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Urinary Polycyclic Aromatic Hydrocarbon (OH-PAH) Metabolite Concentrations and the Effect of GST Polymorphisms Among US Air Force Personnel Exposed to Jet Fuel

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Abstract

Objective—To evaluate the association between inhalation exposure to jet propulsion fuel 8 (JP-8) and urinary metabolites among US Air Force (USAF) personnel, and investigate the role of glutathione S-transferase polymorphisms.

Methods—Personal air samples were collected from 37 full-time USAF personnel during 4 consecutive workdays and analyzed for JP-8 constituents and total hydrocarbons. Pre- and postshift urine samples were collected each day and analyzed for polycyclic aromatic hydrocarbon urinary metabolites.

Results—Work shift exposure to total hydrocarbons was significantly associated with postshift urinary 1-naphthol ($\beta = 0.17$; $P = <0.0001$), 2-naphthol ($\beta = 0.09$; $P = 0.005$), and 2-hydroxyfluorene concentrations ($\beta = 0.08$; $P = 0.006$), and a significant gene-environment interaction was observed with glutathione S-transferase mu-1.

Conclusions—USAF personnel experience inhalation exposure to JP-8, which is associated with absorption of JP-8 constituents while performing typical job-related tasks, and in our data the glutathione S-transferase mu-1 polymorphism was associated with differential metabolism of naphthalene.

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The opinions and assertions contained herein are the private views and opinions of the authors and are not to be construed as official or as reflecting the views of the Army, the Department of Defense, or the Centers for Disease Control and Prevention.

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Jet propulsion fuel 8 (JP-8), a volatile lipophilic kerosene-based fuel, is the main jet fuel used by the US Air Force (USAF). Because of its higher flash point and lower acute toxicity, JP-8 completely replaced JP-4 by 1995.[1] Given that JP-8 is a complex mixture of approximately 228 hydrocarbons, it is a challenge to fully characterize personal exposure to JP-8.[2] Personal and ambient air concentrations of various JP-8 constituents have been previously characterized among personnel on USAF bases, indicating a wide range of exposures, with the highest concentrations among workers who repair and inspect aircraft fuel systems and perform quality control tests on the petroleum products.[3–5] Specifically, naphthalene has been suggested as a useful surrogate measure for exposure to JP-8 as it comprises 0.11% to 0.27% of the fuel on average.[6]

Urinary 1- and 2-naphthol concentrations have been investigated as a measure of absorbed naphthalene among USAF personnel as well as other occupations such as coke plant workers.[7,8] Previous studies have reported significant associations between postshift urinary naphthol concentrations and personal work shift exposure to JP-8 and smoking.[9,10] Because of the various compounds present in JP-8, several urinary metabolites may be used as biomarkers of exposure to JP-8.

Although urinary naphthol concentrations can be used to characterize exposure to naphthalene, smoking and genetic polymorphisms involved in the metabolism of naphthalene have been shown to affect urinary naphthol concentrations. Specifically, smokers with no other exposure to naphthalene with the glutathione S-transferase mu-1 (GSTM1)-null genotype have higher urinary naphthol concentrations than those with the GSTM1-present genotype.[11] Nan et al[12] also reported that the GSTM1-null genotype was significantly associated with higher urinary 2-naphthol concentrations among naphthalene-exposed coke oven workers and naphthalene-unexposed students after adjusting for smoking, though the effect estimate was larger among the coke oven workers ($\beta = -3.5$ vs -0.88).

We previously characterized urinary naphthols in a pilot study of 24 workers at one USAF base,[7] but here we report the results from a larger follow-up study of 73 workers at three USAF bases that includes additional urinary metabolites and evaluates the potential role of GST polymorphisms. The Occupational JP8 Exposure Neuroepidemiology Study was designed to investigate the relationship between exposure to JP-8 and neurological outcomes,[13] using the exposure assessment data presented here. In this article, we aimed to (1) describe pre- and postshift concentrations of urinary metabolites among Air Force personnel exposed to JP-8 at three bases, (2) assess the relationship between urinary concentrations of metabolites and breathing zone concentrations of naphthalene and total hydrocarbons (THC), and (3) investigate the potential interaction of GST polymorphisms and naphthalene air concentrations on urinary metabolite concentrations.

MATERIALS AND METHODS

Study Design

Seventy-four full-time active USAF personnel from three bases participated in this study during 1 workweek between January and April 2008. One participant did not provide

biological samples, resulting in 73 participants in this analysis. All participants had worked for a minimum of 6 months at their current job and were invited to participate to ensure that both workers with routine high exposure to JP-8 and low exposure were included in the study.[13] Participants were categorized a priori into high- and low-exposure groups on the basis of their typical job tasks. Specifically, participants who performed jobs with routine exposure to JP-8 such as fuel cell repair, maintenance, and fuel distribution were categorized as the high-exposure group, whereas those with minimal direct exposure to JP-8 were categorized as the low-exposure group (ie, administrative, clerical, and health care personnel). Each participant provided written informed consent before participation in the study, and all protocols were reviewed and approved by human subjects committees from the Army (US Army Research Institute of Environmental Medicine), Air Force (AF Research Laboratory at Wright Patterson AF Base), Veterans Affairs (VA Boston Healthcare System), and Boston University School of Public Health. The involvement of the Centers for Disease Control and Prevention laboratory was determined not to constitute engagement in human subjects research.

Data Collection

Each participant was monitored during 4 consecutive workdays, beginning on Monday morning after 2 days away from work and ending on Thursday afternoon. All sample collection methods have been described in detail previously.[13,14] Briefly, each participant completed a self-administered baseline questionnaire on the first day of the study to collect information on demographics, behavioral factors such as smoking, alcohol, grilled food, and caffeine consumption, health history, and military work history. Additional surveys were completed at the beginning and end of each work shift to describe more detailed personal exposures during the previous period.

All participants wore a Casella Apex Pro IS personal air monitor (Casella USA, Amherst, New Hampshire) attached to two sorbent tubes using a Y connector, on Monday through Thursday during their work shift to collect an air sample from their breathing zone. The first sorbent tube, a two-section (100/50 mg) Anasorb coconut shell charcoal tube (Anasorb; SKC Inc, Eighty Four, Pennsylvania), was analyzed for benzene, toluene, ethylbenzene, *m-/p-*xylene, *o-*xylene, and THC using National Institute for Occupational Safety and Health method 1501.[15] The second sorbent tube, a Chromosorb 106 tube (Anasorb; SKC Inc), was analyzed for naphthalene according to OSHA method 35.[16] All sorbent tubes were analyzed at the Organic Chemistry Analytical Laboratory at the Harvard School of Public Health in Boston, Massachusetts.

Each participant provided a urine sample at the beginning and end of each work shift, starting with preshift on day 1 after 2 days away from work and ending with postshift on day 4, resulting in eight urine samples per individual. All urine samples were analyzed for 1- and 2-naphthol as well as 2-, 3-, and 9-hydroxyfluorene, 1-, 2-, 3-, and 4-hydroxyphenanthrene, and 1-hydroxypyrene. In addition, urine samples were analyzed for creatinine concentrations to adjust for sample concentration. All urinary analyses were conducted at the Centers for Disease Control and Prevention in Atlanta, Georgia. Briefly, after the enzymatic deconjugation of the target analytes, automatic liquid–liquid extraction into pentene was

performed using the Gilson 215 Liquid Handler (Gilson Inc, Middleton, Wisconsin). The sample extracts were evaporated under a chemical fume hood, and reconstituted in toluene, and then the analytes were derivatized to yield the trimethylsiloxane derivatives. Analytical determination of the target analytes was performed by gas chromatography–isotope dilution high-resolution mass spectrometry, employing a MAT95XP (Thermo Finnigan MAT, Bremen, Germany) instrument.[17] The limits of detection (LODs) were 48 ng/L for 1-naphthol, 42 ng/L for 2-naphthol, 20 ng/L for 1-hydroxypyrene, and 10 ng/L for all other urinary analytes.

A blood sample was collected from each participant post-shift on Thursday. All blood samples were analyzed for GSTM1 and glutathione S-transferase theta-1 (GSTT1) genetic polymorphisms at Brown University using polymerase chain reaction methods described by Schwartz et al.[18]

Statistical Analyses

All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina). Chi-square tests were used to compare categorical variables between the high- and low-exposure groups, and Fisher exact tests were used for categorical variables where cell sizes were small. Wilcoxon ranked sum tests were used to compare continuous variables. Geometric means were calculated for the individual creatinine-corrected urinary metabolites by exposure category (high and low) and shift (preshift and postshift) by exponentiating the mean of the natural log-transformed values. Similarly, the geometric standard deviations were calculated by exponentiating the standard deviation of the natural log-transformed values. The LOD was used for samples below the LOD. Linear mixed-effects models were used for all further analyses to account for the repeated measurements from the participants (eg, air measurements and pre-and postshift urinary samples on 4 consecutive workdays from each individual).

RESULTS

The demographic characteristics of the 73 Air Force personnel who participated in this study are presented in Table 1. For variables that varied by day (ie, the number of cigarettes smoked per work shift and the number of barbeque meals consumed per work shift), we presented data for day 2 only as a representative day. Comparisons by exposure group show that there was no statistically significant difference in age, years of service, body mass index, current smoking status, race, marital status, education level, current military rank, or genetic polymorphisms between those in the high and low-exposure groups. Nevertheless, there was a statistically significant difference in sex ($P = 0.001$), with a greater proportion of males in the high-exposure group than in the low-exposure group. In addition, the high-exposure group had significantly more participants who lived on the base (63% vs 31%; $P = 0.007$). As reported previously, the workers in the low-exposure group were exposed to significantly lower personal air concentrations of THC (0.52 mg/m^3 vs 2.64 mg/m^3), naphthalene (0.37 μg/m^3 vs 2.25 μg/m^3), and other analytes than those in the high-exposure group.[3]

Table 2 presents the comparison of the creatinine-adjusted urinary metabolite concentrations in preshift and postshift urine samples by exposure group and smoking status. The percentage of samples below the LOD ranged from 0% to 29% in the low-exposure group and 0% to 19% in the high-exposure group, with the greatest percentage for 4-hydroxyphenanthrene concentrations. Although the greatest workday differences were observed in naphthols and hydroxyfluorenes among the high-exposure group, postshift urinary concentrations of 1-naphthol, 2- and 3-hydroxyphenanthrene were significantly higher than preshift samples in the low-exposure group among smokers, and 2-hydroxyfluorene concentrations were higher among nonsmokers. In addition, when comparing the postshift urinary concentrations between the high and low-exposure groups, significantly higher concentrations of 1-naphthol, 2-naphthol, 2-hydroxyfluorene, and 3-hydroxyfluorene were observed in the high-exposure group among nonsmokers only (Fig. 1). In contrast, higher 1-hydroxypyrene concentrations were observed in the low-exposure group among smokers (Fig. 2).

Table 3 presents the associations between breathing zone air concentrations of THC and postshift urinary metabolites while adjusting for preshift urinary metabolite concentrations, USAF base, sex, cigarettes smoked per work shift, and postshift urinary creatinine concentrations. Breathing zone concentration of THC was a statistically significant predictor of postshift urinary concentrations of 1-naphthol ($\beta = 0.15$; $P = <0.0001$), 2-naphthol ($\beta = 0.09$; $P = 0.005$), and 2-hydroxyfluorene ($\beta = 0.08$; $P = 0.006$). Specifically, for each additional 10% increase in breathing zone THC, there was approximately a 1% increase in 1-naphthol, 2-naphthol, and 2-hydroxyfluorene. Similarly, breathing zone naphthalene concentrations were a statistically significant predictor of postshift urinary 1-naphthol and 2-naphthol concentrations, with slightly greater effect estimates than observed for breathing zone THC concentrations.

The final multivariate models using air THC concentrations as a predictor of postshift urinary 1-naphthol, 2-naphthol, and 2-hydroxyfluorene concentrations are presented in Table 4, showing that the models explain 85%, 79%, and 72% of the between-worker variability and 19%, 33%, and 39% of the within-worker variability, respectively. In these models, nonadjusted urinary metabolite concentrations were used, and postshift urinary creatinine concentrations were included as a predictor. Preshift urinary metabolite concentrations, postshift urinary creatinine concentrations, and current smoking status were statistically significant predictors of postshift urinary metabolites in addition to the breathing zone THC concentrations. We tested for possible interactions between smoking status and air THC concentrations but found no significant interaction when predicting any of the urinary metabolite concentrations.

The association between naphthalene in personal air and urinary naphthols was significantly different by GST polymorphisms (Table 5). Specifically, the naphthalene concentrations in personal air had a significantly larger effect on urinary naphthols among workers with the GSTM1-present genotype than among those with the GSTM1-null genotype. A significant gene-environment interaction was not observed for GSTT1 genotypes, and we did not observe a main effect of either GSTM1 or GSTT1. No other genetic association was observed with the other urinary metabolites.

DISCUSSION

We investigated the effects of inhalation exposure to JP-8 constituents and the role of genetic polymorphisms on the concentrations of several urinary metabolites among Air Force personnel. Workers who were categorized a priori as having high exposure to JP-8 had higher urinary concentrations of 1-naphthol, 2-naphthol, and 2-hydroxyfluorene, suggesting that the a priori categorization on the basis of workers' typical job tasks and routine exposure to JP-8 can serve as a useful surrogate exposure metric in the absence of actual measurements. Correspondingly, we observed significant increases in urinary metabolites from preshift to postshift and significant associations with personal work shift air THC measurements, suggesting that these urinary metabolites serve as good biomarkers of occupational exposures. In addition, a significant gene–environment interaction was observed, indicating that the GSTM1 polymorphism has an effect on the relationship between personal exposure to naphthalene in air and urinary naphthol concentrations.

Although postshift urinary samples had significantly higher concentrations of some metabolites compared with preshift samples among individuals in the low-exposure group, further analyses among those in the low-exposure group indicated that these differences were mainly observed among smokers (1-naphthol, 2-hydroxyphenanthrene, and 3-hydroxyphenanthrene). Similar urinary concentrations of 2-, 3-hydroxyphenanthrene among the low-and high-exposure groups further support that these concentrations resulted from smoking rather than exposure to JP-8. In contrast, post-shift urinary concentrations of 2-hydroxyfluorene were significantly higher than preshift concentrations among nonsmokers, though the magnitude of the change was comparable and slightly higher for smokers. This significance of the difference in 2-hydroxyfluorene may be due to a greater sample size (22 nonsmokers vs 13 smokers). Others have shown that urinary 2-hydroxyfluorene is a sensitive and specific biomarker of exposure to polycyclic aromatic hydrocarbons, with smokers having significantly higher concentrations than nonsmokers[19,20] and roofers having higher concentrations postshift compared than preshift.[21] Urinary naphthol and 2-hydroxyfluorene concentrations may be influenced by exposure to JP-8 because higher urinary concentrations observed among those in the high-exposure group. Further analyses are warranted to determine the effect of smoking on these urinary biomarkers, possibly using more precise measures of smoking such cotinine concentrations.

In contrast to Serdar et al,[9,10] who observed a decrease in variability explained by the model after adjusting naphthol concentrations for urinary creatinine, postshift urinary creatinine concentration was included as a significant predictor in our final regression models (Table 4) because it explained some of the within-worker variability and there was no decrease in the between-worker variability explained. On the other hand, we observed a significant interaction between naphthalene air concentrations and GSTM1 polymorphism only when urinary metabolite concentrations were not adjusted for creatinine, similar to findings reported by Yang et al.[11]

Although some have shown a significant negative main effect of the GSTM1-present genotype on urinary naphthol concentrations,[11,12] and others have shown a significant positive effect,[22] we did not observe a significant main effect of GSTM1, but we are the first

to report a significant gene–environment interaction with air naphthalene concentrations. In addition, effect modification of GSTM1 by smoking status has been shown,[11] but we are unable to present our results by smoking status because of small sample size and limited power. Another limitation of our study is the lack of other genetic polymorphisms associated with naphthalene metabolism, such as CYP2E1.[23] Similar to other findings, we observed no significant association between GSTT1 polymorphism and urinary metabolite concentrations.[12,22]

Because of the considerable variability in the composition of JP-8, results of the models using THC concentrations in air may not be generalizable to other occupational settings or even all Air Force bases over time.[24] In fact, the average percent naphthalene was 0.10% of THC in air among nonsmokers in this study, but the range was 0.002% to 0.64%, showing some variability in the composition of their exposure.

We collected only one urinary spot sample preshift and post-shift from each participant, but we were able to collect samples over 4 consecutive workdays. Spot samples have greater variability than first-void or 24-hour urine samples, but we were able to reduce variability by adjusting for creatinine concentrations. In addition, the collection of repeated samples reduced the number of participants needed to observe statistically differences in metabolite concentrations.[25]

CONCLUSIONS

Urinary 1- and 2-naphthol concentrations, as well as 2-hydroxyfluorene, reflect occupational exposures to JP-8 during the workday among Air Force personnel and may be used as biomarkers of exposure to jet fuel. It is also important to consider smoking status and GSTM1 polymorphisms. Other routes of exposure, such as dermal, should also be investigated as urinary metabolite concentrations may also reflect exposure through the skin.

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Learning Objectives

- Discuss previous research on individuals exposed to jet propulsion fuel 8 (JP-8), including genetic and environmental factors that may affect urinary naphthol levels.
- Identify the new findings on JP-8 constituents associated with post-shift increases in levels of specific metabolites.
- Outline the new evidence for a significant gene-environment interaction affecting urinary metabolite concentrations after air naphthalene exposure.

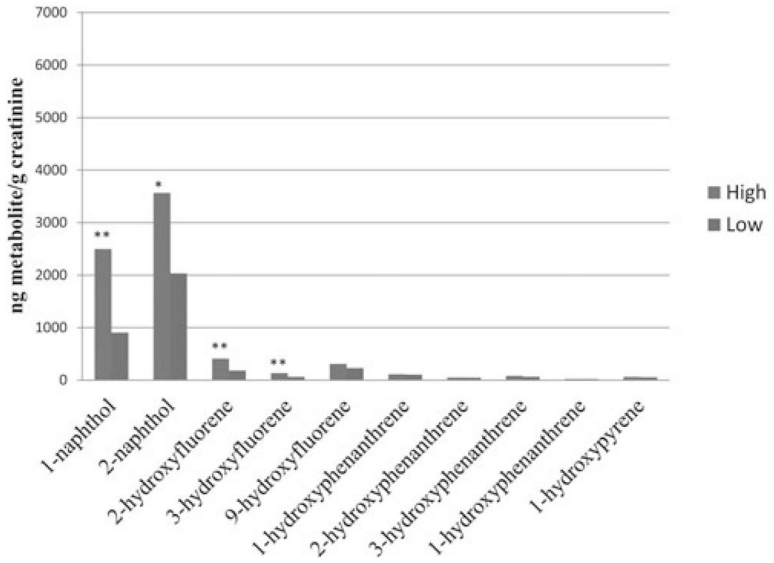

FIGURE 1.

Postshift urinary metabolite concentrations among nonsmokers. ** $P = 0.0001$; * $P = 0.02$.

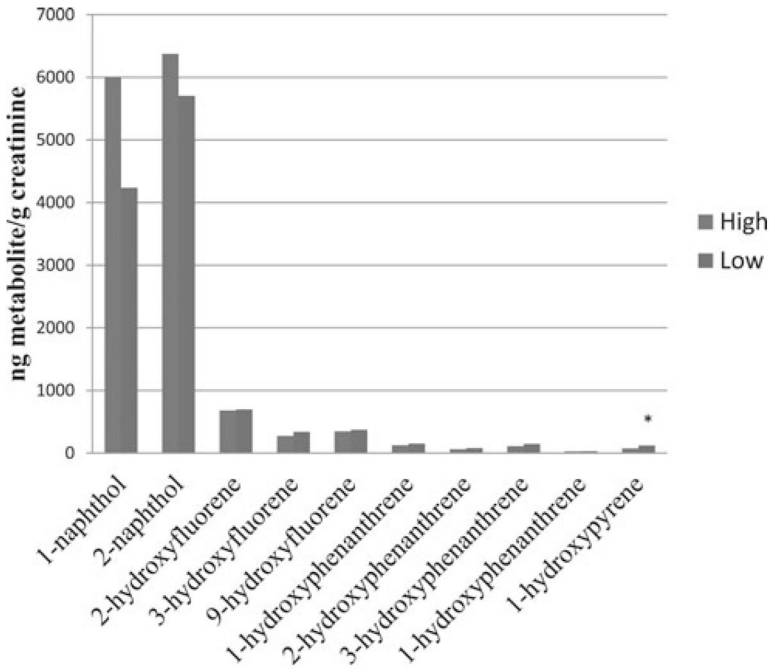

FIGURE 2.
Postshift urinary metabolite concentrations among smokers. *$P = 0.02$.

TABLE 1

Study Population Characteristics by Exposure Group

	Overall *n* = 73	Low *n* = 35	High *n* = 38	*P*
Median age (range)	23.7 (18–43)	23.9 (19–43)	23.6 (18–41)	0.57 *
Median years of service (range)	4.0 (0.5–20)	4.0 (0.5–20)	3.3 (0.5–17)	0.45 *
Median BMI (range)	25.6 (18–34)	25.8 (22–34)	25.6 (18–34)	0.81 *
Sex, *n* (%)				
Male	61 (84)	24 (69)	37 (97)	0.001 †
Female	12 (16)	11 (31)	1 (3)	
Base, *n* (%)				0.02 †
1	20 (27.4)	11 (31)	9 (24)	
2	20 (27.4)	15 (43)	5 (13)	
3	33 (45.2)	9 (26)	24 (63)	
Current smoker, *n* (%)				0.18 †
Yes	33 (45)	13 (37)	20 (53)	
No	40 (55)	22 (63)	18 (47)	
Average cigarettes smoked per day, *n* (%)				0.01 ‡
None	40 (55)	22 (63)	18 (47)	
1/4 pack	19 (26)	8 (23)	11 (29)	
1/2 pack	9 (12)	1 (3)	8 (21)	
1 pack	4 (6)	4 (11)	0	
Missing	1 (1)	0	1 (3)	
Cigarettes smoked during work shift, *n* (%)				
Day 2				0.50 ‡
None	48	26	22	
1/4 pack	18	7	11	
1/2 pack	3	2	1	
Missing	4	0	4	
Number of BBQ/grilled meals during work shift				
Day 2				0.34 ‡
0	56	26	30	
1	8	4	4	
2	2	2	0	
3	1	1	0	
4	2	2	0	
Missing	4	0	4	
Race, *n* (%)				0.83 †
White	53 (73)	25 (71)	28 (74)	
Nonwhite	20 (27)	10 (29)	10 (26)	
Marital status, *n* (%)				0.94 ‡

	Overall *n* = 73	Low *n* = 35	High *n* = 38	*P*
Single	28 (38)	13 (37)	15 (39)	
Married	40 (55)	20 (57)	20 (53)	
Divorced	5 (7)	2 (6)	3 (8)	
Live on base, *n* (%)				0.007†
Yes	35 (48)	11 (31)	24 (63)	
No	38 (52)	24 (69)	14 (37)	
Education, *n* (%)				0.64†
High school	60 (82)	28 (80)	32 (84)	
More than high school	13 (18)	7 (20)	6 (16)	
GSTM1, *n* (%)				0.19†
Null	35 (48)	13 (37)	22 (58)	
Present	34 (47)	18 (51)	16 (42)	
Missing§	4 (5)	4 (11)	0	
GSTT1, *n* (%)				0.45†
Null	9 (12)	3 (9)	6 (16)	
Present	60 (82)	28 (80)	32 (84)	
Missing§	4 (5)	4 (11)	0	

*Wilcoxon ranked sum test.

†Chi-square test.

‡Fisher exact test

§Blood samples were not collected from participants.

BBQ, barbeque; BMI, body mass index; GSTM1, glutathione S-transferase mu-1; GSTT1, glutathione S-transferase theta-1.

TABLE 2

Comparison of Pre- and Postcreatinine-Adjusted Urinary Metabolites (ng/g)

	Low (*n* =13)							High (*n*=20)						
		Pre			Post				Pre			Post		
Smokers	***n***	**%<LOD**	**GM (GSD)**	***n***	**%<LOD**	**GM (GSD)**	***P***	**n**	**% <LOD**	**GM (GSD)**	***n***	**%<LOD**	**GM (GSD)**	***P***
1-Naphthol	52	0	3344 (3.1)	51	0	4234 (3.1)	0.05	79	0	3452 (2.6)	74	0	6006 (2.3)	<0.0001
2-Naphthol	52	0	6284 (2.4)	51	0	5704 (2.3)	0.24	79	0	4633 (2.0)	74	0	6376 (2.0)	0.0002
2-Hydroxyfluorene	52	0	627 (2.2)	51	0	696 (2.0)	0.18	79	0	437 (2.0)	74	0	682 (2.2)	<0.0001
3-Hydroxyfluorene	52	0	312 (2.3)	51	0	337 (2.2)	0.36	79	0	215 (2.4)	74	0	273 (2.4)	0.005
9-Hydroxyfluorene	52	0	334 (2.4)	51	2	373 (2.4)	0.41	79	0	294 (2.2)	73	0	346 (2.0)	0.05
1-Hydroxyphenanthrene	52	0	132 (1.8)	51	0	149 (1.6)	0.10	79	0	118 (2.1)	73	0	124 (2.1)	0.77
2-Hydroxyphenanthrene	52	2	64 (2.3)	51	0	79 (1.8)	0.04	79	0	55 (1.8)	74	0	61 (1.7)	0.11
3-Hydroxyphenanthrene	52	0	120 (2.1)	51	0	147 (1.7)	0.04	78	0	99 (2.1)	71	0	109 (2.0)	0.19
4-Hydroxyphenanthrene	51	22	27 (2.6)	50	22	29 (2.1)	0.47	79	4	22 (2.0)	74	3	24 (1.9)	0.27
1-Hydroxypyrene	50	0	122 (1.8)	51	2	121 (1.8)	0.89	78	1	87 (2.0)	59	2	71 (2.0)	0.04
Nonsmokers	**Low (*n* =22)**							**High (*n* = 18)**						
1-Naphthol	87	0	813 (2.1)	85	0	901 (2.1)	0.25	72	0	1330 (2.6)	69	0	2496 (2.8)	0.0002
2-Naphthol	87	0	2146 (2.1)	85	0	2034 (1.9)	0.44	72	0	2839 (2.3)	69	0	3564 (2.7)	0.007
2-Hydroxyfluorene	87	0	163 (1.9)	85	0	180 (1.8)	0.02	72	0	247 (1.8)	69	0	408 (2.2)	<0.0001
3-Hydroxyfluorene	87	1	59 (1.8)	85	7	62 (1.9)	0.58	72	0	102 (2.1)	69	0	134 (2.2)	0.005
9-Hydroxyfluorene	86	0	208 (1.9)	85	0	228 (1.7)	0.22	72	0	198 (2.0)	69	0	305 (2.3)	0.0004
1-Hydroxyphenanthrene	87	1	107 (1.8)	85	0	105 (1.8)	0.64	72	0	99 (2.0)	69	1	110 (2.2)	0.21
2-Hydroxyphenanthrene	87	7	42 (1.9)	85	6	45 (1.9)	0.23	71	0	43 (2.0)	69	3	51 (2.1)	0.14
3-Hydroxyphenanthrene	87	0	57 (1.6)	85	1	63 (1.6)	0.12	72	0	65 (2.0)	69	1	80 (1.9)	0.03
4-Hydroxyphenanthrene	86	23	20 (2.0)	84	29	21 (2.0)	0.61	72	19	17 (2.4)	69	12	19 (2.5)	0.28
1-Hydroxypyrene	80	9	54 (2.0)	85	19	54 (2.1)	0.66	71	6	67 (2.1)	62	6	61 (2.0)	0.37

GM, geometric means; GSD; geometric standard deviations; LOD, limit of detection.

TABLE 3

Effects of 8-Hour TWA THC and Naphthalene Concentrations in Air*

Predictor	Postshift Urinary Concentration	β (SE)	P
THC, mg/m^3	1-Naphthol	0.17 (0.04)	<0.0001
	2-Naphthol	0.09 (0.03)	0.005
	2-Hydroxyfluorene	0.08 (0.03)	0.006
	3-Hydroxyfluorene	0.04 (0.03)	0.23
	9-Hydroxyfluorene	0.02 (0.03)	0.60
	1-Hydroxyphenanthrene	−0.04 (0.03)	0.20
	2-Hydroxyphenanthrene	0.008 (0.03)	0.75
	3-Hydroxyphenanthrene	−0.01 (0.03)	0.64
	4-Hydroxyphenanthrene	−0.02 (0.03)	0.52
	1-Hydroxypyrene	−0.03 (0.03)	0.38
Naphthalene, μg/m^3	1-Naphthol	0.22 (0.04)	<0.0001
	2-Naphthol	0.11 (0.03)	0.0006

*Adjusted for preshift urinary concentrations, base, sex, cigarettes per shift, and postshift urinary creatinine; 8-hour TWA THC air concentrations, 8-hour TWA naphthalene air concentrations, and urinary metabolite concentrations are natural log-transformed.

SE, standard error; THC, total hydrocarbon; TWA, time-weighted average.

TABLE 4

Final Models of 8-Hour TWA THC in Air ($\mu g/m^3$) and Postshift Urinary Metabolites

	Ln (Postshift Urinary 1-Naphthol)		Ln (Postshift Urinary 2-Naphthol)		Ln (Postshift Urinary 2-Hydroxyfluorene)	
	β **(SE)**	***P***	***β*** **(SE)**	***P***	***β*** **(SE)**	***P***
Intercept	4.59 (0.45)	<0.0001	4.83 (0.46)	<0.0001	3.53 (0.35)	<0.0001
Ln preshift urine concentration	0.33 (0.05)	<0.0001	0.34 (0.05)	<0.0001	0.29 (0.06)	<0.0001
Base		0.17		0.40		0.32
1	−0.29 (0.17)		−0.46 (0.15)		−0.25 (0.16)	
2	−0.23 (0.17)		−0.39 (0.15)		−0.10 (0.16)	
3	Ref		Ref		Ref	
Sex						
Female	−0.007 (0.19)	0.97	0.14 (0.17)	0.40	0.01 (0.18)	0.95
Male	Ref		Ref		Ref	
Cigarettes during work shift		0.0009		0.006		0.002
1/2 pack	0.92 (0.30)		0.65 (0.24)		0.67 (0.24)	
1/4 pack	0.78 (0.15)		0.49 (0.13)		0.61 (0.13)	
None	Ref		Ref		Ref	
Postshift urinary creatinine	0.005 (0.0006)	<0.0001	0.005 (0.0005)	<0.0001	0.005 (0.0004)	<0.0001
Ln 8-hr TWA THC (mg/m^3)	0.17 (0.04)	<0.0001	0.09 (0.03)	0.005	0.08 (0.03)	0.006
Random effects						
σ^2_{bw} (intercept only)	1.23		0.89		0.90	
σ^2_{ww} (intercept only)	0.67		0.42		0.41	
σ^2_{bw} (full model)	0.19		0.19		0.25	
σ^2_{ww} (full model)	0.54		0.28		0.25	
Variability explained by model, %						
Between-worker	85		79		72	
Within-worker	19		33		39	

SE, standard error; THC, total hydrocarbon; TWA, time-weighted average.

TABLE 5

The Effect of GSTM1 and GSTT1 on Postshift Urinary 1-Naphthol and 2-Naphthol Concentrations

	Ln (post 1-naphthol)		Ln (Post 2-Naphthol)	
Predictor Variables	***β*** **(SE)**	***P***	***β*** **(SE)**	***P***
GSTM1				
Intercept	4.31 (0.4)	<0.0001	3.82 (0.5)	<0.0001
Ln (pre 1- or 2-naphthol)	0.49 (0.1)	<0.0001	0.56 (0.1)	<0.0001
Ln (air naphthalene)	0.38 (0.1)	<0.0001	0.26 (0.1)	<0.0001
GSTM1 (present vs null)	−0.07 (0.2)	0.68	0.04 (0.1)	0.77
GSTM1 × ln (air naphthalene)	0.19 (0.1)	0.03	0.15 (0.1)	0.05
GSTT1				
Intercept	4.11 (0.4)	<0.0001	3.71 (0.5)	<0.0001
Ln (pre 1- or 2-naphthol)	0.51 (0.1)	<0.0001	0.57 (0.1)	<0.0001
Ln (air naphthalene)	0.27 (0.05)	<0.0001	0.18 (0.04)	<0.0001
GSTT1 (present vs null)	−0.15 (0.2)	0.51	−0.15 (0.2)	0.48
GSTT1 × ln (air naphthalene)	0.04 (0.1)	0.73	0.05 (0.1)	0.64

GSTM1, glutathione S-transferase mu-1; GSTT1, glutathione S-transferase theta-1.