VOCs and "Sick Building Syndrome": Application of a New Statistical Approach for SBS Research to U.S. EPA BASE Study Data

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ABSTRACT

Causal associations between "Sick Building Syndrome" (SBS) symptoms and specific environmental stressors were explored using a recently developed approach employing Principal Components Analysis (PCA) and Logistic Regression [1]. This approach was applied to data collected by the U.S. EPA from 1995 to 1996 in 28 large U.S. office buildings in the Building Assessment Survey and Evaluation study. PCA was used to apportion measurements of 13 VOC species and carbon monoxide into source-related vectors. A reduced set of four source-based exposure vectors, tentatively identified as photocopiers, automotive emissions, environmental tobacco smoke, and latex paints were derived from the data. Regression analyses indicate statistically significant associations between mucous membrane related symptoms and the PCA photocopier vector (odds ratio=1.2, p=0.04), after adjustment for age, gender, smoking status, presence of carpeting, and thermal exposure. Similar relationships (odds ratio=1.2, p=0.03) were found between sore throat symptoms and the PCA paint vector. Odds ratios are given per unit increase in PCA vector which range over 5-6 units.

INTRODUCTION

Causal associations between "Sick Building Syndrome" (SBS) symptoms and specific environmental stressors have been elusive. Although volatile organic compounds (VOCs) are suspected to be significant contributors to SBS, field studies to demonstrate this relationship have not generally proven successful. Ten Brinke, et al. [1] recently reported a new approach to develop exposure metrics for VOCs that were statistically significant predictors of SBS symptoms reported in the California Healthy Buildings Study. The method utilizes Principal Component Analysis (PCA) to group correlated VOCs into a reduced set of Principal Component vectors (PCs) that are associated with sources. The PCs are then used in a logistic regression analysis to estimate the association between SBS symptoms and these exposure metrics (the calculated PC scores), while adjusting for other building-environmental and occupant-related covariates. This approach has now been applied to a second set of VOC measurements and self-reported SBS symptom data, a subset of the Building Assessment Survey and Evaluation (BASE) study, collected by the U.S. EPA in 1995 and 1996 in 28 large U.S. office buildings.

METHODS

The data analyzed in this paper were collected in 28 large U.S office buildings in 1995 and 1996, a subset of 100 buildings studied from 1994-1998 by the U.S. EPA in the BASE study [2]. These 100 buildings were selected at random to be a representative sample of the nation's office building stock, however at the time that the analyses were conducted, only the '95-'96 data were available and suitable for this analysis. These 28 buildings are located in 11 states (AZ, CA, CO, FL, LA, NE, NV, PA, SC, TN, and TX). Their individual studies were carried out during one-week periods of the winter, spring, or summer months. The BASE protocol includes the collection of an exhaustive database on the physical characteristics of the buildings' construction and HVAC systems; extensive indoor and outdoor environmental monitoring data from a selected space within each building. Data were also collected via questionnaire from all study space occupants within each building. The questionnaire collected information on the occupants' perceptions of their workplace environments, job characteristics, and health and well-being (including symptoms associated with SBS). The BASE study protocol is described in detail elsewhere [2].

VOC samples were collected over 9-hours in canisters and analyzed by gas chromatograph-mass spectrometry for 56 VOC species. Thirteen of the VOCs (Table 1) were selected for inclusion in the present analyses, based upon literature of indoor or outdoor sources common to office buildings, and their similarity to those used in the analyses of Ten Brinke et al. [1].

Nine-hour time-weighted-average (TWA) indoor VOC and indoor minus outdoor CO (ΔCO) concentrations were averaged across the three indoor measurement sites for the Wednesday measurements at each building. A value of half of the limit of detection (LOD) was used to replace values reported as below LOD for individual VOC species. A value of 0.5 ppm was applied to CO data reported below LOD. Table 1 summarizes the VOC and ΔCO data. Thermal exposure (°C-hours) was calculated for each building, as the integrated difference between 5-minute-average-temperature and 20°C, averaged over 3 indoor locations and 2 measurement heights, and normalized to 10-hours of exposure.

Table 1. The geometric mean and standard deviation (GM,GSD), minimum, and maximum 9-hr TWA indoor VOC concentrations for the 28 '95-'96 BASE buildings are shown. Common sources of these VOCs derived from the literature are listed.

Compound	CAS No.	GM (ppb)	GSD	Min (ppb)	Max (ppb)	Common Sources[a]
styrene	100-42-5	0.21	1.5	0.10	1.2	1,2,3,4,13
a-pinene	2437-95-8	0.19	2.5	0.05	0.7	5,6
2-butanone	78-93-3	1.4	2.5	0.23	9.0	7,11,12
1,4-dichlorobenzene	106-46-7	0.13	2.7	0.05	2.4	6,8
toluene	108-88-3	4.8	2.5	1.5	97	1,2,9,11
ethylbenzene	100-41-4	0.38	2.5	0.14	2.6	1,2,3,9
1,2,4-trimethylbenzene	95-63-6	0.63	2.3	0.12	4.7	1,2,4,9
m&p-xylenes	1330-20-7	1.6	2.7	0.24	8.2	3,9,11
n-undecane	1120-21-4	1.2	2.2	0.33	3.6	1,2,4,5,10,14
4-methyl-2-pentanone	108-10-1	0.38	3.2	0.10	15	11
butyl acetate	123-86-4	0.63	3.3	0.13	6.9	7,11,12,14
d-limonene	5989-27-5	0.66	2.6	0.08	6.3	2,5,6,13
ethyl acetate	141-78-6	0.70	2.7	0.11	7.1	7,14
ΔCO (indoor-outdoor, ppm)	630-08-0	0.02	5.7	0.00	4.3	9,13,16

[a]1=Carpet; 2=Undercarpet; 3=Photocopier; 4=Building Materials, 5=Cleaners; 6=Deodorants; 7=Solvent; 8=Air Fresheners; 9=Automotive sources; 10=Latex Paint; 11=Solvent-Based Paints; 12=Spray Paints; 13=Environmental Tobacco Smoke; 14=Adhesives; 15=Inks; 16=Unvented Combustion Sources.

The BASE Study occupant questionnaire was used to derive SBS symptom prevalences (Table 2). These include upper respiratory and mucous membrane (MM) irritation, including the eyes, nose, and throat; chest tightness, difficulty breathing, cough, or wheezing; fatigue;

headache; eye strain; and dry or itchy skin. SBS symptoms are those which are reported to occur when the occupants are in the building and decrease when they leave. In order to qualify as a SBS symptom, the occupant must have reported it to have occurred at least 1-3 days per-week during the month previous to the study.

Table 2. Sick Building Syndrome (SBS) symptoms and average prevalence across 28 BASE '95-96 buildings.

SBS Symptoms	Avg. Prevalence(%)
Mucous Membrane Symptoms (Combined)	30
dry, itching, or irritated eyes	22
sore or dry throat	8.3
stuffy or runny nose, sinus congestion	15
Chest Tightness or Difficulty Breathing	8.2
chest tightness	2.2
shortness of breath	2.3
cough	5.9
wheezing	2.4
Fatigue or Sleepiness	
unusual tiredness, fatigue, or drowsiness	17
Headache	18
Tired or strained eyes	5.1
Dry or itchy skin	5.0

The approach using PCA to derive exposure metrics has been discussed thoroughly by Ten Brinke et al. [1]. In brief, the object of PCA is to convert a set of highly correlated variables (i.e., measured VOC species in office buildings), into a reduced number of uncorrelated vectors which are linearized sums (principal components) of *standardized* individual variables (i.e., normalized between ±1). These PCs represent source types or building materials which emit VOCs, since species originating from the same types of sources tend to co-vary in concentration from one building to the next. Some VOC species can originate from more that one source, so it is possible that they will be associated with more than one PC. Thus, the PCA method is useful because it can apportion the VOC contributions from different source groups. It should be noted that since the PCs represent particular groups of sources, it is likely that they correlate with other (possibly unmeasured) compounds emitted from those sources. In these analyses, PCA correlation matrix eigenvalues of the PCs were used to determine the extent of the PCs interpretability, with a cutoff criterion of ≥ 1.0 used to determine the PCs to be kept in the analysis.

Multivariate logistic regressions (MLR) [3] were used to assess associations between SBS symptoms and both individual VOCs and the PCA-based exposure metrics. Both crude bivariate and multivariate models were adjusted for other risk potential risk factors and confounders. The SBS symptom/environmental exposure associations are presented as odds ratios (OR).

RESULTS AND DISCUSSION

The average (min-max) of informative physical and demographic characteristics needed for this paper follow. Further details for BASE '95-'96 can be found elsewhere [2]. Occupied floor area of buildings (m^2): 17,000 (1,700-54,000); typical building occupancy (persons): 1460 (95-7130); average cooling degree days (°C-days): 1000 (180-2200); average heating degree days (°C-days): 2000 (100-3500); gender of survey responders (% male): 29 (6-70); survey age group mode (years): 40-50; survey participants per building (N): 50 (23-123); RH (%): 33 (10-49); thermal exposure (°C-hours): 33 (7-49); overall prevalence of ever smokers (42.3%); overall prevalence of carpeted workspaces (21.1%). All of the buildings had at least some air-conditioned spaces. The prevalence of operable windows in the buildings was as follows: 60% had 0% operable, 28% had at least 50% operable, and 17% had 100% operable. Some smoking areas were allowed in 32% of the buildings, 1 (4%) building had no smoking

Table 3. Results of Principal Components Analysis on VOCs and Carbon Monoxide from the 28 ‘95-’96 BASE Study Buildings

Compounds	Principal Components 1	2	3	4	Communality
styrene	**0.91**	0.16	-0.08	-0.07	0.94
a-pinene	0.19	-0.04	0.18	-0.11	0.98
2-butanone	**0.83**	0.32	-0.18	-0.02	0.95
1,4-dichlorobenzene	0.18	-0.02	-0.04	0.03	1.00
toluene	**0.83**	**0.45**	0.07	0.00	0.94
ethylbenzene	**0.38**	**0.90**	0.11	-0.01	0.98
1,2,4-trimethylbenzene	**0.66**	**0.64**	0.25	-0.01	0.91
m&p-xylenes	**0.39**	**0.86**	0.15	-0.04	0.95
n-undecane	0.00	0.14	0.09	-0.08	0.99
4-methyl-2-pentanone	-0.07	-0.02	-0.05	**0.97**	0.97
butyl acetate	0.25	0.63	0.40	**0.52**	0.90
d-limonene	0.11	0.07	**0.94**	-0.01	0.93
ethyl acetate	**0.91**	0.22	0.19	0.05	0.94
Indoor – Outdoor CO (ΔCO)	-0.08	0.25	**0.91**	0.00	0.91
Variance (%)	30	21	16	9	Total=66%
Probable Identity of Source:	Photo-copier	Motor Vehicles	Tobacco Smoke	Paint	

restrictions, while smoking was observed in 3 (16%) of the buildings where it was prohibited.

Table 3 presents the results of the PCA analysis for the VOCs in Table 1. Based upon the PC loading patterns and source information from the literature (Table 2), the sources were identified as emissions from photocopiers, motor vehicles outdoors, indoor environmental tobacco smoke (ETS), and latex paints for PC#s 1-4, respectively. PC #1 may also include emissions from under-carpeting or other building materials. PC #3 was identified as environmental tobacco smoke because of the clear correlation between elevated indoor CO and d-limonene levels. The BASE database showed that the buildings with elevated ΔCO and d-limonene also either allowed smoking or had notations regarding observations of unsanctioned smoking activity.

Relative humidity (RH) was found to be significantly correlated ($r = 0.6$, $p= 0.0001$) with 1,2,4 trimethylbenzene (TMB) and PC#1. Humidity levels affect the rates of VOC emissions from materials. Also, due to the obvious dehydrating effects of low RH, especially on MM symptoms, humidity is likely an effect modifier in the VOC-symptom relationship. For these reasons it was deemed inappropriate to directly include RH in the statistical models. The various MLR analyses discussed below were conducted with RH < 20% excluded. The number of observations in these analyses averaged 820±18.

MLRs of individual VOCs against the individual and grouped BR symptoms, after controlling for age and gender, were conducted, and only TMB and 2-butanone (2BU) showed significant positive associations. The TMB associations, per ppb increase, were: grouped MM, OR = 1.14 (p=0.04); dry eyes, OR = 1.12 (0.08); wheezing, OR = 1.27 (0.1). 2BU was found to be associated with grouped MM, OR = 1.09 (0.03); and dry eyes, OR = 1.08 (0.09)).

MLRs were conducted to investigate the association between the SBS symptoms and the PCA source emissions vectors. The models included the 4 VOC vectors (PC #1-4), categorical age, gender, thermal exposure, ever smoker, and presence of carpet in workspace. Statistically significant ($p \leq 0.1$) results are presented in Table 4. The photocopier source is associated with the MM symptoms (OR = 1.17, p = 0.01), especially those of dry and irritated eyes, and stuffy/runny nose and sinus congestion. The association between the photocopier source vector and MM symptoms is biologically plausible. This PC vector contains a number of constituents known to be highly irritating to the respiratory tract. The irritancy of styrene, ethyl acetate, TMB, and m&p-xylene, relative to toluene are 7.9, 7.6, 3.6, and 3.4, respectively [1].

The Latex Paint vector was found to be significantly associated with sore throat (OR = 1.22, p = 0.03), and with chest tightness (OR = 1.33, p = 0.08). Associations between the "Cleaning products & water-based paints" vector and these SBS symptoms was also observed in the Ten Brinke et al. analyses (Throat OR = 1.8, 95% CI = 1.1-3.1; Chest Tightness OR = 1.8, 95% CI = 0.8-4.0). The major component in this vector is butyl acetate, with irritancy relative to toluene being a factor of 6.3 greater.

Statistically significant "protective" associations (those with OR < 1) with a number of symptoms are observed for the ETS source vector. This may be due to some confounding effect or misidentification of the source. If the d-limonene vector actually represents cleaning and deodorizing agents, it is possible that the "protective" association may indicate a positive effect of cleaning activities in reducing overall symptoms. Finally, the analyses indicate an OR of 1.2 for the association between the "tired or strained eyes" symptom and the Motor Vehicle source metric.

Table 4. Association[1] between Principal Component-derived VOC Exposure Metrics and Sick Building Syndrome (SBS) Symptoms in the 28 '95-'96 BASE Study Buildings.

SBS Symptom	VOC Exposure Metric[2] [Odds ratio (95% Confidence Interval)]			
	1 (Photocopier)	2 (Motor Vehic.)	3 (ETS)	4 (Latex Paint)
MM Combined	1.17 (1.04-1.33)		0.84 (0.74-0.96)	
Dry eyes	1.13 (0.99-1.28)		0.83 (0.70-0.97)	
Sore Thrt.				1.22 (1.02-1.47)
Nose/sinus	1.15 (0.99-1.33)			
Chest/breath.				
Chest tight.				1.31 (0.97-1.77)
Short breath				
Cough				
Wheeze				
Fatigue			0.86 (0.73-1.02)	
Headache				
Tired eyes		1.22 (1.06-1.39)	0.82 (0.71-0.95)	
Dry/itchy Skin				

[1] Controlled for Age, Gender, Thermal Exposure, Tobacco User, and Carpet in Workspace. All buildings with average relative humidity ≥ 20%

[2]The listed VOC sources are tentative "best guesses" based on available information.

It should be noted that as with the individual VOC analyses, gender was almost always a significant parameter in the models, with females 1.5 to 6 times more likely to report the SBS symptoms. Thermal exposure was significantly associated with the MM and respiratory symptoms, indicating that symptoms were slightly reduced (OR range = 0.95 to 0.99, p always < 0.1) with exposures above 20°C.

The above results should be interpreted with caution. The OR is defined by the ratio of odds of having a symptom to the odds of not having it, *per unit change* in exposure or risk factor. For the individual VOC analyses the units are merely per- 1 ppb increase in TWA (i.e. the odds of perceiving symptoms increase by a factor of 1-OR per 1ppb exposure increase). For example the 95th percentile TMB concentration is 2.7 ppb, and the OR for wheezing increases from 1.3 to 1.9. In the case of the PCA-based exposure metrics where the unit change of the metric is a composite vector of standardized components, the interpretation is complicated. These vectors range over 5 to 6 units. A comparison with the magnitude of the ORs in the individual VOC analysis indicates that the unit change may be roughly of the same order for the PCA-based associations. Nonetheless, the associations observed help provide one line of evidence regarding specific VOC sources that may be factors in SBS symptoms.

CONCLUSIONS

The application of the new PCA-based technique for developing source-based exposure metrics was successfully applied to a second set of indoor VOC data. Four source-based exposure vectors, tentatively identified as photocopiers, automotive emissions, environmental tobacco smoke, and latex paints were derived from the data. These metrics, which collapsed data from 13 VOC species into four vectors, were useful in conducting logistic regression analyses to identify associations between exposure and SBS symptoms. The regressions indicate statistically significant associations between mucous membrane related symptoms and the PCA photocopier vector, after adjustment for age, gender, smoking status, presence of carpeting, and thermal exposure. Similar relationships were found between sore throat symptoms and the PCA paint vector. Although the PCA was able to apportion the measured VOC species into several meaningful vectors, exact source identification was difficult due to the wide use of organic materials in man-made environments. Further work in this area should include enlargement of the analyses to include all 100 of the BASE Study buildings, to apply irritancy factor weightings to the VOC analyses, and to further develop VOC source fingerprints for materials in order to better specify the identity of the exposure metrics.

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