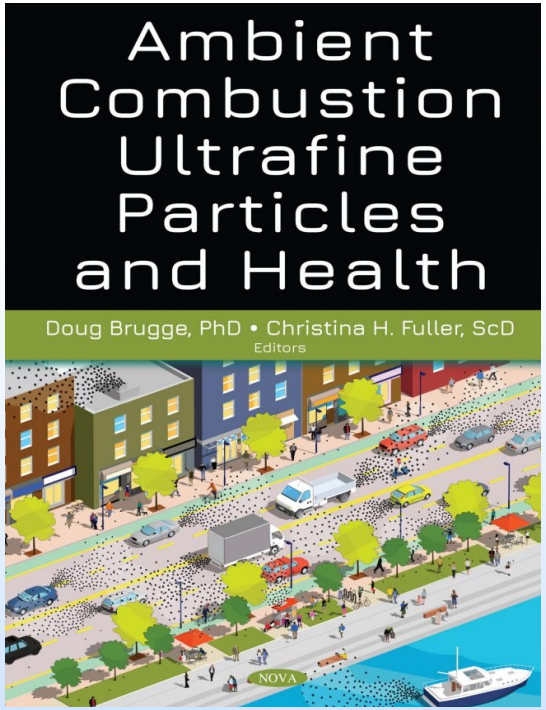
The Role of Ultrafine Particles on Mental Health



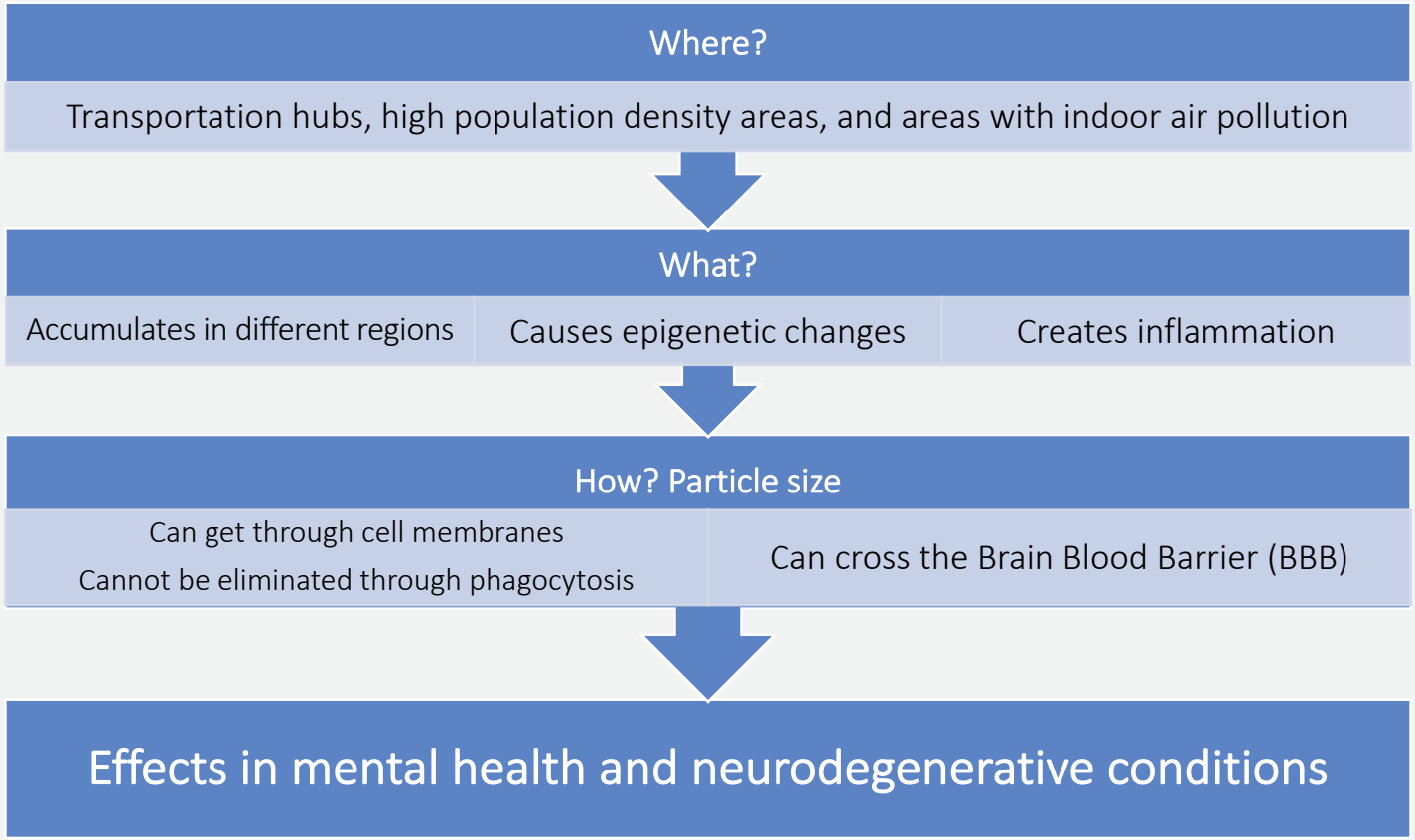
Ben Nephew, Alessandra Torres, Gavin Nephew, Senbao Lu, Ryan Cali and Alicia Howell-Munson

Chapter 12 of “Ambient Combustion Ultrafine Particles and Health”

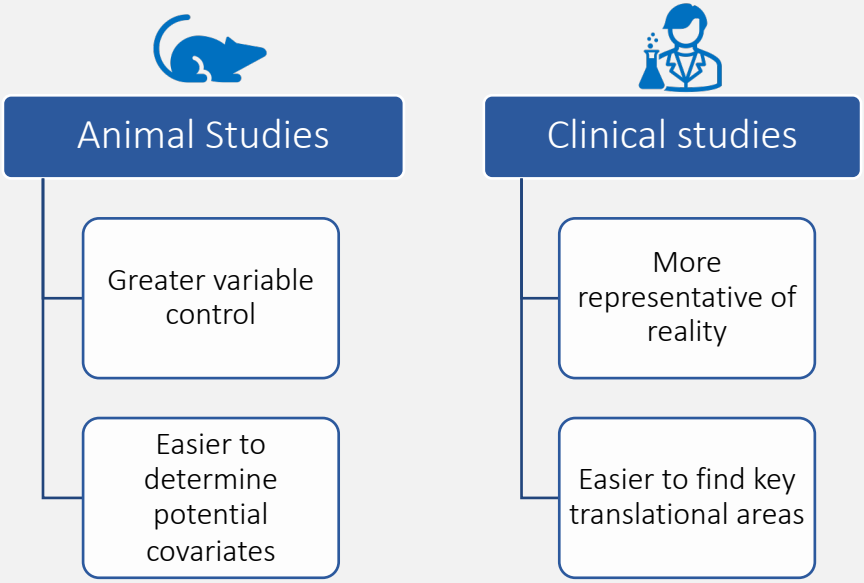
by D. Brugge, PhD and C. Fuller, ScD

Published by Nova in 2021

Health Effects of Ultrafine Particles (UFPs)



Our review shows that findings in animal studies have been consistent and supportive of epidemiological and clinical studies



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**

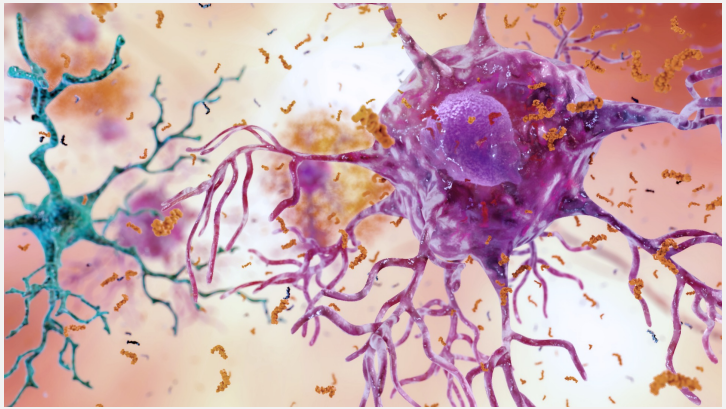


Fig. 1: Neuroinflammation from Alzheimer's disease from the National Institute of Aging, NIH

Studies to identify potential mechanisms

Replicate findings in human studies

- Biomarkers: IL-1 and TNF
- Diesel and gasoline combustion pollutants increase incidence

Calderon-Garcidueñas, et al., 2008
Block & Calderón-Garcidueñas, 2009;
Campbell et al., 2005
Tyler et al., 2016

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. Unchanged

Forns et al., 2017
Pujol et al., 2016
Beauregard, et al, 2018;
Johnson et al., 2015;
Upadhyay et al., 2019
Joshua L. Allen et al., 2014
Joshua L. Allen et al., 2013
Morris-Schaffer et al., 2018

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

Oudin et al., 2019
Wolf et al., 2017
Gong et al., 2017
Newman et al., 2013
Sunyer et al., 2015
J. L. Allen et al., 2017
Sobolewski et al., 2018
J. L. Allen et al., 2014

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

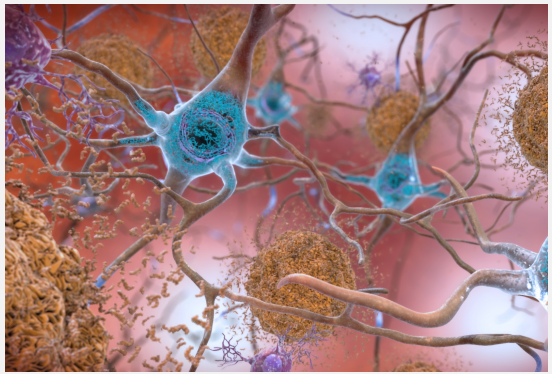


Fig. 4: Beta-Amyloid Plaques and Tau in the Brain from the National Institute of Aging, NIH

Calderon-Garciduenas, et al., 2016
Calderon-Garciduenas, et al., 2020
Cacciottolo et al., 2017
Tyler et al., 2016
Park et al., 2020
Jew et al., 2019

Building Collaborative Tunnels to Study Particulate Matter

Ben Nephew, Alexandra Nemeth, Neelakshi Hudda, Gillian Beamer, John Durant, Ryan Cali, Marcelo Febo, Praveen Kulkarni, Guillaume Poirier, Jean King, Phyllis Mann, Jocelyn Petitto, Doug Brugge

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

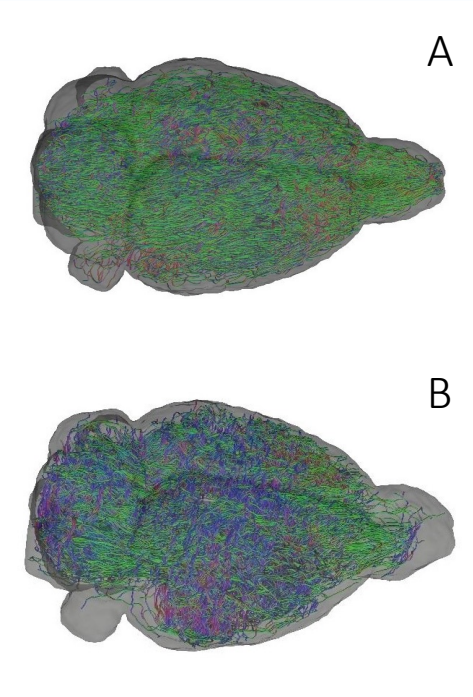
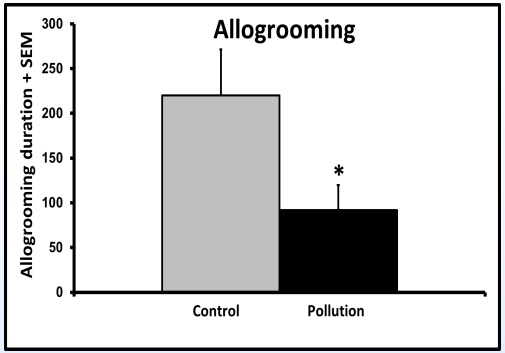
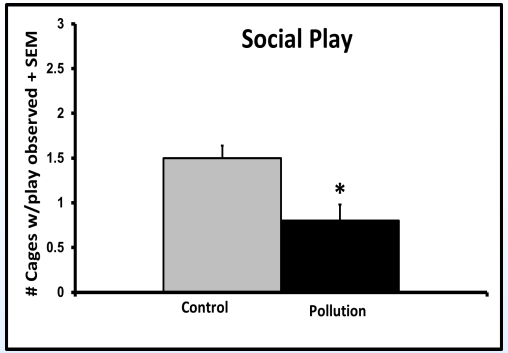
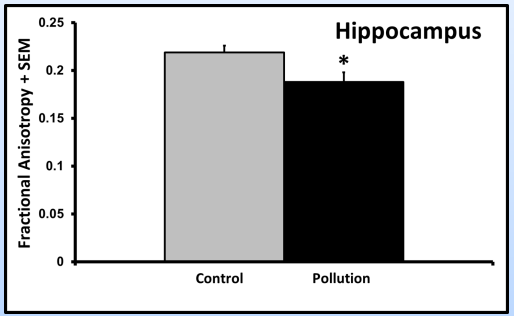
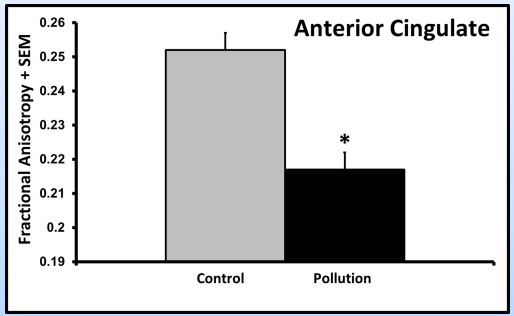


Fig. 5: A. Diffusion tensor MRI of juvenile male rat brains exposed to control air, (A). and PM (b), showing decreased neural integrity and/or disorganized neural tracts in PM exposed brains.



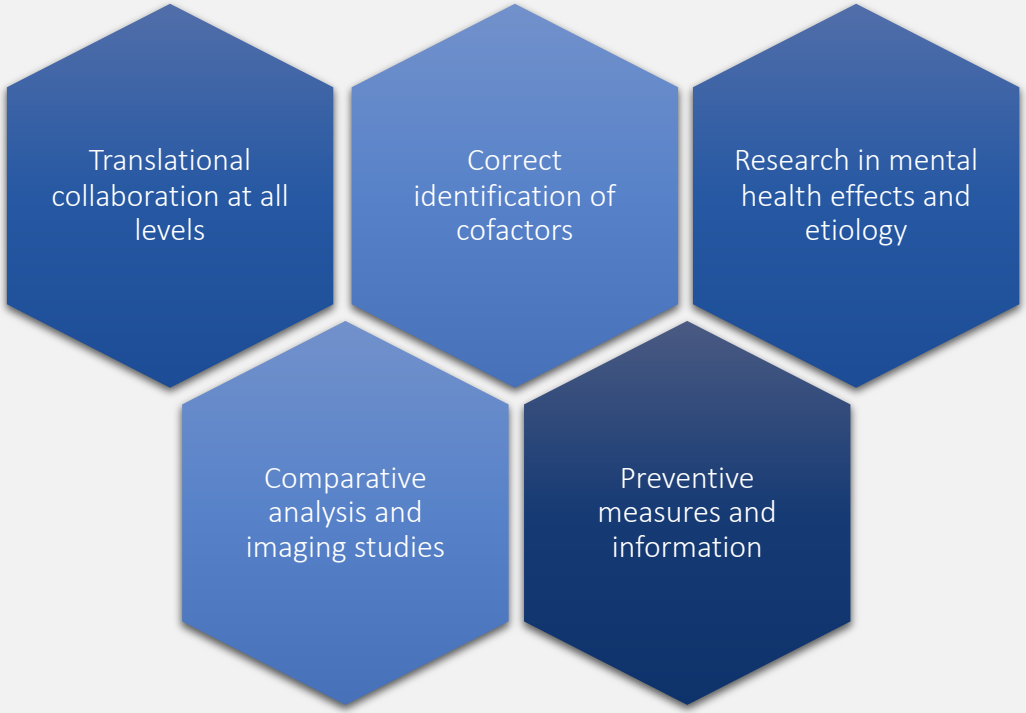






*** = (p<0.05) Rats show decreased social skills and neural integrity**

Future Directions



Further research would:

HELP EARLY DIAGNOSIS

FURTHER OUR KNOWLEDGE OF ETIOLOGY

GUIDE PUBLIC HEALTH AND SAFETY MEASUREMENTS