The Role of Ultrafine Particles on Mental Health

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Health Effects of Ultrafine Particles (UFPs)

Where?
- Transportation hubs, high population density areas, and areas with indoor air pollution

What?
- Accumulates in different regions
- Causes epigenetic changes
- Creates inflammation

How? Particle size
- Can get through cell membranes
- Cannot be eliminated through phagocytosis
- Can cross the Brain Blood Barrier (BBB)

Effects in mental health and neurodegenerative conditions
Our review shows that findings in animal studies have been consistent and supportive of epidemiological and clinical studies.

- **Animal Studies**
  - Greater variable control
  - Easier to determine potential covariates

- **Clinical Studies**
  - More representative of reality
  - Easier to find key translational areas
Neuroinflammation

- Found in children and adults living in larger cities
- Increases in microglia activation, oxidative stress, and cerebrovascular dysfunction
- Can result in central nervous system disease and early onset Parkinson’s disease
- Associated to other conditions

Fig. 1: Neuroinflammation from Alzheimer’s disease from the National Institute of Aging, NIH
Cognitive Development

- Critical period for development: 0 - 6 years
- Impaired neurodevelopment, changes in functional neural connectivity
- Deficit in working memory, 20% decrease cognitive growth
- Standardized testing show lower baseline cognitive scores

Focus on prenatal and neonatal exposure

Learning deficits found even in low exposure conditions

Dysfunction of dopaminergic pathways

Cognitive inflexibility similar to humans

Fig. 2: Children in Math class from Meriwether Lewis Elementary School, Creative Commons
Autism Spectrum Disorder - ASD
Attention Deficit Hyperactivity Disorder - ADHD

- Large scale epidemiological studies: patterns of environment and diagnosis
- Levels of NO$_x$ and elemental C used to determine presence of UFPs
- Potential correlation of fetal exposure and ASD even below WHO standards*
- High exposure during infancy correlated to elevated hyperactivity scores

Mechanisms of developmental delays

- Neuroinflammation, microglial activation and morphometric shrinkage
- Neurodevelopmental toxicity

Behavioral changes

- Impulsivity, preference for immediate reward
- Deficits in social behavior

Fig. 3: “Autism” by Darryl Leja, NHGRI
Alzheimer’s Disease (AD) and Dementia

- Breakdown of epithelial and endothelial barriers
- Significant brain changes in children
  - Early biomarkers: prefrontal inflammatory responses, short memory deficits
- Women 65+: significant drop in cognitive scores where UFP > EPA standards
  - Linked to Alzheimer’s related dementias

**Short term exposure**
Changes in brain regions, including hippocampus
Presence of biomarkers for oxidative stress and AD

**Short term, older mice**
Adverse effects in multiple memory domains
Independent of predisposition to AD

**Chronic exposure 7 months**
Cognitive impairment

Fig. 4: Beta-Amyloid Plaques and Tau in the Brain from the National Institute of Aging, NIH

Calderon-Garciduenas, et al., 2016
Calderon-Garciduenas, et al., 2020
Tavera-Mendoza, et al., 2017
Fink et al., 2020
Jew et al., 2019
Building Collaborative Tunnels to Study Particulate Matter

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Tufts University, Medford, Boston, North Grafton, MA, WPI, UMass Medical School

- Rat mothers and newborns exposed to UFP from Boston traffic tunnels

**Hypothesis:** developmental exposure to TRAP should cause

- systemic increases in inflammation markers
- neuroanatomical changes
- behavioral and cognitive deficits alike those shown in children with ASD
**Results:** Altered behavior, inflammation, anxiety and cognitive impairment

* = (p<0.05) Rats show decreased social skills and neural integrity

Fig. 5: A. Diffusion tensor MRI of juvenile male rat brains exposed to control air, (A), and PM (b), showing decreased neural integrity and/or disorganized neural tracts in PM exposed brains.
Future Directions

- Translational collaboration at all levels
- Correct identification of cofactors
- Research in mental health effects and etiology
- Comparative analysis and imaging studies
- Preventive measures and information
Further research would:

- Help early diagnosis
- Further our knowledge of etiology
- Guide public health and safety measurements