

## Gut Mycobiome Dysbiosis and Its Impact on Intestinal Permeability in Attention-Deficit/Hyperactivity Disorder

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**Abstract :** Background: Dysbiosis in the gut microbial community might be involved in the pathophysiology of attention deficit/hyperactivity disorder (ADHD). The fungal component of the gut microbiome, namely the mycobiota, is a hyperdiverse group of multicellular eukaryotes that can influence host intestinal permeability. This study therefore aimed to investigate the impact of fungal mycobiome dysbiosis and intestinal permeability on ADHD. Methods: Faecal samples were collected from 35 children with ADHD and from 35 healthy controls. Total DNA was extracted from the faecal samples, and the internal transcribed spacer (ITS) regions were sequenced using high-throughput next-generation sequencing (NGS). The fungal taxonomic classification was analysed using bioinformatics tools, and the differentially expressed fungal species between the ADHD and healthy control groups were identified. An in vitro permeability assay (Caco-2 cell layer) was used to evaluate the biological effects of fungal dysbiosis on intestinal epithelial barrier function. Results: The  $\beta$ -diversity (the species diversity between two communities), but not  $\alpha$ -diversity (the species diversity within a community), reflected the differences in fungal community composition between ADHD and control groups. At the phylum level, the ADHD group displayed a significantly higher abundance of Ascomycota and significantly lower abundance of Basidiomycota than the healthy control group. At the genus level, the abundance of *Candida* (especially *Candida albicans*) was significantly increased in ADHD patients compared to the healthy controls. In addition, the in vitro cell assay revealed that *C. albicans* secretions significantly enhanced the permeability of Caco-2 cells. Conclusions: The current study is the first to explore altered gut mycobiome dysbiosis using the NGS platform in ADHD. The findings from this study indicated that dysbiosis of the fungal mycobiome and intestinal permeability might be associated with susceptibility to ADHD.

**Keywords :** ADHD, fungus, gut-brain axis, biomarker, child psychiatry

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