The gut microbiome is altered in schizophrenia and related psychotic illness, but the relationship is complex, as gut microbiome is influenced by diet, exercise, sedentary lifestyle, and antipsychotic (AP) use.1 Also, gut microbes can produce metabolites that can reach the brain and cause neuroinflammation, a possible precursor to psychosis.2 Despite previous studies indicating the microbiome-altering properties of antipsychotics, previous research in SCZ and gut microbiome has been conducted in patients stabilized APs, leading to warranted criticism that studies exploring SCZ-related changes in gut microbiome are largely due to the confounding influence of APs.

In light of this, we present a review of recent literature regarding the relationship of gut microbiota in first episode psychosis in schizophrenia-spectrum disorders compared to healthy controls. We aim to understand if psychotic illness is associated with gut microbiome changes independent of AP use so that the gut microbiome may be explored as a target for future intervention in psychotic illness. Terms: alpha-diversity: within-group diversity; beta-diversity: between-group diversity.

We conducted a literature review using specific key words including schizophrenia, first episode psychosis, microbiome, and dysbiosis to identify controlled studies published on PubMed between 2016-2022. We focused on human studies investigating the relationship of gut microbiota in first episode psychosis in schizophrenia-spectrum disorders compared to healthy controls. Titles and abstracts were screened from PubMed search, relevant full-text articles were assessed for eligibility, and 4 articles met the full criteria.

Table 1: Results of Search

<table>
<thead>
<tr>
<th>Study Design, N</th>
<th>Diversity Findings</th>
<th>Main Findings for Gut Microbiome in FEP</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-control with 1 year prospective cohort -FEP, average AP usage 20 days (N=28) -HC (N=16)</td>
<td>None reported</td>
<td>FEP: increased Lactobacillus Abnormal gut microbiome cluster correlated to decreased remission rates at 12 mo follow-up, controlling for variables like symptom severity, antipsychotic usage.</td>
<td>Schwartz et al., 2018*</td>
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<tr>
<td>Case-control with FEP plus receiving 24 week risperidone treatment and follow-up -FEP, AP-naive (N=41) -HC (N=41)</td>
<td>None reported</td>
<td>FEP: decreased Bifidobacteriaceae, Excherichia coli; Lactobacillus; increased Clostridiom coccoides. FEP before v. after 24-week risperidone treatment: increase in the numbers of fecal Bifidobacteriaceae spp. and E. coli; decrease in Clostridiom coccoides and Lactobacillus. Changes correlated to increased in weight.</td>
<td>Yuan et al, 2018*</td>
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<tr>
<td>Cross-sectional case-control -FEP, AP-naive (N=43) -Chronic SCZ, AP-treated (N=85) -HC (N=85)</td>
<td>Alpha: lower in chronic, AP-treated SCZ v. HC, no difference found between FEP v. HC. Beta: no difference with weighted UniFrac; unweighted showed difference between 3 groups.</td>
<td>-Both SCZ groups (v. HC): increased Christensenellaceae, Enterobacteriaceae. Decreased Pasteurellaceae, Turicibacteraceae. -Chronic SCZ (v. both HC and FEP): increased Enterococcaceae, Lactobacillaceae, Shigellaceae, Streptococcaceae. Veillonellaceae (increased compared to HC, decreased compared to FEP). -Enterococcaceae, Lactobacillaceae, -FEP SCZ (v. both HC and chronic SCZ): Decreased Fusobacteriaceae, Megasphaeraceae, Peptostreptococcaceae, Veillonellaceae. -Right Middle Frontal Gyrus (MFG) volume associated with increased Actinobacteria, Veillonellaceae in FEP SCZ. No association found between microbes and MFGV volumes.</td>
<td>Ma et al, 2020*</td>
</tr>
<tr>
<td>Cross-sectional FEP, AP-naive (N=43), Remission, AP-treated (N=40) HC (N=44)</td>
<td>Alpha: not different between groups Beta: FEP group distinct from HC and chronic groups.</td>
<td>-FEP (v. HC and/or remission): increased Fusobacteriaceae, Actinomyces, Peptostreptococcaceae and Chlamydobacteriaceae -v. HC (v. FEP and/or remission): increased Lachnospira and Coproclostrum.</td>
<td>Zhu et al, 2021*</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Our review shows that psychotic illness is likely associated with altered gut microbiome independent of AP use, but that AP use also influences gut microbiome. This provides preliminary evidence that the gut microbiome may be a useful target for intervention in SCZ. Further studies, especially with temporal components and larger sample sizes, are required.

REFERENCES


4 studies met criteria, shown in Table 1. All studies used 16S RNA sequencing to analyze the bacteria in fecal samples, as a representation of gut microbiome.

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GUT MICROBIOME DYSBIOSIS IN FIRST EPISODE PSYCHOSIS: A REVIEW OF RECENT LITERATURE

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