Cognitive effects may be linked to active transport and urban air pollution

Luc Int Panis

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Air Pollution Ups Risk Of Stroke, Impaired Memory

Common air pollutant linked to mental decline

Air Pollution Linked to Cognitive Decline

Particulates may enter brain

Smog in our brains

Researchers are identifying startling connections between air pollution and decreased cognition and well-being.

Smog May Harm Women's Brains: Study

The more air pollution they were exposed to, the greater their mental decline
New: neurological effects of air pollution

- Direct Mechanisms
  - Soluble Compounds Reach the Brain
  - Adsorbed Compounds Reach the Brain
  - Particulate Matter Reaches the Brain

- Peripheral Mechanisms
  - Cardiovascular System
  - Circulating Monocytes
  - Circulating Cytokines
  - Lung
  - Liver

- CNS Pathology
  - Neuroinflammation (iNOS, TNFα, IL-1β, COX2, NFκβ)
  - Neuron Damage/Loss
  - Microglia Activation (HLA-DR & CD14) (ROS & Cytokine Production)
  - Blood Brain Barrier Damage/Dysfunction (Changes in Inflammatory, Tight Junction, & Transport Proteins)
  - Aβ Accumulation (Neuronal, Vascular, & Diffuse Plaques)
  - Aβ and α-Synuclein Aggregation
  - Lipid Peroxidation
  - Astroglisis (GFAP)
  - DNA Damage
New evidence for Neurological and cognitive effects

» Recently, associations found between chronic exposure to air pollution and negative neurological effects.

» Huge implications: respiratory<cardiovascular<neurological

» Link between ischemic stroke and PM exposure is a well known ("cardiovascular") effect. May impact brain function.

» Post-mortem studies in Mexico city on children and dogs
New evidence for Neurological and cognitive effects

» Calderon et al associations between urban pollution (O₃ and PM);
   » ultrafine particle deposition in the brain
   » Neuroinflammation, disruption of blood-brain barrier
   » accumulation of amyloid-β and α-synuclein
   » and **cognitive decline**

» Others authors have found associations between PM exposure and cognitive decline.
Physical activity

» Good for respiratory and cardiovascular health
Well known.....BUT

Goa et al. 2012 AE in press “Elevated cardiorespiratory fitness observed in physically activate children could be negated by increased amount of inhaled pollutants during exercise”
Cutrufoello et al. 2012 Sports Medicine “healthy athletes ....exercising in urban areas in close proximity to major roadways should consider ambient air pollution ....prior to engaging in vigorous exercise”

» Good for memory, brain plasticity, cognition and mental health
» Aerobic training improves cognitive and visuospatial memory

» WHY?
» mechanism for benefits of exercise remains to be elucidated.
» Better blood transport to brain? (<> air pollution; Louwies et al EHP in prep)
» exercise stimulates neurogenesis and synaptic plasticity
» Even short bouts of exercise induce production and release of neurotrophines such as BDNF and SYN1 in blood and in the brain. (Brain Derived Neurotrophic Factor)

» Our research hypothesis:
“Air pollution exposure cancels the neurological benefits of exercise”
Brain derived neurotrophic factor (BDNF) in urban cyclists (2011)

- Physical exercise increases levels of Brain-Derived Neurotrophic Factor and this contributes to neural plasticity and improved learning and memory.
- Increase in serum BNDF is absent after cycling in traffic.
- Additional experiments in humans (cognition) and animals (brain)

Start to Run experiment

» Goal
  » Effects of aerobic training in urban and rural setting on:
    - cognition
    - inflammation
    - basal serum BDNF

» Design
  » Inactive/sedentary volunteers
  » 12 week *Start-2-Run (S2R)*, 3 sessions/week
  » UFP- contrast
    » S2R in city (Brussels; n=21)
    » S2R in rural area (Mol; n=13)
  » Biological effects before & after S2R
Small and variable UFP (20-1000nm) contrast
larger nano particle contrast (<20nm)
Biological effects studied

» Cognitive tests

» Exhaled NO

» Blood tests
  » Leucocytes
  » Serum BDNF
  » Gene expression
Results

UFP Dose - effect response for inflammation

A. Change in eNO (‰)
B. Change in WBC counts (%)
C. Change in neutrophil counts (%)
D. Change in lymphocyte counts (%)

Rural group vs. Urban group

- A: y = 0.0252x - 143.14
  R² = 0.2417
- B: y = 0.0135x - 80.591
  R² = 0.2632
- C: y = 0.017x - 99.833
  R² = 0.1519
- D: y = 0.011x - 66.016
  R² = 0.2336
Effect of exercise and UFP in rodents

- 4 groups of 6 Wistar rats exposed for 90 minutes to 1 of 4 conditions:
  - UFP (~2.10^7 pt.cm\(^{-3}\) with a 8 nm peak) + exercise (20m.min\(^{-1}\) for 90 min)
  - UFP + rest
  - Ambient air + exercise
  - Ambient air + rest (control)
- Gene expression analysis of
  - Olfactory bulb
  - Prefrontal cortex
  - Hippocampus
Brain gene expression is changed with physical activity & UFP

» BDNF and NFE2L2 hippocampal expression increases with ambient air/exercise
» No BDNF up-regulation in the UFP-exposed group during exercise
» Synapsin1 is down-regulated with UFP

- Bos I., De Boever P., Int Panis L., Sarre S., Meeusen R. 2012. No up-regulation of hippocampal BDNF expression in rats exposed to UFP during exercise, *Neuroscience*
- Air pollution impairs cognition, provokes depressive-like behaviors and alters hippocampal cytokine expression and morphology
  Fonken et al., 2011 in *Molecular Psychiatry*
Conclusions

» Accumulating evidence for urban air pollution effect on the brain
  (e.g. review papers by Block et al. 2012 in Neurotoxicology; Genc et al. 2012 in J. of Toxicology)
  » Neuroinflammation, neurotoxicity, ...
  » Gene expression changes
  » Neurobehavioral changes, (spatial) learning, ...
  » Pathways of effect and neurotoxic fractions of PM not well known

» Interaction with the active transport
  » Physical activity increased exposure
  » Physical activity comes with neurological benefits

» Effects of both can be found even after short exposures with well designed studies (contrast, controls, ....)

Effects need to be taken into account when planning cities for active citizens