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Summary

MICROBIAL DYSBIOSIS, INFLAMMATION, AND THE GUT-BRAIN AXIS IN IRRITABLE BOWEL SYNDROME: INSIGHTS FROM THE DISCOVERIE COHORT

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Gut Microbiota | IBD | Colorectal

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The DISCOVERIE multi-centre study of 743 individuals with multi-omics profiling reveals that IBS is characterised by dysregulated gut neurotransmitter metabolism, with increased GABA degradation and decreased glutamate biosynthesis pathways, alongside elevated IL-6 levels strongly associated with bacterial genera and neurotransmitter-degrading pathways.

KEY POINTS

- IBS subjects showed 17–26% prevalence of the dysbiotic Bacteroides 2 enterotype compared to only 2% in healthy controls and 17% in the general population (chi-squared test, FDR less than 0.05).
- Bacterial metabolic modules in IBS were enriched for degradation of neurotransmitter precursor amino acids, with increased GABA degradation pathways and decreased glutamate biosynthesis modules, suggesting bacteria preferentially degrade rather than produce neurotransmitters.
- Pro-inflammatory IL-6 levels were strongly associated with specific bacterial genera (FDR less than 0.05) and with the metabolic module degrading gamma-hydroxybutyric acid, a neurotransmitter and CNS depressant, suggesting a mechanistic link between low-grade inflammation and depressive symptoms in IBS.
- IBS microbiomes exhibited reduced butyrate synthesis capacity, loss of butyrate-producing taxa, and increased opportunistic taxa compared to non-IBS controls.
- The findings from this international, multi-centre initiative underscore a potential link between elevated IL-6, microbial metabolism, and the gut–brain axis in IBS-related comorbidities.

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