Associations of Volatile Organic Chemicals With Sleep Disorders and Sleep Duration in the National Health and Nutrition Examination Survey

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Abstract **Volatile organic chemicals (VOCs), a common environment pollutant, have been associated with some autoimmune diseases, but it has not been clarified if VOC exposure affects sleep, and if so, which VOCs affect sleep. Our study aimed to evaluate the relationship of individual VOCs with sleep disorders and sleep duration. Our primary analytical techniques were logistic regression models and multinomial logistic regression models.**

After a rigorous verification, specific VOCs N-acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA), mandelic acid (MA), and phenylglyoxylic acid (PGA) showed a statistically significant association with sleep disorders in female individuals in our study. We also determined that N-acetyl-S-(benzyl)-L-cysteine (SBMA), 2-aminothiazoline-4-carboxylic acid (ATCA), N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA), N-acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA), and N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA) showed significant association with sleep duration while maintaining high reliability. We observed that very short sleep duration exhibited a positive correlation with N-acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA) and N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HMPMA), whereas it demonstrated a negative correlation with N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine (MHBMA3) and 3HPMA compared with the normal sleep duration by age group. Our findings indicate a significant association between VOC exposure and sleep, and our study provides novel epidemiological evidence that supports the linkage between environmental pollutants and sleep.

Keywords: sleep disorders, sleep duration, urinary volatile organic chemicals, NHANES

Introduction

Sleep is vital to the human body and accounts for approximately one third of a person's life (Kazaglis et al., 2016). Approximately 4 out of 10 people worldwide reported having a sleep disorder (Jahrami et al., 2022). Poor sleep quality can impair decision making, speed and accuracy of task performance, and recovery from exercise (Troynikov et al., 2018). Sleep disorders can affect cognitive ability, mood, and vitality. Individuals who experience sleep disorders for an extended amount of time have an increased risk of mental disorders and chronic diseases such as diabetes and cardiovascular disease (Sabia et al., 2021), which adversely affect their quality of life. Sleep disorders can be influenced by age, psychological and physiological conditions, and environmental factors.

A growing number of studies suggest that environmental pollution influences sleep quality (Hu et al., 2022) and that higher levels of air pollution exposure could increase the prevalence of sleep disorders (Zhou et al., 2023). To date, research mainly has focused on $PM_{2.5}$, PM_{10}, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) (Tang et al., 2020). Therefore, it is important to explore how these and other modifiable risk factors could potentially contribute to sleep disturbances.

Volatile organic chemicals (VOCs) constitute a prevalent and intricate class of air pollutants. Many of these pollutants pose several health-related problems to humans. VOCs are the main compounds among indoor air pollutants, and formaldehyde, benzene, toluene, and xylene are the most common indoor VOCs (Aladangady, 2017). Among the VOCs detected indoors, benzene is a confirmed human carcinogen.

Other VOCs (e.g., hexane, heptane, octane) can affect the central nervous system (Rao et al., 2006). VOCs can cause not only direct damage to the human body but also indirect damage as VOCs convert into other pollutants. VOC exposure is associated with rheumatoid arthritis (Lei et al., 2023a). VOC derivatives (e.g., acrylamide, 1,3-butadiene, cyanide, ethylbenzene, styrene, propylene oxide, toluene, xylene) have been linked to obesity (Lei et al., 2023b). In homes with high moisture levels, VOCs can lead to asthma and reduced lung function in adults (Wang et al., 2023). Additionally, studies have shown

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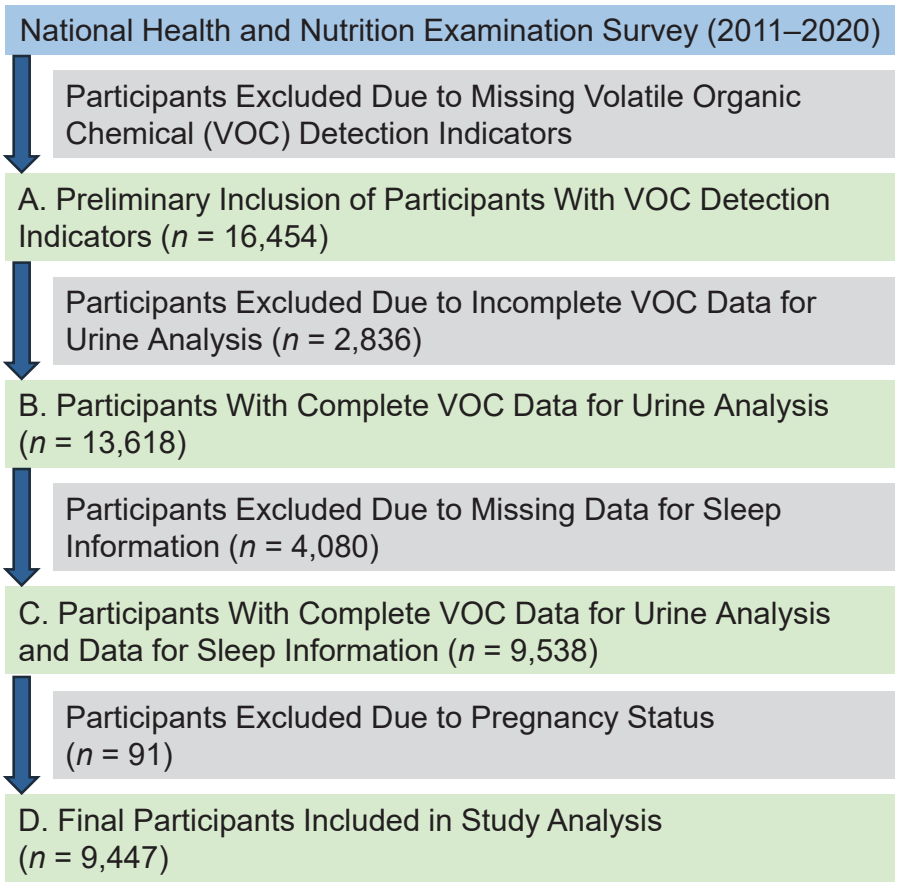
FIGURE **1**

Flowchart of Screening for Eligible Participants From the National Health and Nutrition Examination Survey, 2011–2020



that exposure to VOCs can cause epigenetic changes, leading to impaired motor learning and spatial memory due to neurotoxic effects (Yu et al., 2021). Although there is growing evidence that VOCs can affect human health, limited research has been conducted on the effect of VOCs on sleep.

Therefore, we used data sets from the National Health and Nutrition Examination Survey (NHANES) to determine the relationship between VOC exposure and sleep. Our research can provide new insights into how to improve sleep quality.

Methods

Study Population

NHANES is a federally mandated program that assesses the health and nutrition status of people in the U.S. via data from physical exams, laboratory tests, and surveys. For detailed information on methods, data collection, and ongoing research, see the NHANES website (www.cdc.gov/nchs/nhanes/index.html). The NHANES survey includes demographic, socioeconomic, dietary, and health-related topics (Fang et al., 2021). Participants consented to the survey, which was approved by the National Health Statistics Research Ethics Review Board to maintain ethical standards and protect participant rights.

Our study analyzed five cycles of NHANES data from 2011 to 2020, involving 16,454 individuals with VOC data from urine analysis. After excluding 2,836 participants due to incomplete VOC data and 4,080 without sleep information, along with excluding 91 participants based on pregnancy status, our analysis included 9,447 participants. The participant selection process is detailed in Figure 1.

Measure of VOCs From Urine Analysis

Urine samples were processed, stored, and shipped for analysis to the Division of Laboratory Sciences within the National Center for Environmental Health at the Centers for Disease Control and Prevention located in Atlanta, Georgia. Chromatographic separation was performed using an Acquity UPLC HSS T3 column with 15 mM ammonium acetate and acetonitrile as mobile phases (Alwis et al., 2012).

Assessment of Sleep Disorders and Sleep Duration

Trained interviewers used a computer-assisted personal interviewing (CAPI) questionnaire in participant homes to investigate sleep disorders. Participants were classified into groups based on if they had a diagnosis of a sleep disorder. The questionnaire asked about typical weekday sleep duration, with responses categorized as <5 hr, 5–6 hr, 7–8 hr, or ≥9 hr per night (Giannos et al., 2023; Sun et al., 2020).

Covariates

We considered several covariates: sex, age, race and ethnicity, education, marital status, family income-to-poverty ratio (PIR), body mass index (BMI), smoking, drinking alcohol, work activity, depressive symptoms, hypertension, and diabetes (Table 1). Race and ethnicity categories included non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, and other race. Education levels were categorized as <9th grade, 9–11th grade, high school graduate/GED, some college or associate's degree, college graduate or above, did not answer, and did not know.

Marital status was divided into living with a partner/being married or never married/widowed/separated/divorced. Next, PIR was categorized as <1 and ≥1. BMI categories were listed as underweight (<18.5), normal weight (18.5–24.9), overweight (25–29.9), and obese (≥30). Smoking status was defined as having smoked at least 100 cigarettes in a lifetime. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9), with a score of ≥10 indicating depression (Kroenke et al., 2001).

TABLE **1**

Participant Characteristics by Sleep Disorder Status From the National Health and Nutrition Examination Survey, 2011–2020

Characteristic	Subgroup	Participants With a Sleep Disorder (*n* = 2,468) # (%)	Participants With No Sleep Disorder (*n* = 6,979) # (%)	*p*-Value
Sex	Female	1,111 (45.02)	3,661 (52.46)	<.01
	Male	1,357 (54.98)	3,318 (47.54)	
Age (years)	<40	652 (26.42)	3,004 (43.04)	<.01
	40–59	898 (36.39)	1,952 (27.97)	
	≥60	918 (37.20)	2,023 (28.99)	
Race and ethnicity category	Non-Hispanic White	251 (10.17)	1,013 (14.51)	<.01
	Non-Hispanic Black	230 (9.32)	723 (10.36)	
	Mexican American	1,082 (43.84)	2,167 (31.05)	
	Other race	583 (23.62)	1,751 (25.09)	
	Other Hispanic	322 (13.05)	1,325 (18.99)	
Education	<9th grade	161 (6.85)	603 (9.77)	<.01
	9th–11th grade	274 (11.66)	758 (12.28)	
	High school graduate, GED, or equivalent	572 (24.35)	1,410 (22.83)	
	Some college or associate's degree	827 (35.21)	1,787 (28.94)	
	College graduate or above	515 (21.92)	1,611 (26.09)	
	Did not answer	0(0)	1 (0.02)	
	Did not know	0(0)	5 (0.08)	
Marital status	Living with partner or married	1,297 (55.26)	3,759 (60.92)	<.01
	Never married, widowed, separated, or divorced	1,050 (44.74)	2,411 (39.08)	
PIR category	<1	471 (21.25)	1,312 (21.38)	.90
	≥1	1,745 (78.75)	4,824 (78.62)	
BMI	Underweight (<18.5)	406 (16.45)	1,660 (23.79)	<.01
	Normal weight (18.5–24.9)	523 (21.19)	1,653 (23.69)	
	Overweight (25–29.9)	537 (21.76)	1,785 (25.58)	
	Obese (>30)	1,002 (40.60)	1,881 (26.95)	
Smoking	Yes	1,038 (51.82)	2,097 (38.62)	<.01
	No	965 (48.18)	3,333 (61.38)	
Drinking alcohol	Yes	1,952 (86.14)	4,760 (78.86)	<.01
	No	314 (13.86)	1,276 (21.14)	
Moderate work activity	Yes	847 (42.24)	2,065 (37.46)	<.01
	No	1,158 (57.76)	3,448 (62.54)	
Depressive symptoms	Yes	1,535 (81.39)	4,814 (95.36)	<.01
	No	351 (18.61)	234 (4.64)	
Diabetes	Yes	403 (20.06)	596 (10.82)	<.01
	No	1,536 (76.46)	4,772 (86.61)	
	Borderline	70 (3.48)	142 (2.58)	

Note. BMI = body mass index; PIR = family income-to-poverty ratio.

TABLE **2**

Weighted *OR*s for the Association Between Urine Volatile Organic Chemicals (VOCs) and Sleep Disorders

VOCs (Urine, pg/ml)	Nonadjusted Model *OR* [95% CI]	Model 1 *OR* [95% CI]	Model 2 *OR* [95% CI]
2MHA	0.82 [0.45, 1.50]	0.79 [0.46, 1.34]	1.22 [0.64, 2.34]
3–4MHA	0.99 [0.87, 1.12]	0.99 [0.89, 1.11]	0.89 [0.76, 1.04]
AAMA	0.55 [0.24, 1.25]	1.14 [0.51, 2.53]	1.12 [0.41, 3.08]
AMCC	1.81 [1.28, 2.55]**	1.35 [0.96, 1.92]	1.08 [0.95, 1.22]
CEMA	1.72 [1.01, 2.94]*	1.43 [0.85, 2.41]	1.17 [0.70, 1.94]
CYMA	0.96 [0.33, 2.75]	0.97 [0.33, 2.80]	1.00 [0.21, 4.80]
DHBMA	1.11 [0.77, 1.60]	1.06 [0.73, 1.54]	0.87 [0.56, 1.34]
2HPMA	1.10 [0.87, 1.38]	1.13 [0.87, 1.46]	1.96 [0.92, 4.15]
3HPMA	0.89 [0.77, 1.01]	0.94 [0.83, 1.06]	1.01 [0.89, 1.15]
MA	1.37 [0.82, 2.30]	1.55 [0.93, 2.57]	1.53 [0.87, 2.69]
MHBMA3	3.89 [0, 3,289]	25.39 [0.04, 17,753]	3.81 [0, 13,248]
PGA	0.60 [0.37, 0.97]*	0.66 [0.42, 1.05]	0.71 [0.45, 1.12]
HMPMA	1.10 [0.89, 1.36]	1.04 [0.85, 1.27]	1.00 [0.78, 1.28]

Note. A total of 13 VOCs from urine analysis were entered into the nonadjusted model simultaneously. Model 1 additionally adjusted for age, sex, race and ethnicity, education, and marital status. Model 2 further adjusted for body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity. CI = confidence interval; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.

* $p < .05$. ** $p < .01$.

Statistical Analysis

In this cross-sectional study, we analyzed VOC data from urine analysis to assess association of VOCs with the risk of sleep disturbance and sleep duration. Chi-square tests for comparative categorical data were performed on baseline data for sleep disorder subgroups. A Kruskal–Wallis test was used to determine the VOC levels in urine between different subgroups categorized by sleep disorders. Initially, logistic regression analyses were performed to assess the associations between urine VOC levels and sleep disorders. Additionally, we calculated *OR*s and 95% confidence intervals (CIs) to further quantify these relationships.

In the logistic regression analysis, we constructed a nonadjusted model to directly analyze the relationship between related urine VOC levels and sleep disorders, and then two additional models (model 1 and model 2) with different covariates for further analysis. Furthermore, we conducted a subgroup analysis based on sex and three age groups (<40 years, 40–59 years, and ≥60 years), using model 2 for the subgroup analysis.

We used multinomial logistic regressions to assess the relationships between urine VOC levels and sleep duration, with normal sleep (7–8 hr/night) serving as the reference point. To explore significant disparities in sleep duration among various cohorts, stratified analyses were conducted by sex and age. All statistical analyses were performed using Stata 16.0 software with a 2-sided significance level of $p < .05$.

Results

Associations of VOCs With Sleep Disorders

The total number of participants in this study was 9,447, of which 4,772 were male individuals and 4,675 were female individuals. In total, 26% of the sample had sleep disorders (Table 1). There was a significant difference in sex distribution among individuals with sleep disorders and individuals without ($p < .01$). A statistically significant increase in the prevalence of sleep disorders was observed among older participants ($p < .01$). When compared with participants without sleep disorders, participants who suffered from sleep disturbances were more likely to be male individuals, Mexican American, have a college or associate's degree, live with a partner or be married, have a PIR category ≥1, smoke, be categorized as obese, drink alcohol, report less moderate work activity, and exhibit depressive symptoms (all $p < .01$).

Among participants with sleep disorders, 44% identified their race and ethnicity as Mexican American, and 9% identified their race and ethnicity as non-Hispanic Black. Regarding education, 35% of participants with sleep disorders had a college or associate's degree and 7% reported an education level less than 9th grade. Among participants with sleep disturbances, 41% were categorized as obese and 16% were categorized as underweight, making up the smallest proportion of individuals

TABLE **3**

Weighted *OR*s for Sleep Disorders Across Volatile Organic Chemicals (VOCs) From Urine Analysis by Age in Model 2

VOCs (Urine, pg/ml)	Age Category (Years)		
	<40 *OR* [95% CI]	40–59 *OR* [95% CI]	≥60 *OR* [95% CI]
2MHA	0.60 [0.06, 5.77]	1.04 [0.25, 4.30]	1.31 [0.23, 7.27]
3–4MHA	1.05 [0.84, 1.33]	0.83 [0.57, 1.23]	0.95 [0.77, 1.16]
AAMA	0.45 [0.10, 2.15]	7.49 [1.00, 55.92]	1.34 [0.15, 11.87]
AMCC	1.65 [0.77, 3.52]	0.97 [0.45, 2.11]	1.06 [1.00, 1.12]
CEMA	0.58 [0.14, 2.42]	3.60 [1.14, 11.43]*	0.63 [0.28, 1.39]
CYMA	2.70 [0.35, 20.89]	0.18 [0.01, 3.29]	1.62 [0.03, 97.68]
DHBMA	1.80 [0.60, 5.40]	0.34 [0.16, 0.72]**	2.07 [0.83, 5.17]
2HPMA	3.48 [1.00, 12.17]	1.19 [0.63, 2.24]	2.36 [0.70, 7.97]
3HPMA	0.68 [0.41, 1.13]	0.90 [0.63, 1.29]	1.79 [1.19, 2.69]**
MA	1.31 [0.50, 3.46]	2.20 [0.78, 6.16]	1.21 [0.34, 4.33]
MHBMA3	46.34 [0, 9.19×10^9]	1.29 [0, 3,470,466]	0 [0, 24,567]
PGA	0.41 [0.12, 1.40]	0.68 [0.25, 1.81]	0.46 [0.13, 1.57]
HMPMA	1.19 [0.64, 2.20]	1.12 [0.74, 1.70]	0.81 [0.53, 1.25]

Note. Model 2 adjusted for age, sex, race and ethnicity, education, marital status, body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity.
CI = confidence interval; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.
* $p < .05$. ** $p < .01$.

with sleep disorders. Furthermore, 86% of the participants drank alcohol, 20% were diabetic, 76% were nondiabetic, and 81% exhibited depressive symptoms.

A total of 16 VOCs were included for analysis in our study (Supplemental Table 1). With the exception of 2-aminothiazoline-4-carboxylic acid (ATCA), N-acetyl-S-(benzyl)-L-cysteine (SBMA), and N-acetyl-S-(n-propyl)-L-cysteine (BPMA), participants in the sleep disorder subgroup exhibited significantly higher concentrations of the other 13 urine VOCs when compared with participants in the non-sleep disorder subgroup ($p < .01$) (Supplemental Table 2). In the unadjusted analysis, N-acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC), N-acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA), and phenylglyoxylic acid (PGA) were statistically significant, whereas other VOCs and sleep disorders did not show significant results.

Model 1 incorporated adjustments for age, sex, race and ethnicity, education, and marital status. Model 2 included further adjustments for BMI, smoking, drinking alcohol, diabetes, depression, and physical activity. Both of the models, however, failed to exhibit statistically significant differences between VOCs and sleep disorders (Table 2).

We conducted a stratified study to assess the impact of age on sleep, focusing on the correlation between VOCs and sleep disorders (Table 3). Using model 2 for analysis, the results indicated that among individuals <40 years, no statistically significant differences were observed in the presence of VOCs among subgroups with different sleep disorders. In the age group 40–59 years, a positive correlation was found between CEMA and sleep disorders ($p < .05$), whereas N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine (DHBMA) exhibited a negative correlation with sleep disorders ($p < .05$). Among individuals ≥60 years, a significant positive association was observed between N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA) and sleep disorders ($p < .05$).

After considering the effect of the participant sex on sleep, we conducted an analysis of the relationship between VOCs and sleep disorders using model 2. Our findings indicate that among female participants, CEMA and mandelic acid (MA) were significantly positively correlated with sleep disorders ($p < .05$). Conversely, PGA exhibits a significant negative association with sleep disorders ($p < .05$). Among male participants, no statistically significant differences were observed between VOCs and sleep disorders (Table 4).

Associations of VOCs With Sleep Duration

In the unaltered model, when compared with normal sleep duration (7–8 hr/night), the urinary N-acetyl-S-(2-cyanoethyl)-L-cysteine

TABLE **4**

Weighted *OR*s for Sleep Disorders Across Volatile Organic Chemicals (VOCs) From Urine Analysis by Sex in Model 2

VOCs (Urine, pg/ml)	Sex	
	Female *OR* [95% CI]	Male *OR* [95% CI]
2MHA	2.72 [0.71, 10.47]	0.69 [0.20, 2.42]
3–4MHA	0.80 [0.59, 1.09]	1.01 [0.74, 1.36]
AAMA	0.84 [0.19, 3.76]	1.18 [0.27, 5.14]
AMCC	1.16 [0.62, 2.15]	1.07 [0.96, 1.21]
CEMA	2.23 [1.13, 4.40] *	0.58 [0.25, 1.31]
CYMA	5.32 [0.79, 35.67]	0.15 [0.01, 2.08]
DHBMA	0.58 [0.31, 1.07]	1.33 [0.62, 2.85]
2HPMA	2.79 [0.88, 8.81]	1.37 [0.68, 2.78]
3HPMA	0.92 [0.78, 1.10]	0.95 [0.70, 1.29]
MA	2.60 [1.20, 5.63] *	1.08 [0.38, 3.09]
MHBMA3	0.07 [0, 13,442]	66.44 [0, 5.21 × 10^6]
PGA	0.35 [0.16, 0.76] **	1.45 [0.55, 3.85]
HMPMA	0.90 [0.66, 1.22]	1.25 [0.85, 1.83]

Note. Model 2 adjusted for age, sex, race and ethnicity, education, marital status, body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity. CI = confidence interval; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.

* $p < .05$. ** $p < .01$.

(CYMA) and DHBMA concentrations were positively associated with very short sleep (<5 hr/night), and N-acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA) and 3HPMA concentrations were negatively associated with very short sleep. The urinary CYMA and DHBMA concentrations were positively related to a risk of short sleep (5–6 hr/night). The concentrations of urinary ATCA, DHBMA, and N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HMPMA) exhibited a positive correlation with an increased risk of prolonged sleep duration (≥9 hr/night). A negative correlation was observed between the concentrations of urinary AMCC and SBMA with the risk of prolonged sleep duration (Supplemental Table 3).

A comparison of model 1 with normal sleep duration (Supplemental Table 4) reveals an inverse relationship between the concentrations of urinary 2HPMA and 3HPMA with very short sleep duration. Moreover, we found a positive correlation between urinary levels of N-acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA), ATCA, and DHBMA with an increased risk of prolonged sleep duration. Table 5 presents the fully adjusted model, showing that when compared with normal sleep duration, the concentration of urinary CYMA and HMPMA exhibits a positive association with very short sleep duration. Further, the concentrations of 2HPMA and 3HPMA exhibited an inverse relationship with extremely short sleep. The concentrations of urinary ATCA and DHBMA were positively correlated with an elevated risk of long sleep duration, whereas the concentration of SBMA exhibited an inverse relationship with the risk of long sleep duration.

Table 6 presents the associations between urinary VOC concentrations and sleep duration, stratified by age. In the fully adjusted model, we compared CYMA with different sleep durations among individuals <40 years and found a positive association between this biomarker and very short sleep duration, as well as short sleep duration. A negative association was also observed between urinary AMCC levels and prolonged sleep duration among individuals <40 years.

In adults 40–59 years, HMPMA was positively associated with very short sleep risk; N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine (MHBMA3) was inversely associated with very short sleep risk; and 2-methylhippuric acid (2MHA) and AAMA concentrations were positively associated with short sleep risk. Furthermore, AMCC, DHBMA, and 3HPMA concentrations were positively associated with long sleep risk in adults 40–59 years (Table 6).

In adults ≥60 years, CYMA exhibited a positive correlation with extremely brief sleep durations. Conversely, 3HPMA demonstrated an inverse association with the risk of extremely brief sleep durations in this same subgroup. Furthermore, the concentration of urinary BPMA was negatively associated with brief sleep durations in this subgroup. Lastly, the concentration of urinary MA was positively correlated with longer sleep durations in adults ≥60 years (Table 6).

Table 7 presents the associations between urinary VOC concentrations and sleep duration, stratified by sex. In the fully adjusted model, the concentrations of urinary CEMA and 2HPMA were inversely correlated with very short sleep duration among female individuals, compared with female individuals with normal sleep duration. Moreover, DHBMA was positively associated with a long sleep risk in female individuals, and urinary AMCC, SBMA, and 2HPMA were negatively related to long sleep risk in female individuals.

Furthermore, in male individuals, BPMA and HMPMA exhibited a positive correlation with very short sleep duration. Conversely, SBMA demonstrated a negative association with very short sleep duration in this subgroup. Furthermore, 3HPMA levels were inversely associated with short sleep duration among male individuals, and SBMA and MHBMA3 levels were negatively correlated with long sleep duration (Table 7).

Discussion

We conducted a cross-sectional study evaluating the relationship of urine VOC

TABLE **5**

Association Between Urine Volatile Organic Chemicals (VOCs) and Sleep Duration in Model 2

VOCs (Urine, pg/ml)	Very Short Sleep RRR [95% CI]	Short Sleep RRR [95% CI]	Long Sleep RRR [95% CI]
2MHA	0.67 [0.18, 2.54]	1.66 [0.95, 2.88]	1.28 [0.39, 4.16]
3–4MHA	1.04 [0.90, 1.19]	0.95 [0.90, 1.00]	0.90 [0.68, 1.21]
AAMA	0.97 [0.16, 5.91]	1.20 [0.36, 4.02]	3.10 [0.93, 10.34]
AMCC	1.02 [0.93, 1.12]	0.92 [0.64, 1.34]	0.75 [0.48, 1.18]
SBMA	0.06 [0, 11.05]	0.45 [0.07, 2.76]	0 [0, 0.18]**
BPMA	6.07 [0.28, 129.83]	0.17 [0.01, 2.78]	1.33 [0.11, 16.80]
ATCA	0.89 [0.40, 2.00]	1.07 [0.73, 1.58]	1.75 [1.09, 2.80]*
CEMA	0.83 [0.36, 1.91]	1.04 [0.59, 1.84]	0.46 [0.18, 1.14]
CYMA	12.91 [1.35, 123.78]*	2.52 [0.63, 10.13]	0.56 [0.10, 2.99]
DHBMA	1.18 [0.44, 3.19]	1.43 [0.88, 2.34]	2.86 [1.60, 5.11]**
2HPMA	0.18 [0.05, 0.70]*	0.50 [0.25, 1.00]	0.44 [0.18, 1.08]
3HPMA	0.68 [0.48, 0.95]*	0.86 [0.67, 1.10]	1.03 [0.76, 1.38]
MA	1.50 [0.68, 3.30]	0.97 [0.47, 2.00]	1.31 [0.47, 3.64]
MHBMA3	0 [0, 2.50]	14.19 [0, 277,410]	0.04 [0, 500.47]
PGA	0.69 [0.27, 1.74]	0.88 [0.43, 1.83]	0.84 [0.42, 1.66]
HMPMA	1.69 [1.09, 2.62]*	1.04 [0.76, 1.41]	1.17 [0.82, 1.66]

Note. Model 2 adjusted for age, sex, race and ethnicity, education, marital status, body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity. CI = confidence interval; RRR = relative risk reduction; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; SBMA = N-acetyl-S-(benzyl)-L-cysteine; BPMA = N-acetyl-S-(n-propyl)-L-cysteine; ATCA = 2- aminothiazoline-4-carboxylic acid; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.

* $p < .05$. ** $p < .01$.

exposure with sleep disturbance and sleep duration in U.S. adult NHANES survey participants between 2011 and 2020. VOCs are mainly composed of aromatic hydrocarbons, lipocyclic hydrocarbons, chain hydrocarbons (including saturated hydrocarbons such as alkanes and unsaturated hydrocarbons such as dienes), ketones, and alcohols—all of which are especially significant as dangerous air pollutants (Kheirbek et al., 2012). VOCs in the body can be tested in blood, urine, breath, and sweat. VOCs in the body are mainly metabolized by the digestive system—particularly by liver digestive enzymes—and form water-soluble VOC metabolites (i.e., volatile organic compounds) (Frigerio et al., 2019). Most of the VOCs eventually are expelled from the body through the urine (Li et al., 2021). Therefore, urinary VOCs are more suitable for biomarkers of environmental VOC exposure.

Exposure to air pollution has been associated with a range of health conditions (Hanna et al., 2019). Accumulated epidemiological and experimental evidence indicates that exposure to ambient air pollutants, such as particulate matter and gaseous components such as NO_2 and O_3, has adverse impacts on sleep quality. Air pollutants can be potential triggers for compromised sleep quality through various mechanisms, involving but not limited to the central ventilatory control centers, central nervous system, and both allergic and nonallergic pathways (Cao et al., 2021). VOC-contaminated air is a component of air pollution, which likely is negatively associated with the onset of sleep and sleep quality.

Our study assessed 16 urinary VOCs that were included in the NHANES survey cycles from 2011–2020. Participants were divided into groups based on having a diagnosed sleep disorder or having no known sleep disorder. Baseline data differed significantly between the two subgroups. In the weighted logistic regression model age and sex subgroup analysis, 3 VOCs (i.e., CEMA, 3HPMA, and MA) were identified to be positively associated with sleep disorders. Additionally, 2 VOCs (i.e., DHBMA and PGA) were identified to be negatively associated with sleep disorders. CEMA and 3HPMA are metabolites of acrolein, which was also detected to be positively associated with sleep disorders in our study. Acrolein is a reactive unsaturated aldehyde that can be endogenously produced by lipid peroxidation and by combustion, chemical synthesis, cigarette smoke, and e-cigarette vapor (Henning et al., 2017).

Previous studies have reported that chronic acrolein exposure can cause extensive oxidative stress, inflammation, and apoptosis in animal hearts (Cui et al., 2015). Until now, no epidemiological study has evaluated the association between acrolein and sleep dis-

TABLE **6**

Weighted *OR*s for Sleep Duration Across Volatile Organic Chemicals (VOCs) From Urine Analysis by Age in Model 2

VOCs (Urine, pg/ml)	Very Short Sleep *OR* [95% CI]	Short Sleep *OR* [95% CI]	Long Sleep *OR* [95% CI]
Age: <40 years			
2MHA	0.03 [0.01, 1.16]	1.13 [0.05, 23.45]	4.44 [0.11, 186.53]
3–4MHA	1.45 [1.00, 2.11]	1.00 [0.73, 1.36]	0.83 [0.55, 1.23]
AAMA	0.81 [0.09, 7.44]	0.35 [0.07, 1.76]	2.64 [0.43, 16.18]
AMCC	2.46 [0.66, 9.19]	0.61 [0.24, 1.57]	0.26 [0.09, 0.80] *
SBMA	0 [0, 6.74]	0.57 [0.02, 16.25]	0 [0, 11.69]
BPMA	0.28 [0, 1,339.50]	1.59 [0.06, 39.42]	2.62 [0.01, 1,316.08]
ATCA	0.41 [0.11, 1.53]	1.13 [0.53, 2.40]	1.52 [0.68, 3.42]
CEMA	4.35 [0.57, 33.18]	1.87 [0.42, 8.20]	0.17 [0.02, 1.29]
CYMA	17.98 [1.23, 261.78] *	9.43 [1.24, 71.75] *	1.93 [0.15, 25.35]
DHBMA	1.16 [0.24 ,5.52]	1.17 [0.53, 2.57]	1.12 [0.35, 3.58]
2HPMA	0 [0, 1.73]	0.31 [0.05, 1.80]	1.26 [0.49, 3.24]
3HPMA	0.77 [0.54, 1.10]	0.72 [0.46, 1.15]	0.87 [0.40, 1.89]
MA	1.76 [0.41, 7.63]	0.41 [0.12, 1.40]	0.35 [0.05, 2.50]
MHBMA3	698,408 [0, 2.2×10^{19}]	4.69 [0, 3.81×10^{8}]	49.15 [0, 2.67×10^{9}]
PGA	0.24 [0.01, 4.70]	2.18 [0.79, 5.97]	2.07 [0.67, 6.34]
HMPMA	0.87 [0.33, 2.32]	1.75 [0.86, 3.55]	2.38 [0.90, 6.27]
Age: 40–59 years			
2MHA	0.18 [0.01, 3.14]	2.41 [1.06, 5.46] *	2.23 [0.07, 76.16]
3–4MHA	1.08 [0.87, 1.34]	0.96 [0.85, 1.07]	0.87 [0.38, 1.99]
AAMA	1.99 [0.01, 544.31]	11.7 [1.19, 115.16] *	1.27 [0.05, 32.06]
AMCC	2.80 [0.58, 13.53]	1.05 [0.45, 2.43]	2.73 [1.11, 6.73] *
SBMA	4.66 [0.02, 1,339.68]	0.12 [0, 10.64]	0.03 [0, 13.71]
BPMA	100.88 [0.91, 11,223.63]	0.02 [0, 4.50]	0.01 [0, 5.77]
ATCA	0.11 [0.01, 1.15]	1.41 [0.73, 2.69]	1.01 [0.47, 2.20]
CEMA	1.26 [0.32, 4.98]	2.40 [0.45, 12.96]	0.17 [0.03, 1.10]
CYMA	0.75 [0.01, 52.34]	0.15 [0.01, 3.64]	0.02 [0, 1.52]
DHBMA	0.52 [0.04, 7.12]	1.54 [0.60, 3.95]	6.33 [1.79, 22.36] **
2HPMA	0.11 [0, 4.34]	0.71 [0.30, 1.67]	0.40 [0.11, 1.46]
3HPMA	0.9 [0.47, 1.73]	0.95 [0.58, 1.55]	1.59 [1.05, 2.40] *
MA	1.13 [0.16, 8.02]	1.59 [0.48, 5.27]	0.52 [0.09, 3.03]
MHBMA3	0 [0, 0.06] *	3.60 [0, 1.15×10^{8}]	0 [0, 278.76]
PGA	0.85 [0.12, 6.01]	0.42 [0.14, 1.23]	1.38 [0.32, 5.91]
HMPMA	2.39 [1.27, 4.52] **	0.94 [0.50, 1.77]	1.13 [0.66, 1.94]

continued on page 30

orders. Our findings indicate that acrolein exhibits an inverse relationship with the risk of very short sleep duration among older adults (≥60 years) and female individuals, whereas it is inversely associated with the risk of short sleep duration in male individuals. Conversely, acrolein is positively associated with the risk of long sleep duration in adults 40–59 years. These observations suggest that acrolein could be detrimental for excessive sleep duration and potentially contribute to the development of sleep disorders.

We also looked at 1,3-butadiene, which is mainly produced from tobacco smoke and has been reported to damage human

TABLE **6** continued from page 29

Weighted *OR*s for Sleep Duration Across Volatile Organic Chemicals (VOCs) From Urine Analysis by Age in Model 2

VOCs (Urine, pg/ml)	Very Short Sleep *OR* [95% CI]	Short Sleep *OR* [95% CI]	Long Sleep *OR* [95% CI]
Age: ≥60 years			
2MHA	10.78 [0.87, 132.91]	0.27 [0.01, 7.33]	1.40 [0.10, 19.13]
3–4MHA	0.70 [0.37, 1.31]	1.01 [0.87, 1.16]	0.85 [0.45, 1.58]
AAMA	0.28 [0.01, 10.43]	1.47 [0.04, 54.65]	3.72 [0.18, 78.04]
AMCC	0.26 [0.06, 1.21]	0.95 [0.89, 1.01]	0.45 [0.18, 1.15]
SBMA	0 [0, 104,532.50]	0.29 [0, 27.36]	0 [0, 3.36]
BPMA	0.08 [0, 6,002.03]	0 [0, 0.19] *	1.68 [0.06, 50.22]
ATCA	2.60 [0.78, 8.60]	0.58 [0.21, 1.56]	2.18 [0.78, 6.05]
CEMA	1.59 [0.10, 25.93]	0.64 [0.25, 1.62]	1.19 [0.30, 4.77]
CYMA	202.47 [1.33, 30,896.90] *	0.64 [0.01, 42.56]	0.51 [0.01, 19.04]
DHBMA	4.18 [0.69, 25.44]	1.67 [0.48, 5.73]	1.93 [0.66, 5.65]
2HPMA	0.51 [0.13, 2.01]	0.58 [0.14, 2.36]	0.29 [0.04, 2.11]
3HPMA	0.31 [0.12, 0.82] *	0.86 [0.48, 1.52]	0.71 [0.42, 1.20]
MA	3.99 [0.58, 27.27]	0.92 [0.07, 11.41]	18.59 [4.12, 83.83] **
MHBMA3	0.54 [0, 7.06×10^{11}]	1,139.17 [0, 8.26×10^{13}]	6,071,280 [0.01, 3.66×10^{15}]
PGA	0.78 [0.06, 9.71]	0.57 [0.16, 2.04]	0.25 [0.04, 1.70]
HMPMA	1.22 [0.63, 2.38]	0.90 [0.45, 1.81]	0.83 [0.41, 1.68]

Note. A total of 16 urine VOCs were entered into the nonadjusted model simultaneously. Model 2 adjusted for age, sex, race and ethnicity, education, marital status, family income-to-poverty ratio (PIR), body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity. CI = confidence interval; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; SBMA = N-acetyl-S-(benzyl)-L-cysteine; BPMA = N-acetyl-S-(n-propyl)-L-cysteine; ATCA = 2-aminothiazoline-4-carboxylic acid; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.

* $p < .05$. ** $p < .01$.

health (Boldry et al., 2017). The toxicity of 1,3-butadiene manifests during metabolic processes in vivo, such as enzyme disorders, GSH depletion, and saturable metabolism (Kirman et al., 2010). Further, 1,3-butadiene has been identified as a known carcinogen, with several epidemiological studies demonstrating that exposure to 1,3-butadiene is positively associated with increased incidence of various cancers (Sielken & Valdez-Flores, 2015). Our findings indicate that 1,3-butadiene exhibits a negative correlation with sleep disorders and a positive correlation with longer sleep durations. These observations suggest a potential benefit of 1,3-butadiene in the prevention of sleep disorders. Due to limited published research, however, further comparisons were challenging.

Our study is the first to report a negative association between 1,3-butadiene and sleep disorders, indicating a significant relationship between exposure to 1,3-butadiene and sleep disorders. Additional research is warranted to confirm our findings.

Benzene, toluene, ethylbenzene, and xylenes (collectively referred to as BTEX compounds) constitute a substantial proportion of the VOCs that are released during hookah smoking (Atamaleki et al., 2022). Studies consistently have demonstrated that tobacco smoke serves as a major temporary contributor to indoor BTEX levels (Bolden et al., 2015). Previous investigations have shown that long-term exposure to BTEX can cause biliary tract cancer, lung cancer, and leukemia (Mainka & Kozielska, 2016). The direct adverse health outcomes on renal and congenital disorders are among the most important noncarcinogenic effects of BTEX exposure (Rafiee et al., 2022), but little is known about the effect of BTEX exposure on sleep quality. Based on our findings that 2MHA was beneficial to short sleep among individuals 40–59 years, it seems that xylenes might be adversely associated with sleep duration. We also found that SBMA was adversely associated with long sleep duration and that MA showed a positive correlation with sleep disorders in female individuals in our study.

There were also some VOCs that we found to be associated negatively with sleep duration. These VOCs included acrylamide, acrylonitrile, and crotonaldehyde. Acrylonitrile has been extensively applied as a raw material to manufacture acrylic fibers, plastics, synthetic rubbers, and acrylamide (Benford et

TABLE **7**

Weighted *OR*s for Sleep Duration Across Volatile Organic Chemicals (VOCs) From Urine Analysis by Sex in Model 2

VOCs (Urine, pg/ml)	Very Short Sleep *OR* [95% CI]	Short Sleep *OR* [95% CI]	Long Sleep *OR* [95% CI]
Female			
2MHA	0.27 [0.04, 1.67]	1.41 [0.78, 2.56]	1.22 [0.40, 3.67]
3–4MHA	1.14 [0.95, 1.37]	0.89 [0.79, 1.01]	0.93 [0.72, 1.21]
AAMA	1.54 [0.16, 14.87]	1.08 [0.22, 5.42]	2.54 [0.31, 20.85]
AMCC	2.27 [0.55, 9.44]	0.66 [0.29, 1.50]	0.22 [0.06, 0.83]*
SBMA	0.23 [0, 22.68]	0.25 [0.01, 5.53]	0 [0, 0.11]*
BPMA	2.39 [0, 2,321.73]	0.13 [0, 5.12]	0.09 [0, 1,020,164]
ATCA	0.59 [0.10, 3.34]	0.61 [0.28, 1.33]	2.58 [0.74, 8.95]
CEMA	0.25 [0.07, 0.85]*	0.91 [0.44, 1.88]	0.65 [0.12, 3.55]
CYMA	3.17 [0.18, 57.30]	3.16 [0.32, 31.38]	2.47 [0.27, 22.48]
DHBMA	1.87 [0.64, 5.46]	1.58 [0.83, 3.01]	3.01 [1.11, 8.20]*
2HPMA	0.05 [0, 0.73]*	0.32 [0.10, 1.04]	0.11 [0.01, 0.81]*
3HPMA	0.79 [0.52, 1.19]	0.99 [0.79, 1.23]	0.81 [0.49, 1.32]
MA	1.43 [0.53, 3.82]	0.88 [0.41, 1.92]	1.23 [0.41, 3.70]
MHBMA3	0.12 [0, 3.13×10^{9}]	2,702.78 [0.02, 2.93×10^{8}]	265,540.50 [0, 81.4×10^{13}]
PGA	0.64 [0.21, 1.91]	1.09 [0.63, 1.88]	0.83 [0.39, 1.77]
HMPMA	1.35 [0.76, 2.40]	0.99 [0.70, 1.38]	1.21 [0.70, 2.08]
Male			
2MHA	0.49 [0.08, 3.12]	0.95 [0.21, 4.29]	1.24 [0.09, 16.21]
3–4MHA	1.23 [0.80, 1.90]	1.15 [0.85, 1.57]	0.93 [0.51, 1.71]
AAMA	0.97 [0.08, 11.4]	1.63 [0.21, 12.51]	3.82 [0.53, 27.55]
AMCC	0.70 [0.25, 1.90]	0.83 [0.39, 1.80]	0.92 [0.58, 1.45]
SBMA	0 [0, 0.74]*	0.50 [0.07, 3.77]	0.01 [0, 0.58]*
BPMA	30.05 [1.92, 470.46]*	0.31 [0, 47.85]	1.41 [0.16, 12.81]
ATCA	0.91 [0.37, 2.23]	1.37 [0.76, 2.47]	1.21 [0.70, 2.09]
CEMA	2.33 [0.47, 11.57]	1.16 [0.44, 3.07]	0.27 [0.07, 1.09]
CYMA	14.42 [0.38, 543.11]	0.64 [0.03, 13.07]	0.16 [0.01, 3.56]
DHBMA	0.31 [0.05, 1.86]	0.59 [0.21, 1.63]	1.95 [0.87, 4.36]
2HPMA	0.46 [0.06, 3.48]	0.80 [0.36, 1.79]	0.68 [0.29, 1.62]
3HPMA	0.54 [0.29, 1.01]	0.56 [0.38, 0.82]**	1.31 [0.83, 2.08]
MA	4.88 [0.74, 31.95]	2.62 [0.73, 9.47]	3.10 [0.60, 16.02]
MHBMA3	0 [0, 2.18]	157.95 [0, 2.73×10^{8}]	0 [0, 0.17]*
PGA	1.21 [0.10, 13.80]	1.69 [0.46, 6.18]	2.04 [0.39, 10.64]
HMPMA	2.03 [1.06, 3.86]*	1.36 [0.79, 2.33]	1.19 [0.67, 2.11]

Note. A total of 16 urine VOCs were entered into the nonadjusted model simultaneously. Model 2 adjusted for age, sex, race and ethnicity, education, marital status, family income-to-poverty ratio (PIR), body mass index (BMI), smoking, drinking alcohol, diabetes, depression, and physical activity. CI = confidence interval; 2-MHA = 2-methylhippuric acid; 3–4 MHA = 3- and 4-methylhippuric acid; AAMA = N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC = N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; SBMA = N-acetyl-S-(benzyl)-L-cysteine; BPMA = N-acetyl-S-(n-propyl)-L-cysteine; ATCA = 2- aminothiazoline-4-carboxylic acid; CEMA = N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA = N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA = N-acetyl-S-(3, 4-dihydroxybutyl)-L-cysteine; 2HPMA = N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA = N-acetyl-S-(3-hydroxypropyl)-L-cysteine; MA = mandelic acid; MHBMA3 = N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA = phenylglyoxylic acid; HMPMA = N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine.

* $p < .05$. ** $p < .01$.

al., 2010), and acrylamide was identified early as a genotoxic and carcinogenic compound (Woutersen, 1998).

In our study, urinary CYMA was the major metabolite of acrylonitrile, AAMA was the major metabolite of acrylamide, and HMPMA was the major metabolite of crotonaldehyde. Acrylonitrile was positively correlated with very short sleep among both older and younger adults. Acrylamide was positively correlated with very short sleep among adults 40–59 years, and crotonaldehyde was positively correlated with very short sleep among male individuals 40–59 years old, which might be because the major source of crotonaldehyde is tobacco smoke (Goniewicz et al., 2017). Although little is known about the effect of crotonaldehyde exposure on sleep duration—as smoking is a major risk factor for sleep and smoking is the main source of xylenes, toluene, ethylbenzene, acrylonitrile, and crotonaldehyde exposure—our findings suggest that xylenes, toluene, ethylbenzene, acrylonitrile, and crotonaldehyde might be the main active VOCs responsible for smoking-induced sleep duration.

Our study findings add to improving sleep quality with an environmental perspective. Nevertheless, some limitations should be considered when generalizing our study's conclusions. All data used in this cross-sectional study were collected at the same time, so we were unable to infer the causal relationship between VOC exposure and sleep. More cohort or prospective studies investigating the association between sleep and VOCs could be an effective method to explore this causality. In general, more prospective studies and related experimental studies are needed to further validate the conclusions of our study.

Conclusion

To the best of our knowledge, this research is the first study to carefully examine the relationship between VOC exposure and sleep. We identified several VOCs that are associated with sleep, giving us renewed inspiration for understanding their influence given the widespread presence of these compounds in our daily lives.

Research indicates a link between environmental pollutants and human health, especially sleep quality and duration. While the connection between VOCs and sleep disorders is recognized, the exact mechanisms are not fully understood. Future research should focus on the biological pathways linking VOCs to sleep disruption, examining the effects on the neurotransmitters and hormones involved in sleep regulation. It is also important to study if individuals with respiratory issues or chemical sensitivities are at a higher risk for sleep disturbances due to VOCs. Furthermore, longitudinal studies are needed to understand the long-term effects of VOCs on sleep patterns and identify critical exposure periods and cumulative effects. Public health interventions—such as using low-VOC materials, enhancing ventilation, and educating the public about health risks—are necessary to reduce VOC exposure.

The association between VOC exposure and sleep disorders represents an important area of research that has the potential to inform public health policies and improve the quality of life for individuals affected by sleep disturbances. Future studies should aim to elucidate the underlying mechanisms, identify subpopulations at risk, and evaluate the effectiveness of interventions to reduce VOC exposure and understand their impact on sleep.

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continued on page 34

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