Multi-centre health effect studies on inhaled combustion derived (nano)particles in rats and humans

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Adverse health effects of PM

Epidemiology

• Shortening of life expectancy
• Impaired lung development of otherwise healthy children living near a freeway

In vivo studies

• Emissions from highways result in inflammation of the lung and cardiovascular changes
Routes of exposure to (nano)particles

Figuur 1.21 - Ademhalingsstelsel
Toxicokinetics of PM

Particles

Brain
Nose
Lung
Blood
Spleen
Endothelium
Liver
Heart
Atherogenic plaques

Gut

Courtesy K. Donaldson
Controlled diesel engine exhaust studies – volunteers and rats

Rat studies
1. Sub-chronic exposure (4 weeks; 150 µg/m³)
2. Acute exposure – time series (2 hours; 1.9 mg/m³)
3. Acute exposure – myography (2 hours; 300 µg/m³)
4. Acute exposure – vagus nerve (6 hours 4.9 mg/m³)

Human volunteers
• Acute exposure - plethysmography (2 hours; 300 µg/m³)
• Acute exposure - QEEG (1 hour; 300 µg/m³)
Rat study: Sub-chronic exposure

• Exposure
  - Male Fisher F344 rats (15-16 weeks)
  - Ozone exposure 0.4 ppm for 12 hours
  - 4 weeks; 5 days/week; 6 hours/day
  - 150 µg/m³ diesel engine exhaust
  - Nose-only
  - Characterisation (mass, number, size distribution, sulphate, nitrate, XRF, EC/OC, LPS, volatile organic components)

• Effect assessment
  - 24 hours post-exposure
  - Bronchoalveolar lavage fluid (BALF), blood, tissues
  - Oxidative stress, inflammation, tissue damage
Rat study: Sub-chronic exposure Summary

• Exposure to diesel engine exhaust resulted in an oxidative stress response and impaired fibrinolysis and coagulation

• No inflammation or changes in vascular function
Rat study: Acute exposure – time series Design

• Exposure
  - Male Fisher F344 rats (9 weeks old)
  - 1.9 mg/m³ diesel engine exhaust
  - 2 hours
  - Nose-only
  - Characterisation (mass, number, size distribution, sulphate, nitrate, XRF, EC/OC, volatile organic components)

• Effect assessment
  - 4, 18, 24, 48, and 72 hours post-exposure
  - Bronchoalveolar lavage fluid (BALF), blood, tissues
  - Oxidative stress, inflammation, tissue damage
Rat study: Acute exposure – time series

- Investigate the effect of diesel engine exhaust particles on oxidative stress markers in a time-series study.
Rat study: Acute exposure – time series
Summary

• Exposure to diesel engine exhaust resulted in a time-dependent oxidative stress reaction, followed by an inflammatory response

• Oxidative stress is preceded by a procoagulant reaction in the blood as indicated by concurrent increases in TF activity and the amount of trombin generation
Human volunteers: Acute exposure - QEEG

Inhalation UFP

Irritant receptors

Translocation of NP

Soluble Components, NP

QEEG

VR

HRV

Courtesy: Paul Borm Centre of Expertise in Life Sciences (CEL)

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Study in Umea: diesel exhaust (300 ug/m3)
Dr. Thomas Sandström, Dr. Anders Blomberg

Random order

<table>
<thead>
<tr>
<th>Diesel</th>
<th>Air</th>
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<tbody>
<tr>
<td>Preparation (30 min)</td>
<td>Exposure (60 min)</td>
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<tr>
<td>Post exposure (60 min)</td>
<td></td>
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</tbody>
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Effect of diesel engine exhaust on brain function

During exposure

5'

55'

Post exposure

5'

55'

Sham exposure

5'

55'

Sham post

5'

55'
Human volunteers: Acute exposure – QEEG Summary

• Exposure to diesel engine exhaust influences brain activity

• Physiological meaning however in this context largely unknown
Conclusions

• Automotive emission cannot only cause pulmonary but also systemic effects. The cardiovascular system and the blood are important targets, and also the brain may be directly affected.

• The toxicity may not only be caused by the particles themselves, but can also be caused by chemicals on the surface of particles.
Recommendations

• Impact of exhaust aftertreatment devices such as catalyst and particle traps on the toxicity of the complex mixture is largely unknown

• Impact of new (bio)fuels needs to be investigated for the impact on human health and the environment
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