Alteration of gut microbiota and brain parameters after refeeding in an anorexia nervosa rat model

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P 70

BACKGROUND

It is well known that alterations in the gut microbiota are causally involved in a variety of somatic diseases as well as in psychiatric disorders such as depression and anxiety. Current research suggests that gut microbiota dysbiosis is likewise involved in the pathophysiology of anorexia nervosa (AN). AN is an eating disorder that is characterized by reduced energy intake, disturbed body self-perception, fear of gaining weight and hyperactivity. Using the translational activity-based anorexia (ABA) model, we previously showed gut microbiota changes to be associated with brain volume and astrocyte reductions after chronic starvation (Trinh et al., 2021, J Psychiatr Res. 133). In this study, we analyzed the reversibility of these effects after refeeding.

METHODS

18 female Wistar rats were divided into 2 groups: controls (C) with *ad libitum* food access and ABA with limited food access and running-wheel. After habituation, the ABA group underwent an acute starvation (30% of baseline food intake) to reduce body weight by 25%. Subsequently the animals were kept at this low body weight (chronic starvation). Following, a refeeding with *ad libitum* food access was added to the protocol. Fecal samples were collected after habituation, acute and chronic starvation, and refeeding and a 16S rRNA gene amplicon analysis was applied. After finalization, the volume, the number of GFAP$^+$ astrocytes and the mRNA expression of *GFAP* was measured in the cerebral cortex.

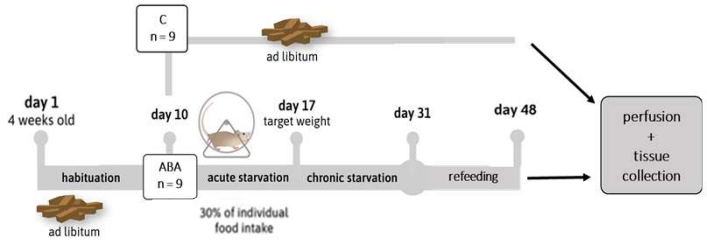

Figure 1: Study design of the activity-based anorexia model.

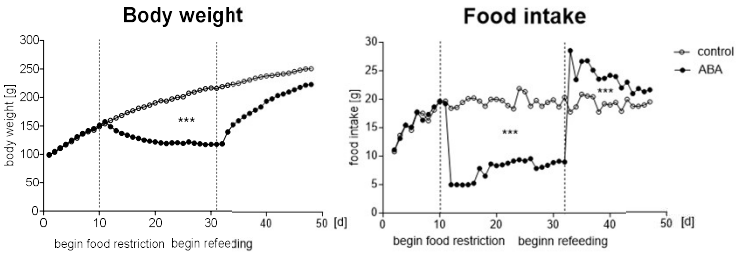

Figure 2: Body weight and food intake profiles. *** p ≤ 0.001

RESULTS

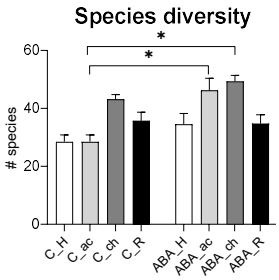

Figure 3: Increased α-diversity (number of species) in ABA rats after acute and chronic starvation and normalization after refeeding.
H habituation, ac acute starvation, ch chronic starvation, R refeeding, * p ≤ 0.05

CONCLUSIONS

The translational ABA animal model is a suitable method to study the gut-brain axis. We again showed significant differences in the gut microbiota composition between ABA rats and controls after acute and chronic starvation. Additionally, we found a reversibility of the microbiota dysbiosis and brain alterations in the cerebral cortex after refeeding. Evidence accumulates that the bacterial composition in the gut could be implicated in the pathophysiology of AN. These findings open a wide range of potential interventions for AN including nutritional therapy, pre- and probiotic supplementation and fecal microbiota transplantation.

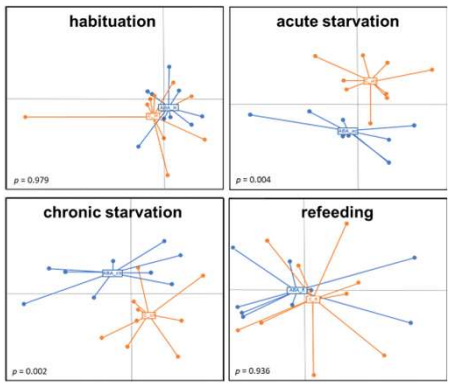

Figure 4: Different β-diversity (species composition) between ABA and controls after acute and chronic starvation; normalization after refeeding.

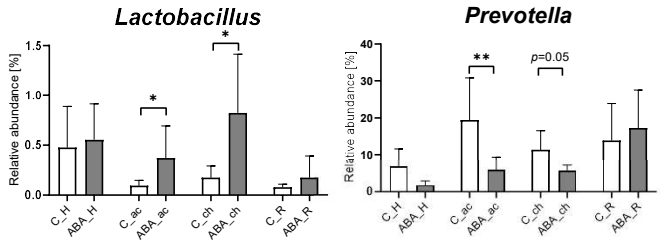

Figure 5: Increase of the genera *Lactobacillus* but decrease of the genus *Prevotella* in ABA rats. H habituation, ac acute starvation, ch chronic starvation, R refeeding, * p ≤ 0.05, ** p ≤ 0.01

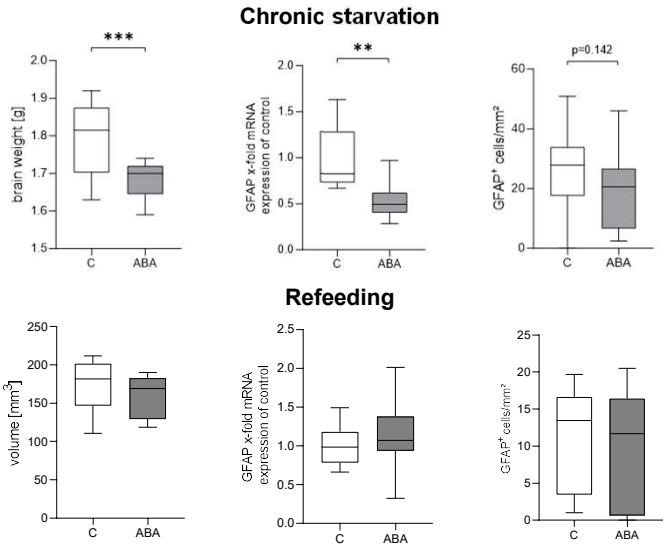

Figure 6: After starvation, decreased volume change, GFAP gene expression and numbers of GFAP$^+$ cells in the cerebral cortex in ABA rats. After refeeding, no differences in these parameters.
** p ≤ 0.01, *** p ≤ 0.001

DISCLOSURE

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