Brain Barrier: Knowns and Unknowns in Health and Disease

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Abstract

The current study indicates lower Candida levels, possibly influenced by factors like geography, lifestyle, diet, or analytical methods. Saccharomyces may play a role in both maintaining a healthy mycobiome and contributing to certain diseases. This suggests a potential strain-specific effect or the broader mycobiome composition's impact on disease development. Further research into the relationship between Saccharomyces, Candida, and other microbiome components in multiple sclerosis is necessary. Investigating fungi's role in disease progression or prevention is crucial. This study provides initial evidence of fungal microbiome disturbance in multiple sclerosis patients, paving the way for future research using advanced sequencing methods and larger sample sizes. Integrating these approaches with mechanistic studies will be essential for understanding fungi's precise role in multiple sclerosis pathobiology.

Keywords: Diabetry • Mycobiome • Multiple Sclerosis• Fungal infection

Introduction

Scientists have been studying these tiny gut residents using special techniques that don't require growing them in a lab for about twenty years now. They've found that in diseases like Multiple Sclerosis (MS), there's something not quite right with the mix of bacteria in the gut. But until recently, most of this research has only looked at bacteria, ignoring the fungi and viruses that also live there.

Now, a new study by Shah and their team has looked at the fungi part of the gut community, called the mycobiome, in people with MS. They found that the fungal makeup in these individuals is different from those without MS. This study, along with another one by Yadav and their team (which hasn't been published yet but is available for others to see), suggests that fungi might play a big role in MS [1-5].

Shat and colleagues looked at the fungal communities (mycobiomes) in 25 people with Multiple Sclerosis (MS) and 22 healthy individuals. They found that those with MS had more types of fungi in their bodies compared to the healthy group, and this didn't change much over six months. Some specific fungi, like *Saccharomyces* and *Aspergillus*, were more common in people with MS. Surprisingly, treatments for MS that fight fungi didn't seem to change the types of fungi present.

The researchers sorted the fungal profiles into two groups, or "Mycotypes." Mycotype 1 had a lot of *Saccharomyces*, while Mycotype 2 had more variety, including *Penicillium*, *Malassezia*, *Mucor*, and *Saccharomyces*. They also found that *Saccharomyces* was linked to higher levels of certain immune cells.

These findings suggest that changes in fungal communities might play a role in MS and its severity. This idea is supported by past research showing different fungal patterns in people with other diseases like inflammatory bowel disease, cancer, heart disease, diabetes, obesity, and liver problems caused by alcohol [6].

Similar to bacteria, fungi are suggested to have a significant (symbiotic) role in maintaining immune balance at mucosal surfaces by regulating both innate and adaptive immunity. Recognition of fungi by innate immune receptors like Dectin-1, Dectin-2, c-type lectin receptors, and macrophage-inducible Ca^{2+} dependent lectin receptor helps modulate immune responses in the gut. Moreover, certain fungi such as Candida and Malassezia are potent stimulators of a systemic Th17 response and facilitate the expansion of the neutrophil population. Recent studies underscore the importance of the mycobiome in T cell activation and granulocyte expansion. These studies reveal that the mycobiome was enriched in the offspring of wild mice that received embryos from laboratory mice, or in laboratory mice reintroduced to the wild. It's noteworthy that laboratory mice, unlike humans, have lower numbers of activated T cells and polymorphonuclear lymphocytes in their blood. These findings suggest that the absence of complex commensal fungi in mice could account for these differences in immune parameters [7-10].

The study discussed here faces limitations due to its small sample size, the classification of fungi at a low resolution, and observed in the current study could be attributed to factors such

as geographic location, lifestyles, dietary habits, or the bioinformatics pipeline utilized. Moreover, Saccharomyces has been linked to both a healthy mycobiome and certain diseases, suggesting either a strain-specific role of Saccharomyces in disease promotion or the influence of the overall composition of the mycobiome, including the bacterial microbiome, on its disease-protective or promoting properties. Further exploration into the correlation between the abundance of Saccharomyces and Candida with other components of the microbiome in the context of multiple sclerosis is warranted.

An important next step in understanding how fungi might contribute to either protecting against or promoting disease is to conduct further research. In conclusion, this study offers initial evidence that the fungal portion of the microbiome is disturbed in individuals with Multiple Sclerosis. This sets the stage for future investigations aimed at characterizing the mycobiome in disease contexts using shotgun metagenomic sequencing and larger sample sizes. Integrating these approaches with mechanistic studies will be crucial in elucidating the precise role of fungi in the pathobiology of multiple sclerosis.

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