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Case Series

Surgical and Medical Management of Mycotoxin Neurotoxicity and Neuropsychological Symptoms via Endoscopic Sinusotomies and Cyclone Antifungal Irrigation

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Abstract

Objective: Neurological and neurocognitive symptoms are commonly seen in chronic rhinosinusitis patients. This case series details significant health improvements in 3 patients with rhinosinusitis and multiple neurological, neuropsychiatric, and neurocognitive deficits.

Method: Three patients, a 40-year-old woman, a 39-year-old man, and a 40-year-old woman exposed to high levels of mold in their individual homes presented with chronic sinus problems and many significant neurological symptoms including hearing loss, tinnitus, suicidal depression, anxiety, chronic fatigue, muscle weakness, cognitive dysfunction, and poor concentration. High indoor mold levels were confirmed by testing for all 3 patients. All 3 also had significant levels of mycotoxins in their urine and nasal mucosal tissue. All 3 also had abnormal brain QEEG's.

Results: All 3 patients' nasal/sinus symptoms cleared and neurological symptoms improved following endoscopic sinus surgery with cyclone antifungal irrigation, neurotherapy, reduction of indoor environmental mold/bacteria exposure, and correction of hormonal and nutritional deficiencies.

Conclusion: Indoor exposure to mold, mycotoxins, microbial volatile organic compounds (MVOC's), bacteria and other bioaerosols are underestimated causes of chronic illness, sinusitis and nasal symptoms, neurological, cognitive, and psychological disorders and other symptoms. Physicians need to test for and rule out mold exposure as a cause to these symptom clusters with urine mycotoxin levels and indoor environmental mold and mycotoxin tests. Many chronic illnesses associated with the previously reported symptoms can often be resolved with outpatient sinus surgery with cyclone antifungal irrigation, reduction of indoor mold exposure, and appropriate medical, hormonal, and nutritional treatments.

INTRODUCTION

Fungal exposure is common in rhinosinusitis patients with one study reporting 94 out of 101 (93%) consecutive CRS surgical patients being diagnosed with fungal CRS. CRS is diagnosed by a number of means including: 1) nasal polyps, 2) allergic mucin, 3) computed tomography (CT) scans consistent with CRS (considered the "Gold Standard" of CRS diagnosis) [1] , 4) positive fungal nasal histology or culture, and 5) type 1 hypersensitivity [2]. Many patients without sinusitis or positive sinus CT scans can have mycotoxicosis and require functional endoscopic sinus surgery (FEES) with antifungal cyclone irrigation to remove it. Many researchers believe that fungal CRS is severely underdiagnosed for several reasons including the fact that CT scans and microbiology are often not done on suspected fungal CRS patients. Additionally, isolating and culturing nasal fungi is extremely difficult, and CT scans are often negative in fungal CRS patients [1,3]. One study reported that CT scans were negative in 50 of a group of 125 (40%) consecutive fungal CRS patients [1]. "Most" CRS patients are being exposed to mycotoxins but not all have sinus-specific symptoms.

Mycotoxins are common in foodstuffs and the environment. Foodborne and indoor molds produce at least several hundred mycotoxins which have a broad range of neurotoxic, immunotoxic, and irritant/inflammatory effects [4]. More than 100 published studies have reported that low-to-moderate levels of many mycotoxins including aflatoxins, ochratoxins, fumonisins, zearalenone, and trichothecenes such as deoxynivalenol are found in human blood, urine, and breast milk [5]. A number of animal in vivo and human and animal cell culture studies have reported that many common mycotoxins are able to readily pass through the blood-brain barrier and or damage the integrity of the blood-brain barrier [6-16]. Exposure to mycotoxins from common

indoor molds has also been shown to severely damage the nasal mucosa. Exposure to satratoxin G from the common indoor mold Stachybotrys induced brain inflammation and olfactory sensory neuron loss in the noses of mice [17] and rhinitis and apoptosis of the olfactory sensory neurons in Rhesus Monkeys [18].

Heavy exposure to indoor molds is associated with many health problems. More than a hundred studies have reported that heavy exposure to indoor molds and their allergens and mycotoxins can cause a wide range of adverse health effects [19-21], especially asthma [21,22], sinusitis [3,22,23], chronic fatigue [24-28], neurological/ neuropsychiatric problems [26,29,30] and hormonal deficiencies [28]. A meta-analysis of 31 indoor air studies reported that visible mold (EE 1.82, 95 % CI 1.56-2.12) and mold odor (EE 2.18, 95 CI 1.76-2.71) were related to significantly greater risk of the development of rhinitis/ sinusitis [24]. A large neurobehavioral study of 105 adults with documented heavy indoor mold exposure reported that the study subjects experienced many significant neurological deficits including delayed reaction time, blink latency, decreased color discrimination, and memory; as compared to 100 unexposed controls (p=0.0001 for many neuropsychiatric test comparisons) [29]. Dennis et al described a group of 79 patients with a history of documented indoor mold exposure, rhinitis, chronic fatigue, and endocrine problems including 81% with hypothyroidism and 51% with growth hormone deficiency [28]. A 2020 summary of 114 worldwide epidemiological studies of indoor mold exposure conducted between 2011-2018 reported that 112 studies (98.2%) showed that indoor mold exposure was associated with a significantly greater rate of adverse health effects [21].

Other bioaerosols besides molds are frequently seen in water-damaged indoor environments. Nine types of bio contaminants from microbial growth are present in water-damaged indoor environments: 1) Indicator fungi, 2) Gram negative and gram positive bacteria, 3) microbial nano-sized and larger particulates, 4) mycotoxins, 5) VOCS (microbial and non-microbial), 6) allergens, 7) endotoxins (LPS) and bacterial exotoxins, 8) Galactomannans, and 9) 1,3-beta D-Glucans [31].

In addition to producing solid mycotoxins which typically are several hundred Daltons in size, molds and bacteria produce over 200 volatile organic compounds (VOCs), many with distinctive odors that account for the mustiness often smelled in damp buildings [32,33]. Exposure to those MVOC's can cause health symptoms like asthma, rhinitis, and eczema [34-36].

Mycotoxins can be found in significant quantities in the nasal mucosa from inhalation. A Texas study reported that measurement levels of the following mycotoxins were found in nasal secretions and sputa for the following mycotoxins: 6 out of 47 (13%) were positive for aflatoxins, 1 out of 26 (4%) for ochratoxins, and 24 out of 63 (38%) for trichothecenes [37]. Case studies have been presented of 3 patients exposed to water-damaged indoor environments who had measurable levels of mycotoxins in their urine or nasal mucosa [38,39]. These 3 patients all improved following endoscopic sinus surgeries, reductions in indoor mold exposure, and treatment with oral/ nasal/ or nebulized antifungal drugs [38,39] and neurotherapy.

Environmental and medical management of mold-related sinus problems can often produce considerable improvement in patients' symptoms. Resolution of rhinosinusitis was seen in 93% (41 of 45) of the Dennis patients reported above who were also able to lower their indoor mold concentrations and who received treatment with nasal saline irrigations, antifungal and antibiotic sprays, and appropriate hormone replacement and nutritional supplements [28].

CASE SERIES

This case series involves three patients who developed chronic sinusitis along with a wide range of neurotoxic, neuropsychiatric and other adverse symptoms related to growth of fungi in their nasal passages. All three patients experienced significant improvement for their multi-system health problems following endoscopic sinus surgery, cyclone (Stryker) antifungal irrigation, and various medical and nutritional treatments along with the reduction of indoor mold exposure and neurotherapy.

PROCEDURE

All three patients had standard FEES surgery on all eight sinuses with generous sinusotomies. Frontal sinusotomies were done with either a balloon or standard FEES depending on degree of pathology. After FEES all sinuses were irrigated with either Amphotericin-B (100 mg/l) or Voriconazole (412 mg/l) with the Cyclone (Stryker) sinus irrigation device using 2, 60 ml syringes for each sinus. All sinuses were irrigated beginning with frontal sinuses followed by maxillary, sphenoid, and ethmoid sinuses. All fluid was suctioned during irrigation to prevent recirculation of mycotoxins.

Patient 1

The first patient is a 40-year-old female who was exposed to heavy indoor mold levels in her home as well as organic chemicals at work. She had a wide range of chronic health problems including chronic nasal blockages, chronic fatigue, problems with concentration, memory loss, anxiety/depression/ irritability, muscle weakness, shortness of breath, skin rashes, and gastrointestinal bloating/diarrhea/gas. She was unable to get off the floor unassisted and could only crawl. When exposed to mold she gets tremors, veins enlarge in her head, and she has pain from her toes to her knees. Her weight dropped from 101 to 87 pounds at 5'1" tall. She was taking Fluconazole 100 mg once daily, nystatin twice daily (500,000 units BID), probiotics and 2.0 grams of magnesium daily.

Her urinary mycotoxin levels were 19.5 ppb ochratoxin (N=<7.5) and citrinin 51.24 ppb (N= <25). An environmental study of her water-damaged home was relatively unremarkable with spore trap testing showing total fungal spores at 507 per cubic meter in her bedroom on 8/16/16.

The CT scan on figure 1 showed bilateral ethmoid opacification, mucosal thickening of the left maxillary sinus, and mucosal thickening of the left posterior sphenoid. Following sinus surgery, her neurocognitive symptoms improved within 3 days. Her total symptom improvement is reported in Table 1.

A summary of the patients' before and after health conditions and subjective health symptoms is reported in Table 1 below.

Table 1: Before Surgical/ Medical Treatment and After Health Symptoms- 0= Healthy 10= Severe Symptoms.

Health Conditions	Patient 1 40 yo ♀		Patient 2 39 yo ♂		Patient #3 40 yo ♀	
	Before	After	Before	After	Before	After
Post Nasal Drip	10	0	10	0	10	2
Energy Level	10	1			10	1
Abdominal Pain	10	4				
Headaches			5	0		
Food Allergy	10	2				
ADHD	10	2	8	5		
Constipation	10	6	0	0		
Diarrhea	10	6	5	2		
Bloating/ Gas	10	6	10	2	4	2
Leaky Gut	10	4	10	2		
Gluten Sensitivity	10	4	10	5		
Gastritis/ Colitis	10	4				
Hyperactivity	10	2	10	5		
Memory Loss/ Concentration	10	2	10	5	8(memory)-9(concentr)	3
Chest Tightness	6	0				
Insomnia	10	1			10	0
Anxiety/ Depression	10	1	10	3	10 (suicidal)	1 (depr) 5 (anxiety)
Skin Rashes/ Psoriasis	10	6				
Eczema/ Hives/ Urticaria	10	4			0	0
Tremors/ Seizures	10	2				
Digital Scale 0 = normal/ healthy and 10 severe.						

The second patient is a 39-year-old male who became ill after exposure to a heavily mold-contaminated house as well as a contaminated CPAP machine. He also had a wide range of chronic health problems including chronic nasal blockage, significant loss of memory/concentration, anxiety/ depression, bloating/ gas, and problems with vision, hearing, tinnitus, and the ability to smell. Before the exposure, he was a powerlifter/bodybuilder, but prior to surgery had lost 20 pounds of muscle and strength, down to 190 pounds. His house had water-intrusion problems with high levels of toxic mold. He had several psychologically traumatic events following the water events in his house. His physician found protozoan and suspected Lyme disease. Another doctor gave him IV nutritional support—amino acids, phosphatidylcholine, and glutathione.

Very high levels of mold were reported in the home of patient # 2 on 3/4/19. Very high mold levels were reported in his office area including-FR South Wall 22,869,330 spores /m^3, FR East Wall 2,149,370 spores/m^3 lower west wall 887.979 spores/m^3, and DR south lower wall 102,620 spores/m^3.

Urinary mycotoxin levels were on 2-28-18, Aflatoxin B 12.96 ppb (N= <0.5), ochratoxin ppb 7.98, (N= <7.5) on 3-26-18 Zearalenone 2.1 ppb(N= <3.2) Roridin 4.17 ppb (N= 0.2), and 3-13-18 Verrucarin A 1.33 ppb, (N= < 1.4).

Patient received CitriDrops Dietary Supplement, amphotericin nebulization (Amphotericin-B 3 mg in 30 ml sterile water with 0.25 mg dexamethasone), Fluconazole (100 mg QD for 30 days), and nystatin (500,000 units tab 1 BID for 60 days), VSL #3 (1 packet BID for 60 or more days, a probiotic containing 450 Billion CFU by VSL Pharmaceuticals). Intramax liquid multivitamin (1 oz qd-415 vitamins, minerals, amino acids, ,vegetables, probiotics, digestive enzymes, all bound to organic carbon for intracellular release and detoxification), Zeobind 500mg 1-3 QD (clinoptilolite, a crystalline Aluminosilicate to bind toxins), oxygen 100%, 8-10 L/min with face mask 1-2 h/day, Acetyl Glutathione 300 mg Bid, Homotaurine 50 mg Bid, Phosphatidylserine 200 mg Bid, Pro DHA 480 mg QD, and Brain Octane 1 TBS QD (MCT medium chain fatty acids). The health improvements of patient 2 before and after treatment is summarized in Table 1. CT scans of patient 2 are presented in Figure 3 below (Figures 1-4).

The third patient is a 41-year-old female. She experienced chronic nasal blockage, chronic fatigue, bloating/gas, significant loss of concentration, muscle and joint pain/fibromyalgia, rashes/hives, memory loss, severe suicidal depression and anxiety, and experienced constant pressure on top of head. The patient experienced severe migratory myalgia's 3 months following birth of 3rd child in June 2017. She was exposed to mold and had very high urinary mycotoxin levels. Urinary mycotoxin levels were 31.71 ppb for Ochratoxin a (N= <7.5) and Gliotoxin levels of 47,320.1 ppb (N= 200). Ethmoid sinus mucosa contained Aflatoxin B 0.479 ppb and Ochratoxin A 0.919 ppb.

Patient had history of flooding in her home and could smell mold. Environmental testing in her home revealed water damage in the basement and high levels of Chaetomium (842 spores per cubic meter as compared to a criteria level of 32 spores per cubic meter.). Chaetomium is a water-loving mold that produces mycotoxins and is found mostly in water damaged environments [40].

Patient experienced severe suicidal depression and anxiety. She had been treated with little benefit with psychotherapy including Dialectical behavior therapy (DBT) and Cognitive

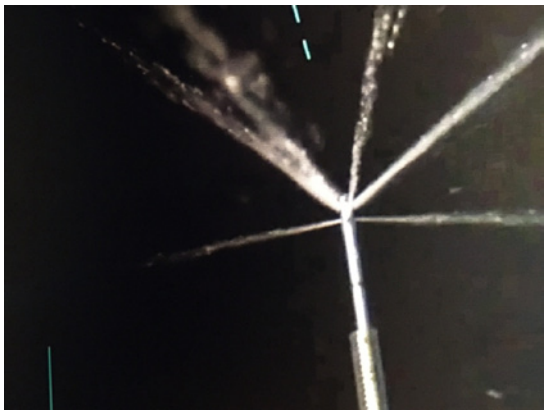
Behavioral Therapy (CBT), 18 ECT electroconvulsive therapy sessions, plus many drugs including Antidepressants: 1. Escitalopram 20 mg QD, 2. Prozac, 3. Zoloft, 4. Trintellix, 5. Effexor, 6 Amitriptyline 150 mg. Benzodiazepines: 1.Lorazepam and 2. Klonopin, Anti-Psychotics- 1. Abilify. Depression completely resolved and anxiety was 80% improved post surgery. The patients' improvement of symptoms is summarized in Table 1 and a CT nasal scan is presented in Figure 4.

See: post op audio link on Patient 3 here:

https://www.dropbox.com/s/zdplxj61cpyqk0k/bAudio%20.mp4?dl=0

Cyclone Endoscopic Surgery video:

https://www.dropbox.com/s/f7ydjcf9768zoqs/21%20Cyclone%20Entellus%202.mp4?dl=0



Stryker Cyclone

QEEG BEFORE AND AFTERWARDS

Patient1

Chief complaint was anxiety, OCD, brain fog, problems with sustained attention and focus and hypersensitivity to perceived exposure to mold and allergens (whether actually exposed or not) (Figure 5A and Figure 5B).

Patient 2

Chief complaint was anxiety, short-term memory loss, brain fog, problems with sustained attention and focus (Figure 6A and 6B).

Patient 2 J Neurotherapy results:

Chief complaint upon beginning neurofeedback therapy was anxiety, OCD, issues with short-term memory and ADD. Patient noted some neurological problems, such as occasional numbness and limited use of right extremities.

Brain maps indicated slightly elevated tempero-posterior Delta 1.5-4 Hz), indicating possible TBI/Concussion, reduced Alpha (8-12Hz) indicating issues with anxiety and depression, and decreased Beta ((12-20 Hz) indicating attentional problems. Hibeta (20-40 Hz) was elevated temporally, indicating muscle tension/jaw clenching. Hyper-Coherence was noted in Delta.

Upon completing 30 sessions of neurofeedback the client reported a significant reduction in anxiety and depression, as well as improved focus and memory. Increased strength in right extremities was also reported.

Brain maps indicated significant reduction in Delta (both amplitude and coherence) which reflects the client's improvement in focus and memory. An increase in Alpha likely contributed to the improvement in anxiety and depression. Increase in Beta contributes to improved attention [41].

Patient 3

Chief Complaint: Suicidal Depression, anxiety, brain fog, short-term memory loss, issues with emotional regulation and sustained focus.

Excessive coherence tends to indicate two or more areas of the brain being overly connected or locked together, too rigid. The brain is not efficiently processing and executing information, resulting in poor day-to-day performance. Client may experience a range of symptoms from over-arousal (hyperactivity and agitation) to under-arousal (daydreaming and "spacey") (Figure 7A and 7B).

EO 3 (Post-Neuro) shows normal coherence in Delta and

Figure 1 Patient 1. Sinus CT Scan and ethmoid mucosa showing mycotoxins in brown halo around the tissue in an SDA agar plate.

Figure 2 Patient 1 before and 3 days after Voriconazole Cyclone irrigation of all sinuses.

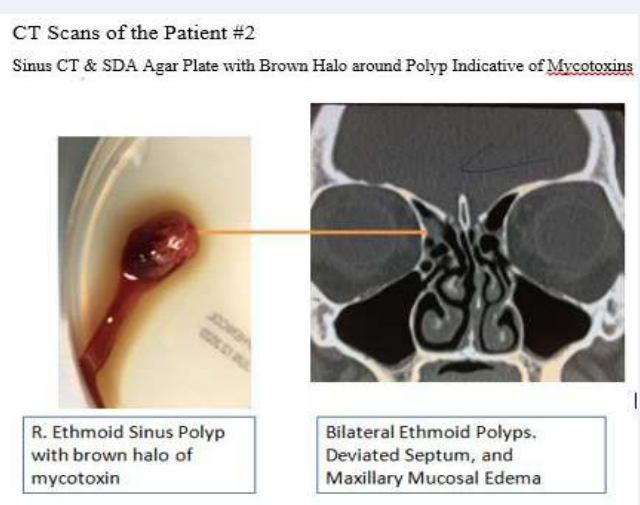


Figure 3 Patient 2. CT Scans of the Patient #2. Sinus CT & SDA Agar Plate with Brown Halo around Polyp Indicative of Mycotoxins.
Video link of patient post op.
https://www.dropbox.com/s/nwjpygslkif026e/J%20video%20PO.MOV?dl=0

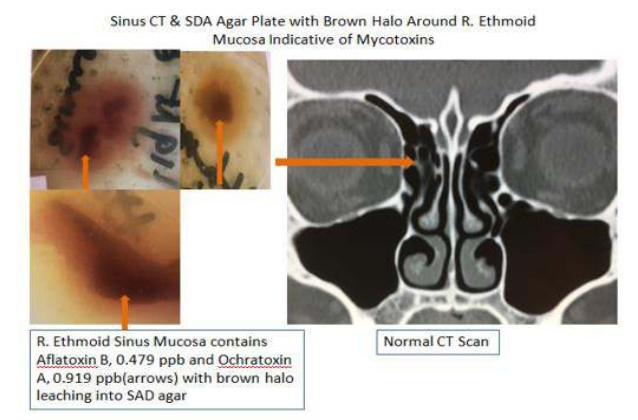


Figure 4 A Sinus CT scan of patient 3 is presented Above.

Theta connections which resulted in the client experiencing improved attention, focus and processing. It was noted that, after neurotherapy sessions, the client was able to carry on coherent and focused conversations where it had been difficult to follow along before beginning therapy.

(Significant muscle tension artifact was noted at left temporo-posterior, which commonly reflects in Beta and hibeta as seen in figure 7C).

DISCUSSION

Mold, mycotoxin, MVOC's and bacteria are unrecognized triggers for nasal and associated neurological problems. When patients are in a toxic, moldy environment, known or unknown, they are breathing approximately 2,904 gal. of air per day consisting of a soup of mold spores (which produce more mycotoxins), mycotoxins, MVOCs, bacteria, and other toxins [31]. These toxins readily pass the blood-brain barrier and quickly communicate with the brain in real time (like sniffing glue). Thus, when the urine is positive for mycotoxins from breathing mycotoxins in the air, the concentration of mycotoxins in the sinus mucosa becomes high, forcing these neurotoxic chemicals into the brain. Functional endoscopic sinus surgery (FESS) using cyclone irrigation/suction of all 8 sinuses with an antifungal (Amphotericin-B or Voriconazole) can safely remove mucosal toxins, preventing, them from entering the brain to cause multi-system disruption, thus yielding dramatic improvement of systemic, neurological, and psychiatric symptoms. Just as ceasing glue sniffing resolves the intoxication symptoms and allows the brain to heal, removing the mycotoxins from the sinus mucosa ceases the ongoing release of mycotoxins in the body and allows the patient to heal and to respond better to all other interventions.

The Cyclone irrigator (Stryker ENT) technology is the key to successful removal of the toxins from the mucosa because of the dual antifungal irrigation and simultaneous suction, so the toxins cannot reabsorb into adjacent mucosa. Some patients have obvious sinus CT pathology while others may have a negative sinus CT scan but have positive urine for mycotoxins. Thus, the connection may be made that the highest mycotoxin concentration is in the sinus mucosa [38,39] and severe neurological and/or neuropsychiatric symptoms will improve with this therapeutic approach as it prevents the mycotoxins in the sinuses from continuing to cross the blood-brain barrier

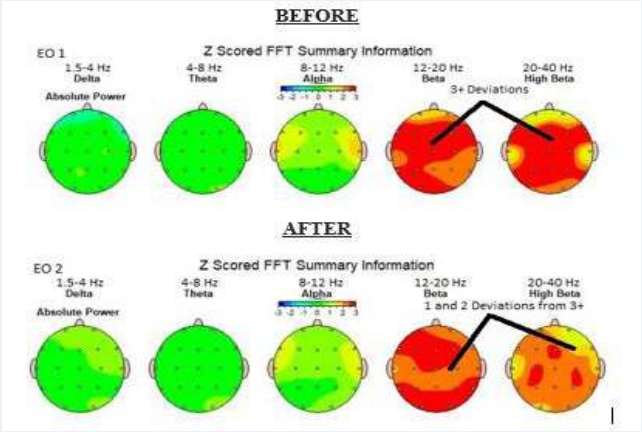


Figure 5 5A: EO 1 Above shows a summary of 3+ deviations in Beta and Hibeta in the intake brain map.
Findings: Significantly elevated Beta and Hibeta (fight or flight) brainwaves (12-20 and 20-40 Hz) of 3+ deviations indicating anxiety, ADD/attentional issues, OCD/rumination, and insomnia.
Primary Training Protocol: Inhibit Beta 20-24 Hz with EO at F3/F4-FZ/CZ.
Note Improvement at Black pointers below from 3+ to 2 or less (Best score is yellow to green)
Figure 5B. EO 2 shows a reduction in deviations from 3+ to 2 or less deviations over a significant area in both Beta and Hibeta
Primary Training Protocol: Inhibit Beta 20-24 Hz with EO at F3/F4-FZ/CZ.
Findings: Reduced Beta and Hibeta (fight or flight) brainwaves (12+20 and 20-40 Hz) indicate a reduction in anxiety, attention and sleep disruptions.
Patient reported feeling calmer, happier, and more focused, as well as having no significant reactions to known allergens or short-term mold exposure during and after completing the program.42

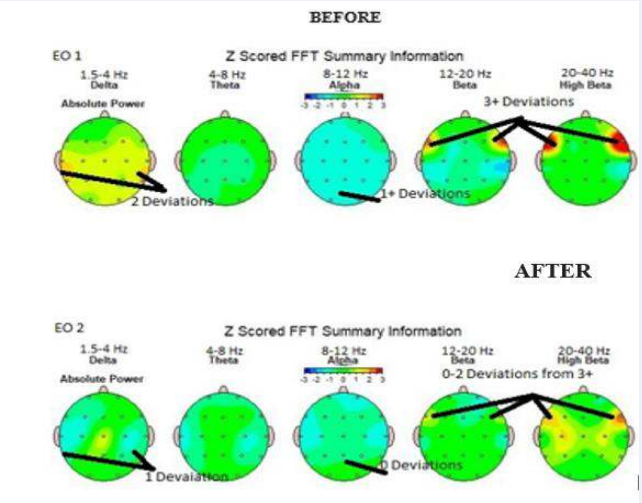


Figure 6 AEO 1 shows a summary of 2 deviations in Delta and 3+ Deviations in Beta and Hibeta in the intake brain map. Alpha showed a negative 1 deviation.

Findings: Elevated tempero-posterior Delta (1.5-4 Hz) indicating possible TBI/ABI or concussion, learning disability, emotional processing, and list acquisition problems. Elevated Beta and Hibeta (fight or flight) brainwaves (12-20 and 20-40 Hz) of 3+ deviations indicating anxiety, ADD/attentional issues, OCD/rumination, and insomnia. Reduced posterior Alpha (8-12 Hz) can indicate depression and traumatic stress.

Primary Training Protocol: Alpha/Theta training with EC.

EO 2 Black pointers shows a reduction in deviations from 2 to1 in Delta, 1 to 0 in Alpha and 3+ to 2 or less deviations in both Beta and Hibeta.

Findings: Improved deviations in Delta (1.5-4 Hz) indicates improved ability to learn and process new information. Decreased Beta and Hibeta (fight or flight) brainwaves (12+20 and 20-40 Hz) indicate a reduction in anxiety, improved attention and less sleep disruptions. Increased Alpha (8-12 Hz) from negative 1 deviation to 0 can indicate improved overall mood.

Patient reported feeling more relaxed and significantly less depressed, as well as having more focus and improved short-term memory for the first time in many years.

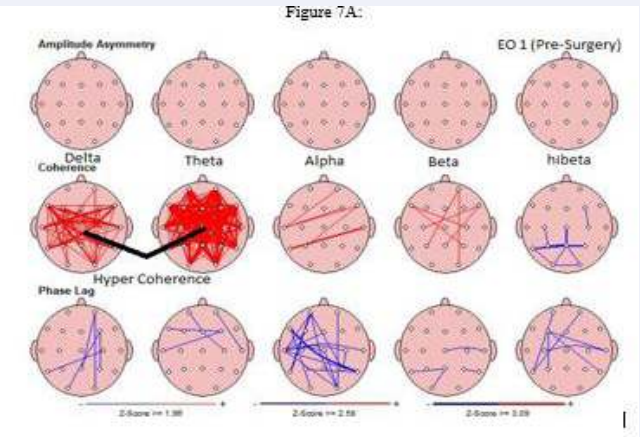


Figure 7a EO 1 (Pre-Surgery) shows hyper coherence in Delta and Theta connections. Excessive coherence tends to indicate two or more areas of the brain being overly connected or locked together, too rigid. The brain is not efficiently processing and executing information. resulting in poor day-to-day performance. Client may experience a range of symptoms from over-arousal (hyperactivity and agitation) to under-arousal (daydreaming and "spacey").

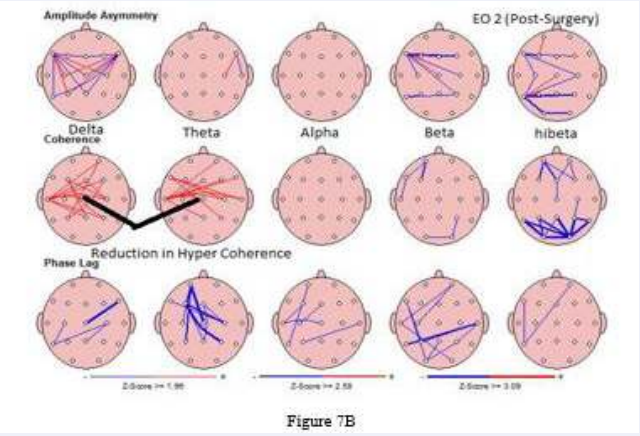


Figure 7b EO 2 (Post-Surgery) shows a reduction in hyper coherence in Delta and Theta connections from the previous brain map.

A reduction in hyper coherence in Delta and Theta connections can result in the client experiencing less agitation and brain fog, more sustained focus and better processing [42].

Patient reported a 95% reduction in treatment resistant suicidal depression after surgery.

to influence mood, cognition, behavior, hormones, and more. QEEG is key in identifying brain damage that does not respond to surgical and conventional medical therapy. Neuropsychiatric symptoms such as OCD, and rumination are physiologic reactions that can be caused by continuous exposure to mycotoxins secreted in the sinus mucosa from previous mold and/or chemical environment exposures. This is often seen in patients where the symptoms remain, but the environment is clear such that the person continues to discard belongings and continues to move to another environment, but not improve. Neurotherapy is effective in these patients if they complete the course and receive appropriate counseling.

The chief items that lead to treatment failure include remaining in a moldy indoor environment or other toxic environment, having gut overgrowth of Candida promoted by antibiotics, steroids, or a diet rich in sugar and other refined carbohydrates, or failure to address hormonal deficiencies [28].

Pituitary damage is also very common in mold-exposed patients. Most often we see deficiencies in thyroid, cortisol, and growth hormone. In our previous study we found 51% (40/79) of mold-exposed patients were Growth Hormone deficient. Primary or secondary hypothyroidism in T3 and/or T4 was seen in 81% (64/79) of patients; 75% (59/79) had adrenocorticotrophic hormone (ACTH) deficiency [29]. Failure to identify and correct these deficiencies results recovery failure, so informed endocrine consult is helpful. Most of these patients experience optimal health when hormone levels are in middle- to high-normal range.

Remediation of indoor environments is helpful in some, but not all, cases. A 2015 meta-analysis of 12 published studies reported that professional remediation of mold- and water-

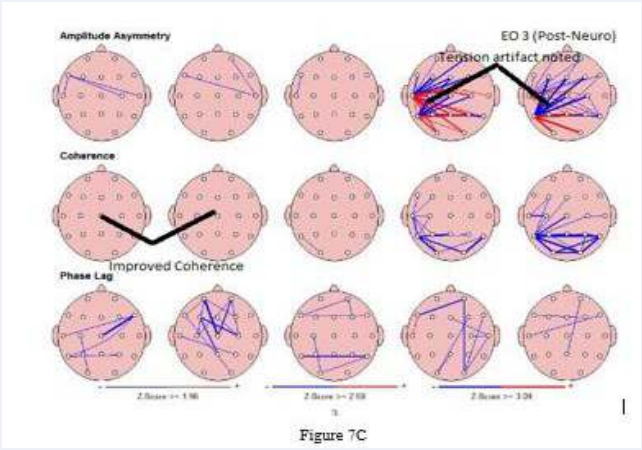


Figure 7c EO 3 (Post-Neuro) shows normal coherence in Delta and Theta connections which resulted in the client experiencing improved attention, focus and processing. It was noted that, after neurotherapy sessions, the client was able to carry on coherent and focused conversations where it had been difficult to follow along before beginning therapy.
(Significant muscle tension artifact was noted at left temporo-posterior, which commonly reflects in Beta and hibeta as seen in figure 7C).

damaged homes was associated with significant reductions in wheezing (OR 0.64, 95% CI 0.55-0.75) and rhinitis symptoms (OR 0.57, 95 % CI 0.49-0.66) [42]. However, in sinusitis patients with severe neuropsychiatric symptoms, we find that detailed professional environmental remediation most often fails due to the fact that they are breathing into their nose 2,904 gallons of contaminated air per day and the patients genetically cannot excrete the toxins at a normal rate. Thus, they are already overloaded with toxins, are hypersensitive to them, and the fungal spores in their sinuses are manufacturing more mycotoxins and MVOCs. Mycotoxins (which often travel on sub-spore particles smaller than 0.3 μm [43]) and MVOCs can penetrate all surfaces, sheetrock, wood, furniture etc. and therefore re-expose an already sick person to more toxins. The continuous and often unavoidable mycotoxin exposure causes treatment failure. A delay in moving can exacerbate the symptoms and waste critical time and resources. Getting into a safe place, meaning a place in which the patients knows they are improving and not bringing items from the contaminated space with them into the safe space is the single most important item for recovery [44].

Earlier research has reported that surgical or medical treatment of chronic rhinosinusitis is associated with significant improvements of many types of cognitive and neuropsychiatric function as measured by quality of life, disease burden, and cognitive failure instruments [45,46].

The mechanisms by which surgical and medical treatment may improve cognitive and neuropsychiatric conditions are not entirely clear, but may be related to significantly reducing the toxic, allergenic, and inflammatory burden in the body, so that the effects of environmental mold and mycotoxins, as well as bacteria and other bioaerosols found in moldy environments [32] are not so overwhelming to the body.

In summary, ENT physicians need to be aware that indoor exposure to mold, mycotoxins, bacteria and other bioaerosols is a major cause of both nasal problems and associated neurological, neuropsychiatric, and neurocognitive problems. Proper surgery and medical care, along with reduction in environmental exposures, and nutritional hormonal replacement can produce dramatic symptom improvements in mold-exposed patients.

REFERENCES

1. Ferguson BJ, Narita M, Yu VL, Wagener MM, Gwaltney JM, Jr. Prospective observational study of chronic rhinosinusitis: environmental triggers and antibiotic implications. Clin Infect Dis. 2012; 54: 62-68.
2. Bent JP 3rd, Kuhn FA. Diagnosis of allergic fungal sinusitis. Otolaryngol Head Neck Surg. 1994; 111: 580-588.
3. Ponikau JU, Sherris DA, Kern EB, Homburger HA, Frigas E, Gaffey TA, et al. The diagnosis and incidence of allergic fungal sinusitis. Mayo Clin Proc. 1999; 74: 877-884.
4. Brase S, Encinas A, Keck J, Nising CF. Chemistry and biology of mycotoxins and related fungal metabolites. Chem Rev. 2009; 109: 3903-3990.
5. Fromme H, Gareis M, Volkel W, Gottschalk C. Overall internal exposure to mycotoxins and their occurrence in occupational and residential settings--An overview. Int J Hyg Environ Health. 2016; 219: 143-165.
6. Alonso-Garrido M, Tedeschi P, Maietti A, Font G, Marchetti N, Manyes L. Mitochondrial transcriptional study of the effect of aflatoxins, enniatins and carotenoids in vitro in a blood brain barrier model. Food Chem Toxicol. 2020; 137: 111077.
7. Baldissera MD, Souza CF, Zeppenfeld CC, Descovi SN, Moreira KLS, da Rocha MIUM, et al. Aflatoxin B1-contaminated diet disrupts the blood-brain barrier and affects fish behavior: Involvement of neurotransmitters in brain synaptosomes. Environ Toxicol Pharmacol. 2018; 60: 45-51.
8. Patel R, Hossain MA, German N, Al-Ahmad AJ. Gliotoxin penetrates and impairs the integrity of the human blood-brain barrier in vitro. Mycotoxin Res. 2018; 34: 257-268.
9. Park S, Lim W, You S, Song G. Ochratoxin A exerts neurotoxicity in human astrocytes through mitochondria-dependent apoptosis and intracellular calcium overload. Toxicol Lett. 2019; 313: 42-49.
10. Behrens M, Huwel S, Galla HJ, Humpf HU. Blood-Brain Barrier Effects of the Fusarium Mycotoxins Deoxynivalenol, 3 Acetyldeoxynivalenol, and Moniliformin and Their Transfer to the Brain. PLoS One. 2015; 10: e0143640.
11. Guo P, Liu A, Huang D. Brain symptoms damage and neurological induced by T-2 toxin in rat brain. Toxicol Lett. 2018; 286: 96-107.
12. Weidner M, Huwel S, Ebert F, Schwerdtle T, Galla HJ, Humpf HU. Influence of T-2 and HT-2 toxin on the blood-brain barrier in vitro: new experimental hints for neurotoxic effects. PLoS One. 2013; 8: e60484.
13. Ravindran J, Agrawal M, Gupta N, Rao PV. Alteration of blood brain barrier permeability by T-2 toxin: Role of MMP-9 and inflammatory cytokines. Toxicology. 2011; 280: 44-52.
14. Krug I, Behrens M, Esselen M, Humpf HU. Transport of enniatin B and enniatin B1 across the blood-brain barrier and hints for neurotoxic effects in cerebral cells. PLoS One. 2018; 13: e0197406.
15. Taevernier L, Bracke N, Veryser L, et al. Blood-brain barrier transport kinetics of the cyclic depsipeptide mycotoxins beauvericin and enniatins. Toxicol Lett. 2016; 258: 175-184.

16. Karunasena E, Larranaga MD, Simoni JS, Douglas DR, Straus DC. Building-associated neurological damage modeled in human cells: a mechanism of neurotoxic effects by exposure to mycotoxins in the indoor environment. Mycopathologia. 2010; 170: 377-390.

17. Islam Z, Harkema JR, Pestka JJ. Satratoxin G from the black mold Stachybotrys chartarum evokes olfactory sensory neuron loss and inflammation in the murine nose and brain. Environ Health Perspect. 2006; 114: 1099-1107.

18. Carey SA, Plopper CG, Hyde DM, Islam Z, Pestka JJ, Harkema JR. Satratoxin-G from the black mold Stachybotrys chartarum induces rhinitis and apoptosis of olfactory sensory neurons in the nasal airways of rhesus monkeys. Toxicol Pathol. 2012; 40: 887-898.

19. Curtis L, Lieberman AD, Rea W, Stark M, Vetter M. Adverse human health effects of indoor molds. Journal of Nutritional and Environmental Medicine. 2004; 14: 261-274.

20. Hope J. A review of the mechanism of injury and treatment approaches for illness resulting from exposure to water-damaged buildings, mold, and mycotoxins. Scientific World Journal. 2013; 2013: 767482.

21. Dooley M. MSW. A Comprehensive Review of Mold Research Literature From 2011-2018. Internal Medicine Review. 2020; 6: 1-39.

22. Quansah R, Jaakkola MS, Hugg TT, Heikkinen SA, Jaakkola JJ. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. PLoS One. 2012; 7: e47526.

23. Jaakkola MS, Quansah R, Hugg TT, Heikkinen SA, Jaakkola JJ. Association of indoor dampness and molds with rhinitis risk: a systematic review and meta-analysis. J Allergy Clin Immunol. 2013; 132: 1099-1110 e1018.

24. Brewer JH, Thrasher JD, Straus DC, Madison RA, Hooper D. Detection of mycotoxins in patients with chronic fatigue syndrome. Toxins. 2013; 5: 605-617.

25. Zhang X, Norback D, Fan Q, Bai X, Li T, Zhang Y, et al. Dampness and mold in homes across China: Associations with rhinitis, ocular, throat and dermal symptoms, headache and fatigue among adults. Indoor air. 2019; 29: 30-42.

26. Hyvonen S, Poussa T, Lohi J, Tuuminen T. High prevalence of neurological sequelae and multiple chemical sensitivity among occupants of a Finnish police station damaged by dampness microbiota. Arch Environ Occup Health. 2020: 1-7.

27. Hyvonen S, Syrjala H. Asthma Case Cluster during Renovation of a Water-Damaged and Toxic Building. Microorganisms. 2019; 7.

28. Dennis D, Robertson D, Curtis L, Black J. Fungal exposure endocrinopathy in sinusitis with growth hormone deficiency: Dennis-Robertson syndrome. Toxicol Ind Health. 2009; 25: 669-680.

29. Kilburn KH. Neurobehavioral and pulmonary impairment in 105 adults with indoor exposure to molds compared to 100 exposed to chemicals. Toxicol Ind Health. 2009; 25: 681-692.

30. Hyvonen SLJ, Tuumien T. Moist and Mold Exposure is Associated with High Prevalance of Neurological Symptoms and MCS in a Finnish Workers Cohort. Saf Health Work. 2020; 11: 173-177.

31. Thrasher JD, Crawley S. The biocontaminants and complexity of damp indoor spaces: more than what meets the eyes. Toxicol Ind Health. 2009; 25: 583-615.

32. Korpi A, Jarnberg J, Pasanen AL. Microbial volatile organic compounds. Crit Rev Toxicol. 2009; 39: 139-193.

33. Inamdar AA, Morath S, Bennett JW. Fungal Volatile Organic Compounds: More than Just a Funky Smell? Annual review of microbiology. 2020; 74: 101-116.

34. Kim JL, Elfman L, Mi Y, Wieslander G, Smedje G, Norback D. Indoor molds, bacteria, microbial volatile organic compounds and plasticizers in schools--associations with asthma and respiratory symptoms in pupils. Indoor air. 2006; 17: 153-163.

35. Araki A, Kanazawa A, Kawai T, Eitaki Y, Morimoto K, Nakayama K, et al. The relationship between exposure to microbial volatile organic compound and allergy prevalence in single-family homes. The Science of the total environment. 2012; 423: 18-26.

36. Choi H, Schmidbauer N, Bornehag CG. Volatile organic compounds of possible microbial origin and their risks on childhood asthma and allergies within damp homes. Environ Int. 2017; 98: 143-151.

37. Hooper DG, Bolton VE, Guilford FT, Straus DC. Mycotoxin detection in human samples from patients exposed to environmental molds. Int J Mol Sci. 2009; 10: 1465-1475.

38. Dennis D, Thrasher J. Nasal Fungal Pathology and Trichothcenes Associated with Water-Damaged School and House. Austin Journal of Otolaryngology. 2016; 3: 1072.

39. Dennis D, Thrasher J. Surgical and managment of sinus mucosal and systematic mycotoxicosis. Otolaryngol Reconstructive Surgery. 2017; 3: 111-117.

40. Samson RA HJ, Thrane U, Frisvad JC, Andersen B. Food and Indoor Fungi. Utecht, The Netherlands: CBS- KNAW Fungal Biodiversity Centre; 2010.

41. Crago BR, Gray MR, Nelson LA, Davis M, Arnold L, Thrasher JD. Psychological, neuropsychological, and electrocortical effects of mixed mold exposure. Arch Environ Health. 2003; 58: 452-463.

42. Sauni R, Verbeek JH, Uitti J, Jauhiainen M, Kreiss K, Sigsgaard T. Remediating buildings damaged by dampness and mould for preventing or reducing respiratory tract symptoms, infections and asthma. Cochrane Database Syst Rev. 2015; 2015: Cd007897.

43. Brasel TL, Douglas DR, Wilson SC, Straus DC. Detection of airborne Stachybotrys chartarum macrocyclic trichothecene mycotoxins on particulates smaller than conidia. Appl Environ Microbiol. 2005; 71: 114-122.

44. Rea WJ. A Large Case-series of Successful Treatment of Patients Exposed to Mold and Mycotoxin. Clin Ther. 2018; 40: 889-893.

45. Rowan NR, Schlosser RJ, Storck KA, Ganjaei KG, Soler ZM. The impact of medical therapy on cognitive dysfunction in chronic rhinosinusitis. International forum of allergy & rhinology. 2019; 9: 738-745.

46. Alt JA, Mace JC, Smith TL, Soler ZM. Endoscopic sinus surgery improves cognitive dysfunction in patients with chronic rhinosinusitis. International forum of allergy & rhinology. 2016; 6: 1264-1272.

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