

AGGRESSION: A GUT REACTION?

THE EFFECTS OF THE GUT MICROBIOME ON AGGRESSION

Dr. Sondra Turjeman

Future of the Microbiome Winter Summit 2024

The Microbiome-Gut-Brain Axis

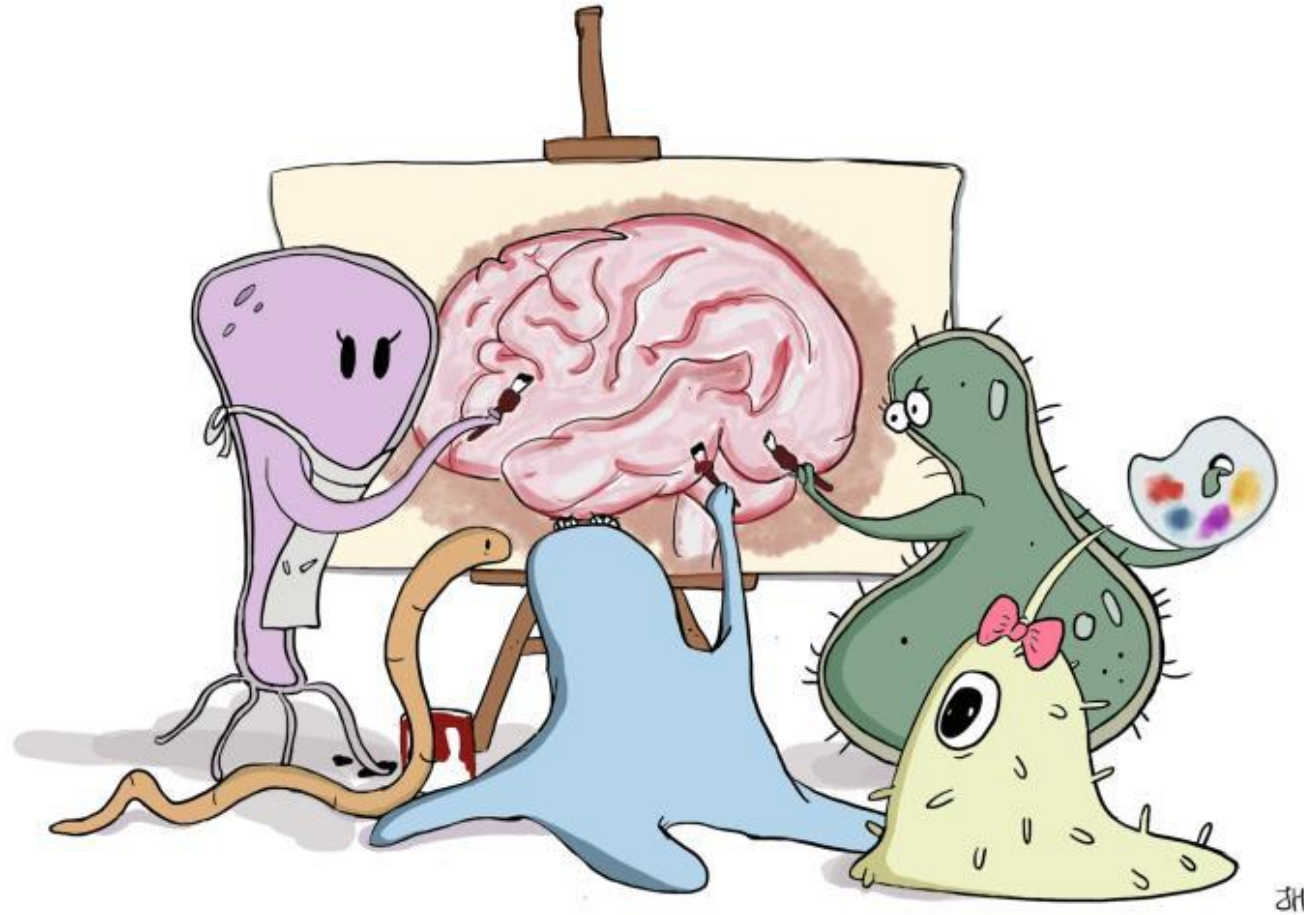
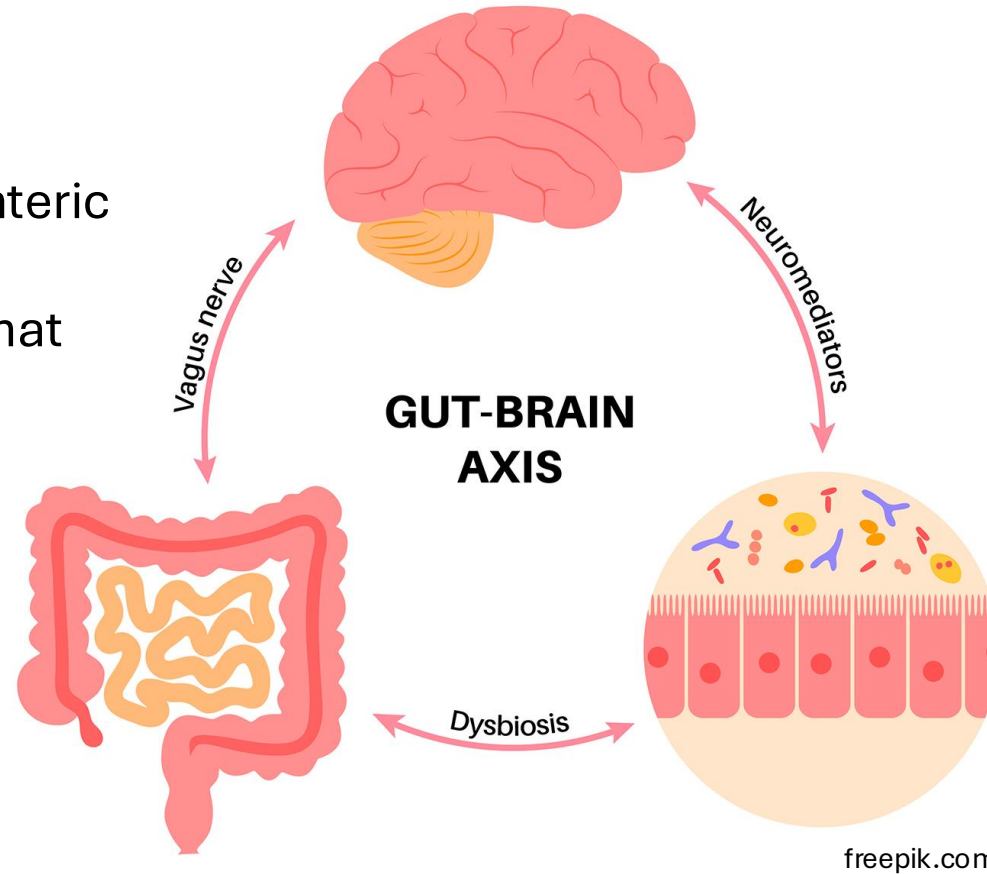


Image: KinesisMagazine – Feb 2020

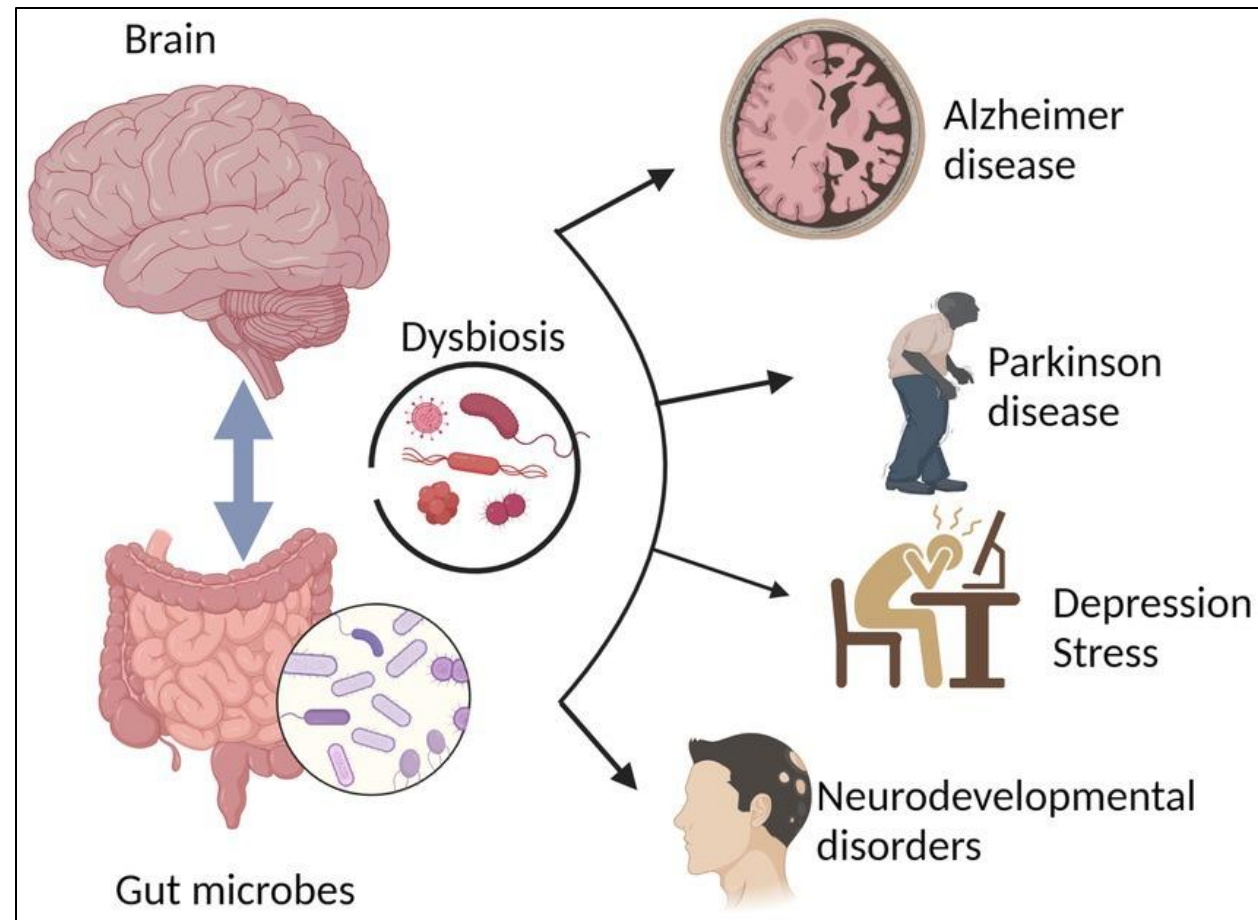
The Microbiome-Gut-Brain Axis

The vagus nerve and enteric nervous system form a bidirectional network that regulates digestive and neural functions



Metabolites produced in the gut can travel through the circulatory system to impact brain function

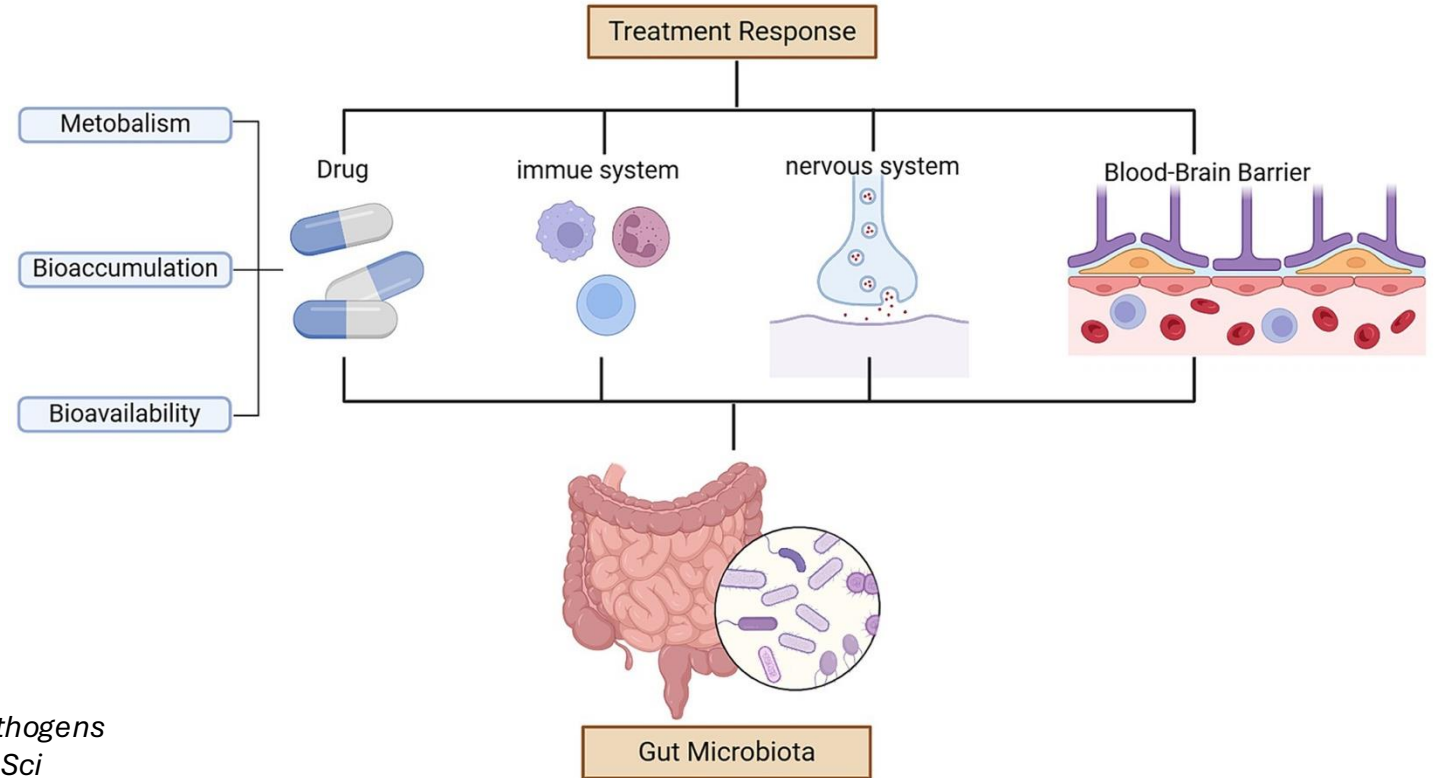
Microbial dysbiosis is associated with psychiatric and behavioral disorders



Ullah et al. 2023, *Front NeuroSci*

Dysbiosis is also associated with treatment outcomes

- Non-response rates in psychiatric disorders are 30-60% depending on diagnosis
- The microbiota play a role!



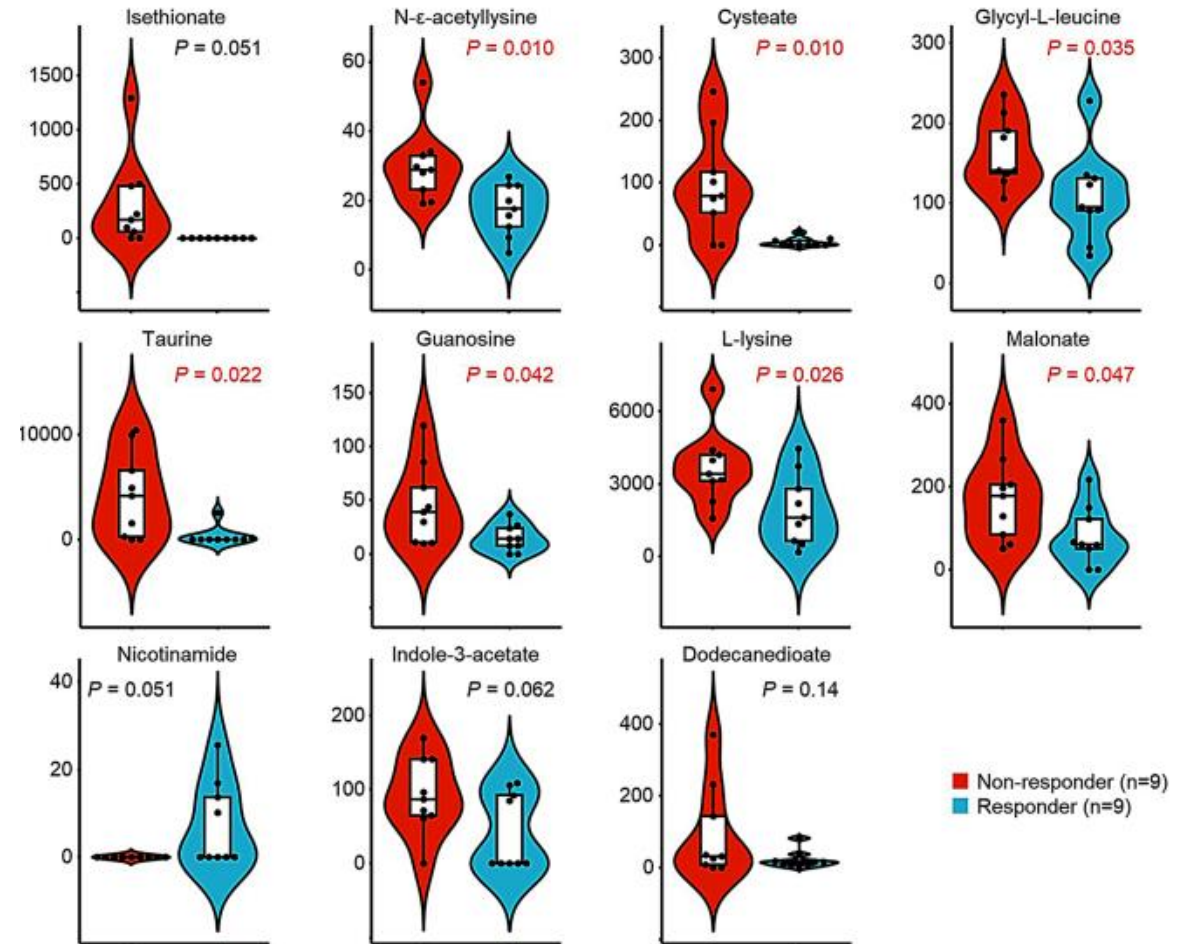
Matsuzaki et al. 2024, *Gut Pathogens*
Dong et al. 2022, *Front NeuroSci*
Xie et al. 2024, *Front. Microbiol*

Xie et al. 2024, *Front Microbiol*

Dysbiosis is also associated with treatment outcomes

- Microbiota composition and microbial metabolites have been associated with individual response to treatment

Matsuzaki et al. 2024, *Gut Pathogens*
Dong et al. 2022, *Front NeuroSci*
Xie et al. 2024, *Front Microbiol*



Matsuzaki et al. 2024, *Gut Pathogens*

Our Research: Social behavior and the microbiome, with a focus on aggressive behavior in flies, mice, and men.



How does microbiota dysbiosis affect aggressive behavior?

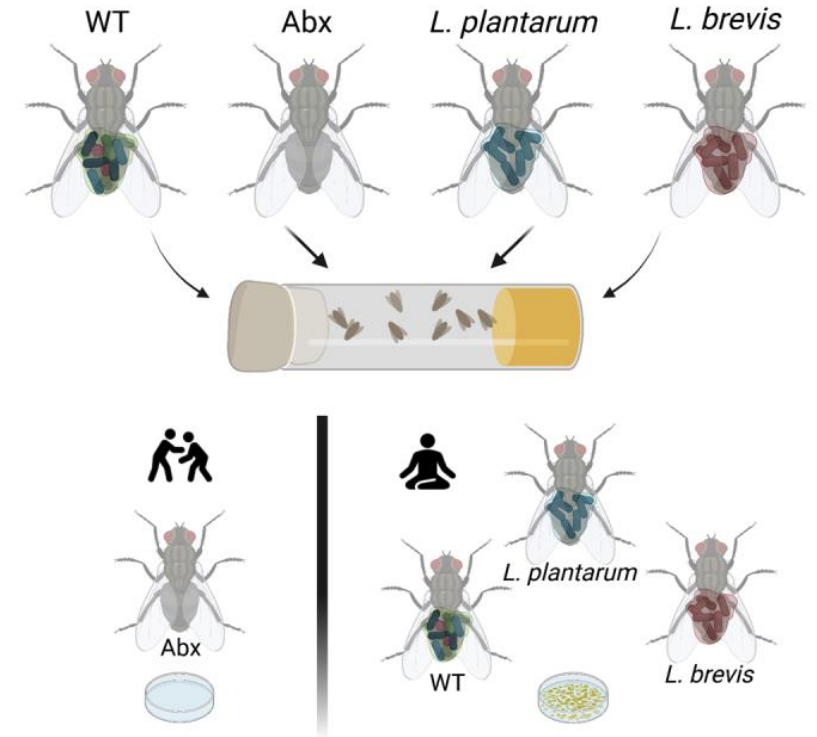
iScience

Article

Antibiotics increase aggression behavior and aggression-related pheromones and receptors in *Drosophila melanogaster*

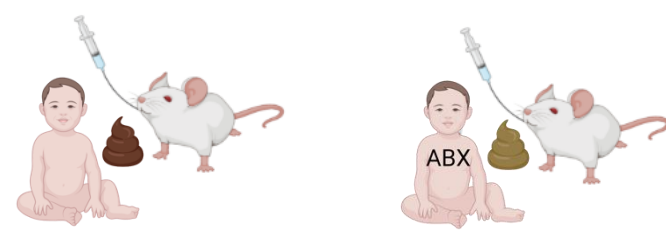
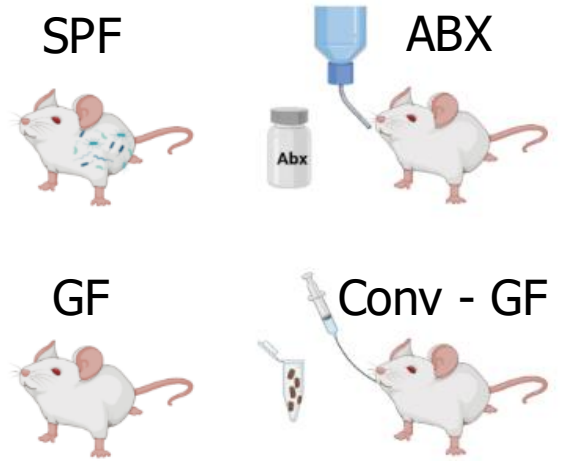
M. Grinberg,¹ R. Levin,¹ H. Neuman,^{1,2} O. Ziv,¹ S. Turjeman,¹ G. Gamliel,¹ R. Nosenko,¹ and O. Koren^{1,3,*}

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2022



Microbiome & Aggression in Two Parts

Part I: Direct effects



Atara Uzan-Yulzari

Part II: Indirect (*in utero*) effects



Lelyan Moadi

Measuring aggression in mice

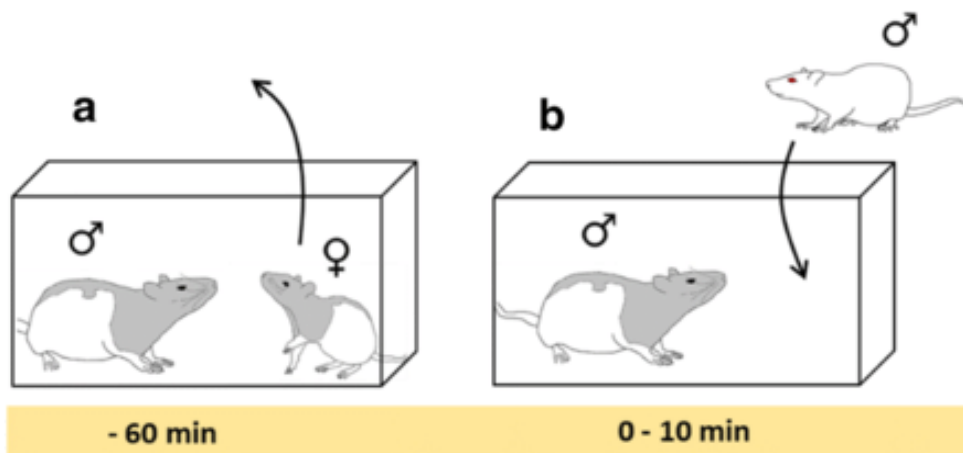
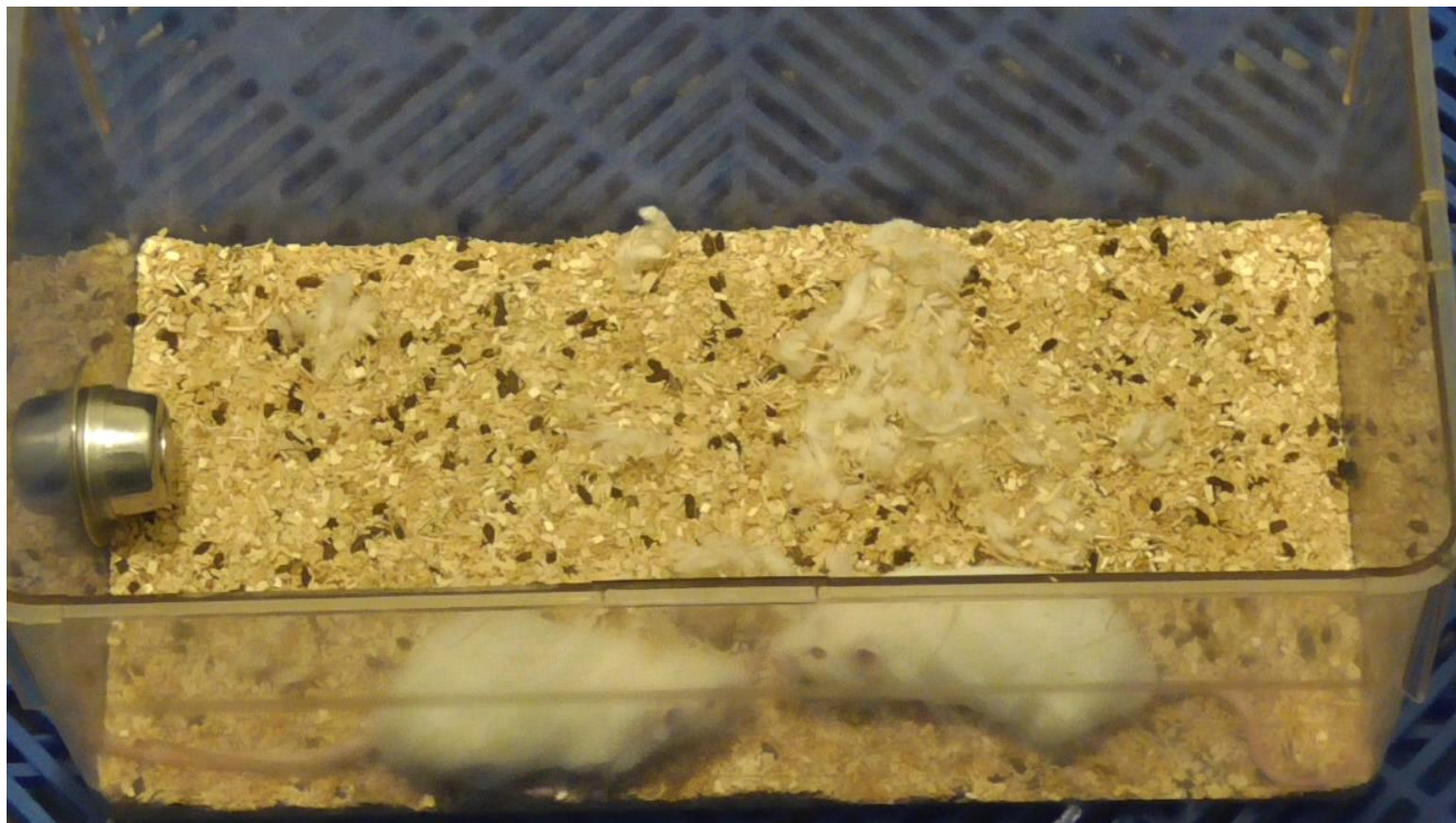
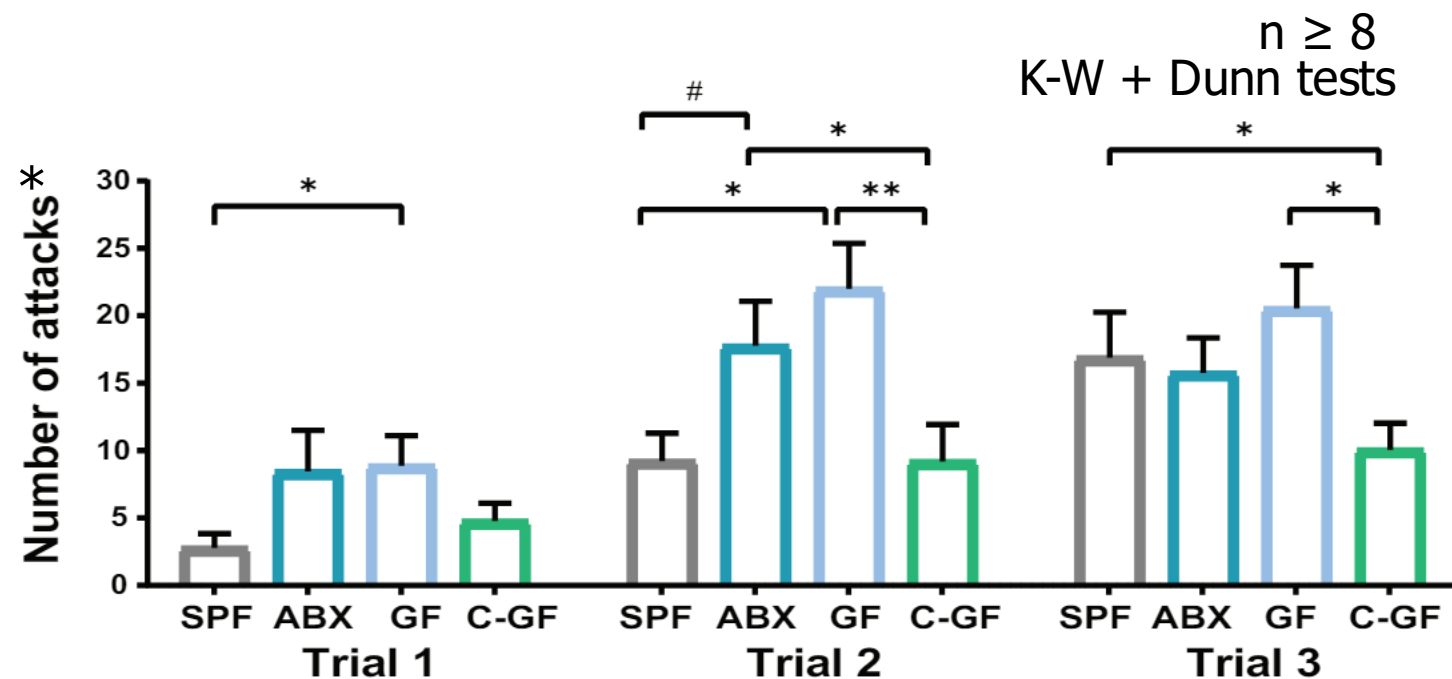
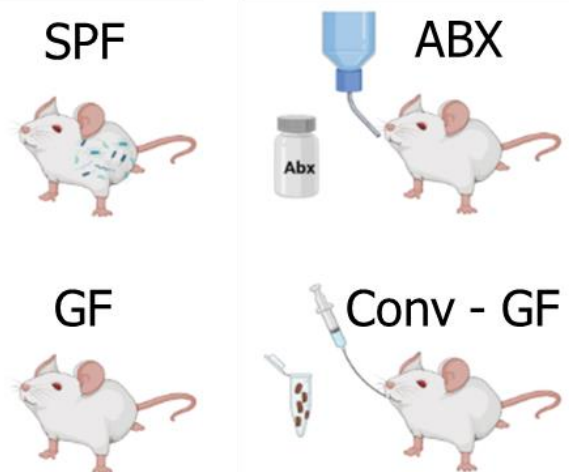


Image: Rajalingman et al. BMC Neuroscience 2020



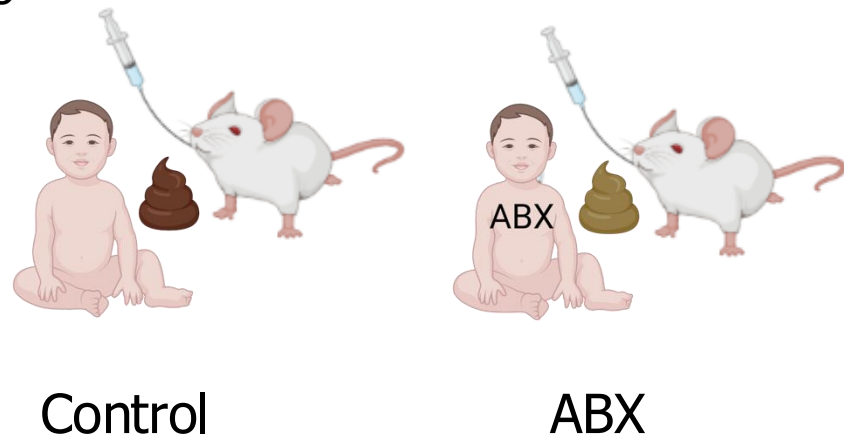
Microbiota manipulation increases aggression – driven by altered brain gene expression and metabolome



* Time to attack was also significantly reduced in the GF and ABX groups and restored in C-GF (not shown).

Humanized mouse model (FMT) further confirms this!

n = 8



ABX in first 48 hr of life



Feces collected at 1 mo

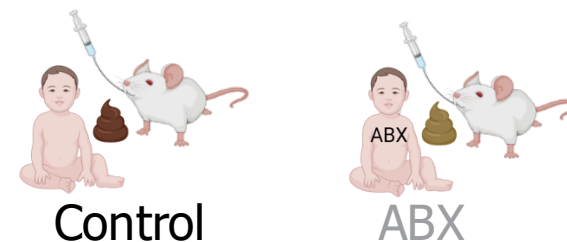


FMT to GF mice at 5 wks

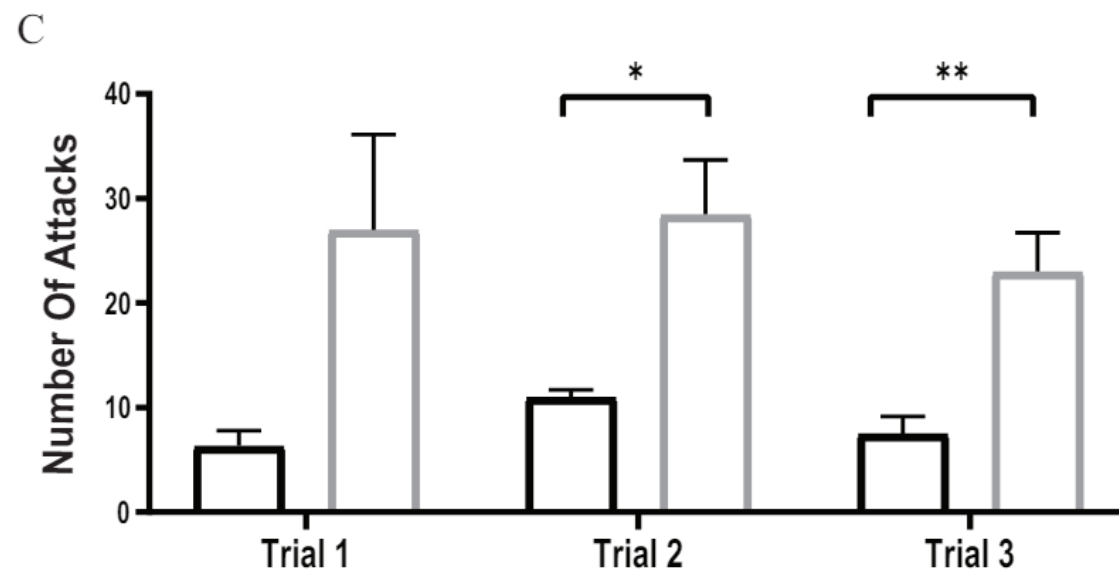
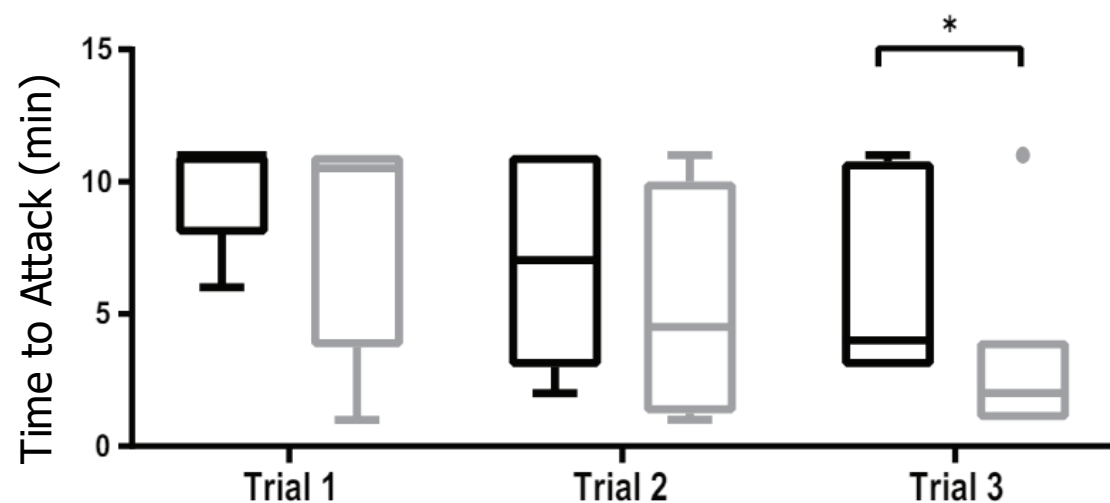


Behavior assay at 8-12 wks

FMT following ABX treatment induces aggressive phenotype in mice

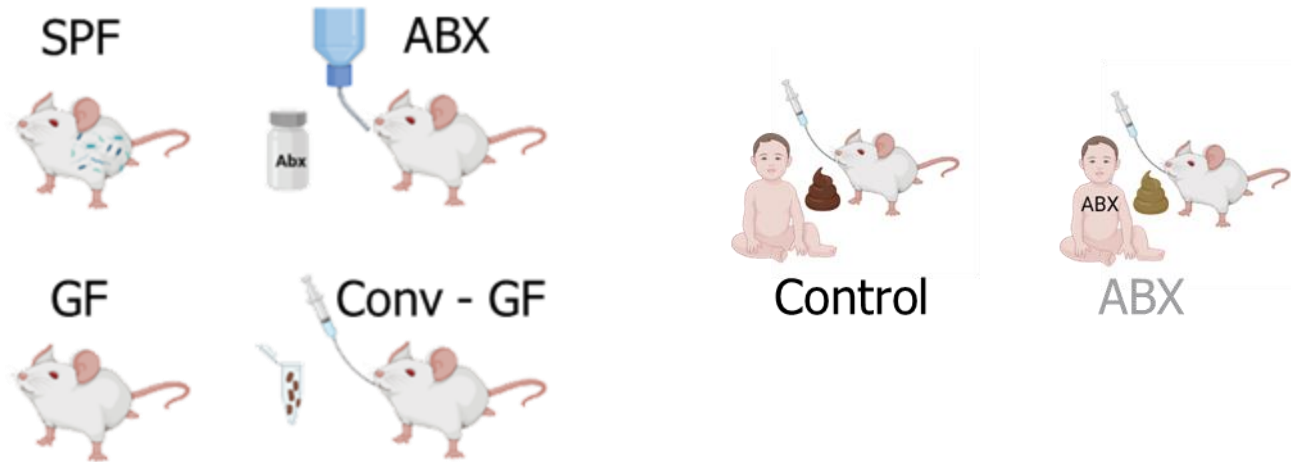


● Control
● ABX
n = 8



Dysbiotic gut microbiota - or complete absence - leads to increased aggression.

Can this phenomenon be vertically transmitted?



Going with the flow – how research is born

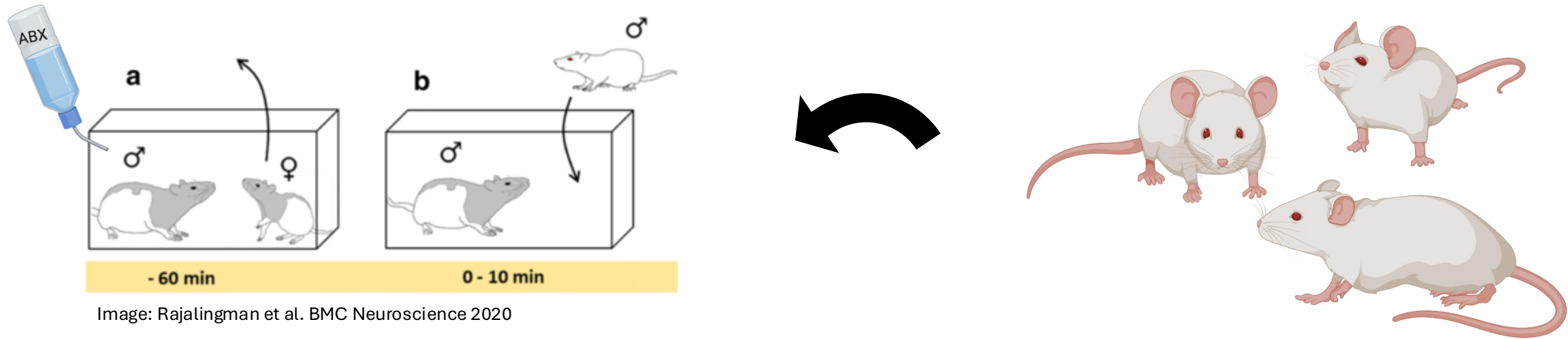
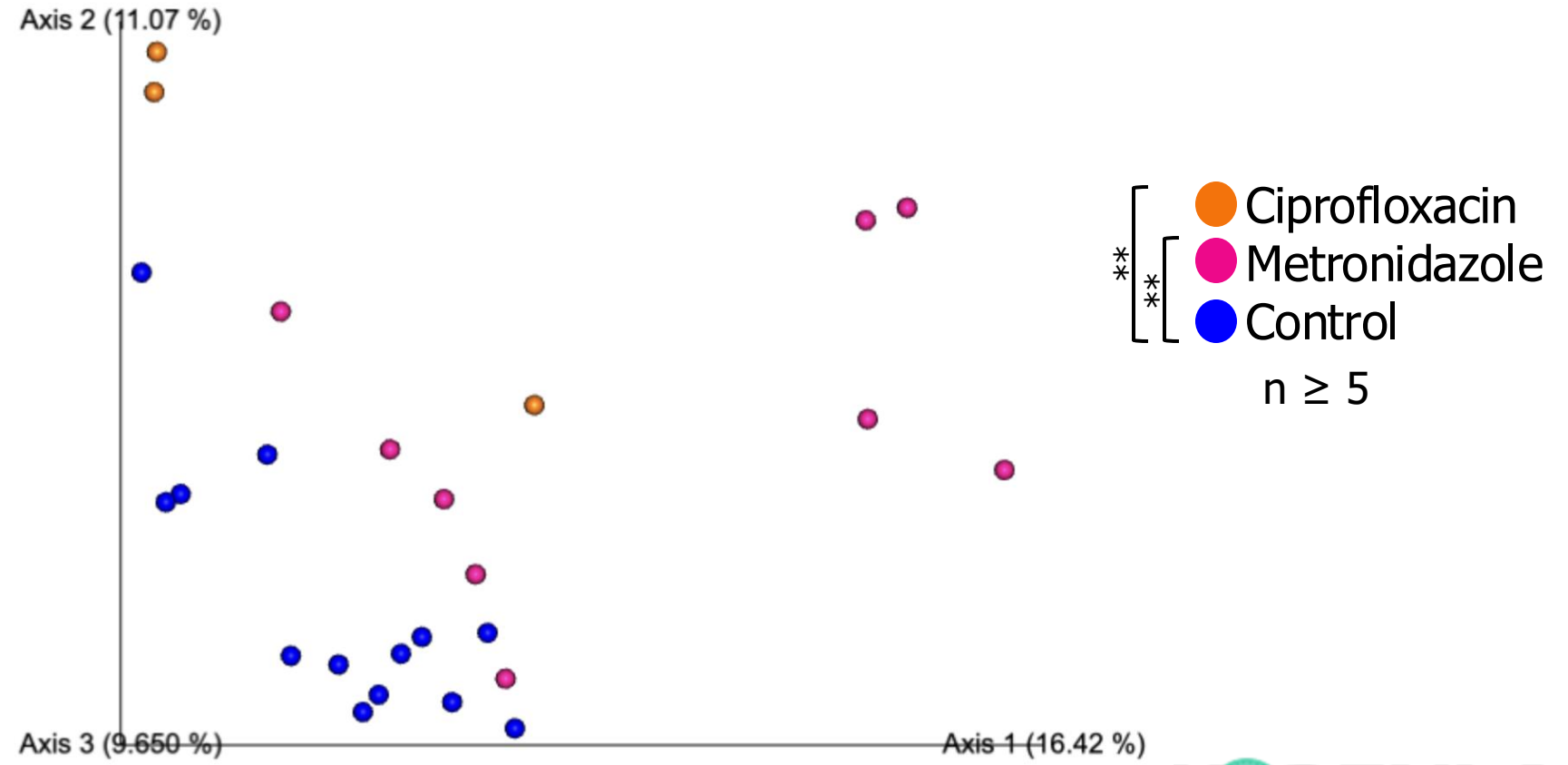
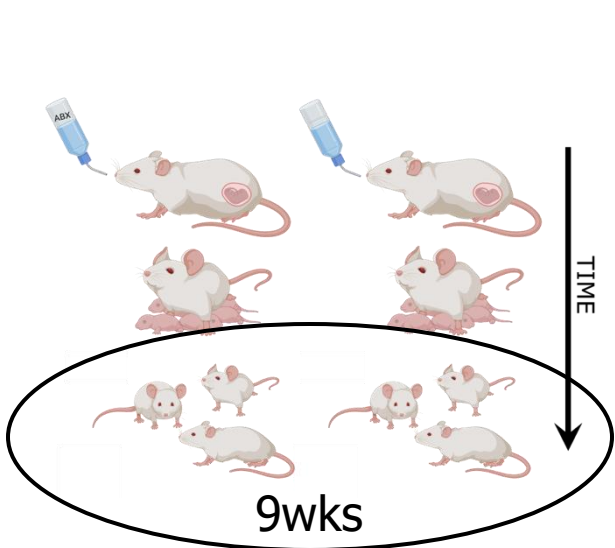


Image: Rajalingman et al. BMC Neuroscience 2020

Vertically transferred maternal microbiota dysbiosis is maintained through adulthood and increases offspring aggression



Microbiota-Gut-Brain Axis + Aggression

The gut microbiota is intimately associated with aggression

Antibiotic exposure (direct and *in utero*) can lead to increased aggression

Effects of antibiotics are long-reaching in murine models

**Remember – antibiotics are lifesaving drugs essential to modern medicine

Moving Forward: Microbiota + Aggression

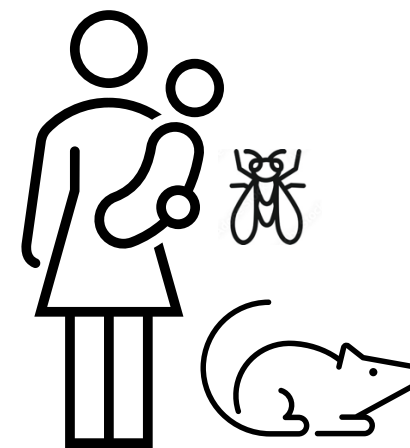
- Human adult and (longitudinal) childhood cohorts
- Identification of conserved, microbially-associated pathways in humans, mice, and men

PLOS GENETICS

Of Fighting Flies, Mice, and Men: Are Some of the Molecular and Neuronal Mechanisms of Aggression Universal in the Animal Kingdom?

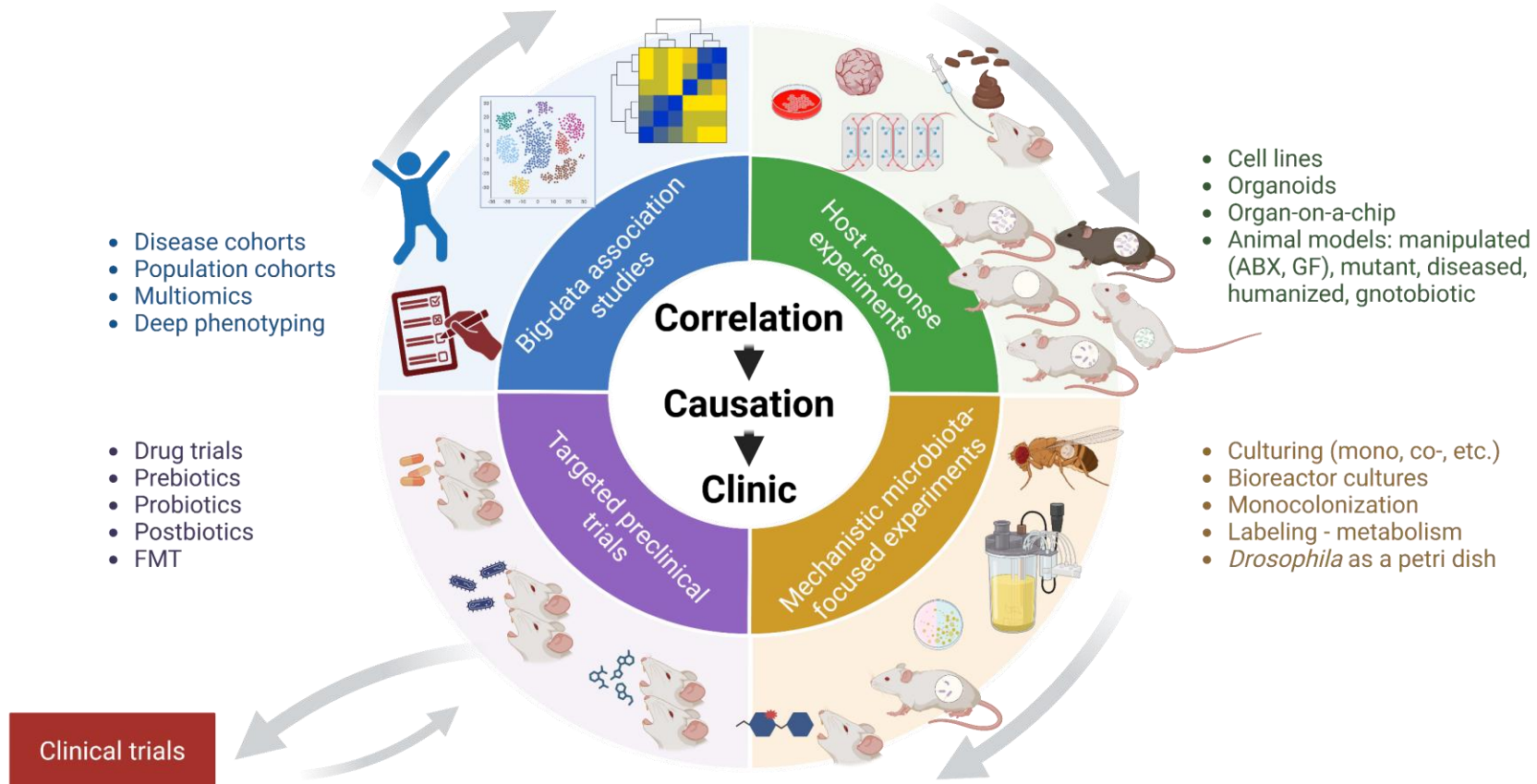
Amanda L. Thomas , Shaun M. Davis , Herman A. Dierick 

Published: August 27, 2015 • <https://doi.org/10.1371/journal.pgen.1005416>





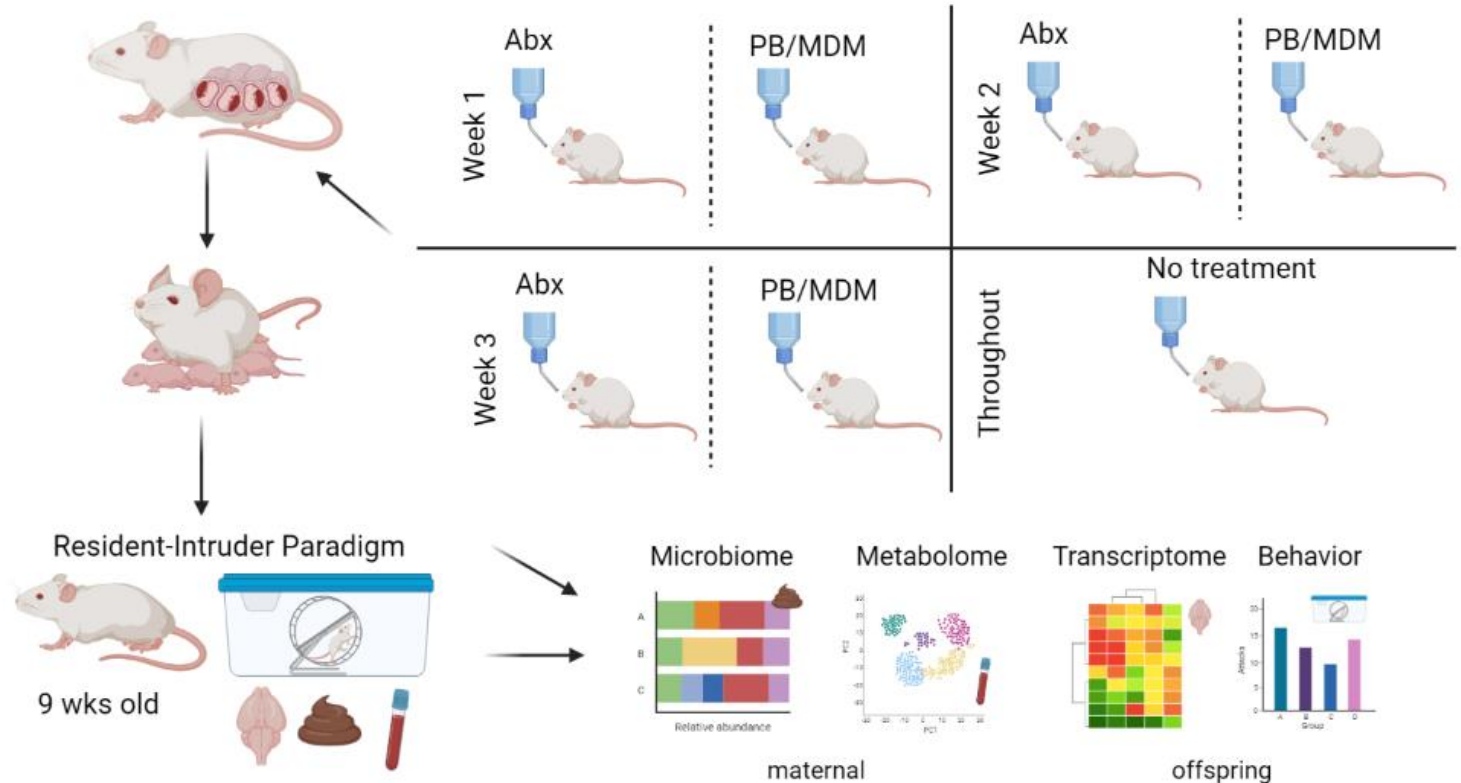
Translating findings to the clinic



Turjeman et al. *In Revision*

Translating findings to the clinic

- Probiotics (PB) or microbially derived metabolites (MDM) to be taken:
 - routinely during pregnancy and nursing
 - with or after a course of antibiotics



It takes a village!



Atara Uzan-Yulzari



Lelyan Moadi

Microbiota-Gut-Brain Axis | Aggression

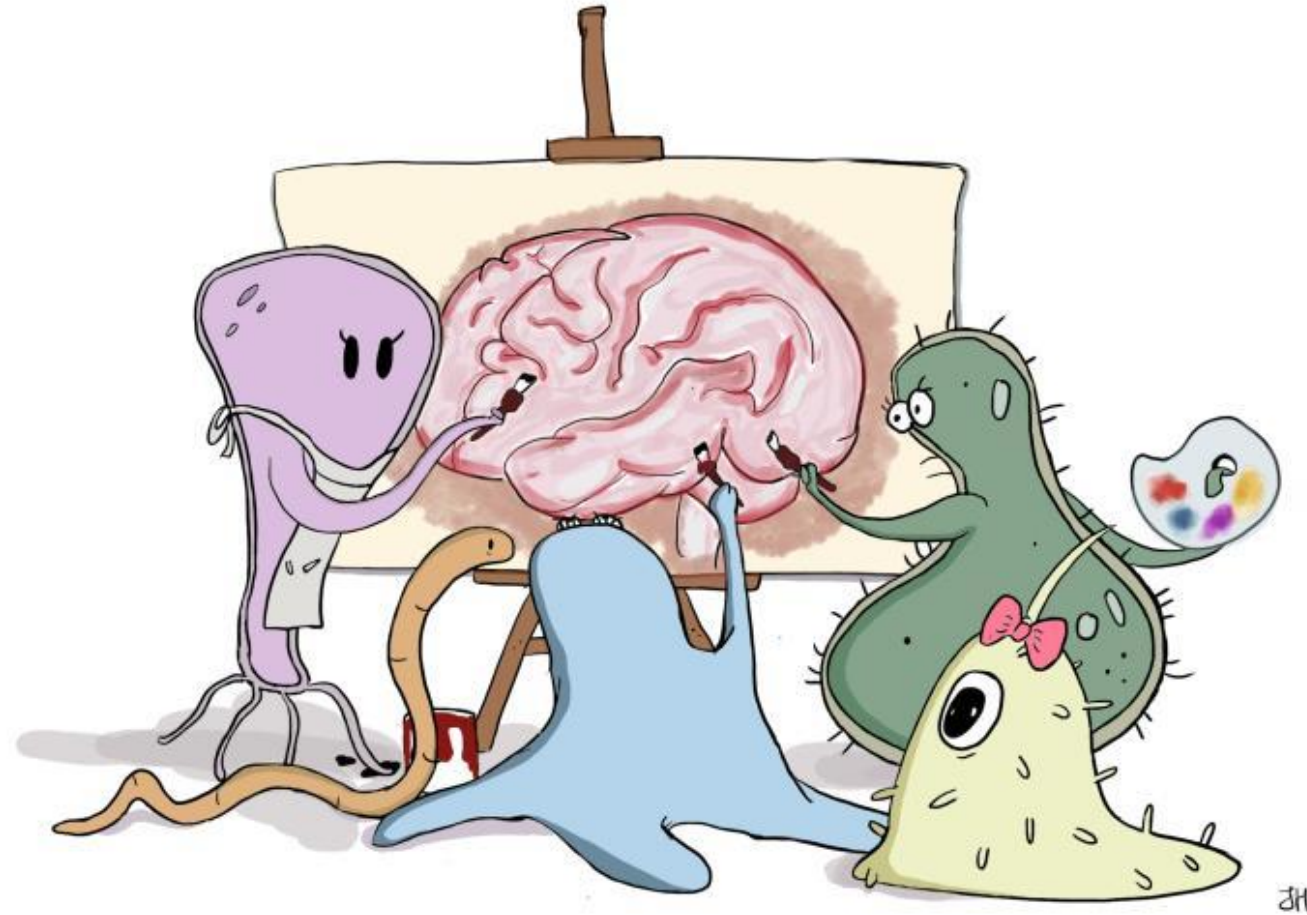


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