

GUT MICROBIOTA FUNCTIONAL REMODELING IN PEDIATRIC MIGRAINE: A MULTI-OMIC INSIGHT INTO NEUROACTIVE AND IMMUNOMETABOLIC PATHWAYS

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Background. Pediatric migraine is increasingly linked to alterations of the microbiota–gut–brain axis, but the functional activity of the gut microbiota remains poorly characterized. We integrated fecal metaproteomics and untargeted metabolomics to investigate gut microbiota-associated functional and metabolic signatures in children with migraine.

Methods. Stool samples from 50 migraine patients and 24 healthy controls were analyzed by LC–MS/MS-based metaproteomics, while metabolomics was performed on 83 migraine patients and 41 controls. Microbial protein groups were functionally annotated using COG and KEGG-based approaches, and fecal metabolites were annotated from untargeted metabolomic profiles.

Results. Metaproteomics revealed selective remodeling of microbial pathways related to nitrogen metabolism, arginine/citrulline and glutamate–glutamine turnover, aromatic amino acid metabolism, and short-chain fatty acid-associated functions. These changes converged with fecal metabolomic alterations involving arginine-related metabolites, glutamate/GABA-associated compounds, tryptophan- and tyrosine/phenylalanine-derived metabolites, purine intermediates, and lipid-related molecules. The nitrogen and arginine/citrulline signature suggested a potential link with nitric oxide-related pathways, whereas glutamate/GABA and aromatic amino acid alterations pointed to remodeling of neuroactive microbial functions. Changes in lipid/acyl-CoA, butanoate/propanoate, and purine-related pathways suggested an altered intestinal immunometabolic environment potentially relevant to barrier integrity, mucosal immune regulation, purinergic signaling, and microbiota–gut–brain communication.

Conclusions. Integrated metaproteomic and metabolomic profiling identified selective remodeling of gut microbial functions and fecal metabolic outputs in pediatric migraine, supporting a functional microbiota signature potentially linked to nitric oxide-related metabolism, neuroactive amino acid pathways, purine signaling, and intestinal immunometabolic homeostasis.