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Physical and psychological stress along with candle fumes induced-cardiopulmonary injury mimicking restaurant kitchen workers

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ABSTRACT

Restaurant kitchens are work areas where involve strict and hierarchal environments that promote opportunity for bullying and workplace aggression and violence. These physical and psychological stress and fumes ultimately trigger severe occupational stress by disrupting the body's homeostasis that might induce cardiopulmonary injury. The study aimed to investigate the physical and psychological stress and candle fumes on cardiopulmonary injury in an animal model mimicking a restaurant kitchen worker. Social disruption stress (SDR) mice were exposed to scented candle fumes (4.5 h/d, 5 d/wk) in an exposure chamber for 8 weeks. Exposure to burning scented candles failed to reduce serum corticosterone level and increased proinflammatory cytokines levels and NF-ƙB activity in the lung. In addition, burning scented candle fumes synergistically increased SDR-induced serum LDH, CPK, CKMB levels, proinflammatory cytokines production as well as NF-ƙB activation in the lung and heart. Further, cardiac HIF-1α and BNP levels were also increased. We conclude that the physical and psychological stress along with candle fumes might induce cardiopulmonary injury in mice. These results could be extrapolated to restaurant kitchen workers.

1. Introduction

Occupational stress is defined as “a psychological syndrome of emotional exhaustion, depersonalization and reduced personal achievement that can occur among individuals who work with other people” (Maslach, 1993). Several work features lead to stress, such as long work hours, high levels of responsibility, multiple tasks (DeFraia, 2015). In addition, conflicts between staff and the atmospheres are a critical contributor to chronic stress (Colligan and Higgins, 2006). The chef is one of the famous work categories exposed to a high level of occupational stress (Cerasa et al., 2020). Work is more important for the chefs, and they are less capable of mentally distancing themselves from their work (Hartung et al., 2010). Physical violence and psychological abuse are widespread in kitchens were reported (Johns and Menzel, 1999). Physical violence may vary from kicking, throwing objects to burning with hot food. Psychological stress includes the pressure to conform to the strict hierarchy of authority in place, working under time pressure during peak periods, managing discontented customers (Hartung et al., 2010).

Scented candles are used in hotels, restaurants, and spas as room fresheners and aromatherapy to provide psychological relief with a healing effect (Bagheri-Nesami et al., 2014). Scented candles are only one source of volatile organic compounds, semi-volatile organic compounds, or particulate matters in the indoor environment (Sarigiannis et al., 2011; Isaacs et al., 2013). Candle burning affects indoor ultrafine particle concentrations in homes and restaurants (Neuberger et al., 2013; Deffner et al., 2016). Studies found the human health risk associated with scented candle fumes (VITO, 2006; VITO, 2008; Petry et al., 2013; Petry et al., 2014).

To date, no study has been undertaken to investigate the occupational restaurant stress along with its indoor environmental exposure to burning candles in restaurant workers in inducing cardiopulmonary injury. There is no animal model available to represent the exact restaurant kitchen worker's physical and psychological stress. The Social Disruption stress (SDR) mice model was adopted to mimic restaurant kitchen workers' occupational physical and psychological stress. Further, under SDR, mice were exposed to controlled scented candle fumes to investigate cardiopulmonary injury.

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2. Materials and methods

2.1. Animals

Male 7–8 weeks old C57BL/6 mice (N = 8) were purchased from the Animal Center of National Cheng Kung University. Animals were given a pellet feed diet and water *ad libitum*. Animals were maintained on a 12-hour light–dark cycle at a controlled temperature (25 °C). The animal care and experimental protocols were followed as per nationally approved guidelines (IACUC No.99054).

2.2. Experimental Design

Mice were divided into four groups of eight each. Group I served as untreated healthy controls. Group II underwent SDR (1 h/d, 3 d/wk) for 8 weeks. Group III mice exposed to scented candle fumes (4.5 h/d, 5 d/wk) for 8 weeks. Group IV mice exposed to SDR (1 h/d, 3 d/wk) followed by candle fumes (4.5 h/d, 5 d/wk) for 8 weeks. After 8 weeks, mice were killed, and blood and lung, heart tissues were collected for biochemical analysis (Fig. 1).

2.3. Social disruption induction

The social stress model is based on the repetitive social defeat experience of group-housed male mice in their home cage exposed to daily confrontations with a violent intruder mouse. An aggressive male C57BL/6 male mouse 3 months older compared to the experimental animals were used. Intruder mouse was individually housed over months to induce high levels of offensive agonistic behavior such as an attack, chase, and tail ratting against unknown mice. Every day at the start of the active dark period, an intruder mouse was introduced into a cage with resident mice. The intruder attacked the unknown resident mice within the first 5 min of the confrontation, and the resident mice displayed submissive behavior such as flight, defensive upright posture, retreat, and crouch. The intruder mice were replaced if they did not display offensive agonistic behavior against the resident mice. After 1 h of confrontation, the intruder mice were removed from the residents' cages. The stress model was performed three days every week for eight weeks (Curry et al., 2010).

2.4. Scented candle exposure

Commercially available scented candles were used. The same type of scented candles was used throughout the study. An exposure chamber was established to provide a stable operating environment to expose the mice to scented candle fumes. The chamber was made of acrylic and Teflon and divided into three parts: air inlet end, candle burning area (volume 50 cm × 50 cm × 50 cm), and exposed area (volume 40 cm × 40 cm × 40 cm). The inlet side provides a steady flow of air (including humidity and inlet airflow) for the scented candles to the burn test space and the exposure space, and the supply of air within the exposure chamber does not change. The chamber is connected to an external air compression system with a diffusion dryer, activated carbon filter, and a high-efficiency particulate air filter to control the ventilation rate of indoor air exchange rate 1.5 ACH (air exchange rate). A humidifier (Nafion® FC 125, Perma) was used to maintain the 70% humidity of the exposure chamber. In addition, CO_2, O_2, and CO concentrations were measured in the scented candle fumes exposed area to confirm that the mice were not exposed to an anoxic environment. Aluminum honeycomb panels were used in the front end of the chamber for uniform distribution of scented candle fume exposure from burning space to exposure space. The combustion test space mainly provides stability for burning scented candles, and the mixing space serves as space for mixing pollutant discharge. Scented candle fumes are emitted in exposure space for animal exposure (Fig. 2A). After stabilizing the humidity and air exchange rates, the mice were placed on the exposure area for 4.5 h daily for 5 days a week for 8 weeks. The stability and homogeneity of the scented

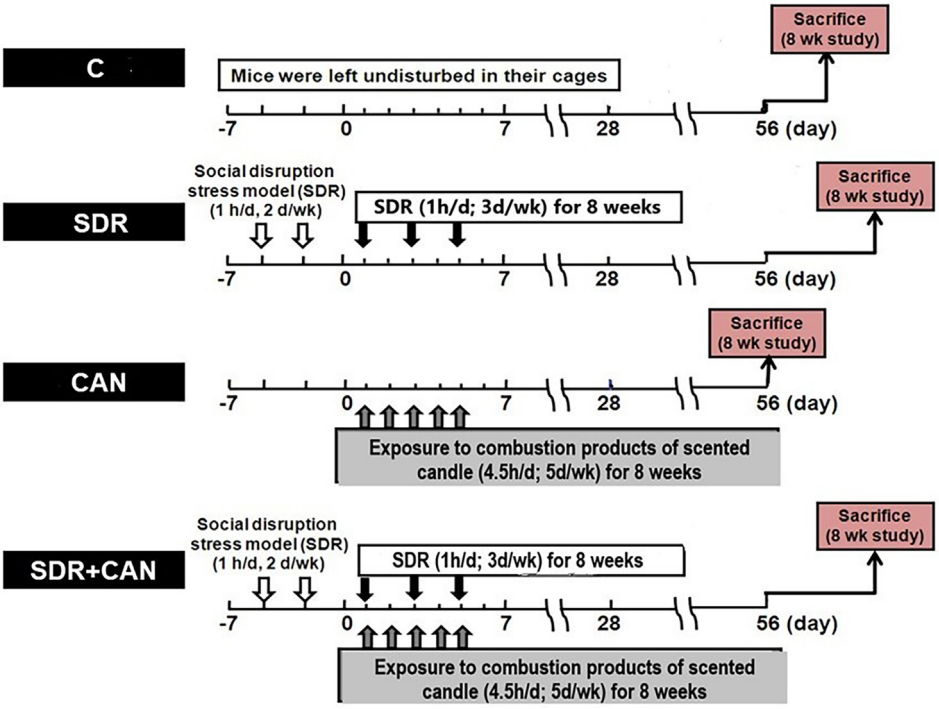
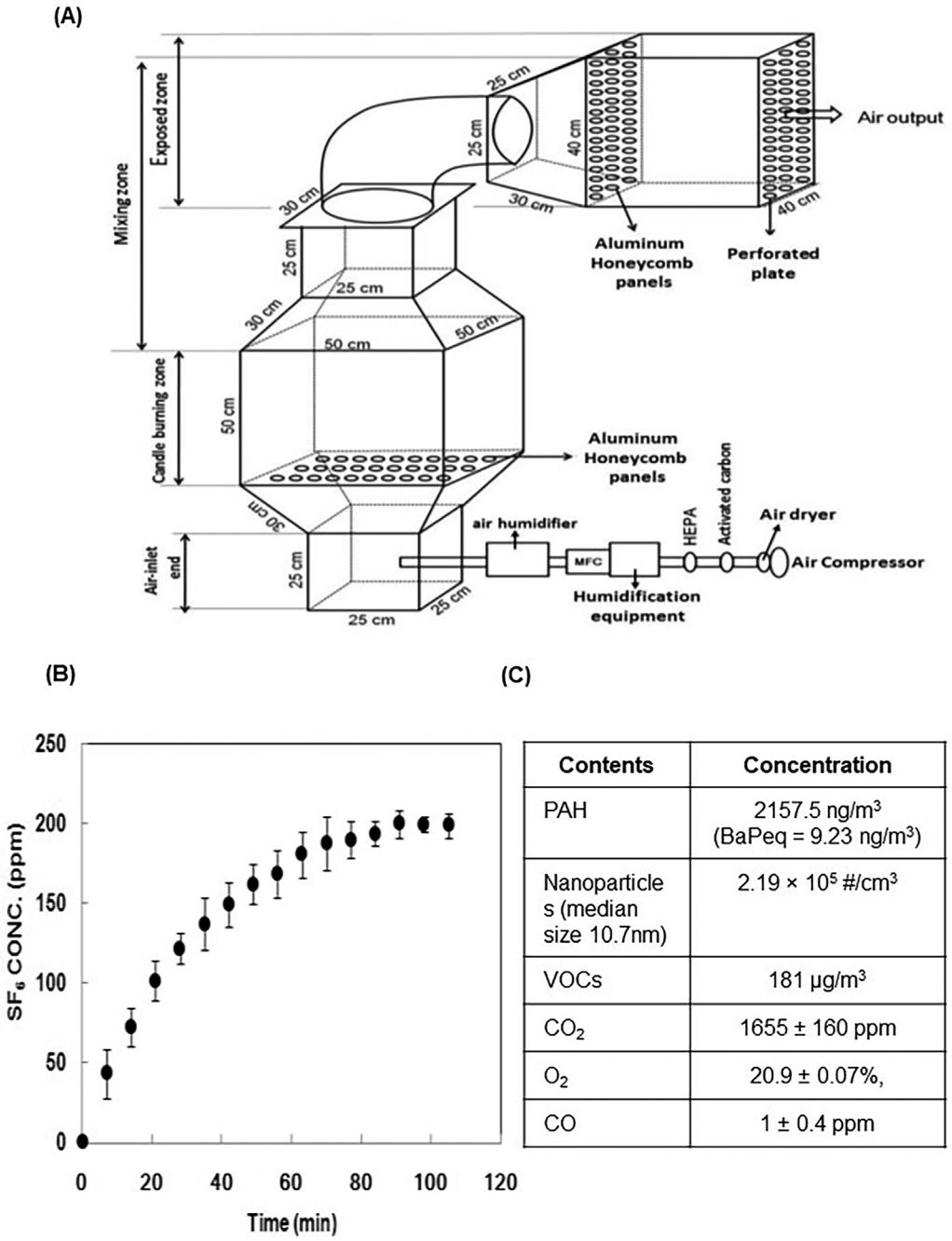


Fig. 1. Experimental Design. Mice were divided into four groups. Control group (C): mice were left undisturbed in their cages; SDR group (SDR): mice were subjected to social disruption stress; Candle group (CAN): mice were exposed to the scented candle fumes; and social disruption stress plus candle group (SDR + CAN): mice were exposed to scented candle after social disruption stress challenged.



Contents	Concentration
PAH	2157.5 ng/m^3 (BaPeq = 9.23 ng/m^3)
Nanoparticles (median size 10.7nm)	2.19 × 10^5 #/cm^3
VOCs	181 μg/m^3
CO_2	1655 ± 160 ppm
O_2	20.9 ± 0.07%,
CO	1 ± 0.4 ppm

Fig. 2. Exposure chamber and uniformity and stability testing.

candle exposure chamber were measured (model 1302 Photoacoustic Multi-gas Monitor and model 1309 Multipoint Sampler, Innova AirTech Instruments, DK-2750 Ballerup, Denmark) using a tracking gas (SF6). The primary air pollutants PAHs, VOCs, and nanoparticles emitted from aromatic candles were measured (Fig. 2B,C).

2.5. Blood biochemical analysis

Mice were anesthetized using pentobarbital sodium (10 mg/kg), 1 mL of blood was collected from the hepatic portal vein in a serum separation tube. After 30 min, serum was separated by centrifugation at 15,000 rpm for 10 min at 4 °C. Cardiac dysfunction was assessed by measuring the level of LDH, CPK, and CKMB in serum using a biochemistry analyzer (Fujifilm Dri-Chem 3500s; Fujifilm, Kanagawa, Japan). Fifty microliters of serum were used to measure corticosterone levels using a mouse corticosterone ELISA kit (Cayman Chemicals, Inc., MI, USA).

2.6. Broncho-Alveolar lavage fluid (BALF)

Mice were anesthetized using pentobarbital sodium (10 mg/kg), the skin from the jaw to thoracic cavity was cut open. The trachea was opened by pulling the neck muscle layer. A blunt 19 G needle was inserted near the cut of the larynx and tightened the needle to the trachea using a switcher thread. Sterile PBS (1 mL) was injected slowly into the lungs and flushed by pumping in and out, repeating three times, and the solution was removed.

2.7. Estimation of cytokines levels

BALF was centrifuged for five minutes (2000 rpm, 4 °C), and 50 μL of re-suspended supernatant was used. Heart and lung tissue 30 mg each were homogenized in added Milli Q water (10:1, w/v). The homogenate was centrifuged at 12,000 rpm for 30 min at 4 °C, and 50 μL of homogenized supernatant was used. Mouse cytokine duoset ELISA kit (R&D System, Inc., Minneapolis, MN) was used to measure TNF-α, IL-1β, and IL-6 levels, and the absorbance was measured at 450 nm with an ELISA reader.

2.8. NF-ƙB analysis

Heart and lung tissue (30 mg) were used for analysis. A nuclear and cytoplasmic extraction kit (Pierce Biotechnology Inc. Rockford, IL) was used to extract the nuclear protein. NF-ƙB p65 transcription factor kit (Pierce Biotechnology Inc. Rockford, IL) was used to measure NF-ƙB levels using 20 μL of nuclear protein. Fluoroskan ascent FL microplate fluorometer and luminometer (Pierce Biotechnology Inc. Rockford, IL) under dark conditions were used for the measurement.

2.9. Plasma BNP level analysis

Mice were anesthetized with pentobarbital sodium (10 mg/kg), 1 mL of blood was collected from the hepatic portal in a collection tube containing K_2 EDTA anticoagulant. After 30 min, plasma was separated by centrifugation at 15,000 rpm for 10 min at 4 °C. Mouse BNP-45 ELISA kit (Phoenix Pharmaceuticals Inc. CA, USA) measured BNP levels at 450 nm with an ELISA reader.

2.10. Heart HIF-1α analysis

A heart tissue of 30 mg was used for HIF-1α analysis. Nuclear and cytoplasmic extraction kits (Pierce Biotechnology Inc. Rockford, IL) extract the nuclear protein. Mouse HIF-1α transcription factor assay kit (Cayman Chemical Inc. MI, USA) was used, and the absorbance was measured at 450 nm with an ELISA reader to measure the HIF-1α levels.

2.11. Histopathological analysis of lung and heart tissue

A small piece of lung and heart tissues was placed in 10% buffered formalin. The tissues were processed and fixed in paraffin blocks. Five micrometer thick sections were made and stained with Hematoxylin and Eosin (H&E). The mounted tissues were observed under a microscope (magnification: 100×) for pathological changes.

2.12. Statistical analysis

The statistical analysis was done using the SPSS v. 17 software (SPSS Inc., IL, USA). All the data were presented as mean ± SD. One-way ANOVA followed by Fisher's Least Significant Difference (LSD) methods was used to compare groups. $P < 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Effect of scented candle fumes on social disruption stress-induced corticosterone level

Serum corticosterone is a measure of psychological and physiological stress. Serum corticosterone level was increased significantly ($P < 0.05$) in the SDR group relative to the control group. However, exposure to the scented candle did not significantly ($P < 0.05$) reduce the serum corticosterone level induced by SDR (Fig. 3).

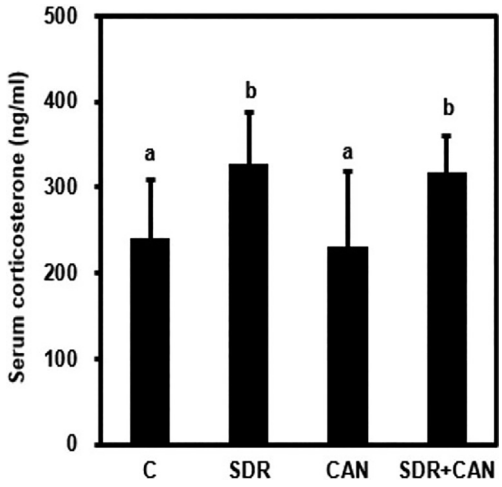


Fig. 3. Effect of exposure to scented candle fumes and SDR on serum corticosterone levels. Four groups were referred to as Fig. 1 legend. Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

3.2. Effect of scented candle fumes on social disruption stress-induced inflammation in BALF, lung and heart tissues

Cardiopulmonary injury is characterized by inflammatory reactions related to cytokines and the activity of transcription factor NF-κB. Both lung and BALF; SDR group, a candle alone and SDR + candle group showed significant ($P < 0.05$) increase in TNF-α, IL-1β, and IL-6 compared to control. In heart tissue, the SDR group and SDR + candle group showed a significant ($P < 0.05$) increase in TNF-α, IL-1β, and IL-6 compared to the control and candle-alone group. However, in BALF, lung, and heart tissues, the SDR + candle group showed a significant ($P < 0.05$) in TNF-α, IL-1β, and IL-6 than the SDR group and candle-alone group (Fig. 4A–I). NF-κB activity was found to increase in the SDR group, a candle alone, and SDR + candle group in lung tissue, whereas it increased only in the SDR group. However, the SDR + candle group significantly ($P < 0.05$) increased NF-κB activity than the SDR group and candle-alone group in lung and heart tissues (Fig. 5).

3.3. Effect of scented candle fumes on social disruption stress-induced cardiac function and plasma BNP level and heart HIF-1α

LDH, CPK, and CKMB levels were significantly ($P < 0.05$) increased in the SDR group and SDR + candle group compared to control and candle alone (Fig. 6). Except in control and candle alone groups, the plasma BNP and heart HIF-1α were significantly increased in SDR + candle groups (Fig. 7).

3.4. Effect of scented candle fumes on social disruption stress-induced cardiopulmonary injury

SDR group, a candle alone, and SDR + candle group depicted lung injury relative to control. However, the SDR + candle group showed significant ($P < 0.05$) damage than the SDR and candle-alone groups. Lung injury is characterized by infiltration of white blood cells in the interstitium and alveolar compartments, pulmonary edema, and mild-to-moderate interstitial thickening. SDR + candle group showed severe interstitial thickening and thickening of the bronchial cartilage (Fig. 8). However, no significant histopathological changes were observed in the heart tissue (Data not shown).

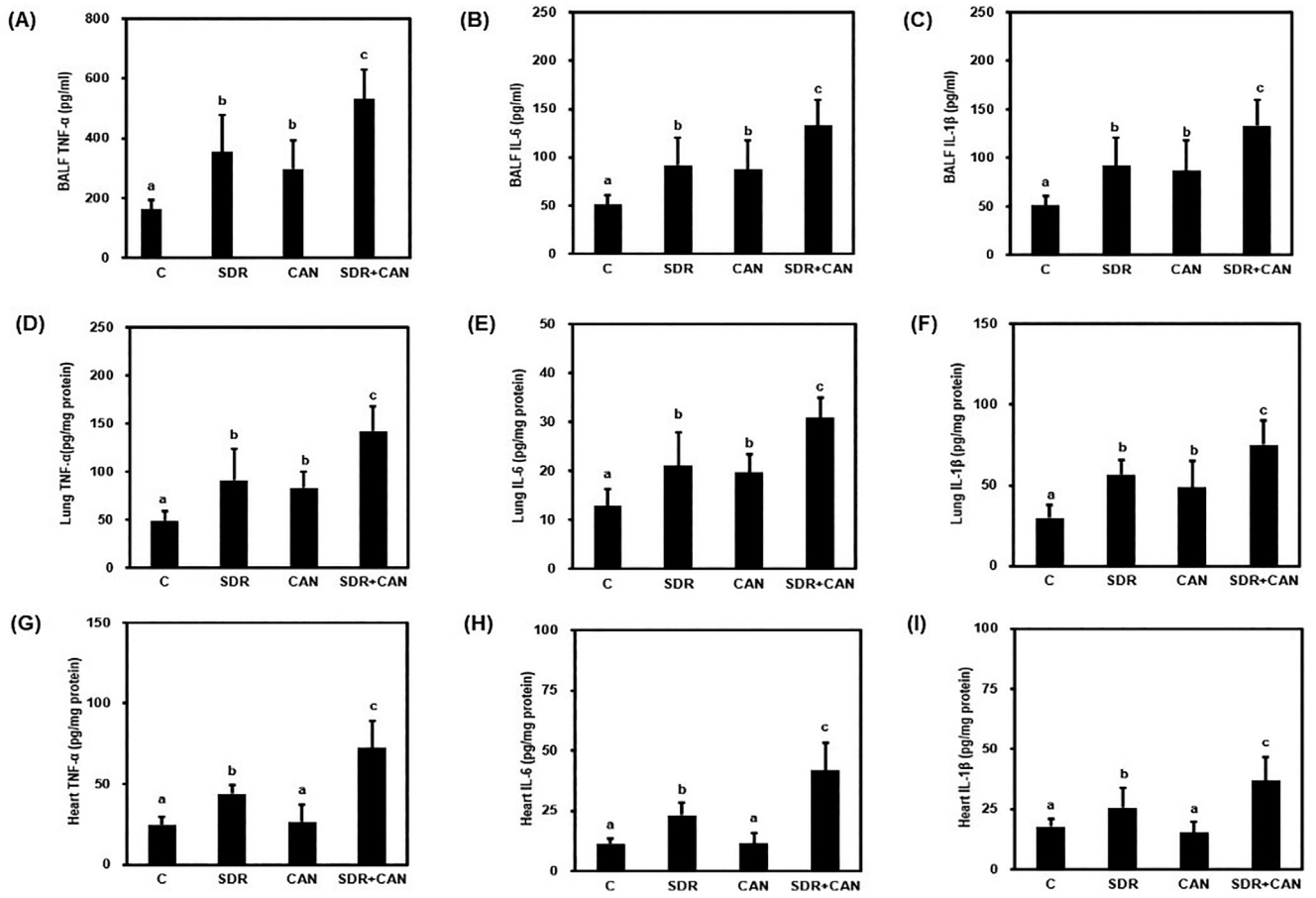


Fig. 4. Effect of exposure to scented candle fumes and SDR on proinflammatory cytokines in BALF, lung, and heart tissues. Four groups were referred to as Fig. 1 legend. The levels of TNF-α, IL-6, IL-1β in BALF (A–C), lung tissue (D–F), and heart tissue (G-I) were measured. Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

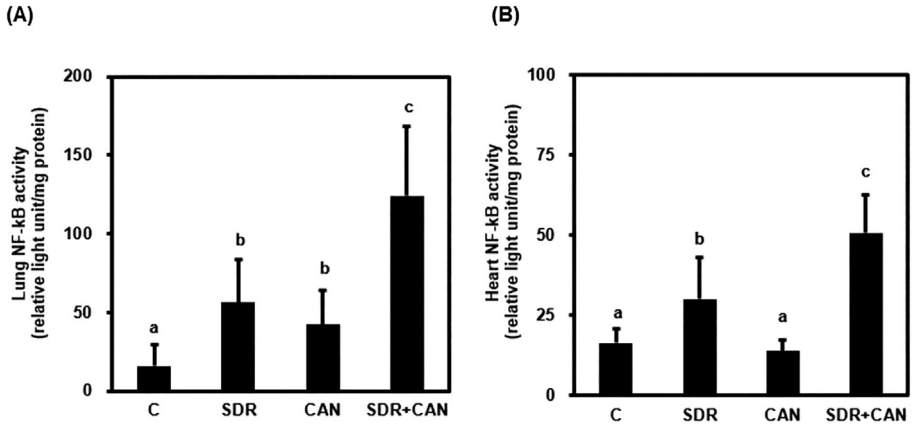


Fig. 5. Effect of exposure to scented candle fumes and SDR on transcription factor NF-κB activity in lung and heart tissues. Four groups were referred to as Fig. 1 legend. Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

4. Discussion

We found that physical and psychological stress, along with candle fumes, induced cardiopulmonary injury in mice. Although there is a general acceptance that scented candles often used in hotels, spas, and restaurants play an essential role in calming effect or reducing stress, in the present study, scented candles and social disruption stress did not reduce corticosterone levels.

SDR and candle exposure significantly increased proinflammatory cytokines. As a result of chronic stress, increasing the circulating glucocorticoids is associated with excessive cytokine and proinflammatory responses. Glucocorticoids regulate gene expression through interaction with other transcription factors NF-κB, thereby increasing proinflammatory cytokines such as IL-1, IL-6, and TNF (Sternberg, 2006). SDR increased neutrophils within the lungs by two-fold. The neutrophils were in an activated state and increased inflammatory

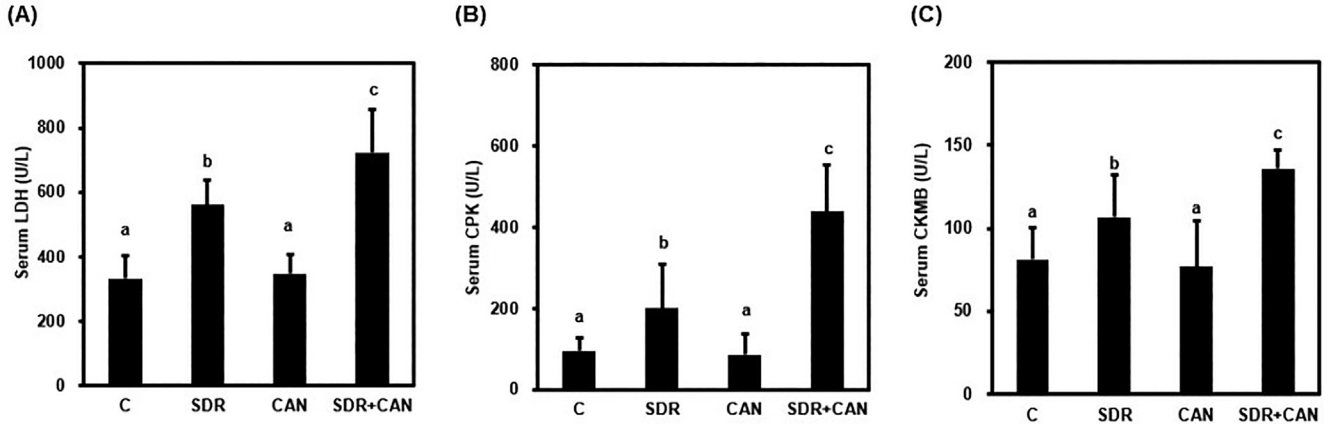


Fig. 6. Effect of exposure to scented candle fumes and SDR on cardiac marker levels in serum. Four groups were referred to as Fig. 1 legend. Cardiac dysfunction was assessed by LDH (A), CPK (B), and CKMB (C). Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

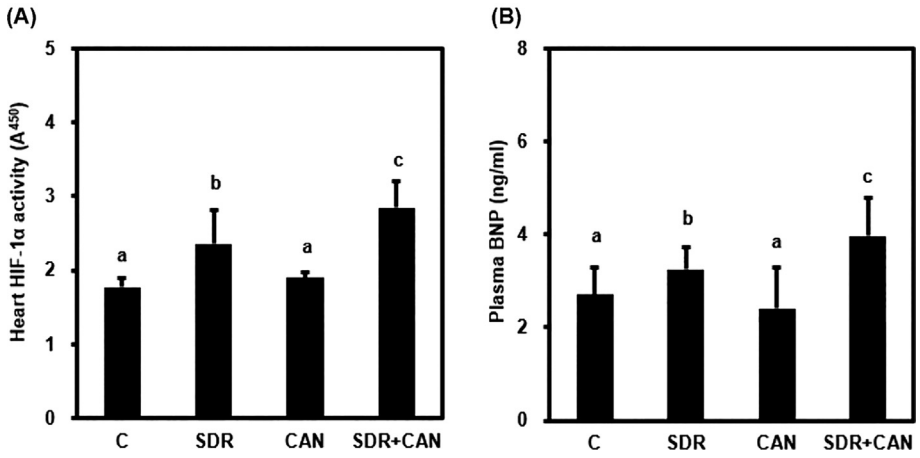


Fig. 7. Effect of exposure to scented candle fumes and SDR on cardiac hypoxia. Four groups were referred to as Fig. 1 legend. Cardiac hypoxia was assessed by the levels of heart hypoxia-inducible factor 1α (HIF-1α) activity (A) and plasma β-type natriuretic peptide (BNP) (B). Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

cytokine, IL-1β, in the lungs of SDR mice (Nishikori, 2005; Verstrepen et al., 2008). Burning scented candles indoors produces harmful substances such as PAHs and VOCs (NCA, 1999). These air pollutants can cause inflammation that may lead to coronary artery heart disease or chronic obstructive pulmonary disease (Ware and Matthay, 2000; Gan et al., 2004; Barnes, 2008; Bringardner et al., 2008). Proinflammatory cytokines may alter pulmonary vascular permeability by disrupting the cytoskeleton, interrupting tight junctions between epithelial cells, and altering cellular ion channels leading to pulmonary edema (Eisenhut, 2011). In the present study, corticosterone levels in the blood increased and subsequently triggered the inflammatory responses by increased production and release of TNF-α, IL-6, and IL-1β and enhanced the NF-κB activation and expression through a positive feedback mechanism, thereby enhancing the inflammation in the lungs.

In the heart of SDR and SDR + candle exposed mice, a significant increase in the expression of HIF-1α, plasma BNP, NF-κB, and proinflammatory cytokines inducing inflammation; however, no apparent myocardial injury was observed in histology. Stress causes ventricular wall tension or increased ventricular pressure, leads to myocardial oxygen demand, ultimately causing myocardial hypoxia. Myocardial hypoxia induces the activation of HIF-1α and synthesis of HIF-1α heterodimers that bind to specific HRE sequence, and in turn, activate the downstream gene target BNP and NF-κB leading to the release of BNP into the blood and inducing an inflammatory response (Bateman et al., 2007; Weidemann et al., 2008; Casals et al., 2009). IL-1β and TNF-α stimulate the activation of NF-κB and increase the expression of HIF-1α by positive feedback, thereby enhancing myocardial hypoxia (Weidemann et al., 2008; Jiang et al., 2010). Exposure to indoor air pollutants such as candle burning and cooking is associated with a more significant burden on the heart, and mechanisms of inhalation-mediated cardiovascular toxicity include activation of proinflammatory pathways (Simkhovich et al., 2008). Although all the biochemical and inflammatory changes were observed, they were not reflected in the myocardial tissue level, and it may be because the exposure duration is not long enough. However, further investigation is needed to confirm this.

In the present study, we evaluated the role of SDR in combination with exposure to scented candles as generally accepted to reduce stress. However, the combined SDR and scented candle exposure were found to escalate the stress level. This stress escalation might be due to the cardiopulmonary inflammatory response of the stress and candle fumes, which could be directly related to restaurant workers. Physical and psychological stress and candle fumes induced-cardiopulmonary injury in mice can be extrapolated to restaurant workers. Restaurant kitchen abuse, both physical and psychological, might be an expected part of the culture of a commercial kitchen and is supported by both historical and social structures (Bloisi and Hoel, 2008). Restaurant

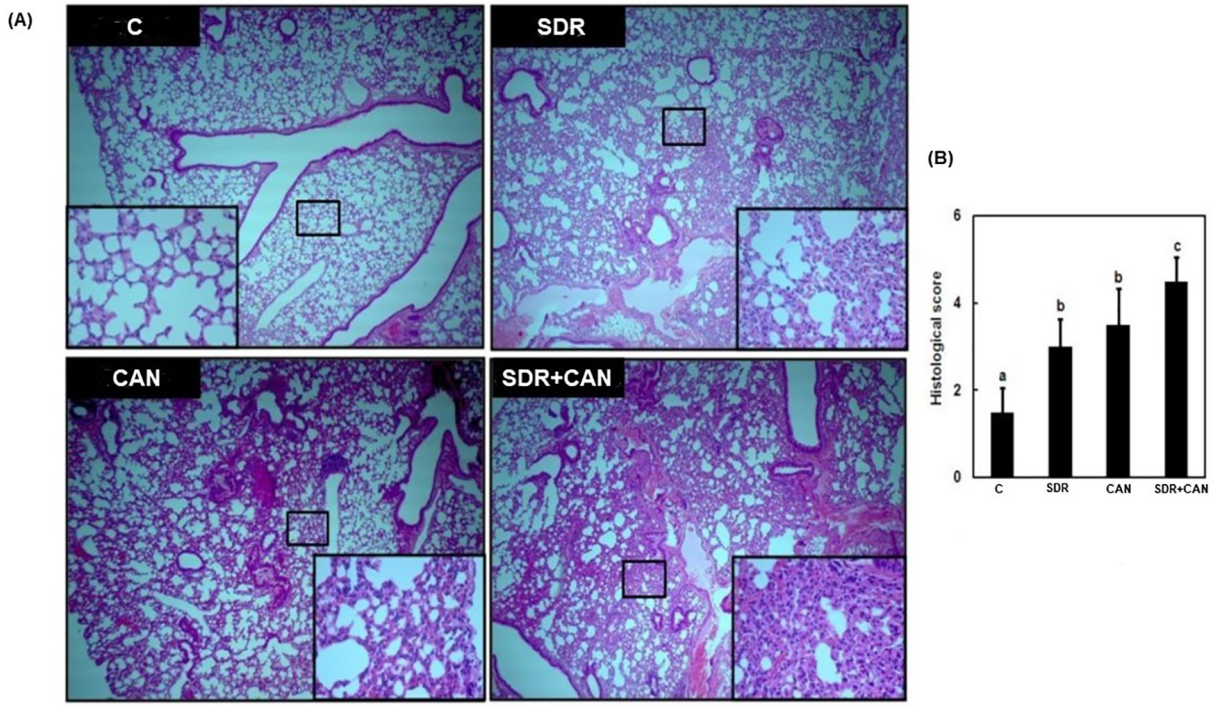


Fig. 8. Effect of exposure to scented candle fumes and SDR on the pulmonary injury. Four groups were referred to as Fig. 1 legend. The pulmonary injury was assessed by histological changes (100 ×) (A) and histological scoring (B). Data were means ± SD. Different letters indicate statistically significant differences between groups ($P < 0.05$).

workers undergoing physical and psychological stress in a kitchen environment for a long duration might result in cardiopulmonary injury. Often restaurant workers' health was related to diet and other habitual issues. Therefore, care should be taken to address the physical and psychological stress and kitchen environment for accessing the health of restaurant workers.

CRediT authorship contribution statement

Victor Raj Mohan Chandrasekaran: Conceptualization, Writing - original draft. **Srinivasan Periasamy:** Methodology. **Se-Ping Chien:** Supervision. **Chu-Han Tseng:** Investigation. **Perng-Jy Tsai:** Conceptualization, Supervision. **Ming-Yie Liu:** Conceptualization, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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