Effect of gut microbiotafrom children with autism spectrum disorder (ASD) on behavior and ASD-related biological markers in germ-free mice

Léa Roussin

Effect of gut microbiota from children with autism spectrum disorder (ASD) on behavior and ASD-related biological markers in germ-free mice

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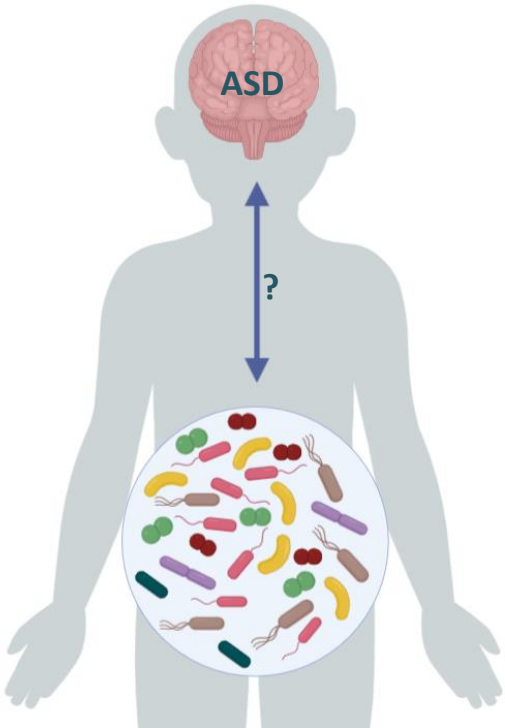
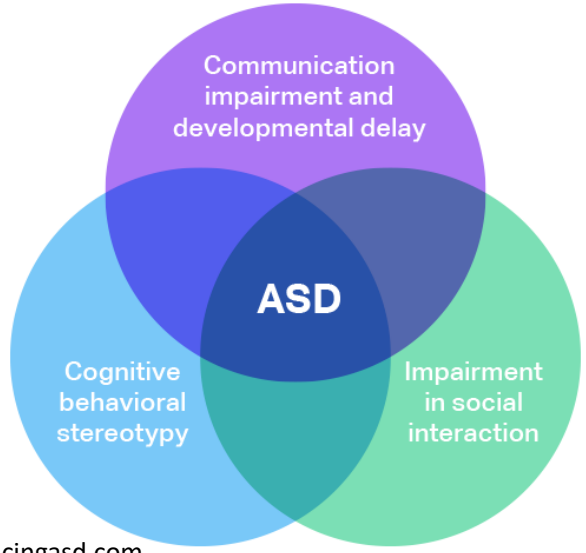
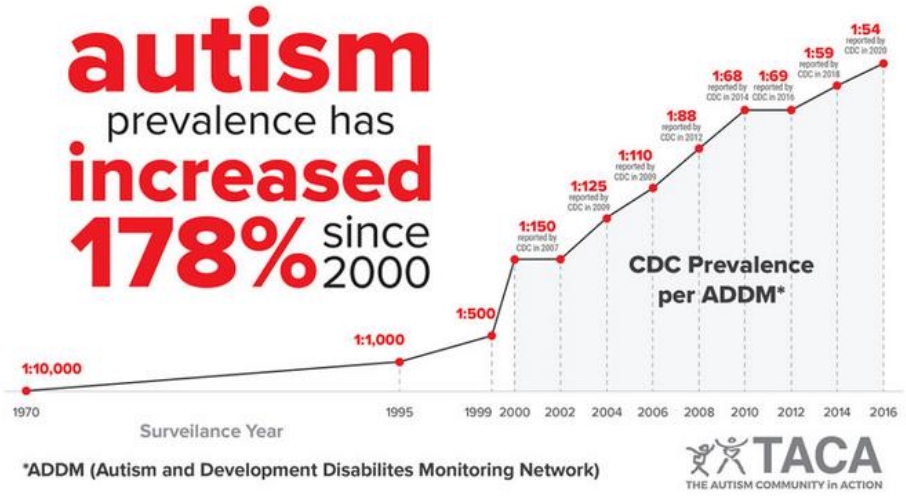


Autism spectrum disorder



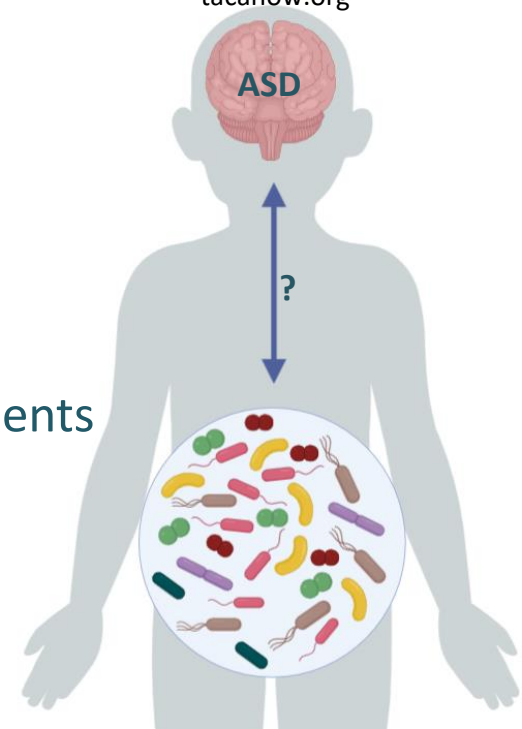
embracingasd.com



tacanow.org

- Genetic heritability is reported to be around 50%
  also a strong environmental impact.

- High prevalence of gastrointestinal (**GI**) disorders in ASD patients



Role of microbiota-gut-brain axis in ASD ?

Role of the gut microbiota in ASD

• Several studies observe differences in the composition of the microbiota between people with ASD and neurotypical people. The presence of GI symptoms seems to also have an impact.

• Little inter-study consensus on the bacterial genera or species modulated, probably due to differences in geography, diet, and choice of control groups (siblings or not).

•A few studies show improvment of behavior and/or GI symptoms after microbiota modulation (FMT, probiotics) in ASD patients or mice models of ASD

GEMMA
Multi-Omics Research in Autism

16 partners from 7 countries

Clinical

Identify early life biomarkers of ASD

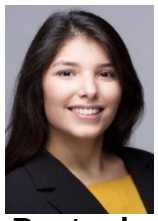
Preclinical

Effect of microbiota of children with ASD in mice models

INRAE

Utrecht University

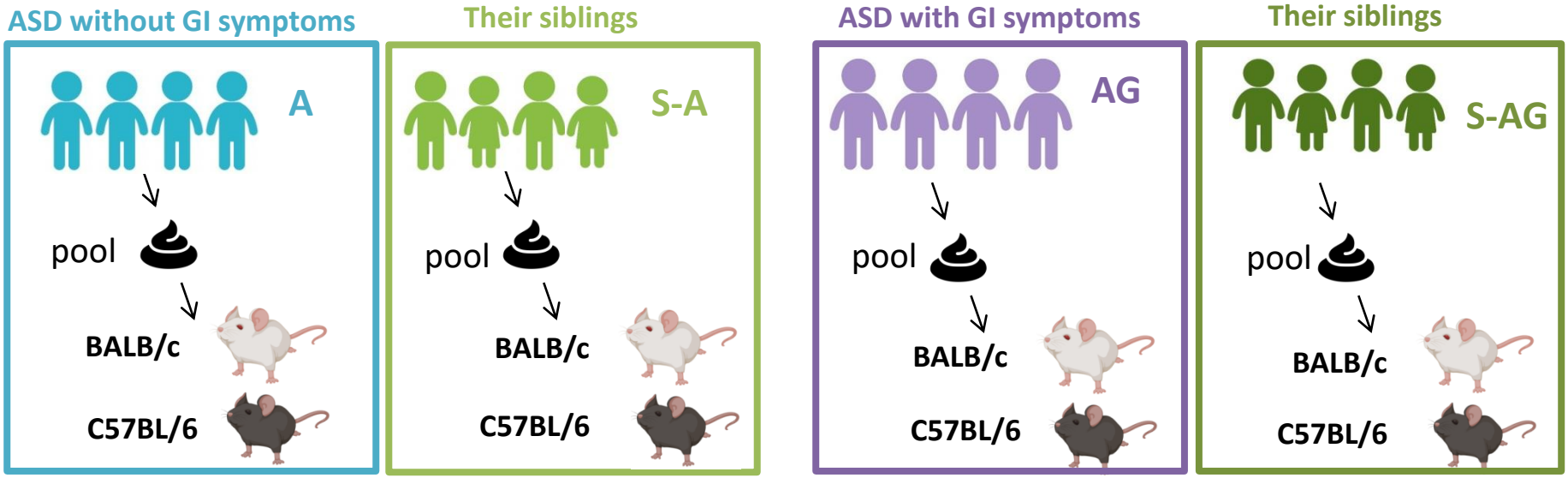
Talk by Lucia Marzal this afternoon

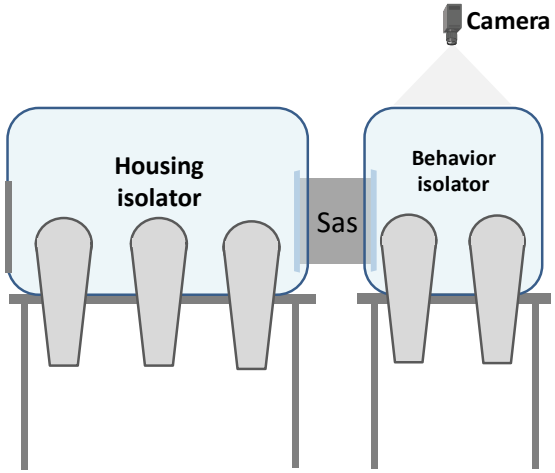


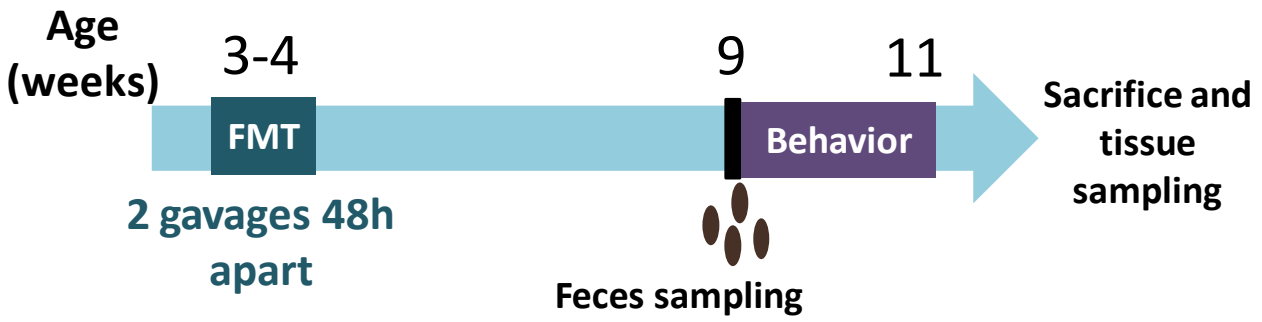
Poster by Naika Prince

GEMMA project-Preclinical part

Effect of the gut microbiota from children with ASD on behavior and ASD-related biological markers in germ-free mice







-ASD related behavior
-Gut microbiota composition, gut permeability, gut and brain inflammation, serotonin

Microbiota composition (16S rDNA)- ASV analysis

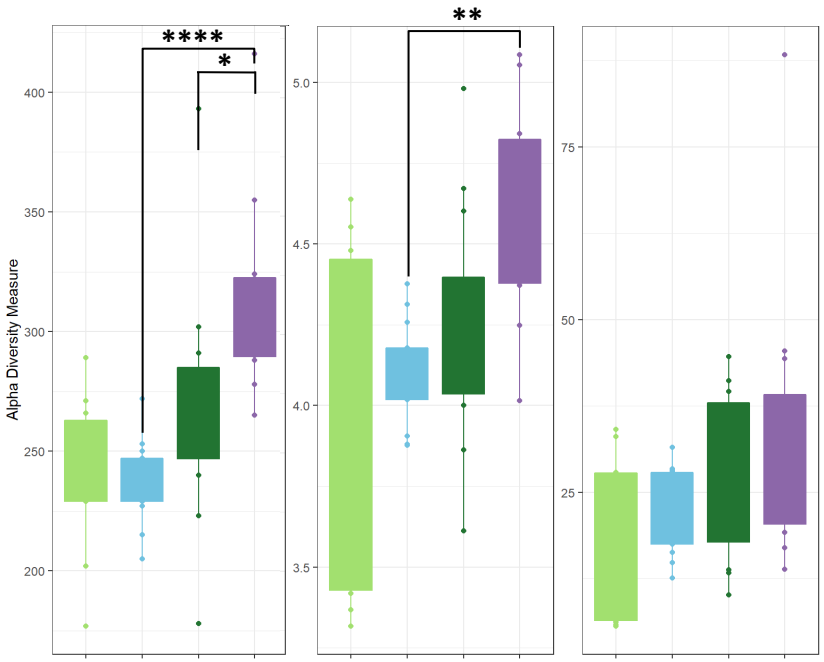
Alpha-diversity (intra-group)

BALB/c

Group:
- S-A
- A
- S-AG
- AG

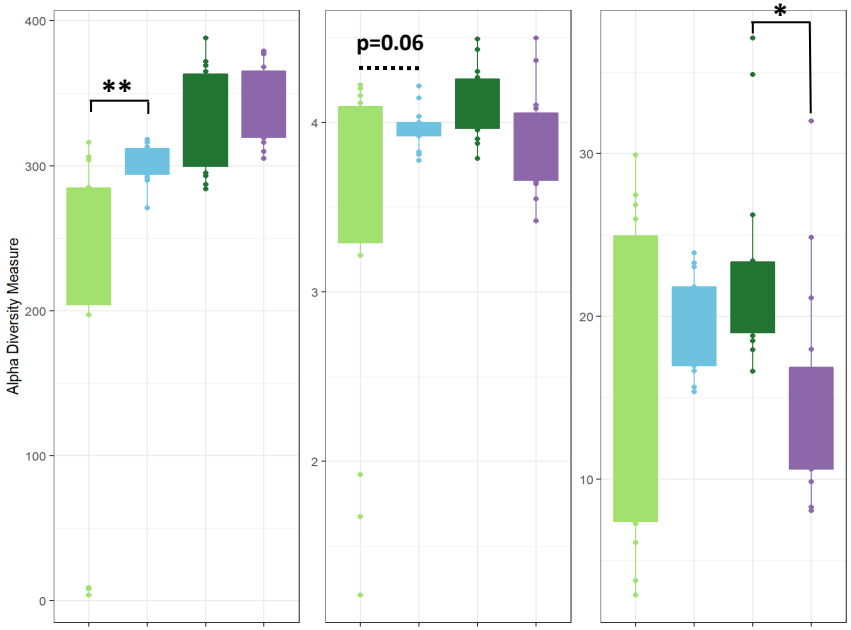
C57BL/6

Observed: **Shannon:** **InvSimpson:**



Overall greater diversity in the AG group

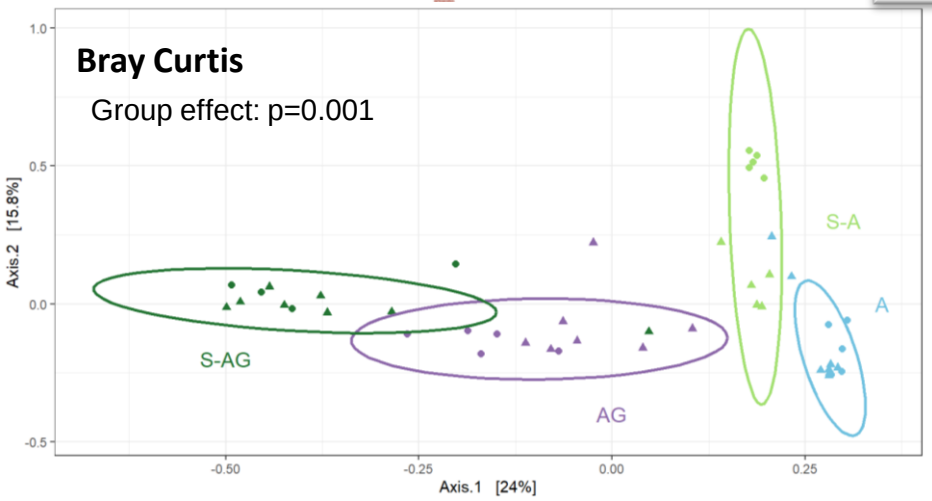
Observed: **Shannon:** **InvSimpson:**

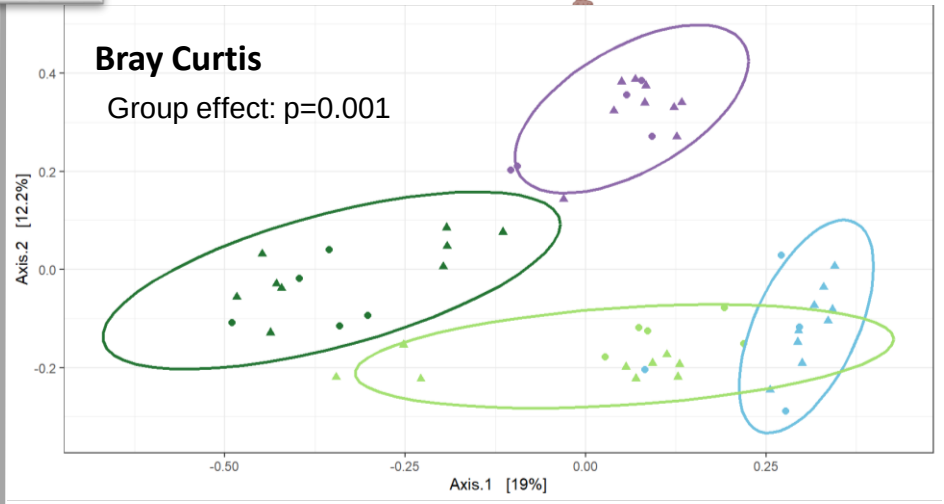


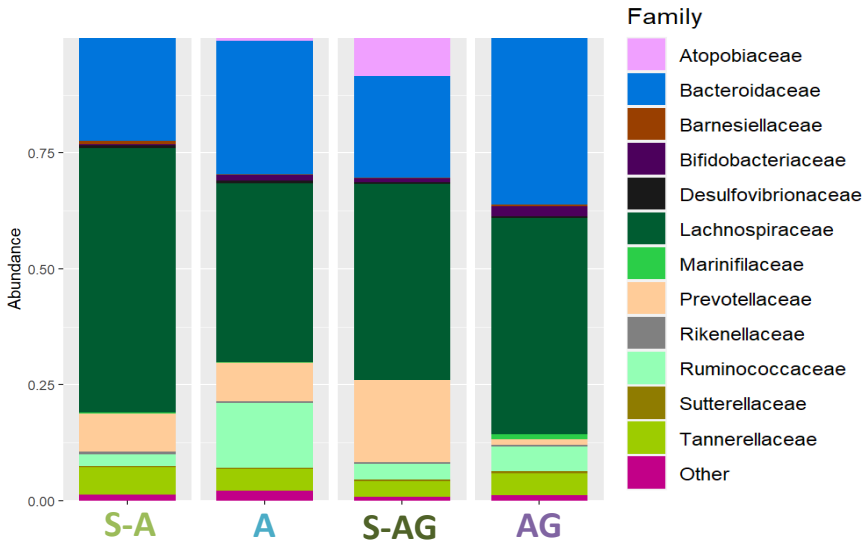
Slightly higher diversity in group A, variable according to the chosen index.

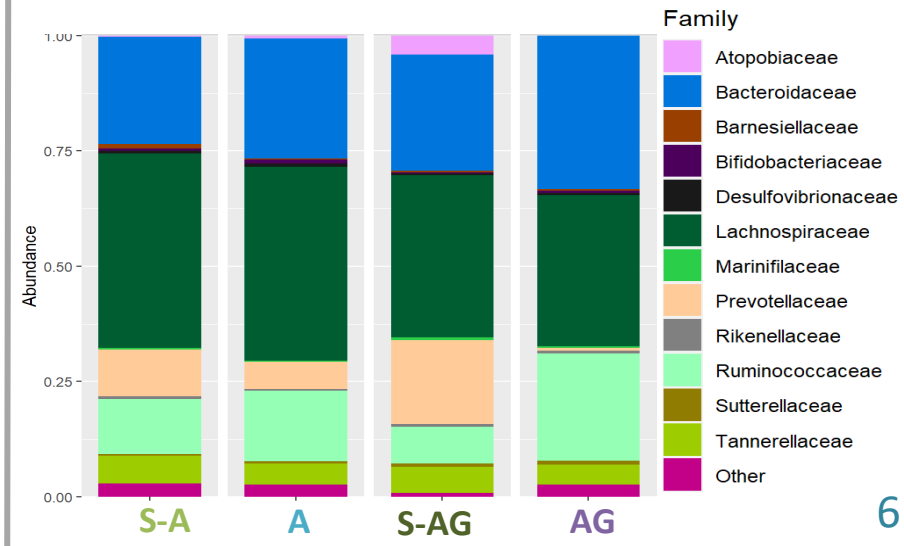
Microbiota composition (16S rDNA)

Beta-diversity and Family composition

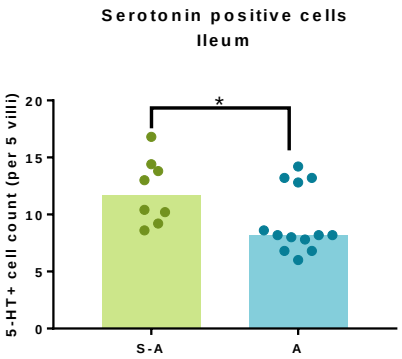


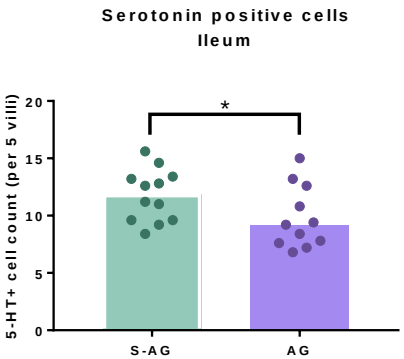


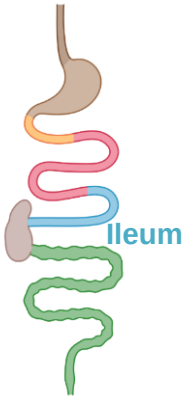


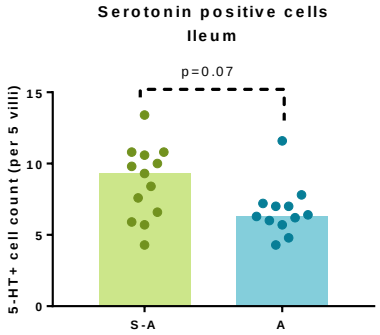


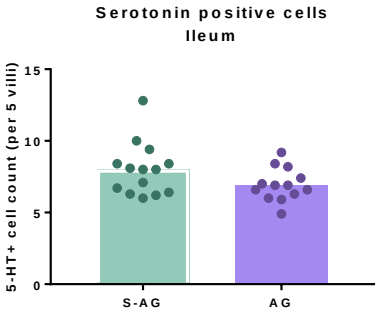
Gut serotonin



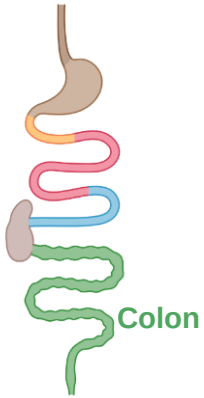


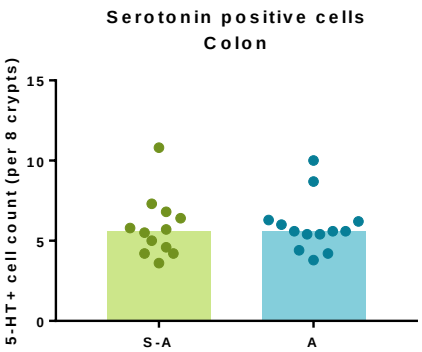


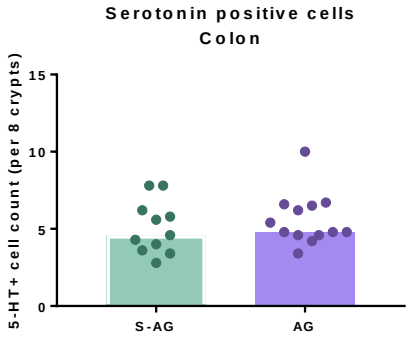




Colon: In progress





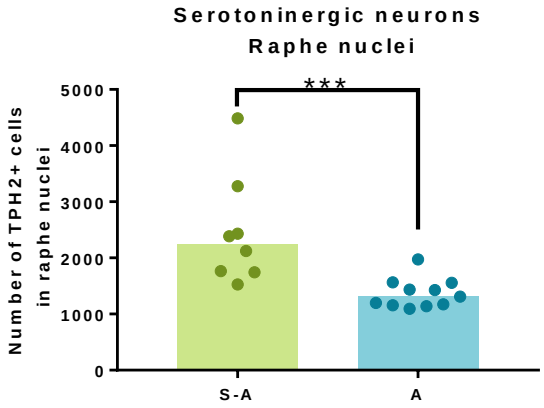


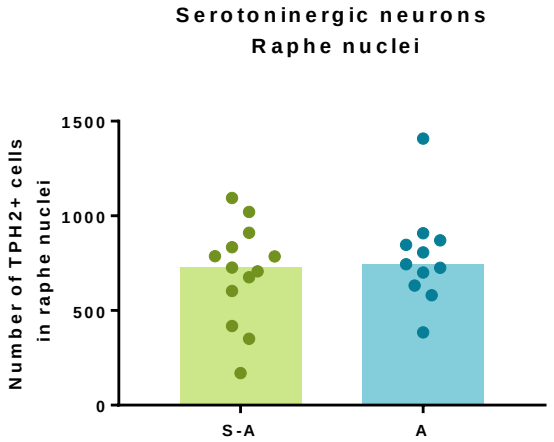
- Less serotonin positive cells in the ileum of A and AG mice in BALBc and a trend for group A in C57BL/6

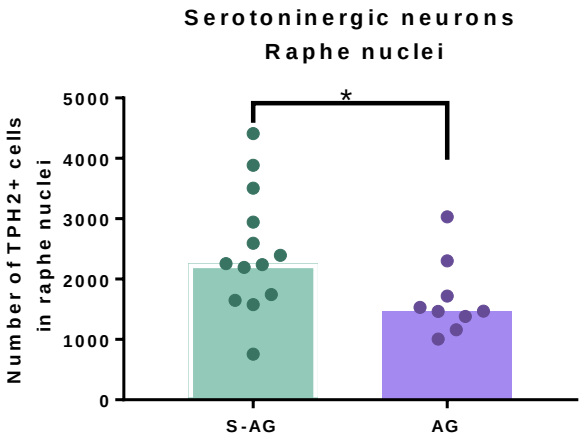
Brain serotonin

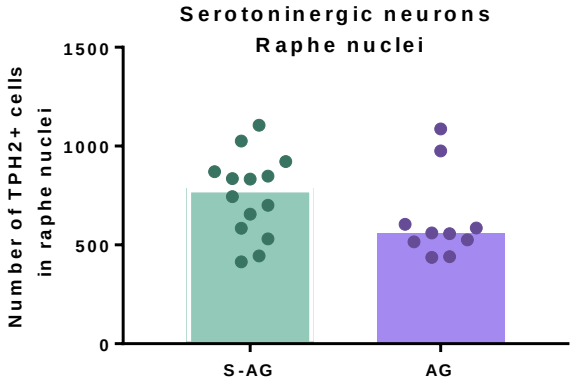
Serotonin neurons in the raphe nuclei

raphe nuclei









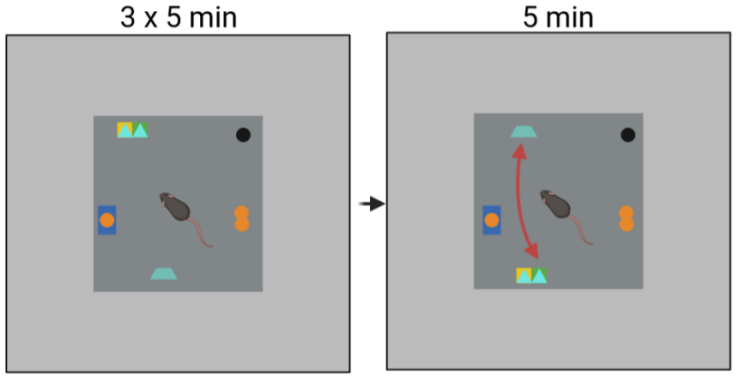
- Reduced number of serotonergic neurons in raphe nuclei in groups A and AG only for BALBc

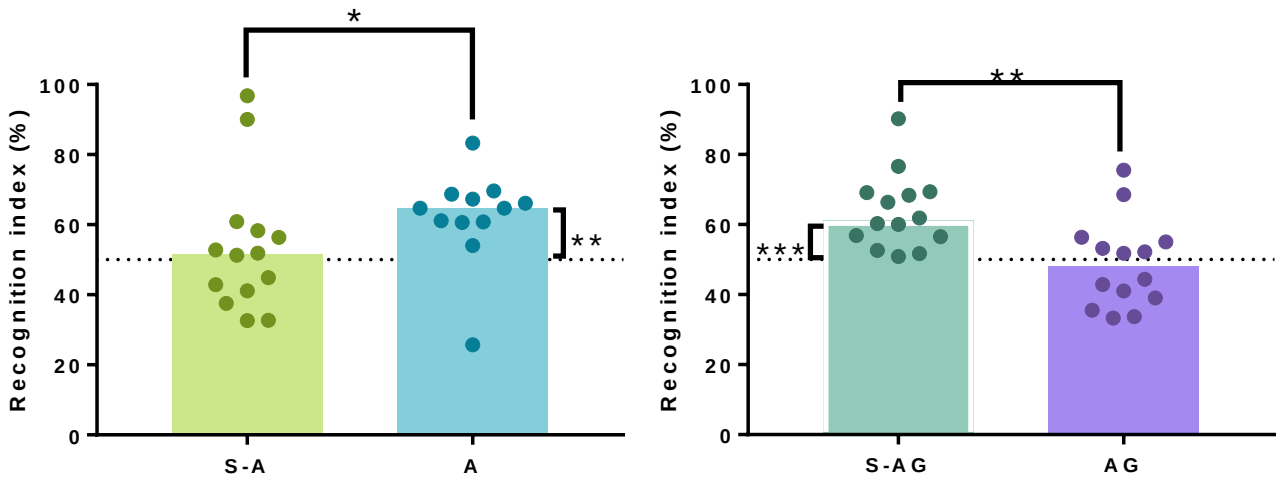
Behavior

•No difference in anxiety, social behavior and stereotyped behavior

Spatial memory:

C57BL/6

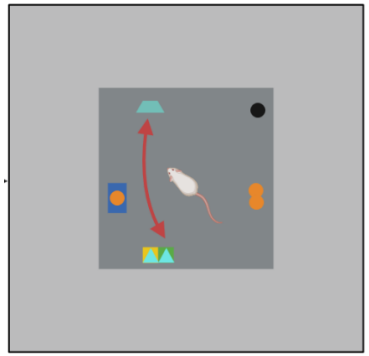




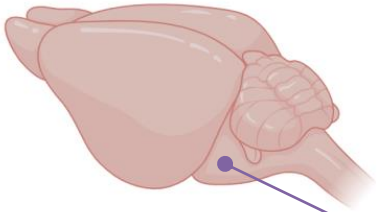
→ Lower recognition index in AG than S-AG mice

→ Lower recognition index in S-A than A mice

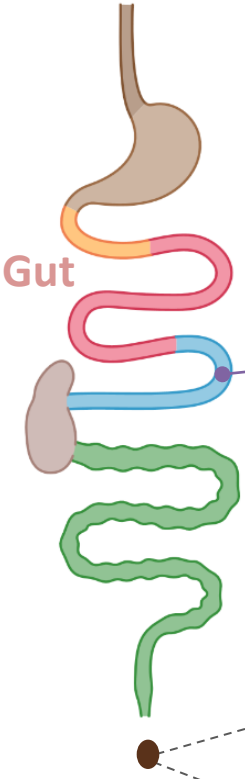
Conclusion:

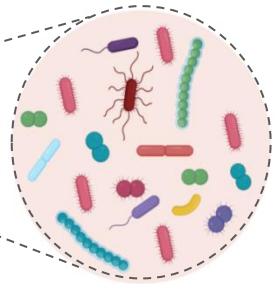


No difference in behavior aside from altered spatial memory (C57BL/6)



Decreased number of serotonin positive cells or serotoninergic neurons in A and AG groups (BALB/c)





Distinct composition and fermentation activity (SCFAs profile)

- A more in depth statistical analysis is planned
- Some analysis are still ongoing (quantification of gene expression in the brain)

Thank you for your attention!

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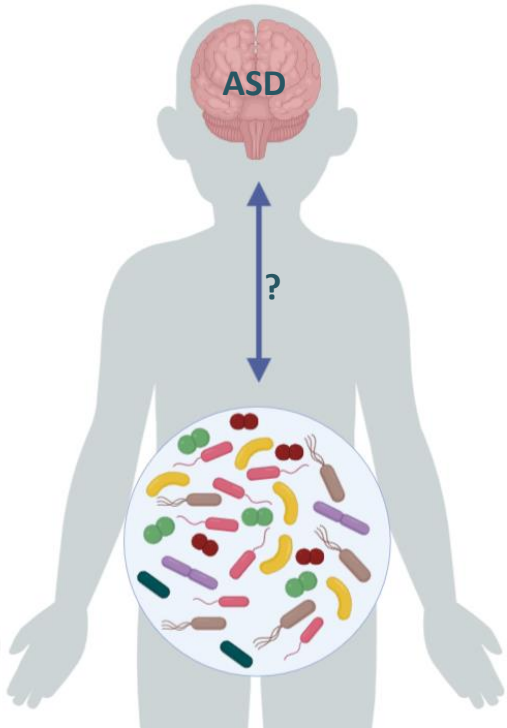


Extras

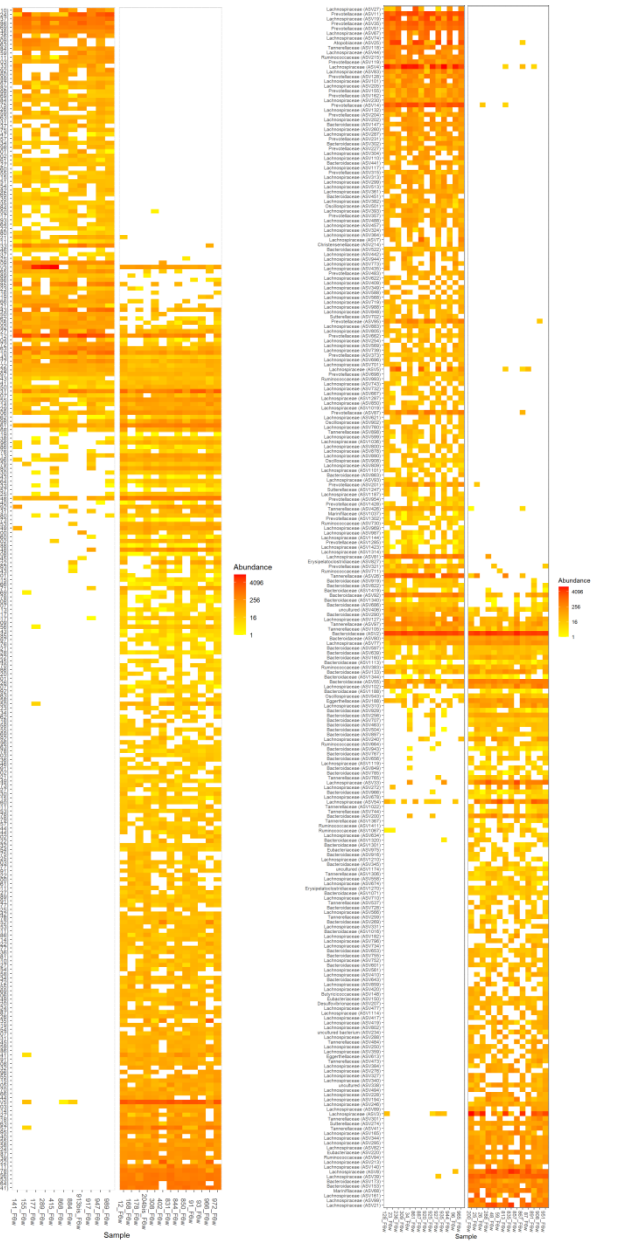
Differential abundances (ASV)

pval = 0.01 ; min abondance = 50

log2foldchange >3

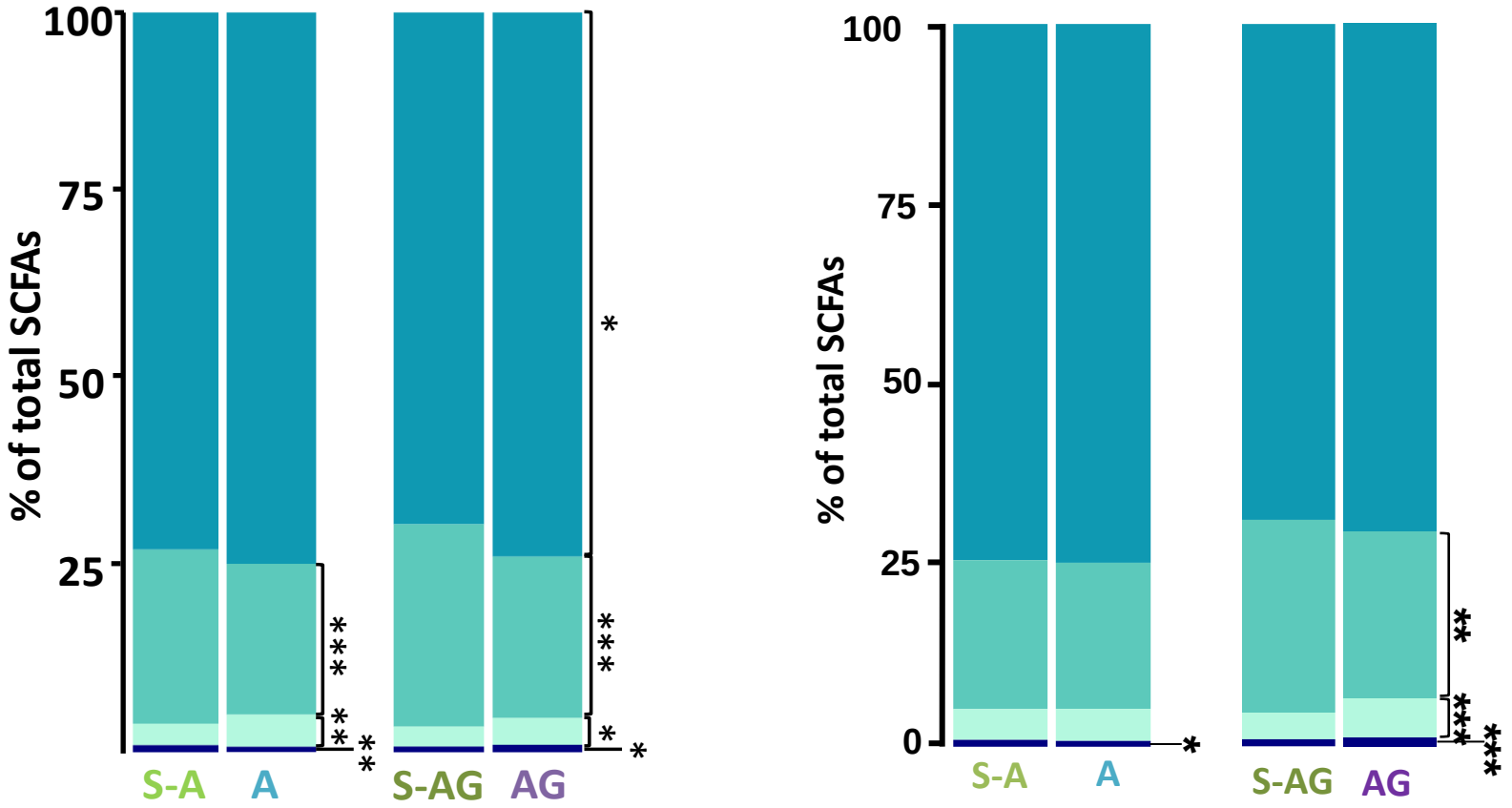
S-A A S-AG AG

S-A A S-AG AG



Short chain fatty acids

Fermentation activity of the microbiota



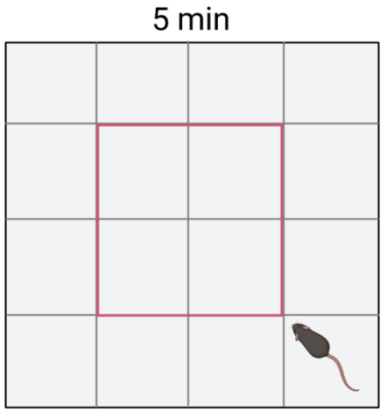
- Inter-group differences in caecal SCFA profiles

Behavior

BALB/c 

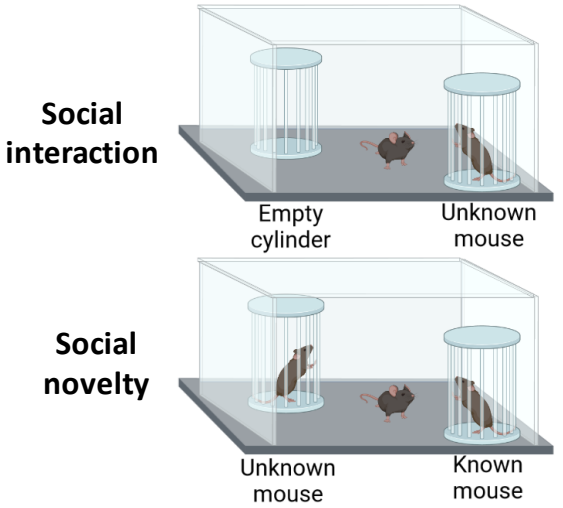
C57BL/6 

Anxiety (Open-field)



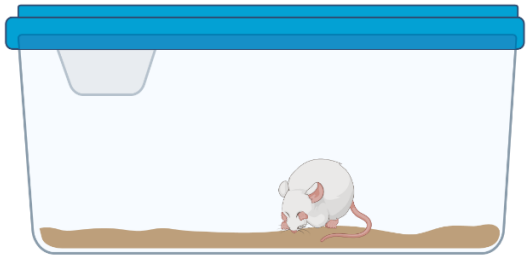
No difference between groups

Social behavior



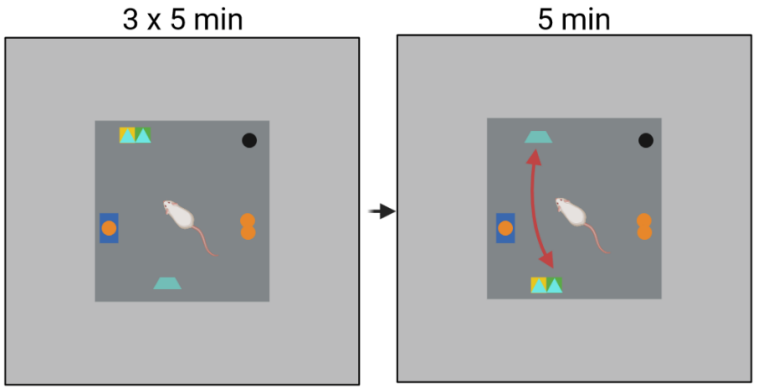
No difference between groups

Repetitive behavior (self-grooming)



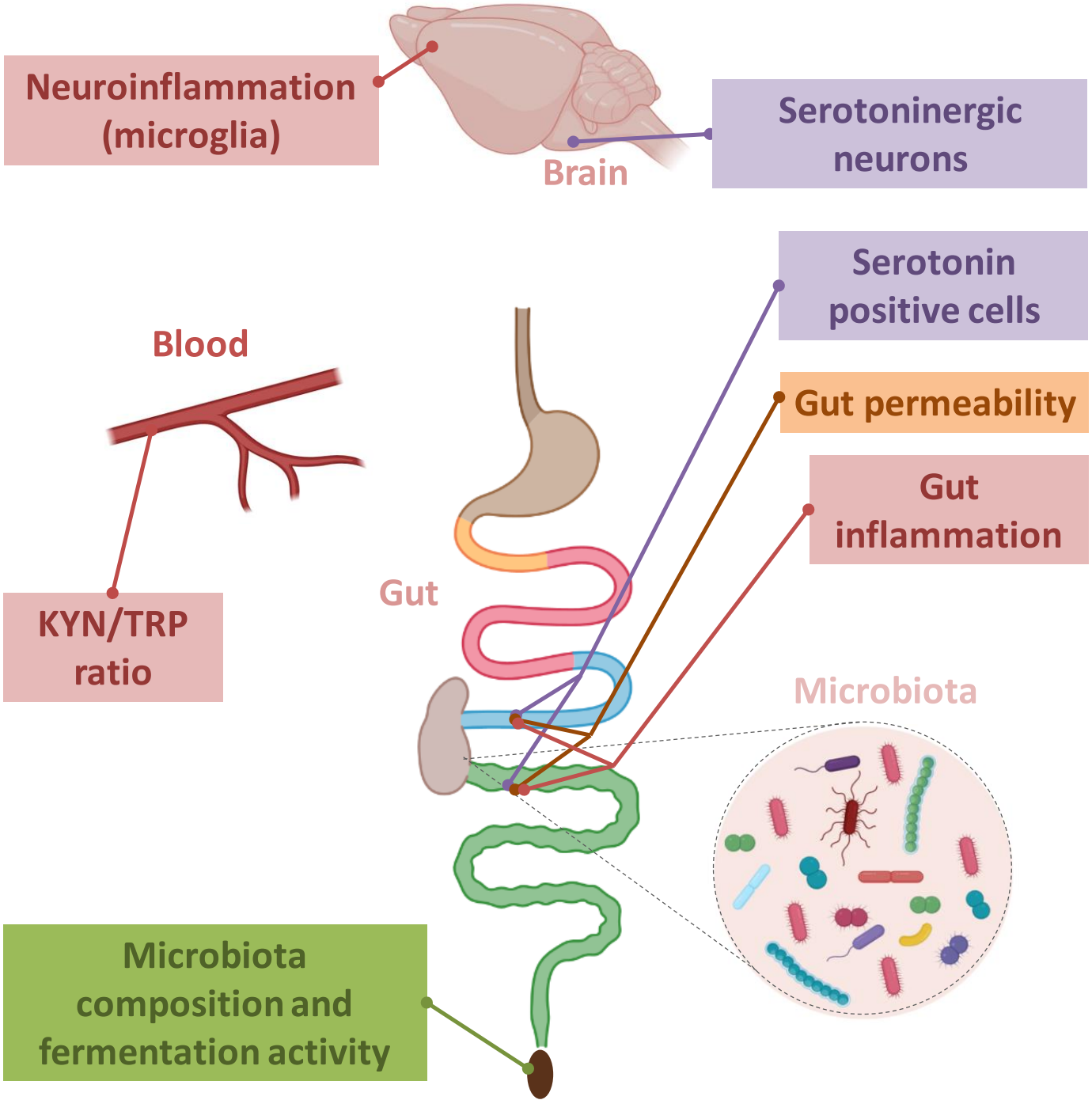
No difference between groups

Cognition (spatial memory)



Difference between groups

C57BL/6


Neuroinflammation (microglia)
Brain
Serotoninergic neurons
Serotonin positive cells
Blood
Gut permeability
Gut inflammation
KYN/TRP ratio
Gut
Microbiota
Microbiota composition and fermentation activity