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Impact of gut microbiota on severity of obsessive-compulsive disorder (OCD) - a short review

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Abstract

Introduction and purpose
Obsessive-compulsive disorder (OCD) has an unclear etiology. Genetic and environmental factors dominate among the etiologic factors. The disorder is characterized by the presence of obsessions (repetitive and persistent thoughts, images, impulses or urges) and compulsions (rituals; repetitive behaviours or mental acts that the individual feels driven to perform in response to an obsession). This disorder has less than 4% of the population. Treatment is a long and difficult process, and the best results are with SSRIs (e.g., fluoxetine) and cognitive behavioral therapy (CBT). The aim of the study was to review articles linking gut microbiota and obsessive-compulsive disorder issues.

A brief description of the state of knowledge

The gut microbiota-gut-brain axis perhaps has an impact on the etiology of psychiatric diseases. Its existence has been well researched in animals. Researches suggest that there possibly may be changes in the composition of the gut microbiota in people with obsessive-compulsive disorder. Quantitative and qualitative changes in the gut microbiota composition may worsen the patient's condition. The use of probiotics may help improve the patient's condition and reduce symptoms of the disorder.

Summary (conclusions)
More research is needed to explore the potential impact of the gut microbiota on obsessive-compulsive disorder. This could perhaps lead to future applications of probiotics, e.g., in the adjunctive treatment of obsessive-compulsive disorder.

1. Introduction and purpose

Obsessive-compulsive disorder (OCD) is a disorder affecting less than 4% of the population [1-3]. The etiology is unclear. The most important etiologic factors are genetic and environmental. Abnormalities of the gut microbiome and dysfunction of the gut-brain axis have been discussed among etiologic factors for some time [1].
ICD-11 diagnostic criteria [3,4]:

- "Presence of obsessions and/or compulsions.
    - Obsessions are repetitive and persistent thoughts (e.g., of contamination), images (e.g., of violent scenes), or impulses/urges (e.g., to stab someone) that are experienced as intrusive, unwanted, and are commonly associated with anxiety. The individual attempts to ignore or suppress obsessions or to neutralize them by performing compulsions.
    - Compulsions (or rituals) are repetitive behaviours (e.g., washing, checking) or mental acts (e.g., repeating words silently) that the individual feels driven to perform in response to an obsession, according to rigid rules, or to achieve a sense of "completeness".
- Obsessions and compulsions must be time-consuming (e.g., take more than 1 hour per day) to warrant the diagnosis. •The symptoms result in significant distress or significant impairment in personal, family, social, educational, occupational, or other important areas of functioning".

Systematic review by A. G. Guzick showed that in the early phases of the COVID-19 pandemic, OCD symptoms intensified. The effect was especially visible in patients with symptoms of SARS-COV-2 infection [5].
Among the established and most effective methods of treatment are SSRI (Selective Serotonin Reuptake Inhibitor) class drugs and cognitive-behavioral therapy (CBT) [6-8]. The combination of both methods of treatment is more effective than monotherapy [6,7]. Clomipramine is no more effective than SSRIs [6]. Research is appearing that not only CBT has a positive effect on treatment, but also behavioral therapy, exposure and response prevention (ERP) and EMDR (Eye Movement Desensitisation and Reprocessing) [8,9].

Drug-resistant OCD is treated additionally with antipsychotic or glutamatergic agents, e.g., risperidone, lamotrigine, aripiprazole, among others, which improve the effect of SSRIs [10].

2. Description of the state of knowledge

The gut microbiota consists of trilions microorganisms. It is involved in metabolism. The gut microbiota-gut-brain axis is a relatively new issue and there are little high-quality studies, e.g. randomized control trials on a large group of patients, studying this issue in depth. Review papers are available including its impact on the development of neurological or psychiatric diseases. Research in animals confirms its existence and the dual directionality of this pathway. However, there is a lack of human clinical studies to definitively determine whether there is a link between disturbances in the gut microbiota and the development of OCD or other psychiatric diseases. The fact that serotonin is present as a transmitter in the gastrointestinal tract and brain is one of the grounds for studying this issue [11-17].

J. Turna et al. analyzed the gut microbiome profiles in stool samples from 43 patients. The patients were divided into two groups: 1) 21 patients with OCD currently unmedicated, 2) 22 control group - non-psychiatric patients. The impact of factors that may affect the presented gut microbiome profile were excluded. Dietary differences were corrected using the EPIC Norfolk FFQ, as diet influences the presented gut microbiome profile. The OCD patient group had lower species richness α-diversity and lower relative abundance of the three butyrate-producing genera than the control group [18].

The results of a study conducted by L. Domènech et al. were published in 2022, in which stool samples from 64 patients were examined. That was 32 patients in the OCD group and 32 patients in the control group, matched for age and gender. The OCD patients' stool samples had lower bacterial α-diversity. The researchers also found an imbalance in the gut and oropharyngeal microbiome of OCD patients. No significant changes were observed in the Bacteroidetes to Firmicutes ratio [19].

Fecal microbiota transplantation (FMT) was performed in 10 patients with IBD. A significant decrease in BDI, SCL-90-R and MOCI was observed 1 month after the procedure compared to pre-treatment values, and the severity of anxiety, depression and obsessions decreased. The authors conclude that the reduction in psychiatric symptoms may be a primary effect - the neuropsychiatric effect of FMT, or a secondary effect resulting from improvement in gastrointestinal symptoms [20].

P. A. Kantak et al. performed an experiment on house mice with induced OCD-like behavior. They observed that the administration of Lactobacillus rhamnosus blocked the induction of OCD-like behavior just like the administration of fluoxetine [21].

A case report by V. Kobliner et al. reports that administration of Saccharomyces boulardii to a 16-year-old boy reduced symptoms of OCD and self-injurious behavior [22]. Furthermore, D. Tao et al. found that S. boulardii can increase gut microbiota diversity and reduce depressive symptoms through the gut-brain axis pathway [23].

N. S. Sanikhani conducted an experiment on Wistar rats with induced OCD-like symptoms. A reduction in symptoms was observed in groups of rats given Lactobacillus casei Shirota, fluoxetine or a combination of both. The beneficial effects of L. casei were likely due to modulation of serotonin-related gene expression [24].

C. D'Addario tested DNA methylation levels in the blood and saliva of 115 patients. A group of 64 OCD patients and a control group of 51 age- and gender-matched patients.
In the OCD patients, the DNA methylation level of the oxytocin receptor gene was lower than in the control group, and the level of gene expression was reduced. Actinobacteria abundance was also found to be higher in OCD and a correlation with epigenetic changes in the oxytocin receptor gene was found [25]
The study conducted by T. K. Murphy involved 31 young patients (4–14 years old). They were divided into two groups: 1) 17 patients received azithromycin and probiotic, 2) 14 patients received only probiotic. Patients who received azithromycin reported a significant reduction in the intensity of OCD on the CGI-S OCD scale [26].

3. Summary

Animal testing confirms the existence of the gut microbiota-gut-brain axis and its potential role in the pathogenesis of psychiatric disorders. Human studies are sparse, including on changes in the gut microbiota of OCD patients. Single studies involving the use of probiotics or FMT appear promising. However, further studies on large groups of patients are necessary for a definitive conclusion. This could possibly lead to the use of probiotics in the adjunctive treatment of OCD patients.

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