Subchronic exposure to ambient particulate matter induces oxidative stress responses in brain tissue of ApoE$^{-/-}$ mice

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Abstract

Studies with rodents have shown that the brain may be adversely affected after inhalation of ambient particulate matter (PM) by inducing oxidative stress, pro-inflammatory responses and tissue injury[1-4]. In this study the induction of oxidative stress responses were evaluated in mice exposed subchronically to fine (≤2.5 µm) concentrated ambient particles (CAPs). Specifically, apopoliprotein E knockout (ApoE$^{-/-}$) mice were exposed to either CAPs or particle-free air for 5 hours a day, 5 days per week, for a period of 6 months. The whole-body inhalation exposures were conducted in two urban cities (Seattle, WA and Detroit, MI) with distinct sources and chemical composition of PM. Brain tissue was collected after the exposures were completed and analyzed for biomarkers of oxidative stress. The antioxidant glutathione (GSH) was reduced in the brains of mice exposed to CAPs in Michigan but not in Washington. In contrast the lipid peroxidation product 4-hydroxyalkenal (HNE) was significantly increased in the membrane fraction of brain tissue of mice exposed to CAPs in Washington but not in Michigan. No significant differences were observed in protein carbonyl levels, a biomarker of protein oxidation, although the levels were slightly higher in the cytoplasmic fraction of brain tissue from animals exposed to CAPs when compared to controls regardless of exposure site. The results suggest that PM from different sources can modulate oxidative stress responses in a distinct fashion and that different subcellular fractions in the brain can be more susceptible to the effects of PM.

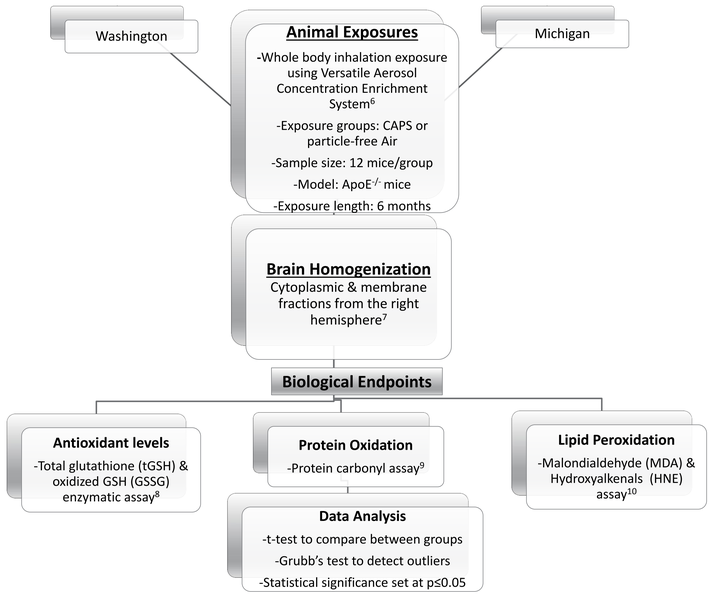
Introduction

- Studies have shown that the brain maybe adversely affected by particulate matter (PM) exposure[1-4]
- Exposure to particulate matter has been shown to induce oxidative stress and tissue injury in the brains of mice[4]
- Oxidative stress results when an abundance of reactive oxygen species (ROS) exceeds the cell's ability to quench them[5]
- The presence of oxidative stress parameters has been found in the brains of patients with neurodegenerative diseases such as Alzheimer's and Parkinson's disease[5]
- Therefore the extent of how exposure to PM may lead to neurotoxicity and neurodegeneration needs further investigation

Objectives

- Determine whether oxidative stress responses were present in the brains of the in the brains of ApoE$^{-/-}$ mice exposed for six months to fine CAPS at two different cities in the US
- Determine if the effects of fine CAPs in the CNS of ApoE$^{-/-}$ mice are related to the source and composition of PM
- Elucidate whether specific subcellular fraction in the brain are more susceptible to the oxidative stress responses induced by fine CAPs

Methods



Results

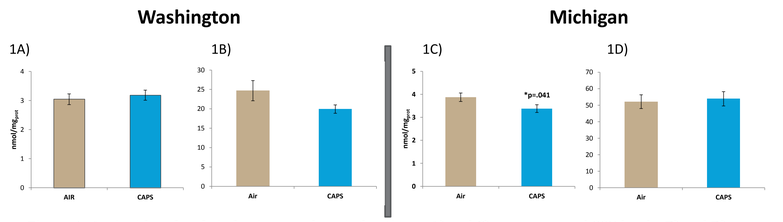


Figure 1. Antioxidant levels in brain cytoplasmic fractions. A) and **C)** represent total GSH levels; **B)** and **D)** represent the ratio between reduced GSH and GSSG. GSH levels were normalized by the protein content of sample. Bars represent mean ± standard error (SE). *Represents significant statistical differences from the control group.

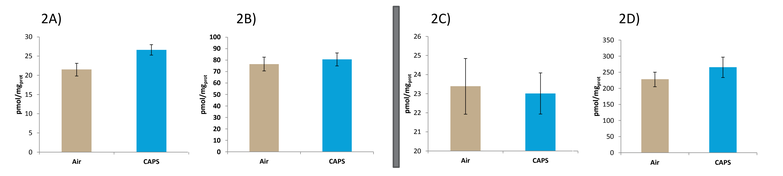


Figure 2. Protein oxidation in brain subcellular fractions. Protein carbonyl content in cytoplasmic fractions **2A)** and **2C)**; and membrane fractions **2B)** and **2D)**. Protein carbonyl levels were normalized by the total protein content of the sample. Bars represent mean ± standard error (SE).

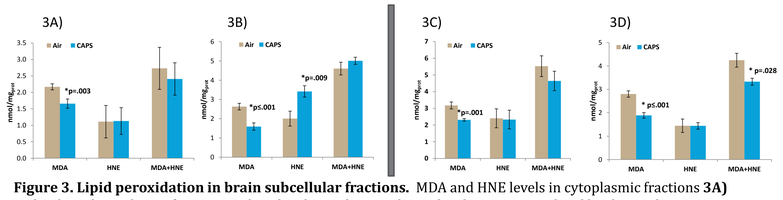


Figure 3. Lipid peroxidation in brain subcellular fractions. MDA and HNE levels in cytoplasmic fractions **3A)** and **3C)**; and membrane fractions **3B)** and **3D)**. Lipid peroxidation levels were normalized by the total protein content of the sample. Bars represent mean ± standard error (SE). *Represents significant statistical differences from the control group.

Conclusions

- Total GSH levels were reduced in brain samples of mice exposed to CAPs in MI but not in WA
- The ratio between reduced and oxidized GSH were not significantly changed when compared to controls suggesting that antioxidant levels were not altered by the CAPs exposure
- A slight non-significant increase in protein carbonyl content in different subcellular fractions were observed brain samples of animals exposed in WA (cytoplasmic) and MI (membrane)
- Lipid peroxidation products in the subcellular fractions of brain tissue had differing outcomes
- Baseline levels of MDA were higher than those for HNE and were actually reduced after exposure to CAPs
- In contrast, HNE levels in the membrane fraction of brain samples from mice exposed in Washington were significantly increased
- In overall, the results suggest that PM from different sources can modulate oxidative stress responses in a distinct fashion and that different subcellular fractions in the brain can be more susceptible to the effects of PM.

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