EDITORIAL

The Brain and Mycotoxins

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YOUR BRAIN

You are what your brain is. Your brain makes you how you are: your personality, your character, your ability to be happy and enjoy life, your emotions, your ability to learn, your daily actions and reactions, how and what you pay attention to, all of these and much more derives from your brain. Your brain's health is vital to your well-being.

Our brain is a unique and extremely complex organ, and the only one completely surrounded and protected by bone: the skull. It weighs about 3 pounds, about 2% of our body weight, yet uses 20% of our calories and of our oxygen, and 30% of our glucose. The brain receives the freshest and most oxygenated blood as it is pumped out from the heart. The brain has the texture of tofu and is made up of approximately 100 billion neurons and we have 400 miles of blood vessels to bring oxygen and nutrients to all those neurons. Each neuron has approximately 1000 synapses.

According to the World Health Organization, diseases caused by mycotoxins are many and mycotoxins are known as the "Great Masquerader" of the 21st century due to their ability to present in patients a number of nonspecific clinical signs and symptoms and not routinely suspected by the medical establishment.[1] Many patients get misdiagnosed with Lyme disease, Chronic Fatigue Syndrome, Fibromyalgia, or eventually psychiatric disorders such as adjustment disorder, depression, and others.[2]

For the most part, conventional medicine is the treatment of symptoms with a prescription drug. This is a well-established system, with a code book for insurance companies to plug in a number for the approval of treatment and reimbursement. These drugs eventually can cause other symptoms and health problems, so they add another drug to control the symptoms of other drugs. It's a vicious cycle. Instead of taking the time to sit down with the patient to discuss the benefits of changing their lifestyle, nutrition, diet, and exercise, the patient may be given an impersonal handout, one size fits all.

When a patient has a several or many non-specific complaints, the conventional doctor will usually order common laboratory tests. When these are normal, the patient may undergo imaging studies and, if these are normal as well, they may be referred to a specialist. When the specialist orders tests on this patient and they return as normal, this patient may be then sent to another specialist, and another, etc. Somewhere along the line, a doctor may refer this unfortunate person to a psychiatrist.

Psychiatry is different from other medical specialties. It doesn't have all the technical advances or tests. However, there has been one major change in psychiatry: it is now a drug intensive specialty with prescriptions. This has taken place over the last 35 or so years, and psychiatry has developed into a specialty where a patient is given a drug, usually an antidepressant. Many of these are as effective as a placebo and some have worrisome side effects.[3-6] If the patients need counseling or psychotherapy, they are sent to a psychologist or social worker. This heavy use of psychotropic drugs has been noted by the pharmaceutical industry, and it has liberally given money and samples to psychiatrist. When Vermont and Minnesota passed a law requiring pharmaceutical companies to divulge payments made to doctors, psychiatrists received more money than any other medical specialty. The American Psychiatric Association gets 20% of their annual budget from pharmaceutical companies.[7] Is it really surprising that psychiatrist give out prescriptions and leave the mental health counseling to others? The patient, who may be suffering from the effects of exposure to molds and mycotoxins, may spend months or years in this cycle of specialists and psychiatrists.

THE EFFECTS OF MYCOTOXINS ON THE BRAIN: AUTISM SPECTRUM DISORDER, MULTIPLE SCLEROSIS, AMYOTROPHIC LATERAL SCLEROSIS, AND DEMENTIA.

Autism

According to the Centers for Disease Control and Prevention (CDC) Autism Spectrum Disorder (ASD) now affects 1 in 54 children; in the year 2000 it was 1 in 150. It is a developmental condition characterized by impaired communication and obsessive behavior.

A study published in 2017 looked at 172 children with ASD and 61 controls. The authors showed statistically significant differences comparing mycotoxin antibody levels

between the two children groups, with the ASD group having more elevated levels of mycotoxin antibodies.[8] In a subsequent study of ASD, these researchers linked ASD to ochratoxin A.[9]

Another 2018 study from Tufts University School of Medicine found evidence implicating mycotoxins in the pathogenesis of ASD. The effects of mycotoxins were via different pathways and included the secretion of pro-inflammatory cytokines from mast cells.[10] Their conclusion was: "…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." A follow up publication by the same institution in 2019 reconfirmed these findings.[11]

Alzheimer's Disease

On the other end of the spectrum of life we have Alzheimer's Disease (AD). In a 2016 study, Dr. Dale Bredesen found 3 subtypes of AD: type 1 (inflammatory), type 2 (non-inflammatory or atrophic), and type 3 (cortical). He reported that type 3 Alzheimer's disease can be due as the result of exposure to mycotoxins.[12]

Another study published in 2017 looked at why Finland has the highest dementia mortality rate in the world. The authors looked at environmental factors and linked a climate that is both very cold and humid resulting in housing frequently harboring molds that are capable of producing neurotoxic mycotoxins.[13]

In a 2009 study, the mycotoxin ochratoxin A (OTA), which is produced by Aspergillus and Penicillium subspecies, the authors found that OTA induced apoptosis that was accompanied by a loss of mitochondria membrane potential. This indicated that OTA is neurotoxic at relatively low concentrations and may contribute to the pathogenesis of neurodegenerative diseases (e.g. Alzheimer's and Parkinson's disease) in which apoptotic processes are centrally involved.[14] In 2014, von Tobel et al. demonstrated that the neuroinflammatory response results in demyelination, axonal instabilities, and astrocyte disturbances resulting in neurodegenerative disorders.[15] Park et al. published a study in 2019 showing how ochratoxin A exerts neurotoxicity through anti-proliferation and mitochondria-dependent apoptosis in human astrocytes.[16]

Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)

Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease (MND) in adults and is also known as Lou Gehrig's disease. The well-known scientist at Cambridge University, Dr. Stephen Hawking who recently died suffered from this disease. It is a progressive and fatal disease and approximately 90% cases of ALS are sporadic, with 5-10% due to genetic mutations. A 2019 review of ALS looked at exposure of neurons to mycotoxins. They showed how these mycotoxins elicits a significant increase in glutamate production which stimulate TDP-43 translocation and modification, providing a link between mycotoxins and one of the molecular and histologic hallmarks of sporadic ALS.[17] This is another disease of the brain linked to exposure to mycotoxins.

Multiple Sclerosis

Multiple sclerosis (MS) is one of the most frequent and severe demyelinating neurological diseases, mainly affecting young people, eventually leading to their becoming disabled. It is 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. A 2010 study from Rutgers Medical School showed how a coherent relationship can be made between multiple sclerosis and mycotoxins. This study stated: "We propose here that fungal toxins are the underlying cause of multiple sclerosis and thus may offer an avenue towards an effective cure."[18] Several studies have previously shown that mycotoxin exposure leads to neural antibodies and as myelin degrades it triggers the onset of multiple sclerosis and its associated symptoms. A 1998 publication showed in both in vivo and in vitro that the mycotoxin gliotoxin causes demyelination leading to MS.[19]

DEMYELINATION IN THE BRAIN AND PERIPHERAL NERVOUS SYSTEM

There are numerous publications demonstrating that the effects of mycotoxin as measured in serum as antibodies that result in the formation of antibodies to neural tissues bringing about demyelinating diseases. Mycotoxins have been shown to cause demyelination of sensory or motor neurons or both in a number of studies. Furthermore, mycotoxins antibodies can form covalent protein adducts in vitro and in vivo that cause inflammation of the brain such as trichothecene mycotoxins.[20] This was demonstrated in a study of 119 patients exposed to molds and mycotoxins and in which all tested positive to mycotoxins antibodies.[21] The study concluded: "All groups (119) showed significantly increased autoantibodies titers for all iso-types (IgA, IgM, IgG) of antibodies to neural antigens when compared with 500 healthy controls."

Another study concluded that satratoxin antibodies form adducts in both in vitro experiments and in vivo in humans and animals.[22] A case study in a home with water damage showed the development of Chronic Inflammatory Demyelinating Polyneuropathy in the two inhabitants.[23] Patients can also develop demyelinating optic neuritis from exposure to molds and mycotoxins.[24]

THE BLOOD BRAIN BARRIER

Mycotoxins can alter the blood brain barrier. The cytotoxic effects of the trichothecene mycotoxin T-2 toxin are already well described in the medical and scientific literature with apoptosis being a major mechanism of action. A recent publication states: "T-2 toxin can cross the blood-brain barrier and accumulate in the central nervous system (CNS) to cause neurotoxicity.[25] A study investigated the effects of T-2 on the blood-brain barrier (BBB). Besides

strong cytotoxic effects on the BBB as determined by the CCK-8 assay, impairment of the barrier function starting at low nanomolar concentrations were observed for T-2 toxin, clearly indicating the ability of T-2 toxin to enter the brain via the BBB.[26]

A study looked at the mycotoxin deoxynivalenol (DON), which is produced by Fusarium fungi. The authors investigated and compared the effects of DON on the blood-brain barrier and found that DON reduced the barrier integrity and caused cytotoxic effects at very low concentrations.[27] A more recent publication from 2018 looked at the mycotoxin gliotoxin (GTX) produced by Aspergillus and Penicillium fungi on the BBB using brain microvascular endothelial cells (BMECs). In both acute (2 h) and prolonged (24 h) exposure to GTX at low concentrations compromised BMECs monolayer integrity and altered the blood-brain barrier integrity.[28] Lastly, there is a good review of the blood-brain barrier in a 2016 publication.[29]

Testing: Blood Serum Antibodies to Mycotoxins

The testing to detect mycotoxins in the body for any patient exhibiting symptoms or having been given a diagnosis of the diseases and disorders above is by serum antibody testing.

Blood serum testing for mycotoxin antibodies using the ELISA method have been used for more than 20 years and are highly accurate and, just as importantly, are validated tests used in research and by clinical laboratories. It is the gold standard of laboratory testing. The specificity and sensitivity of blood serum testing for the presence of IgG and IgE antibodies to mycotoxins are of the highest degree. There are a number of publications that review mycotoxin antibodies in the diagnosis of patients affected by molds and their mycotoxins.[30-32] Very importantly, when there are mycotoxin antibodies in the blood, these can form adducts and bind to human tissue, triggering autoimmunity.[33] There are over 100 autoimmune diseases, affecting approximately 10% of the world's population; some are calling it an epidemic, as genetic predisposition accounts for only 30% of all autoimmune diseases, while 70% are due to environmental factors, including exposure to mycotoxins.[34] Furthermore, antibodies to mycotoxins also give the clinician the added information of body burden. All of the mycotoxins mentioned that affect the brain in this article are available for blood serum antibody testing.

According to the National Institute for Occupational Safety and Health (NIOSH), a part of the Centers for Disease Control and Prevention (CDC), low levels of mycotoxins are found in many foods in parts-per-billion. For that reason, they are routinely present in the urine of healthy people. Therefore, mycotoxin metabolites in urine testing does not mean that the person is suffering from any disease or disorder related to molds or mycotoxins; it does not indicate pathology. The most important point is that if you have mycotoxins in urine it is a good thing: the body is doing its job of getting rid of mycotoxins from foods and beverages. Furthermore, some mycotoxins cannot be measured in urine, such as ochratoxin. Almost all, 99.8%, of the ochratoxin in the body is very tightly bound to the body's main protein, albumin, so it cannot be excreted through the kidneys. It is reabsorbed from any part of the nephron by both active and passive transport and by passive diffusion.[35] Lastly, the CDC (Centers for Disease Control and Prevention) states that urine testing for mycotoxins is an unvalidated test and should not be used for diagnostic purposes in clinical medicine.[36] (*Altern Ther Health Med.* 2020;26(6):8-11).

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AUTHOR DISCLOSURE STATEMENT

Dr. Campbell is the medical director of Mymycolab.

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