Associations between Gut Microbiome and Migraines in 7-18-year-old Children: the American Gut Cohort Analysis

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Conflict of Interest Disclosure

Author’s conflicts of interest: None

Educational Objectives

• Understand the concept of gut microbiome
• Be familiar with the microbiome-gut-brain axis
• Assess associations between the gut microbiome and Migraines
Significance

- 10% children suffer from migraine
- Migraine can result in more school absences and lower academic performance
- The gut microbiome may impact migraines through the following pathways:
  - Intestinal epithelial permeability
  - Inflammation
  - Microbiome-gut-brain axis

Definition of Gut Microbiome

- A collection of microorganisms and their genomes in human GI tract
- Human gut hosts tens of trillions of microbes, 500 species on average
- Gut microbiome changes across the lifespan

Mechanism of Gut Microbiome in Pain

- Neural: Vagus nerve & spinal
- Metabolic: SCFAs (butyrate, propionate, and acetate)
- Immune: cytokines
- Tryptophan & neurotransmitters

Microbiome-Gut-Brain Axis

a. Neural: Vagus nerve & spinal
b. Metabolic: SCFAs (butyrate, propionate, and acetate)
c. Immune: cytokines
d. Tryptophan & neurotransmitters
Research Purpose

- **Profile** the gut microbiome in children aged 7-18 years from the American Gut Project (AGP)
- **Examine** the associations between the gut microbiome and migraines among a cohort of children aged 7-18 years from AGP

Methods

- AGP is an ongoing national project
- All de-identified AGP data have been deposited into the European Bioinformatics Institute sequence repository
- Following the Illumina MiSeq 515f-806r amplification protocol, 16S rRNA V4 gene was sequenced
- All data except confidential information is openly and freely for use

- Eligible participants: 7-18-year-old children and had the gut microbiome data available
- Raw 16S rRNA sequencing and metadata were obtained from the AGP Public Repository
- In this study, 16S rRNA single-end sequencing data (~150bp reads) per sample and metadata were obtained from the EBI repository before data analysis
Methods

- Quality control of 16S rRNA data used DADA2
- Alpha-diversity (observed-OTUs, Shannon, Faith's PD) and beta-diversity metrics (weighted-, unweighted-UniFrac, Bray-Curtis distances) were analyzed
- Taxonomic and abundance analyses were conducted using QIIME 2

Results

- 381 children (341 without migraines and 40 with migraines) were analyzed.
- These children had mean age of 11.5 years and mean BMI of 18.0.
- Migraine children were more White (p=0.04), more boys (p=0.01), younger (p=0.002) and more underweight (p<0.001).

- Compared with those without migraines, children with migraines showed lower estimates in observed-OTUs, Shannon and Faith's PD (p<0.01)
**Results**

- The Bray-Curtis (LEFT) and weighted-UniFrac (RIGHT) distances displayed the gut microbial dissimilarities between children with and without migraines (p=0.001)

**Results**

- Children with migraines had higher abundances in genus
  - Actinobacteria (e.g., Bacteroides, Parabacteroides, Eggerthella, Odoribacter),
  - Firmicutes (e.g., Lachnospira, Dorea, Veillonella)
  - Proteobacteria (e.g., Sutterella) than children without migraines.

**Conclusion**

- Associations between gut microbiome diversity and abundances and migraines in children suggested potential biological mechanisms of migraines
- Future work needs to examine how the metabolites of gut microbes impact migraines in children
- The microbiome-gut-brain axis should be further studies in children with migraines
- Personalized interventions can be designed towards migraine control
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