Effects of Mycotoxins on Neuropsychiatric Symptoms and Immune Processes

Aarane M. Ratnaseelan, MBS[1]; Irene Tsilioni, PhD[2]; and Theoharis C. Theoharides, MS, MPhil, PhD, MD[1,2,3,4,5]

[1]Graduate Program in Biomedical Sciences, Tufts University School of Medicine, Boston, Massachusetts; [2]Molecular Immunopharmacology and Drug Discovery Laboratory, Department of Immunology, Tufts University School of Medicine, Boston, Massachusetts; [3]Sackler School of Graduate Biomedical Sciences, Tufts University, Boston, Massachusetts; [4]Department of Internal Medicine, Tufts University School of Medicine and Tufts Medical Center, Boston, Massachusetts; and [5]Department of Psychiatry, Tufts University School of Medicine and Tufts Medical Center, Boston, Massachusetts

ABSTRACT

Purpose: The effects of air pollutants have been receiving increased attention both clinically and in the media. One such pollutant is mold, fungal growth in the form of multicellular filaments known as *hyphae*. The growth of molds is omnipresent not only in outdoor settings but also in indoor environments containing excessive amounts of moisture.

Methods: PubMed was searched for relevant articles using terms such as *mold, mycotoxins, fungi, immunity, inflammation, neurodevelopment, cognition, Alzheimer's,* and *autism*.

Findings: Exposure to molds is most commonly associated with allergies and asthma. However, it is now thought to be associated with many complex health problems, since some molds, especially *Trichoderma, Fusarium* and *Stachybotrys* spp, produce mycotoxins that are absorbed from the skin, airways, and intestinal lining. People exposed to molds and mycotoxins present with symptoms affecting multiple organs, including the lungs, musculoskeletal system, as well as the central and peripheral nervous systems. Furthermore, evidence has recently implicated exposure to mycotoxins in the pathogenesis of autism spectrum disorder. The effects of mycotoxins can be mediated via different pathways that include the secretion of pro-inflammatory cytokines, especially from mast cells.

Implications: The information reviewed indicates that exposure to mold and mycotoxins can affect the nervous system, directly or through immune cell activation, thus contributing to neurodevelopmental disorders such as autism spectrum disorder.

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Key words: autism, brain, cognition, fungus, inflammation, mast cells, mold, mycotoxins.

INTRODUCTION

Mold is a type of fungus grown in multicellular filaments on moist food and other surfaces. While generally thought to be an outdoor problem, mold contamination in buildings is quite common.[1–8] One study from Harvard University (Cambridge, Massachusetts), in 13,369 white children aged 8 to 12 years from 24 communities across North America, reported that the prevalence of indoor mold growth was between 22% to 57%, affecting >50% of households in 5 communities. The reported prevalence of asthma symptoms ranged from about 3% to 11% of the children.[9] Another study in 5951 children from 9 cities in Russia reported positive associations between water damage or the presence of molds in the home and asthma, wheezing, dry cough, bronchitis, and respiratory allergy.[10]

Many studies describe the adverse health consequences of mold-contaminated indoor environments, and especially mycotoxins,[11,12] on the skin and respiratory systems.[13] Some indoor molds, including *Trichoderma, Fusarium,* and *Stachybotrys* spp, produce mycotoxins,[1–8,14] exposure

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to which occurs through dermal contact, inhalation, and ingestion.[11] Inhabitants of affected dwellings typically report headaches and respiratory and musculoskeletal symptoms.[9,15–17] Some studies have also reported that mold-exposed groups had altered neurologic functioning, including changes in body balance, blink-reflex latency, visual fields, reaction time, and color discrimination, compared with controls.[18–21] The exposed groups also demonstrated depression.[22]

Increasing evidence has implicated the pathogenic potential of nanoparticulate fragments of fungi, and more specifically mycotoxins.[23–26] Moreover, while a single mycotoxin may not produce any effect, a combination of mycotoxins could induce toxicity at very low levels.[27] The major classes of mycotoxins include ochratoxin (A, B, and C), produced by *Penicillium* and *Aspergillus* spp, as well as the trichothecenes (T2).[14] Ochratoxin A is the most common mycotoxin found in foods and water-damaged buildings, and has been associated with serious health problems,[28] including severe neurologic issues, in humans.[29,30]

The trichothecene mycotoxins are subclassified as nonmacrocyclic, produced mostly by *Fusarium* spp, and macrocyclic, produced mostly by *Myrothecium*, *Stachybotrys,* and *Trichothecium* spp. Trichothecene mycotoxins can be released at ~300-fold the concentration of spores.[24] These are commonly detected in the air of contaminated buildings, and exposed persons have significantly more T2 mycotoxins in their sera as compared to controls.[25,31–33] These toxins can cause multisystemic effects, including gastrointestinal, cardiovascular, and neuropsychiatric complications.[23] One study reported neurotoxic effects on human cells exposed to satratoxin A at levels found in water-damaged buildings.[34] Trichothecene mycotoxins released by *Stachylobotrys* spp, such as satratoxins G and H, have been shown to produce neurotoxicity in humans.[35,36] The nonmacrocyclic T2 fumonisin B1 has also been associated with neurotoxicity.[37]

Here we review the risk factors, signs and symptoms, diagnoses, and mechanisms of action of mycotoxins, especially as they relate to neuropsychiatric effects.

MATERIALS AND METHODS

PubMed was searched for relevant articles using terms such as *mold, mycotoxins, fungi, immunity, inflammation, neurodevelopment, cognition, Alzheimer's,* and *autism*. The reference lists of identified articles were searched manually for additional papers eligible for inclusion. Data from articles that were prior to 1990 and those in languages other than English were excluded from the review.

RESULTS

A total of 150 articles were identified from the database search. After the exclusion of articles that were [reasons for exclusion], data from 16 articles (N = 1580 patients) were included in the present review. The Table summarizes most of the key studies reviewed.

Neuropsychiatric Effects From Mold Exposure

Findings in Adults

Individuals exposed to mold report an extensive range of symptoms, including malaise, fatigue, and cognitive impairment, which appear to be related to the duration of exposure.[18–21] In one study, patients who had been exposed to mold were impaired on a variety of cognitive measures, including verbal learning, visuospatial learning and memory, psychomotor speed, and emotional functioning.[20] Mold-exposed patients in other studies also displayed similar symptoms of neurologic dysfunction as compared to controls, including an inability to stand on one's toes, inability to walk in a straight line with eyes closed, short-term memory loss, altered blink-reflex latency, verbal recall impairments, as well as issues with color discrimination and reaction time.[38,40]

Another group of researchers assessed the psychological, neuropsychological, and electrocortical effects of exposure to mixed colonies of toxigenic molds in 182 patients with a confirmed mold-exposure history.[19] The patients reported moderate to severe levels of cognitive, physical, and emotional symptoms, mostly depression, while quantitative electroencephalography results showed hypoactivation in the frontal cortex, which could potentially be due to brain stem involvement and insufficient excitatory input from the reticular-activating system.[19] Neuropsychological testing also indicated impairments similar to those seen in mild traumatic brain injury, in which there were findings of impaired functioning on multiple cognitive tasks when compared to premorbid estimates of intelligence.[19] This picture is consistent with that from another study, in which neuropsychological data from and symptoms in 31

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