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OPEN Effect of welding fume on heart rate variability among workers with respirators in a shipyard

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Welding fume exposure is associated with heart rate variability (HRV) reduction. It is still unknown whether respirator can reduce effect of welding fume on HRV among welding workers in a shipyard. We recruited 68 welding workers with respirator and 52 welding workers without respirator to measure HRV indices, including standard deviation of normal-to-normal intervals (SDNN) and square root of the mean squared differences of successive intervals (r-MSSD) by ambulatory electrocardiographic (ECG). Personal exposure to particulate matter less than or equal to 2.5 µm in diameter (PM_{2.5}) was measured by a dust monitor. The association between 5-minute mean PM_{2.5} and log₁₀-transformed HRV indices was analyzed by mixed-effects models. We found 5-minute mean PM_{2.5} was associated with 8.9% and 10.3% decreases in SDNN and r-MSSD. Effect of PM2.5 on HRV indices was greatest among workers without respirator {SDNN: 12.4% (95% confidence interval = -18.8--6.9); r-MSSD: 14.7% (95% confidence interval = -20.8--8.6}. Workers with respirator showed slight decreases in HRV indices {SDNN: 2.2% (95% confidence interval = -6.3--1.9); r-MSSD: 4.0% (95% confidence interval = -6.4--1.6). We conclude that respirator use reduces the effect of PM_{2.5} exposure on HRV among workers performing welding in a shipyard.

Welding is a fabrication process to join materials, such as metal, by intense heat. Electric welding by electrode is frequently used to improve the assembly of the larger metal pieces in shipyard. Welding fume, a complex mixture of metals, gases and particles, arises from the base metal, especially from electrodes while welding¹. Previous studies have reported that welding workers are exposed to welding fumes generated during the welding process². The majority of welding fume particles is found to be in coarse and fine size ranges by mass concentration³. Compared with coarse particles, fine particles {particulate matter (PM) less than or equal to $2.5 \,\mu$ m in diameter (PM2,5)} is often measured due to its ability to penetrate deep into the alveolar regions of the lung and induce adverse cardiovascular effects (4. Evidence from epidemiological studies suggest that heart rate variability (HRV) can be used as an early disease marker of PM-induced adverse cardiovascular effects⁵⁻⁷. Decrease in HRV has been reported to alter the heart's ability to respond to external signals, leading to myocardial infarction and sudden cardiac death⁸.

Recent studies have shown that workers exposed to metal fume are associated with HRV changes. Magari et al.⁹ reported that exposure to high levels of PM25 was associated increased standard deviation of normal-to-normal intervals (SDNN) among a cohort of 39 boilermakers9. Cavallari et al.¹⁰ found that high concentrations of PM_{2.5} were associated with decreased night square root of the mean squared differences of successive intervals (r-MSSD) for 26 male boilermaker construction workers ¹⁰. Fan et al.¹¹ observed that acute decline of HRV was associated with exposure to welding PM2.5 among 66 welders¹¹. On the other hand, Scharrer et al.¹² found no effect of clinical significance of a short-term high-level exposure to welding fumes on time- and frequency-domain parameters of HRV among 20 healthy individuals¹². According to these studies, the findings on the association between welding

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				ANOVA		
	All workers	With respirator	Without respirator	p-value	Scheffe's test	
Respirator usage, no						
Yes	68	68	0	—	—	
No	52	0	52	_	—	
Smoking, no						
Yes	45	25	20	_	—	
No	75	43	32	_	—	
Age, year						
Mean \pm SD	51.1 ± 10.3	50.1 ± 9.7	52.4 ± 8.9		_	
Range	26-61	26-59	30-61	0.65		
No	120	68	52			
BMI, kg/m ²						
Mean ± SD	24.8 ± 2.4	23.8 ± 1.9	25.2 ± 2.6		_	
Range	19.2-29.1	19.2-28.4	21.3-29.1	0.72		
No	120	68	52			
Seniority, year		l.				
Mean \pm SD	27.6 ± 12.5	27.2±11.9	27.8 ± 12.1		_	
Range	1-45	1-45	1-45	0.82		
No	120	68	52			
PM _{2.5} , mg/m ³		l.				
Mean \pm SD	1.3 ± 0.8	1.8 ± 1.1	1.1 ± 0.7		_	
IQR	0.7	0.8	0.6			
Range	0.1-5.4	0.1-5.4	0.1-4.9	0.84		
No	11520	6528	4992			
Temperature, °C		l.				
Mean ± SD	28.2 ± 3.4	27.7 ± 2.9	28.4 ± 3.1			
Range	24.7-33.1	24.7-32.6	25.5-33.1	0.72	_	
No	11520	6528	4992			
Relative humidity, %						
Mean ± SD	74.2 ± 6.7	76.6 ± 5.9	68.2±6.9			
Range	52.1-78.4	52.1-78.4	52.7-75.3	0.67	_	
No	11520	6528	4992			
Log ₁₀ SDNN, mse	c	L				
Mean ± SD	1.64 ± 0.32	1.79 ± 0.17	1.51 ± 0.13			
Range	0.89-2.11	0.99-2.56	0.89-2.11	< 0.05	With/Without	
No	11520	6528	4992			
Log ₁₀ r-MSSD, ms	ec					
Mean ± SD	1.51 ± 0.21	1.63 ± 0.15	1.39 ± 0.26			
Range	0.49-2.07	0.52-1.91	0.49-2.07	< 0.05	With/Without	
No	11520	6528	4992			

Table 1. Summary statistics for participants' characteristics, and $PM_{2.5}$ exposure, heart rate variability and climate conditions at 5-minute mean. BMI, body mass index; $PM_{2.5}$, particulate matter less than or equal to 2.5 µm in diameter; r-MSSD, square root of the mean squared differences of successive intervals; SDNN, standard deviation of normal-to-normal intervals.

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particles and HRV changes are still inconsistent. Moreover, it is still unknown whether respirator can reduce adverse effect of welding fume on HRV.

In order to answer whether occupational exposure to welding fume is associated with impaired cardiac autonomic control and the effectiveness of respirator on protecting workers from welding fume, we recruited a panel of welding workers in Taiwan to clarify these scientific questions.

Results

Summarized statistics for 120 participants' characteristics, heart rate variability monitoring, $PM_{2.5}$ exposure and climate conditions are presented in Table 1. The study participants were adult workers with a mean age of 51.1 years {standard deviation (SD) = 10.3 years}, 37.5% were current smokers, and 56.7% used respirator while working. There were no female workers among our population. No significant different was observed in age, BMI and seniority between workers with and without respirators. For $PM_{2.5}$, temperature and humidity monitoring, no significant difference was observed in $PM_{2.5}$ exposure and climate conditions between workers with and without

	All workers N = 11520	With respirator N = 6528	Without respirator N = 4992
Log ₁₀ SDNN	-8.9	-2.2	-12.4
	(-14, 5, -3.3)	(-6.3, 1.9)	(-18.8, -6.0)
Log ₁₀ r-MSSD	-10.3	-4.0	-14.7
	(-15.8, -4.8)	(-6.4, -1.6)	(-20.8, -8.6)

Table 2. Percentage changes^a in heart rate variability indices for an interquartile range change of 5-minute mean $PM_{2.5}$ in mixed-effects models. $PM_{2.5}$, particulate matter less than or equal to $2.5 \,\mu$ m in diameter; r-MSSD, square root of the mean squared differences of successive intervals; SDNN, standard deviation of normal-to-normal intervals. ^aThe values are presented as percentage changes and 95% confidence interval for interquartile range changes after adjusting for age, body mass index, smoking, temperature and relative humidity in all models.

	With respirator		Without respirator		
	Smokers N = 2400	Non-smokers N = 4128	Smoker N = 1920	Non-smoker N = 3072	
Log ₁₀ SDNN	-3.6	-1.8	-14.8	-11.6	
	(-7.4, 0.2)	(-4.5, 0.9)	(-19.2, -10.4)	(-13.8, -9.4)	
Log ₁₀ r-MSSD	-5.8	-3.1	-17.2	-12.1	
	(-8.1, -3.5)	(-6.5, 0.3)	(-22.1, -12.3)	(-15.7, -8.5)	

Table 3. Percentage changes^a in heart rate variability indices for an interquartile range change of 5-minute mean $PM_{2.5}$ in mixed-effects models stratified by smoking. $PM_{2.5}$, particulate matter less than or equal to $2.5 \,\mu m$ in diameter; r-MSSD, square root of the mean squared differences of successive intervals; SDNN, standard deviation of normal-to-normal intervals. ^aThe values are presented as percentage changes and 95% confidence interval for interquartile range changes after adjusting for age, body mass index, temperature and relative humidity in all models.

respirators during the study period. For HRV monitoring, the workers with respirators had significantly higher values of HRV indices (Log_{10} SDNN and Log_{10} r-MSSD) than did the workers without respirators.

The results of associations between concurrent $PM_{2.5}$ and HRV indices estimated by the mixed-effects models are shown in Tables 2. With age, BMI, smoking, temperature and relative humidity being adjusted in all mixed-effects models, we found that $PM_{2.5}$ exposure was associated with HRV changes for welding workers in general. It is noteworthy that $PM_{2.5}$ exposure significantly decreased HRV indices for workers without respirators. Log₁₀ SDNN decreased by 12.4% per IQR of $PM_{2.5}$ at 5-minute mean among workers with respirators. No significant association between PM2.5 and Log₁₀ SDNN was observed among workers with respirators. Likewise, r-MSSD decreased by 14.7% per IQR of $PM_{2.5}$ at 5-minute mean among workers without respirators but only decreased by 4.0% among workers with respirators.

Table 3 shows the results of associations of concurrent $PM_{2.5}$ with HRV indices estimated by the mixed-effects models stratified by smoking. With age, BMI, temperature and relative humidity being adjusted in all mixed-effects models, we found that $PM_{2.5}$ exposure was associated with HRV reduction for both smoking and non-smoking workers without respirators. No significant association of $PM_{2.5}$ with HRV reduction was observed among workers with respirators except Log10 r-MSSD in smoking workers.

We further assessed effect modification in mixed-effects models and found an effect modification of $PM_{2.5}$ by respirator usage (Table 4). Workers without respirators showed a decrease of 7.4% in Log_{10} SDNN, which was associated with an increased 5-minute mean $PM_{2.5}$. In contrast, workers with respirators showed no significant change in Log_{10} SDNN. Likewise, workers without respirators showed a decrease of 10.2% in Log_{10} r-MSSD by $PM_{2.5}$ exposure, but workers with respirators only showed a mild decrease of 3.5% in Log_{10} r-MSSD.

Discussion

Welding fume has been commonly measured as total dust or inhalable particles in past studies. However, fine particles, which can reach the alveoli, are more specific with regard to cardiopulmonary diseases and systemic particles exposure from welding fume¹⁴. Previous studies demonstrate the association of environmental exposure to $PM_{2.5}$ with decreased HRV in human subjects⁵⁻⁷. Recent studies further report the association between occupational exposure to $PM_{2.5}$, mainly from welding, and HRV changes in workers⁹⁻¹². The present study confirms that occupational exposure to $PM_{2.5}$ has comparable magnitudes of effects on decreasing HRV indices in workers. Magari *et al.*⁹ showed that SDNN decreased by 1.4% per 1 mg/m³ of concurrent $PM_{2.5}$ (-0.77 msec) among 39 boilermakers⁹. Cavallari *et al.*¹⁰ reported that total $PM_{2.5}$ exposure was associated with decline in night r-MSSD by 18.8% (-0.006 msec/µg/m³) among 26 boilermakers¹⁰.

In addition to the $PM_{2.5}$ effects on HRV indices, the present study shows respirator could modify the association between $PM_{2.5}$ and HRV. As the results of mixed-effects model with effect modifier showed (Table 3), workers without respirators had higher effects of $PM_{2.5}$ on HRV reduction compared to those in workers with respirators. This finding is the first one to demonstrate the protective effect of respirator on reducing $PM_{2.5}$ exposure and cardiovascular adverse effects. Our finding also provides further evidence to support that respirator can be the

	Log ₁₀ SDNN N = 11520	Log ₁₀ r-MSSD N = 11520	
Respirator usage			
Yes	-1.8 (-2.2, 0.4)	-3.5 (-6.8, -0.2)	
No	-7.4 (-9.8, -5.0)	-10.2 (-13.7, -6.7)	
P-value for interaction	0.03	0.04	

Table 4. Effect modification of association of heart rate variability with 5-minute mean $PM_{2.5}$ among 120 study participants. BMI, body mass index; $PM_{2.5}$, particulate matter less than or equal to $2.5 \,\mu m$ in diameter; r-MSSD, square root of the mean squared differences of successive intervals; SDNN, standard deviation of normal-to-normal intervals. ^aThe values are presented as percentage changes and 95% confidence interval for interquartile range changes after adjusting for age, body mass index, smoking, temperature and relative humidity in all models.

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last resort in controlling welding fume exposure to worker in the aspect of occupational safety and health management system^{15,16}.

The possible pathophysiological mechanism between $PM_{2.5}$ and autonomic alteration has been well discussed in previous studies. In brief, inhaled $PM_{2.5}$ may exacerbate the autonomic function of the heart via induced inflammation in lung and proinflammatory cytokine expression in cardiac macrophages¹⁷. The time course of $PM_{2.5}$ on HRV in workers at 5-minute mean is in agreement with the findings of previous studies among workers¹⁸, young adults¹⁹ and general population²⁰. It has been reported that fine particles can affect both sympathetic and parasympathetic nervous systems immediately. The biological mechanism is PM-induced activation of pulmonary neural reflexes secondary to autonomic alteration after PM inhalation²¹⁻²³.

Several limitations should be addressed in the present study. First, the measurement of $PM_{2.5}$ might not be representative of welding fume exposure in this study because it was monitored by only personal dust monitor. There might be unmeasured gaseous pollutants that could contribute to the observed HRV reduction. However, if the present findings were driven by gaseous pollutants, there would be no effect modification by respirator status. Therefore, the observed HRV reduction was less likely due to gaseous pollutants as gases travel freely through respirators. Second, the unmeasured meteorological variables, such as wind speed and wind direction, were likely to influence the level of personal $PM_{2.5}$ exposure²⁴. Such limitation might lead to exposure misclassification and bias the pollution effects on HRV reduction toward null²⁵. Third, we could not exclude the respiration's confounding effects on the association of personal $PM_{2.5}$ exposure with HRV reduction because our participants' physical activities and breathing patterns were not measured in the present study²⁶. Lastly, short-term reduction of HRV has not been associated with higher risk of cardiovascular disease clinically. Cohort study is needed to elucidate the effect of respirator on the relationship between welding fume and cardiovascular health.

Conclusion

The present study found that personal exposure to welding fume was significantly associated with decreased HRV. Such adverse cardiovascular effect was lower among welders with respirators than among welders without respirators. The use of a respirator is therefore beneficial for occupational health management and welder health improvement. Therefore, we encourage employers to provide suitable respirators and adequate training for employees.

Methods

Ethics. The Ethics Committee of the Taipei Medical University-Joint Institutional Review Board approved the study protocol. The methods were carried out in accordance with the approved guidelines. All subjects received written and oral information prior to inclusion and provided informed consent.

Study participants. We recruited 120 healthy male welding workers from a shipyard located in Taiwan as our study participants for this panel study in July and August in 2013 and 2014. The main duty of these welding workers was to weld all types of steel plates of varying sizes and shapes with electric welder. The company was obligated to provide respirators and training courses for all welding workers before they performed arc welding. The type of respirator was disposable activated-carbon facemask. We assigned a well-trained assistant to conduct eight-hour continuous personal PM_{2.5} exposure monitoring and HRV monitoring for each participant while working (from 09:00 am to 17:00 pm). Each participant's age, body mass index (BMI), smoking, work history, current health status, respirator usage and work-activity pattern, including sitting, walking, talking, welding, dining, etc. were obtained from a questionnaire by a professionally trained nurse. None of participants had hyperthyroidism, hypoxemia, acute cardiopulmonary failure and paced cardiac rhythm. They were informed of the objective of this study, the benefits and possible danger to health. The ethic committee of the Taipei Medical University Joint Institutional Review Board (Taipei, Taiwan) approved this study (TMU-JIRB No.: 201306041). An informed consent was obtained from each participant before the study embarked and the individuals were allowed to give up at any moment.

HRV monitoring. We performed continuous ambulatory electrocardiographic (ECG) monitoring for each participant while working by using a PacerCorder 3-channel device (model 461A; Del Mar Medical Systems

LLC, Irvine, CA, USA) with a sampling rate of 250 Hz (4msec). All ECG tapes were analyzed by using a Delmar Avionics model Strata Scan 563 (Irvine, CA, USA). Each 5-minute segment of normal-to-normal (NN) intervals was taken for HRV analysis. The time domain measurements of HRV were SDNN and r-MSSD. Each participant obtained approximately 12 successful segments of 5-minute HRV measurements per hour for data analysis.

Personal PM_{2.5} **exposure monitoring.** We conducted continuous monitoring of $PM_{2.5}$ and meteorological conditions for each participant while working. $PM_{2.5}$, temperature and relative humidity were measured continuously by a personal dust monitor (DUSTcheck Portable Dust Monitor, model 1.108; temperature and humidity sensor, model 1.153FH; Grimm Labortechnik Ltd., Ainring, Germany), which measured and recorded 1-min mass concentrations of $PM_{2.5}$ as well as temperature and relative humidity in the breathing zone. After monitoring, the raw data for 1-min PM_{2.5}, temperature and relative humidity were matched with the monitoring time of HRV for data analysis.

Statistical analysis. We applied mixed-effects models to examine the association of $PM_{2.5}$ with SDNN and r-MSSD for our study participants by running R statistical software version 2.15.1. The SDNN and r-MSSD were log_{10} -transformed to improve normality and stabilize the variance. We treated each participant's age, BMI, smoking (Yes vs. No), respirator usage as time-invariant variables, while 5-minute mean $PM_{2.5}$, 5-minute mean temperature, 5-minute mean relative humidity, log_{10} SDNN and log_{10} r-MSSD as time-varying variables in our data analysis. The outcome variables were log_{10} SDNN and log_{10} r-MSSD, and the exposure variables were 5-minute mean $PM_{2.5}$. We treated each participant as a random effect in our mixed-effects models. In further analyses, we investigated if $PM_{2.5}$ effects differed among smokers and non-smokers using mixed-effects models stratified by smoking.

Effect modification by respirators usage (Yes vs. No) was assessed in a separate mixed model by including interaction terms between $PM_{2.5}$ exposure and respirators usage among all workers. Minimizing Akaike's Information Criterion (AIC)¹³ was used as the criteria of model selection. The pollution effects are expressed as percent changes in HRV by an interquartile range (IQR) change in pollution levels for $PM_{2.5}$.

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Author Contributions

B.-C.H., I.-J.L., H.-C.C., C.-H.P. performed air sampling and heart rate variability monitoring, and wrote the manuscript. K.-J.C., designed research, performed air sampling, analyzed data, and wrote the manuscript.

Additional Information

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