Why should we care about demyelination?

This post is a summary of two recent posts:

- *Good News/Bad News about Multiple sclerosis Research* (7/26/2018)
- *Demyelination, continued*. (7/28/2018)

Why Care about Demyelination?

We need to care about demyelination as a society because it may be a factor underlying many conditions that have been occurring at increasing rates. The high cost of health care is not just due to the cost of individual medications or the price of hospitalization but is due to the additive cost of increased numbers of individuals needing care. Autism care alone is estimated to likely reach $500 billion by 2025 for care in the U.S. alone, (link), demyelination or disordered myelin formation is thought to be involved. Our food supply may provide calories but it may no longer be supporting health due to imbalance in some nutrients and lack of sufficient amounts of other nutrients – in addition to personal choices for some people leaning toward convenient and tasty foods that provide very few nutrients besides calories.

The other reason to care about demyelination as a society is because the early symptoms can occur for years without clear reasons and may disrupt relationships or the ability to hold a job – personality changes including anxiety and anger, paranoia and a short temper – problems with impulse control and the ability to follow through on planned actions or with communication and the ability to tell the truth instead of substituting other statements that may seem illogical and obviously far from the truth. Problems with impulse control and a tendency toward mood problems may also include an increased risk for suicide or self injury or violence towards others. Gun control is important but self control is also important. A forensic psychiatrist discusses the increased problem with knife violence in the U.K. and how strategies to control knives has helped reduce risk – he suggests kitchen knives should be made with blunt tips. (link) What will be next? No loose stones allowed in the world? We can not provide everyone with a suit of bubble wrap or take away everyone's car keys.

Addition: nothing against the forensic psychiatrist trying to increase safety however as someone who has had first hand experience with self harm problems and lived to tell the tail – controlling the urges is the most important strategy because there are many ways to harm oneself or others. At my worst I did hide the kitchen knives and I didn't

travel on my own because I didn't trust myself around tall bridges. We can not bubble wrap the world or coat it in knife resistant mesh or put everyone in a suit of armor, but we could distribute food supplies more evenly and waste less and we could work towards more effective preventative health care strategies instead of medicating symptoms and not addressing the underlying causes of mental and physical ill health – they are frequently connected.

Neurologists are busy people. With my variety of health symptoms and unidentified problems I have seen one – once. I was left with the impression that since I wasn't dragging one foot when I walked and slurring my speech I had completely wasted his time with my slight issues. I've had that impression though from a few specialists and my lasting impression of specialists is try to avoid them. The co-pays and appointment time adds up and the special tests add more time and co-pays and are not focused on preventative care – they are focused on the very sick in their specialty and preventative care requires attention to slight changes before they get to the point of being very sick, very severe symptoms. So my lasting impression was – if the lab tests say normal, I do not want to find out what really sick feels like – and that I have to figure out how to get back to my own understanding of normal health on my own. Fortunately I have the help of the internet and all of the medical research and other material available online. *Specialists are very important – and busy. I did receive an answer to one question I had for the neurologist and it helped lead me to more information online which did help me improve my health so he got a paycheck and I did get better health – fair deal.

The medical research is complex and hasn't put all the loose threads together yet, so I will summarize my summary points in a more concise list and combine them with the work of the other summary article:

Strategies to help prevent the breakdown of myelin or help promote regeneration of myelin:

1. Vitamin B1, thiamin deficiency, chronic, severe – Wernicke's encephalopathy may be more of a risk for severe alcoholics and people with anorexia – severe lack of appetite or the eating disorder anorexia nervosa.
2. Vitamin B12 deficiency – may be more of a risk for people with low stomach acidity, due to older age or chronic use of calcium type antacids; or due to genetic reasons limiting production of Intrinsic Factor; or due to a vegan diet without supplementation of vitamin B12 or inclusion of Nutritional yeast flakes in the diet.

3. Zinc deficiency (22) or copper excess (link).
4. Adequate but not excessive lithium may increase myelin production. (22)
5. Adequate but not excessive iron intake is needed for production of myelin.
6. Magnesium deficiency or poor intestinal absorption of magnesium, or lack of adequate protein and phospholipids in the diet for the body to be able to store magnesium in the normal manner within the intracellular fluid.
7. Inadequate calcium or vitamin D can be a factor but excessive intake of either can also be a factor in cell breakdown and risk of demyelination. If taking vitamin D as a supplement the vitamin D3 form may be most bioactive and taking vitamin K2 with it may help with myelin production (22) and protect against osteoporosis. Green leafy vegetables are good sources of vitamin K.
8. Adequate intake of cholesterol is needed as a building block for our own production of vitamin D and other steroid hormones and as a building block for myelin. (22) Pregnenolone is a steroid hormone precursor that may benefit some people when used as a supplement. It and other steroid hormones are involved in signaling increased production of myelin. Testosterone insufficiency may also negatively affect myelin production. (22)
9. Excessive intake of free glutamate or aspartate – excitatory amino acids that are commonly used as flavoring or sweetening agents in foods or may occur naturally in fermented foods or alcoholic beverages.
10. Adequate protein is needed to support a variety of body functions in addition to supporting magnesium levels. Uridine is a nucleotide base (part of DNA that is a combination of a type of sugar and an amino acid) that is also is involved in energy metabolism, fasting occasionally may increase our own production (more info). Insufficient amounts may negatively affect myelin production and use as a supplement may help some people. (22)
11. Insufficient calories to provide the body enough glucose to support mitochondrial health. They can use protein or fats for energy but it shifts the metabolism more towards oxidative stress.
12. Occasional fasting and/or a low carbohydrate diet may help promote autophagy due to increased use of ketones for energy (22) but may cause health problems due to excess oxidative stress or an increased burden of nitrogen waste removal for the kidneys when followed long term.
13. Lack of antioxidants due to lack of Nrf2 within the body to promote our own production of antioxidants internally; and/or lack of antioxidants within the diet, including vitamin C, (22), would decrease our ability to detoxify the reactive oxidative chemicals produced during normal metabolism or which are produced at increased rates when protein or fats are being used for energy instead of glucose.

14. Use of the herb ashwagandha or Gingko biloba (22) may help protect against oxidative stress and protect against demyelination by promoting Nrf2. (ashwagandha & Nrf2) (an overview of Nrf2 metabolism, its potential benefits for conditions such as Multiple sclerosis, and Gingko biloba and pomegranate are mentioned as promoters of Nrf2: nutricology/newsletter, see first article) (other Nrf2 promoting phytonutrients/foods and menu ideas: G10: Nrf2 Promoting Foods.) Flavonoids are one of the groups of phytonutrients that helps promote Nrf2; and also may help protect myelin production. (22) Medicinal mushrooms, including Hericium Erinaceus, Lion's Mane Mushroom,(22), may also help protect myelin production and prevent breakdown by reducing oxidative stress (link) and promoting Nrf2. (link)
15. Having a healthy balance of omega 3 fatty acids and omega 6 fatty acids in the diet helps reduce risk of inflammation/oxidative stress and also helps us build healthy membranes which are necessary to control flow of minerals and other chemicals from the exterior to interior of cells and organelles such as the mitochondria.
16. Inadequate iodine for healthy thyroid hormone production, (22); may be a combined problem of excess presence of bromide, fluoride and perchlorate in the diet or environment.
17. Lack of oxygen due to poor air quality, or smoking, or health problems causing inadequate breathing function. Emotional or physical stress may also increase the need for oxygen or increase the tendency to hold our breath; *Take ten deep breaths and think before you speak* is good advice for any emotionally stressful situation because oxygen is needed to think rationally and we tend to hold our breath when we are upset.
18. Avoid extreme physical and emotional stress.
19. Avoid toxins.
20. Get adequate sleep at night, and a brief nap during the day may be beneficial for some people. Melatonin helps promote myelin production and inadequate sleep and having lights on at night can disrupt our production of melatonin. (22)
21. Adequate exercise (22) and stretching regularly helps move nutrients throughout the body and remove toxins in the lymphatic fluid for further detoxification and eventual removal from the body.
22. Wear a helmet for any activity that may cause head trauma and avoid sports which may cause frequent closed head trauma and especially when helmets are not used (sorry soccer, football, hockey, (link), and boxing fans).
23. Adequate phospholipid and other phosphonutrients or cannabinoids may be necessary to include from external sources if genetic differences or other health problems or age interferes with the body's internal production capability. Dark

cocoa products, cardamom powder, pomegranate and pumpkin seeds are a few legal dietary sources.

24. Use of ibuprofen and/or ginger (approximately 1/2 teaspoon per day) may help prevent breakdown of our body's supply of cannabinoids, breakdown of which may then lead to increased breakdown of cells and may then lead to increased degeneration of myelin.
25. Lack of any B vitamins or genetic differences in the ability to remethylate folate and vitamin B12 may disrupt the ability of mitochondria to generate usable energy from glucose or proteins and fats, and may reduce production of myelin. (22) Inositol and choline may be particularly important for myelin production. They are considered to be in the B vitamin group but was discovered more recently than the numbered series of B vitamins. (22)
26. Low Level Laser Therapy – I am not familiar with this, see #10: (22), but I have read elsewhere that certain types of light can stimulate activity levels. (Haier)
27. Practice, practice, practice – new things. (22) Myelin is produced in response to learning [45] so remaining mentally stimulated with new experiences and learning new topics or techniques keeps signalling the body to produce myelin.
28. Brain-derived Neurotrophic Factor, (BDNF), the brain's growth factor, may help increase production of myelin by increasing production of brain cells, which include oligodendrocytes. (22) Ways to promote BDNF (link, from within 22) fortunately overlap with the strategies for protecting against demyelination already mentioned above or included in the list of Nrf2 promoting foods.
29. Reducing exposure to electromagnetic fields (EMF) – energy leakage from laptops, smartphones, WiFi, televisions, and other strong sources of electicity may help protect against myelin degeneration. (22)

References and more details for some of this information were included in the last two posts:

- *Good News/Bad News about Multiple sclerosis Research* (7/26/2018)
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Good news/Bad news about Multiple sclerosis research

The good news about Multiple sclerosis (MS) research is that there seems to have been a major breakthrough in treatment, the bad news is that research regarding demyelinating disorders which includes MS seems to have slowed down (1) – finding a solution, a medical answer, that isn't politically approved of or one that is able to be easily patent protected may be the reason for the bad news. Finding an answer that you don't like shouldn't mean we stop asking the question. The goal of medical research ideally is to lead to the prevention or cure of chronic illness, not just to create a patent protected high cost medication for the management of chronic illness.

Cannabinoids seem to be the good news treatment for MS, whether as purified extracts of medical marijuana or as the whole product which can contain many cannabinoids and medically active terpenes. An overview published in 2016 regarding the role of cannabinoids in neurology in various types of autoimmune disease: (2). An overview of the role of cannabinoids in neuroinflammatory conditions published in 2008: (3). An opinion article published in 2018 regarding the potential role of cannabidiol (a non-euphoric cannabinoid) to improve mobility for patients with Multiple sclerosis: (4).

What is Multiple sclerosis?

Multiple sclerosis is a chronic condition that seems to be autoimmune in nature where the body is breaking down the protective coating around the branching segments between nerves. The coating is called the myelin sheath and it acts a little like the plastic coating around an extension cord. Myelin on a nerve fiber or plastic on an extension cord keeps the electrical signals on the inside and out of danger of creating sparks elsewhere along the path of the cord or nerve fiber.

What are cannabinoids?

Cannabinoids are directly involved in making strong and flexible cell membranes as they are building blocks that make up portions of the membrane, like bricks in a wall. They can also be signaling chemicals that can be activated when released from the

membrane. Excess calcium inside of a cell can be a signal that causes the release of cannabinoids. Once they are released they break down into their two basic components, phospholipids and a free fatty acid, often arachidonic acid. The problem is two part – 1) both of the components of cannabinoids once they are released from the membrane can become signaling chemicals that can lead to increased inflammation, NSAID pain killers (aspirin, naproxen, ibuprofen helped reduce level of fatigue experienced by MS patients) may help block the negative effects of excess free arachidonic acid (21); 2) if too many bricks are released from the wall, then the wall may no longer function – the plastic coating on the extension cord may allow sparks through that can be a risk for an electrical fire. In the case of Multiple sclerosis the nerve damage and lack of myelin sheathing around nerve fibers causes difficulties with muscle control and the patient may have increasing difficulty walking and doing other normal daily tasks.

Preventing the increased release of cannabinoids from the membrane walls would likely to the best plan for preventing the resulting increase in inflammatory signaling chemicals they form and the reduction in membrane function. The amount of cannabinoids present can cause opposite effects, small or medium amounts can have beneficial effects while large amounts may have significantly different effects. Mitochondria are the main energy production center of the cell, where sugar is turned into a usable form of energy with the chemical shorthand name ATP or ADP. Both are phosphochemicals differing in the number of phosphate groups, adenosine tri-phosphate and adenosine di-phosphate. The amount of calcium within the cell and within the mitochondria may be different and cannabinoid can affect the movement across the mitochondrial membrane and cause differenct effects depending on the amount of calcium in each area and the amount of cannabinoids that are present. It's complicated is the short story. This article goes into a longer but still simplified description of the chemistry. (23)

And part of the point is that having adequate cannabinoids and adequate phosphonutrients and adequate but not excessive calcium are all important for cellular health and the ability to produce energy – and to not be fatigued – excessively tired all of the time. And in order to have adequate calcium but not excessive the cells need adequate magnesium and adequate protein and phosphonutrients in order to hold it ready for use – like taxicabs circling the block ready to discharge magnesium as a free ion when and where it is needed. The topic of magnesium, and the need for protein and phosphonutrients was introduced in a recent post. Magnesium blocks entry of excess calcium from being able to enter the interior of the cell, where it can cause increased release of cannabinoids from their storage positions within the cell membranes.

Ibuprofen, but not other NSAIDs such as naproxen, also help reduce the amount of breakdown of cannabinoids. (pp 82-83, 24)

What are oligodendrocytes?

A type of specialized brain cell called oligodendrocytes are responsible for building or repairing the myelin sheath. Multiple sclerosis involves increased loss of oligodendrocytes. The specialized cells have calcium permeable glutamate receptors and are more susceptible to oxidative stress than average cells so they are particularly at risk for being damaged by ongoing emotional or physical stress or a traumatic brain injury. (6) Sphingomyelin is one of the building blocks of the myelin sheath, (7), and is formed by oligodendrocytes. (8)

The body is complicated and needs many/all of the nutrients for optimal health. More nutrients and other lifestyle issues that may benefit myelin production or increase risk are discussed in a list of tips for regenerating myelin, phosphatidylserine, a phospholipid, is one of the recommendations; other conditions that may include myelin breakdown besides Multiple sclerosis are also mentioned: (22).

Problems with vitamin D availability may also be involved in the body being more prone to autoimmune reactions by the immune system (attack on our own healthy cells instead of only attacking foreign or damaged cells); and on the natural building or repair of the myelin sheath. (5) And just to keep things interesting – iron is important but too much within the oligodendrocytes may increase risk for MS; polyunsaturated fats are also important but their reactivity may increase risk to the oligodendrocytes from oxidative stress; lack of Nrf2 may be involved in the susceptibility to oxidative stress in the development of MS due to damage to the oligodendrocytes; and the oligodendrocytes have an abundance of calcium permeable glutamate receptors so excess glutamate may increase risk of excess calcium entry into the cells which can lead to cell death. (8)

Summary points for protecting oligodendrocytes –

- all nutrients are important, (22), but balance is also important.
- Avoid excess emotional and physical stress if possible.

- Adequate iron is important because the oligodendrocytes need more than average in order to be able to make the myelin sheath. Some patients may have an underlying genetic difference that leads to their needing supplementation of a well absorbed form of iron throughout their life. Genetic screening and individualized metabolic guidance may be needed for optimal treatment of patients with MS as it may have differing causes. A true autoimmune antibody/antigen has not been identified. (10)
- In general however, avoid excess iron (fortified breakfast cereals and meats for example; men and menopausal women who eat large servings of very iron-fortified foods or large servings of iron rich meats can be more at risk for iron overload. Donating blood occasionally can benefit society and may help protect against the risk of iron overload for people who do not menstruate. Food sources of iron and more information about donating blood: (9) Iron overload can be a cancer risk and tends to be more common than iron deficiency in the non-menstruating population.(11))
- and avoid excess free glutamate (frequently used in seasonings and naturally found in fermented products such as soy sauce. It is in many processed foods, (12)).
- Eat a balance of omega 3, (22), and omega 6 polyunsaturated fatty acids.
- Eat plenty of antioxidant rich foods regularly that also include Nrf2 promoting phytonutrients and other phospholipid containing nutrients. Here is some Nrf2 promoting foods and menu ideas: G10: Nrf2 Promoting Foods.
- And cannabinoids or other phospholipid/phosphonutrient containing foods include these, many of which are also Nrf2 promoting foods:

Food Sources of Phospholipids and other phospho-nutrients, a partial list:

Hemp seed kernels and oil; Artemisia turanica/wormwood leaf; amaranth seed; asparagus; avocado fruit or the inner kernel, dried and powdered; beans/legumes; cardamom seeds and powder; carrots; celery stalks and leaves; cocoa beans and cocoa powder, baker's chocolate, dark chocolate and to a lesser amount milk chocolate and chocolate syrup; coconut; cumin seed/powder; fennel seed, flax seed, pine nuts; sesame seeds, pumpkin seed kernels, squash seeds; butternut squash and pumpkin; gingko leaf; grapefruit and orange juice with the pulp; Jerusalem artichoke (this is a root vegetable rather than a green artichoke); lettuce, spinach and mustard leaves and other leafy green vegetables and herbs; nuts/peanuts, cashews, walnuts; oats; okra seeds; onion root, leek leaves, garlic; parsnip root; pomegranate seeds and pomegranate peel extract;rice, white or brown but the bran is the best source; rosemary; sorghum; sweet

potato or yam; buckwheat (a seed botanically that is not wheat and is gluten free); wheat. (G.26)

The current treatments for Multiple sclerosis are very costly, and may not help all patients while also tending to cause negative side effects.

Returning to the original question – why has the ratio of research being published about demyelinating disorders declined since 2013? It is possible that the answer might be that medical marijuana or a recommendation to eat more dark cocoa and beans, nuts, and seeds is not as profitable as the older MS treatments may average $60,000 per year and newer treatments cost 25-60% more than that, (13), which would be an average prescription cost of $75,000-96,000 per year per patient with Multiple sclerosis. Good quality cocoa is expensive but can fit within most grocery budgets. Being a medical marijuana patient might cost around $12,000 per year for a patient using it several times each day. Use of ibuprofen daily might cost a few hundred dollars per year depending on the amount used and whether it was a name brand or off brand. (21) (24) (Note – long term use of ibuprofen may cause intestinal problems, ginger (about 1/2 teaspoon) can be healing for the intestines and help with pain relief as well as ibuprofen and provided better pain relief when used in combination with ibuprofen in a study with arthritis patients. Ginger may be reducing inflammation by reducing the amount of cannabinoid breakdown to free arachidonic acids and preventing transformation into inflammatory eicosanoids. (27))

Efficacy and negative side effects are also worth considering – for that $60,000-96,000/year price tag only half of the patients may gain health benefits while many will experience negative side effects in addition to needing time and copays for office visits to receive some types of treatments. Fewer than half of patients receiving interferon-β treatment were found to benefit medically and many experienced side effects. (13)

The pharmaceutical industry frequently does medical research involving new drug treatments. The use of medical marijuana for the treatment of Multiple sclerosis or other demyelinating disorders is not legal at the Federal level as the herb is still scheduled as a substance with no medical benefit. Private research in states that have legalized medical use could possibly be performed however. Enrolling patients would likely need to be by self selection though, and for comparison purposes an experimental group of patients could be given a phospholipid rich diet plan to follow and a control group of

patients receiving standard pharmaceutical treatments could also be followed to compare health outcomes with the current standard of care.

How many patients have Multiple sclerosis?

More math – there are about 400,000 people in the U.S. with Multiple sclerosis and about 10,000 newly diagnosed patients each year. (14) Averaging the cost of standard treatments to $78,000 per year would mean the 400,000 patients require $31,200,000,000 per year in pharmaceutical care. Thirty one billion dollars would buy a lot of cocoa. The number of patients living with the condition globally is estimated to be around 2.3 million people. (15) If they all received treatment at the average U.S. cost it would require $179.4 billion in care.

People living farther from the equator tend to have a greater risk for developing Multiple sclerosis so vitamin D deficiency may be involved.

Looking at the global distribution map on the link does visually suggest that vitamin D deficiency may be involved – it is not as much of a risk for nations around the equator where more sunshine would consistently be available. Genetic differences may also be involved as it is more of a risk for Caucasians and people of central and northern European descent. It is rare for Inuits, Aborigines and Maoris. (14) (The Inuit native diet is rich in vitamin D from seafood sources.) A map of distribution risk across the U.S. also suggests a sunshine factor – rates below the 37th parallel are reduced compared to farther north. (15)

Sphingomyelin is found in the diet but needs to be made by the oligodendrocytes.

Why discuss eating cocoa or sources of phospholipids or vitamin D? Why not just eat sphingomyelin? We do eat some but our digestive systems break it down into smaller types of fats, (16), and then our oligodendrocytes have to rebuild it. Sphingomyelin tends to be found with cholesterol within the body, and both can affect the digestion of the other. (16)

Genetic differences may be involved in risk for MS. Variations in genes involved in Vitamin D metabolism may be a risk factor. There also may be differences in the cannabinoid metabolism involved or in other metabolic pathways.

Vitamin D can be made out of cholesterol when our skin is exposed to adequate sunshine. Genetic differences in vitamin D metabolism may be why some people are more prone to developing multiple sclerosis than others – speculatively. Genetic differences in vitamin D metabolism have been studied in relation with multiple sclerosis risk and a correlation was found however studies with supplementation have been inconclusive. (17) One nutrient solutions can not solve multiple nutrient problems – adequate iron but not too much, adequate balance of polyunsaturated fats to promote health without increasing inflammation, avoiding excess free dietary glutamate, and having adequate phospholipids and Nrf2 promoting foods in the diet may also all be important – in addition to having adequate vitamin D in the diet or from sunshine or tanning lights.

Vegetarian based diets include many foods that help reduce inflammation & protect against oxidative stress, & may save money.

Some more good news – a vegetarian based diet can provide many of those dietary factors and save money (about $750/year, (18)) compared to a meat based diet (which tends to be more inflammatory – i.e. oxidative stress promoting). More math – the economical vegetarian diet (2015 U.S. prices) was estimated to cost about $2,762/year which would add up to $6,353 million per year for the 2.3 million global population of people with MS instead of the $179.4 billion that would be needed for current pharmaceutical treatments for Multiple sclerosis. Phosholipid rich, Nrf2 promoting foods can also provide a good balance of omega 3 fatty acids and include sources of vitamin D and iron and tend to include many high quality vegetarian sources of protein such as nuts, beans, and seeds.

Cocoa has been found to reduce fatigue for MS patients and is a good source of phospholipids and Nrf2 promoting flavonoids.

Better news – cocoa, which is made from a bean that is rich in flavonoids, which are Nrf2 promoting phytonutrients, G10: Nrf2 Promoting Foods, and is a good source of phospholipids, (G.26), has been found to help reduce fatigue levels in patients with Multiple sclerosis while not increasing high blood sugar risk factors. (19)

Skip the sugar if possible, Insulin resistance may increase breakdown of the myelin sheath.

I add a spoonful of dark cocoa powder (unsweetened Baking cocoa) to my coffee – like mocha coffee without the syrup. Once you stop using sugar your taste buds adjust to not needing as much sweet taste – or add a little sugar or honey but artificial sweeteners may not be that helpful because the sweet taste is still signaling the body to increase insulin levels which then increases appetite and studies have found snacking calories are then increased -resulting in no overall reduction in calorie intake. Avoiding insulin resistance, frequently a problem with Type 2 Diabetes and Metabolic Syndrome, may also help protect against Multiple sclerosis risk as it may have something to do with the breakdown of the myelin sheath. (20)

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Demyelination, continued.

The last post got a little long and it included a link to another health writer who was summarizing a large amount of material on the topic of demyelination – it is amazing what you can learn by reading. I only mentioned the article, (22), briefly because it was already a long postand I hadn't checked the other writer's references, (it is primarily all medical research from peer reviewed journals (22.1)); and some of his recommendations are not typical, however I had read of them elsewhere so it seemed thorough and well written. The truly intriguing part for me was just how many other conditions there are that may be susceptible to demyelination and increased negative symptoms due to nerve degeneration.

I have a few of the problems that were mentioned and I have had early symptoms of nerve numbness and pain in my extremities – fingertips particularly. Health is easier to maintain then to restore once chronic conditions develop. I have managed to reverse the nerve numbness and occasional pain that I was having in my fingertips but it is with several daily or weekly health habits, not just a simple take-this-medication-once-a-day solution.

The list of psychiatric conditions that may also have demyelination summarized in an article about possible ways to regenerate myelin, (22):

- *Attention deficit hyperactivity disorder*
- *Depression*
- *Bipolar disorder*
- *Dyslexia*
- *Language disorders*
- *Stuttering*
- *Autism*
- *Obsessive-compulsive disorder*
- ***Cognitive decline***
- *Alzheimer's disease*
- *Tourette's syndrome*
- *Schizophrenia*
- *Tone deafness*
- *Pathological lying*
- (22)

That is quite a list – protect your oligodendrocytes, because they protect your ability to think and communicate, to control your ability to control your movements and to have stable moods, reduce anxiety, and control your ability to be able to read and speak and to be able to control your impulses and ability to prevent yourself from lying or saying things you don't intend to say, and to be able to understand that your thoughts are your own thoughts, and to be able to hear accurately. The reference given for the information is this article: [45].

Neurology is the study of the nervous system, Psychiatry or Psychology is the study of mental health and neuropsychiatry is the study of mental symptoms caused by neurological conditions.

This topic of psychiatric conditions and other conditions that may also have demyelination is also reviewed in a summary of Neurotoxicology for neurologists: (Neurotoxicology). Neurology is the study of the nerves and nervous system. The nervous system includes the brain and spinal cord and all of the nerves throughout the body. It is subdivided into two main categories: the Central Nervous System (CNS) refers to the brain, the spinal cord and nerves of the brain and spinal cord; and the Peripheral Nervous System (PNS) refers to the nerves throughout the rest of the body. Neurologists are medical doctors who specialize in conditions affecting the nervous system. They may focus on a subspeciality within the field of neurology (What is a neurologist?, HealthLine) Interestingly dementia, chronic headaches, and Multiple sclerosis are mentioned as possible conditions they treat but all the other psychiatric conditions mentioned in the list that may involve demyelination are not mentioned.

The overview article on Neurotoxicology does mention that psychiatric symptoms may occur in patients with neurological conditions but that the symptoms tend to be dismissed by neurologists, and are not studied in depth, so more reliable information is needed about psychiatric symptoms presenting with neurological disorders – see "*Psychiatric and behavioural disorders*." (Neurotoxicology) An article for neurologists goes into more detail about psychiatric symptoms that might deserve consultation with a neurologist rather than having the patient only see a psychiatrist: *Neurological syndromes which can be mistaken for psychiatric conditions*. Early symptoms of Multiple sclerosis for example sometimes may be mistaken for a psychiatric condition. (Neurological syndromes) Talk therapy or psychiatric medications are not going to help a patient regenerate their myelin after all. Neuropyschiatrists are neurologists that also

have a degree in psychology and specialize in treating patients with mental health and behavioral symptoms related to neurological disorders. (neuropsychiatrists)

PTSD was also mentioned as a psychiatric condition that may have demyelination.[45]

Reading the article that was referenced for the list of psychiatric conditions that may also have demyelination [45] provided an additional condition that was not added to the list in the summary article about potential ways to help regenerate myelin (22) – PTSD also may involve demyelination, and confirmed the rest of the list were mentioned [45] . The article also includes more background information about the function and development of the myelin sheath in learning and behavior.

Nerves with myelin provide a much faster signal and oligodendrocytes myelinate several different nerves so there is additional benefit in signals that work in a coordinated manner to also improve speed of function. The myelination occurs over time so the phrase practice, practice, practice applies. Peak time of life to learn skills is in our youth because that is when the majority of myelination occurs -starting in early childhood and continuing until the early twenties even up to age thirty. Healing after injury or learning a new skill later in life would still require the practice, practice, practice so the speedy pathways between groups of nerve cells develop their myelin sheaths in coordinated connections. [45]

This information may help show the difficulties faced by people with PTSD or other psychiatric conditions – the brain connections are coordinated in patterns learned from traumatic memories or are stuck in Obsessive Compulsive patterns. The problem with impulse control might also make more sense if there is simply “leaky” wiring in the brain. Signals that were intended to do one thing might end up activating other behaviors because the myelin sheath is no longer functioning as expected.

A cognitive therapy technique, involving frequent practice/repetition of new ways to talk to yourself – it might help strengthen more positive neural networks with new myelin sheath connections.

Learning new patterns of thinking, replacing traumatic or anxious thoughts that were learned as a child or during a traumatic phase of life can take time and a lot of repetition but it is possible, just like it can be possible to relearn how to walk or do other basic life skills after a stroke or traumatic physical injury. A book by Shad Helmstetter, PhD discusses how to rephrase your own internal self talk to be more positive and gives examples for a number of different types of concerns. I found the technique helpful for emotional overeating and share phrases that I wrote regarding healthy eating and lifestyle and a link to the book in a previous post: "*What to Say When You're Talking to Yourself*." The recommendation that I followed was to read the statements several times every day – for a while, months even. I don't remember how long I read them daily but it was for quite a while and I still have the little ring binder of statements that I wrote.

Often changing behavior patterns is easier when the new pattern is created first, rather then trying to stop the old first. Build the new and then the old is no longer needed.

A new way to think about demyelination – what is the underlying problem? Possibly excess cell death, at rates above the ability to breakdown and remove nucleotides (ATP, ADP, UTP, UDP).

The article on demyelination and cognitive disorders, [45] , also mentioned that adenosine plays a role in signaling oligodendrocytes to make myelin and an article with more information on the topic mentions that increased amounts of ATP, ADP, UTP, UDP can signal breakdown of myelin. Increased presence of those chemicals was suggested to possibly be due to increased cell death without normal clearing away of the old cellular material. And some types of Multiple sclerosis seems to involve increased levels of the enzyme that breaks down adenosine so there would be less available to signal the production of myelin. (adenosine in MS)

Take home point – protect against excessive cell death by not having excessive glutamate or aspartate – excitatory amino acids that may be overly available in the modern processed food diet – and by having adequate magnesium to protect the cells from their interior by providing the needed energy to block ion channels in the cell membrane and prevent excessive amounts of calcium, glutamate or aspartate from being able to cross the cell membrane and enter the cell's interior.

As usual however, it is not that simple, (not that avoiding glutamate and aspartate in the diet is easy, they are in many processed foods), other things can also cause excessive cell death.

- Exposure to toxins in the environment or due to drug use, illicit or legal, can cause excessive cell death and lead to demyelination disorders. An overview:(Neurotoxicology)
- Lack of oxygen can also be a cause. Lack of nutrients in general can increase the breakdown of cellular parts to provide enough nutrients however if malnutrition is severe and ongoing the breakdown (autophagy) can become excessive. (Metabolic Stress, Autophagy & Cell Death)
- Traumatic injury and infection can increase the rate of cell death above the level that the body's detoxification systems can cope with clearing away the cellular material. Traumatic injury is associated with increased risk for infection for reasons that are not well understood, the immune system is considered functionally suppressed: (Immunobiology of Trauma) Also mentioned briefly in the *Skeletal Muscle* section of this overview: (Neurotoxicology).
- Anything that causes excess oxidative stress may cause increased rates of mitochondria breakdown so protecting against stress is protecting the mitochondria which is protecting the cells. (Metabolic Stress, Autophagy & Cell Death) Mitochondria are the main energy producers within cells and make up about thirty percent of the volume of cardiac/heart cells. Other type of mitochondrial problems can also increase risk of their switching from promoting health through energy production into a mode that promotes cell death. One of the roles mitochondria play in normal health is storage of excess intracellular calcium. If the mitochondria become dysfunctional then the extra calcium is released into the cell where it can signal increased activity such as release of cannabinoids from the membranes. (mitochondria in CVD)

This is approaching really long again, so I am stopping here for now.

/Disclosure: This information is provided for educational purposes within the guidelines of fair use. While I am a Registered Dietitian this information is not intended to provide individual health guidance. Please see a health professional for individual health care purposes./

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Glymphatic system and sleep

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Following up on Friday's easy answer day (previous post) - yes, the glymphatic system of the brain does help protect against Alzheimer's dementia, (7, 8, 14, 17), and sleep, especially one of the deeper stages of sleep (low-delta), is important. (10, 11, 13) Sleeping on your right side may help promote better fluid drainage through the glymphatic system of the brain (sleeping on your right side puts the left side of your

body with your heart farther up above the rest of your body, a pillow between your knees and a neck support may also help). (Social media link, reference source: Neurology Reviews, 2) (12) The circulation by the heart can help move fluid through the brain but only indirectly due to the on/off pressure of the arterial pulse. The regular lymphatic system of the body is a drainage system for the brain fluid system but the blood brain barrier prevents direct interaction. Specialized water pumps in some types of brain glial cells help provide circulation within the brain by pumping water in two directions within the second layer of thick membranes that separate the soft brain tissue from the bony skull. (3)(4)(15)(16)
Overall the fluid within the brain does circulate and there is a visible, small, pulsing movement that has been amplified and can be observed in a video: (5). The spread of a dye within the brain can be observed in a different type of brain scan, the fluid diffusion is not rapid taking 24 hours to reach a maximal point, and the movement of the dye was most prevalent (see color chart) near the skull: (6). The glymphatic system as defined as the specialized glial cells with water pump channels is located in the area near the skull. (4) Diffusion of fluid throughout deeper areas of the brain where the blood brain barrier is not found can occur to a small extent through membranes. (9)

Exercise may also help the glymphatic system function better. (18) The lymphatic vessels and lymph nodes in the neck are the initial drainage route for the glymphatic system cleansing of the various fluid filled areas of the brain. Stretching exercises and rhythmic walking type exercise can help move lymphatic fluid from farther areas of the body to the torso and urinary system for eventual excretion.

Small amounts of alcohol - one third of a serving; to moderate - one or two servings per day; may help the detoxification of the brain fluid by mechanisms that are not well understood yet but which seem to involve the glymphatic system. (19, 20) The mechanism may involve the effect of alcohol on GABA receptors, it can activate them which in general would have a calming/inhibitory effect, (23), however GABA receptors also are involved in promoting more production of the water pump Aqaporin 4 channels in neural stem cells within the subependymal zone. (24) The subependymal zone is in the lateral part of the lateral ventricle which is a cerebrospinal fluid filled area near the center of the brain, (27), which is involved in fluid balance and drainage of the glymphatic system. (25) GABA receptors are also involved with flow of chloride ions across membranes (for an inhibitory effect on nerve signaling, (pp 126-131, 1), and affect fluid balance in areas of the brain without the blood brain barrier which makes diffusion of water across the brain membranes more possible. (26)

Alcohol also inhibits the action of the excitatory neurotransmitter glutamate, particularly at the NMDA receptor, (23), which is an excitatory ion channel and also allows calcium to enter the cell where the mineral can activate many functions within the cell. (pp 120-126, 1) If drinking alcohol is not preferred or legal due to age or advised due to pregnancy or possibility of becoming pregnant then GABA (gamma-aminobutyric acid) is available as an over the counter supplement, typically in a form that melts in the mouth to promote more direct absorption. While it is not typically referred to as an amino acid due to its role as a neurotransmitter, it is simply an amino acid, a smaller molecule from which proteins can be formed. Or sleep, in the form of a short nap, may also help promote GABA. Naps may benefit our health in part because of a beneficial effect on GABA promotion by increased glymphatic action in the brain - twenty minutes of sleep may be adequate. (28)

An overview of the glymphatic system and lifestyle and dietary tactics that might improve its function are described in a video by a nutritionist: (21); and also in a self-help style article by a different person: (22).

Some types of magnesium supplements including magnesium threonate may also help. Magnesium within the brain has many functions including inhibiting the NMDA glutamate receptor which would prevent excess calcium from entering the cell. (pp 120-126, 1)

We tend to hear about neurotransmitters such as serotonin for depression or dopamine and Parkinson's disease, yet we rarely hear that calcium is the mineral that signals the release of both of those and over one hundred other neurotransmitters that are involved in nerve signals within the brain or throughout the body (page 85, 1.Neuroscience, 6th Ed.). Neurotransmitters include excitatory and inhibitory chemicals and they activate or inhibit the firing of a nerve signal. GABA can be a calming/inhibitory neurotransmitter that may be low when anxiety is a problem. Magnesium is the mineral inside cells which helps control how much calcium will be allowed to enter. Excess calcium can cause excess release of neurotransmitters. Magnesium deficiency can also be involved when anxiety is a symptom.

Adequate fluid is also likely important for adequate cleansing of waste from the brain by the glymphatic system. Problems with edema/swelling in other areas of the body or problems with hypertension may indicate problems with the lymphatic system in general. Moderate exercise helps the muscle power of movement also move extracellular fluid and lymphatic fluid through the lymphatic vessels to lymph nodes to be filtered by blood cells. Waste is removed into blood vessels for later excretion by the kidneys.

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