

Diesel exhaust inhalation and stress response: a mechanism for systemic health impacts

Errol Thomson

Research Scientist, Inhalation Toxicology Laboratory, Environmental Health
Science and Research Bureau, Health Canada

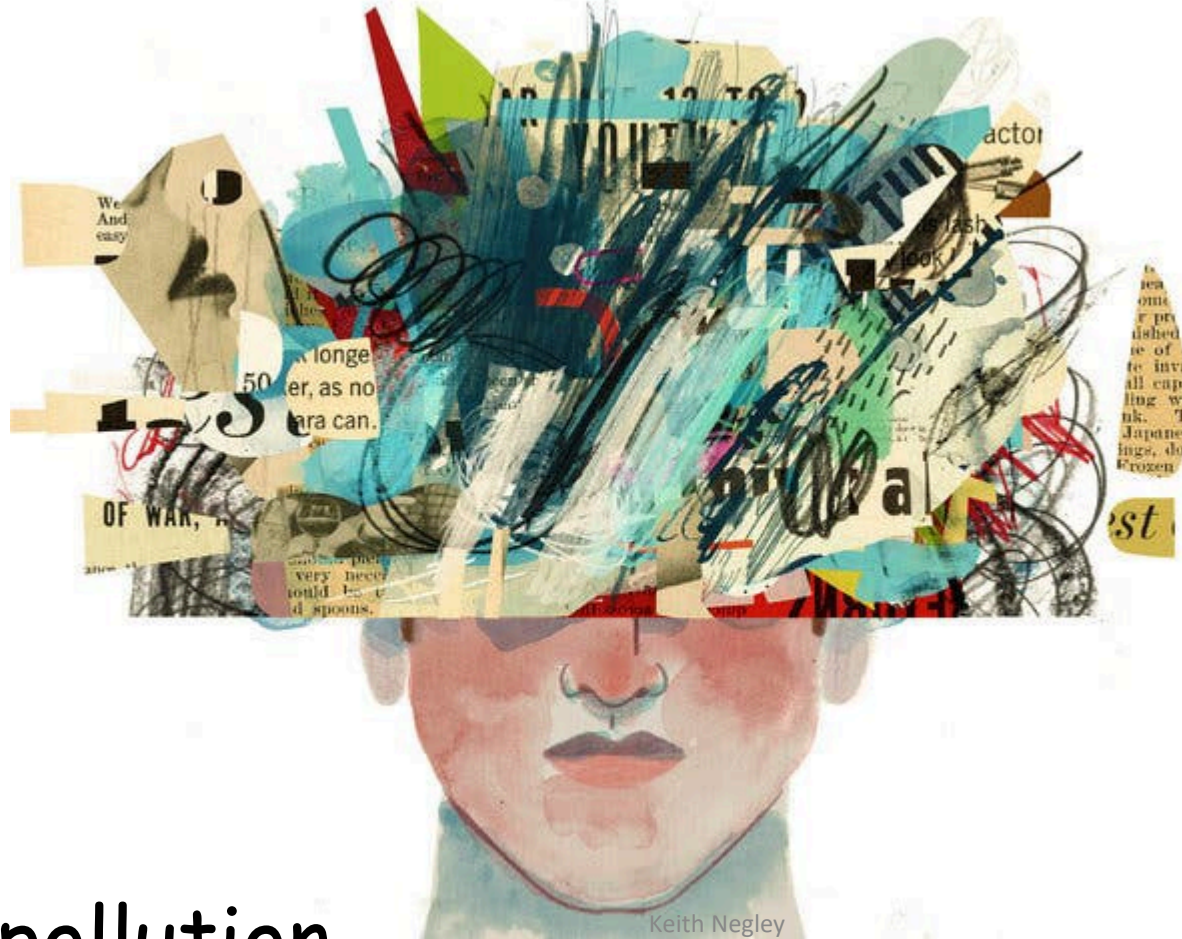
Adjunct Professor, Department of Biochemistry, Microbiology & Immunology,
Faculty of Medicine, University of Ottawa

MDEC, Toronto, ON, October 7, 2026

YOUR HEALTH AND SAFETY... OUR PRIORITY.



The New York Times



More stress?



Air pollution

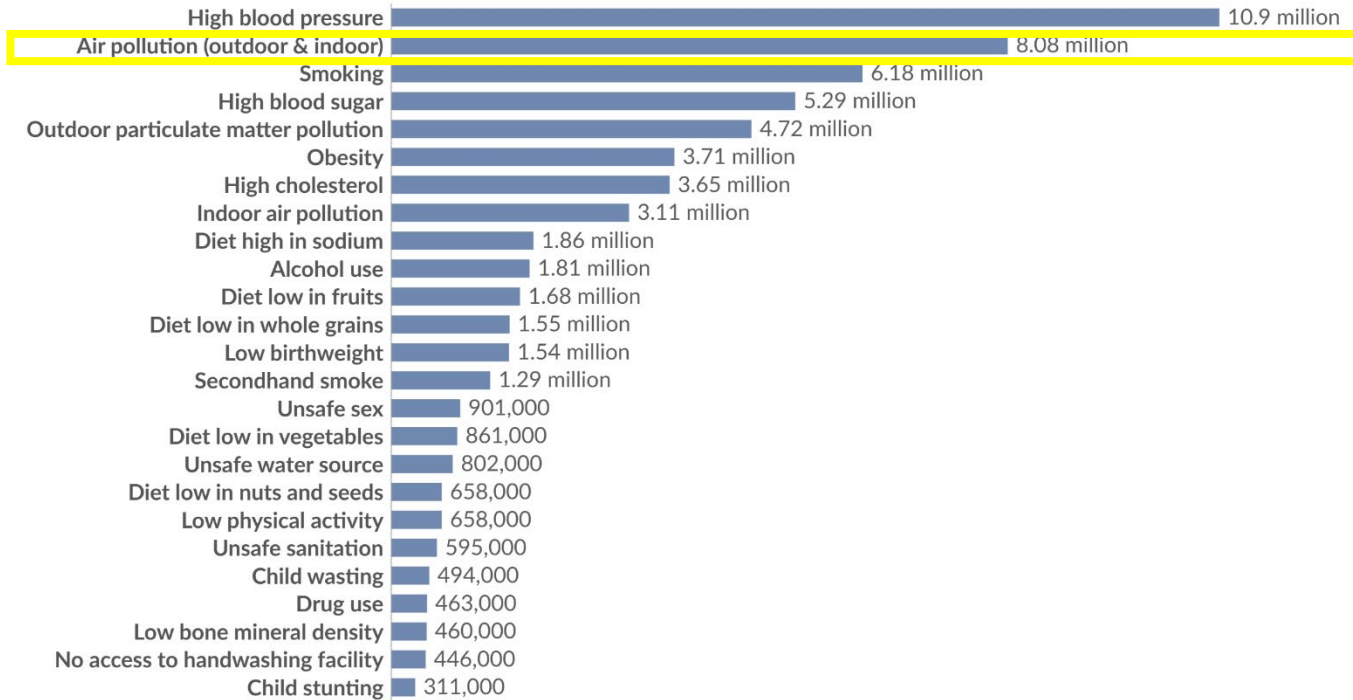
~~Stress~~ Can Make You Sick. Take
Steps to Reduce It.



Deaths by risk factor, World, 2021

Our World
in Data

The estimated annual number of deaths attributed to each risk factor¹. Estimates come with wide uncertainties, especially for countries with poor vital registration².

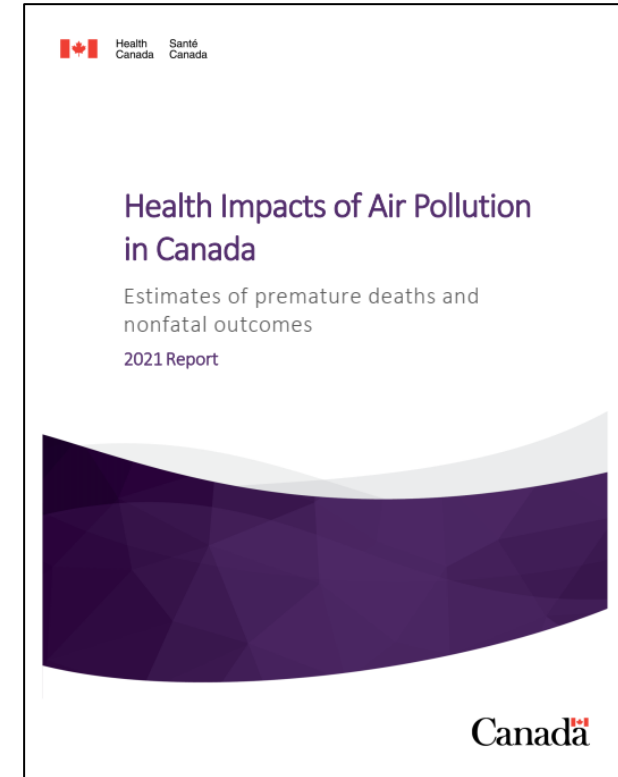


Data source: IHME, Global Burden of Disease (2024)

OurWorldinData.org/causes-of-death | CC BY

Note: Risk factors¹ are not mutually exclusive. The sum of deaths attributed to each risk factor can exceed the total number of deaths.

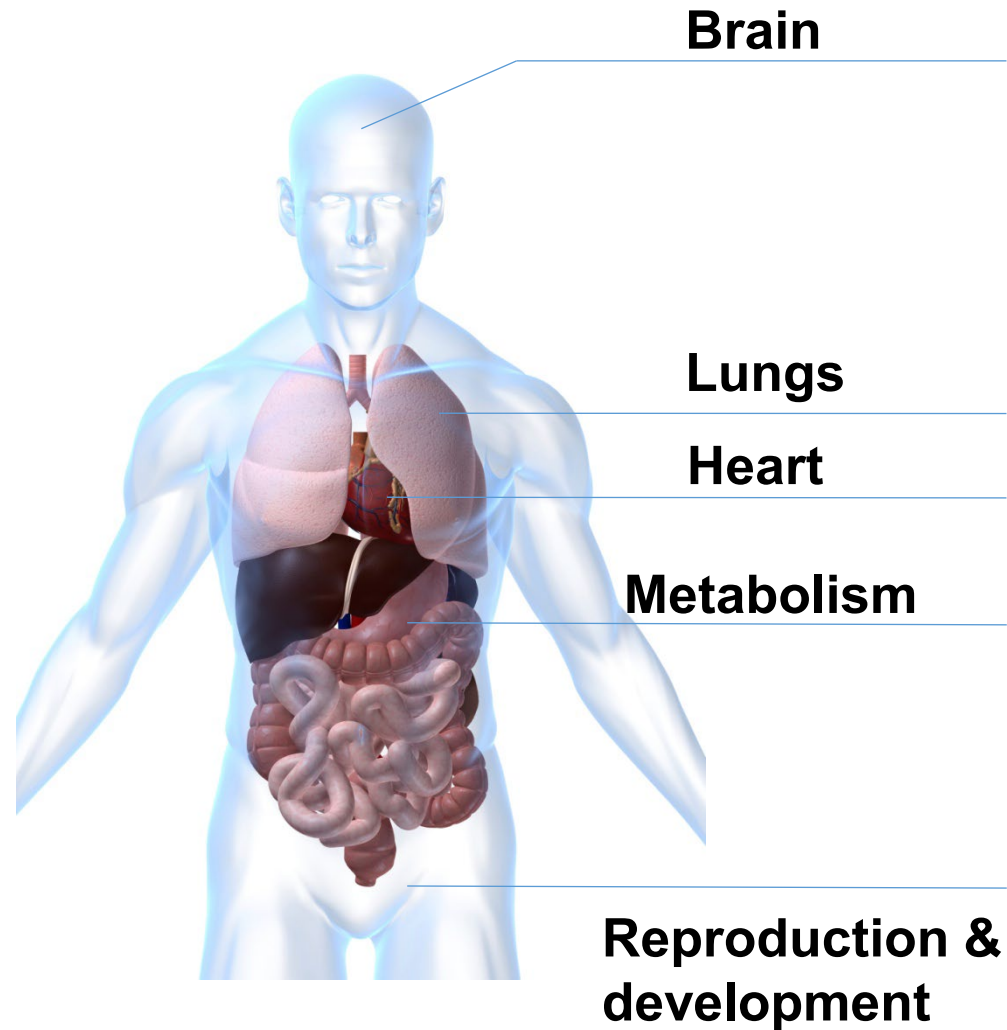
1. Risk factor A risk factor is a condition or behavior that increases the likelihood of developing a given disease or injury, or an outcome such as death.



Estimates for Canada:

- Over 15,000 premature deaths/year
- 2.7 million asthma symptom days and 35 million acute respiratory symptom days per year
- Economic costs of health burden estimated at \$120 billion (2016)

Air pollution health effects



Cognitive decline, dementia, anxiety, depression, stroke, suicide

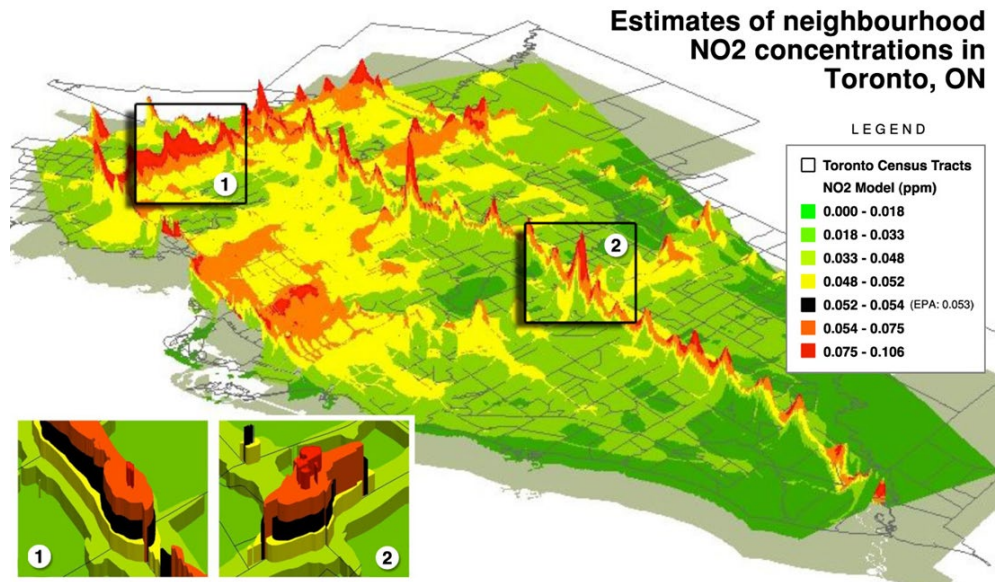
Reduced lung function, asthma, COPD, lung cancer

Heart disease, changes to heart rhythm, atherosclerosis

Metabolic dysfunction, obesity, diabetes

Fertility, low birth weight, developmental programming

Near-road exposures



Buzelli and Jerrett, Can J Reg Sci 30: 195-210 (2007)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2007;357:2348-58.

Respiratory Effects of Exposure to Diesel Traffic in Persons with Asthma

James McCreanor, M.R.C.P., Paul Cullinan, M.D., Mark J. Nieuwenhuijsen, Ph.D., James Stewart-Evans, M.Sc., Eleni Malliarou, M.Sc., Lars Jarup, Ph.D., Robert Harrington, M.S., Magnus Svartengren, M.D., In-Kyu Han, M.P.H., Pamela Ohman-Strickland, Ph.D., Kian Fan Chung, M.D., and Junfeng Zhang, Ph.D.

Living near major roads and the incidence of dementia, Parkinson's disease, and multiple sclerosis: a population-based cohort study

Lancet 2017; 389: 718-26

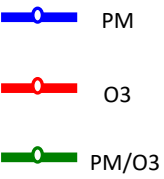
Published Online

January 4, 2017

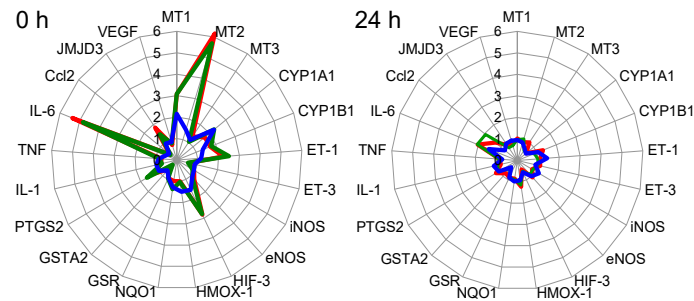
[http://dx.doi.org/10.1016/S0140-6736\(16\)32399-6](http://dx.doi.org/10.1016/S0140-6736(16)32399-6)

Hong Chen, Jeffrey C Kwong, Ray Copes, Karen Tu, Paul J Villeneuve, Aaron van Donkelaar, Perry Hystad, Randall V Martin, Brian J Murray, Barry Jessiman, Andrew S Wilton, Alexander Kopp, Richard T Burnett

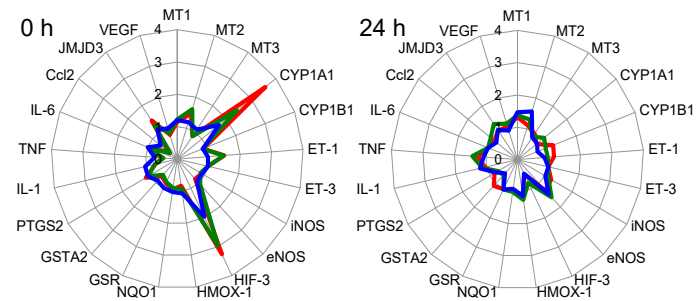
UN



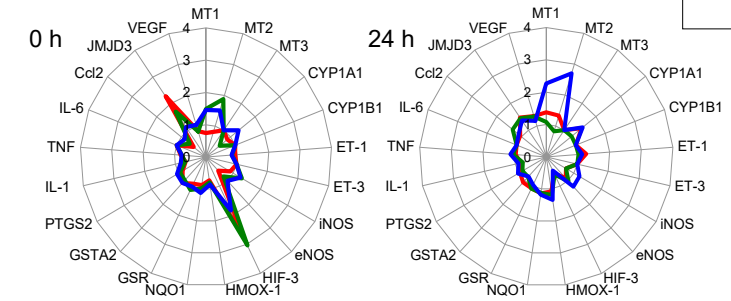
Lungs



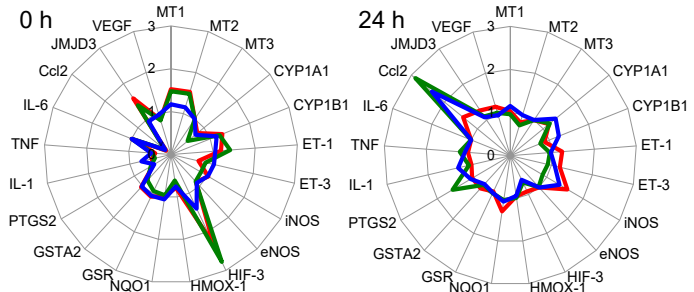
Heart



Liver

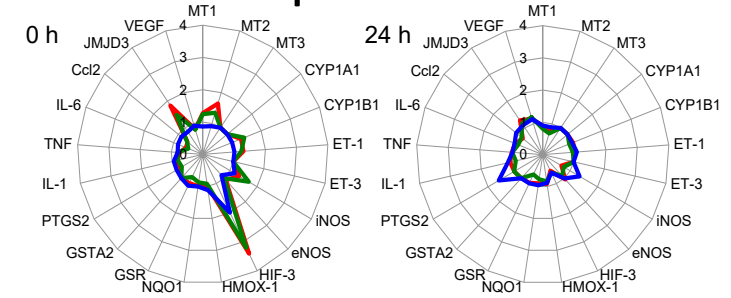


Kidney

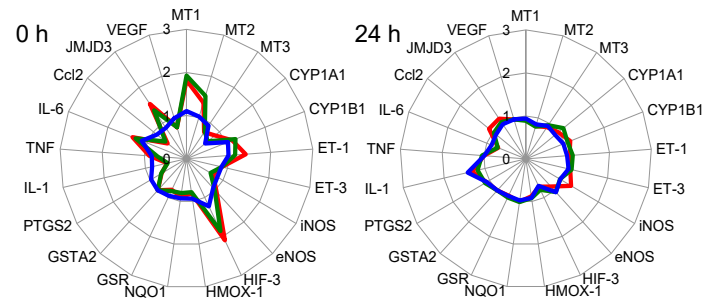


Mapping pollutant effects on the body

Spleen



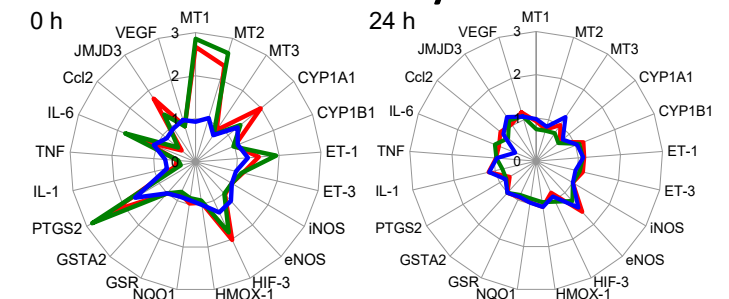
Brain



Surprise # 1:

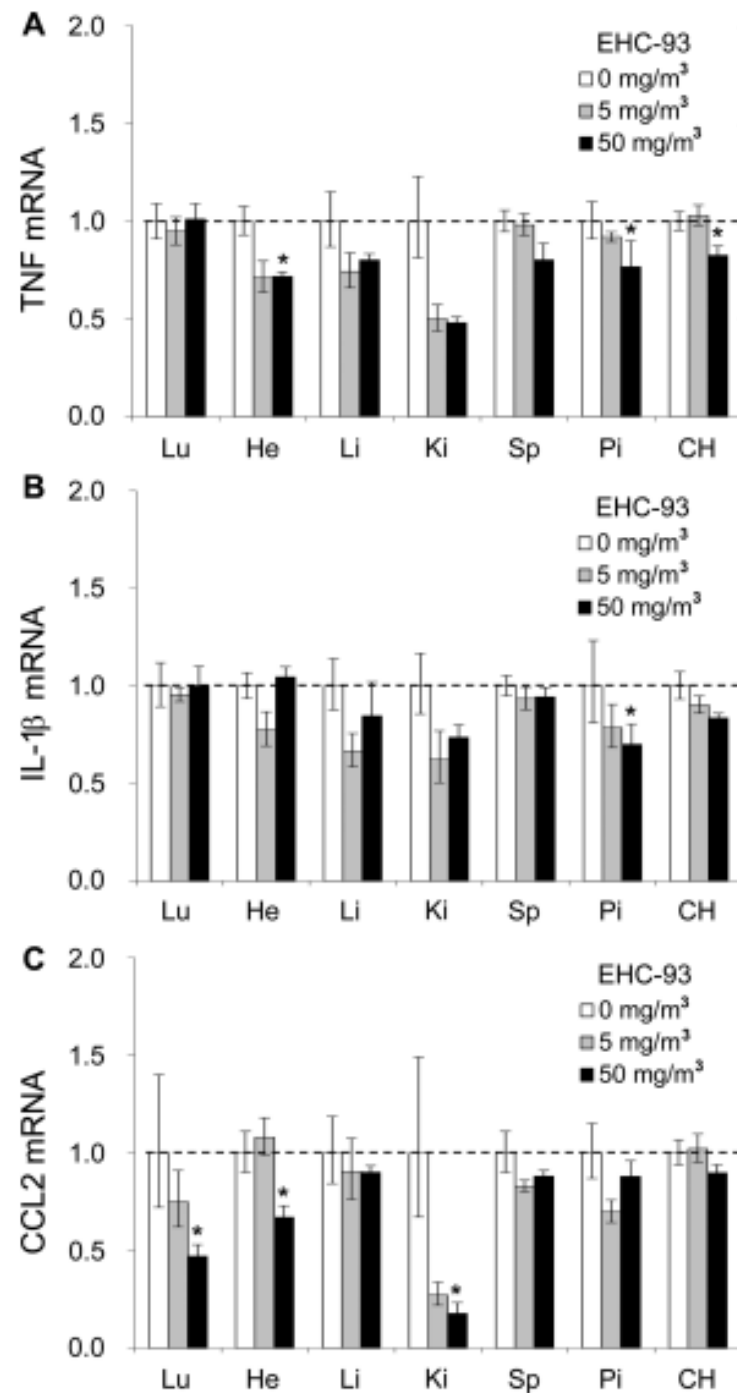
Every tissue was affected

Pituitary



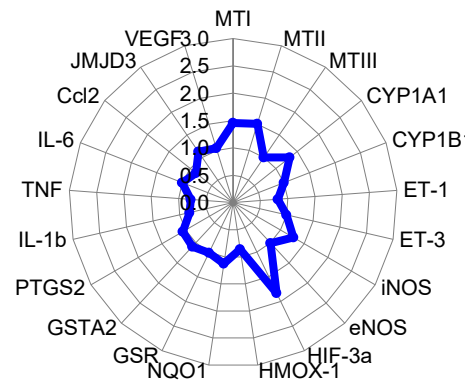
Surprise # 2:

Air pollutants didn't increase inflammatory signaling, they decreased it

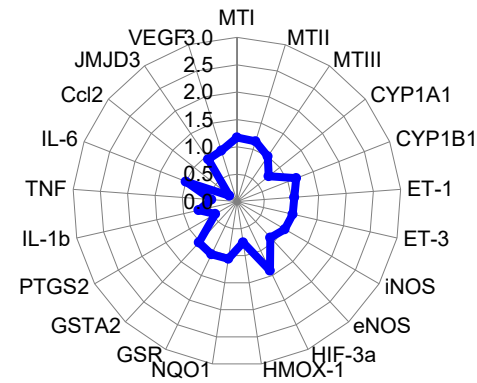


Surprise # 3: similarity of profiles across tissues

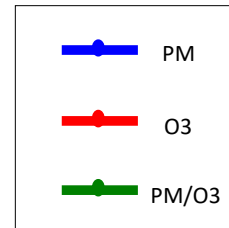
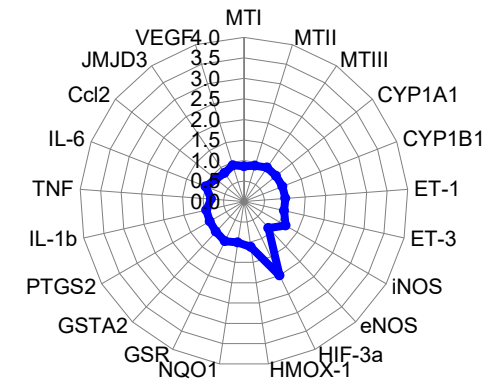
Liver



Kidney

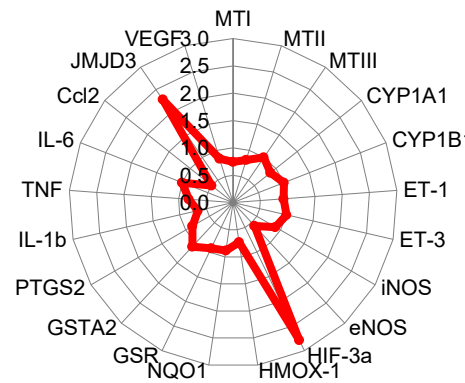


Spleen

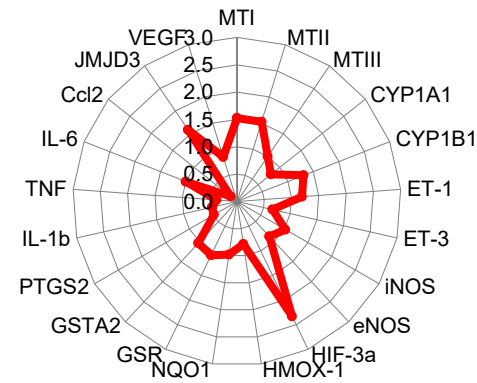


Surprise # 3: similarity of profiles across tissues

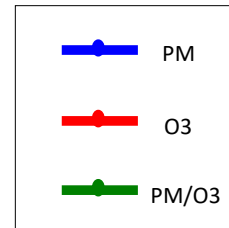
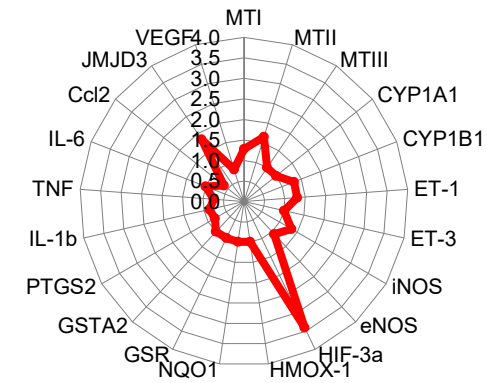
Liver



Kidney

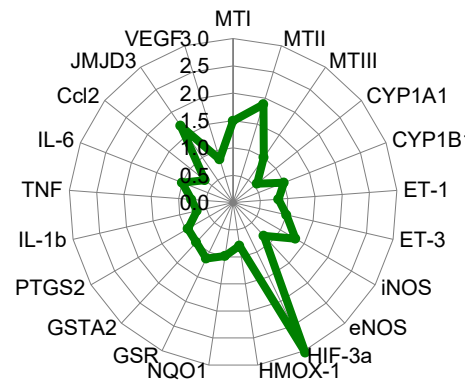


Spleen

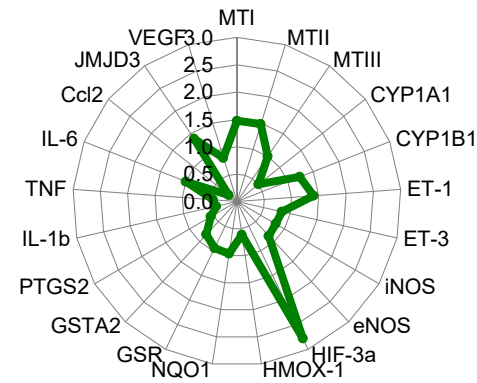


Surprise # 3: similarity of profiles across tissues

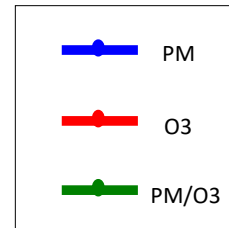
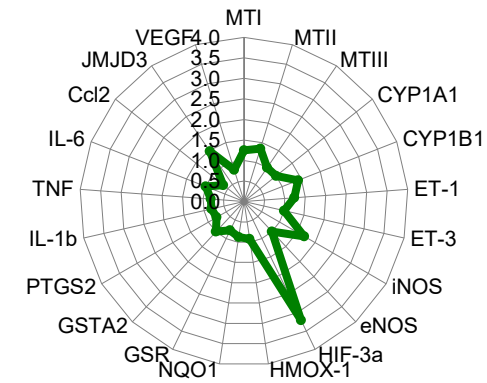
Liver



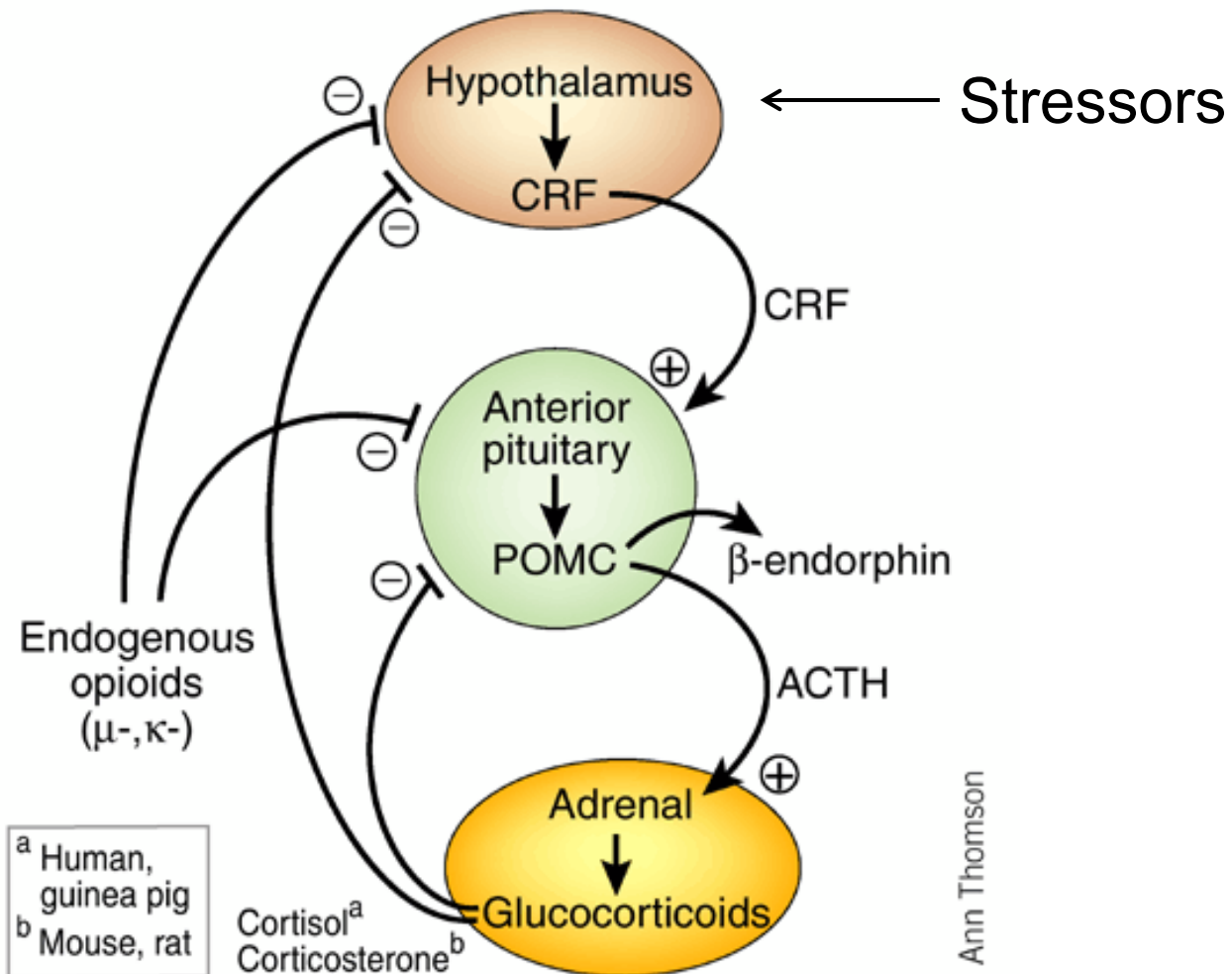
Kidney



Spleen



Hypothalamic-pituitary-adrenal (stress) axis



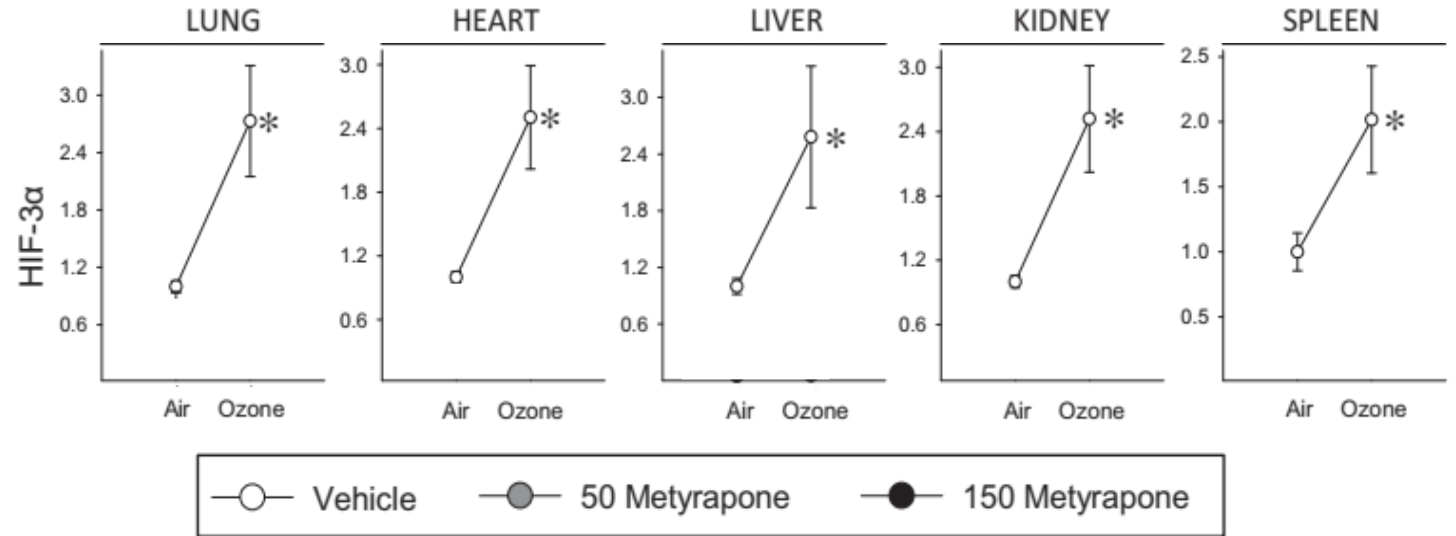
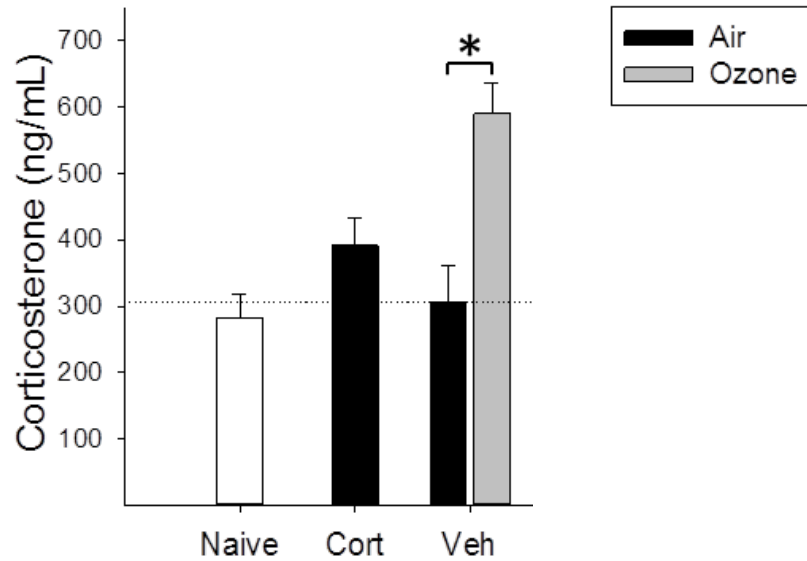
Glucocorticoids:

- anti-inflammatory (acutely)
- metabolic effects
- oxidative stress
- immunosuppressive
- hypertension
- impaired cognitive ability
- depression

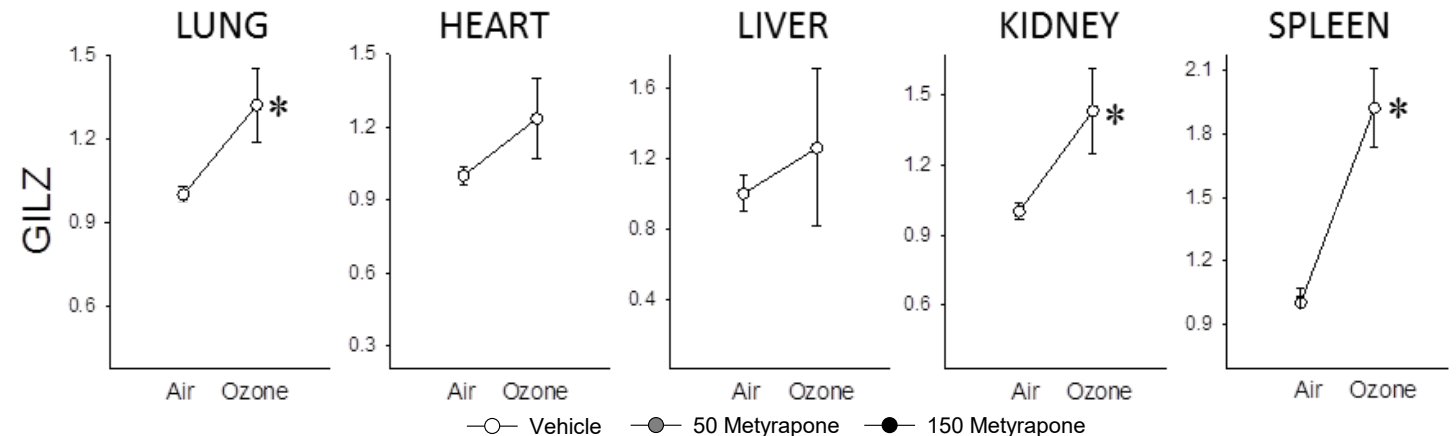
Chronic activation and dysfunction is implicated in many disease states.

Stress hormones drive systemic effects of pollutants

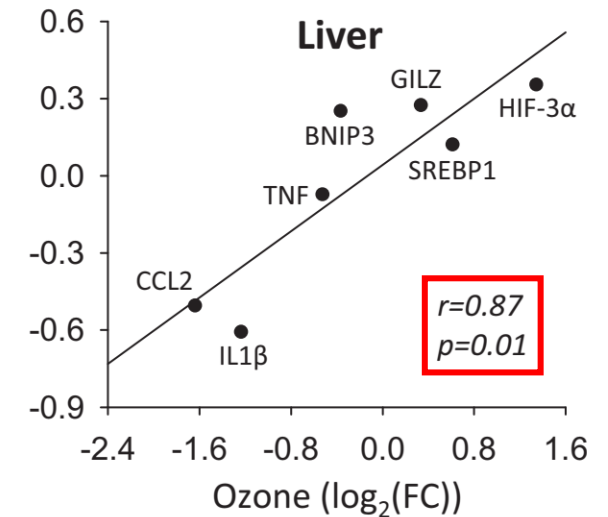
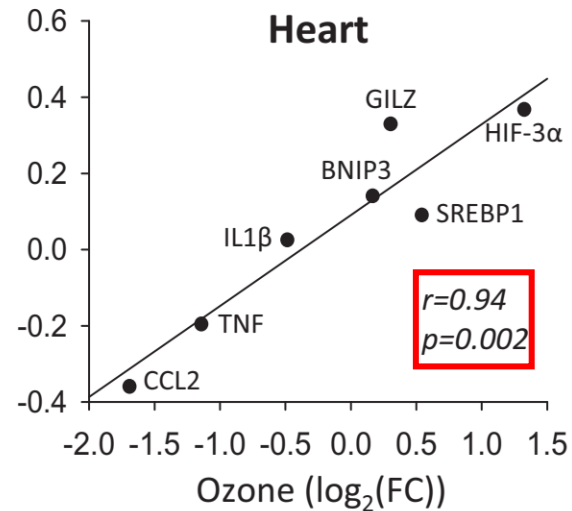
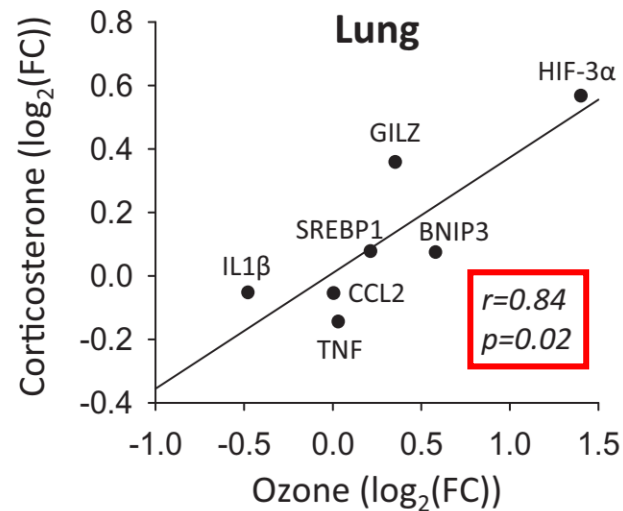
Metabolic



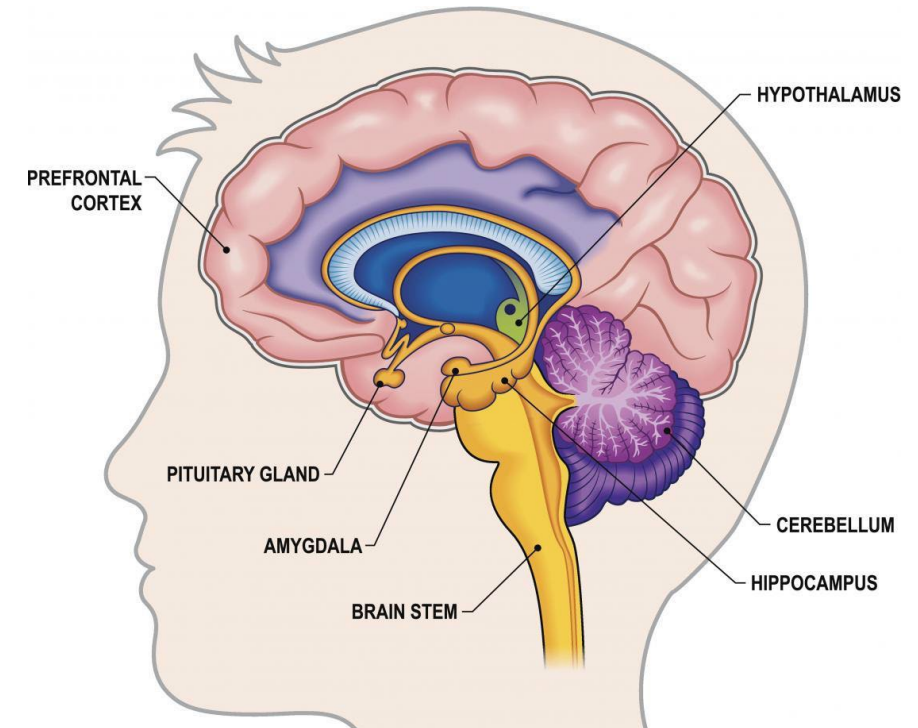
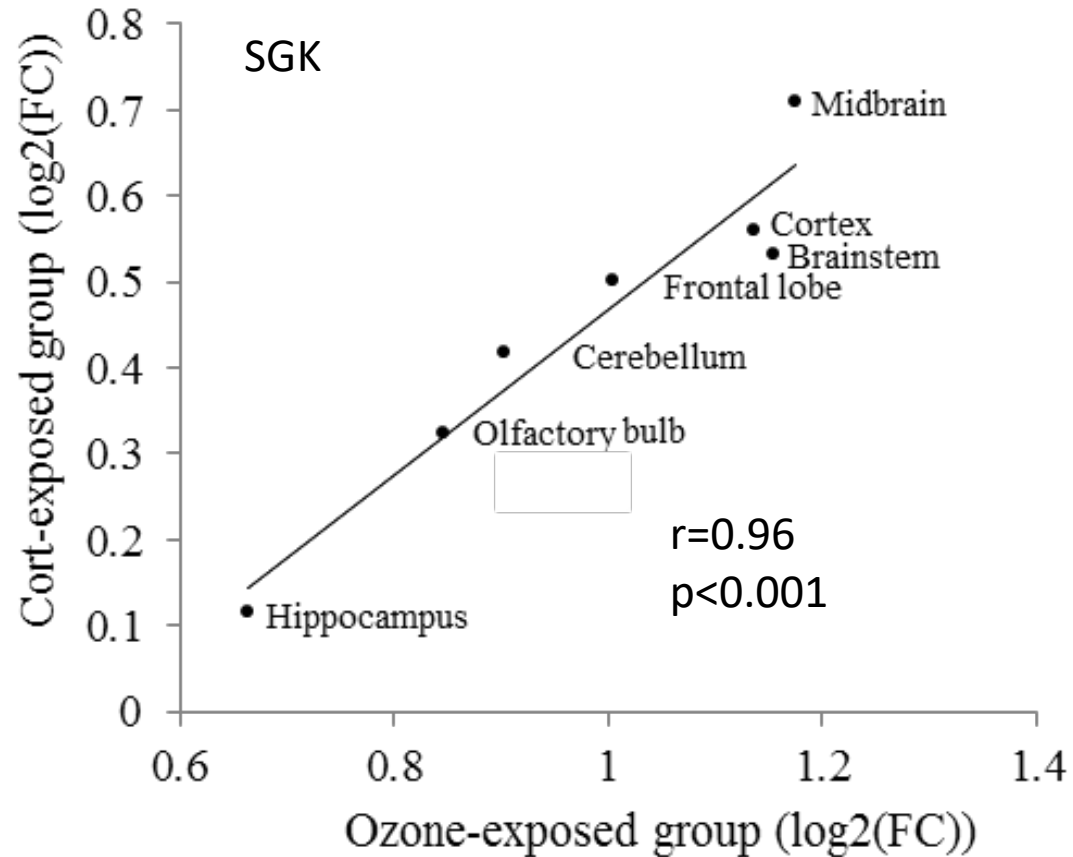
Immune



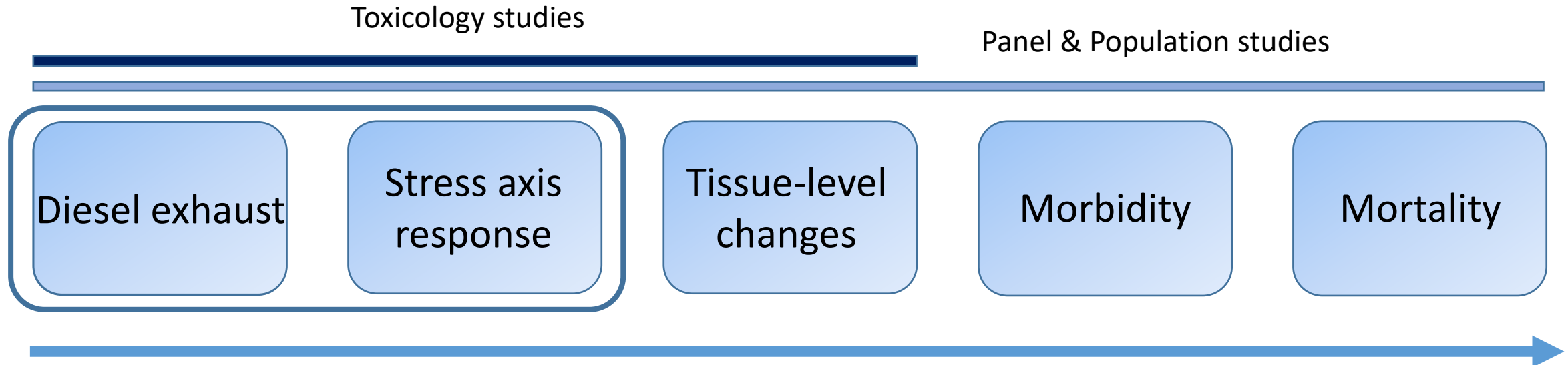
Air pollution effects reproduced with a shot of stress hormone



What about effects in the brain?

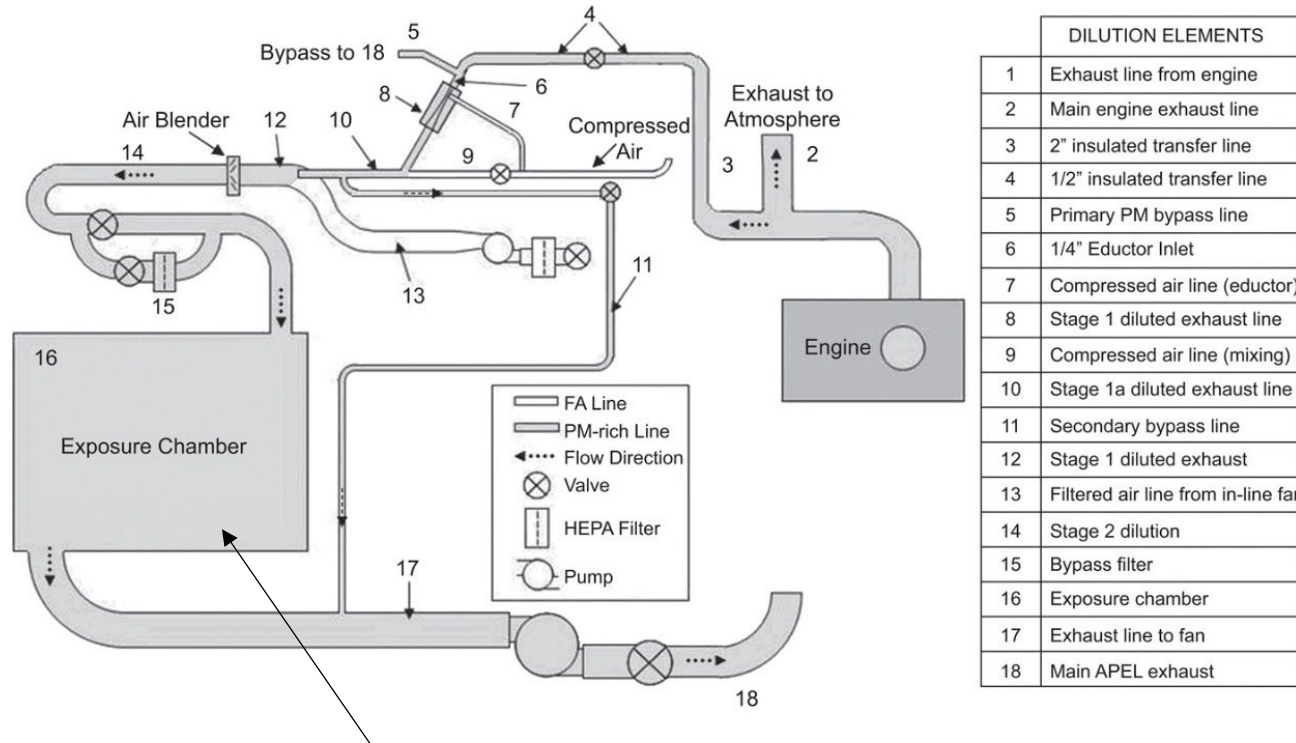


Coherence of evidence



Does exposure to diesel exhaust increase stress hormone levels?

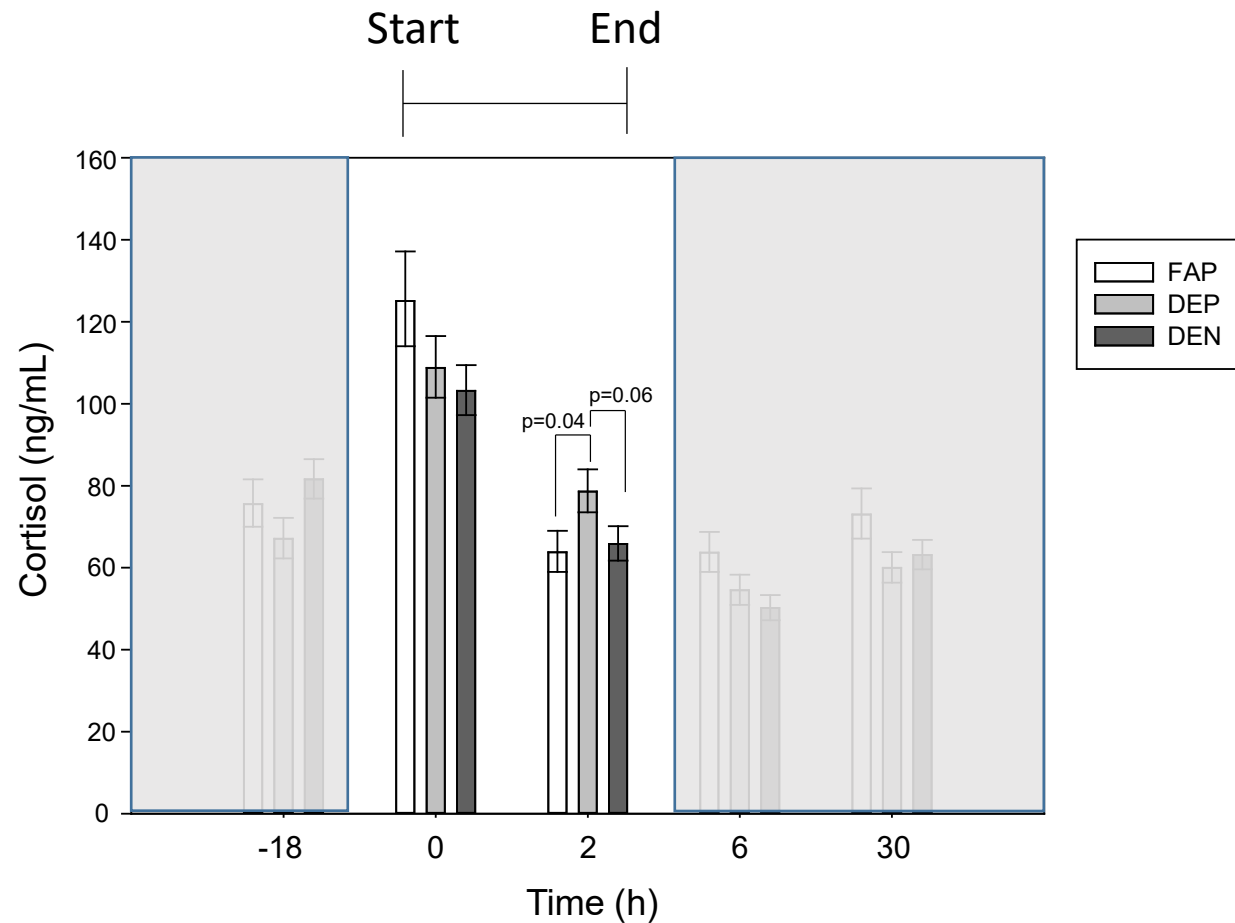
Panel study on acute effects of diesel exhaust



Birger et al., Inhal Tox 23:4 (2011)

- **Participants:** N= 19; 14 with asthma (7 females, 7 males), 5 without (3 females, 2 males)
- **Randomized double-blind crossover design**
- **Exposures:** 3 exposure conditions
 - Filtered air with placebo (FAP)
 - Diesel exhaust with placebo (DEP)
 - Diesel exhaust with N-acetylcysteine (DEN)
 - Target concentration: 300 $\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$
- Minimum 2 week washout period between exposures
- **Measures:** Cortisol measured before and after each 2 h exposure

Cortisol response to diesel exhaust



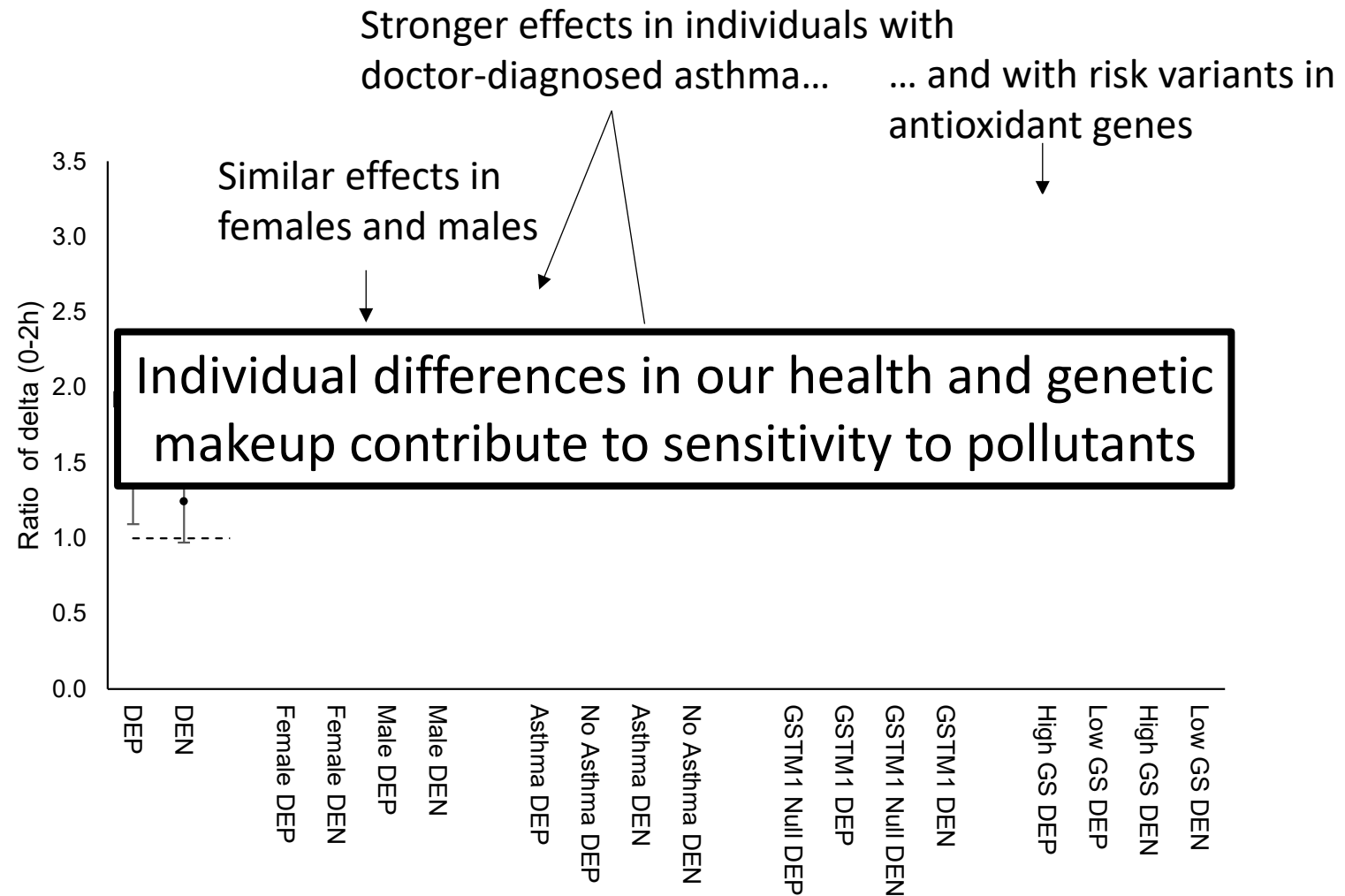
- Diesel exhaust rapidly increased cortisol levels (compared to filtered air)
- N-acetylcysteine tended to reduce the effect
- Effects were transient

Exposure x Time interaction, $p < 0.0001$



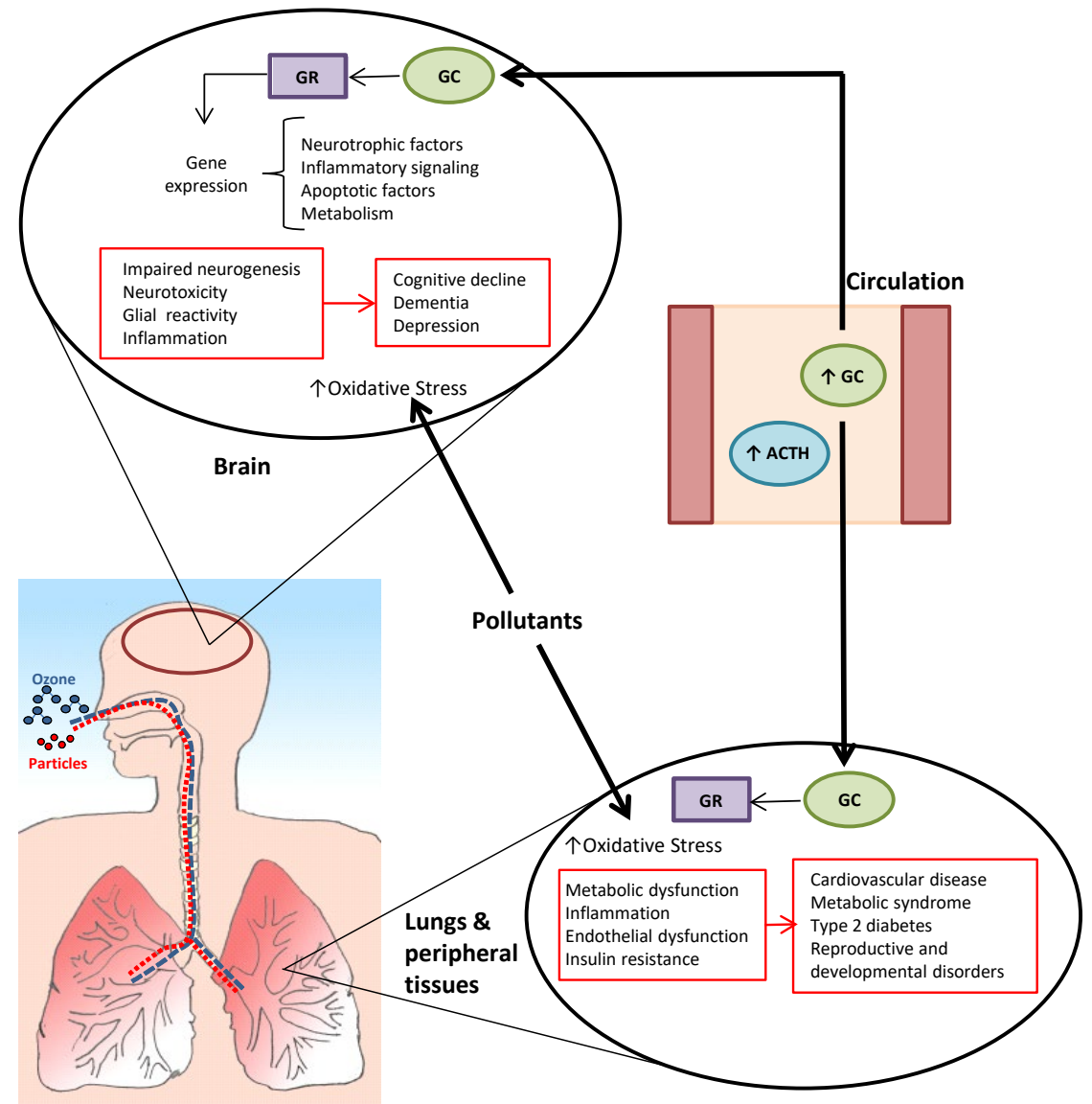
Stress
response?

Answer: It depends...

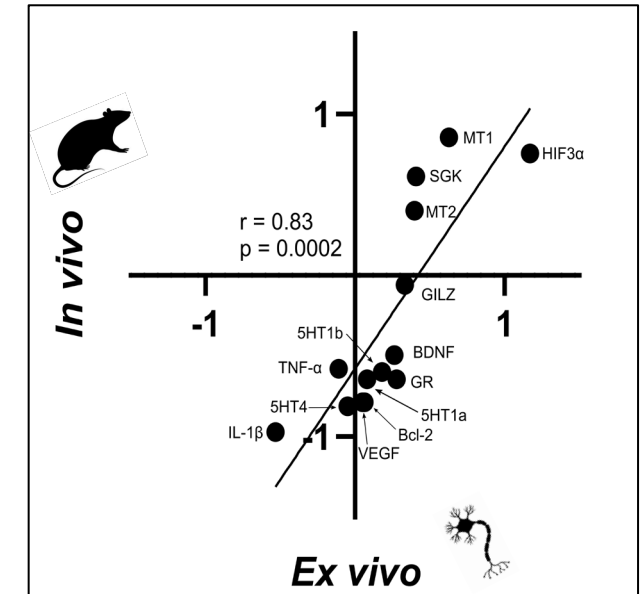
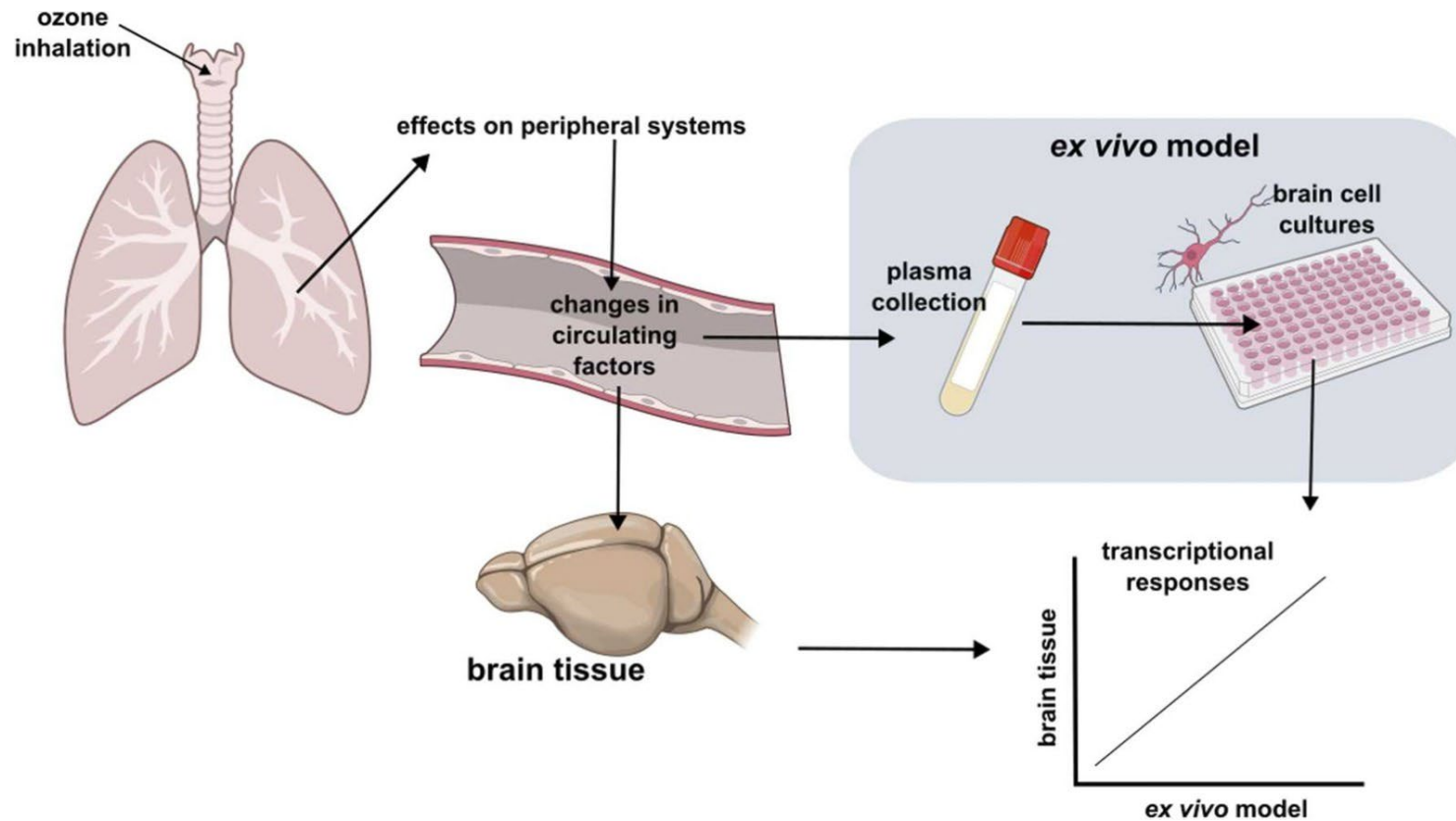


Mechanisms

- Direct and indirect pollutant effects
- Oxidative stress, inflammation: important for disease processes
- Early responses include “fight-or-flight” stress axis activation
- Air pollution, like stress, affects the whole body
- Chronic air pollution = chronic stressor



An ex vivo model of pollutant effects on the brain



Rose and Thomson, Toxicology, 2025

Now translated to human participants to study effects of diesel exhaust on the brain



Screening for toxicity determinants



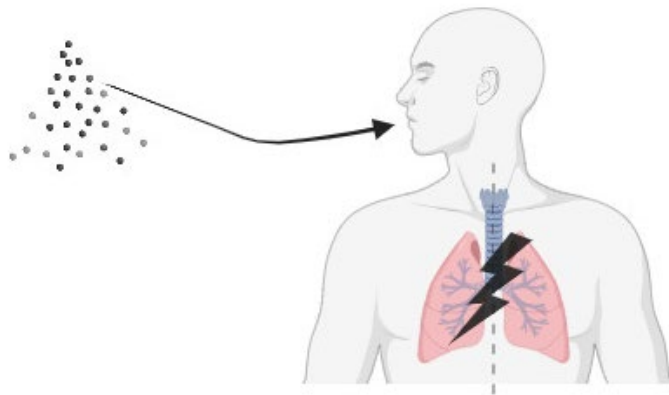
EXPOSURE



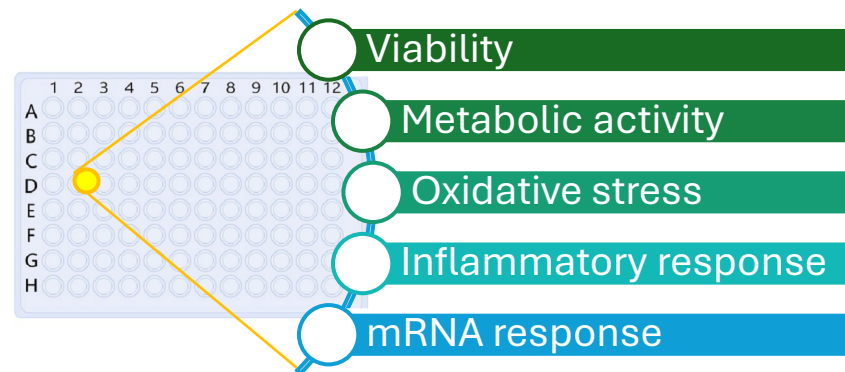
TOXICITY



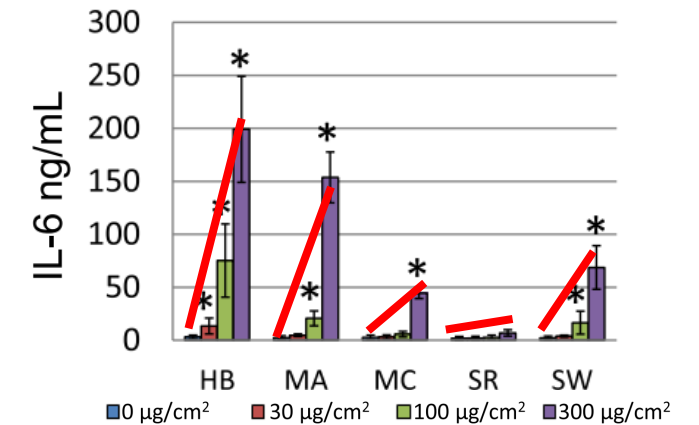
DATA REDUCTION AND INTEGRATION



- Tools to assess PM, gases, mixtures

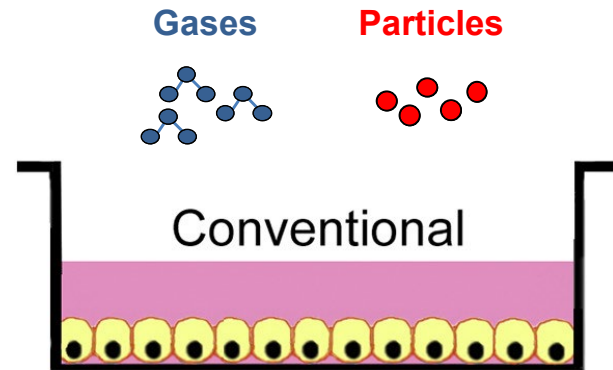


- Multiple biological endpoints

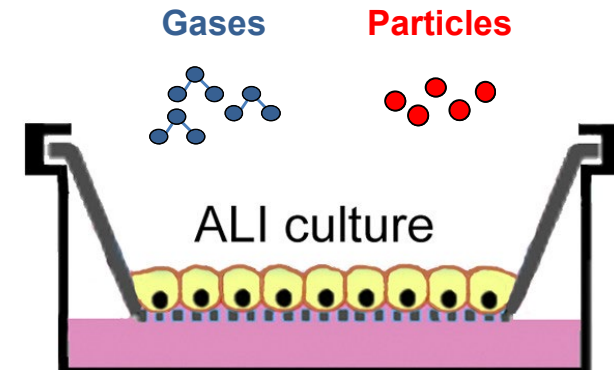


- Relate potency to constituents

In vitro exposure methods



- Relatively **high-throughput**
- Less technically challenging
- **Uncertain dosimetry**, especially for nano/UFP
- Potential **modification** of the test agent in the media



- **Physiologically-relevant** exposures
- Exposure to the **actual atmospheres** to which people are exposed
- Dose: **we measure what the cells “see”**
- More **human-relevant data** in support of regulatory needs

Disentangling cumulative effects on health of near-road exposures

Broader exposure context

- Air pollutants
- Noise
- Individual characteristics
- Contextual factors

Complex pollutant mix

- Traffic
- Ambient

Specific pollutant

- Brake wear
- Tire wear
- Diesel
- Ozone

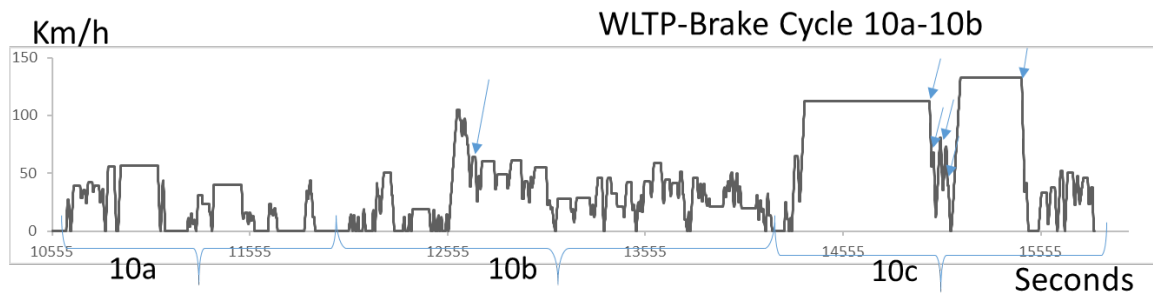
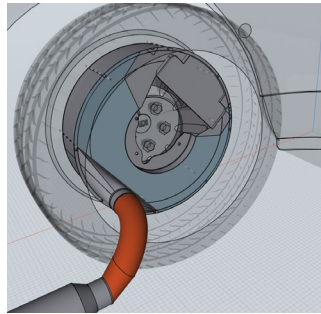
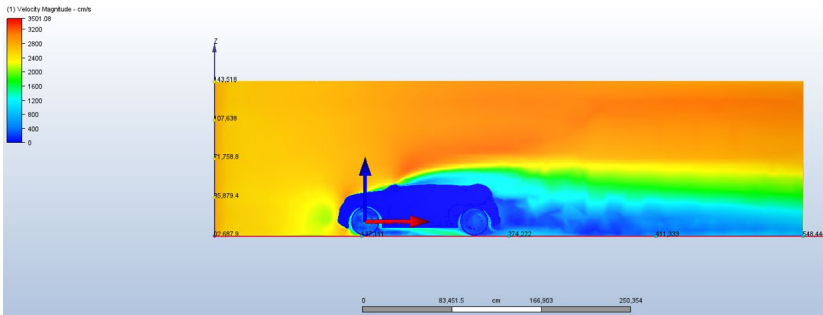
Population studies (HC, ISGlobal)

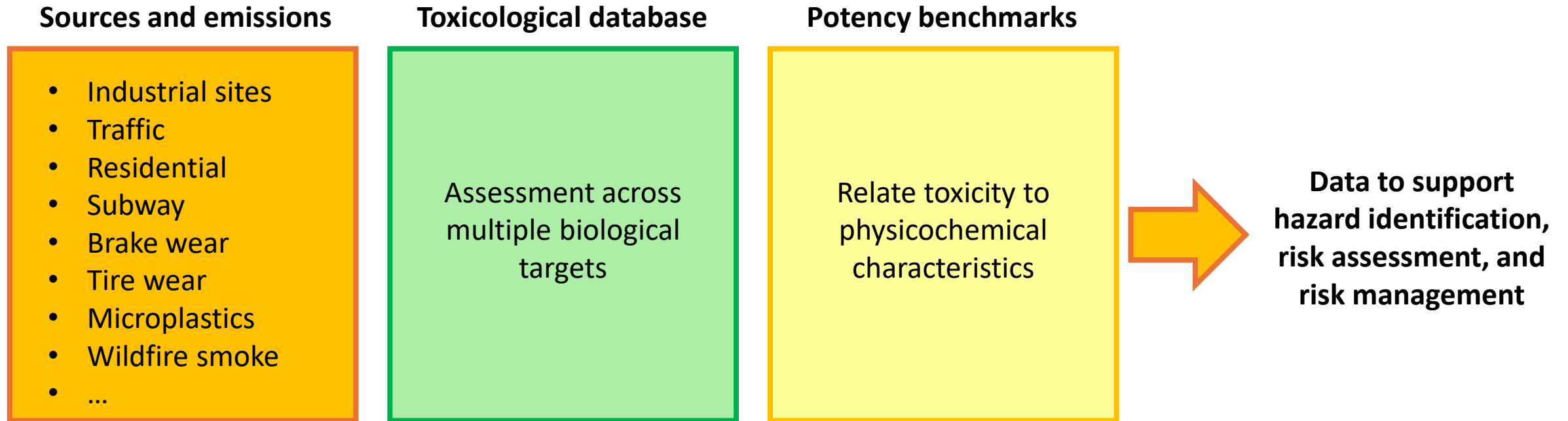
Collection and characterisation (HC, ECCC)
Inhalation toxicology (HC)

Materials procurement and fleet characterisation (TC)
Emission generation, collection, characterisation (HC, ECCC)

Panel study (UBC)

Exposures to freshly-generated brake wear





Team

Inhalation Toxicology Laboratory

Dalibor Breznan
Kevin Curtin
Alain Filiatreault
Marjolaine Godbout-Cheliak
Josée Guénette
Andres Henriquez
Miranda Jordens
Shinjini Pilon
Jith Thomas
Renaud Vincent
Djordje Vladislavljevic

Environmental Health Science and Research Bureau

Ella Atlas
Rick Burnett
Harun Kalayci
Prem Kumarathanan
Brittany Halverson-Duncan
Mietek Szyskowitz
Mike Wade
Mike Walker
Andrew Williams

Water and Air Quality Bureau

Gary Mallach
Keith Van Ryswyk

Environment and Climate Change Canada

Jeff Brook (now UofT)
Valbona Celo
Eva Dabek-Zlotorzynska
Elisabeth Galarneau
Debbie Rosenblatt
Jonah Veenendaal

Statistics Canada

Tanya Christidis
Lauren Pinault
Mike Tjepkema

Funding

Clean Air Regulatory Agenda
Addressing Air Pollution Horizontal Initiative
Air Quality Program

University of British Columbia

Chris Carlsten
Chris Rider

University of Ottawa

Steffany Bennett
Ian Colman

McMaster University

Alison Holloway

University of New Brunswick

Dan Crouse (now HEI)

University of Toronto

Greg Evans
Nicole Trieu

ISGlobal (Barcelona)

Mònica Guxens
Yuchan Mou

Students

Cheuk Kei Yeung
Chanele Polenz
Kunal Patel
Sidonie Ward
Caroline Illman
Michael MacLeod
Milaan Thirukumaran
Nivetha Srikanthan
Joel Bennoit
Avril Metcalfe-Roach
Nathan Bullen
Mercedes Rose
Tristan Woo
Marie-Claire Wasson
Linda Chan
Arunemathi Shanmugam
Thushani Chandrakumar
Julia Loftus
Ipshita Tomar
Fady Ghattas
Tara Ferguson
Michelle Miller
Sathana Sivasegaran
Jaya Kapur
Vanessa Cen
Katie MacDonald