Fungal toxins and multiple sclerosis: A compelling connection

Catherine B. Purzycki*, Daniel H. Shain1
Department of Biology, Rutgers, The State University of New Jersey, 315 Penn Street, Camden, NJ 08102, United States

Abstract

Multiple sclerosis occurs as a consequence of central nervous system neuronal demyelination. Decades of research suggest that the primary suspects (e.g., viruses, genes, immune system) are associative rather than causative agents, but a surprisingly coherent relationship can be made between multiple sclerosis and fungal toxins. Specifically, certain pathogenic fungi sequester in non-neuronal tissue and release toxins that target and destroy CNS astrocytes and oligodendrocytes. Without these glial support cells, myelin degrades triggering the onset of multiple sclerosis and its associated symptoms. We propose here that fungal toxins are the underlying cause of multiple sclerosis and thus may offer an avenue towards an effective cure.

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stirring correlations have been made between MS and fungal toxins, leading to a surprisingly coherent story of MS development. And while no definitive link has been made, many researchers remain open to an infectious micro-organism as the causative agent of MS [18]. In our proposed scenario, certain pathogenic fungi (e.g., species of Aspergillus and Candida) – masked from the immune system by their mannan coats – sequester in non-neuronal tissue, steadily releasing toxins (e.g., gliotoxin) into the bloodstream. Once across the blood–brain barrier, these toxins target CNS astrocytes, which are integral for maintaining this barrier; and oligodendrocytes, which provide nutritive support for myelin. Without proper glial support, the blood–brain barrier weakens and myelin degrades, generating myelin debris that triggers a full scale immune response in the CNS. Thereafter, the characteristic progression of MS ensues: further demyelination, conduction failure, redistribution of sodium channels, ion imbalances, anoxia, mitochondrial depletion and axon degeneration.

Experimental evidence for this putative fungal-based etiology is limited but strongly suggestive. Fungi are recognized by the human immune system due to polymeric beta-glucan in their cell walls [29]. Some fungal pathogens, including clinically important dimorphic fungi, are able to mask themselves with a mannoprotein coat that evades the host’s immune system [29], thus enabling them to colonize certain areas of the body (e.g., gastrointestinal tract) while their cyotoxic metabolites create the neurological havoc associated with MS.

Different mycotoxins may in fact be responsible for different forms of MS. Fumonisin B(1), isolated from species of Fusarium, which contaminates both animal feed and human food, disrupts forms of MS. Fumonisin B(1), isolated from species of Aspergillus, which is found in wheat, corn and all corn-based products, can reach 0.15–0.5 mg; the acute lethal dose in human is ~10 mg [11]. Thus, continuous exposure to grain-based fungi and their airborne spores in northern regions may constitute a key environmental component of MS, and contribute to the perplexing distribution of MS cases worldwide.

Can fungal metabolites be the missing pathogenic factor in MS? Are toxic metabolites targeting astrocytes and oligodendrocytes while also impairing myelin synthesis and blood–brain barrier integrity? As the scientific community struggles to understand the complex nature of this disease, and clinicians attempt to ameliorate symptoms with drugs whose side effects can be worse than the disease itself, perhaps it is time to determine the definitive role that fungal toxins play in MS etiology.

References


