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Field Study

Plasma Catecholamine Levels and Neurobehavioral Problems in Indian Firefighters

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Abstract: Plasma Catecholamine Levels and Neurobehavioral Problems in Indian Firefighters: Manas R. RAY, *et al*. Experimental Hematology Unit, Chittaranjan National Cancer Institute, India— Firefighting is a stressful and hazardous job. Persons engaged in firefighting are highly exposed to work-related stress as well as to smoke containing a host of chemicals potentially harmful to human health. In order to elucidate whether firefighting affects neuroendocrine and behavioral responses of firefighters, plasma catecholamine (CA) levels and the prevalence of neurobehavioral symptoms in 62 firefighters (all males, mean age 43 yr) and 52 control subjects matched for age and sex were examined in this study. Self-reported neurobehavioral symptoms data were obtained from a questionnaire survey and personal interview. Concentrations of epinephrine (E), norepinephrine (NE) and dopamine (DA) in plasma were measured by high-performance liquid chromatography with electrochemical detection. Compared with matched controls, the firefighters showed higher prevalence (p<0.05) of neurobehavioral symptoms such as burning sensation in the extremities, tingling and numbness, transient loss of memory, and depression, but no significant difference was recorded in the prevalences of anxiety, vertigo and dizziness. The firefighters demonstrated a more than two-fold (p<0.05) rise in plasma levels of E and NE, but the plasma DA level was relatively unchanged. Controlling age and smoking as possible confounders, firefighting was found to be associated with raised E (OR=2.15; 95% CI, 0.98–4.52), and NE levels (OR=2.24 95% CI, 1.22–3.61). In conclusion, the job of firefighting appears to be associated with stimulation of sympathetic activity and a rise in the prevalence of neurobehavioral symptoms. *(J Occup Health 2006; 48: 210–215)*

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Fire is one of the most serious problems that affect modern life. Firefighters are entrusted with the important task of putting out fires, saving materials and precious lives. However, the job of firefighting is stressful and hazardous in nature, and work-related stress may cause cardiovascular problems[1)], hemostatic abnormality[2)], musculoskeletal disorders[3)] and oxidative DNA damage[4)]. Firefighters work round the clock in shifts, and studies have shown that workers employed in 3-shift jobs suffer more from work-related stress than do day workers[5)]. In addition, fire produces a complex toxic environment that includes flame, heat, oxygen depletion, smoke and toxic gases. Smoke from synthetic polymers, which are increasingly used in buildings as furniture, decorative items, electric wiring covering, insulation etc., is more toxic and faster-acting than smoke of natural polymers like cotton and wood[6)]. During fire episodes, a number of toxic chemicals like hydrogen cyanide and hydrogen chloride are released from synthetic materials besides well known smoke constituents such as carbon monoxide, formaldehyde, acrolein, benzene , benzo(a)pyrene and respirable particulates, posing a chemical hazard to the firefighters[6–9)]. Therefore, in accomplishing their assigned duties, persons actively engaged in firefighting face health-impairing work stress and inhale a wide spectrum of combustion and pyrolysis products, many of which are potentially harmful to human health[7–10)].

Smoke inhalation, rather than burns, is the principal toxicity of fire among firefighters[5)] . A number of studies have been carried out on the health impact of smoke inhalation in firefighters, and several impairments including respiratory[10)], cardiovascular[11)] and genotoxic changes have been documented[12)]. It has also been reported that a substantial number of firefighters leave their job for health reasons[13)]. These investigations were centered primarily on physical health, leaving the

psychological and behavioral aspects of a stressful job like firefighting relatively uninvestigated. It seems important to mention in this context that an animal study showed brain damage following exposure to a high level of airborne pollutants[14]; and formaldehyde, a major component of smoke, impairs the function of the central nervous system in humans[15]. Moreover, work-related stress has been shown to affect the pattern of diurnal cortisol secretion[16]. In view of these reports, we were interested to know whether the firefighters suffer from neurobehavioral problems that could be attributed to their occupation. Accordingly, we examined the prevalence of neurobehavioral symptoms and plasma catecholamine (CA) levels in a group of firefighters working in Kolkata, India.

Materials and Methods

Subjects

A total of 114 adult male individuals volunteered for this study. Of these, 62 (mean age 45 yr) were fire service personnel of the twin cities of Kolkata (former Calcutta) and Howrah, in eastern India. They were actively engaged in firefighting for 10–37 yr and worked 8 h/d, 6 d/wk in the morning (8.00–14.00 h), evening (14.00–22.00 h), or night (24.00–8.00 h) shifts in rotation. The remaining 52 individuals were gender- and age-matched (mean age 44 yr) controls consisting of administrative staff of West Bengal Fire Service not engaged in fire fighting, and working 8 h/d (10.00–18.00 h), 6 d/wk for the last ten years or more. Only apparently healthy subjects who were not under medication for the last one month were enrolled in this study. Descriptive characteristics of the study populations are compared in Table 1. The Institutional Ethical Committee of Chittaranjan National Cancer Institute, Kolkata, approved the study protocol.

Self-reported neurobehavioral problems

The firefighters and the controls were interviewed in Bengali and Hindi (local languages) at their working places by the research staff. They were asked to furnish information regarding age, family, smoking and chewing habits, history of medication, type and duration of employment etc. In addition, a neurobehavioral symptom questionnaire, adopted from the subjective symptom questionnaire accompanying the World Health Organization Neurobehavioral Core Test Battery[17], Wechsler's memory scale[18], and Beck depression inventory[19] was administered to them. The questionnaire focused mainly on symptoms like burning sensation in the extremities (feeling of burn in distal and terminal portions of the body such as hand and foot), tingling (repetitive moving pin prick-like sensation), numbness (temporary loss of sensation), transient loss of memory (short-term memory loss, usually lasting for a few hours), depression (mental state with feelings of sadness, despair and discouragement), anxiety (unpleasant emotional state in anticipation of imagined danger), vertigo (an illusionary sensation that the body or surrounding environment is revolving), and dizziness (sensation of unsteadiness with a feeling of movement within the head, giddiness). A five-point rating scale using simple and clear words like 'never', 'rarely', 'sometimes', 'frequently' and 'very frequently' was used in the questionnaire to elicit a better response[20]. Afterwards, answers like 'never' and 'rarely' were considered as absence of that symptom, while responses like 'sometimes' 'frequently' and 'very frequently' were recognized as having such symptoms[20].

Plasma catecholamine (CA) assay

Venous blood (5-mL) was collected after obtaining informed consent in vacutainer tubes (Becton Dickinson,

Table 1. Characteristics of the study population

Variable	Control (n=52)	Firefighter (n=62)
Mean age in year (range)	44 (27–55)	45 (29–57)
Mean duration of service (range) in yr	19 (10–33)	21 (10–37)
Current smoker (%)	42.3	46.8
Ex-smoker (%)	1.9	3.2
Tobacco, betel quid chewer (%)	25.0	27.4
Use of mosquito repellant at home (%)	96.1	95.2
Cooking fuel at home (%)		
Liquified petroleum gas	90.4	91.9
Kerosene	5.8	4.8
Biomass	3.8	3.2
Food habit (%)		
Vegetarian	5.8	6.4
Mixed	94.2	93.5

Table 2. Prevalence (%) of neurobehavioral symptoms

Symptom	Control (n=52)	Firefighter (n=62)
Burning sensation in extremities	11.5	54.8*
Tingling / numbness	12.9	37.1*
Transient loss of memory	21.1	72.6*
Depression	28.8	51.6*
Anxiety	38.4	40.3
Vertigo/dizziness	13.4	16.1

*: $p<0.05$ compared with control in χ-square test

USA) containing K_3EDTA as an anticoagulant. The control subjects and firefighters were requested to rest in the supine position in a relaxed environment for 30 min before blood drawing to measure basal plasma CA level[21]. For better comparison with control subjects, blood samples were collected from firefighters in the middle of the morning shift usually on day 2–4 (Tuesday–Thursday) of every week at a fixed time (10.30–11.30 h) at their respective working places. Plasma was separated by the standard procedure. NE, E and DA were measured by high performance liquid chromatography with electrochemical detection using established methodology[22]. In brief, 200 μL of 3, 4 dihydroxybenzylamine prepared as 0.1 μM solution in 0.1 M perchloric acid (containing 400 μM sodium metabisulphite) was added as internal standard to 2 mL of plasma samples. Then 400 μL of 0.5 M tris HCl (pH 8.6) and 20 mg of activated alumina were added and the contents of the tube were shaken gently for 15 min. Following centrifugation at 600 × G for 2 min, the supernatant was removed and the catecholamines were eluted from alumina into 50 μL of 0.6 M perchloric acid containing 400 μM sodium metabisulphite. The mixture was centrifuged at 800 × G for 30 min and 20 μL of the supernatant was injected into a reverse phase high performance liquid chromatographic column (Waters Novapak C 18 column, 3.9 × 150 nm, coupled to an electrochemical detector, Waters 464 pulsed ECD; Waters, USA). The mobile phase consisted of 780 mL of acetate-citrate buffer pH 5.2; 220 mL of methanol and sodium octane-1 sulphonate (5 mM) were filtered through 0.45 μM Millipore filter and degassed prior to use; and the flow rate was set at 1.2 mL/min.

Statistical analysis

The results were statistically analyzed by Student's *t* test and the χ-square test, and $p<0.05$ was considered significant. Logistic regression models were used to calculate the adjusted odds ratio (OR) and the 95% confidence interval (95% CI) for individual symptoms after controlling for the potential confounders. The analysis was done with Systat 9.0 (SPSS, Chicago, IL, USA) statistical package.

Results

Prevalence of neurobehavioral symptoms

The prevalence of self-reported neurobehavioral problems is summarized in Table 2. Transient loss of memory, reported by 73% of firefighters, was 3.5-times more prevalent than among the controls. Significant increases ($p<0.05$) were also noted in the prevalences of burning sensation in the extremities, tingling, numbness, and depression. However, we did not find any significant change in the prevalence of anxiety, vertigo or dizziness. Controlling for age and smoking as possible confounders, firefighting was found to be associated with increased prevalences of transient loss of memory (odds ratio [OR]=2.23; 95% confidence interval [95% CI], 1.23–4.12), burning sensation in extremities (OR=3.87; 95% CI, 2.16–5.34), tingling or numbness (OR=1.95; 95% CI, 1.10–3.21), and depression (OR=1.23; 95% CI, 0.73–2.05).

Changes in plasma CA levels

The firefighters showed a 2.4-fold increase in plasma E level (Fig. 1). They had 1.35 ± 0.81 (SD) nmol E per liter of plasma (range 0.52–2.94 nmol/L) against a control value of 0.56 ± 0.22 nmol/L (range 0.05–1.57 nmol/L). Likewise, a 2.7-fold rise was recorded in plasma NE among the firefighters (Fig. 1). They showed 8.74 ± 3.04 nmol/L (range 2.3–16.0) plasma NE compared with 3.22 ± 0.78 nmol/L (range 0.24–5.7) in controls. After controlling age and smoking as possible confounders, the job of firefighting was found to be associated with rises in plasma E (OR=2.15; 95% CI, 0.98–4.52), and NE (OR=2.24 95% CI, 1.22–3.61) levels. In contrast, the concentration of DA in plasma remained relatively unchanged in firefighters. For example, compared with 2.05 ± 0.03 nmol/ L (range 0.25–4.32) plasma DA in controls, the firefighters had 1.92 ± 0.2 nmol/L (range 0.17–3.52) of DA, showing a modest decline of 6% ($p>0.05$).

A subject's period of employment as an active firefighter was used to estimate the quantum of

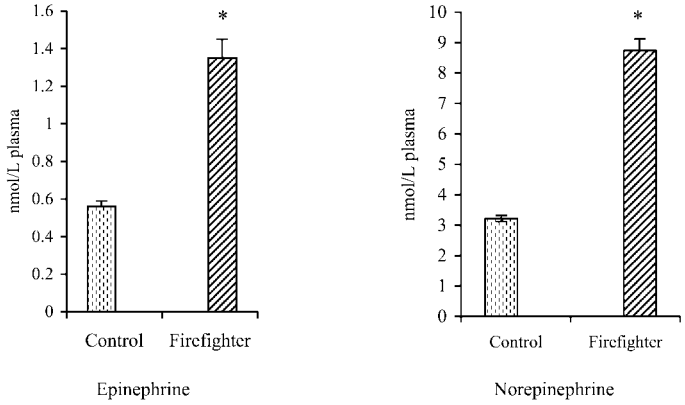

Fig. 1. Plasma epinephrine and norepinephrine levels of firefighters and their matched controls. The bars represent standard error of mean, and *, $p<0.05$ compared with respective control values.

Table 3. Plasma catecholamine levels (mean ± S.D) of firefighters with respect to duration of employment

	10–19 yr service (n=24)	20–37 yr service (n=38)
Epinephrine (nmol/L)	0.90 ± 0.7	1.63 ± 1.2*
Norepinephrine (nmol/L)	6.12 ± 3.5	9.75 ± 3.9*
Dopamine (nmol/L)	1.83 ±0.8	1.97 ± 0.6

*: $p<0.05$ compared with 10–19 yr service

combustion fumes and chemicals he was likely to have been exposed to as well as the duration of this exposure. This was categorized into two broad groups: Group I, (moderate exposure) with <20 yr of employment, and Group II (high exposure) with 20–37 yr of employment. A comparison of plasma CA concentrations in firefighters in these two groups revealed a more intense rise in E and NE levels in Group II, and the difference in E and NE concentrations between these two exposure groups was statistically significant ($p<0.05$). However, no such difference was found in the plasma DA level (Table 3).

Discussion

The present report documents alterations in plasma CA levels and higher prevalences of some neurobehavioral symptoms in firefighters. The plasma concentration of NE generally varies between 0.09–1.8 nmol/L in the general population[21], although a higher upper limit (3.54 nmol/L) has been reported by some investigators[23]. The latter value is closer to the mean plasma NE level found in the control subjects of this study. Compared to these, the plasma NE level in firefighters was significantly increased. Since plasma NE is used as a measure of sympathetic activity[21], stimulation of sympathetic activity in firefighters is indicated, but the mechanism by which both E and NE levels are increased in firefighters is currently unknown. Smoking is a well known enhancer of plasma CA[24]. Likewise, smoke exposure during fire episodes might raise plasma CA. While the smoke component(s) responsible for this activity is as yet unknown, carbon monoxide can be excluded, as it has no significant effect on plasma CA levels[25]. Besides smoke exposure, higher plasma CA in firefighters compared to their colleagues with office jobs can be attributed to the more strenuous and stressful job of firefighting that often requires standing for long hours. Support for this argument comes from a report that upright posture such as standing for 5 min increases the plasma NE level by 2- to 3-fold, while strenuous exercise and mental stress cause significant increases in both plasma E and NE levels[15, 18]. Emotional or physical stress can increase plasma E up to 8-fold, whereas physical stress elevates plasma NE level more acutely than emotional stress[26]. Therefore, elevated plasma E and NE levels in firefighters could be attributed, in part, to occupation-related stress.

The rise in the prevalence of neurobehavioral symptoms seen in firefighters in this study could be the fall-out of neurological changes. Behavior is an outcome of multiple mechanisms within the central nervous system (CNS), and changes are sensitive indicators of nervous system dysfunction. It is now well established that ultra-fine particles present in combustion products cross the

alveolar-capillary barrier, reach the blood stream[27], and influence the activities of all vital organs including the CNS[14]. The twin cities of Kolkata and Howrah where the study was conducted have very high air pollution levels (annual average PM_{10} level> 200 $\mu g/m^3$). Therefore, it is an interesting proposition to explore whether cumulative exposures to combustion products along with high background air pollution level mediate changes in CNS function that, in turn, result in neurobehavioral symptoms.

The net impact of elevated plasma CA in firefighters might be an alteration of the activity of all major organ systems. CA stimulates vasoconstriction and increases heart rate and cardiac output. Cardiac stimulation increases myocardial oxygen consumption, a major factor in the pathogenesis of myocardial ischemia. Indeed, a rise in plasma NE is considered a potential cardiovascular risk[21] which is common among firefighters[11]. A rise in plasma E and NE might also alter the immune function by increasing the number of natural killer cells, T-suppressor/cytotoxic cells and total WBC, and by depleting T-helper cells and B cells in peripheral blood[28, 29]. In essence, this study, the first of its kind in India, has clearly demonstrated stimulation of the sympathetic nervous system and increased prevalence of several neurobehavioral symptoms in firefighters with a minimum of 10 year's experience as active firefighters in at least 4 episodes of fire per week. The consequence of these findings could be far reaching, because the physiological and behavioral changes may interfere with job tasks resulting in costly injuries and loss of productivity[30].

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