (*white bars*: yes-yes and yes-no), and false sensory irritation detections (*grey bars*: yes-yes and no-yes). [The blanks constitute 25% of the presentations in both experiments]

50% probability of missing this same 'something' (no-no) is 65 ppb for formaldehyde and 76 ppb for pyridine.

Comparing upper diagrams with lower diagrams in Fig. 2 shows that sensory irritation alone (no-yes) was rarely reported (open square); the irritation curve (yes-yes, no-yes; filled square) is close to identical in form to the curve for the yes-yes responses alternative (upper: open triangles). The elevated only-irritation frequencies at low concentrations suggest that formaldehyde, but not pyridine, was mixed up with the clean-air presentations (see false alarms, Table 2). Indeed all three false alarms were higher in the formaldehyde experiment (23%) than in the pyridine experiment (18%). In comparison, for pyridine, odor detection dominates systematically over sensory irritation detection for every concentration (Fig. 2, right hand diagram), whereas for formaldehyde, odor detection starts to dominate systematically over sensory irritation detection at 23 ppb. Particularly at low concentrations, the sensory quality of formaldehyde was also more

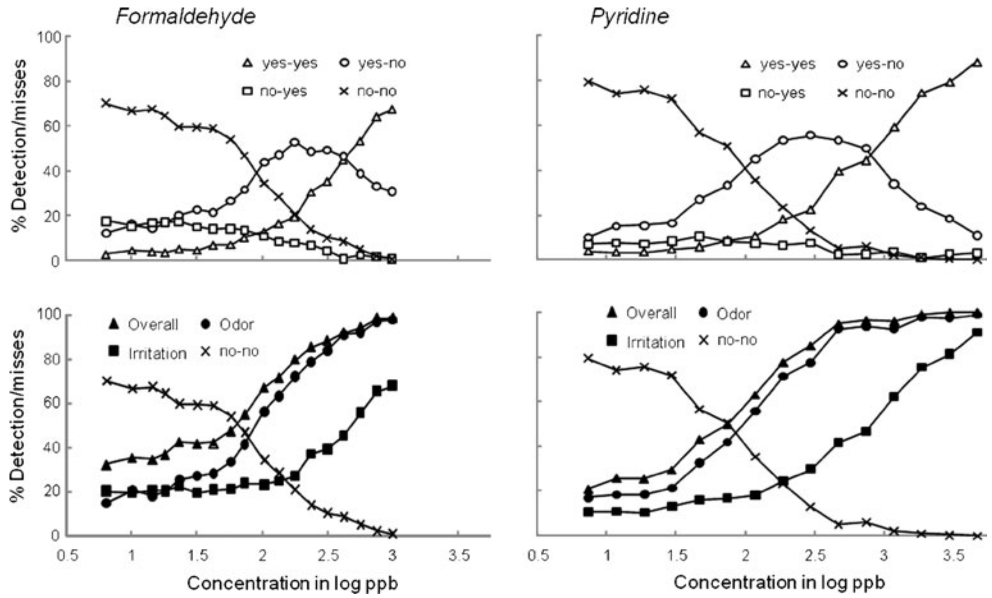


Fig. 2 Odor and/or sensory irritation detections (AM over 31 subjects) of formaldehyde (*left diagrams*) or of pyridine (*right diagrams*) as a function of 18 or 15 concentrations, respectively. *Upper two diagrams* show detections (yes) or misses (no) for four response alternatives for odor (first position) and/or sensory irritation (second position): yes-yes (*open triangle*), yes-no (*open circle*), no-yes (*open square*), and no-no for misses (*cross* in all four diagrams). *Lower two diagrams* show four sensory classes: overall detection = yes-yes, yes-no, no-yes (*filled triangle*), odor detection = yes-yes, yes-no (*filled circle*), irritation detection = yes-yes, no-yes (*filled square*), and the misses = no-no (*cross*)

easily mixed up with the sensory quality of the blanks than was the case for the sensory quality of pyridine (upper two diagrams of Fig. 2).

Psychometric Functions for Individual Data

To evaluate the quality of the data, the individual psychometric functions were plotted as percentage of detections for odor or sensory irritation (sensory class) against concentrations in log parts per billion, separately for formaldehyde and pyridine (cf. Cain and Schmidt 2009). For odor detection, individual psychometric functions were determined for all the 31 subjects for formaldehyde and all the 31 subjects for pyridine. For sensory irritation detection of pyridine, made jointly with the odor detection (= same sniff), individual psychometric functions were also determined for all the 31 subjects. However, for sensory irritation detection of formaldehyde, all but one of 25 subjects produced only parts of the psychometric function (see Fig. 4, last right-hand diagram) including 100% detection at the highest concentration (= Sw. TLV of 1 ppm). The remaining six out of the 31 subjects produced close to random scatter of detections with increasing concentration.

The individual psychometric plots for odor detection of formaldehyde and pyridine exhibit a close to linear trend with the logarithm of concentration, rather than the expected ogive which is characteristic of the group functions (cf. Cain et al. 2005, 2007; Cain and Schmidt 2009; for formaldehyde see Berglund and Nordin (1992)); see examples in the six left diagrams of Figs. 3 and 4 (for pyridine and formaldehyde, respectively). The 32 psychometric functions for sensory irritation have similar appearance (right-hand diagrams of Figs. 3 and 4). The slopes of the individual psychometric functions relative to log concentration were on average steeper for formaldehyde odor than for pyridine odor (different subjects, different odorous irritants), that is on average 82.7% per log ppb ($N=30$; SD=21.4% per log ppb and range 50.3–136.7% per log ppb) as compared to 68.5% per log ppb ($N=31$; SD=21.3% per log ppb and range 39.3–117.3% per log ppb). But the slopes for sensory irritation detection of pyridine were the same as for odor detection, that is, on average 68.2% per log ppb ($N=28$; SD=23.2% per log ppb; range 36.0–126.2% per log ppb). For pyridine, similar slopes of the detection functions may be related to the bisensory method with yes-yes responses dominating over the yes-no and no-yes response alternatives. If such response tendencies go with the bisensory method, we would have expected a similar outcome also for formaldehyde.

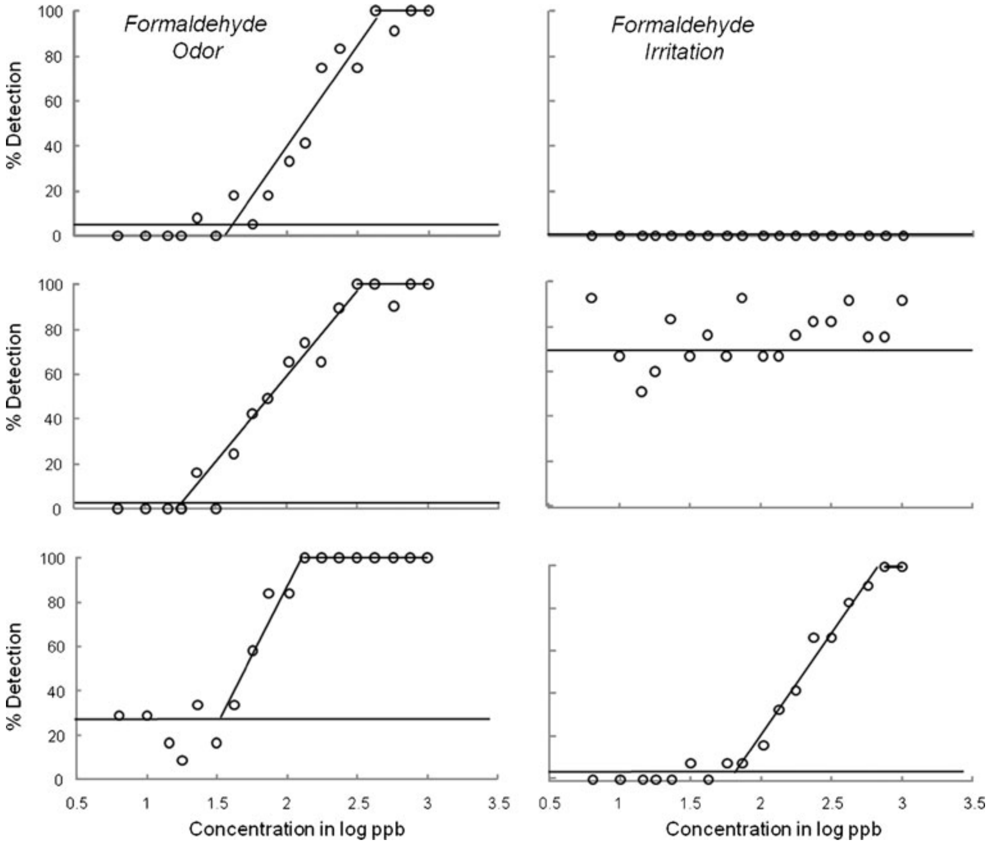
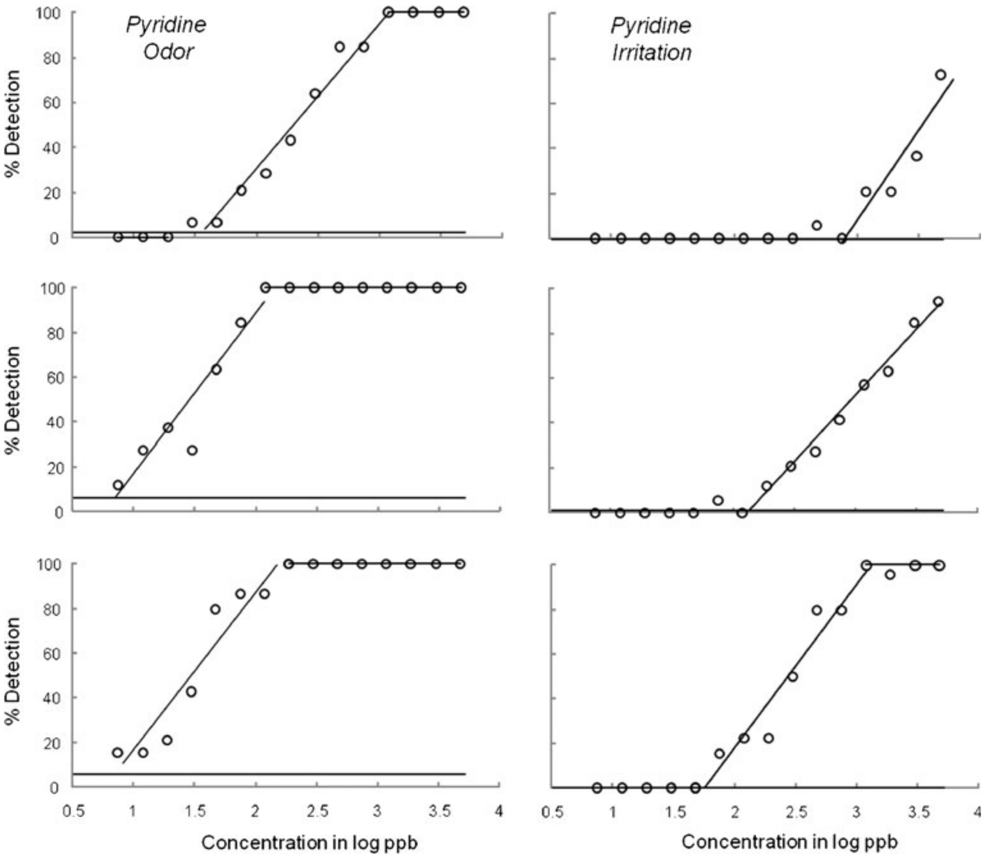


Fig. 3 Formaldehyde odor (*left*) and sensory irritation (*right*) detections (%) plotted as a function of increasing concentration in log parts per billion for three subjects (*top*, *middle*, and *bottom diagrams*) typical of the 31 tested. The *horizontal line* indicates the false alarms for odor and for sensory irritation upon presentation of blanks

Fig. 4 Pyridine odor (*left*) and sensory irritation (*right*) detections (%) plotted as a function of increasing concentration in log parts per billion for three subjects (*top*, *middle*, and *bottom diagrams*) typical of the 31 tested. The *horizontal line* indicates the false alarms for odor and for sensory irritation upon blanks



Psychometric Functions for Group Data

The detection probability functions for the group were calculated for the two sensory classes of odor and sensory irritation and plotted against log concentration for formaldehyde (Fig. 5, left) and pyridine (Fig. 5, right). Moreover, the false alarms for the two sensory classes of odor and sensory irritation were added to the diagrams as horizontal line of comparison (13% for formaldehyde and 10% for pyridine). The psychometric curves would reflect the position and variation in the close to linear slopes with log concentration of the individual psychometric functions. Notably, for sensory irritation of formaldehyde, the pooled data for the group exhibit a smooth curve up to ca. 65% probability of detection.

Although the average slopes of the individual psychometric functions were the same for pyridine odor and pyridine irritation, the group data of average probabilities of detection (Fig. 5, right) for the various concentrations seem ‘distorted’. Two reasons are: (1) the concentrations were not high enough for all the 31 subjects to reach 100% detection of sensory irritation (cf. Fig. 4, right, for

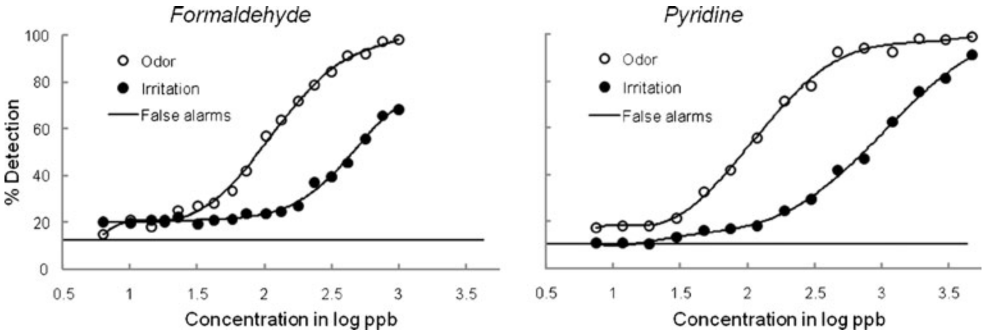


Fig. 5 Psychometric functions for formaldehyde and pyridine for the two groups of 31 subjects: detection percentages for the two sensory classes of odor (*open circles*) and of sensory irritation (*filled circles*) plotted against formaldehyde (*left*) and pyridine (*right*) concentrations in log parts per billion. The *horizontal line* in each diagram indicates the average size of the false alarm rates for odor and for sensory irritation as measured with the blanks (for exact values see Table 2)

formaldehyde) and (2) the other more important reason is that (cf. Fig. 2, top right) the yes-yes responses (both odor and irritation) increased monotonically with increasing concentration and the no-yes (only sensory irritation) decreased monotonically to zero, whereas the yes-no (only odor) increased to a maximum and then decreased, but not all the way to the level of the false alarms. Inevitably, if the odor threshold is lower than the sensory irritation threshold, then with increasing concentration the probability for always detecting odor together with sensory irritation will be increasing, whereas the probability for perceiving sensory irritation alone will decrease. Simultaneous perceptions of odor and sensory irritation exist in everyday life, and potential perceptual interactions ought to happen in many of our odor detection experiments.

Table 3 Odor and sensory irritation detection: the effective threshold (P_0), the absolute thresholds (P_{25}, P_{50}, P_{75}) with the interquartile (P_{75}–P_{25}) range, and the complete detection threshold (P_{100}) for the two groups of 31 subjects in the formaldehyde and pyridine experiments

Detection probability	Formaldehyde (ppb)		Pyridine (ppb)	
	Odor	Irritation	Odor	Irritation
P_0	23.0	–	19.9	89.8
P_{25}	50.1	–	52.7	265.8
P_{50}	109.8	–	76.5	620.3
P_{75}	240.5	–	241.4	1581.6
P_{100}	505.1	–	613.0	3656.1
P_{75}–P_{25}	178.6	–	178.5	1205.5

Geometric means calculated for 31 subjects' threshold concentrations in parts per billion

Absolute Odor and Sensory Irritation Thresholds

In order to determine the absolute threshold for odor or sensory irritation, the individual data sets from the 62 subjects were corrected for false alarms according to Eq. 1 (Engen 1971):

$$P_c = 100 \times \frac{P_{\text{hits}} - P_{\text{false alarms}}}{100 - P_{\text{false alarms}}} \qquad (1)$$

where P_c is the percentage of positive response corrected for false alarms, P_{hits} is the percentage of a positive response (odor or sensory irritation) in the presence of an odorous irritant (formaldehyde or pyridine), and $P_{\text{false alarms}}$ is the percentage of a positive response (odor or sensory irritation) in the presence of the blank.

For each subject's odor or sensory irritation detections, separately, straight lines were fitted to the data points relating P_c to log concentration, including the concentration closest or equal to the false alarms (P_0 in Eq. 1) up to the lowest concentration representing 100% detection (P_{100} in Eq. 1). P_0 here represents the effective threshold, that is, the highest concentration at which the probability of odor (or sensory irritation) detections equals the probability of false alarms for odor (or sensory irritation). Moreover, for each of the 31 subjects in the formaldehyde and in the pyridine experiments, the absolute thresholds at P_{25}, P_{50}, and P_{75}, and the interquartile (P_{75}–P_{25}) range were determined.

As shown in Table 3, the average P_{50} odor thresholds were 110 ppb (range 23–505 ppb, N=31) for formaldehyde and 77 ppb (range 20–613 ppb; N=31) for pyridine, and for pyridine sensory irritation 620 ppb (range 90–3,656 ppb, N=31). Notably, the interquartile range of the distributions was the same for the two odorous irritants, 178.5 ppb. (Geometric means were used because for formaldehyde expressed in log parts per billion, Ahlström et al. (1986) obtained a strongly positively skewed odor threshold distribution over concentration in log parts per billion for a larger group of 64 subjects, and in addition, our distribution for formaldehyde seems to be log normal (left diagram of Fig. 6). The effective thresholds (P_0) for formaldehyde odor and for pyridine odor were found to be close to equal: 23.0 and 19.9 ppb, respectively, and the P_{100} detection thresholds were 505 and 613 ppb, respectively. For pyridine irritation, the effective threshold (P_0) was 89.9 ppb, which is close to the P_{50} absolute odor threshold for pyridine (76.5 ppb). For formaldehyde, the sensory irritation thresholds were not possible to determine at the individual level but for a few of the subjects.

Figure 6 shows the interindividual distributions of the P_{50} absolute thresholds of the one group of 31 subjects for formaldehyde odor (left diagram) and the other group of 31 subjects for pyridine odor and pyridine sensory irritation (right diagram). Because the majority of the 31 subjects did not reach 100% detection for formaldehyde irritation, only the threshold distribution for odor is presented. The two individual threshold distributions for pyridine odor and sensory irritation are distinctly negatively skewed when expressed in log parts per billion (Fig. 6, left diagram). To enhance comparability, geometric means were used for calculating group mean thresholds also for pyridine (see Table 3).

Discussion

Detection thresholds for formaldehyde and pyridine odor and sensory irritation were measured by a bisensory method with the aid of 62 subjects. The individual psychometric functions for both odor and sensory irritation detection were rectilinear. The odor thresholds were always lower than the sensory irritation thresholds for both formaldehyde

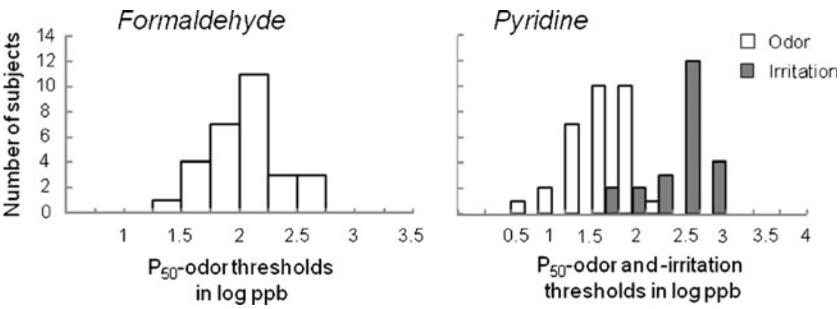


Fig. 6 Distributions of absolute thresholds (50% probability of detection) for formaldehyde odor (*left*) for one group of 31 subjects and for pyridine odor (*right*, *white bars*) and pyridine irritation (*right*, *grey bars*) for the other group of 31 subjects

and pyridine. Earlier research has used a lateralization method in which monorhinal stimulation in one nostril is perceived as sensory irritation in the other nostril (Schneider and Schmidt 1967; Kobal et al. 1989; Wysocki et al. 1992: Dalton et al. 2000). Cometto-Muñiz and Cain (1998) showed that nasal localization was well suited for measuring nasal irritation in normosmic persons; the threshold was the same for anosmics and normosmics. The bisensory method was tried in the present research because our primary aim was to develop a method, which allowed natural breathing conditions, similar to how we would breathe indoor air. A future intended use of the bisensory method would be, for example, to investigate sensory irritation together with odor of air sampled into the hood from various rooms in buildings (cf. Berglund et al. 1982).

Formaldehyde and Pyridine Thresholds

The P_{50} absolute thresholds were determined for formaldehyde odor to 110 ppb (GM; range 23–505 ppb, N=31; AM: 148 ppb), for pyridine odor to 77 ppb (GM; range 20–613 ppb; N=31; AM: 97 ppb), and for pyridine sensory irritation to 620 ppb (GM; range 90–3,656 ppb, N=31; AM: 769 ppb); see Table 1. The sensory irritation threshold for formaldehyde was not located inside a maximum of 1,000 ppb (Swedish TLV). In the bisensory method, the subject's task was to report if odor and/or irritation were present in every single sniff. Our results show that for every subject, the thresholds and the transient range for the psychometric functions are located at lower concentrations for odor than for sensory irritation. This is true for both odorous irritants tested, formaldehyde and pyridine, although our formaldehyde exposures were too low for determining every subject's psychometric function for irritation, including concentrations for 100% detection.

For formaldehyde, Ahlström et al. (1986) reported a range of 10–1,000 ppb (GM: 50 ppb; method of limits) for 64 subjects' odor thresholds, within which range our 31 subjects' odor thresholds are located (23–505 ppb: GM 110 ppb). In a recent critical review, Wolkoff and Nielsen (2010) reported odor thresholds between 56 and 295 ppb, based on experiments by Berglund and Nordin (1992), Nagata (2003), and Lang et al. (2008). Our highest exposure for formaldehyde was 1,000 ppb (Sw. TLV value), which turned out to be a too low concentration for covering the transient part of the psychometric function and measuring the individual sensory irritation thresholds for all but one of our 31 subjects.

The odor and sensory irritation thresholds for pyridine have been more researched than those for formaldehyde. Cometto-Muñiz and Cain (1990) reported pyridine threshold differences which are a factor of three to four between normosmic (odor and irritation) and anosmic (irritation only) subjects. The 'pure' pyridine irritation threshold was approximately 4,000 ppb if the 'overall' odor-and-irritation threshold is accepted to be 1,000 ppb. However, the odor-and-irritation threshold for their normosmics was found to be quite high compared to the only-odor threshold of 660 ppb reported by Amoore (1991; elderly subjects included) or of 42 ppb reported by Stevens et al. (1988), but falls within the approximate odor threshold range of 1,000–10,000 ppb reported by Cain and Gent (1991, 22–59 years old; focus on aging). Cain et al. (1987), Berglund et al. (1988b), Stevens et al. (1989) and Nordin et al. (2011) reported low pyridine odor thresholds of 106, 95, 100 and 105 ppb, respectively, all close to our threshold of 97 ppb calculated as an arithmetic mean over 31 subjects (GM was 77 ppb). Stevens et al. (1989) obtained their pyridine odor threshold of 100 ppb for 63 young persons, as compared with 950 ppb for 77 elderly. Several of these experiments used the sniff-bottle technique, which may partly explain the large variation in pyridine odor thresholds, although, obviously, age is a very strong factor explaining variation in odor detection.

In animal experiments, Abraham et al. (2003) reported pyridine eye irritation thresholds of 562 ppb (draize rabbit test scores), which they claim are perfectly compatible with human eye irritation thresholds. Obviously, our 31 subjects' average nasal sensory irritation threshold for pyridine is close to the same, 620 ppb. From selected properties of chemical compounds, Abraham and co-workers have developed a QSAR equation (Quantitative Structure–Activity Relationship) by which they estimate the odor-detection and nasal-pungency thresholds for pyridine to be 1.3 ppb and

1288 ppb, respectively (Abraham et al. 1996, 1998, 2007). Compared to our (geometric) mean P_{50} thresholds for pyridine odor (GM: 77 ppb; AM: 97 ppb) and sensory irritation (GM: 620 ppb; AM: 769 ppb), the QSAR equation underestimates the odor threshold. If nasal-pungency thresholds ought to be perceived as somewhat 'painful', 1288 ppb is also low in comparison with the P_{50} absolute threshold range for 'sensory irritation' obtained for our 31 subjects (90–3,656 ppb).

Our steepest psychometric function was found for formaldehyde odor (82.7% per log ppb). Interestingly, for pyridine, the steepness was on average the same for odor (68.5% per log ppb) as for sensory irritation detection (68.2% per log ppb). This latter finding may have to do with our bisensory detection method in which the frequency of detections of odor and irritation (yes-yes response) dominantly co-varied with the only-irritation response. A large set of odorous irritants has to be investigated before any conclusions can be drawn on co-variation between odor thresholds and sensory irritation thresholds for the same individuals.

The Practical Use of the Bisensory Method for Odor and Irritation Detection

In their extension, our research results contribute important new knowledge in the areas of occupational and environmental health. In particular, this involves the protection of the general population from unwanted low-concentration odorous irritants, i.e. in the indoor air or in the emissions from building materials in homes, schools, and offices (e.g. Wolkoff et al. 2006; Wolkoff and Nielsen 2010). The bisensory method has great promise for future determination of psychometric functions and of human thresholds of odorous irritants, particularly in field situations, where indoor-air samples cannot be repeated exactly. Particularly, more knowledge is needed about low-concentration, persistent irritants of the upper airways or of the eye. These parts of the body are involved in many environmental syndromes such as the 'sick building syndrome' or 'multiple chemical sensitivity' (Cain et al. 1986; Cullen 1987; Baird et al. 1994; Dalton et al. 1997; Kunkler et al. 2011).

One interesting finding was that at the lowest concentrations, formaldehyde was more frequently detected as sensory irritation than as odor, whereas this was not the case with pyridine. Moreover, formaldehyde was also more frequently mixed up with the clean air (blanks); this could not be a leakage in the olfactometer because formaldehyde concentrations were measured in hood samples also for the blanks. Formaldehyde is one of the suspected sensory irritants involved in the 'sick buildings' (Ahlström et al. 1986; Cain et al. 1986). One explanation could be that formaldehyde has some other capacity to affect the trigeminal system and/or the mucosa. For example, Cain et al. (1986) showed that sensory irritation to formaldehyde took time to develop. In this respect, formaldehyde may work as a TRPA1 agonist (Cain et al. 2010) (TRPA1 stands for a receptor named 'transient receptor potential A1'). Kunkler et al. (2011) pointed out that TRPA1 receptors mediate environmental irritant-induced meningeal vasodilatation in the nasal and oral mucosa and respiratory lining. The activation of these receptors is the mechanistic link between the environmental irritants (for example formaldehyde and toluene) and neurogenic inflammation. One could speculate that during our 4-h experiment, such processes have been activated in the nasal pathways during the formaldehyde experiment, but not the pyridine experiment. This could potentially explain why the low formaldehyde concentrations were sensory-irritation detected at a frequency equal to the odors, but the pyridine concentrations were not.

On a more technical level, the main strength of the bisensory method for future joint detection of odor and sensory irritation is that both the experimental and stimulus contexts are invariant during the perceptual measurement of every exposure of an odorous irritant. We find that the bisensory method would be particularly well suited for testing building materials as well as indoor air quality in residential and occupational environments. The bisensory method is intended to be used in environmental research where it is often the case that indoor air consists of broadband mixtures of unknown compounds at very low concentrations (Berglund 2011). It is then often impossible to repeat experimentally identical stimulus exposures. At very low concentrations, single compounds may not be chemically detectable, but total exposures may still be odorous and sensory irritating (Berglund et al. 1988a).

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