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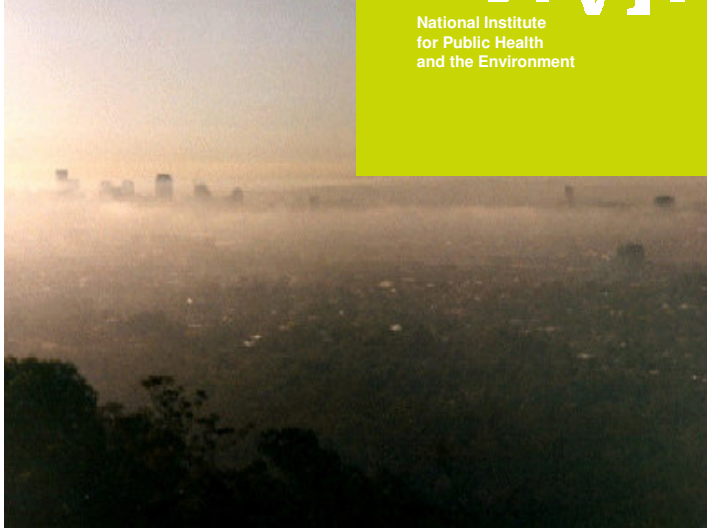

Multi-centre health effect studies on inhaled combustion derived (nano)particles in rats and humans

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Adverse health effects of PM

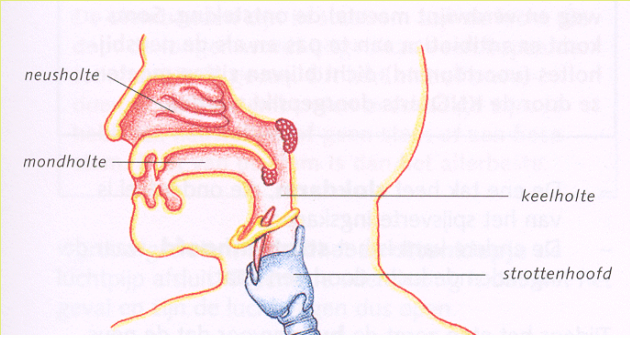
Epidemiology

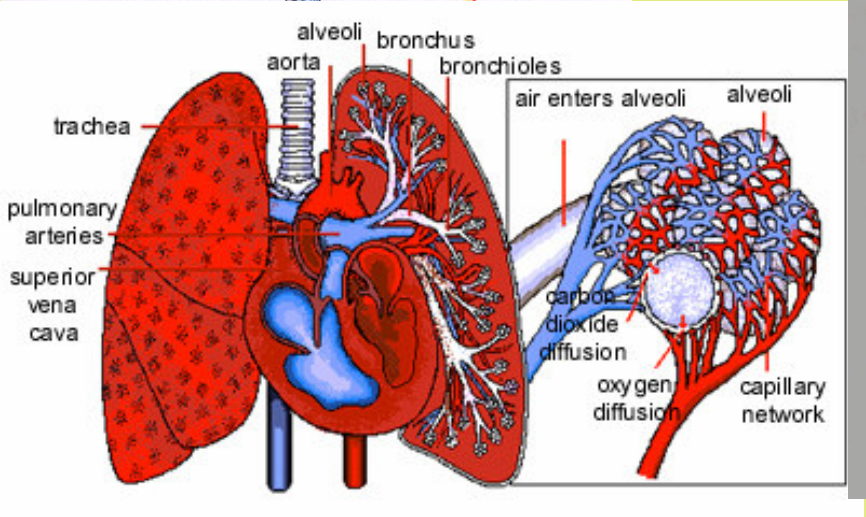
- Shortening of life expectancy
- Impaired lung development of otherwise healthy children living near a freeway

In vivo studies

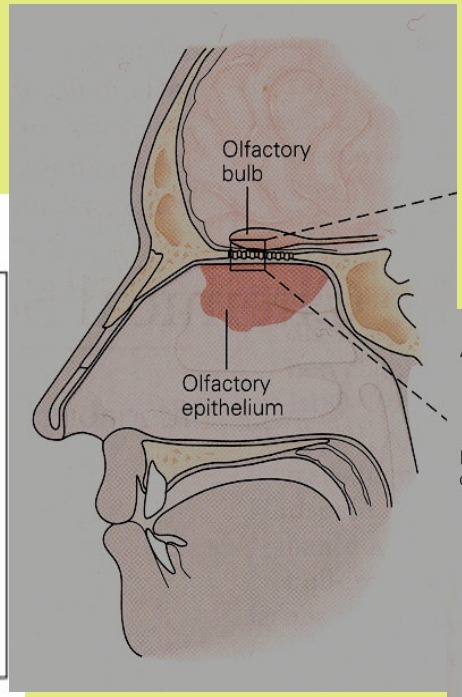
- Emissions from highways result in inflammation of the lung and cardiovascular changes

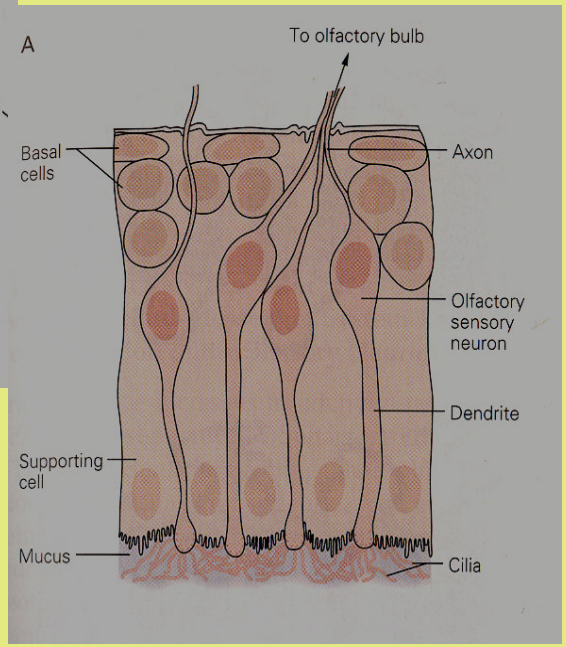
Routes of exposure to (nano)particles



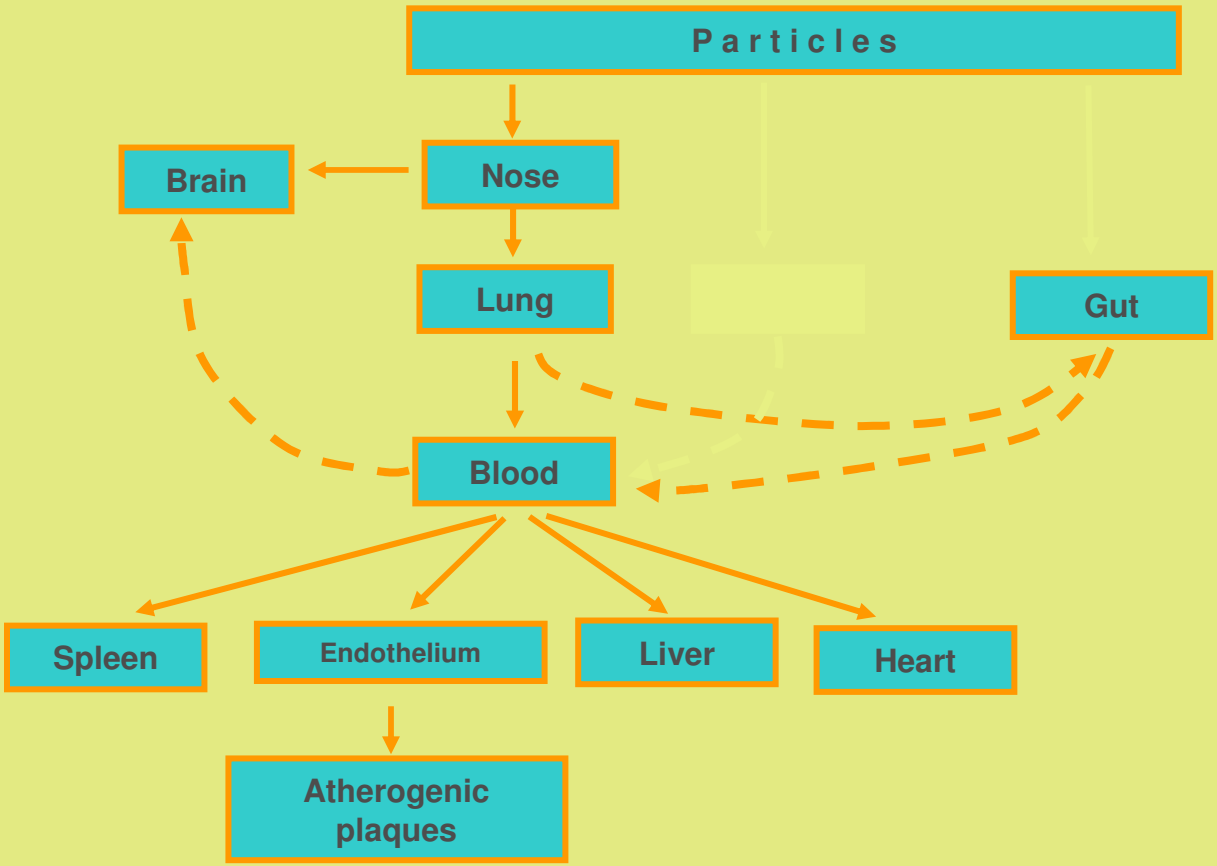


Figuur 1.21 Ademhalingsstelsel





Toxicokinetics of PM



Courtesy K. Donaldson

Controlled diesel engine exhaust studies – volunteers and rats

Rat studies

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

Human volunteers

- Acute exposure - plethysmography (2 hours; 300 µg/m^3)
- Acute exposure - QEEG (1 hour; 300 µg/m^3)

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; 6hours/day
  - **150 µg/m^3 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

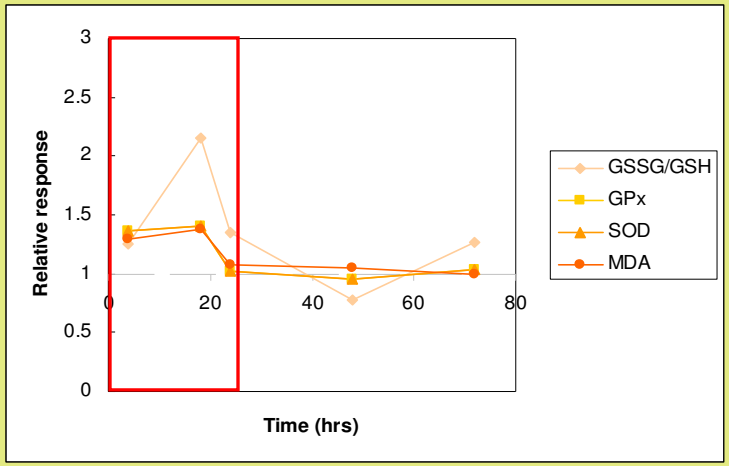
Rat study: Acute exposure – time series Design

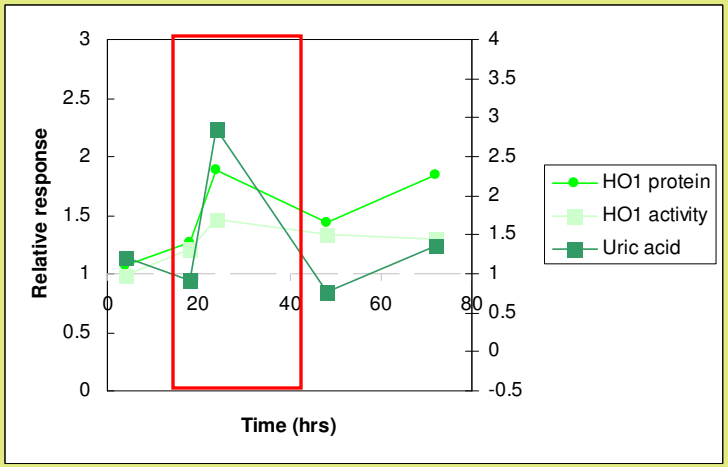
- Exposure
  - Male Fisher F344 rats (9 weeks old)
  - **1.9 mg/m^3 diesel engine exhaust**
  - 2 hours
  - Nose-only
  - Characterisation (mass, number, size distribution, sulphate, nitrate, XRF, EC/OC, volatile organic components)

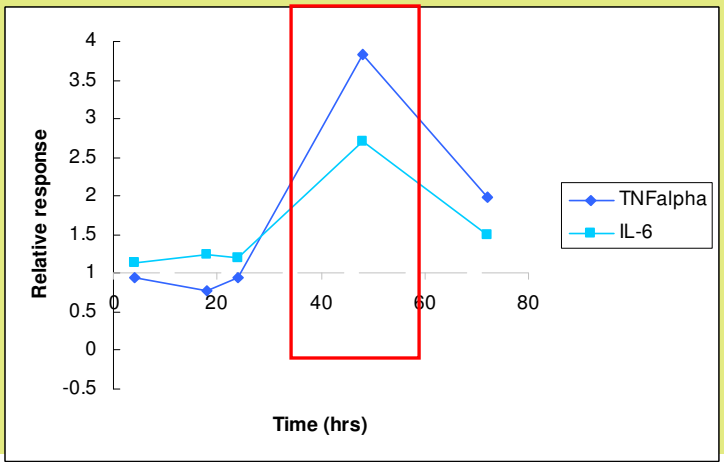
- Effect assessment
  - 4, 18, 24, 48, and 72 hours post-exposure
  - Bronchoalveolar lavage fluid (BALF), blood, tissues
  - Oxidative stress, inflammation, tissue damage

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

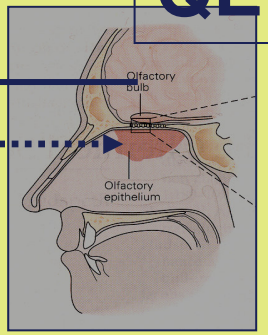
- Oxidative stress is preceeded by a procoagulant reaction in the blood as indicated by concurrent increases in TF activity and the amount of trombin generation

Human volunteers: Acute exposure - QEEG

Inhalation UFP

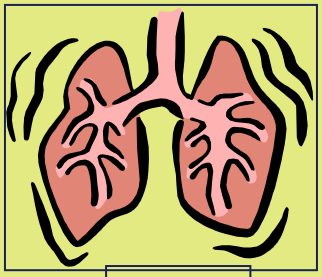
Translocation of NP

QEEG

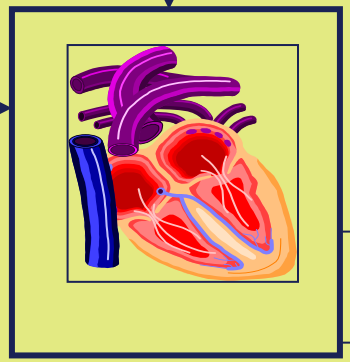


Irritant receptors

Soluble Components, NP



VR



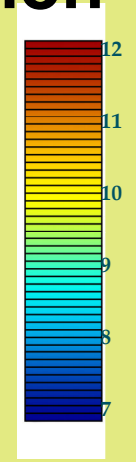
HRV

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

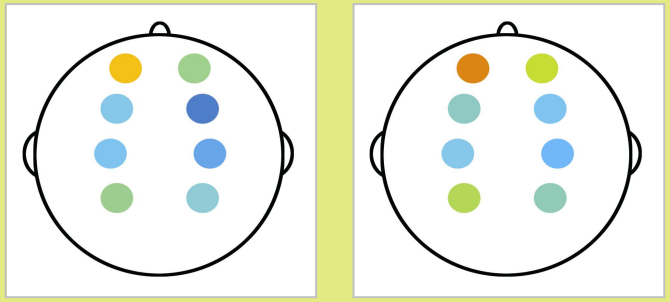
Study in Umea: diesel exhaust (300 ug/m3)

Dr. Thomas Sandström, Dr. Anders Blomberg

Effect of diesel engine exhaust on brain function

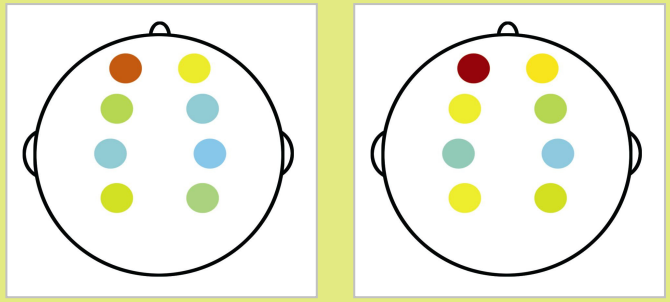


During exposure



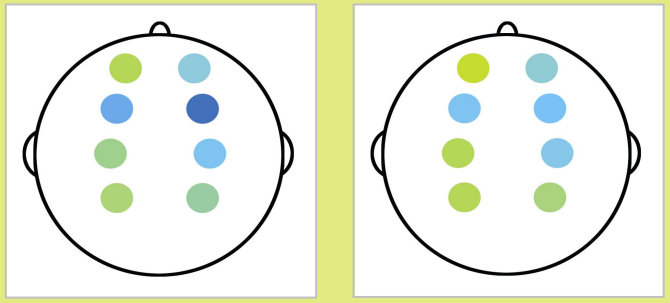
5′ 55′

Post exposure



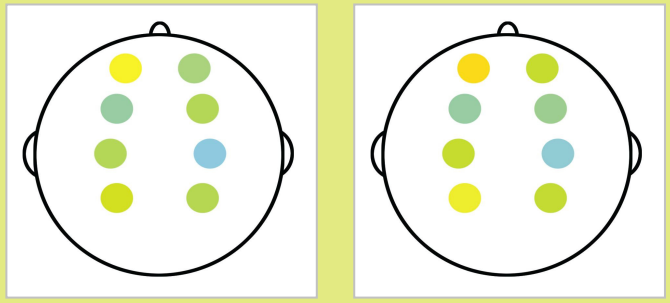
5′ 55′

Sham exposure



5′ 55′

Sham post



5′ 55′

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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 aftertreatement 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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