PP026

Restoring balance: How ketogenic diet mitigates the long-lasting effect of prenatal stress

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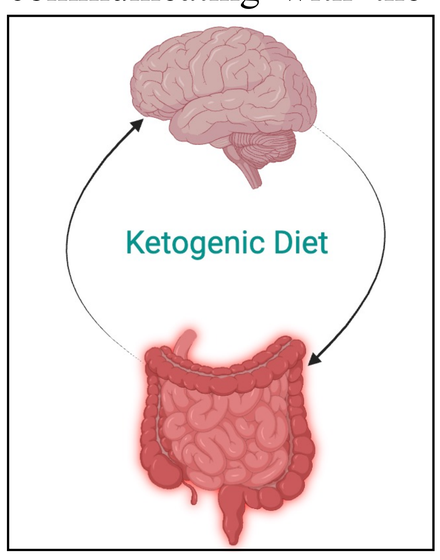
ABSTRACT

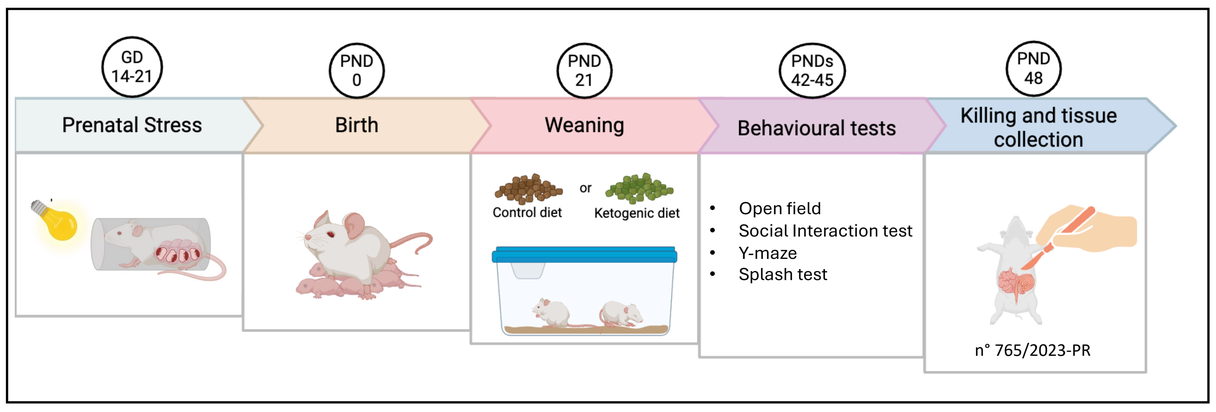
Early-life stress induces various negative outcomes, including increased anxiety-like behaviours, cognitive impairment, and neurodevelopmental dysfunction [1]. These adverse effects are often driven by changes in biological mechanisms, including the hypothalamic-pituitary-adrenal (HPA) axis or inflammatory responses [2]. Emerging research highlights the crucial role of gut microbiota in modulating these stress-related outcomes [3]. Indeed, the intestinal microbial community plays a pivotal role in stimulating the immune system and communicating with the brain, thereby impacting host behaviour.

The ketogenic diet (KD), characterized by high fat and low carbohydrate intake showed promising results in reducing symptoms associated with several psychiatric disorders [4]. However, the biological mechanisms underlying the effect of KD are still unclear. This study investigated the effect of the KD in response to early-life stress by regulating the gut microbiota.

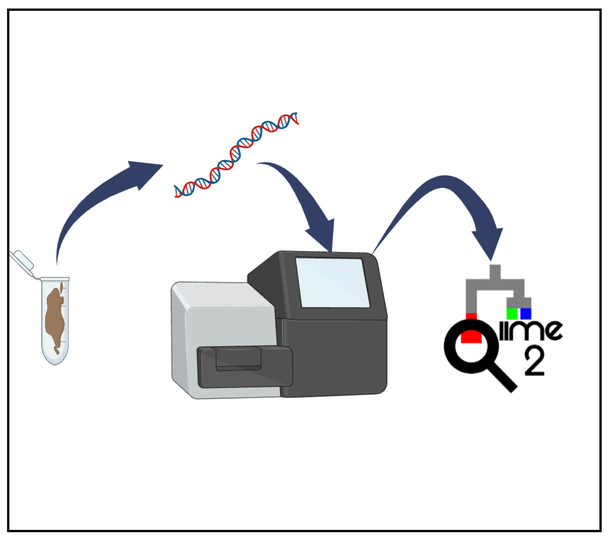


METHODS

Pregnant Sprague-Dawley rats were exposed to a well-established Prenatal Stress Paradigm (PNS) from the gestational day 14 to 21. After weaning (PND 21), control and stress-exposed male offspring were randomly assigned to receive KD or control diet. Animals underwent behavioral assessments during adolescence (PND 40) and were sacrificed at PND 48 where several tissues were collected.

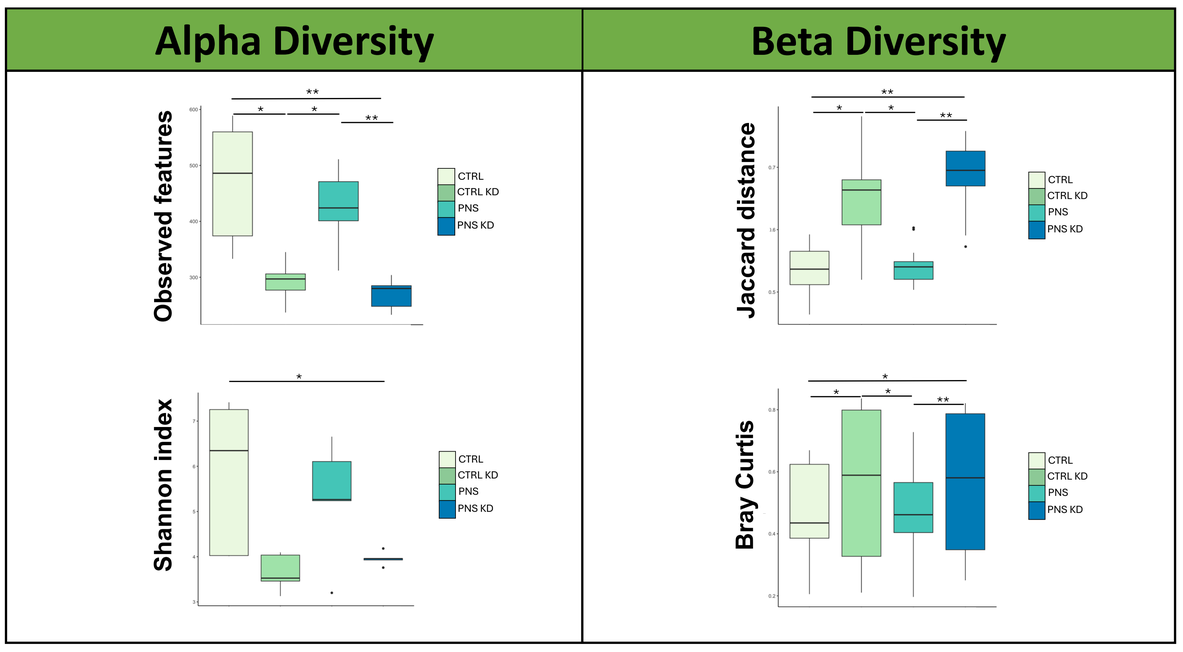


DNA extracted from the cecum microbiota was amplified using primers targeting the V3-V4 region of the bacterial 16S rRNA gene. Raw sequencing data were imported into QIIME2 to analyze the alpha and beta diversity while the assessment of compositional changes of bacteria at the genus level was performed using MaAsLin2.



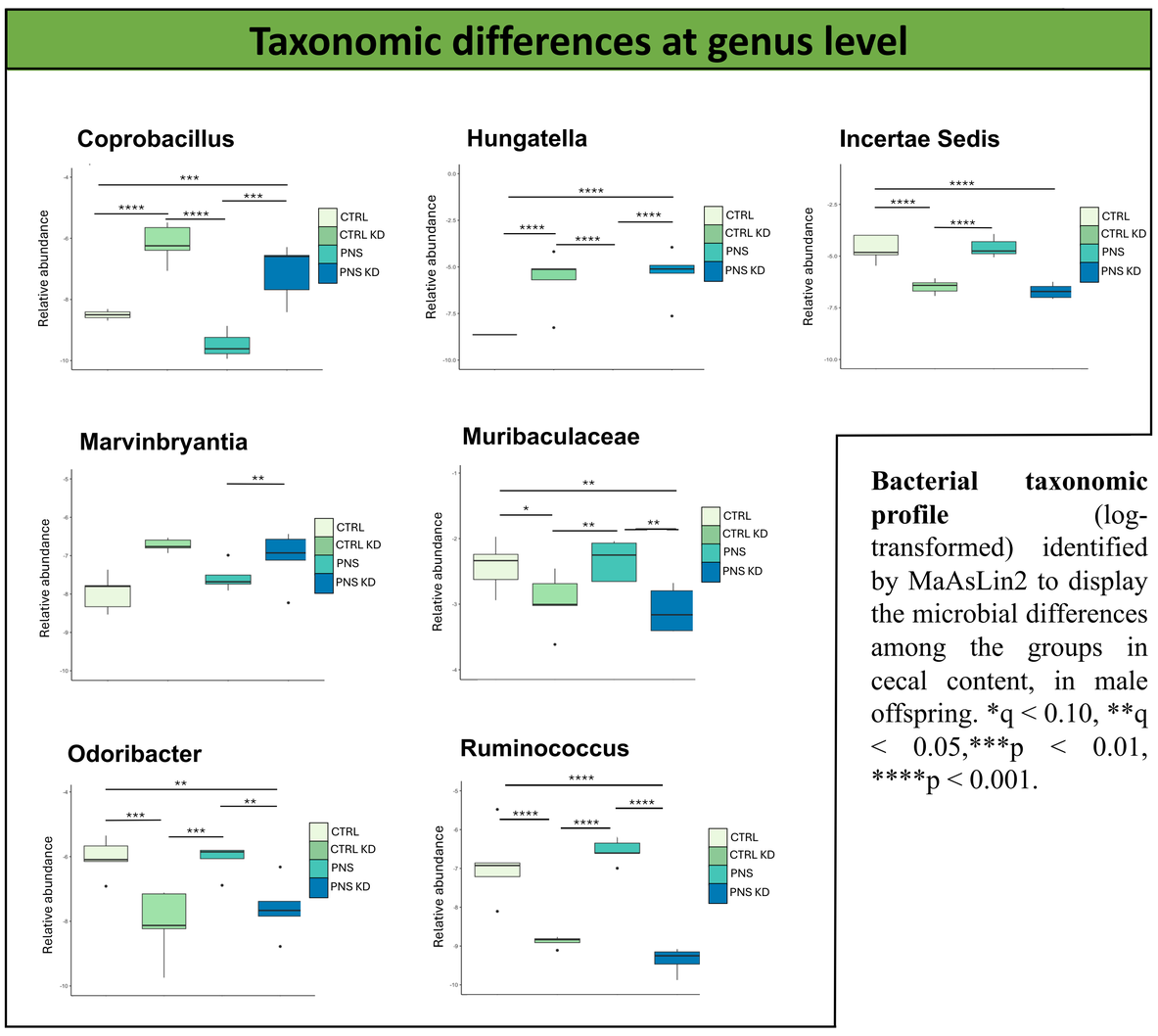
RESULTS

KD reduced alpha diversity (Observed ASVs) in both CTRL and PNS animals ($q \leq 0.024$). The beta diversity, on the other hand, shows an opposite trend.



Analysis of the alpha and beta diversity of the cecal content in male offspring. Boxplot of alpha diversity by Observed features and Shannon, and beta diversity by Jaccard distance and Bray Curtis. *p < 0.05, **p < 0.01.

MaAsLin2 analyses allowed a comparison between PNS and CTRL KD-fed and CTRL animals fed with the control diet, showing that KD increased the relative abundance of different taxa such as *Coprobacillus, Hungatella* and *Marvinbryantia*. In contrast, other taxa including *Incertae Sedis*, *Muribaculaceae*, *Odoribacter* and *Ruminococcus* had been reduced.



Bacterial taxonomic profile (log-transformed) identified by MaAsLin2 to display the microbial differences among the groups in cecal content, in male offspring. *q < 0.10, **q < 0.05,***p < 0.01, ****p < 0.001.

CONCLUSIONS

In conclusion, these results suggest that KD modulate the cecum microbiota composition. These changes are likely to have a positive impact on gut-brain communication, consequently improving mental health outcomes. Future studies that consider behavior and brain areas in the analyses will be needed to uncover the mechanisms underlying these interactions.

References

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