

## **Gut microbiome specific changes in different behavioral profiles in a mouse social defeat stress model**

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The gut microbiome has arisen as one important modulator of general health, including brain function. In fact, disturbances in brain health are commonly mirrored in the microbiome, which could be contributing to pathology. One of the most common brain disorders is depression, which is tightly linked to environmental factors such as stress and drives alterations in regular behavior. However, not much is known about the role of the gut microbiome in response to stress and its relationship to behavior.

In this study, the social defeat stress (SDS) paradigm was used as a depressive-like symptoms inducer in 8 w.o. male C57BL/6J mice for 10 days. Mice were segregated in stress resilient and sensitive according to behavior using K-means clustering and behavioral data was interpreted using principal component analysis. Then, the mice microbiome was extracted from fecal pellets after the stress protocol. DNA was extracted and purified followed by 16S (V3-V4) region amplification for sequencing. These data were analyzed to obtain diversity indexes and identify bacterial taxa within samples and groups.

Data revealed that mice responded differently to the same stressor. Half the mice were found to have mild depressive-like symptoms whereas the other half showed profound alterations. Behavioral data was found to be explained in three factors: anhedonia, exploration, and motility. Stressed mice showed overall differences in their microbiome, being less diverse and populations associated with higher inflammation. Moreover, the healthy gut associated *Verrucomicrobiae* class was only identified in stress resilient mice, suggesting a possible relationship with their behavioral phenotype.

Altogether, these results show a different behavioral response to stress in animals that reflects in their microbiome, which could be a key factor in determining stress resilience.

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