Research Update on Air Pollution and the Brain

California Environmental Protection Agency
Air Resources Board

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Recent Headlines

Background

- Air pollution-related cardiovascular and respiratory health effects well documented
- Less known about brain impacts
  - U.S. EPA, Health Effects Institute: more brain/PM studies needed[1,2]
- More studies published since reviews
- Today's focus: neurodegenerative effects

[1]U.S. EPA (2009) Integrated Science Assessment for Particulate Matter.

[2]HEI Review Panel on Ultrafine Particles (2013) Understanding the Health Effects of Ambient Ultrafine Particles.

Observational Evidence: Mexico City

Children from Mexico City vs. less-polluted areas:

- Breakdown of brain protective layer and nasal cavity lining
- Signs of early-stage Alzheimer's disease
- Cognitive deficits

Note:

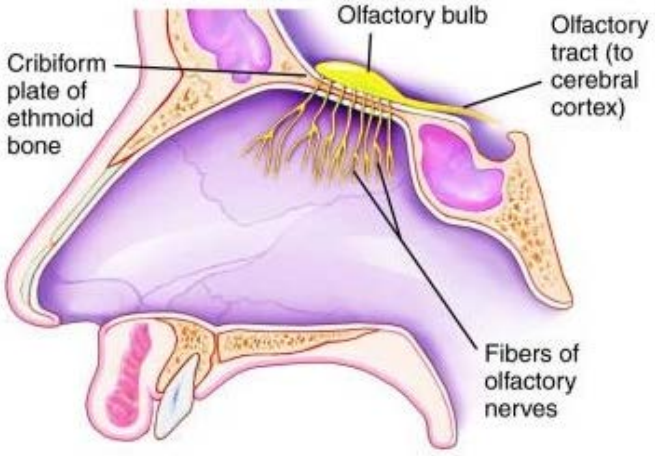
- Lack pollutant measurements

Outline for Today's Talk

- Can inhaled pollutants enter the brain?
- What have we learned from animal studies?
- Are effects observed in exposed populations?

Can Inhaled Pollutants Enter the Brain?

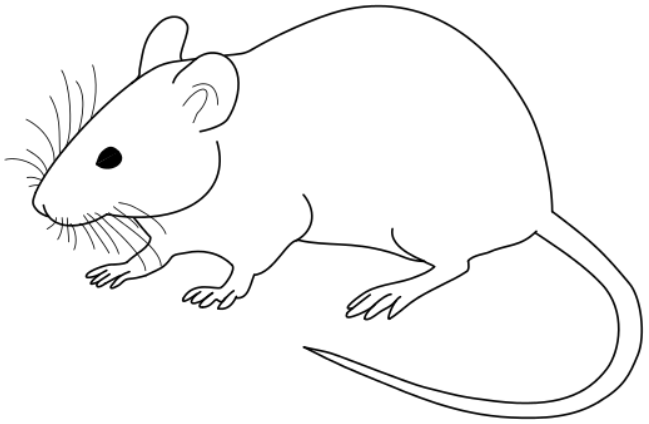
- Direct particle entry via olfactory nerve
- Blood-brain barrier (BBB) protects brain
  - Ultrafine PM can penetrate BBB
  - BBB can be compromised
- Other indirect pathways likely



What Have We Learned from Animal Studies?

Air pollution exposures lead to:

- Brain inflammation = potential mechanism
  - Normal response to harmful stimuli
  - If chronic: can contribute to disease
- Impairments in learning & memory
- Behavioral changes



Are Effects Observed in Exposed Populations?

Ontario, Canada Study

- >2 million adults (55-85 years), 2001-2012
- Residential distance from major roads 5 years prior
- Accounted for age, sex, pre-existing disease

⇒ Increased dementia risk near busy roads:

- <50 meters: ↑7%
- 50-100 meters: ↑4%
- 101-200 meters: ↑2%

- No increased risk for Parkinson's disease

*Chen et al. (2017) Living near major roads and the incidence of dementia, Parkinson's disease, and multiple sclerosis: a population-based cohort study. *Lancet* 389(10070):718-726.

Are Effects Observed in Exposed Populations? (cont.)

U.S. Nationwide Study

- Women's Health Initiative Memory Study: 3,647 women (65-79 years, European ancestry)*
- Residential PM2.5 exposure, 1999-2010
- Accounted for age, BMI, SES, lifestyle, clinical factors

$\Rightarrow$ For PM2.5 > annual national standard (12 $\mu g/m^3$):

- Cognitive decline: ↑81%
- Dementia risk: ↑92%
- Even larger increases for women with gene related to Alzheimer's disease risk

*Cacciottolo et al. (2017) Particulate air pollutants, APOE alleles and their contributions to cognitive impairment in older women and to amyloidogenesis in experimental models. *Translational Psychiatry* 7(1):e1022

Conclusions

- Can inhaled pollutants enter the brain?
  - Yes
- What have we learned from animal studies?
  - Brain inflammation, cognitive impairment
- Are effects observed in exposed populations?
  - Emerging evidence

Additional questions:

- Which pollutants pose greatest risk, over what time frame; who is most at risk?

Related Research Activities

- Completed ARB Study: Central nervous system effects of ambient PM2.5
  (M. Kleinman, UC Irvine)
- Current ARB Study: Ultrafine PM exposure and Parkinson's disease in a mouse model
  (A. Cho, UCLA)
- Other Research:
  - Possible neurological add-on to current ARB epidemiological study of ultrafine PM and mortality
  - SCAQMD studies on brain tumors

What ARB is Doing

- Diesel regulations led to decreasing ultrafine PM emissions:
  - I-710: About 70% decrease in ultrafine PM emission factors from heavy-duty trucks (2009-2016)
- Truck Field Enforcement / New Screening Technologies
- Just released: "Strategies to Reduce Air Pollution Exposure Near High-Volume Roadways" (https://www.arb.ca.gov/ch/landuse.htm)
- Longer-term: Transportation electrification

Thank You