

ABSTRACT

The purpose of this literature review was to explore the effects of probiotics on the gut microbiota of women diagnosed with anorexia nervosa. Anorexia nervosa is a psychiatric disorder with a high mortality rate and is diagnosed if a patient experiences strong self-restraint to consume foods. The gut microbiota plays a direct role in the patient's ability to gain weight after being altered due to starvation. The gut microbiome consists of varying bacterial strains depending on the type of birth the patient experienced (cesarian or vaginal), types of foods consumed, and stress levels. The gut microbiome can be improved by altering the diet and implementing both pre- and probiotics. Several studies have highlighted that implementing probiotics, specifically liquid probiotics, can aid in the proliferation of beneficial bacteria in the gut lining leading to weight restoration. Continued research is needed to better understand anorexia nervosa as a psychiatric disorder, probiotic implementation as a nutrition therapy option, and probiotic effects for anorexia nervosa.

BACKGROUND

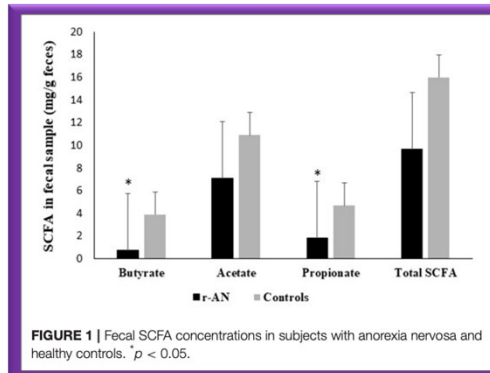
- Anorexia nervosa (AN) incidence rate is 100-200/100,000 females ages 15-19 and has the highest mortality rate of all psychiatric disorders.¹
- Those struggling with AN could have altered hunger cues and exhibit strong self-restraint to consume foods caused by differing factors.² Primarily, this is due to patients' altered self-image and struggle with body dysmorphia.³
- In the body, the gut microbiome's role is to protect the intestinal lining from pathogens and toxic substances that are ingested.² The gut microbiome consists of varying bacterial strains depending on the type of birth the patient experienced (cesarian or vaginal), types of foods consumed, and stress levels.
- The gut microbiome can be improved by altering the diet and implementing both pre- and probiotics. Probiotics are necessary within the diet to "feed" the probiotics and are defined as non-digestible compounds that ferment in the gastrointestinal (GI) tract to aid in proliferation of healthy microbes.⁴ Probiotics help to improve the effectiveness of the probiotics and are found in fruits, vegetables, leeks, whole grains, garlic, etc.⁵

METHODS

- The Tennessee Technological University Volpe Library Database and The Academy of Nutrition and Dietetics were utilized to find articles that were relevant to this review.
- Terms such as "anorexia nervosa and gut health", "effects of probiotics on patients with anorexia nervosa", "probiotic intervention", etc. were searched.
- Articles were selected if written during the years 2011-2021 and peer-reviewed to gather relevant and up-to-date information on the topic.

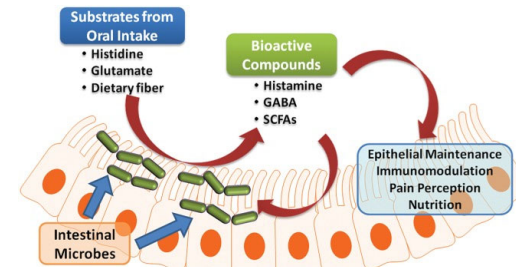
ANOREXIA NERVOSA EVALUATED

- Patients with AN had a higher level of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST), lower food intake, higher levels of depression and anxiety, significantly higher levels of eating disorder psychopathology, and the intestinal microbiota was altered for all bacterial species in patients with AN.³
- The operational taxonomic unit, or OTU, was negatively related to BMI.
- BMI was also found to be negatively correlated with obsessive-compulsive disorder, depression, and anxiety.
- The ClpB in patients with AN and concluded that those with AN had a higher production of ClpB. ClpB, or caseinolytic protease b, interferes with an alpha-melanocyte-stimulating hormone which is responsible for anxiety and satiety signaling.³ Meaning, patients with AN could have altered communication between the gut-brain axis due to the increased ClpB.
- The data showed decreased insulin levels in AN patients and a correlation of the *Roseburia* species and insulin metabolism.³
- Fecal samples were also evaluated to determine SCFA composition using gas chromatography, and differences were recorded using Wilcoxon's rank test. It was found that the observational group had a much lower BMI due to low energy intake and was positively correlated with butyrate and propionic acid.⁷



PROBIOTICS

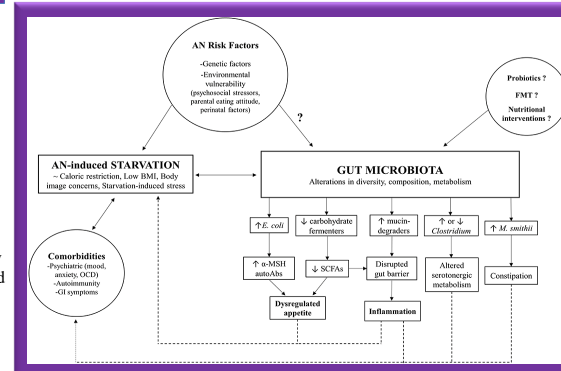
It was recommended that patients consume a liquid probiotic since the liquid probiotics can withstand the low pH of stomach acid. Gaisford highlighted that with a 3-week implementation of probiotics, the gut microbiota was positively altered. In such, the "good" bacteria and butyrate increased.⁸ Gaisford noted in his interview that he believes that if probiotics can reach the action site, participants can see positive results.⁸ Thus, probiotic implementation could increase butyrate in the gut which could aid in decreasing AN symptoms. Specifically, utilizing lactobacilli can help to reduce permeability in the intestine and decrease inflammation.¹ Probiotics are noted to have the ability to improve mental health specifically in those that suffer from anxiety and depression.⁹ A study was conducted that included healthy volunteers that have experienced chronic stress and were given Diazepam, an antidepressant drug, or probiotics. The volunteers that were given probiotics showed improved psychological effects and decreased cortisol levels.⁹ The benefits of probiotic therapy versus traditional prescription therapy are reduced cost, ease of availability, decreased side effects, and improved immune response.⁹



THE GUT LINING

The intestinal lining of patients with AN has been found to contain a high count of mucin-degrading Firmicutes and Verrucomicrobia and a low count of carbohydrate-degrading species Bacteroidetes. Because of the altered bacterial count, there is a higher chance of the intestinal lining's protective layer being digested as it has no protection from the harmful bacteria. Therefore, the intestinal lining has a greater opportunity for bacteria translocation, immune response, and system-wide inflammatory response.³

Alterations in the microbiome can lead to anxiety and/or depression, which are side effects of AN. The microbes within the intestinal lining have been linked to the excretion of dopamine, serotonin, norepinephrine, and Gamma-amino butyric acid (GABA).⁴ Insulin and blood sugar regulation are also influenced by the intestinal microbiome. The hormone, estrogen, is decreased in females with amenorrhea which is a common symptom of AN; in addition, estrogen decreases the bacterial virulence in the intestinal lining. Starvation can increase cortisol, a stress hormone, levels throughout the body; therefore, indicating the microbiome plays a direct role in regulating one's stress responses.³ The bacterial composition in the gut lining determines the energy that is harvested. For example, it is highlighted that patients who were overweight had an altered gut microbiome which caused them to harvest more energy from food. Patients who are critically ill with AN have a lower bacterial count in the gut, or Bacteroidetes, which limits the amount of energy that can be absorbed by the body; however, when the patient increased body weight, the Bacteroidetes increased.³



LIMITATIONS

- Probiotics are not regulated by the FDA (Food and Drug Administration) which allows producers to have increased flexibility when creating products. This has caused the public and health authorities to question the composition of supplements such as probiotics.⁷
- Probiotics have yet to be properly evaluated due to the small-scale clinical trials that have been conducted and show negative effects resulting in a stigma that probiotics are not beneficial.⁷
- AN is also continually researched, but doctors are only beginning to understand the correlation between the intestinal microbial lining and the symptoms of AN.
- The differing categories of AN (restrictive and purging) are new to research as psychologists and physicians are learning the different characteristics of patients with AN.

IMPLICATIONS

- Translocating bacteria across the intestinal wall can aid in stimulating the release of hunger hormones such as ghrelin to increase food consumption to assist in weight gain.¹
- Implementing Lactobacilli can aid in reducing intestinal permeability and inflammation.¹
- Further research is needed to be conducted on probiotics specifically to determine the effectiveness of the supplement.
- Refeeding mechanisms are also needed to be further researched to determine the most efficient way to assist in growing the beneficial bacterial colonies in the gut lining for optimal healing.¹
- It is noted that AN therapy should include pre- and probiotics to increase the bacterial content in the intestinal lining and therefore increase the ability for AN patient to absorb energy from foods to gain weight and aid in decreasing gut permeability, inflammation, and antibody formation.¹
- Quality research is needed to better understand the gut microbiome and which bacterium aid in absorption of energy from food and how the bacteria are altered in healthy patients and in those with AN.

CONCLUSION

Overall, probiotic implementation can be useful to restore the gut microbiome after starvation, and patients should be given foods that are meant to proliferate the bacteria, foods that contain prebiotics. By restoring the bacterial content in the intestinal lining, AN patients can absorb more energy from foods leading to weight gain. In two consecutive studies, it has been found that weight restoration aids in increasing the bacterial diversity in the gut.³ Weight restoration was also shown to increase alpha diversity in patients with AN and thereby decreasing AN symptoms such as anxiety and depression.¹

REFERENCES

1. Saito J, Balthazar M, Schulz N, Demytten A, Baines JF, Herpertz-Dahlmann B. The Impact of Starvation on the Microbiome and Gut-Brain Interaction in Anorexia Nervosa. *Front Endocrinol (Lausanne)*. 2019;10(4):1-8. doi:10.3389/fendo.2019.00044
2. Herpertz-Dahlmann B, Saito J, Baines J. Food matters: How the microbiome and gut-brain interaction might impact the development and course of anorexia nervosa. *Eur J Child Adolesc Psychiatry*. 2017;26(9):1011-1044. doi:10.1007/s10808-017-0284-2
3. Francesca B, Alessandro R, Alberto R, Maria C, Sara B, Stefania G, Simona A, Sotgiu S, Antonio P, Giulio M, Elisa B. Microbiota in anorexia nervosa: The strong between bacterial species, metabolites and psychological traits. *PLoS One*. 2017;12(6):1-11. doi:10.1371/journal.pone.0179739
4. Clapp M, Anorexia N, Herrera L, Blaric M, Wilson E, Wakefield S. Gut microbiota's effect on mental health: The gut-brain axis. *Clin Pract*. 2017;7(9):7131-136. doi:10.4081/CP.2017.987
5. Homanova P, Vavralova J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuroendocrinology. *Ther Adv Gastroenterol*. 2013;6(1):29-51. doi:10.1177/1756285X12459294
6. Klotz C. Probiotics and probiotics: creating a healthier you. <http://www.oxfordjournals.org/abstract/doi/10.1093/oxfordjournals/oxford-journals.nutrition.a0000000>. Accessed September 24, 2023.
7. Chiodonello A, Park H, Bhanji PV. The Gut Microbiome in Anorexia Nervosa: Friend or Foe? *Front Psychiatry*. doi:10.3389/fpsyt.2020.61477
8. Speranza E, Caffè I, Santarpia L, et al. Fecal Short Chain Fatty Acids and Dietary Intake in Italian Women With Restrictive Anorexia Nervosa: A Pilot Study. *Front Nutr*. 2018;5:119. Published 2018 Nov 26. doi:10.3389/fnut.2018.00119
9. Gaisford S. The gut microbiome and the potential of probiotics: an interview with Simon Gaisford. *Future Microbiol*. 2019;14:263-265. doi:10.2217/fmb.2019.0040
10. Clapp M, Anorexia N, Herrera L, Blaric M, Wilson E, Wakefield S. Gut microbiota's effect on mental health: The gut-brain axis. *Clin Pract*. 2017;7(9):7131-136. doi:10.4081/CP.2017.987