Air Pollution Exposure is Associated with the Gut Microbiome as Revealed by Shotgun Metagenomic Sequencing


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Health Effects of Air Pollution

https://www.stateofglobalair.org
Image: www.wikiwand.com/Pollution
Air Pollution Exposure is Associated With Obesity and Type 2 Diabetes

ADULTS

• ↑Air pollution exposure (NO\textsubscript{x}, NO\textsubscript{2}, and PM\textsubscript{2.5}) associated with greater risk for obesity and type 2 diabetes\textsuperscript{1-3}

• ↑Annual and shorter-term exposure to NO\textsubscript{2} and PM\textsubscript{2.5} had adverse effects on fasting glucose and insulin sensitivity\textsuperscript{4}

CHILDREN

• ↑NRAP exposure associated with increased annual BMI\textsuperscript{5,6}

• ↑NO\textsubscript{2} and PM\textsubscript{2.5} exposure associated with increased insulin resistance (HOMA-IR)\textsuperscript{7,8}

• ↑NO\textsubscript{2} and PM\textsubscript{2.5} exposure associated with declined insulin sensitivity and β-cell function\textsuperscript{9}

\textsuperscript{1}Chen et al., 2013; \textsuperscript{2}Weinmayr et al., 2015; \textsuperscript{3}Li et al., 2016; \textsuperscript{4}Chen et al., 2016; \textsuperscript{5}Jerrett et al., 2014; \textsuperscript{6}McConnell et al., 2014; \textsuperscript{7}Kelishadi et al., 2009; \textsuperscript{8}Thiering et al., 2013 and 2016; \textsuperscript{9}Alderete et al., 2017
Overarching Hypothesis: Air Pollution Contributes to Obesity/Type 2 Diabetes via the Gut Microbiome

- Exposure to Air Pollutants
- Increased Inflammation
- Altered Basal Metabolism
- Gut Microbiome
- Obesity
- Type 2 Diabetes
The Gut Microbiome and Obesity

Tremaroli & Backhed, 2012
Exposure to Air Pollutants and the Gut Microbiome

- **Inhalation and diffusion** from lungs, absorbed into systemic circulation and delivered to gut via the blood stream
- **Cleared** from the airways by cilia and then ingested
- **Ingestion** of contaminated food/water
Does Air Pollution Exposure Alter the Gut Microbiome (Composition/Function) in Young Adults?

- Exposure data in overweight and obese young adults
- Detailed assessment of the gut microbiome using WGS

**Hypothesis:** Higher exposure to air pollutants would be associated with:

1) Specific gut bacteria (species)
2) Gut bacteria function (genes/pathways)
Cross-Sectional Study

• Inclusion criteria at study entry
  • Young adults from Southern California (2014-2017)
  • 17-21 years of age (n=101)

• Exposure assessments (Sonoma Technologies, Inc.)
  • Individual residential ambient air pollution
    • Air quality stations (AQS) using inverse-distance squared weighting
  • Individual residential near roadway air pollution (NO$_x$)
    • California-line dispersion model (CALINE4)

• The gut microbiome
  • Whole genome sequencing
  • Multivariate and univariate linear models
Exposure to Air Pollutants was Associated with the Gut Microbiota and Phylum and Species Level Using WGS

Fouladi et al., Env Int 2020
Ozone was Associated with the Relative Abundance of Gut Bacteria (Phylum Level) using WGS

Associations also seen at species level...

FDR adjusted **p<0.01 and *p<0.05

Fouladi et al., Env Int 2020
Exposure to O₃ was Positively Associated with the Relative Abundance of Taxa Belonging to the Bacteroides Genus using WGS
Exposure to O$_3$ was Negatively Associated with Gut Bacterial Diversity using WGS

# of bacteria and how abundant

Fouladi et al., Env Int 2020
Exposure to O₃ was Significantly Associated with Multiple Gene Pathways Using WGS

FDR adjusted **p<0.01 and *p<0.05

Fouladi et al., Env Int 2020
Gene Pathways Associated with O₃ have the Potential to Impact the Gut Permeability

• L-ornithine de novo biosynthesis:
  • Polyamines: necessary for cell growth¹,²
  • Nitric Acid: antiproliferative properties (cytotoxicity)³

• Pantothenate (Vit. B) and coenzyme A (CoA) biosynthesis:
  • Pantothenate and CoA biosynthesis: role in fatty acid synthesis/degradation⁴
  • CoA Derivatives: inhibit insulin release⁵,⁶ elevated in T2D / obesity⁷

¹Selamnia et al., 1998; ²Hölttä et al., 1993; ³Kumar et al., 2015; ⁴Leonardi et al., 2007; ⁵Davaapil et al., 2014; ⁶Webster et al., 2008; ⁷Bandyopadhyay et al., 2006
Exposure to Air Pollutants may Alter the Composition of the Gut Microbiome and Gut Permeability

Ozone:
- Known to stimulate HPA axis → release of catecholamines and steroid hormones
- Alter gut bacteria via adrenergic neuron stimulation (gut lamina propria)
- Damage gut barrier through immune activation
Ongoing Research

• Metabolomics

• Association between targeted and untargeted metabolites and air pollution exposure
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Thank You!

Questions?
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