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THE IMPACT OF GUT MICROBIOTA ON DISORDERS OF GUT-BRAIN INTERACTION IN CHILDREN: A SYSTEMATIC REVIEW

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THE IMPACT OF GUT MICROBIOTA ON DISORDERS OF GUT-BRAIN INTERACTION IN CHILDREN: A SYSTEMATIC REVIEW

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Disorders of gut-brain interaction, also known as functional gastrointestinal disorders, are common in children, but the pathophysiology is still partly unknown.These disorders affect 10-15% of children. The symptoms are typically abdominal pain, constipation, and diarrhea that occur weekly.

There is clear data connecting adults' functional gastrointestinal symptoms and the composition of their gut microbiome. However, evidence in children remains limited. This study is a systematic review, where current knowledge is gathered.
The data search was done in May 2024 in PubMed -database. Studies where the subjects were 1-18 years old, had a diagnosis on functional gastrointestinal disorders and their gut microbiome was analyzed, were chosen to be part of this study. Exclusion criteria included animal studies, studies of children under 1 year of age, studies focusing on individual bacterial species, and review articles. Seven articles were chosen.

The results in the chosen studies varied widely. Two studies found a connection between the symptoms and a smaller alfa-diversity of microbiota. Three studies found a difference in beta-diversity between the groups. Findings regarding individual bacterial species varied considerably, making it difficult to draw definitive conclusions. This is due to the vast diversity of gut microbiota. A few studies also found preliminary results about symptomatic children having a less dynamic microbiome than healthy controls.

As a conclusion, the association between children´s gastrointestinal symptoms and gut microbiome is possible, but not definitive because of the inconsistent results. Further research is needed, particularly longitudinal studies and standardized research methods, to allow for more meaningful comparisons in future studies.

The Impact of Gut Microbiota on Disorders of gut-brain Interaction in Children: A Systematic Review

1 INTRODUCTION

1.1 Functional gastrointestinal disorders in children

Disorders of gut-brain interaction (DGPI) in children refer to digestive symptoms for which no clear structural or biochemical cause can be identified. These symptoms include abdominal pain, constipation and diarrhea. Typically, the symptoms recur in a similar pattern 1–3 times per week and cannot be treated with medication with current knowledge. (Kuitunen 2023) Functional gastrointestinal disorders are common, affecting approximately 10–15% of children. They are most prevalent among children aged 6 to 12 years (Kuitunen 2023). The impact of these disorders is significant, both for the child and their family. Doctor visits and medical examinations related to these symptoms also burden the healthcare system. Even though these disorders are common, it is still necessary to rule out inflammatory diseases and intolerances, such as celiac disease and lactose intolerance, since they can present in similar ways.

Some research has already been conducted on this topic in children and adults, and the aim of this work is to compile the information regarding paediatric patients and examine whether they have left gaps that require further investigation.

1.2 Gut microbiota and gastrointestinal health

The gut microbiota refers to the microbial community in the intestine, which consists primarily of millions of bacteria. Its composition is unique to each individual and is influenced by various factors such as dietary habits, medication, and environmental conditions. (Karahan F. 2024)

In adult patients, gut microbiota is considered to play a significant role in the development of various diseases and symptoms, including functional gastrointestinal disorders.(Shin A et al. 2019). It has also been observed that children's risk for allergies and infections, as well as the development of their nervous system, are partly influenced by the microbiota. (Pantazi AC et al. 2023) This provides reason to suspect that the etiology of gastrointestinal symptoms in children may also be linked to the gut microbiota. By examining the connection between children's gut microbiota and gastrointestinal symptoms more closely, we can gain deeper insight into the underlying causes and maybe move one step closer to effective treatment. The aim of this work is to systematically review the literature on disorders of gut-brain interaction and gut microbiota in children.

2 METHODS

A systematic review was conducted following the guidelines outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA 2020) statement (Page et al., 2021).

2.1 Data Sources

The material search was conducted in May 2024 using the academic database PubMed. The search terms were formed from the main topics of the study, which were microbiota, ("microbiota" OR "microbiome" OR "bacteria" OR "bacterial" OR "metagenome" OR "16S"), children ("child*" OR "adolescence" OR "toddler" OR "pediatric" OR "paediatric") and various functional gastrointestinal symptoms ("functional gastrointestinal disorder" OR "functional bowel disorder" OR "functional abdominal" OR "functional constipation" OR "irritable bowel disorder" OR “FGID” OR "functional reflux" OR "functional dyspepsia" OR "cyclic vomiting"). The aforementioned search terms were combined into a search query using the Boolean operator "AND" to obtain results that are as relevant to the topic as possible:

("functional gastrointestinal disorder" OR "functional bowel disorder" OR "functional abdominal" OR "functional constipation" OR "irritable bowel disorder" OR FGID OR "functional reflux" OR "functional dyspepsia" OR "cyclic vomiting") AND ("child*" OR "adolescence" OR "toddler" OR "pediatric" OR "paediatric") AND ("microbiota" OR "microbiome" OR "bacteria" OR "bacterial" OR "metagenome" OR "16S")

2.2 Eligibility criteria

This study included all research where the subjects were 1-18 years old, had diagnosed functional abdominal disorders or assessed symptoms of thereof, and their gut microbiota had been analyzed either using a amplicon or sequencing the whole genome, e.g. 16s rRNA

sequencing or metagenomic sequencing. Study types were cohort and case-control. Intervention studies were included if the gut microbiota was analyzed at the baseline and the findings were studied in relation to symptoms.
The age limit was set to one year to focus on other functional abdominal disorders than colic, since there is multiple research done on that and the point was to find out what science already knows about older children's functional gastrointestinal disorders.

The exclusion criteria was decided to be:

1. Studies written in other languages except English
2. Studies only visible in chargeable platforms
3. Studies that focused on oral or other non-GI microbiota
4. Narrative reviews
5. Guidelines
6. Studies where the microbiota analysis was done at the endpoints of an intervention
7. Testing done on animals
8. Studies related to single organisms such as Blastocystis related studies or Helicobacter related studies
9. Babies suffering from colic, children under 1 year old
10. Full-text article not available openly or through the institution

2.3 Study selection and data extraction

The articles were collected from PubMed using Zotero (Version 6.0.36). Each article was screened by title and abstract to pass the inclusion and exclusion criteria by the reviewer. The articles that did not fit the inclusion criteria were removed as well as the ones that matched one or many exclusion criteria. The reasons behind the removal were listed in a *spreadsheet*. After this, the remaining articles were read through and assessed for their eligibility. Ineligible articles were again excluded.

After the study selection reviewers created a set of variables that would comprehensively categorize the information from the articles. These were:

- ☐ author(s)
- ☐ country
- ☐ title
- ☐ publication year
- ☐ DOI-address
- ☐ study type
- ☐ number of subjects
- ☐ participant demographics including sex and age
- ☐ how DGPI was diagnosed
- ☐ the leading symptom(s)
- ☐ sequencing method, primer (if 16S-data was used)
- ☐ how the microbiota sample was collected
- ☐ exposure to medications, antibiotics and probiotics
- ☐ the association of symptoms with the alpha and beta diversity of the GM and individual microbiota species
- ☐ other notable findings

Then a spreadsheet was made and the aforementioned information was collected from the articles and listed it on the spreadsheet. Later this information was evaluated and synthesized.

3 RESULTS

3.1 Study selection

The search resulted in 159 articles. They were transferred to the Zotero research assistant. Zotero's duplicate removal feature deleted 11 articles.
After the search, the articles were screened by one of the reviewers and 75 articles were excluded based on their title and abstract for not meeting the inclusion criteria or matching with the exclusion criteria (Figure 1). Of these, 52 were off-topic, meaning they did not address functional gastrointestinal disorders in children and the microbiota of the colon. Eight articles were animal studies, which was an exclusion criteria. In two publications, the subjects were adults. One publication included both adults and animals as subjects. Twelve articles were reviews or guidelines, which was also an exclusion criterion.

In the next phase, the remaining 73 articles were analyzed by their full text or until an exclusion criterion was met (Figure 1). Of these, 33 studies were found to be narrative studies, reviews, or study protocols. Four articles were excluded because they were only accessible through paid services, two were duplicates of a previous article and one was otherwise unavailable. One article was excluded because it was published in a language other than English.
In 23 studies, the gut microbiota of the subjects was not analyzed or only a single bacterial species was examined (Figure 1). Since this review focuses on the broader picture of the gut microbiota, the presence of a single bacterium is not relevant to this work.
In two studies, the subjects were too young to meet the inclusion criteria.

After going through all the articles, only 7 articles remained and were selected for the study for further analyzing (Figure 1).

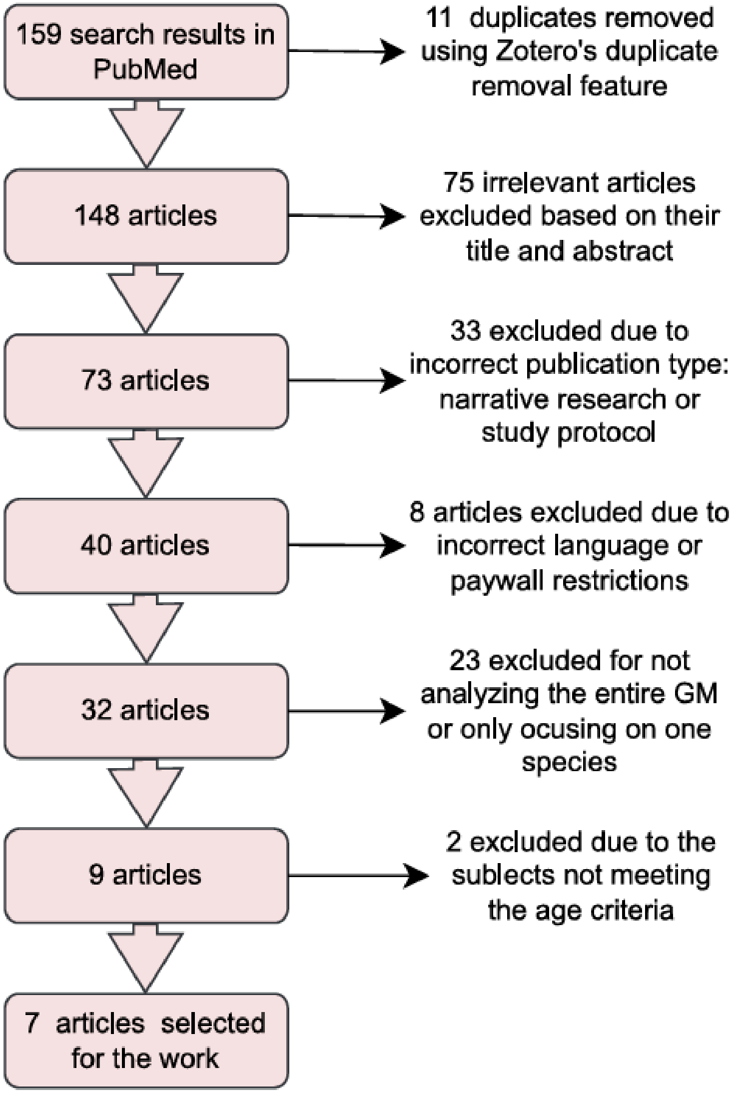

Figure 1: *Flow chart of study selection*

3.2 Study characteristics

In all the studies included in this work, there were a total of 504 participants. 284 of them were diagnosed with DGPI and 220 were healthy controls. Two of the selected articles had the same population (n=) and it has been taken into account in the results. The study with the highest number of participants was by Tim G H de Meij et al. (2016), which had 137 participants. The study with the fewest participants was by Ruth Ann Luna et al., which included 35 participants. The articles were published between the years of 2015 and 2024.

Gender distribution of the participants was balanced: all the studies had 231 girls combined, making up 46% of the participants.

In four studies, the participants did not have any other diagnoses than DGPI. In two studies, there were groups of children with autism spectrum disorders and in another study children with cerebral palsy. All of the studies had a group of completely healthy control participants who did not have issues with their gut.

Articles represented three different study types: four of them were case-control studies, two prospective longitudinal studies and one clinical trial (Table 1).

3.3 Study populations

Study populations had differences. Four studies had only two groups that they compared; DGPI-diagnosed group and a healthy control group. In three other studies there was also a comorbidity group. Son et al. compared the GM and symptoms of children in the autism spectrum to their neurotypical siblings. Luna et al. had a group of children with ASD and DGPI, a group of neurotypical children with DGPI and a control group of children without any diagnosis. Huang et al. compared children with cerebral palsy to a group of healthy children. Both of the Abomoelas studies had the same population. Their research question was different: the earlier published focused merely on the differences in microbiota in DGPI-children and healthy children. The latter compared the changes in microbiome in DGPI-children and healthy controls during different times of school year; holiday versus semester. Both of the studies were included in this work.

Six of the seven studies were conducted in the western countries: four in the USA, one in Poland and one in the Netherlands. Huang et. al´s study was conducted in China, which is important to knowledge since the environment affects the composition of gut microbiome (Lozupone CA).

In all studies, the use of antibiotics and probiotics before participating in the study was prohibited because it is known to affect the gut microbiome. However, the required time since the discontinuation of antibiotics or probiotics varied from two weeks to three months. Three studies used a three-month exclusion, and other three used a two-week exclusion. The remaining study exclusion time was one month.

Authors	Study type	Study population	N of girls	Age range	Country
Son et al. 2015	Case-control	59 with ASD, 44 NT controls	37	7-14, mean age 10,2	United States of America
Meij et al. 2016	Case-control	76 DGPI-children, 61 healthy controls	69	4-18, mean age 8,0	Netherlands
Luna et al. 2017	Case-control	14 with ASD+DGPI, 15 NT+DGPI, 6 Healthy NT	3	3-14, mean age 8,8	United states of America
Abomoelak et al. 2021	Prospective longitudinal	28 Children with DGPI, 54 healthy controls	43	7-16, mean age 11,0	United States of America
Abomoelak et al. 2022	Prospective longitudinal	28 children with DGPI, 54 healthy controls	43	7-16, mean age 11,0	United States of America
Huang et al. 2022	Clinical trial	35 with CP, 21 healthy controls	16	Range not mentioned, mean age 13,5	China
Kwiatkowska et al. 2024	Case-conrtol	57 Children with DGPI, 34 healthy controls	59	Above 3, mean age 7,5	Poland

ASD = Autism Spectrum Disorder, CP = Cerebral Palsy, NT = Neurotypical

Table 1: *Table of Basic Information on the Studies*

3.4 DGPI diagnoses

Six of the seven articles used the Rome criteria to diagnose DGPI. Three of them used the older version, Rome III and the rest used Rome IV. Rome III and IV are internationally used criteria to diagnose disorders of the gut-brain interaction. All the studies using the older version of Rome criteria were published earlier than the ones using Rome IV, which explains the difference.

The remaining one article, by Huang et al, did not mention the diagnostic criteria for DGPI, they only mentioned that the participants had experienced functional constipation.

Since DGPI is a group of disorders involving chronic gastrointestinal symptoms, there was some variation in the symptom-profile in which the studies focused on. Three studies focused on functional constipation, and three on functional abdominal pain. Only one study focused on all types of DGPI (Son et al.). They took into account a wider range of symptoms, such as constipation, diarrhea, abnormal stool smell, bloating, excessive gas, severe abdominal pain and vomiting.

3.5 Sequencing techniques and used primers

Almost all of the studies used Illumina MiSeq for sequencing DNA from the samples (Table 2). Meij et al. was the only one that used a different technique, IS-pro.
Most of the studies using Illumina MiSeq -technique used the same hypervariable region V3-V4 (Table 2). Two used different ones; Son et al. V1-V3 and Luna et al. V1V3 and V4. Meij et al., who used the IS-pro technique, used FirISf, BacISf, DUISr1-3 regions (Table 2).
Most of the microbiome samples were collected from a fecal sample (Table 2). Luna et al. used a rectal biopsy to collect the microbiome sample. The biopsy was taken during a colonoscopy.

Author	Sequencing technique	Hypervariable region	Microbiome collection method
Son et al. 2015	Illumina MiSeq	V1-V3	Fecal sample
Meij et al. 2016	IS-pro	FirISf, BacISf, DUISr1-3	Fecal sample
Luna et al. 2017	Illumina MiSeq	V1V3 and V4	Rectal biopsy
Abomoelak et al. 2021	Illumina MiSeq	V3-V4	Fecal sample
Abomoelak et al. 2022	Illumina MiSeq	V3-V4	Fecal sample
Huang et al. 2022	Illumina MiSeq	V3-V4	Fecal sample

Kwiatkowska et al. 2024	Illumina MiSeq	V3-V4	Fecal sample

Table 2: *Table of the used sequencing methods*

3.6 Findings

3.6.1 Alpha diversity and functional gastrointestinal disorders

Alpha diversity is used to describe the variety and abundance of species within a specific community or a sample, for example a gut microbiome in this case. Only two of the seven studies in this work noticed a difference in alpha diversity in the gut microbiome. These studies were by Abomoelak et al (2021) and Huang et al. Both of their results indicated that the alpha diversity was decreased in children with DGPI. Having a decreased alpha diversity means having a lower variety and abundance of species within a single participant than the ones in the other group.

3.6.2 Beta diversity and functional gastrointestinal disorders

Beta diversity is used to measure the differences in microbial community composition between different samples or environments. Four studies did not find any notable difference in beta diversity between healthy children and DGPI diagnosed children. Three studies found a difference between groups. Abomoelak et al. found a difference between a healthy control group and the DGPI-children. In Huang et al.’s intervention study there was a difference at the baseline, but the difference narrowed during the intervention. Luna et al. found a difference between autism spectrum DGPI-children and neurotypical children.

3.6.3 Differences regarding single bacterial genus or species

All of the studies noticed differences in individual bacterial genera and species, except the one that compared the microbiome at different times; Abomoelak et al. (2022). Son et. al´s results showed some differences in the prevalence of rare and low abundance bacterial genera, such as *Sutterella* spp., *Prevotella* spp. and *Bacteroidetes* spp., in association with DGPI and ASD, but these findings were not statistically significant.

Most differences in the prevalence of the bacteria identified Abomoelak et al. They identified differences in as many as nine bacterial species, the highest number among all the studies.

Summarizing and connecting the findings is challenging, as the studies' results differ significantly concerning bacterial genera. There are only a few bacterial genuses which are mentioned in more than one study, and even for these, prevalence has been compared across different symptom profiles. According to studies, genus Bacteroides increase in constipation and abdominal pain but generally decrease in DGPI overall. This result is highly contradictory, as DGPI encompasses both constipation and abdominal pain.

Another bacterial genus that was mentioned in two studies was Faecalibacterium. In both of them, it´s abundance was noticed to be decreased.

Lajit / suvut	Constipation	FAPD	DGPI
Firmicutes		↓[4]	
Alistipes	↓[2]		
Akkermans		↓[4]	
Bacteroides	↑[2]	↑[4]	↓[6]
Bifidobacterium -lajit			↑[6]
Christensenellaceae	↓[7]		
Clostridium lituseburense			↑[3]
Dialister		↓[4]	
Faecalibacterium		↓[4]	↓[6]
Fusicatenibacter	↓[7]		
Lachnoclostridium bolteae			↑[3]
Parabacteroides	↓[7]		
Prevotella			↑[6]
Romboutsia	↓[7]		

Lajit / suvut	Constipation	FAPD	DGPI
Ruminococcus		↓[4]	
Subdoligranulum	↓[7]		
Sutterella		↓[4]	
Veillonella		↓[4]	
Verruca Microbiota		↓[4]	

Table 2. [1]Son et al. 2015, [2] Meij et al. 2016, [3]Luna et al. 2017, [4]Abomoelak et al. 2021, [5]Abomoelak et al 2022, [6]Huang et al. 2022, [7]Kwiatkowska et al. 2024

3.7 Differences in study methods and findings

Two studies, Huang et al. and Abomoelak et al. were the only ones to identify connections to all of these aspects. This might be a coincidence, but there is a few things that could explain the differences. First of all, Huang et al. was the only study conducted in a non-western country, China, where the microbiota might be different overall. Abomoelak et al. on the other hand focused exclusively on functional abdominal pain, disregarding constipation and other functional symptoms. They identified differences in as many as nine bacterial species, the highest number among all the studies. They also found most connections between the abundance of certain bacterial genera and the symptoms.

Assessing the prevalence of individual microbial genera is also difficult based on these studies, as the bacteria identified varied greatly between findings. Only a few bacterial occurrences were statistically significant in more than one study.

One study, Meij et al., was the only one to use a different sequencing technique than the others and they also had a wider spectrum of symptomes that they examined. Still, the findings were similar to the other studies.

3.7 Other findings

The studies also revealed other intriguing findings related to the microbiota and children's digestive issues. Meij et al discovered that using a Ridge-regression analysis, they can distinguish children suffering from constipation from healthy ones with 82% accuracy. This means it could aid in developing efficient, non-invasive diagnostic methods and deepen understanding of the gut microbiome's role in gastrointestinal health.

Luna et al. noticed that pro-inflammatory cytokines and serotonin metabolites were elevated in children with ASD-DGPI, indicating alterations in neuroimmune signaling.

Abomoelak et al, in both of their studies, noticed that the gut microbiota of FAPD-children was much more static than the control group´s. This was discovered when they compared the GM of both groups between holiday season and school term. School term affected mostly the abundance of Enterobacteria and Megasphaera.

Kwiatkowska et al. collected saliva samples in addition to fecal samples from the participants and analyzed the oral microbiota. However, no differences were observed in the salivary microbiota between those with gastrointestinal symptoms and healthy individuals.

4 DISCUSSION

4.1 Context and key findings

The main objective of this review was to gather and analyze information on the possible connection between the gut microbiota and functional gastrointestinal disorders in children, as well as to identify possible gaps in current knowledge. At present, there is limited information on this topic regarding children, whereas some more data is available for adults and it seems to show that there could be a connection. Functional gastrointestinal disorders are common, as approximately 10-15% of children experience them. The impact of these conditions is significant, both for the affected child and their family. Medical visits and examinations related to these disorders also burden healthcare services. Understanding the etiology of the symptoms could help identify effective treatments.

4.2 Findings regarding GM composition

Summarizing the findings of these studies is challenging, as there is no clear consensus between the studies on the relationship between alpha diversity, beta diversity, and individual bacterial genera with functional gastrointestinal disorders. Two studies, Huang et al. and Abomoelak et al. were the only ones to identify connections to all of these aspects. This might be a coincidence, but there are a few things that could explain the differences. First of all, Huang et al. was the only study conducted in a non-western country, China, where the microbiota might be different overall.. Secondly, Huang et al. had a wider spectrum of symptoms, since they did not differentiate between the various symptoms of DGPI but grouped them together. Abomoelak et al. on the other hand focused exclusively on functional abdominal pain, disregarding constipation and other functional symptoms. They identified differences in as many as nine bacterial species, the highest number among all the studies.

4.2.2 Alpha diversity

Out of the seven studies included in this work, only two observed a variation in alpha diversity within the gut microbiome. These studies, conducted by Abomoelak et al. (2021) and Huang et al., both found that children with DGPI exhibited a reduced level of alpha diversity. This could be related to the aspects mentioned in the previous paragraph regarding the nationality of the study participants and the research question.

Children suffering from constipation had significantly lower abundances of rare bacterial genera such as Christensenellaceae R-7, Fusicatenibacter, Parabacteroides, Romboutsia, and Subdoligranulum.

4.2.3 Beta diversity

Among the seven studies reviewed, four did not observe a significant difference in beta diversity between healthy children and those diagnosed with DGPI. However, three studies did identify a distinction between groups. Abomoelak et al. reported a difference between DGPI-affected children and a healthy control group. They also compared the GM of the children between school term and holiday season and noted that a healthy GM is more dynamic than a symptomatic one. In Huang et al.'s intervention study, an initial difference was noted at baseline, but this gap diminished over the course of the intervention where they gave the children Compound Dietary Fiber (CDF) supplementation for 1 month and probiotics (lactic acid-producing and butyric acid-producing) for 6 months.

Luna et al. found a difference in beta diversity when comparing DGPI-children on the autism spectrum with neurotypical children. This may be due to the elevated levels of proinflammatory cytokines and serotonin metabolites observed in children from the ASD-DGPI group, suggesting alterations in neuroimmune signaling, as the researchers found.

4.2.4 Taxonomic level findings

Most of the associations between individual bacterial genera and DGPI were only observed in one individual study. Several possible factors may influence this, including differences in nutrition, age, environment and methods used analyzing the GM.
Bacteroides was the only genus that was observed in three studies: Meij et al., Abomoelak et al. and Huang et al. However, the associations differed across studies: *Bacteroides* abundance was increased in patients with constipation (Meij et al.) and FAPD (Abomoelak et al.), whereas it was decreased in patients with DGPI (Huang et al.). This is contradictory, as the concept of DGPI encompasses both constipation and abdominal pain as presenting symptoms.The *Bacteroides* genus plays a significant role in the human GM and can have many effects on gut health, because they break down complex carbohydrates producing short-chain fatty acids like butyrate, which supports gut health (Lensu & Pekkala, 2021). They also compete with several harmful microbes in the colon and can prevent their overgrowth promoting a healthy gut environment.
Bifidobacterium species were found in larger amounts in -childrens gut microbiota in Huang et al.´s work. They had excluded participants who had used probiotics in the last two weeks before the baseline, but it might still affect the GM at that point especially since it looks like the DGPI-patients have a less dynamic GM. Another option could be that the participants did not follow the restriction.

In Kwiatkowska et al. ‘s analyze, *Christensenellaceae bacteria* was noticed to be decreased in DGPI-children compared to healthy ones. According to current understanding, Christensenellaceae bacteria play a significant role in gut health. This relationship has been observed in both humans and animal models, where Christensenellaceae abundance correlates with reductions in inflammatory biomarkers and better gut health (Akbuğa-Schön et al., 2024). The prevalence of *Enterococcus faecalis* was reduced in both FAPD patients (Abomoelak et al. 2021) and DGPI patients (Huang et al. 2022). This bacterium is abundant in the gastrointestinal tracts of humans, where it participates in maintaining the gut homeostasis while also having the capability to cause opportunistic infections under certain conditions (Zhang et al., 2022; , Mason et al., 2011). Research indicates that *enterococcus faecalis* can help regulate gut microbiota composition, potentially by producing bacteriocins, which are antimicrobial peptides that may inhibit the growth of other bacterial strains (Fu et al., 2025).

Fusicatenibacter is known to produce butyrate, which can induce the motility of the colon and reduce constipation. (Zhang et al. 2021) It produces short-chain fatty acids (SCFAs) which play an important role in maintaining the integrity of the intestinal mucosa and immune balance. *Prevotella* species are especially abundant in individuals consuming a fiber-rich and plant-based diet, indicating that they have the capacity to utilize plant polysaccharides. (Abdelsalam, Hegazy & Aziz, 2023) In Huang et. al´s study, they noticed that the children with DGPI had more *Prevotella* bacteria in their gut. This may indicate either a connection between DGPI and diet or a connection between DGPI and *Prevotella* presence in the gut microbiome. *Prevotella* participates in utilizing fiber creating short-chained fatty acids that may have influence on the host, potentially contributing to gastrointestinal symptoms. (Chen et al., 2017)

4.3 The role of intestinal transit time and diet

Intestinal transit time plays a significant role in the bacterial composition of the colon as well as the symptoms the patient experiences. IBS symptoms can be divided into three categories according to transit time: constipation-predominant, diarrhea-predominant and a mixed-type.
In constipation-predominant state, where intestinal contents remain in the colon for a prolonged time, bacteria have more time to break down fibers and other substrates. This may lead to an excessive or imbalanced production of gases and SCFAs can promote the growth of methane producing archaea, which slows intestinal motility even more (Pimentel *et al.*, 2006).
In diarhhea-predomintant state, the transit time is shorter than the average. This means that there is less time for microbial growth and fermentation, which may lead to lower bacterial richness and diversity (Aatsinki et al. bioRxiv 2025). Some beneficial, fiber-fermenting bacteria, for example Faecalibacterium prausnitzii and Bifidobacterium, may decrease in this type (Tottey et al., 2017; Procházková et al., 2023).
In the mixed-type, the alternating transit speed exposes microbes to instable conditions.
This instability can potentially reduce overall microbial resilience and favor opportunistic or stress-tolerant species over stable commensals such as *Faecalibacterium prausnitzi*i and *Bifidobacterium*.
(Procházková et al., 2023)
As mentioned earlier, diet is known to influence the gut microbiome, although the relationship is not necessarily straightforward. Experiencing DGPIs can modify a patient’s dietary habits, while specific dietary patterns may also affect DGPI symptoms. When intestinal transit time and the gut microbiome are also taken into account, since all these factors may interact with both diet

and symptoms, the overall relationship becomes increasingly complex. These overlapping influences make it difficult to determine the direction of causality especially with individual variability.

4.4 Possibilities for Further Research

There is no clear consensus between the studies on the relationship between alpha diversity, beta diversity, and individual bacterial genera with disorders of gut-brain interaction. Because of the small amount of research on the subject, the statistical power is inadequate and the perspective is narrow. Much more data is needed so that a meta-analyze could be done to gain generalizability and maybe even solutions for clinical use.
As some of the research covered in this work suggested, the dynamism of the GM could explain part of the manifestation of symptoms. It could be useful, if this would be studied more by taking multiple samples from the same patients and comparing them to symptoms at the time.

4.5 Clinical relevance

In this review, no clinically relevant findings were identified. The results varied widely across studies and did not reveal any consensus on the bacterial species underlying the symptoms. The findings from these studies do not show unanimously affected bacterial groups in the children suffering from DGBI that could be used in developing microbe-based interventions. However, in the study by Meij et al., ridge regression analysis was able to identify most of the children experiencing DGPIs within their population. This suggests that machine learning–based methods can detect complex multivariate patterns that conventional statistical analyses may fail to reveal.

4.6 Limitations of this review

This review had a few limitations. First, there were only seven articles that passed the eligibility criteria, and the data search was conducted using only one scientific database, PubMed, which may have limited the comprehensiveness of the literature coverage. Secondly, the search and the screening were performed by a single author, which increases the risk of selection bias and reduces the reliability of the review process.

5 CONCLUSION

This review highlights that current evidence on the connection between gut microbiota and functional gastrointestinal disorders in children remains inconclusive. Heterogeneous study designs, small sample sizes and inconsistent findings on alpha and beta diversity, as well as divergent associations at the genus level, prevents from making firm conclusions. Consequently, there is no clear bacterial targets for microbiota-targeted therapies such as probiotics or fecal transplants in this population.

The limited number of studies and narrow research perspectives makes larger, longitudinal investigations important in the future. Standardized sampling protocols and taking into account also functional readouts (for example metabolomics and immune markers) will be crucial to gain more understanding on dynamic microbiome–symptom relationships and maybe find clinically actionable insights.

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