

Microbiota influence on behavior: Integrative analysis of serotonin metabolism and behavioral profile in germ-free mice

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Introduction

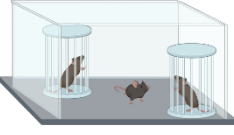
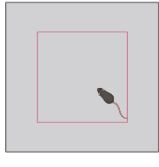
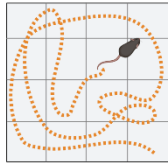
Previous studies on **germ-free (GF)** animals have described **altered anxiety-like and social behaviors** together with **dysregulations in brain serotonin (5-HT) metabolism** compared to conventional (CV) animals. In other studies, **alterations in circulating 5-HT levels and gut 5-HT metabolism** have also been reported in GF mice. We aimed to further this evidence through an **integrative approach**. We conducted an integrative analysis of **various behaviors** as well as markers of **5-HT metabolism** in the **brain** and **along the GI tract** of **GF male mice compared to CV ones**.

Methods

Conventional (CV)

Germ-free (GF)

Behavior

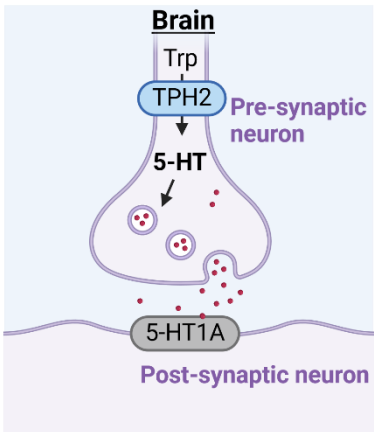
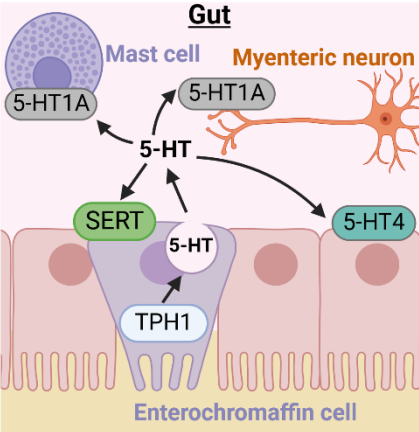


Locomotor activity

Anxiety like behavior

Social behavior

Gut and brain 5-HT metabolism



Conclusion

- A **strong decrease in locomotor activity**, accompanied by **signs of increased anxiety-like behavior** and a **trend to improved sociability** were observed in **GF mice compared with CV mice**. More in-depth analysis of locomotion and motor function in GF mice could be interesting.
- These results **add to previous evidence** that the **microbiota is involved in regulation of behavior**, although **heterogeneity among studies** suggests a strong **impact of genetic and environmental factors** on this microbiota-mediated regulation.
- Brain gene expression** analysis showed **no differences** in expression of genes coding for **5-HT1A and TPH2**. It is possible that measuring **other markers** or studying **other brain regions** would have yielded different results.
- However, **substantial differences in gut 5-HT metabolism** were noted, with **tissue-dependent results** indicating a **varying role of microbiota along the GI tract**. The **behavioral alterations** we observed **could be** in part linked to those **changes in gut 5-HT metabolism** through its action on the **immune system and the vagus nerve**.
- As the **gut is at the interface between intestinal microbiota and the central nervous system**, it should be considered more systematically in future studies evaluating the influence of the gut microbiota on brain function and behavioral responses.

This work was recently published :



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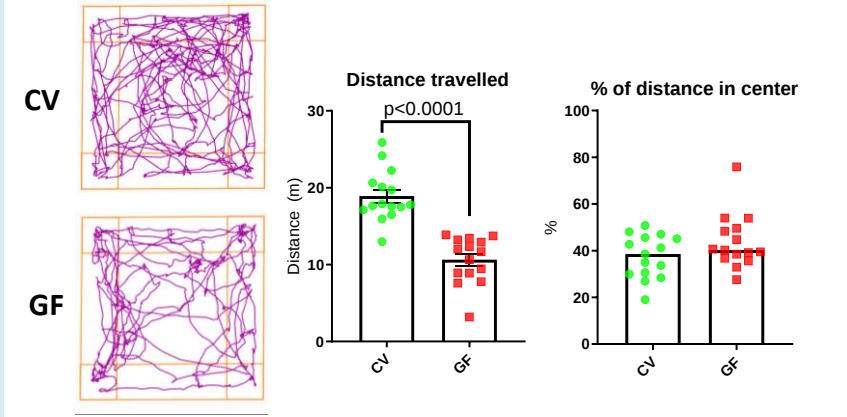
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Results

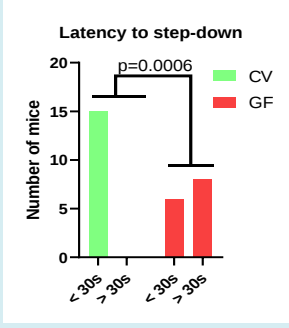
Behavior

Open-field test

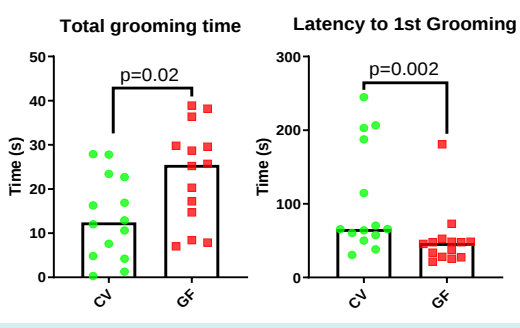


→ Strongly **reduced locomotor activity** in GF mice
→ No difference in anxiety like-behavior in this test

Step-down test

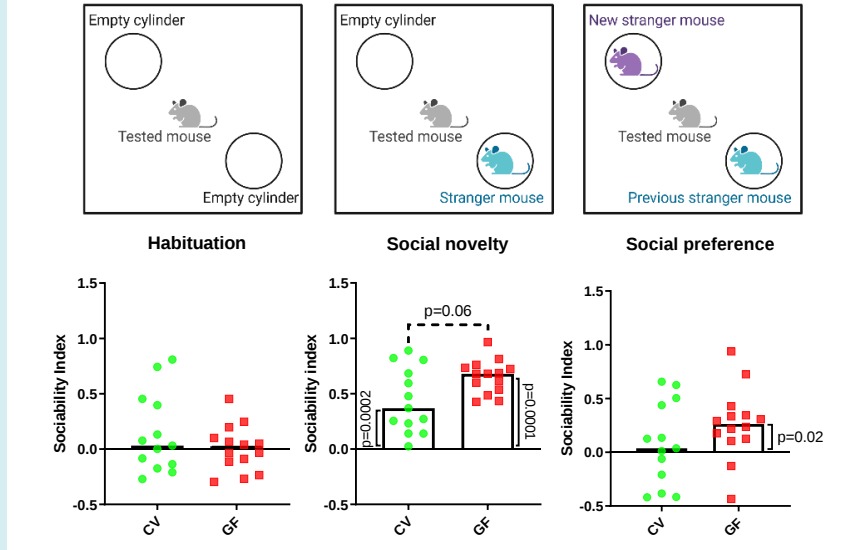


Self-grooming test



→ Signs of **increased anxiety** in GF mice compared to CV in the step-down and self-grooming tests

Social behavior



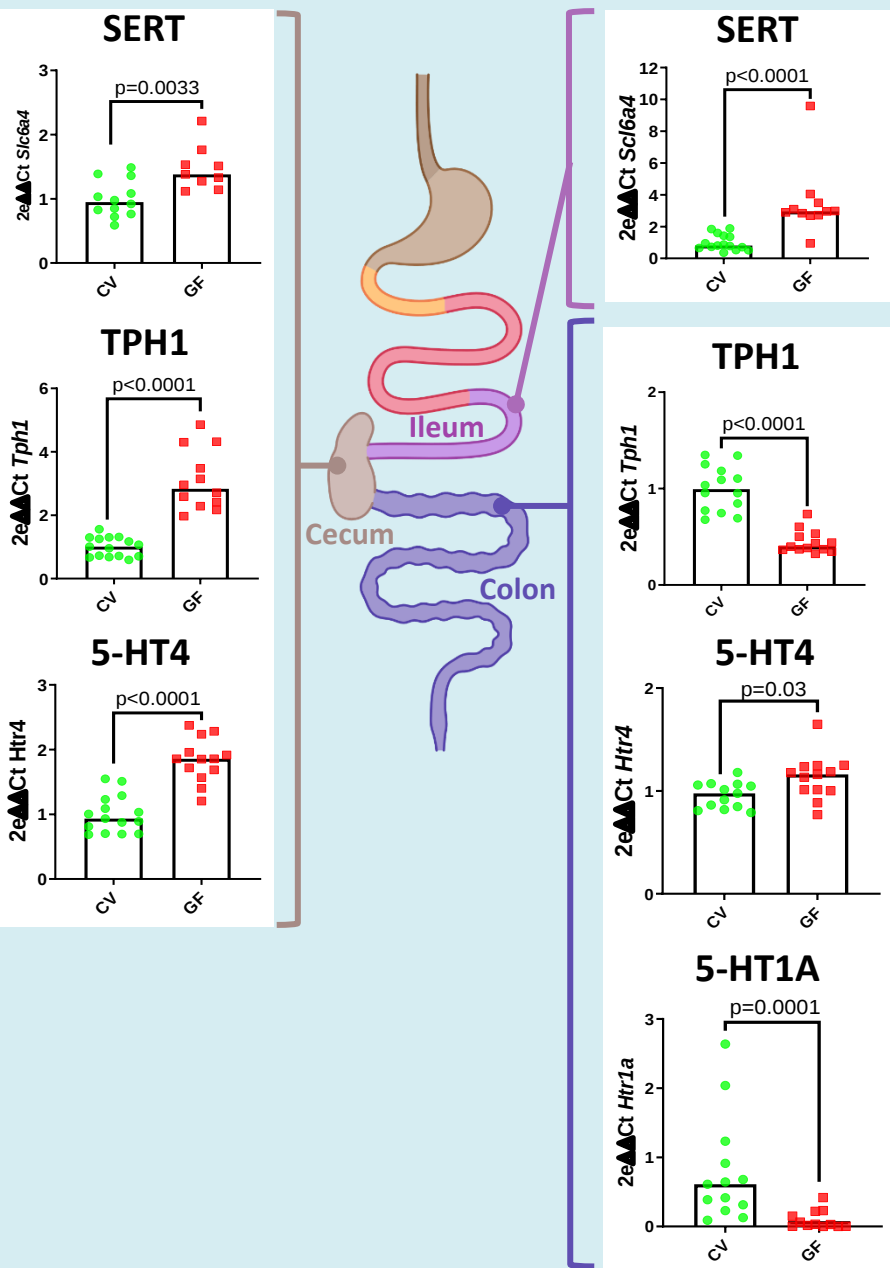
→ Trend to an **improved social behavior** in GF mice compared to CV

No difference in repetitive behaviors and spatial memory were found.

Brain 5-HT metabolism

→ We investigated gene expression of genes coding for **TPH2 and 5-HT1A** in the **PFC, hippocampus, nucleus accumbens and cerebellum** but found **no differences between groups**.

Gut 5-HT metabolism



→ Expression of the gene coding for **SERT** is **increased** in GF mice compared to CV in ileum and cecum.

→ Expression of the gene coding for **TPH1** is **increased** in the cecum of GF mice but **decreased** in their colon compared to CV.

→ Expression of the gene coding for the **5-HT4** receptor is **increased** in GF mice compared to CV, in cecum and colon.

→ Expression of the gene coding for the **5-HT1A** receptor is **decreased** in the colon of GF mice compared to CV.