In-Theater Combustion Exposure Using an *In Vivo* Rat Inhalation Model

Annie Wang[1], Noah Benn[1], Jacob Janssen[1], Kelsey Evans[1], Katie Beam[1], Ava Zapf-Rickards, PhD[1], Lily Thibodeaux[1], Allison Mills[1], Mackenzie Ellis[1], Kailen Watson[1], Michelle Racine[1], Abigail Methvin[1], Justin Tressler[1], Bryan McCranor, PhD[1] , Erik Johnson, PhD[1]

[1]U.S. Army Medical Research Institute of Chemical Defense (USAMRICD), Aberdeen Proving Grounds, MD 21010

Introduction

- Smoke inhalation injury is the leading cause of fire-related deaths
  - Toxic gases
  - Chemical irritants
  - Particulate matter
- Military service members are disproportionately affected
  - Dioxins
  - Heavy metals
- Long term health risks
  - Respiratory damage
  - Pulmonary dysfunction
  - Systemic chronic inflammation
- Evaluation of physiological and molecular toxicity of military-specific combustion products

Methods

- *In vivo* rat model using adult, male Sprague-Dawley rats
- Smoke generation using a **combustion chamber**
  - Wood – 77.8%
  - Paper – 10.5%
  - Rubber – 7.8%
  - Styrofoam – 3.9%
  - Saturated with 32.6 wt% of diesel fuel
- Side-stream directed to a whole-body **plethysmography chamber** for controlled exposure, observation, and recording
- Exposed for 2, 3, or 4 hours per day for 4 consecutive days
- Control rats exposed to room air for 4 hours
- All data collected via the FinePointe program

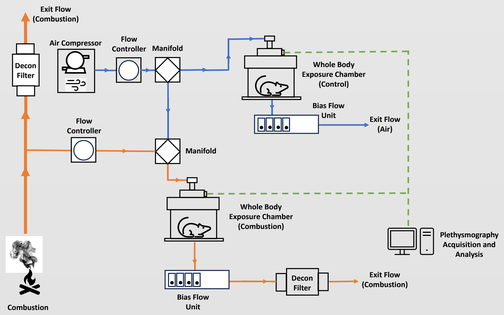

Figure 1. Combustion exposure system. A combustion chamber generates smoke that is vacuum-pulled by a Buxco Bias Flow pump into a mixer with air before diffusing into whole-body plethysmography chambers equipped with temperature/humidity probes and pressure sensors that measure respiratory parameters.

Frequency

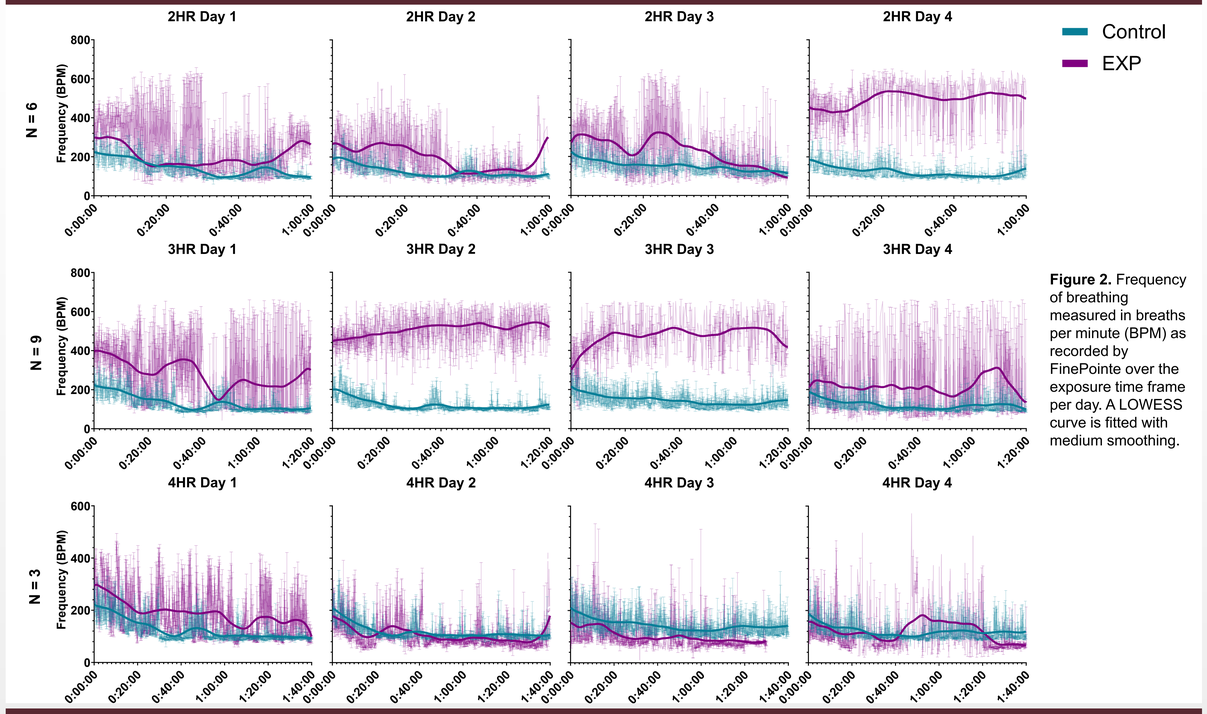

Figure 2. Frequency of breathing measured in breaths per minute (BPM) as recorded by FinePointe over the exposure time frame per day. A LOWESS curve is fitted with medium smoothing.

Tidal Volume

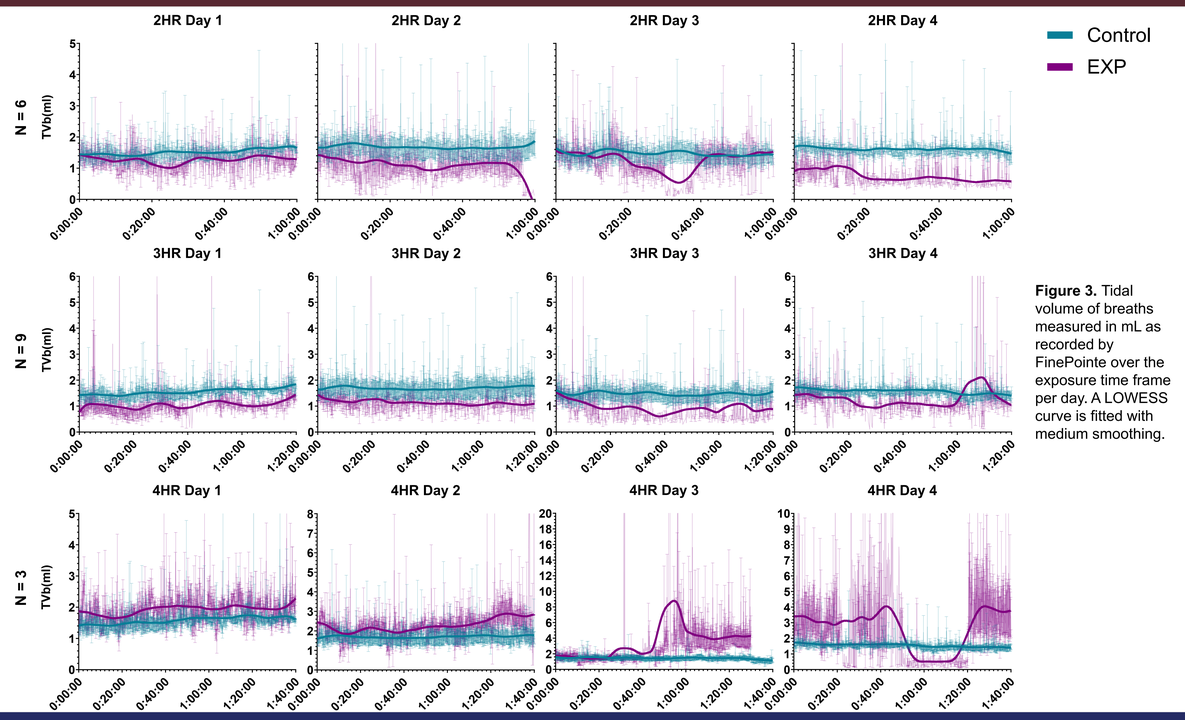

Figure 3. Tidal volume of breaths measured in mL as recorded by FinePointe over the exposure time frame per day. A LOWESS curve is fitted with medium smoothing.

Enhanced Pause

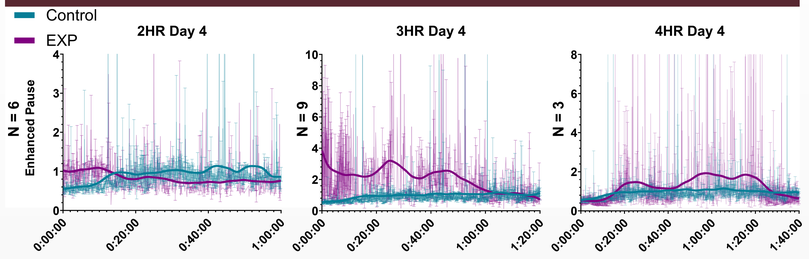

Figure 4. Enhanced pause between breaths as recorded by FinePointe over the exposure time frame per day. A LOWESS curve is fitted with medium smoothing.

Results

- Increased breathing frequency and decreased tidal volume in the 2- and 3-hour exposure groups
  - Absent in 4-hour group
- Increased and erratic tidal volume and increased enhanced pause in 4-hour group on penultimate days of exposure

Conclusions

- Changes in respiratory parameters in shorter exposure groups could have resulted from acute respiratory irritation due to inhalation of particulate matter and carbon monoxide
  - Faster, shallower breaths
- Longer exposure periods can potentially contribute to bronchoconstriction, restricting breathing functionality and leading to decreased breathing frequency and increased tidal volume
  - Slower, deeper breaths
- True injury phenotype may be presenting in the 4-hour and on the last day of the 3-hour exposure period

Future Directions

- Further investigation of the 4-hour exposure period and potentially more extended time frames to solidify exposure guidelines
- Different animal model to more closely mimic human respiratory response (i.e. ferrets)
- Evaluation of potential therapeutics geared towards military service members

Disclaimers

This research was supported in part by an appointment to the Department of War (DoW) Research Participation Program administered by the Oak Ridge Institute for Science and Education (ORISE) through an interagency agreement between the U.S. Department of Energy (DoE) and the DoW. ORISE is managed by ORAU under DoE contract number DE-SC0014664. All opinions expressed in this paper are the author's and do not necessarily reflect the policies and views of DoW, DoE, or ORAU/ORISE.

This work was supported by funds collected via 10 U.S. Code § 4123.

The experimental protocol was approved by the Animal Care and Use Committee at USAMRICD, and all procedures were conducted in accordance with the principles stated in the Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966 (P.L. 89-544), as amended.

To learn more, visit:
https://usamricd.health.mil