In Male Rats High-Fat Diet, Microbiome-Gut-Brain Axis Signaling, and Anxiety-like Behavior Observed

A recent study published the impact of a high-fat diet (HFD) on gut microbiome diversity and its subsequent effects on the expression of brainstem serotonergic genes associated with anxiety-related symptoms.

Study

The current study hypothesized that HFD modifies gut microbiome diversity and composition, thereby increasing serotonergic gene expression in the cDRD, which triggers anxiety-related defensive behavioral responses in male rodents.

To this end, rodents were subjected to HFD or control diet (CD) for nine weeks, following which their gut microbial composition and diversity were assessed. Additionally, tph2, htr1a, and slc6a4 gene expression in the brainstem raphe nuclei were evaluated, along with the rats' defensive behavioral responses.

Rats were kept under controlled noise (60-80 dB) and temperature (23 ± 1 ºC) conditions with free access to food and water for nine weeks. Fecal pellets were collected for microbial analysis.

At the end of the study, all rats were euthanized using rapid decapitation and brains were analyzed using in situ hybridization histochemistry to measure tph2, htr1a, and slc6a4 mRNA expression, pontomesencephalic reticular formation, median raphe nucleus, and B9 serotonergic cell levels. Adipose tissues were also collected to determine the effects of HFD on adiposity.

Results

As compared to CD, HFD consumption impacted serotonergic gene expression in the pontine raphe nuclei and midbrain, as demonstrated by increased tph2, htr1a, and slc6a4 mRNA expression in subregions of the DR. In previous studies, the increased expression of these genes has been associated with anxiety-like responses in the cDRD or dorsomedial DR. Moreover, increased serotonergic gene expression can lead to serotonergic projections to forebrain anxiety circuits.

These findings strongly suggest that HFD triggers anxiety-like behavioral symptoms in rats. Furthermore, as compared to CD, HFD caused obesity, which was associated with reduced alpha diversity in the gut microbiome.

Although dissimilar gut microbiome composition was observed in HFD-rats relative to CD-rats, significant changes in gut microbial diversity were also observed in CD-rats across life stages. This observation implies the importance of life stages in microbiome community structure.

A relatively lower abundance of Prevotella and Lactobacillus, as well as higher levels of Blautia, were observed in the gut microbiome profile of HFD rats as compared to CD rats. The HFD diet also increased the Firmicutes/Bacteroidetes (F/B) ratio relative to CD, which has been associated with obesity. Furthermore, a positive correlation was observed between the F/B ratio, adipose index, and final weight in HFD rats.

Prevotella is a beneficial bacterium that is present in high concentrations following the consumption of a fiber-rich diet. Previously, a high abundance of Prevotella was negatively correlated with slc6a4 mRNA expression in the cDRD. Therefore, a lower abundance of Prevotella may promote stress-like conditions due to increased slc6a4 mRNA expression.

Conclusion

The current study highlights that nine weeks of exposure to HFD impacted gut microbiome diversity and composition, which influenced serotonergic gene expression in the brain and caused anxiety-like behavioral responses in rats. Taken together, these findings provide new insights into the possibility of developing microbiome-based interventions to prevent stress-related psychiatric disorders like anxiety.

Source:

https://www.news-medical.net/news/20240620/High-fat-diet-triggers-anxiety-in-male-rats-through-gut-brain-axis-disruption.aspx