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Mini Review

# Fecal Microbiota Transplantation and Anorexia Nervosa

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## Abstract

Anorexia nervosa (AN), a complex and debilitating eating disorder, is characterized by distorted personal body image and fear of gaining weight, accompanied by severe weight loss and high psychiatric comorbidity. It has difficult treatment, since it involves environmental genetic factors and alterations of the microbiome. Metabolo-psychiatric process, which leads to extreme mortality, with approximately half of the patients recovering in the very long term.

For the above reason, we delved into the topic, especially detecting the importance of fecal microbiota transplantation (FMT) in its management.

Most of the articles reviewed lead to improvement, which usually lasts up to 12 months and is directly related to the presence of specific bacterial alterations, such as *Firmicutes*, the main producer of butyrate and consequently generator of short chain fatty acids (AGCC). Likewise, *Lactobacillus* spp. (Homeostasis Rehabilitator). *Akkermansia muciniphila* (Uses mucins as an energy source). *Methanobrevibacter smithii* (Fermentation of polysaccharides that eliminates excess hydrogen from bacteria) and others, which, being detected decreased prior to FMT, increase after the procedure and, although briefly, lead to clinical improvement.

Due to this knowledge, I raise the question that in order to maintain the corrections given by the increase in beneficial microorganisms, FMT must be received again at least a year after the first, or once the symptoms begin to subside decline, and as a complement use biotics, paraprobiotics, postbiotics or bacteriophages.

Finally, it is necessary to consider bacterial metabolites (MB), since they are a primary factor in human health, through the development and strengthening of the intestinal immune barrier.

***Keywords:*** *Anorexia Nervosa (AN); Fecal Microbiota Transplantation (FMT); Short Chain Fatty Acids (SCFA); Bacterial Metabolites (BM); Probiotics, Prebiotics and Symbiotics (BIOT)*

## Introduction

Anorexia nervosa (AN), an eating disorder with extreme weight loss, due to fear of gaining weight, with added somatic disorders and a mortality rate of 5.86 [1]. Low weight is usually resistant despite high-calorie diets. Even though good results have been observed with

FMT from obese patients with AN. It has been a topic of constant discussion, once proteomic and metagenomics sequencing studies have been modernized and routinized [2].

de Clercq NC and his group [3] report weight gain through FMT, because the intestinal microbiome has been determined to regulate body weight. And although it is only one case, we must turn our eyes towards it.

There are studies in progress that have visualized the need for several FMTs, and carry out 4 procedures, one per week, with follow-up at 2 and 6 months [4].

AN is one of the psychiatric conditions with the highest mortality rate, and only half of patients experience long-term recovery [5].

Over the last decade, advances in metagenomic and proteomics sequencing technologies have allowed us to deeply interrogate the composition and function of these microbial communities, including the regulation of appetite and weight [6], as well as their comorbid symptoms, such as mood alteration [7] and gastrointestinal symptomatology [8], through various immune, neuroendocrine and metabolic pathways [9]. In addition to the aforementioned physical problems, other important complications include anxiety and co-morbid depressive disorders [10]. A well-known study, "The Minnesota Famine Experiment" [11], which was carried out during World War II, clearly showed that famine significantly affected both physical and psychological conditions.

## BALB/c mice

BALB/c germ-free (GF) mice were originally obtained from the Central Institute for Experimental Animals (Kawasaki, Japan) [12]. These mice had been raised for more than 10 generations in isolators without bacterial contamination in the laboratory. To guide the AN process, pairs of male and female GF mice were selected as grandparents of experimental mice, and their first offspring were used as parents of gnotobiotic mice. Parental mice were orally administered "fresh" feces [13].

## Dysbiosis

## Alteration in bacterial metabolites

## Intestinal permeability and immunological mechanisms

The *Bacteroidetes* phylum is decreased in patients with AN. Likewise, intestinal dysbiosis (ID) has been demonstrated in patients with AN [14]. Although precise characterization of the IM was not the focus of this study, gut microbes in AN patients were different based on 16S rRNA gene pyrosequencing of fecal samples. Another study that demonstrates that ID is a determining factor in AN is that of Morita C and her group [15]. Those who determine that although the pathophysiological mechanism of AN is not clear, it can be determined that there is an intestinal microbial imbalance, that is, ID. They point out the above, finding a minimum amount of total bacteria, as well as obligate anaerobes. Sudo N [16] points out that the gut microbiota is a significant participant in neuropsychiatric disorders, including AN.

**Alteration in bacterial metabolites:** There are articles that highlight the role of genetics in AN, as well as the complexity of IM [17]. Highlighting dysbiosis due to the incidence of energy and nutrients, as well as the functional and metabolic disorders of the intestinal microbiome itself. Bacterial metabolites (BM) play a predominant role in the development of the disease.

Patient with small intestine bacterial overgrowth (SIBO), and AN, very common, combined processes - was administered several FMTs, resulting in improvement; In them, the various markers were determined, highlighting short-chain fatty acids (SCFAs), which are an important source of energy for the epithelial cells of the intestine [18].

There are numerous studies that link the alteration of IM with AN. Like Reed K, and her group [19], who point out that IM is linked to their psychopathology and nutrition; Therefore, they suggest therapies based on intestinal microbioma.

**Intestinal permeability and immunological mechanisms:** The immunological role in AN has been underestimated, even though the presence of pro-inflammatory cytokines, increased oxidative stress, changes in IM and the pathological microenvironment of the bone marrow have been determined in the disease [20]. Regarding Intestinal permeability, little has been noted about its incidence in AN [21]. However, in the intestine there is deregulation of the immune response, which translates immunoglobulins against appetite-regulating peptides. On the other hand, the involvement of the intestinal barrier is not fully elucidated, even though if it is involved, it is a possible therapeutic source [22].

## Comments

Although IM research in AN is still in its infancy, evidence supports the key role of ID, marked by perturbations in diversity and taxonomic composition, in both the somatic and psychological manifestations of this complex multifactorial disorder.

What we cannot ignore is the constant bi-directional communication between the intestine and the brain, through the gut-microbiota-brain axis [23], and its metabolic production. However, it is unclear whether the microbial changes observed in patients with AN are a non-specific consequence of chronic caloric restriction or a causal factor [24]. The definition of AN as a psychiatric condition is increasingly questioned, since the number of articles that highlight IM is overwhelming [25]. And therefore, every day the possibility that IM contributes to the behavioral and central phenotype of AN is raised [26]. Although there are detractors who comment that a greater understanding of how biological mechanisms act in AN is required [27].

## Responses to treatment

Treatment of the patient with AN, led to improvement of intestinal barrier function, which was impaired before FMT [28]. It has been determined that the richness of bacterial species, as well as their uniformity, increases in patients with psychological deterioration, with FMT, decreasing fungal alpha diversity [29]. The levels of SCFAs gradually increased after FMT, in patients with psychiatric processes [30]. Among them, acetate, propionate, butyrate stand out, used by colonocytes.

Another finding in AN, is that the *Firmicutes* were decreased before FMT [31]. Let us remember that *Firmicutes* are the main producers of Butyrate, which decrease 12 months after transplantation.

Some other facts that occur are that *Lactobacillus* spp, which is rehabilitative of homeostasis and decreased before transplantation, also increases, strengthening the process [32]. *Bacteroides* spp varies and the highest number is observed 30 days after FMT [33]. Fan Y, and his group, conclude the following:

- "Our "omic" and mechanistic studies imply that a disruptive gut microbiome may contribute to the pathogenesis of AN" [34].
- There are other investigations, in which it is determined that the alteration of IM causes alteration of the intestinal barrier, increasing permeability [35].

## Conclusion

- The intestinal microbiota affects the genesis of anorexia nervosa.
- Intestinal dysbiosis may contribute to the specific features of AN, including decreased body weight and mental disorders [36].
- Good results have been observed with FMT in obese patients.
- Since the intestinal microbiome has been determined to regulate body weight, FMT is an option in AN, carriers.
- Multiple transplants of fecal microbiota usually give good results.
- Intestinal permeability is affected in patients with AN.
- SCFAs, which are decreased in AN, increase with TMF.

## Conflicts of Interest

The authors declare that do not have affiliation or participation in organizations with financial interests.

## Ethical Approval

This report does not contain any study with human or animal subjects carried out by the authors.

## Informed Consent

The authors obtained informed written consent from the patients, in order to develop this article.

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