The Gut Microbiome in First-Episode Psychosis

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• The human commensal microbiota plays important roles in physiology, nutrition, and immune function[1]

• The gut-brain axis appears to be a bidirectional means of communication involving neuronal, hormonal, and immunological pathways, and gut microbiota may modulate behavior

• There is increasing evidence that gastrointestinal inflammation may play a role in the pathophysiology of psychotic disorders[2]
• Schwarz and colleagues[3] investigated the composition of the fecal microbiota in patients with first-episode psychosis (FEP) and healthy controls

• They also explored whether fecal compositional differences were associated with symptom severity and remission after 2 months and 1 year of treatment for FEP
The authors recruited patients age 18 to 40 with FEP from the catchment area of the Helsinki University Hospital, Finland. They included subjects with all primary psychotic disorders but excluded subjects with substance-induced psychosis and psychosis secondary to general medical condition.

Patients with FEP had a score of 4 or greater on the delusions (unusual thought content) or hallucinations item of the Brief Psychiatric Rating Scale—Extended (BPRS-E). Controls were matched by age, sex, and region of residence.
Patients with FEP were assessed at baseline clinical contact, and after 2 and 12 months of treatment; controls were assessed only at baseline.

Fecal samples were analyzed at baseline only.

Food habits, physical activity, and blood metabolic parameters were also assessed.
Fecal DNA was extracted from samples, and fecal bacterial numbers were analyzed for 7 different bacterial groups using qPCR analyses, which is based on 16S ribosomal RNA copy numbers.

Genetic analyses of fecal DNA (metagenomics) were also performed.

Metagenomics data were analyzed using the linear discriminant analysis effect size method, which is a combined assessment of statistical significance and biological relevance.
28 Subjects with FEP and 16 controls were included in the study. Patients with FEP and controls were well matched regarding age, sex, BMI, and markers of glucose and lipid metabolism.

Half of the patients received a diagnosis of schizophrenia at the 1-year follow-up.

The median duration of antipsychotic treatment at baseline was 20 days.
There were no significant differences in the numbers of bacteria within the 7 analyzed groups between patients with FEP and controls.

In subjects with FEP, bacterial numbers for Lachnospiraceae, *Bacteroides* spp, and *Lactobacillus* group were significantly positively correlated with total psychopathology.

Higher bacterial numbers were most strongly correlated with greater negative symptoms and poorer functioning.

Duration of antipsychotic treatment was not correlated with bacterial numbers.
Metagenomic analyses identified 5 significant differences at the family level: Lactobacillaceae, Halothiobacillaceae, Brucellaceae, and Micrococcineae were increased, and Veillonellaceae were decreased in patients with FEP versus controls.

Given the effects of physical activity on microbiota composition, Lactobacillaceae remained increased and Veillonellaceae decreased in physically active patients with FEP versus controls.
12-Month follow-up data were available for 19 of 28 patients with FEP. Patients with microbiota that clustered with (ie, were similar to) controls had a significantly higher remission rate than patients with “abnormal” microbiota composition (70% versus 28%).

This association was not confounded by higher baseline illness severity, physical activity, BMI, diagnosis, food habits, or duration of antipsychotic treatment.
Discussion

• The authors conclude that findings of this small, preliminary study support the involvement of microbiota alterations in psychotic illness.
• Associations between microbiota composition and outcome raise the possibility that modulation of the fecal microbiome might influence treatment response and remission.
• Replication of these findings in larger samples is warranted.


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Dr. Miller is Associate Professor in the Department of Psychiatry and Health Behavior at Augusta University in Augusta, GA, and Schizophrenia Section Editor for *Psychiatric Times*. He reports no conflicts of interest concerning the subject matter of this article.