Particulate Matter Air Pollution: Neurological and Psychiatric Disorders

Marc G. Weisskopf, PhD, ScD
Cerebrovascular Link

- Air pollution, especially particulate matter, has established consequences for cardiovascular disease
  - Vascular risk factors are often associated with cognition or dementia
  - Subclinical cerebrovascular disease is implicated in dementia
  - Subclinical cerebrovascular disease may also be involved in late-onset depression

http://med.uc.edu/neurosurgery/divisions/cerebrovascular.aspx
Particulates can reach the brain
Particulate matter exposure appears to lead to...

All of these suggested negative consequences of particulate exposure are evident in multiple neurodegenerative and psychiatric diseases.
Fig. 2. CAPS exposure leads to increase in lateral ventricle size; effects were graded with the example demonstrating the most severe effects shown here. Panels A–C: Rostral to caudal section of air exposed males at PND 14 with lateral ventricle (LV) becoming ...


*Developmental neurotoxicity of inhaled ambient ultrafine particle air pollution: Parallels with neuropathological and behavioral features of autism and other neurodevelopmental disorders*

NeuroToxicology, 2015, Available online 22 December 2015

http://dx.doi.org/10.1016/j.neuro.2015.12.014
The maternal interleukin-17a pathway in mice promotes autism-like phenotypes in offspring

Gloria B. Choi,1* Yeong S. Yim,1* Helen Wong,2,6,* Sangdo Kim,4 Hyunju Kim,4 Sangwon V. Kim,6 Charles A. Hoefler,3,6† Dan R. Littman,2,6,* Jun R. Huh4,6†
Particulate Matter and Autism Spectrum Disorders (ASD): Nurses’ Health Study II

Average predicted PM$_{10}$, 1988-2007

- A spatiotemporal model incorporating information from:
  - Monitoring networks
  - Meteorology
  - A collection of GIS-based predictors
- Linked to nurses’ addresses by month
- Average PM$_{10}$, PM$_{2.5}$
  - During pregnancy
  - 9m before pregnancy
  - 9m after pregnancy
- Difference= PM$_{10}$-PM$_{2.5}$

Yanosky et al. Environ. Health 2014 (PM$_{2.5}$ too)
### OR for ASD by IQR PM$_{2.5}$ over 9 months before, during, and after pregnancy

*Raz et al., Environ. Health Perspect., 2015*

<table>
<thead>
<tr>
<th>Exposure Period</th>
<th>Unadjusted OR (95% CI) per 4.40 µg/m$^3$ PM$_{2.5}$ (IQR)</th>
<th>Adjusted OR (95% CI) per 4.40 µg/m$^3$ PM$_{2.5}$ (IQR)</th>
<th>Mutually adjusted OR (95% CI) per 4.40 µg/m$^3$ PM$_{2.5}$ (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 months before pregnancy</td>
<td>1.20 (0.98-1.47)</td>
<td>1.32 (1.04-1.69)</td>
<td>0.83 (0.58-1.19)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1.37 (1.09-1.71)</td>
<td>1.50 (1.16-1.94)</td>
<td>1.63 (1.08-2.47)</td>
</tr>
<tr>
<td>9 months after pregnancy</td>
<td>1.19 (0.96-1.49)</td>
<td>1.29 (1.00-1.67)</td>
<td>0.96 (0.65-1.40)</td>
</tr>
</tbody>
</table>

*Adjusted for child sex, year of birth, month of birth, maternal age at birth, paternal age at birth, census income*
Odds ratio for ASD per IQR PM by pregnancy trimester

Adjusted for:
- All trimesters
- child sex
- year of birth
- month of birth
- maternal age at birth
- paternal age at birth
- census income

PM_{2.5} IQR = 4.40 \mu g/m^3
PM_{10-2.5} IQR = 5.17 \mu g/m^3
• Windham et al., 2006
• Volk et al., 2011, 2013
• Becerra et al., 2012;
• Roberts et al., 2013
• Kalkbrenner et al., 2015
• Talbott et al., 2015
Anxiety and Cognitive Function

(c) Early Stage AD
- Aβ oligomers
- Synapse loss

(d) Late Stage AD
- Tau tangles
- Amyloid plaques
- Microgliosis and neuronal degeneration

Current Opinion in Neurobiology
Anxiety: Nurses’ Health Study I
Power et al., BMJ, 2015

- Crown Crisp Index Phobic Anxiety Scale
  - Asks about fearfulness and desire to avoid common situations or environments (e.g. disliking “going out alone”) as well as tendency to worry (i.e. “about getting some incurable illness”)

15% have “Elevated Anxiety Symptoms”
PM$_{2.5}$, but not PM$_{10}$ or distance to road, is associated with increased odds of elevated anxiety symptoms.

Adjusted for month of questionnaire return, nurse's education, husband's education, age, age squared, whether the nurse has a partner, employment status, physical activity, percent of residential census tract that is white, percent of residential census tract adults who lack a high school education, median home value of residential census tract, geographic region, residence within a metropolitan statistical area, and social support.
Shorter averaging periods may be more relevant than longer averaging periods.

Adjusted for month of questionnaire return, nurse’s education, husband’s education, age, age squared, whether the nurse has a partner, employment status, physical activity, percent of residential census tract that is white, percent of residential census tract adults who lack a high school education, median home value of residential census tract, geographic region, residence within a metropolitan statistical area, and social support.
Black Carbon and Cognitive Function

*Power et al., Environ. Health Perspect., 2011*

Normative Aging Study,

Elderly men,
Greater Boston, Massachusetts
Black Carbon and Cognitive Function

*Power et al., Environ. Health Perspect., 2011*

**Table 2. Adjusted associations for a doubling in BC concentration on the natural scale and cognitive test score(s).**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Effect per doubling in BC concentration (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1: age adjusted</td>
</tr>
<tr>
<td>Low MMSE score OR</td>
<td>1.4 (1.1 to 1.6)</td>
</tr>
<tr>
<td></td>
<td>Model 2: age and education adjusted</td>
</tr>
<tr>
<td></td>
<td>1.3 (1.0 to 1.5)</td>
</tr>
<tr>
<td></td>
<td>Model 3: multivariable adjusted</td>
</tr>
<tr>
<td></td>
<td>1.3 (1.1 to 1.6)</td>
</tr>
<tr>
<td>Global analysis estimate</td>
<td>−0.073 (−0.122 to −0.023)</td>
</tr>
<tr>
<td></td>
<td>−0.052 (−0.100 to −0.004)</td>
</tr>
<tr>
<td></td>
<td>−0.054 (−0.103 to −0.006)</td>
</tr>
</tbody>
</table>

*Adjusted for age, education, first language, computer experience, physical activity, alcohol consumption, diabetes, dark fish consumption, percentage of residential census tract that is nonwhite, percentage of residential census tract adults with a college degree, indicator for first cognitive assessment, and indicator for part-time resident.*
Particulate Matter and Neurological Disease: Medicare Data

Kioumourtzoglou et al., Environ. Health Perspect., 2015

City specific PM
PD, AD, Dementia
PM$_{2.5}$ and Parkinson Disease, Alzheimer’s Disease, and Dementia Hospital Admissions

### Table 1. Number of subjects, cause-specific admissions, and estimated hazard ratios for Parkinson's disease, Alzheimer’s disease, and dementia.

<table>
<thead>
<tr>
<th>Results</th>
<th>PD</th>
<th>AD</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total population</td>
<td>9,817,806</td>
<td>9,817,806</td>
<td>9,817,806</td>
</tr>
<tr>
<td>Number of admissions</td>
<td>119,425</td>
<td>266,725</td>
<td>203,463</td>
</tr>
<tr>
<td>HR (95% CI) per 1 µg/m$^3$</td>
<td>1.08 (1.04, 1.12)</td>
<td>1.15 (1.11, 1.19)</td>
<td>1.08 (1.05, 1.11)</td>
</tr>
<tr>
<td>HR (95% CI) per 5 µg/m$^3$</td>
<td>1.44 (1.22, 1.70)</td>
<td>2.00 (1.70, 2.35)</td>
<td>1.46 (1.29, 1.66)</td>
</tr>
<tr>
<td><strong>Excluding cases in the first 2 years after enrollment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total population$^a$</td>
<td>8,011,978</td>
<td>7,976,136</td>
<td>7,897,538</td>
</tr>
<tr>
<td>Number of admissions</td>
<td>80,788</td>
<td>202,614</td>
<td>143,888</td>
</tr>
<tr>
<td>HR (95% CI) per 1 µg/m$^3$</td>
<td>1.07 (1.03, 1.11)</td>
<td>1.15 (1.10, 1.19)</td>
<td>1.07 (1.04, 1.11)</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer’s disease; HR, hazard ratio; PD, Parkinson’s disease.

$^a$The number of total subjects for this sensitivity analysis is different by outcome, depending on the number of excluded cases in the first 2 years of follow-up by outcome.

http://dx.doi.org/10.1016/j.tins.2009.05.009
Personal Characteristic/Behaviors

Outcome

Personal air pollutant exposure

Indoor air pollutant estimate

Ambient air pollutant estimate
The Total Indoor Environmental Quality Lab is housed at Syracuse Center of Excellence. The lab was used to simulate conditions observed in different office environments.

1. Multivariable test for building types:
   - Conventional
   - Green
   - Enhanced Green
   - i.e., Typical Office
   - Low VOC
   - Low VOC and High Ventilation

2. Single-variable test for carbon dioxide:
   - Low CO₂
   - Moderate CO₂
   - High CO₂
Many thanks to my collaborators

Raanan Raz
Melinda Power
Marianthi-Anna Kioumourtzoglou

Weisskopf Environmental Neuroepidemiology Group
Figure 2. Chronic activation of microglia by air pollution. Microglia can become toxically activated by either pro-inflammatory stimuli or in response to neuronal damage. Regardless of how the neuron is damaged, microglia respond to form a chronic cycle of tox...

Michelle L. Block, Lilian Calderón-Garcidueñas

Air pollution: mechanisms of neuroinflammation and CNS disease

null, Volume 32, Issue 9, 2009, 506–516

http://dx.doi.org/10.1016/j.tins.2009.05.009
Figure 1. Potential roles of microglia in the healthy and diseased brain. (a) During early postnatal development, microglia (illustrated in green) help refine excessive synaptic connections (illustrated in blue). Insert highlights microglial engulfment of synapses.

Soyon Hong, Lasse Dissing-Olesen, Beth Stevens

**New insights on the role of microglia in synaptic pruning in health and disease**

Current Opinion in Neurobiology, Volume 36, 2016, 128–134

http://dx.doi.org/10.1016/j.conb.2015.12.004
To summarize

Air pollution

- Neuroinflammation
- Oxidative Stress
- Protein Aggregation
- CNS Dysfunction

Systemic Inflammation

Subclinical cerebrovascular disease

Blood brain barrier disruption
Exposure Assessment

- Estimated PM2.5 and PM2.5-10 prior to anxiety symptom assessment in 2004:
  - Prior 1 month
  - Prior 3 months
  - Prior 6 months
  - Prior 12 months
  - 1988-2003
- Distance to road

Yanosky et al. Environ. Health 2014 (PM$_{2.5}$ too)