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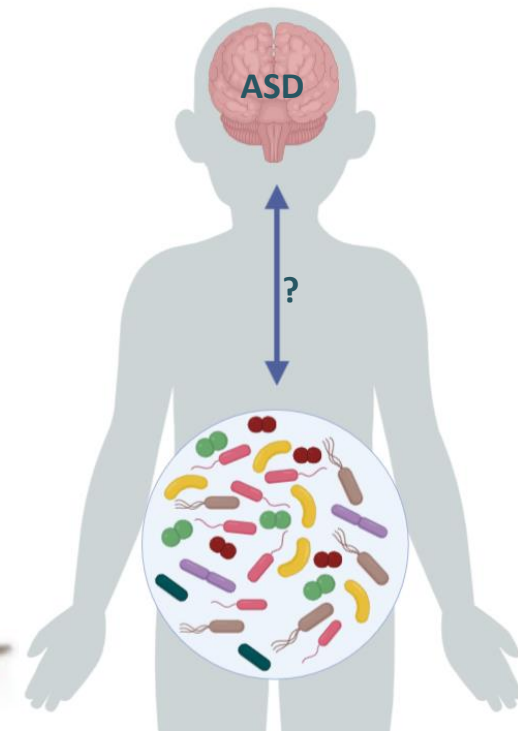
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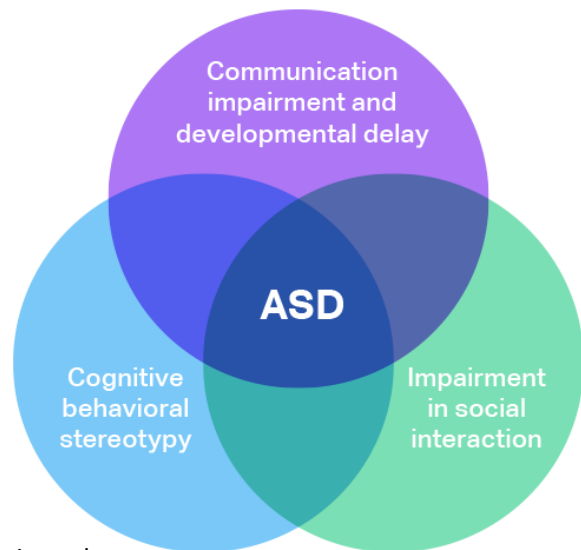
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➤ Effect of gut microbiota from children with autism spectrum disorder (ASD) on behavior and ASD-related biological markers in germ-free mice

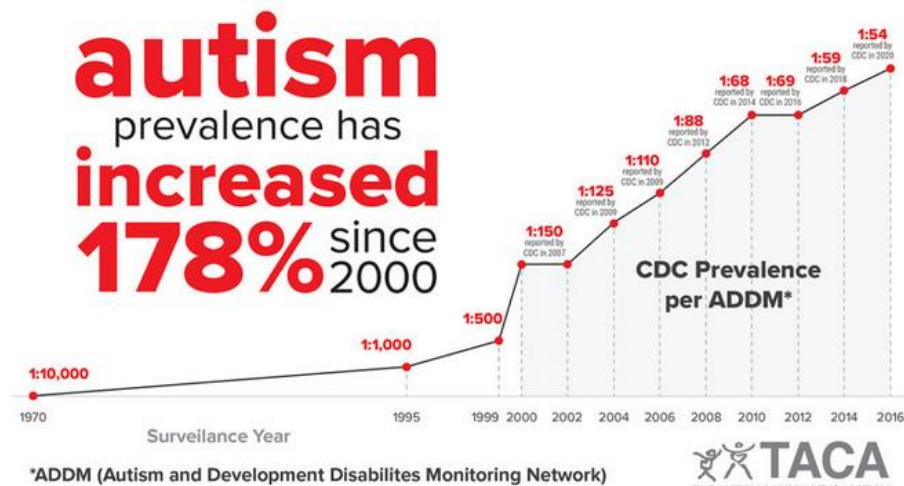
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# ➤ Autism spectrum disorder



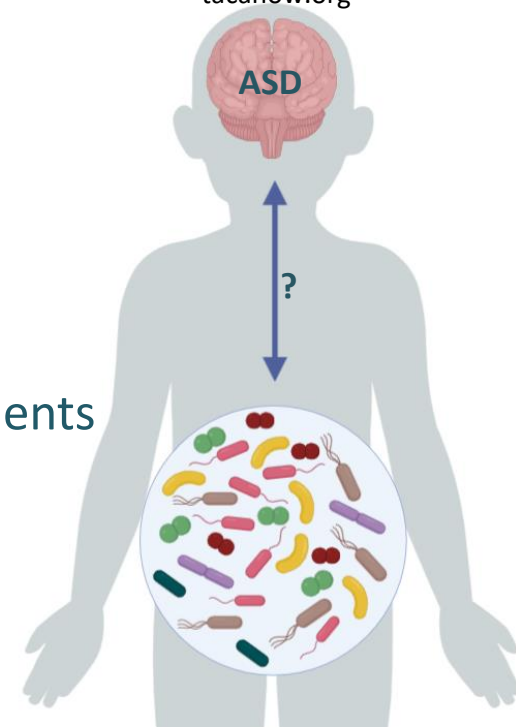
embracingasd.com



- Genetic heritability is reported to be around 50% also a strong environmental impact.
- High prevalence of gastrointestinal (GI) disorders in ASD patients

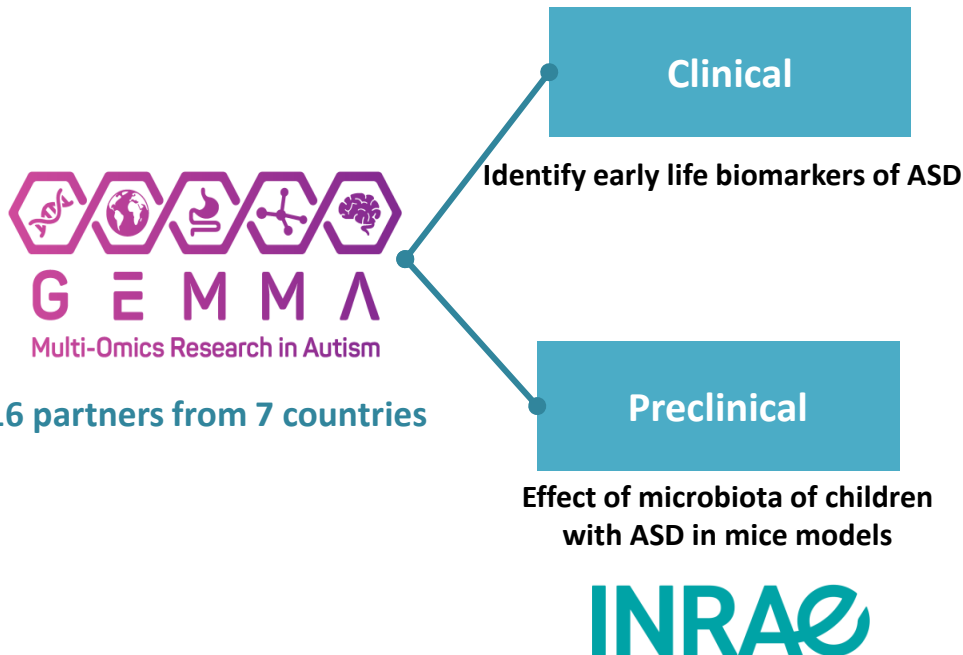


Role of microbiota-gut-brain axis in ASD ?



# ➤ 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 improvement of behavior and/or GI symptoms after microbiota modulation (FMT, probiotics) in ASD patients or mice models of ASD



Utrecht University



Talk by Lucia Marzal this afternoon

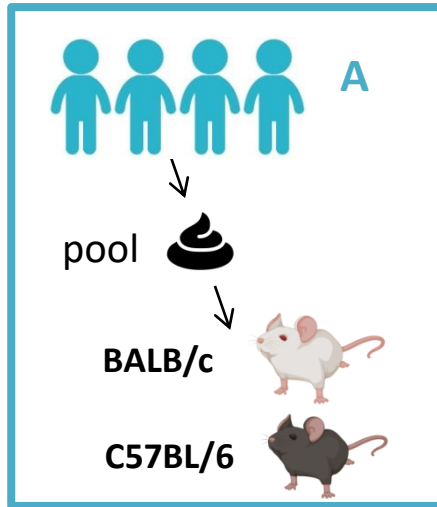


Poster by Naika Prince

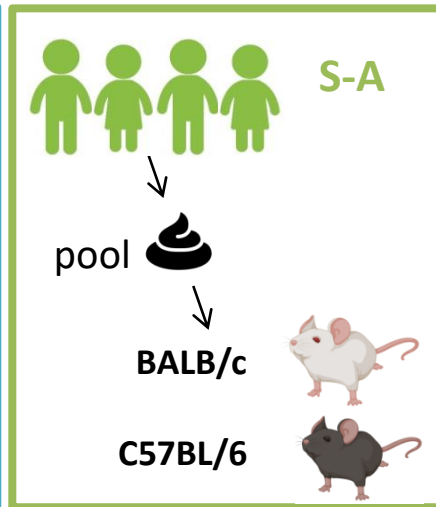
# ➤ GEMMA project-Preclinical part

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

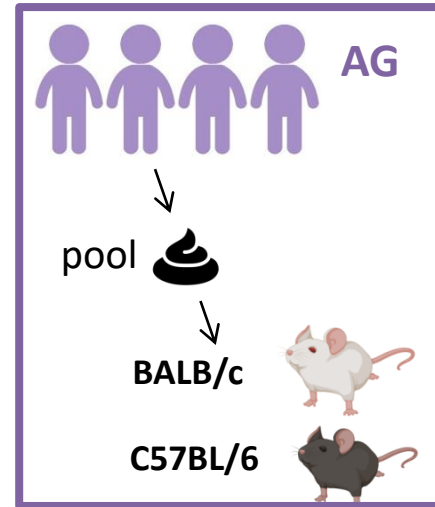
ASD without GI symptoms



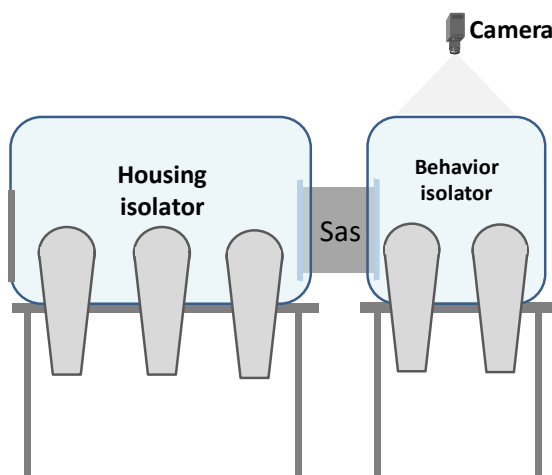
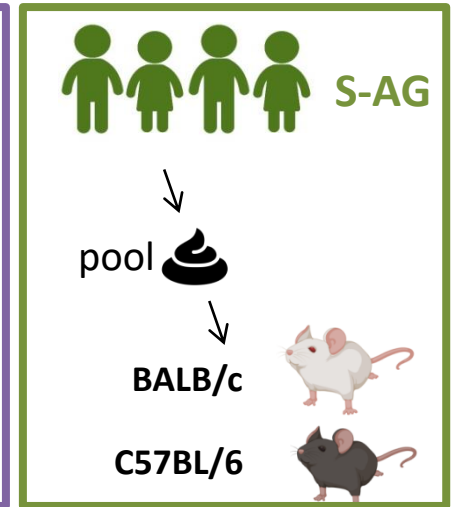
Their siblings



ASD with GI symptoms



Their siblings



Age (weeks)

3-4

FMT

2 gavages 48h apart

9

Behavior

Feces sampling

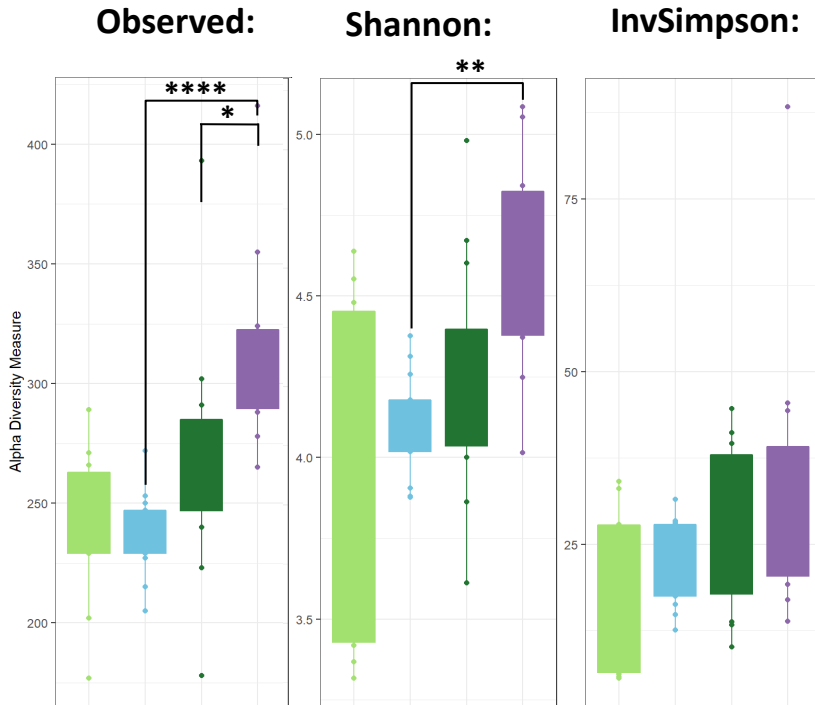
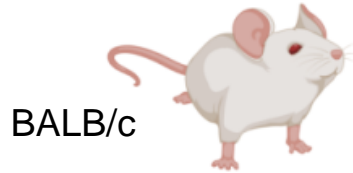
11

Sacrifice and tissue sampling

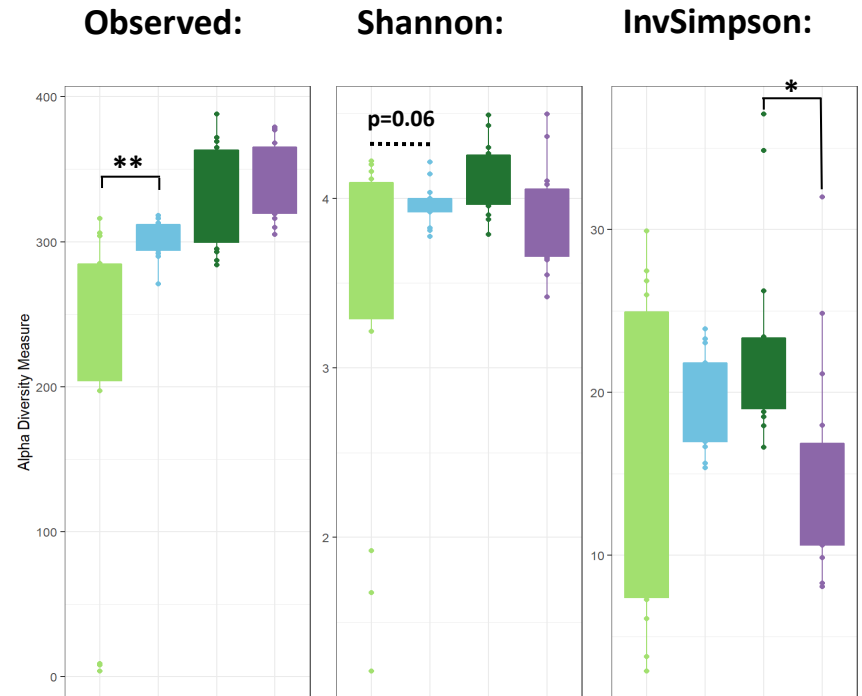
- ASD related behavior
- Gut microbiota composition, gut permeability, gut and brain inflammation, serotonin

# Microbiota composition (16S rDNA)- ASV analysis

## Alpha-diversity (intra-group)



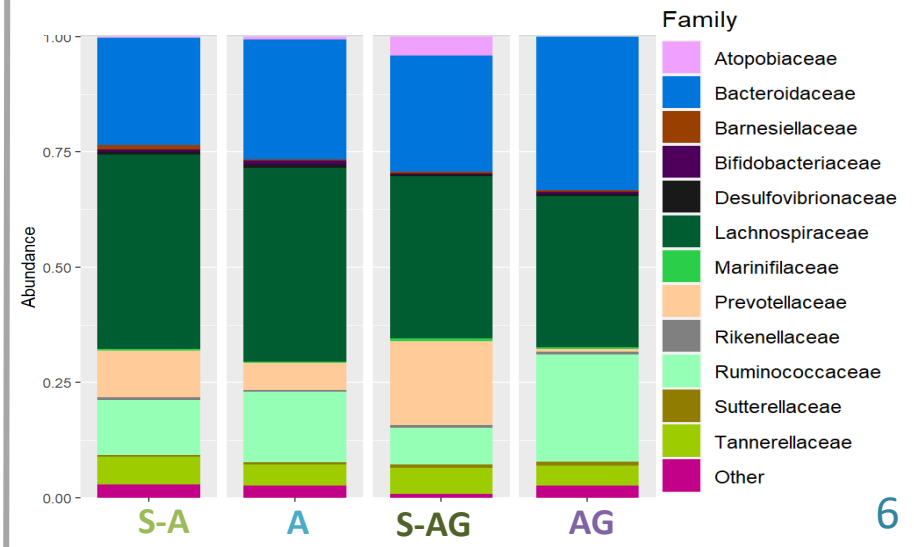
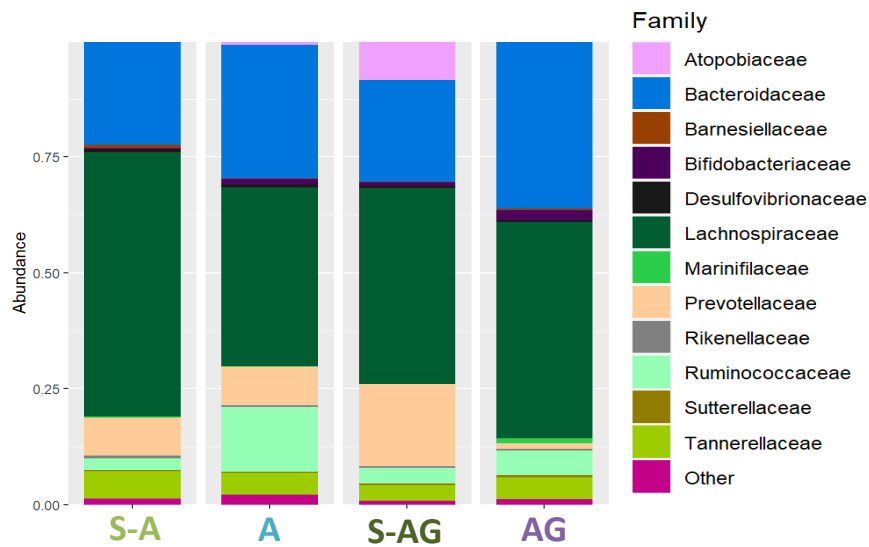
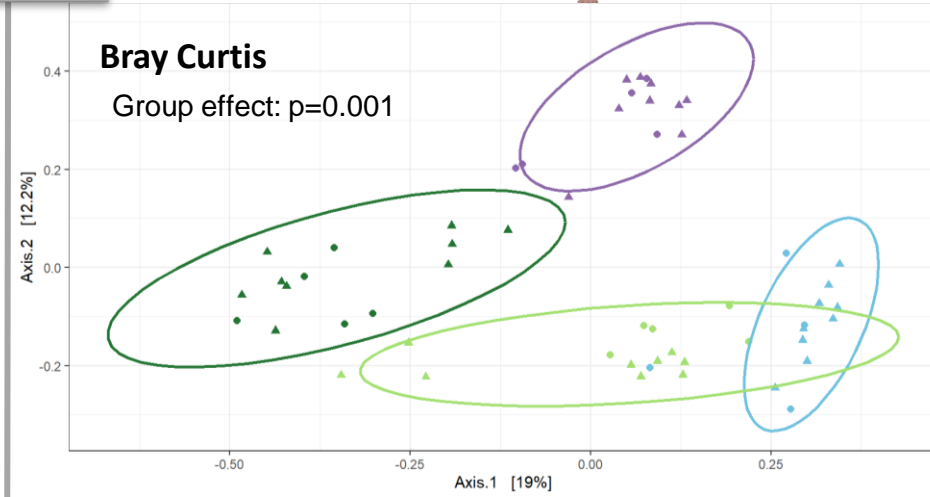
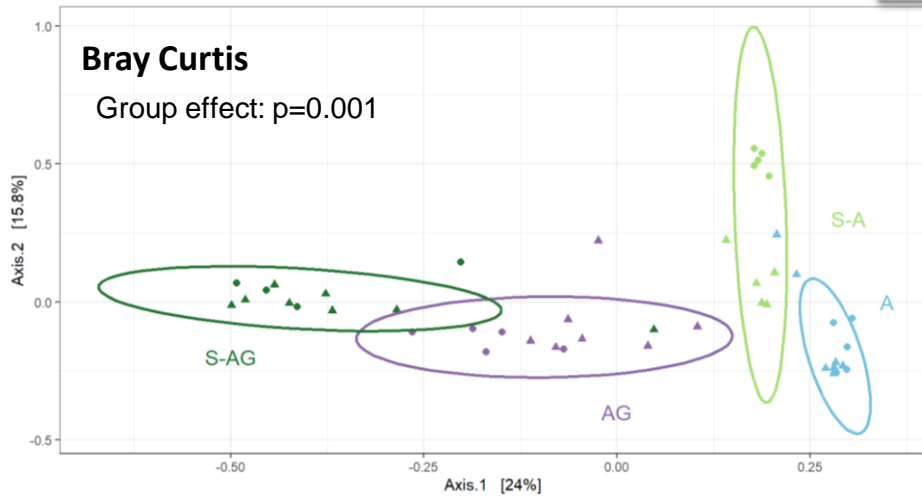
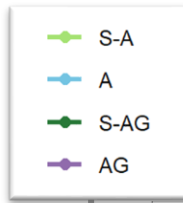
Overall greater diversity in the AG group



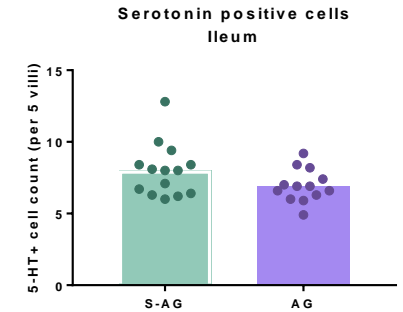
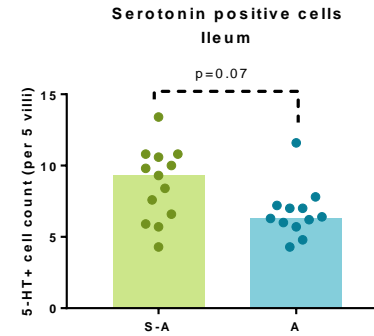
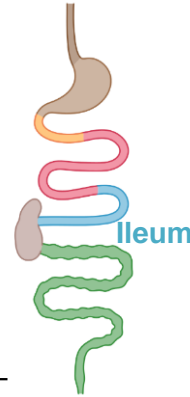
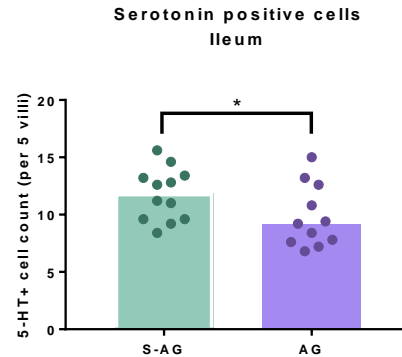
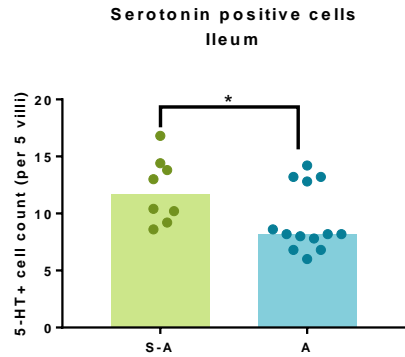
Slightly higher diversity in group A, variable according to the chosen index.

# Microbiota composition (16S rDNA)

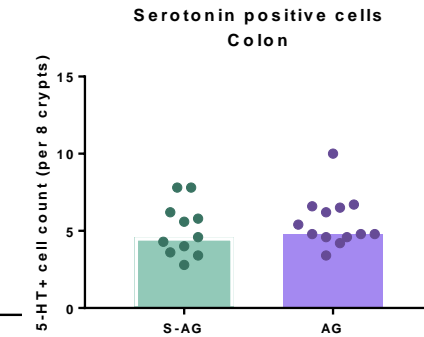
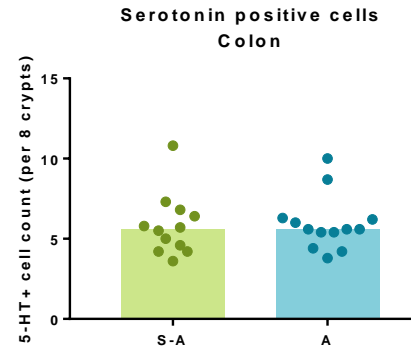
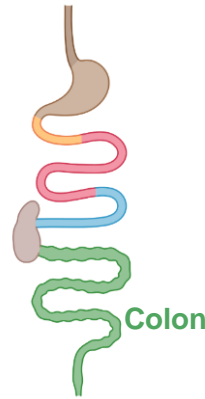
## Beta-diversity and Family composition



# Gut serotonin



*Colon: In progress*



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

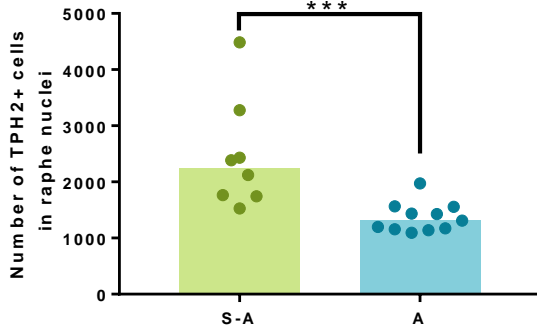


# Brain serotonin

## Serotonin neurons in the raphe nuclei



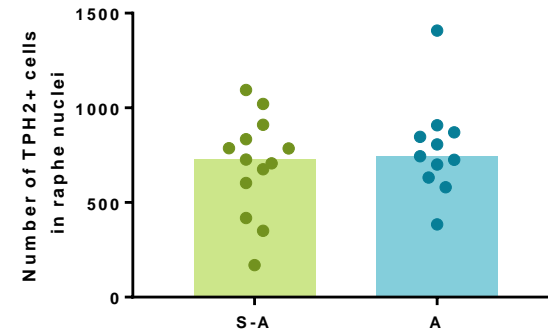
Serotonergic neurons  
Rape nuclei



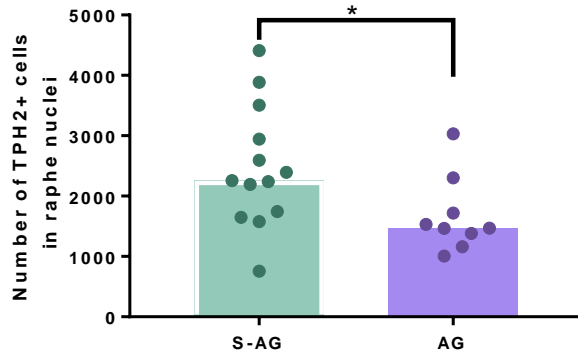
raphe  
nuclei



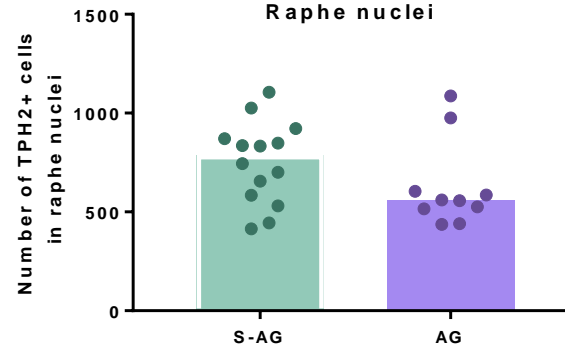
Serotonergic neurons  
Rape nuclei



Serotonergic neurons  
Rape nuclei



Serotonergic neurons  
Rape nuclei

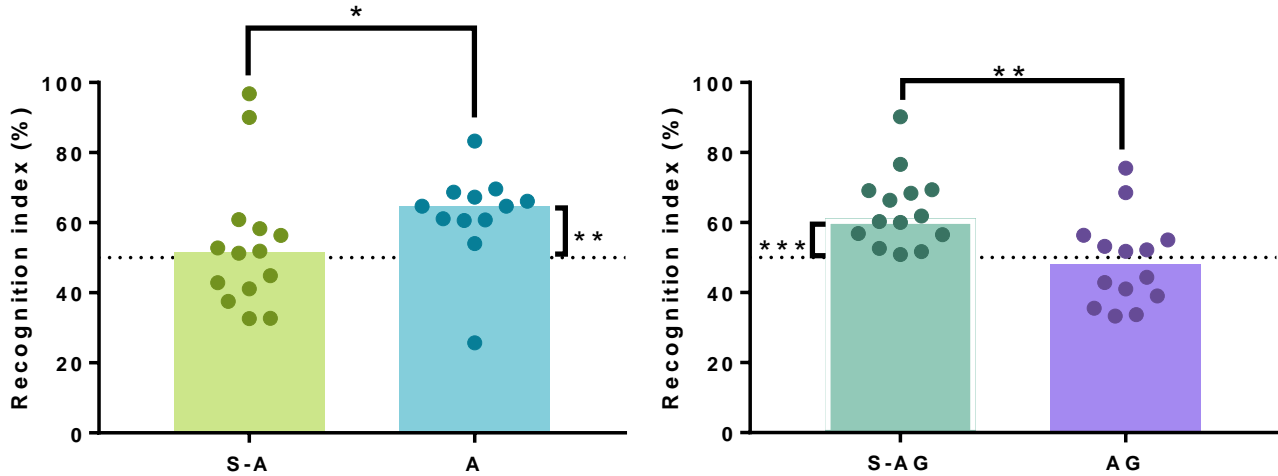
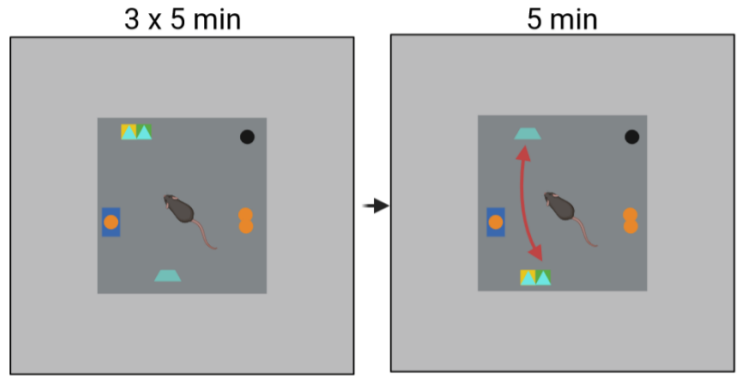
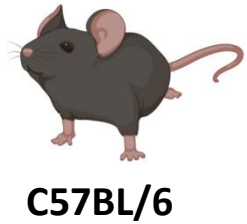


•Reduced number of serotonergic neurons in raphe nuclei in groups A and AG only for BALBc

# Behavior

- No difference in anxiety, social behavior and stereotyped behavior

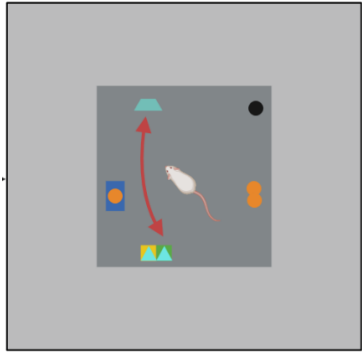
## Spatial memory:



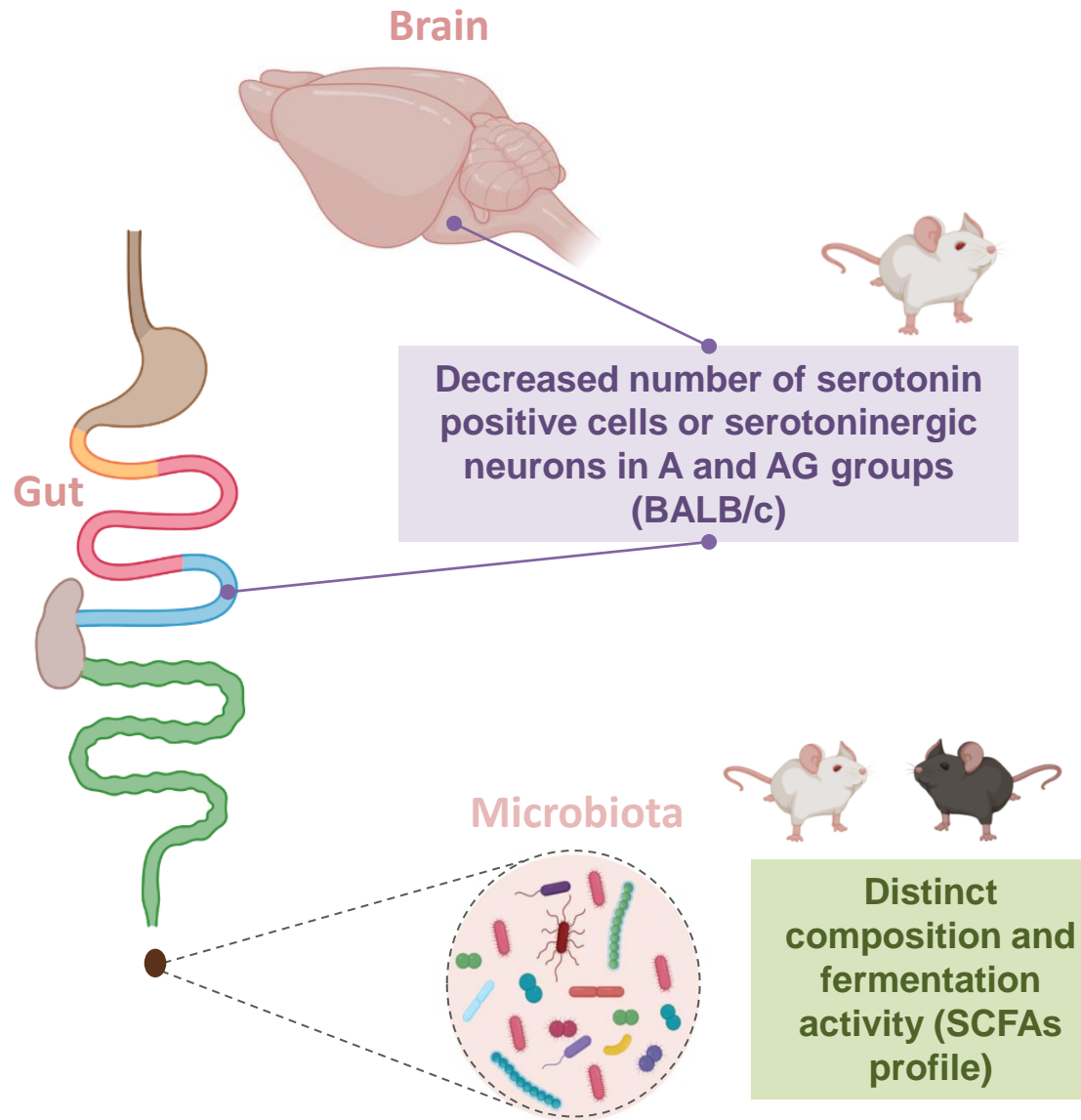
→ Lower recognition index in AG than S-AG mice

→ Lower recognition index in S-A than A mice

# Conclusion:



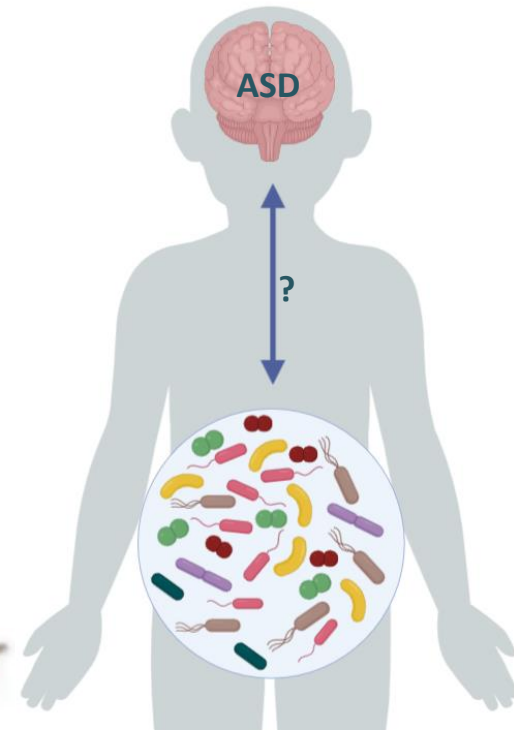
No difference in behavior aside from altered spatial memory (C57BL/6)



- 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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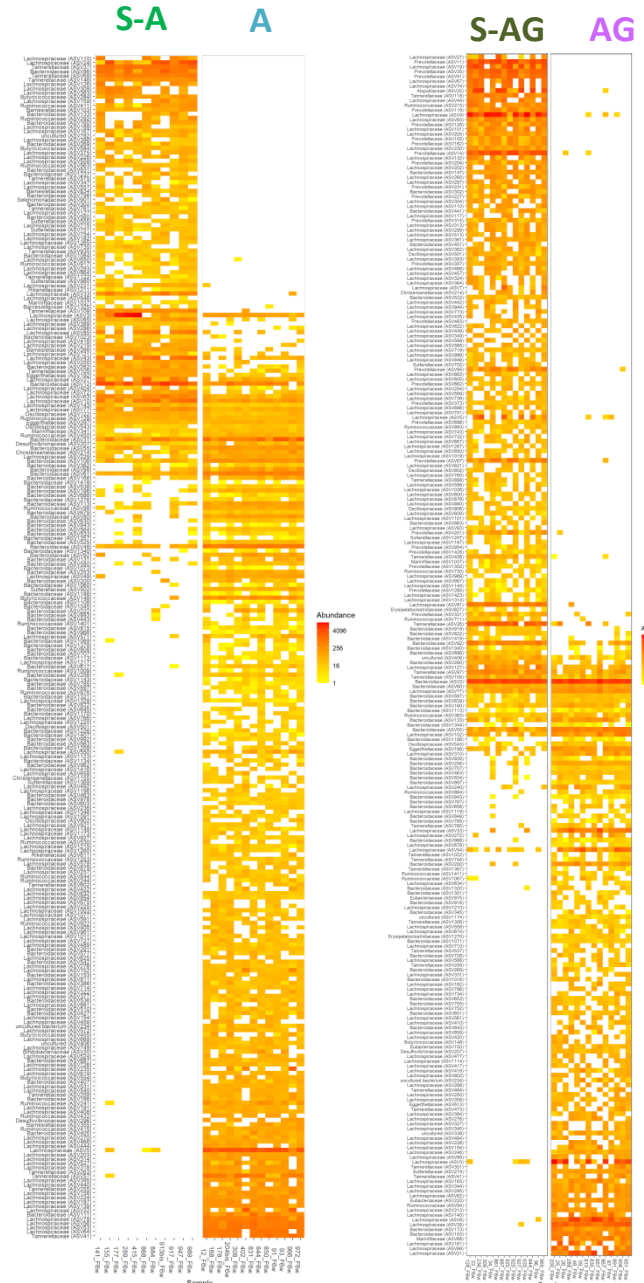
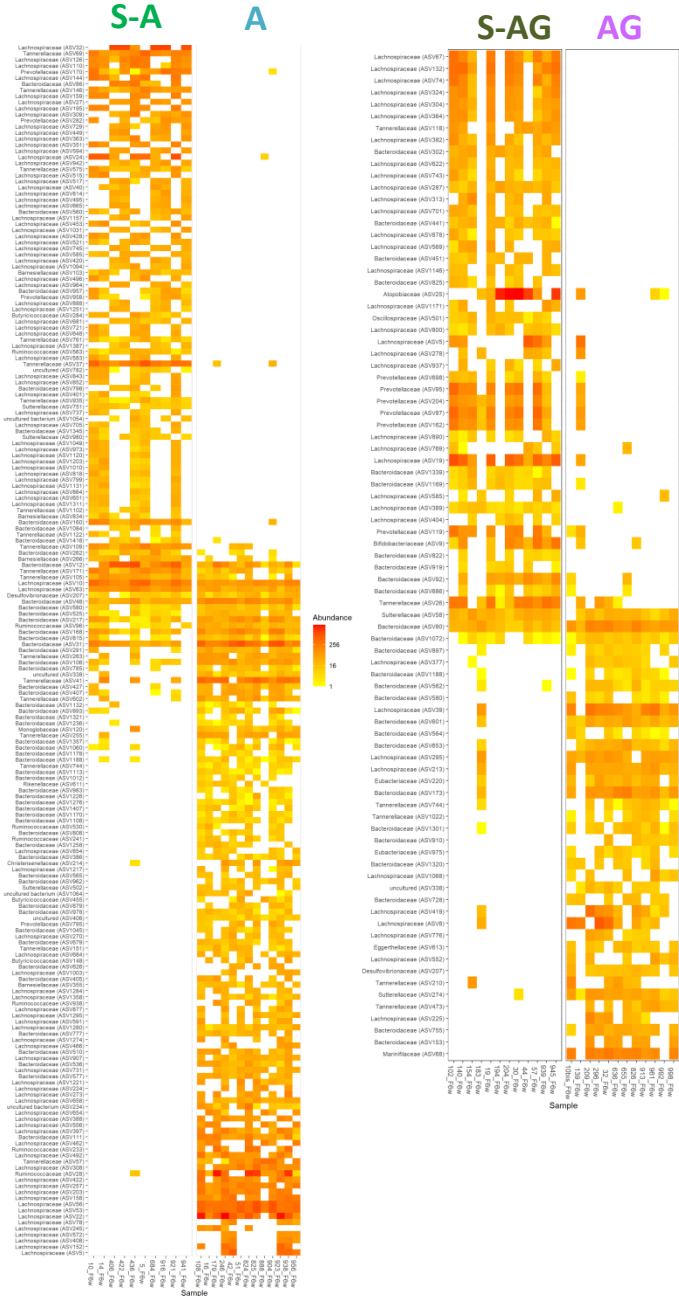


Extras



# Differential abundances (ASV)

pval = 0.01 ; min abundance = 50  
log2foldchange >3

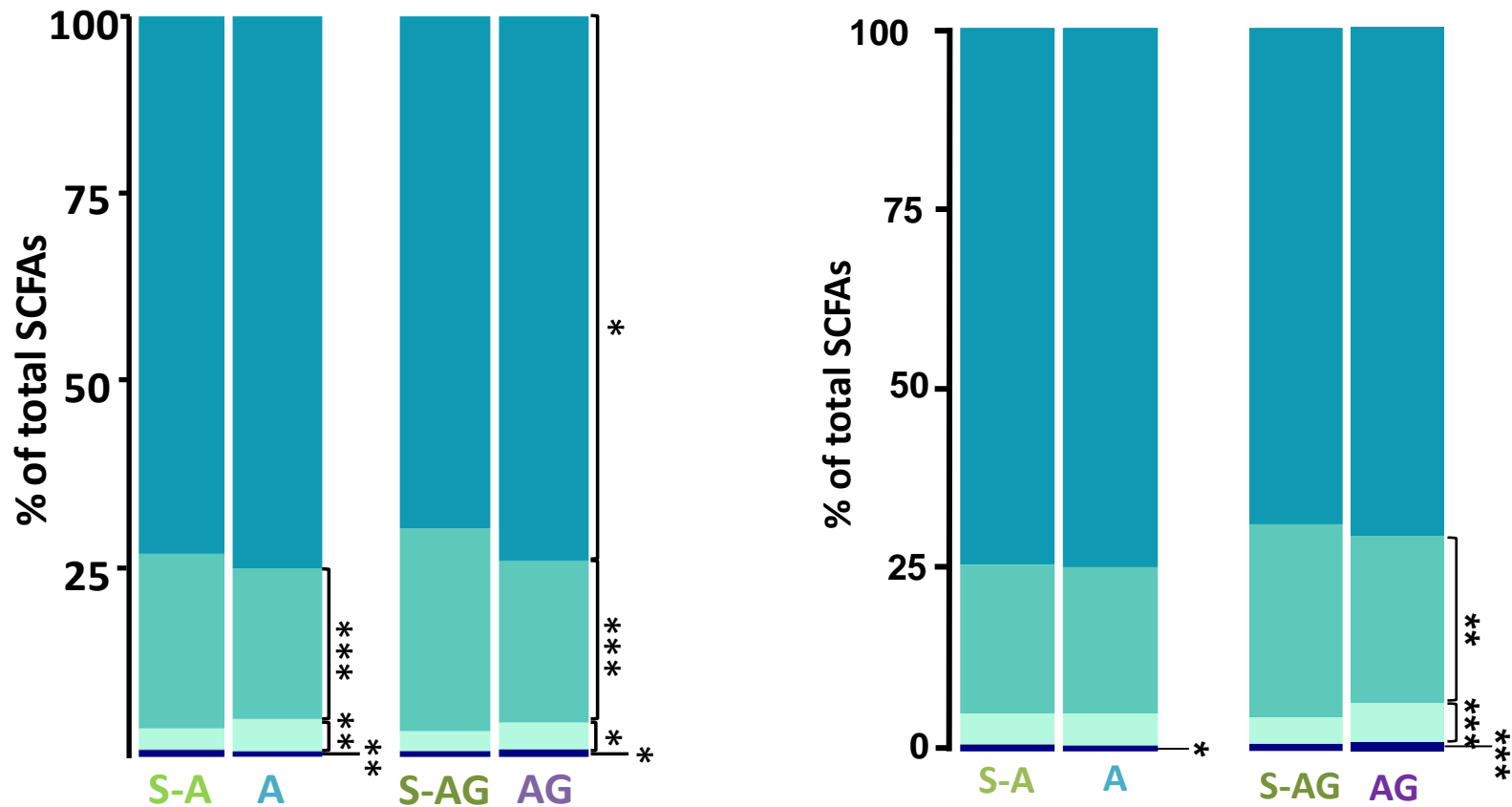


# ➤ Short chain fatty acids

Fermentation activity of the microbiota



Acetate Butyrate  
Propionate Branched and long chain



• Inter-group differences in caecal SCFA profiles

# Behavior

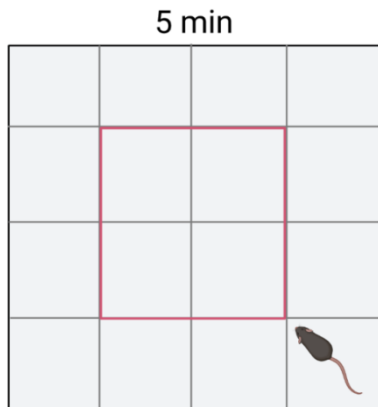
BALB/c



C57BL/6

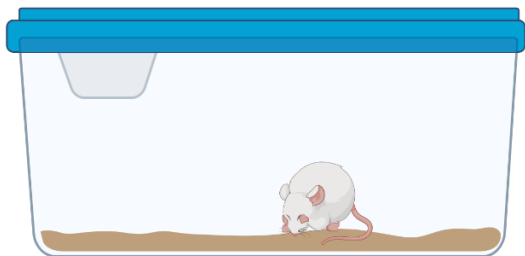


## Anxiety (Open-field)



No difference between groups

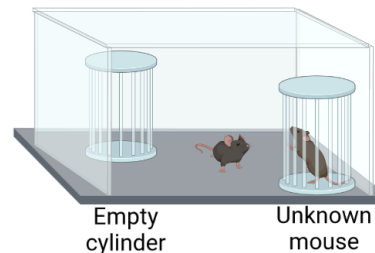
## Repetitive behavior (self-grooming)



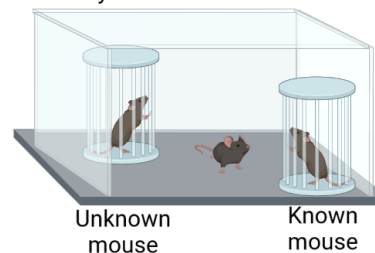
No difference between groups

## Social behavior

Social interaction



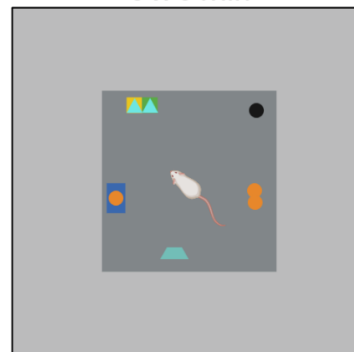
Social novelty



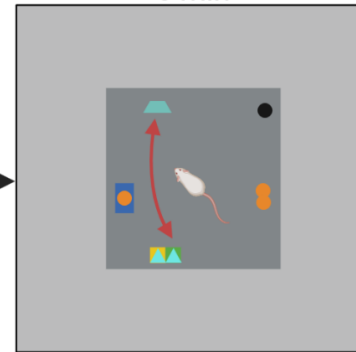
No difference between groups

## Cognition (spatial memory)

3 x 5 min



5 min



Difference between groups



C57BL/6



