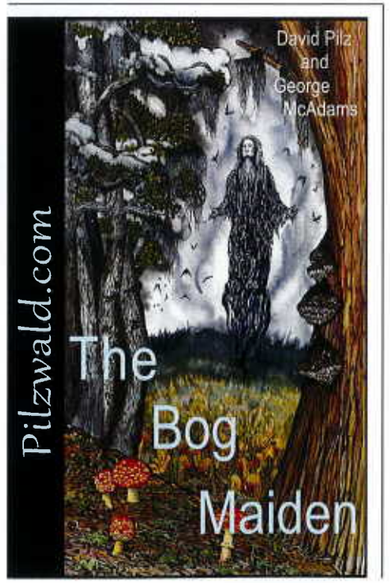
Neurodegeneration and Medicinal Mushrooms

Robert Dale Rogers

Even if all the experts agree,
they may well be mistaken.
- Bertrand Russell

First, the bad news

Neurodegenerative conditions are estimated to affect some 90 million people, of the 65+ age group, by the year 2050. (Acosta and Wortmann, 2009). I personally observed my own mother's suffering through a half decade of declining cognitive ability, possibly related to Alzheimer's disease (AD). Incidence of Parkinson's disease (PD), multiple sclerosis, myasthenia gravis and numerous other auto-immune conditions are dramatically on the rise.



There is a strongly established correlation between widely used anticholinergic drugs and dementia. This means that medicines taken by millions of people for depression, asthma, and allergies may be affecting brain metabolism and atrophy (Risacher et al., 2016). Antihistamines, anti-depressants, cardiovascular medications, heartburn medications, anti-Parkinson's drugs, muscle relaxants, motion sickness remedies, and medications for urinary incontinence are some of the more than one hundred over-the-counter and prescription drugs that work in this way. The study looked at the brains of 451 men and women, with 60 taking one or more anticholinergic medicines. Researchers found those taking one of the medicines "were four times more likely to develop either mild cognitive impairment or dementia," than those not taking these medicines, according to lead author Dr. Shannon Risacher. This followed an earlier retrospective cohort study by Cai et al. (2013), which looked at long-term use of anticholinergic drugs in 3,690 older adults, and found a significant correlation with cognitive impairment and dementia. Over 800 developed dementia, and if the drugs were taken for three years or more, there was a 54% higher dementia risk than taking them for three months.

Benzodiazepine use has also been linked to AD. A team of researchers in France and Quebec looked at nearly 2,000 men and women over 65 diagnosed with AD. They then randomly selected 7,000 others without AD, who were matched for age and sex, and then looked at drug prescriptions for five to six years before diagnosis. Those taking drugs such as Ativan, Serex, Xanax, Elavil, Serzone, Halcion and other anti-anxiety / anti-depression / insomnia medications for three to six months had a 32% greater risk, and those taking one for more than six months had an 84% greater risk than those who took none. This makes sense when you remember that these medications block the transmission of acetylcholine or boost GABA (gamma-aminobutyric acid) in the brain.

People aged 75 years or older, and using proto pump inhibitors (PPIs), have a 44% greater risk of developing dementia including AD (Gomm et al., 2016). This was a seven-year study involving 74,000 participants.

An earlier study by Akter et al. (2015) examined cognitive effects of short term use in 60, otherwise healthy, young adults, aged 20-26 years. Six groups received a different PPI or placebo for seven days. All the drug groups had a statistically and clinically significant impairment in cognitive function. In just one week! Imagine the implications for long-term use.

Several medicinal mushrooms appear beneficial for brain health, in some early *in vivo* and preliminary human clinical trials.

But here's the good news

Lion's mane mushroom (*Hericium erinaceus*) has been studied for its possible benefit in the treatment of brain and nerve-related conditions (Wong et al., 2012; Mori et al., 2009) and is showing promise. The ability of small molecules to cross the blood brain barrier and induce production of nerve growth factor is indeed, an exciting possibility for further research.

It is important to note that oven-dried *Hericium* products lose the ability to stimulate neurite outgrowth (Wong et al., 2007). I now recommend this mushroom

Hericium erinaceus
courtesy Jan Hammond.

Ganoderma tsugae, courtesy David Work.

be freeze-dried, or juiced and frozen, rather than tinctured. This suggests its future use as a regularly ingested functional food.

Funding for the research of natural products derived from mushrooms has been extremely difficult to access, due in large part to an inability to receive patent protection, and gain market share in the mono-molecular world of pharmaceuticals.

Ganoderma lucidum has been reported to encourage neurite growth and improve neuronal health benefits. Reishi extracts contain neuro-active compounds that induce neuronal differentiation and prevent apoptosis (self-programmed death) of cells, albeit in a rat study (Cheung et al., 2000).

Work by Phan et al., (2013) found water extracts of reishi, *Lignosus rhinoceros* , *Grifola frondosa*, and ethanol extracts of *Cordyceps militaris* significantly promote brain neurite growth, and may be useful for brain and cognitive health. Both reishi and hen of the woods (*G. frondosa*) water extracts have been shown to promote nerve growth factor in work by Ling-Sing et al. (2013).

Even the inedible bitter hedgehog (*Sarcodon scabrosus*) contains cyathane diterpenoids called scabronines, that showed neurite outgrowth in a study by Obara et al. (1999).

All of this is interesting and worthy research. But perhaps the answer to the large increase in chronic neuro-degenerative disease, lies in roles played by our immune system and inflammation. There are at present, no pharmaceutical drugs that will improve immune response and reduce inflammation at the same time. That is, cortisone reduces inflammation but suppresses the immune system.

Auto-immune conditions respond well to medicinal mushrooms due to their ability to up-regulate the immune system when deficient, or down-regulate whenever there is inflammation and destruction of tissue. The optimizing of immune function and reduction of inflammation in the body may be the key to longevity and increased quality of life. And hence the interest in medicinal mushrooms.

A new book by Michal Schwartz (2015), *Neuroimmunity*, explores the relationship between the immune system and the brain. She published an earlier paper that proposed immune cells keep the brain healthy, and how they do it. Not that many years ago, scientists believed that immune cells were kept out of the brain. Early studies into multiple sclerosis looked at how immune cells attack nerve tissue. But maybe we have been looking at it all wrong. Her work suggests that immune cells control formation of the brain's stem cells, shape cognitive performance and affect our mood and ability to cope with stress. This all happens at a special border of the brain, so that when called upon, the immune cells assist via molecules delivered to the brain, or by controlled entry to help repair the damaged or diseased brain.

Sir Frank Macfarlane Burnet was awarded a Nobel Prize in 1960 for his work on auto-immune cells. Since that time, scientists have considered such cells to be associated with auto-immune disease, but such is not the case. In fact, these cells are not only harmless, but are essential for generation of new nerve cells and the preservative of learning and memory.

Michal Schwartz calls these "the immune cells of wisdom." Her team found that immune cells communicate with the brain from a site located at the border between the brain and circulating blood. This is a thick layer of epithelial cells called the choroid plexus. This area controls the access of immune cells to the brain tissue when called upon. It filters our blood of compounds needed to keep the brain healthy, and creates cerebrospinal fluid. In fact, it was thought for decades that its only role was for the production of this fluid. Immune cells interact with a healthy brain without actually entering the tissue, but under certain conditions this site acts as a gate that selects and shapes the immune cells that enter the brain. The blood brain barrier remains sealed to immune cells under all conditions and if by-passed, may result in pathological inflammation. In turn chronic inflammation is cited and treated with immune suppressing drugs. Physiological inflammation, if not resolved, can lead to pathological inflammation, so practitioners try to shut down this response. But this denies the diseased brain the immune assistance it needs from the blood.

The creation of inflammation in the body is connected to heat, pain and discomfort. Acute inflammation, such as the raising of body temperature to fight a viral, bacterial or fungal infection, is a natural process. In fact, it is the body's only mechanism of dealing with invasive pathogens. The Russian biologist Élie Metchnikoff emphasized, against the common wisdom of the day, the benefits of inflammation in fighting pathogens, repairing tissue and maintaining a healthy body. A variety of over the counter and prescription drugs are widely available to individuals wishing to suppress this condition.

But there is a cost. By continuing to suppress the ability of body tissue to throw off toxins, more chronic states of inflammation later result. As the body attempts to move from a chronic state to an acute state and restored homeostasis, there is fever, pain, and inflammation.

By supporting the body through this period of time, the acute state will abide and the body continues its natural state of well-being and balance.

It is the pathway of disease and healing crisis which I teach to my herbal students at our college. But if these symptoms are

suppressed, the vicious cycle continues. This is why anti-inflammatory drugs fail to treat neurodegenerative disorders.

Tens of millions of people take sleep medications with acetaminophen on a nightly basis. The OTC sales of anti-inflammatory drugs is staggering. In 2015, a total of 2.9 billion retail trips were made to purchase over the counter drugs. The average US consumer makes 26 trips a year to purchase OTC products, and yet visit their physician only three times per year. Acetaminophen is the most commonly used children's medication for reducing fever and pain. Benadryl, Dimetapp and Palgic, for allergies and colds contain anticholinergics. Twenty three percent of American adults use acetaminophen in any given week (Kaufman et al., 2002). Some epidemiological and laboratory studies suggest NSAIDs (non-steroidal anti-inflammatory drugs) reduce the risk of AD, by lowering levels of inflammation. Work by Szekely et al. (2008) found acetominophen and ibuprofen did not lower the risk of dementia or AD.

Using a drug that indiscriminately shuts down your immune response, reduces the physiological inflammation required for healing. Stronger anti-inflammatory medications reduce this body inflammation, but at the cost of suppressing the choroid plexus and its interaction between the immune system and the brain.

Medicinal mushrooms, on the other hand, reduce inflammation in the body and at the same time optimize our immune response (immune modulation). Yet another reason to add medicinal mushrooms to your dietary and supplement regime.

References Cited

Acosta, D., and M. Wortmann. 2009. World Alzheimer Report. In: *Alzheimer's Disease International.* Prince M. J. Jackson (Eds). London pp.1-92.

Akter, S., M.R. Hassian, M. Shahriar, et al. 2015. Cognitive impact after short-term exposure to different proton pump inhibitors: assessment using CANTAB software. *Alzheimer's Research and Therapy* 7: 79.

Cai, X., N. Campbell, B. Khan, C. Callahan, and M. Boustani. 2013. Long-term anticholinergic use and the aging brain. *Alzheimer's and Dementia* 9: 377-385.

Cheung, W.M., W.S. Hu, P.W. Chu, S.W. Chiu, and N.Y. Ip. 2000. Ganoderma extract activates MAP kinases and induces neuronal differentiation in rat pheochromocytoma PC12 cells. *FEBS Letters* 486: 291-296.

Gomm, W., K. von Holt, F. Thome, et al. 2016. Association of proton pump inhibitors with risk of dementia: A pharmacoepidemiological claims data analysis. *Journal of the American Medical Association Neurology* 73(4): 410-416.

Kaufman, D.W., J.P. Kelly, L. Rosenberg, et al. 2002. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *Journal of the American Medical Association* 287: 337-344.

Ling-Sing, S.S., M. Naidu, P. David, K.H. Wong, and V. Sabaratnam. 2013. Potentiation of neuritogenic activity of medicinal mushrooms in rat pheochromocytoma cells. *BMC Complementary and Alternative Medicine* 13(157): 13-15.

Mori, K., S. Inatom, K. Ouchi, Y. Azumi, S. Kinugasa, S. Inatomi, et al. 2009. Improving effects of the mushroom Yamabushitake (*Hericium erinaceus*) on mild cognitive impairment: A double-blind, placebo-controlled clinical trial. *Phytotherapy Research* 23: 367-372.

Obara, Y., N. Nakahata, T. Kita, Y. Takaya, H. Kobayashi, S. Hosoi, et al. 1999. Stimulation of neurotropic factor secretion from 1321N1 human astrocytoma cells by novel diterpenoids, scabronines A and G. *European Journal of Pharmacology* 370: 79-84.

Phan, C.W., P. David, M. Naidu, K.H. Wong, and V. Sabaratnam. 2013. Neurite outgrowth stimulatory effects of culinary-medicinal mushrooms and their toxicity assessment using differentiating Neuro-2a and embryonic fibroblast BALB/3T3. *BMC Complementary and Alternative Medicine.* 13: 261.

Risacher, S.L., B.C. McDonald, and E.F. Tallman. 2016. Association between anticholinergic medication use and cognition, brain metabolism, and brain atrophy in cognitively normal older adults. *Journal of the American Medical Association Neurology* 73(6): 721-732.

Schwartz, M. 2015. *Neuroimmunity.* Yale University Press. New Haven and London.

Szekely, C.A., J.C.S. Breitner, A.L. Fitzpatrick, T.D. Rea, B.M. Psaty, L.H. Kuller, and P.P. Zandi. 2008. NSAID use and dementia risk in the cardiovascular health study: Role of APOE and NSAID type. *Neurology* 70(1): 17-24.

Wong, K.H., S. Vikineswary, M. Naidu, and R. Keynes. 2007. Activity of aqueous extracts of Lion's Mane mushroom *Hericium erinaceus* on the neural cell line NG108-15. *International Journal of Medicinal Mushrooms* 9: 57-65.

Wong, K.H., M. Naidu, P. David, R. Bakar, and S.Vikineswary. 2012. Neuroregenerative potential of Lion's Mane mushroom, *Hericium erinaceus*, in the treatment of peripheral nerve injury (Review). *International Journal of Medicinal Mushrooms* 14: 427-446.

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Prayer for the Great Shroom

Gratitude to Fungi

Gift to the clans
from the powers below ground
The de-composers
Breaking down
strings of amino acids
& fatty woodwind arpeggios

Composting dead trees into
creekside
kettledrums. Orchestrating
the grand wheeling
kiva crescendo of
singing
cycling & recycling

Sparked by nature's
spore plugs of regeneration
Edulis
Cibarius
Esculenta

Polypores. Puffballs
Stinkhoms. Earthstars
Corals & Clubs
[Antiphonal]
[Bard:]
In our hearts, minds
stomachs & synapses
so be it...
[The Assembled]
So be it!

And gratitude to the Fungophiles
The Salzmans
Lincoffs
Andrew Weil
Paul Stamets & Dusty Yee
Corbin. Klite. Norris
The Gillmans & the Adamses

Tie-dye locals & suit&tie regulars
And to all us pot-hunting
mountain crazies
jonesing for another foray

Throwbacks to an earlier dawn
Of earth dancers
Soil singers

Not Homo sapiens but Humus
ludens
Hunting & gathering once again
on Lizard Head slopes
& in Sheep Mountain forests
encircling
To-Hell-u-Ride

Playful mud men & mud wymyn
getting down dirty to
dig up stipes

Or
cross-species dressing up
to parade down Colorado Ave.

Swearing fealty
to the sacred
Shroom

[Antiphonal]
[Bard:]
In our hearts, minds
stomachs & synapses
so be it...
[The Assembled]
So be it!

Honor the goddess in all her
guises
Be she healing tonic
gourmet treat or
amatoxin hell
for those who pick without respect

And may we all experience
(if just once)
the whiz-bang
berserker inebriation of
amanita muscaria

Yes!
We love Mushrooms!

So raise high the galactic
roofbeam
Sasha. Terence.
Dolores LaChapelle

& let us enter
the flavor of xerampolina
The aroma of matsutaki
The ling chi tea of Chinese
longevity

Let us bioassay
(at least once)
& join in praise of all entheogens
but particularly cubensis

Entangling us in the power
the glory & the mycelial
warp of black holes
dark matter & death's mystery

[Antiphonal]
[Bard:]
In our hearts, minds
stomachs & synapses
so be it...
[The Assembled]
So be it!

Art Goodtimesw