Exposure to wildfire particulate during infancy influences adolescent innate immune responses and lung growth

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Abstract

Rationale: The long-term health effects of acute wildfire smoke exposure are not known.

Objective: To determine if exposure to wildfire smoke during infancy is associated with alterations in innate immunity and lung function.

Methods: We evaluated a cohort of adolescent outdoor-housed rhesus macaque monkeys that were exposed as infants to ambient wood smoke from a series of Northern California wildfires in the summer of 2008. A second cohort of animals born in 2009 served as a control group. Peripheral blood mononuclear cells (PBMC) and pulmonary function measures were obtained when animals were 3 years of age. PBMC were cultured with either LPS or flagellin, followed by measurement of secreted IL-8/IL-10 protein or toll-like receptor (TLR) pathway mRNA analysis.

Measurements and Main Results: LPS or flagellin-induced IL-8 protein synthesis was significantly reduced in PBMC cultured from female animals with a prior history of wildfire smoke exposure. In contrast, LPS or flagellin-induced IL-10 protein synthesis was significantly reduced in PBMC cultures derived from male animals with a prior history of wildfire smoke exposure. Baseline and TLR ligand-induced expression of the transcription factor RelB was greatly modulated in PBMC from wildfire smoke-exposed female monkeys, with additional TLR pathway genes affected in a ligand-dependent manner. Wildfire smoke-exposed animals displayed a reduction in lung volume relative to control animals.

Conclusion: Our findings suggest that ambient wildfire smoke exposure during infancy can alter innate immunity and lung function in a sex-dependent fashion that is maintained into adolescence.

The Environment, the Immune System, and Lung Development

- A large body of evidence shows associations between wildfire smoke exposure and increases in hospitalization, emergency room visits, doctor’s visits for respiratory illness or heart disease, and asthma inhaler use.
- Children are particularly susceptible to the negative effects of air pollution because their undeveloped lungs are more vulnerable to injury. No data have been published specifically on wildfire smoke particulate.
- Current studies describing the effects of air pollution on the immune system are biased toward acute effects immediately following experimental exposures. Long-term sequelae are rarely described.
- In June 2008, an outbreak of wildfires in Northern California caused a spike in particulate air pollution levels. A cohort of monkeys studied here were 3 years old and housed outside at the time of the wildfires. Differences in lung volume and immune function compared to unexposed animals were still apparent 3 years later.

Summary

- Animals born in 2008 were exposed to a peak in particulate matter during development, while animals born in 2009 were not.
- Different sex-specific changes in the immune response were seen in males and females.
- PBMCs taken from wildfire-exposed animals 3 years after exposure exhibited significantly reduced IL-6 responses to bacterial components.
- PBMCs taken from wildfire-exposed males 3 years after exposure exhibited significantly reduced IL-6 responses to bacterial components.
- Wildfire smoke exposure was associated with reduced lung volumes in both males and females without changes in airways resistance or airway hyperresponsiveness.
- There is increased RelB expression in PBMC from wildfire smoke-exposed animals, suggesting that transcription factor regulation might be a target for air pollutant exposures.

Conclusions

We conclude from this study in rhesus monkeys that exposure to wildfire PM during the postnatal period of development can result in dysfunction of innate immune responses towards infectious agents and lung function decrements at adolescence. Our data suggests that children who underwent similar exposures to wildfire smoke PM, in 2008 as infants/toddlers may exhibit a similar health profile, with the caveat that unlike local children, the animals in this study were housed completely out of doors for the duration of the study. Furthermore, because rhesus macaques develop at a faster rate than children, the relative impact of a short-environmental exposure may differ. Nevertheless, the ability to quantitatively assess exposure impact on immune parameters using a non-invasive peripheral blood assay also makes our approach developable for rhesus macaques feasible for a large population-based human study.

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