Does Exposure to Air Pollution Contribute to Neurodegenerative Diseases?

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Atmospheric Emissions
Photo: Owen Byrne
Outline

- Particulate Matter (PM) in Air Pollution
- Mortality due to cardiovascular causes attributed to PM exposure
- Brain another potential target?
- Chronic neuroinflammation and neurodegeneration
- Exposure to ambient PM activates inflammatory markers in rodent brains
- Pilot study in an animal model of Alzheimer’s Disease
- Summary & Conclusion
Sources of ambient particulates
Premature Mortality Risk Attributable to PM$_{2.5}$

Deaths per 100,000 adults

- Blue: <25
- Green: 26–50
- Yellow: 51–75
- Orange: 76–100
- Red: 101–125
- Pink: <125

Brain as another potential target

http://science.nationalgeographic.com/science/photos/brain/
Route of Entry

Neurons, astrocytes & microglia

human neurons (10X)

human astrocytes (40X)

human microglia (20X)

http://www.sciencellonline.com/site/productInformation
Innate Immune Responses in the Brain

Chronic Neuroinflammation

Diesel Engine exposure Study Design

- Male Fischer F344/CrlBR rats (15-16 wks old) were exposed to diluted Diesel Engine Exhaust (DEE) generated by a stationary diesel engine using a nose-only exposure system (~ 150 μg/m³).
- Animals were pre-exposed to 0.4 ppm ozone for 12 hrs prior to the PM exposure.
- Rats were exposed (6 hrs/day, 5 days/wk for 4 weeks). Control animals were exposed to filtered air.
- The brain was divided into:
  - Cerebellum
  - Hippocampus
  - Olfactory bulb + Tubercles (OB + T)
  - Striatum
  - Cortex
Exposure unit at RIVM
TNF-α Levels

Gerlofs-Nijland et al., 2010 Particle & Fibre Toxicology 7: 12.
IL-1α Levels

Gerlofs-Nijland et al., 2010 Particle & Fibre Toxicology 7: 12.
Results by other research groups

Levesque et al., 2011 Environmental Health Perspectives • volume 119 pp:1151-1152
Neurodegenerative disorders target specific areas of the brain

Alzheimer’s Disease
http://www.alz.org/braintour/healthy_vs_alzheimers.asp

Parkinson’s Disease
http://neuropathology-web.org

Huntington’s Disease
http://kobiljac.msu.edu
Alzheimer’s Disease

- Most prevalent neurodegenerative disorder
- Learning and memory impairment
- Hallmarks are senile plaques and neurofibrillary tangles

LaFerla et al. Nature Reviews Neuroscience 8, 499-509 (July 2007)
Pilot study to assess PM-exposure in an animal model of AD

- Three months old transgenic mice containing the human Swedish mutation in APP (Tg2576)
- Whole body exposure (5hrs/day, 3 days/week for 7 weeks)
- Particulate matter (PM$_{2.5}$) collected near highway in downtown Los Angeles
NF-κB activation & IL-1β Levels in the brain
Toll-like Receptors

Microglia and TLR2 Immunostaining in the hippocampus
Summary

- Exposure to PM causes an Inflammatory response in the brain.
- Inflammation has been associated with both neuroprotection & neurodegeneration.
- More studies are warranted before it could be concluded that exposure to PM is potentiating pathogenesis of neurodegenerative disorders.
Interaction of aging, genetic predisposition, and environmental exposures in Neurodegeneration

- Age-related deterioration of brain microvasculature
- Compromise of BBB
- Activation of innate immune responses
- Environmental exposure
- Genetic predisposition
- Chronic neuroinflammation
- Oxidative stress
- Neural cell loss
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