

Children's Mental Health and the Gut Microbiome

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Abstract

Scientific and public interest in the relationship between the gut microbiota and the brain has grown as a result of its potential to explain psychiatric risk. While several mental health issues have been linked to variations in gut microbiome composition, the majority of the evidence for this association has come from small-scale human research and animal models. In this cross-sectional investigation, we examined the relationships between the gut microbiota and 1,784 ten-year-old children from the multi-ethnic, population-based Generation R Study. Stool samples were used to analyse the gut microbiota using 16S rRNA sequencing. The maternally evaluated Child Behavior Checklist was used to measure general mental symptoms as well as particular categories of emotional and behavioural issues. Although there was a correlation between greater overall and particular mental health disorders and reduced gut microbiome diversity, the link was not statistically significant. After multiple testing corrections, we also failed to detect any taxonomic characteristic linked to mental health issues, despite intriguing results showing the disappearance of taxa like *Hungatella anaerotruncus*, and *Oscillospiraceae* that have previously been linked to psychiatric diseases. All mental health issues had the same compositional abundance differences that had been established. Last but not least, we did not discover any appreciable enrichment for certain microbial activities in connection to mental health issues. Based on the biggest sample analysed to date, we draw the conclusion that there is no conclusive evidence between the diversity, taxonomy, or functions of the gut microbiome with mental health issues in the general pediatric population. To determine whether and when relationships between the gut microbiota and mental health arise throughout development and into adulthood, longitudinal designs with repeated assessments of microbiome and psychiatric outcomes will be essential in the future.

Keywords: Microbiome; Child Mental Health; Gut-Brain-Axis; Epidemiology; Psychiatry

Introduction

As knowledge of the crucial role microbiome may play in mediating communication between the stomach and the brain (the so-called "gut-brain" axis) has grown, so has interest in the association between the gut microbiota and mental health. The brain is influenced by the gut microbiota in a variety of ways, including as vagus nerve stimulation, immune system activation, the manufacture of neurotransmitters like serotonin, and the generation of neuroactive metabolites like short-chain fatty acids. Furthermore, it has been demonstrated that a number of environmental variables, such as stress exposure, drugs, and food, that affect the brain and psychiatric risk also affect the gut microbiota. As a result, the gut microbiome has become an intriguing candidate for a mechanism driving variations in brain function, behaviour, and risk for developing mental illnesses [1].

The majority of research on the gut-brain axis to date has been based on studies done on animals. These studies have shown the significance of gut bacteria for neurodevelopment and behaviour, including learning and memory, social interactions, stress response, and behaviours resembling anxiety and depression. Fecal microbial transplantation studies, which show that translocation of fecal bacteria from human donors with a psychiatric disorder (e.g., depression, anxiety, or schizophrenia) associate with reduced microbial diversity and increased psychiatric symptoms in animals, have further supported a causal effect of the microbiome on the brain. The human literature is somewhat limited and consists virtually exclusively of clinical investigations. These have mainly concentrated on major depressive disorder in adulthood, with the first large-scale, population-based studies reporting robust and independently replicated associations with lower abundance of *Prevotellaceae*, *Coprococcus* and *Faecalibacterium*. These have also implicated lower abundances of *Enterococcus*, *Escherichia coli*, *Bacteroides*, and *Bifidobacterium* in patients compared to healthy controls for autism spectrum disorder. Preliminary research

reveals a reduced abundance of particular taxa in relation to diseases such attention-deficit hyperactivity disorder, schizophrenia, and generalized anxiety disorder, although other psychiatric symptoms have gotten far less study (for a summary of the known information. In addition to connections with clinical illnesses in adults, a lesser number of studies in babies have revealed links with temperamental traits and subclinical mental health issues (e.g., emotional and behavioural issues) [2-4].

Despite this fast growing body of knowledge, significant gaps still need to be filled. First, studies on the relationship between the gut microbiome and mental health have relied on small sample sizes, which are susceptible to flaws like selection bias, a lack of clarity regarding the generalizability of findings, and a lack of statistical power to identify associations with negligible effects. The use of multiple testing correction, covariate adjustment, and investigation of the gut microbiome at various taxonomic levels, among other methodologies, has led to a broad range of research, which limits the comparability of results. This has spurred requests for larger, better powered, and planned studies that look at the gut microbiota from a variety of angles (e.g., from global diversity measures to individual taxonomic units). Third, despite the fact that more than half of mental diseases appear earlier in childhood as emotional and behavioural issues, current research has focused nearly exclusively on either newborns or adults.

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Therefore, it is yet unknown if connections found in adult research are also noticeable in children. Finally, despite evidence that psychiatric symptoms frequently co-occur, research have concentrated on isolated psychiatric outcomes. As a result, it has been unable to determine whether the identified variations in gut flora are exclusive to mental disorders or widespread [5, 6].

Discussion

To fill up these gaps, we looked at cross-sectional relationships between the gut microbiota and typical mental health issues in a sample of approximately 1,800 10-year-olds from the general community. We used a thorough methodology to evaluate relationships between the makeup of the gut microbiome at several taxonomic levels (genus level, functional pathway analysis, and alpha and beta diversity assessments) and general mental symptoms in children. We further investigated links between the gut microbiota and eight distinct categories of emotional and behavioural issues as follow-up investigations [7].

We anticipated correlations between the gut microbiome and mental health based on earlier research, but we did not have any a priori assumptions about the direction of connections or the taxa implicated. The PICRUSt2 tool was used to estimate the functional composition of the gut microbiome from the ASV-level abundance tables. The anticipated composition was then incorporated in annotated MetaCyc pathways, run as univariate models using linear regression while accounting for variables. Ten pathways were discovered to have nominally significant correlations with both general and specialized mental health issues. These relationships did not endure multiple testing corrections, similar to previous findings [8].

Conclusion

Based on this extensive population-based analysis, we find less evidence that the gut microbiota and typical childhood mental health issues are related. Our analysis suggests that relationships are likely of minor amplitude in the overall pediatric population at this age but does not conclusively support a link between the gut microbiota and child mental health issues. To increase statistical power to identify minor connections, joint projects pooling data from numerous research will be necessary in the future. Additionally, using longitudinal

data from early childhood to maturity will be a vital step in figuring out how connections between these variables grow over time and comprehending the function of the gut microbiota in the emergence of mental illnesses [9, 10].

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Conflict of Interest

None

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