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Letter to the Editor

Resetting the gut-brain axis in AN: the promise and pitfalls of FMT

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Dear Editor,

Anorexia nervosa (AN) is an eating disorder characterized by persistent dietary restriction and an intense fear of weight gain despite maintaining low body weight. It remains one of the most lethal psychiatric disorders, yet therapeutic advancements continue to lag behind its clinical burden. With its onset in the early teen years, AN affects up to 4% of adolescent girls[1] and disproportionately affects young women, with 90% of sufferers being female.[2] Currently, the bidirectional link between the gastrointestinal tract and the central nervous system, known as the "microbiota-gut-brain axis," has attracted increased research interest in metabolic and psychiatric diseases such as AN.

Complex microbial communities can be found in the human digestive tract, and the gut microbiota (GM) plays an important role in host metabolism. Growing evidence shows that in the active phase of illness, individuals with AN have a dysbiotic GM, with lower microbial diversity and reduced stool levels of serotonin, GABA, dopamine, butyrate, and acetate compared to healthy controls (HCs).[3] The process of communication between the gut and brain takes place via neural, endocrine, and immune systems.[4] Microbial metabolites have an effect on gut-brain communication through activation of vagal afferent signaling and on secretion of appetite-regulating hormones like glucagon-like peptide-1 (GLP-1).[4]

Fecal microbiota transplantation (FMT) is a promising new procedure that involves the transfer of GM from a healthy donor to a recipient to restore microbial balance and improve health outcomes. FMT is a standard procedure used to treat recurrent C. difficile infections. Microbial diversity and production of microbial metabolites are restored with FMT, potentially normalizing the communication between the gut and the brain, leading to better gastrointestinal homeostasis and the alleviation of symptoms, including constipation, but the role of FMT in the regulation of appetite is still being investigated. FMT has shown promising findings in adult case reports of AN, with improvements in gut microbial diversity, gut barrier function and participants experiencing weight gain despite no reported increase in caloric intake.[5]

Despite increasing interest in FMT in AN, current evidence is still limited and unclear. Most available data comes from animal studies and small pilot human studies, while randomized controlled trials are still lacking. Existing research is also limited by the lack of standardized protocols for donor selection, route of administration, and the frequency of treatment, resulting in reduced reproducibility across studies.[6]

FMT in AN also brings up important ethical and safety concerns, especially because adolescents and young adults represent a vulnerable patient population. Obtaining informed consent can be difficult in severely malnourished individuals with impaired cognitive and psychological functioning. Additionally, the long-term neurodevelopmental, metabolic, and psychiatric consequences of altering the gut microbiome are not understood properly.

Although there is increased evidence that the gut microbiome plays a role in AN, there are key knowledge gaps, such as whether the timing of onset affects the relationship between genetic susceptibility, diet and gut microbiome. Future work should therefore extend beyond the observational studies towards understanding how certain microbial taxa interact with the host in order to develop microbiome-based interventions (e.g., probiotics, and FMT) as adjuncts to standard therapy.

ETHICAL DECLARATIONS

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