

Background

- Firefighters, like many other occupational groups, perform long work shifts involving nightshift and thus remain sleep deprived¹.
- Increasing evidences suggest that sleep deprivation (SD) induces stress or injury², in multiple organs and thus may predispose individuals to development of different diseases.
- Indeed, SD has been associated with many disease like type 2 diabetes mellitus³, obesity⁴, cancers⁵, cardiovascular disease⁶, infections⁷, among others.
- Firefighters undergo stress due to sleep deprivation and exposure to hazardous chemicals such as in the firefighting foams (e.g perfluorooctanoic acid/PFOA).
- Independent human studies have shown that SD leads to alteration in immune function in multiple ways, such as inducing IFN- γ secretion, decreasing phagocytosis in peripheral blood cells⁸, decreasing lymphocyte proliferation, decreasing NK cell count and target cell killing activity^{9,10} and decreasing antibody production from plasma B cell¹¹.
- PFOA is widely used in fire extinguishing foams and a number of industrial and consumer products and has been frequently detected in food-chain and drinking water¹² and bioaccumulates in kidneys, liver and blood¹³.
- Animal studies have suggested that PFOA has immune suppressive effects¹⁴ and causes different type of cancer in rodents¹³. In mice, PFOA causes decreased T cell-dependent antibody production¹⁴. Serum PFOA levels were negatively associated with response to diphtheria and tetanus vaccination in children¹⁴.
- **Hypothesis:** Collectively, these facts coupled with the reports of sleep deprivation associated stresses in high risk jobs lead us to hypothesize **that occupational SD-induced chronic stress modulates immune homeostasis and function, which may be further exacerbated by co-exposure to perfluorooctanoic acid (PFOA)**. This alteration in immune parameters, may at least in part, can serve as a tool for finding novel biomarkers and help understand the mechanism of different disease conditions as a result of firefighting- related exposures.

Objectives

Aim 1: To assess sleep deprivation (SD)-associated chronic stress in an SD mouse model based on biomarkers.

Aim 1a: We will use the established multiple platform method to induce sleep deprivation and chronic stress mice model.

Aim 1b: To analyze sleep deprivation induced chronic stress associated bio-markers (cortisol and C-reactive protein) by ELISA in serum.

Aim 2: To examine the effects of co-exposure (SD + PFOA) on stress and immune function in the SD mouse model.

Aim 2a. Immune cell phenotyping and immune mediator profile will be measured based on qRT-PCR analysis. (Gene- T-bet, Fox-p3, IL-10, TNF- α , IL-1 β , IL-6, IFN- γ , Cxcl5, NK1.1, Cxcl11)

Study plan

A mouse model of sleep deprivation based on the reported modified multiple platform method will be set up by using 6-8 week old C57BL/6 mice (n=8 mice/ group). Briefly, in this method, the mice will be placed in a water cage (e.g. 42 cmx28 cmx18 cm high), containing six platforms (3 cm in diameter), surrounded by water up to 1 cm beneath the platform surface for 24 h. Ad libitum food and sterile water will be given to mice during the sleep deprivation period. Chronic stress will be induced by following the sleep deprivation scheme outlined in **Figure-1** without or with weekly co-exposure to PFOA (@ 1ug/kg mice body weight, which is equivalent to the range of reported PFOA level in firefighters) by oral gavaging on day 7, 14 and 21.

Modified multiple platform techniques



Image.1 Modified multiple platform: Six round platforms of 3-cm-diameter each, in water tanks of (42 cmx28 cmx18 cm high) size.

Experimental design

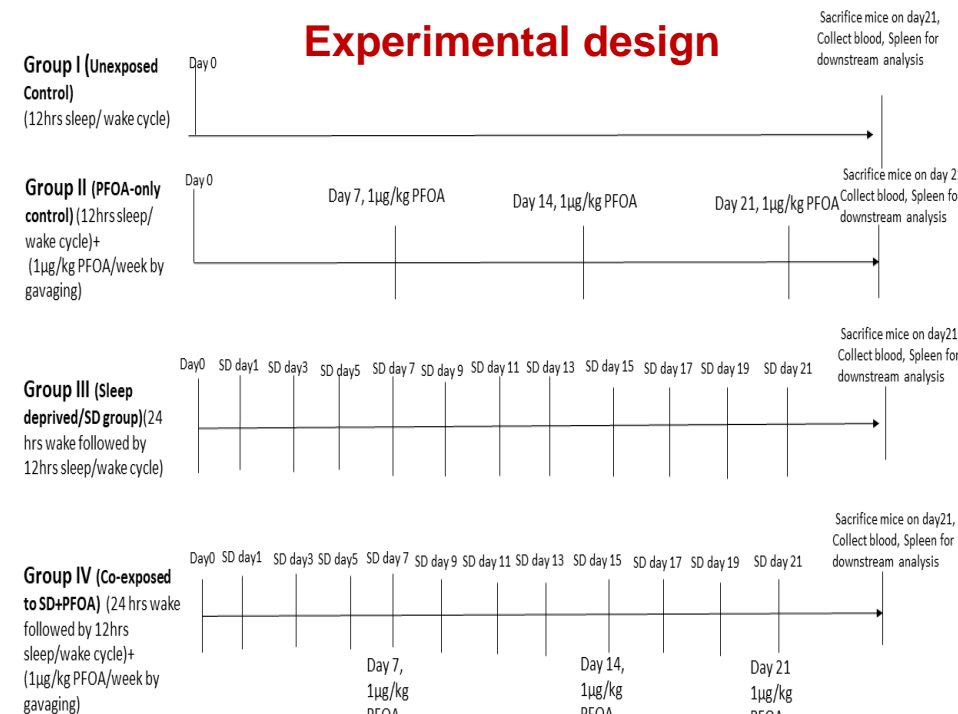


Figure1: Experimental design (work flow) of the proposed study.

Limitations

We anticipate no specific technical problems in inducing SD and performing PFOA exposure given our prior experience in mouse studies in mentor's laboratory. We expect no obvious problems in sampling and immunological analysis considering the PI's specialization in immunology and mentor laboratory's track record in environmental immunology and established routine lab techniques. However, it is possible that some mice may die due to SD induced stress in the middle of the experiment. In that case, we will continuously monitor the mice and shorten the duration of the SD cycle to a level enough to induce measurable stress indicators.

Expected results

1. We expect to identify alterations in immune cells profile in mice with the SD-induced stress without and with PFOA exposure, in a differential manner. This information is expected to provide insights into the interplay between the SD induced stress and PFOA exposure
2. we expect to identify novel specific immune biomarker candidates associated with SD-induced stress and/or PFOA exposure

Future directions

1. This study will unravel the risks as result of chronic stress due to occupational risk factors sleep deprivation and PFOA exposure.
2. This work will reveal specific deployable biomarkers in different body fluids as a result of altered immune status.
3. Preliminary data obtained through this pilot study will be used to submit a larger grant to NIOSH to pursue future expanded studies on role of firefighting-associated chronic stress factors in immune dysfunction of occupational workers and associated health disorders and diseases in firefighters.

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Title	Author	Affiliation
A Lead-Free Carbon-Based Shielding Material to Protect Healthcare Workers	Devika Chauhan	University of Cincinnati Mechanical and Materials Engineering
IoT based AI Application for Posture Recognition to Reduce Workplace Injuries	Aditya Milind Deshpande	University of Cincinnati Mechanical and Materials Engineering
Dual-Functionality Heatable Carbon Nanotube Air Filters for Healthcare Providers	Yanbo Fang	University of Cincinnati Mechanical and Materials Engineering
Designing Next-Generation Solid Electrolyte via a Multiscale Computational Scheme to Avoid Workplace Battery Hazard	Yao Fu (Mengze Ma)	University of Cincinnati Aerospace Engineering and Engineering Mechanics
Neurotoxicity of Polyfluoroalkyl Substance (PFAS) Mixtures in Firefighting Materials	Ola Wasel	Purdue University School of Health Sciences
Heavy Metal Sensor for Construction Workers Based on 3D Graphene	Mahnoosh Khosravifar	University of Cincinnati Mechanical and Materials Engineering
Assessing Volunteer Workers' Exposure to Dust, Metals and Bioaerosol During Equine Assisted Activities/Therapies: An Exploratory Study	Kimberly Tumlin	University of Kentucky Preventative Medicine and Environmental Health
Characterizing Fine and Ultrafine Particle Exposure Among Home Healthcare Workers	Ashley Turner	University of Cincinnati Environmental Health
Role of Firefighting-Associated Chronic Stress Factors in Immune Dysfunction in Mouse Model	Brijesh Yadav	University of Cincinnati Environmental Health
Invited Posters		
Home Health Care Workers' Occupational Exposure to Bioaerosols and Potential Association with Respiratory Health Issues	Yao Addor (Targeted Research Training Poster)	University of Cincinnati Environmental Health

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