Effects of dietary exposures to pesticide residues on the gut microbiome

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The gut microbiota: a major player in the toxicity of environmental pollutants?

Recommended reading


What is a pesticide?

- Pesticides are chemical compounds that are used to kill insects, rodents, fungi and plants.

- They can be natural or synthetic.

- Plants generally produce compounds acting as pesticides to protect themselves against herbivores and insect attacks.

- Synthetic pesticides are vastly inspired from natural pesticides which have been modified to be more stable, more specific, and more toxic.
Some synthetic insecticides have health effects in agricultural workers or following domestic applications

Sagiv et al., 2019. PNAS. 116 (37) 18347-18356
Larsen et al., 2017 Nature Communications 8, Article 302

Little is known about the effects of long-term exposures to dietary pesticide residues
Are organic food consumers healthier?

- Increased organic food consumption
  - sufficient evidence

- Decreased exposure to synthetic pesticides
  - insufficient evidence

- Health benefits
  - sufficient evidence

Organic food consumer demographic and lifestyle covariates

- More education
- Less smoking
- More physical activity
- Healthier dietary choices
- Placebo effect of marketing

Health benefits include:
- More education
- Less smoking
- More physical activity
- Healthier dietary choices
- Placebo effect of marketing
The gut microbiome is a mediator of insecticide resistance

- *Enterococcus* sp. enhanced resistance to the insecticide chlorpyrifos in the diamondback moth
  

- Fenitrothion-degrading *Burkholderia* strains in bean bug *R. pedestris*
  

- *Drosophila melanogaster* gut-derived *Lactobacillus plantarum* metabolize chlorpyrifos and affects its toxicity
  
Gut microbiota mediate caffeine detoxification in the primary insect pest of coffee

*Pseudomonas* species subsist on caffeine as a sole source of energy

Perturbation of the gut microbiome may contribute to the neurotoxicity of organophosphate pesticides

Roman et al., 2019. NeuroToxicology 75, Pages 200-208

- In rats or mice, no human study
- High doses, unrealistic
- Effects are secondary to systemic effects
- Mostly using 16S rRNA sequencing
- More studies are needed to reflect real-life exposure scenarios
Glyphosate-based herbicides are the most heavily applied herbicide in the world and usage continues to rise.

Human exposures to glyphosate are rising.

Does glyphosate pose risks to human health?

https://www.fera.co.uk

https://www.ceh.ac.uk
Glyphosate is frequently found in the food chain because it is directly sprayed on edible crops. It is sprayed on cereals before the harvest to accelerate ripening, or to clear weeds during cultivations of Roundup-tolerant genetically modified crops.

Fig. 1. Residues of glyphosate and AMPA in individual soybean samples ($n = 31$).

Bohn et al. 2014, Food Chem. 53:207-15
Glyphosate has been patented as an antiparasitic agent to treat pathogenic infections provoked by *Toxoplasma gondii*, *Plasmodium falciparum* (the parasite that causes malaria) and *Cryptosporidium parvum* (U.S. Patent No 7771736 B2).
Can glyphosate affect the gut microbiome?

- **Tap water**
- **Glyphosate** (0.5, 50 and 175 mg/kg bw/day)
- **MON52276** (0.5, 50 and 175 mg/kg bw/day)

- 90 days
- X12 per group

**Gut microbiome**
- Caecum metabolomics
- Caecum metagenomics

**General toxicity**
- Liver and kidney histopathology
- Biochemistry
- Serum metabolomics

**Liver molecular profiles**
- Transcriptomics
- Methylation profiles
Caecal metabolomics reveals that glyphosate inhibits the EPSPS pathway in the rat gut microbiome.
Analysis of shotgun metagenomics data

Data analysis with Metaphlan2 and Humann2 did not reveal effects of glyphosate, a new analysis using a gene catalogue of the Sprague-Dawley rat gut metagenome is ongoing.
Evaluating the effects of synthetic pesticide exposure through analysis of the faecal microbiome in twins discordant for organic food consumption.

Exposure to 571 synthetic pesticides in 65 twin pairs

Data from pilot study

Urinary analysis of pesticide residues in 5 twin pairs reveals exposure to the herbicide glyphosate in British individuals

<table>
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Faecal samples in 65 twin pairs that are discordant for an organic diet are studied by shotgun metagenomics and metabolomics to understand if pesticide exposure associates with changes in the faecal microbiome.

\[ N = 110 \]

**Ongoing analysis**

3-dehydroshikimic acid level correlate with metagenome composition.

Can glyphosate exposure affect 3-dehydroshikimic acid level in the human faecal microbiome?
Next steps?

1/ Completing the study of associations between pesticide exposure and faecal microbiota composition

2/ Can organophosphate exposure be associated with changes in gut microbiome composition?

3/ Evaluation of the metatranscriptome in rats exposed to glyphosate

4/ Evaluate if an increase in shikimic acid levels can have health consequences
Thank you research Collaborators!

Thank you for your attention!
Questions?

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