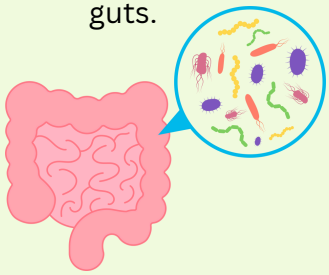
LINKING SYNTHETIC PESTICIDE EXPOSURE TO THE GUT MICROBIOTA AND BRAIN FUNCTIONING

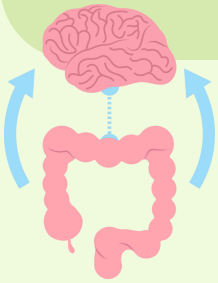
- **Gut microbiota live within a dynamic ecosystem** which is affected by several factors, including exposure to synthetic pesticides
- **The widespread use of pesticides in agriculture** makes it important to understand the long-term effects of exposure in the gut microbiota, both in terms of composition and function
- Exposure studies using animal models have found that **pesticides can have negative impacts on microbiota and behaviour**
- This review explores **whether pesticide-induced changes to gut microbiota are driving changes in behaviour**
- The mechanisms of how pesticides lead to behaviour change resulting from gut microbiota change are still poorly understood - **more research is needed.**

WHY GUT MICROBIOTA?

The gut microbiota is the diverse range of different microorganisms that live in our guts.



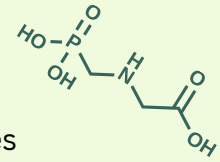
Healthy and diverse gut microbiota are essential for human and animal health and is known to have a major effect on brain functioning and behaviour.



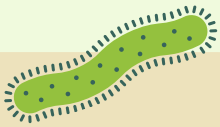
LINKING THE GUT MICROBIOTA TO THE BRAIN

Our gut microbiota and central nervous systems communicate with each other. These communications are essential for brain function and can affect our behaviour.

PESTICIDES AND THE GUT MICROBIOTA



Chemicals such as pesticides can affect communications between the gut microbiota and the brain, including by affecting microbial function. Pesticides have been found to disrupt gut microbiota composition and have negative impacts on cognitive function in humans.



PESTICIDE EXPOSURE - HOW?

- **Pesticides are very widespread in the environment** due to their intensive use in agriculture
- A recent study measured pesticide levels in >300 soil samples taken from across the EU. **Over 80% of soil samples contained pesticide residues**
- **Several pesticide mixtures have been detected in fruits and vegetables**
- Pesticide residues can **enter our bodies through inhalation, ingestion, or by being absorbed through our skin**
- However, our bodies are **able to detoxify pesticides** with help from our livers and gut microbiota
- When these chemicals reach our gut microbiota before being metabolised and made less toxic by our livers, this **can have negative consequences for our health.**

This factsheet is based on research by Matsuzaki et al (2023), conducted as part of the EU Horizon 2020 SPRINT project.

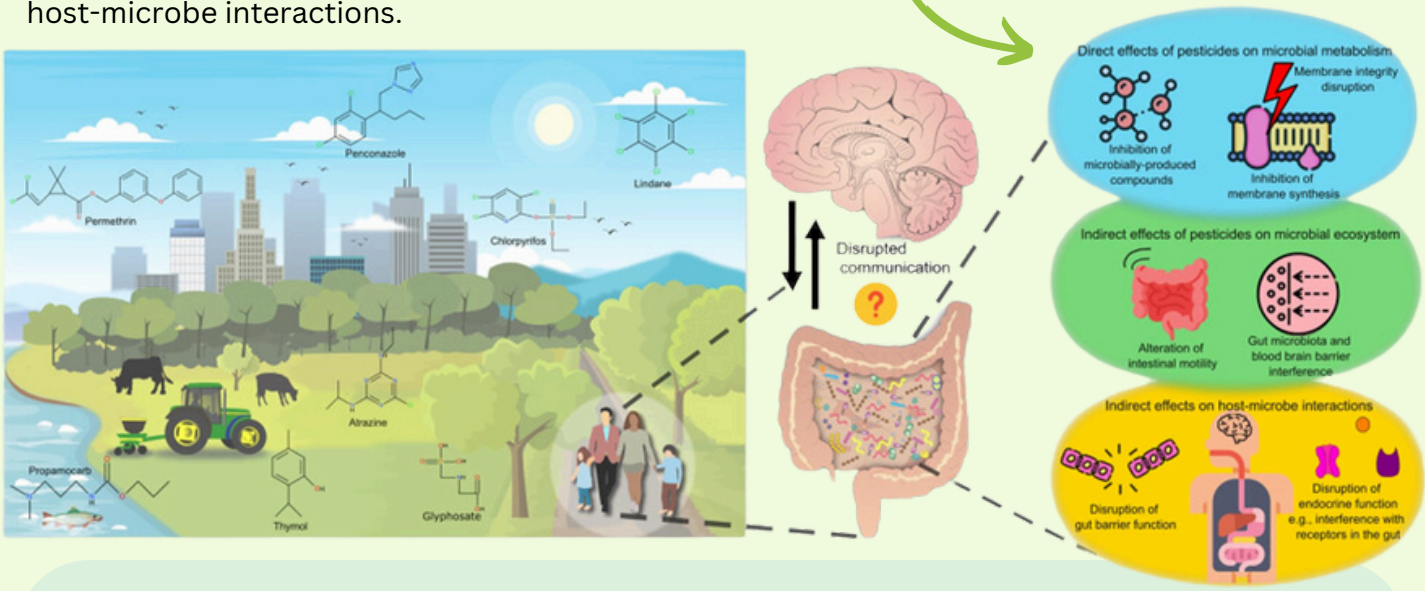
Underlined text? Click me!

...turn over for more!

HOW ENVIRONMENTAL PESTICIDES AFFECT THE MICROBIOTA-GUT-BRAIN AXIS

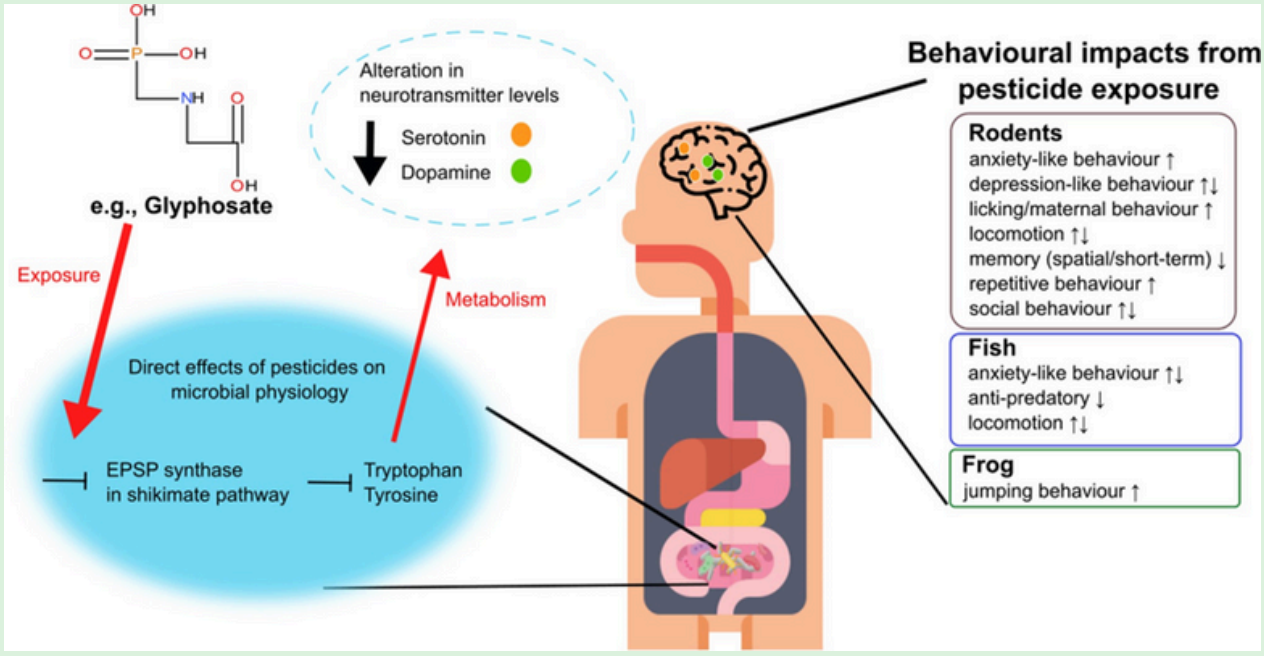
Pesticides present in air, soil, water, and food, can enter our bodies and **disrupt communication between our guts and brain**. The figure below provides an overview of proposed ways in which pesticides present in the environment can affect microbial metabolism, the microbial ecosystem, and host-microbe interactions.

Further mechanisms are still being discovered but these pathways are expected to contribute to behavioural impairments.



EFFECTS OF SYNTHETIC PESTICIDES ON ANIMAL BEHAVIOUR

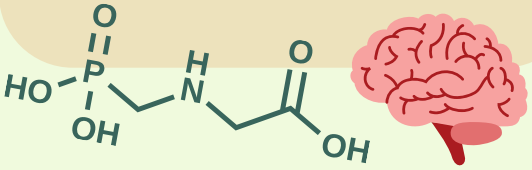
The infographic below shows how Glyphosate may affect microbial physiology and in turn, the effects this has on neurotransmitter levels. These neurotransmitters affect our behaviour. Possible **behavioural impacts due to pesticide exposure may include anxiety and depression-like behaviour, decreased memory, reductions in anti-predation behaviour, and affected social behaviour**, depending on the species (see below).



GLYPHOSATE: A KEY SYNTHETIC PESTICIDE

Glyphosate is the active component of many widely used herbicides, including 'Roundup'. This pesticide acts by inhibiting a key functional process used by plants, which mammals don't use. As a result, the human health risk has been seen as low. However, **an increasing body of research is finding that glyphosate has negative impacts on non-target species**, including those found in the gut microbiota. This can result in behaviour change. **In mice exposed to Glyphosate-containing products, this caused increased anxiety and depressive-like behaviour and reduced social interaction.**

Research has found that **glyphosate can enter the brain and increase inflammation levels**. This includes increases in a key cytokine linked to Alzheimer's disease.



HOW PESTICIDES ALTER THE GUT MICROBIOTA

Several studies support the idea that **altered signalling to the brain due to changes to the gut microbiota may explain changes to behaviour**. Existing research has found that pesticides such as Thymol (fungicide), glufosinate ammonium (herbicide), and permethrin (insecticide) can all interfere with nervous system signalling in some way. Overall, findings indicate that gut microbiota affected by pesticide exposure can result in behavioural impairments via the microbiota-gut-brain axis. However, more research is needed to understand how gut microbiota are specifically involved in the process.

HOW PESTICIDES AFFECT GUT AND BRAIN BARRIERS

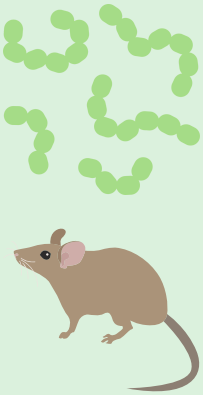
- Pesticide exposure may cause increased permeability of the gut and brain barriers, leading to behavioural impairments
- **The gut microbiota plays a key role in protecting the intestinal barrier from damage. If the gut microbiota are being affected by pesticides, this may be impacted.**
- **Exposure to an insecticide, imidacloprid, was found to affect the populations seen in the gut microbiota of mice. A loss of key microbiota resulted in disrupted bile acid metabolism and colon barrier function.**
- Other research has found that several pesticides also affect the physical gut barriers linked to the gut microbiota, each of which can lead to behaviour changes.

PESTICIDES AND THE IMMUNE SYSTEM

- **Immune system health can be affected by the gut microbiota.**
- Exposure to certain synthetic pesticides including chlorpyrifos have been found to induce immune responses in mice. The resulting **inflammatory reactions are known to be linked to anxiety and depression symptoms.**

- Atrazine, a synthetic herbicide, is known to disrupt endocrine systems in amphibians and mammals. Research found that frogs exposed to this chemical had **reduced gut microbiota diversity and expressed altered behaviours.**
- Research on wasps suggests that **gut bacteria changes can result in changes to the immune system which, in turn, cause changes to behaviour.**

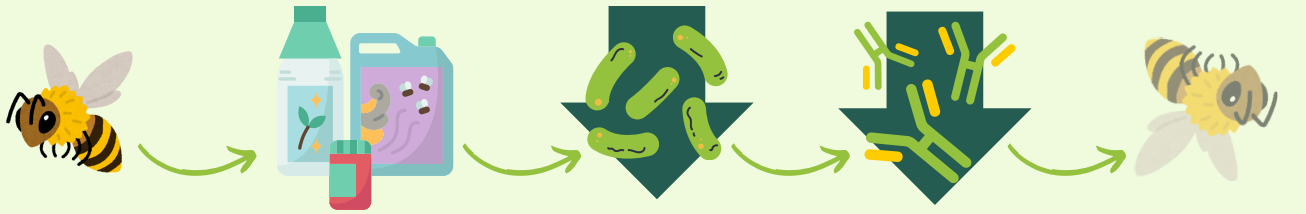
KEY MICROBES AFFECTED BY PESTICIDE EXPOSURE IN MAMMALS



- Mammal studies have found a **reduction in the abundance of particular bacterial species within *Bacillota***, a key group of gut microbiota, when animals including mice and rats are exposed to herbicides including Glyphosate
- ***Lactobacillus* is one type of bacteria within this group and is known for being useful for enhancing intestinal health**
- Some strains are also probiotic while certain others are involved in the immune system
- While *Lactobacillus* levels are **reduced in mammals exposed to certain synthetic pesticides, they appear to increase in insects**
- This shows that the **gut microbiota of different groups of animals are affected in different ways when exposed to pesticides**

KEY MICROBES IMPACTED BY PESTICIDE EXPOSURE IN HONEYBEES

- Honeybee populations have declined in recent years
- **Pesticides can have direct physiological impacts on honeybees but alterations to bee gut microbiota also occur**
- For example, glyphosate exposure results in a reduction of two *Pseudomonadota* microbial groups (see figure below)
- **These microbes are important for immune response and, and research has found that bee populations are more susceptible to bacterial pathogens where they are exposed to glyphosate**



PESTICIDES AND THE MICROBIOTA: A NEED FOR FUNCTIONAL ANALYSIS

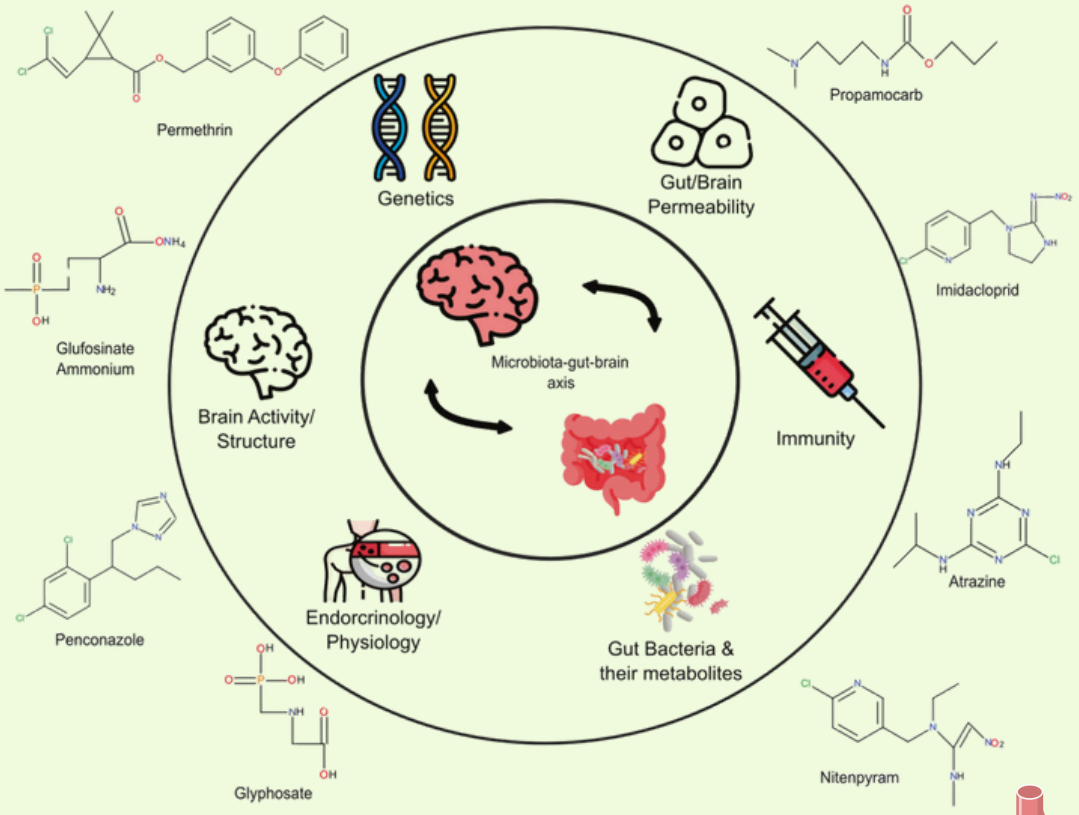
- **Not many studies have explored the direct functional implications of microbiota changes**
- This is important because functional-based molecular approaches can provide rich insights into our health
- **Existing studies have found pesticide-related impacts on biological functions including detoxification, amino acid metabolism, intestinal barrier function, and inflammation**
- Functional analysis can help us to understand the implications of gut microbiota changes and examine the direct impacts, which may not align with the functions of specific microbiota

FUTURE RESEARCH NEEDS

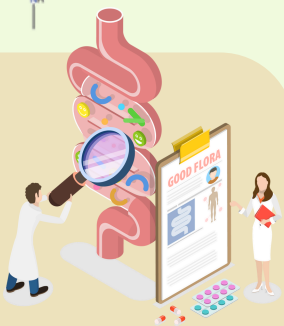
- More research is needed to understand the impacts of changes to the gut microbial ecosystem as a whole
- **There is a lack of research on whether changes in the gut-brain axis are caused by pesticide exposure, or just associated with it**
- Methods that can assess whether behavioural changes are caused by microbiota changes are needed - one of which involves administering host faeces to a donor, thus creating the same microbiota in the donor's gut
- **We also need to understand more about the direct interactions between pesticides and the gut microbiota - it is not understood how tolerance and susceptibility to pesticides happens**

PESTICIDES INFLUENCING ANIMAL BEHAVIOUR: POTENTIAL MEDIATORS

How pesticide exposure results in behavioural disorder is still largely unknown. **It is possible that these behaviour changes are caused by changes in endocrinology/physiology, brain activity/structure, genetics, gut/brain permeability, immunity, or gut bacteria.** Further research is needed.



CONCLUSIONS



This review has examined research into how pesticide exposure affects the gut microbiota, and in turn, behavioural impairments because of interactions between the microbiota and the brain.

There is substantial evidence that pesticide exposure both before birth and throughout the lifetime results in changes to the gut microbiota and host behaviours. This can include anxiety/depressive-like behaviours and memory loss.

More research is needed to understand whether the negative behavioural changes seen in those exposed to pesticides are directly caused by changes to the gut microbiota.

INTERESTED IN READING MORE?

Access the full paper by Matsuzaki et al (2023) by clicking here.

Any questions?
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