

Optimizing Brain Function

What is optimal brain functioning? Optimal Brain Function is the ability to think clearly and creatively, to learn efficiently, to concentrate, and to focus. There are many reasons why someone would be unable to do this. The reasons someone can not function at an optimal state is a matter of their unique brain chemistry, their conditioned response to environmental stressors, and the nutrition they take in. Before asking yourself “what can I take to relieve my ailment?” ask your mind-body if it needs water, rest, exercise, or nutrition. In light of this, there are ways to enhance the process of achieving an optimal state. In this paper we will discuss both changes one can make to their lifestyle, mindset, and nutritional supplements one can take to restore brain function to an optimal state.

In order to help get a better picture of what optimal brain functioning will look, we will take a look at neurotransmission and the different neurochemicals that are involved. We will look at the dopaminergic, serotonin, GABA/glutamate as well as acetylcholine systems. Each of these systems interact with one another and understanding how they work will give you a better understanding of how your brain can work more efficiently. Then we will look at the essential role of B vitamins in brain functioning. Next we will look at herbal extracts that interact with these neurotransmitter systems. Although I will be sharing what I have learned through my personal experience, education, and research, there is always more to learn about how the brain works and ways to make it work more efficiently. I encourage all readers to do their own research and see what works for them.

We live in high stress societies, we have a stress response that has been hijacked into survival mode for a lot of people. We are taught through fear that we are here to survive. Actually the opposite is true; we are here to thrive. There are steps you can take to eat better, and exercise and take care of your mental health but we realize that sometimes we do not have the time, energy, or money to spend getting to an optimal state. This is why supplementing your lifestyle with herbs and vitamins may be beneficial. They work with your mind-body's natural striving towards homeoflux. The only constant is

change, flux, and flow. We naturally flow with the flux of the existence but we are taught to be afraid of change and flux. Your mind-body uses adaptation to achieve balance, it will attempt to adapt to whatever environment by learning from the stressors in that environment. It naturally strives to harmonize and flow with its environment with the goal to learn and grow from it. If that environment is not conducive to growth then there will be incongruence which can lead to feelings of anxiousness and hopelessness. If the environment that was supposed to be conducive to loving, learning, growing was not for long enough, they may come to believe that every environment will be the same and their neural networks will change accordingly.

The state of one's brain functioning is determined by their adaptation to their environment and their willingness to learn and grow in that environment. Within the brain we call this adaptation neuroplasticity. Neuroplasticity is the ability of the brain to create and prune away neuro networks in order to adapt to the person's environment. This creating and pruning is determined by importance of the network which is determined by how often these pathways are used. For example the network for my connection with my parents is constantly reinforced and therefore remains whereas my connection with the grocer I met once will be pruned away without reinforcement. On a deeper level, if I was treated with indifference, neglect or abuse by those who were supposed to love me, then a network that connects the ideas of love with abuse and neglect may be reinforced as opposed to one that connects the idea of love with compassion and understanding. We are either adapting to a higher state of consciousness or a lower one with each network that we reinforce. We are here to vibrate at our highest state of consciousness.

Optimizing brain function is about aligning yourself with your inner guidance. We naturally strive to flow with the flux of existence and learn and grow from it.

There are natural remedies which can help to get in touch with our mind-body striving towards homeoflux but there is not one right way to get to this point but many depending on what may be

distracting you. There is not one right way to do anything but many ways based on your experience and understanding. A lot of natural remedies work synergistic with others and some will work for some and not for others. Taking the time to figure out what is coming in and going out of your mind-body should be the first step in figuring out what will work for you. When you have an awareness of what you are taking in already, then you can consider taking in more or less. Next understanding the basics of neurochemistry, you will be better able to supplement that neurochemistry to make it work more efficiently. I will be describing neurochemistry for the layman. This is in no way a complete story of how neurochemicals interact.

We'll start with the basics of neurotransmission; the transmission of a neurochemical across the synapse by brain cells or neurons. Neurons have dendrites to receive neurochemicals which move across the synapse and are sent by the axons of the giving neuron. If a certain amount of charge is developed through this transmission the receiving neuron sends their message to the next neuron and neural circuits are made or enhanced. These neural circuits can be inhibitory or excitatory or a mix of both. Dopamine is the main excitatory neurotransmitter associated with motivation, focus, concentration, and pleasure.

We will start here with dopamine, epinephrine, and nor-epinephrine, known collectively as catecholamines. ADD medications work to maintain higher levels of these neurotransmitters. Attention Deficit Disorder is defined as a developmental disorder that is marked especially by persistent symptoms of inattention (such as distractibility, forgetfulness, or disorganization) or by symptoms of hyperactivity and impulsivity (such as fidgeting, speaking out of turn, or restlessness) or by symptoms of all three and that is not caused by any serious underlying physical or mental disorder. Medication works by blocking reuptake of catecholamines or by increasing their release into the synapse. In order to synthesize catecholamines, your body takes amino acids from foods, some of these are the amino acids phenylalanine and tyrosine. These are the building blocks of catecholamines and essential for their production. (Kaufman&Milstein 2013) notes Dopamine synthesis begins with the

amino acid phenylalanine, and proceeds sequentially through tyrosine, DOPA, and then dopamine.

Tyrosine hydroxylase is the rate-limiting enzyme in this pathway. Another important enzyme is DOPA decarboxylase, which decarboxylates DOPA to form dopamine. That same enzyme acts on both naturally occurring DOPA and L-dopa (levodopa), the Parkinson disease medicine. Dopamine is further converted into nor-epinephrine and then epinephrine. Dopamine is essential for motivation, attention and focus as well as pleasure. Tyrosine and L-DOPA is essential for its production.

Sometimes one's affliction has to do with one's mood. Dopamine and serotonin are inherently involved in one's mood and follow a lot of the same pathways in the brain. I have found that if I am lacking serotonin, my brain does not function as well as it could. Again it starts with one's diet. Within one's diet is an amino acid called tryptophan. Tryptophan is converted into 5htp which is then converted into serotonin. The release of serotonin is associated with feelings of well being, happiness, and accomplishments. One of the ways that serotonin and dopamine interact is in the completion of goals.

(Ruden & Byalick 2003) noted in order to focus and be motivated towards one's goals dopamine must be active. Once a goal is accomplished, serotonin is released giving a person a sense of satisfaction and accomplishment. There are other ways that these neurotransmitters interact but this will give one a basic understanding of how they are inherently connected and how the ability to focus and be motivated involves both systems. When one is motivated towards a goal and they complete that goal, a sense of accomplishment is accompanied by a sense of progress but without that serotonin this cannot happen. Essentially, motivation leads to accomplishment, satisfaction, and progress which motivates one to strive towards more goals. (Meditation?) Next we will look at two more neurotransmitters that are inherently connected; GABA(gamma aminobutyric acid) and glutamate (glutamic acid).

GABA is the brains main inhibitory neurotransmitter and glutamate is the main excitatory neurotransmitter. Overly simplifying a complex process, GABA can be converted into glutamate and

glutamate can be converted into GABA through glutamine conversion . This balancing is essential for neuroplasticity which is involved in learning and memory. Too much glutamate and the neuron can be overexcited and cause damage. Too much GABA and you be inhibited in your thinking and actions, such as a drunk person or someone abusing benzodiazepines. This is how they balance each other by breaking down the excess of one into the other.

Neuroplasticity is the brains ability to mold itself for optimal functioning. “Neurotrophic factors and glutamate interact to regulate developmental and adult neuroplasticity. For example, glutamate stimulates the production of brain-derived neurotrophic factor (BDNF) which, in turn, modifies neuronal glutamate sensitivity, Ca²⁺ homeostasis and plasticity...Excessive sustained activation of glutamate receptors can kill neurons, particularly under conditions of reduced energy availability and increased oxidative stress. This phenomenon, which is called excitotoxicity...Glutamate stimulates the production of BDNF in neurons, and BDNF promotes neurogenesis ” (Mattson 2008) Neurotrophic factors are expression of genes that allow for growth of new neurons which is a part of neuroplasticity; the ability of the brain to change itself by creating and pruning neuropathways.

Neuroplasticity is essential to understanding how to improve your brain's efficiency. As the authors noted glutamate is inherently involved in both the production on new neurons and the killing of them. This exemplifies why it is so important to manage your input effectively and excite your neurons as needed. In order to improve your brain's efficiency and allow neuroplasticity to work for you, one must understand how cortisol effects neuroplasticity. Simply put, excess cortisol disrupts the brains ability to encode new memory thus make new neural pathways.

Cortisol is the brains main stress hormone. (Payne) noted that there are dense concentrations of cortisol receptors in the hippocampus and frontal cortex and when cortisol is high it can impair memory tasks which are dependent on the functioning of the hippocampus. Stress manipulations showed how cortisol enhanced emotional information encoding and long term memory while decreasing the encoding and long-term memory of neutral events. “The stress manipulation also

increased salivary cortisol, catecholamines as indicated by the presence of α -amylase, heart rate, and subjectively reported stress. Stressed subjects reported more false memories than non-stressed control subjects, and these false memories correlated positively with cortisol levels, providing evidence for a relationship between stress and false memory formation” (Payne, 2007). Not only does stress disrupt the encoding of memory but helps encode emotionally charged memories. If one is stressed, it is likely that those are not positive emotionally charged memories and probably false memories as well. Excess cortisol can make you tell yourself lies about yourself such as I'll never be good enough or my brain will never work without this drug.

Its important to note the relationship between catecholamines and cortisol. In the craving brain ... outlines the necessity of cortisol and its relationship to dopamine for survival. It is cortisol that tells the dopamine to to release so that one may focus to get its survival need met. If there is no survival need to be met yet cortisol is too high this will lead to a state of incongruence which can lead to a cycle of anxiety and depression. When we feel as though we have a survival need to be met yet there is not one present to us, then we can learn to feel helpless. Excess cortisol is associated with the release of dopamine. “Findings from the longitudinal analyses indicated that cortisol responses to AMPH were positively associated with DA release in the LVS and the left dorsal putamen” (Oswald,2005). Catecholamines include dopamine, nor-epinephrine, and epinephrine which are all increased using traditional pharmaceutical medicines for ADD and other mental disorders. These medicines are associated with an increase in cortisol which interferes with memory formation yet they used to treat a disorder that could be its cause. In some cases lack of dopamine may be the cause of the symptoms of mental disorders but how is one to know whether it is excess cortisol interfering with memory formation and focus or its lack of dopamine? Is it possible that the child is too stress to focus and just needs to find a way to adapt to their stressors? We will talk more about ways to adapt later but let us return to GABA and its relationship to cortisol and stress first.

Many stress and anxiety medications work by increasing GABA. This may work in some cases

but sometimes relaxing is not going to help you recover from the onslaught of chronic stress. In a lot of cases this is simply a band-aid at best. Benzodiazepines are commonly prescribed to treat anxiety disorders. They have a host of side effects including memory problems and are very addictive. Excess cortisol can interfere with GABA production but increasing GABA production does not necessarily decrease cortisol production. “Despite the finding of slightly lower evening cortisol levels in daily and infrequent BZD users compared to nonusers, results indicate that long-term BZD use is not convincingly associated with HPA axis alterations. We did not find significant differences in the cortisol awakening response, diurnal slope, or in the dexamethasone suppression test”(Manthey, 2010). Although there is some short-term alterations in cortisol with the use of benzodiazepines, there is no significant change in the course of cortisol throughout the day.

In a review of the research (Vorspan, 2018) noted that older studies show that short term efficacy of benzodiazepines was demonstrated but was poor. Apparent long term efficacy could be the result of rebound effect or discontinuation symptoms when the treatment is quit and symptoms removal when treatment is started again. Severe withdrawal syndrome is noted when treatment is quit. This review of the research elucidates the efficacy of these drugs and their side effects. Side note benzodiazepines and alcohol are the only drugs which you can die from withdrawals. As one doctor told me as he prescribed them to me, “this is alcohol in a pill”.

So what if you are not stressed but your memory is still impaired? Well it is likely your cause is rooted in the production and transmission of the neurotransmitter acetylcholine. Acetylcholine is made of two parts acetyl and choline. “Pantothenic Acid (Vitamin B5) is a substrate for the synthesis of the ubiquitous coenzyme A (CoA). Beyond its role in oxidative metabolism, CoA contributes to the structure and function of brain cells via its involvement in the synthesis of cholesterol, amino acids, phospholipids, and fatty acids. Of particular relevance, pantothenic acid, via CoA, is also involved in the synthesis of multiple neurotransmitters and steroid hormones” (Kennedy, 2016) The acetyl group comes from acetate which is a by-product of the production of CoA. Coenzyme A provides the acetyl

group for many biological processes and b5 pantothenic acid is essential for the production of CoA. Choline exists in many foods with the highest amounts being in eggs, beef, fish, and mushrooms among many others. Acetylcholine is the main neurotransmitter involved in learning and memory. (Pepeu & Giovannini, 2010) noted acetylcholine is essential in encoding, attention, working, spatial and explicit memory, as well as skill learning but not consolidation. Experiments from humans confirm animal studies. Acetylcholine is essential for learning and memory and its production is dependent on b vitamins.

The essential nature of b vitamins in the production of neurochemicals and optimal brain functioning cannot be overstated. (Kennedy, 2016) noted that research shows that a significant amount of the population of developed countries are deficient in B-vitamins and without an adequate diet, they should be supplemented at doses beyond currently recommended by the government in order to preserve brain health. So why are the government recommendations insufficient?

(Kennedy, 2016) noted RDAs are population statistics which represent rough estimates and for most micronutrients the information needed to calculate RDAs is not completely available. Therefore they are based on some assumptions and can have considerable variations. Despite emerging evidence of individual differences in the processing of vitamins in the past 40 years, these figures have had minimal changes. Since there is no normal population but individuals, some would say that RDAs are arbitrary numbers. We won't suggest what the dosage should be here but simply give you more information on the essential nature of b vitamins in many biological processes and the signs of deficiency.

We'll start with b1 thiamine, (Kennedy, 2016) noted it is a coenzyme which is necessary in the synthesis of fatty acids, steroids, nucleic acids and the aromatic amino acid precursors necessary for neurochemicals essential for brain function. It is heavily involved in the acetylcholine system. Food sources include Cereals (esp. whole grain), brown rice, green vegetables, potatoes, pasta, liver, pork, eggs. Mild deficiencies result in general fatigue/weakness, gastro-intestinal symptoms, irritability,

emotional disturbances, confusion, disturbed sleep and memory loss. Deficiency known as Beri-beri could involve peripheral nerve damage, cardiovascular dysfunction leading to pain, impaired sensory perception; swelling, weakness and limb pain; shortness of breath, irregular heart rate, heart failure. Deficiency of the brain is called wernicke- korsakoff syndrome and can include neurodegeneration, Ataxia, abnormal motor function and eye movement, amnesia, apathy, confabulation. This disease is most associated with alcoholism.

(Kennedy, 2016) noted B2 Riboflavin is involved in many biological processes most notable for our discussion is its involvement in the synthesis, conversion and recycling of niacin(B3), folate(B9), and b6. It is also involved in the regulation of thyroid hormones. Food sources include dairy products, leafy vegetables, legumes, liver, kidneys, yeast, mushrooms. Its deficiency can be involved in the many cases of brain dysfunction. Deficiencies are associated with weakness, oral pain/tenderness, burning/itching of eyes, dermatitis, anemia, fatigue, personality change and brain dysfunction.

B3 Niacin is involved in the function of all peripheral and brain cells. It is involved in energy production, oxidative reactions, antioxidant protection, DNA metabolism and repair, cellular signaling events and folate conversion. Its levels are involved in schizophrenia and Parkinson's disease. Food sources include meat, fish, whole grain cereal, legumes, mushrooms, nuts. Deficiency known as Pellagra: dermatitis/photo dermatitis, alopecia, muscle weakness, twitching/burning in the extremities, altered gait, diarrhoea, depression, anxiety, progressing to vertigo, memory loss, paranoia, psychotic symptoms, aggression (Pellagrous insanity). Its deficiency is related to alcohol abuse. We previously spoke about b5 involvement in acetylcholine production. Food sources include meat, whole grain cereals, broccoli. Its deficiencies involve numbness/burning sensations in extremities, dermatitis, diarrhoea, encephalopathy, behavior change, demyelination.

B6 pyridoxine is necessary for the synthesis of dopamine, serotonin, GABA, noradrenaline and melatonin. As well as its essential nature in these synthesis's, it also has direct effects on the immune

system and gene transcription/expression as well as brain glucose regulation. Food sources include Meat, fish, legumes, nuts, bananas, potatoes. Its deficiencies involve anemia, irritability, impaired alertness, depression, cognitive decline, dementia, autonomic dysfunction, convulsions. It can be related to Alcohol abuse, age-related malabsorption, contraceptive medications.

B7 biotin is essential for glucose metabolism and is involved in type 2 diabetes. Food sources include eggs, liver, pork, leafy vegetables. Its deficiencies involve seborrheic eczematous rash, tingling/burning of the extremities, depression, lethargy, hallucinations, seizures and can be related to type II diabetes, poor gluco-regulation. B9 folate is inherently connected to B12 and both are necessary for the folate cycle to function efficiently, which is necessary in the production of serotonin, melatonin, dopamine, noradrenaline, adrenaline and nitric oxide. Deficiencies in both can result in megaloblastic anemia, peripheral neuropathy, spinal cord lesions, metabolic abnormalities, affective disorders, behavior changes, psychosis, cognitive impairment/decline, dementia (inc Alzheimer's disease and vascular dementia) B9 food sources include leafy vegetables, legumes, citrus fruits. Its deficiencies can be related to common genetic polymorphisms, low Riboflavin and B12. B12 food sources include meat, fish and other animal products. Its deficiencies can involve age-related malabsorption, vegetarians, vegans, Genetic polymorphisms.

We'll take a quick look at the neurochemistry involved in meditation and positive affirmations. Many natural enhancers of optimal brain functioning work synergistically with one another and many find benefits from combining meditation and positive affirmations with supplementing. If you're telling yourself the same story expecting it to be different because you took something, you may not find benefits from these medicines.

We will now look at science that shows how certain herbs can possibly assist your brain in functioning optimally. We will start with adaptogens as we live in a high stress society. "Adaptogens are natural compounds or plant extracts that increase adaptability and survival of organisms under

stress.....several adaptogenic herbal extracts in brain cells culture... The extracts affected many genes playing key roles in modulation of adaptive homeostasis, indicating their ability to modify gene expression to prevent stress-induced and aging-related disorders” (Panossian, Seo, & Efferth, 2018).This shows how these substances work on a genetic level to enhance adaptability to stress. They may also work with glucose metabolism. (Liao, 2018) noted the positive effects of adaptogens on stress hormones, the pituitary adrenal gland axis and glucose metabolism. These are just some of the research that has been done but there is more to do in order to fully understand how these medicines work, but the science is there to support that they work.

There are two types of adaptogens are sometimes categorized as primary and secondary. (Liao, 2018) noted primary adaptogens affect the hypothalamic-pituitary-adrenal (HPA axis) as it is stimulated by external stress. They can maintain or recover homeostasis, allostasis and promote anabolic recovery. They can produce a positive stress response with an associated hormone expression. They can also help regulate energy use by improving the function of the neuroendocrine system and enhancing cellular energy transfers. Secondary adaptogens cannot influence the HPA axis directly but do affect the immune, nervous and endocrine systems. They can enhance anabolism but are lacking in research.

We will focus on 3 adaptogens and their medicinal benefits. We'll look at ginseng, bacopa, and maca root. Ginseng is possible the most well known adaptogen. There are a few different types of ginseng but most of the research is based on panax ginseng known as Asian ginseng. In a review of the studies(Huang, Li, Pu, Zhang, & Wang, 2019) noted Ginseng has been used since ancient times and recent research displays how its neuroprotective properties could possible prevent neurological damage and disease without any serious side effects. This is based on some evidence from animal and other from human studies. One study with humans showed its effects on glucose and cognitive function. “These results confirm that Panax ginseng may possess glucoregulatory properties and can enhance

cognitive performance.” (Reay, Kennedy, & Scholey, 2006) Personally I used a combination of ginseng, ginkgo biloba and yerbe mate to relieve myself of a 16 year dependency on Adderall. (Scholey & Kennedy, 2002) described a study of young adults showing the benefits of combining ginseng and ginkgo on cognitive functioning.

Bacopa is an adaptogenic herb from the Ayurveda tradition with many active constituents and benefits. It may help to alleviate depression, anxiety and memory problems. (Aguiar & Borowski, 2013) noted studies that suggest that bacopa could protect neurons from oxidation, enhance acetylcholine production, reduce plaque build up associated with Alzheimer's, increases blood flow to brain and helps modulate acetylcholine, serotonin and dopamine pathways. Therefore Bacopa could have potential value in the treatment of dysfunction of these neurotransmitters. “*Bacopa* alcohol extract has shown memory-enhancing effects in three double-blind, randomized, placebo-controlled studies. *Bacopa* recipients displayed a decrease in depression and combined state plus trait anxiety scores with the placebo recipients increasing on both. Participants also had slightly lower heart rates after taking *Bacopa* while those taking the placebo displayed an increase in heart rate”(Calabrese, 2008). As an adaptogenic herb, the research suggests how its medicinal properties may work through enhancing memory and decreasing depression and anxiety symptoms.

One root that has shown to be promising as an adaptogen is Maca. “Maca is a plant with great potential as an adaptogen and appears to be promising as a nutraceutical in the prevention of several diseases. Scientific evidence showed effects on sexual behavior, fertility, mood, memory, osteoporosis, metabolism, and the treatment of some tumor entities”(Gonzales, 2012). There are a few different types of maca which some call the Peruvian ginseng. Their effects varied a bit so its important you find the right one for you.

Although some of these adaptogens work with the acetylcholine system, we will now explore other herbs that some say can be used to enhance learning and memory through the cholinergic

systems. We will look at huperzine A and lions mane mushroom. (Garcia 2017) noted HupA is a potent acetylcholinesterase (AChE) inhibitor as it became known in the treatment of dementia. Its noted pharmacological effects include antioxidant, anti-inflammatory, anti-apoptosis, anti- β -amyloid peptide fragmentation, inhibition of oxygen-glucose deprivation, and NMDA receptor antagonism. It can improve memory and behavior in Alzheimer's patients by acting in the beta-amyloid peptide processing, which reduces neuronal injury. "The beta-amyloid protein involved in Alzheimer's comes in several different molecular forms that collect between neurons. It is formed from the breakdown of a larger protein, called amyloid precursor protein. One form, beta-amyloid 42, is thought to be especially toxic. In the Alzheimer's brain, abnormal levels of this naturally occurring protein clump together to form plaques that collect between neurons and disrupt cell function"(What) Huperzine A is able to inhibit the breakdown of acetylcholine allowing learning and memory happen more efficiently. It also assists in the breakdown of amyloid plaque preventing neuronal damage.

Lions mane mushroom is also shown to remove amyloid plaque as well. (Hu, Jun-Hao) noted this study showed how Erinacine S, produced in *Hericium erinaceus* mycelia (lion's mane mushroom) can penetrate the blood-brain barrier and is able to reduce amyloid plaque growth and improve neurogenesis in aged brain of rats. It has been reported to possess anti-cancer, immuno-modulating, anti-hyperglycemic, anti-hyperlipidemic, anti-oxidant, anti-osteoporotic, anti-bacterial, wound healing, anti-neurodegenerative, neurogenesis-inducing, and memory-improving activities. Moreover, it has been shown to prevent ischemia injury, Alzheimer's disease, Parkinson's disease, and depression in animal models. This study provided support for the use of lions mane mushroom to treat neurological diseases among others. "Myelin sheaths, wrapping axons, perform the following important functions: support, protection, feeding and isolation..Recently it was shown that extract from mushroom *Hericium erinaceus* had activating action on the nerve tissue. The process of myelination in the presence of the extract began earlier as compared to controls and was characterized by a higher rate. Thus, extract of H.

erinaceus promoted normal development of cultivated cerebellar cells and demonstrated a regulatory effect on the process of myelin genesis process in vitro” (Kolotushkina EV). This research provides further support for the utilization of lion's mane mushroom in the process of myelination. Next we will discuss herbal remedies for anxiety and stress.

If one's anxiety cannot be attributed to external stressors then GABAergic substances could optimize brain functioning. We will consider three options for enhancing the production and utilization of GABA; Chamomile, L-theanine, and kava. Chamomile has been used for many years as a bedtime tea but its extraction has captured the attention of some researchers. “Chamomile extract produced a clinically meaningful reduction in GAD symptoms over 8 weeks, with a response rate comparable to those observed during conventional anxiolytic drug therapy and a favorable adverse event profile”(Keefe, John R. 2016).It was able to reduce symptoms of Generalized Anxiety Disorder comparable to other drug treatments and had fewer side effects. “Long-term chamomile was safe and significantly reduced moderate-to-severe GAD symptoms” (Mao, Jun J.,2016).These studies showed its safety and effectiveness both in the short-term and the long-term. Although it did not reduce the rate of relapse, it can be stopped without withdrawal and the memory problems associated with benzodiazepines.

Another herbal compound to treat anxiety without the side effects of traditional treatments is L-Theanine. L-Theanine is amino acid found in green tea. “Anxiolytic effects have been reported, whereby 200 mg L-theanine reduced acute stress responses (subjective perception, heart rate and salivary immunoglobulin A) induced by a mental arithmetic task, and a 250 mg dose of L-theanine slowed reaction time on a visual probe task, indicating reduced anxiety”(Ogawa, Shintaro,2017). This study suggested its effectiveness at reducing anxiety in humans.

This next study looks at changes in hippocampal and anxiolytic activity in rats. “Our findings demonstrate that repeated systemic l-theanine administration at a relatively low dose elicits significant anxiolytic effects in WKY rats, which are accompanied by decreased glutamate and increased methionine levels in the CSF. Our findings further indicated that l-theanine treatment produces increases in hippocampal activity as measured using FDG-PET. Collectively, our results suggest that l-theanine enhances hippocampal activity and exerts anxiolytic effects, which may be mediated by changes in glutamate and methionine levels in the brain”(Ogawa, Shintaro,2017). As we discussed before the hippocampus activities can be impaired by excess cortisol. As this study shows L theanine can enhance hippocampal activity. Another option for treating anxiety naturally is kava. “In clinical trials, kava extracts are superior to placebo in reducing anxiety, and are generally well tolerated with negligible to mild side effects. Despite reports of alleged kava-induced hepatotoxicity... systematic reviews and meta-analyses conducted over the last 15 years found a clear positive benefit-to-risk ratio for kava”(Chua, Han Chow,2016). Although some have claimed that kava is toxic, studies have shown that the benefits outweigh the risks. Next we will consider devils claw and kratom in the treatment of pain.

Devils Claw has been used for centuries in Africa to treat pain and other disorders. This study using devils claw to treat arthritis supports this use. “The most striking results of the study were seen in pain reduction. Indeed, pain levels were significantly reduced in all joints affected by general rheumatic disorders during this study. In addition, more than 60%of patients taking analgesics for joint pain at baseline had either reduced their intake or completely stopped taking them at endpoint thus showing that Hp had a positive impact on concomitant medication. There were also statistically significant reductions in mean pain scores for hand, wrist, elbow, shoulder, hip, knee and back pain. Quality of life measurements (SF-12) were significantly increased from baseline and 60% patients either reduced or stopped concomitant pain medication. Harpagophytum is an effective and well-tolerated serious

treatment option for mild to moderate degenerative rheumatic disorders providing improved quality of life measure”(Warnock, Mary,2007). A review of research on devils claw for non-specific lower back pain showed that “Strong evidence exists for the use of an aqueous Harpagophytum extract at a daily dose equivalent of 50 mg harpagoside in the treatment of acute exacerbations of chronic NSLBP” (Gagnier, Joel J,2004). These studies provide evidence of the efficacy of devil's claw extracts to treat pain and improve the quality of life for those who suffer from pain.

Another potential way to treat one's pain is kratom. Kratom is a tree that grows in southeast Asia and its leaves are used to treat pain and fatigue. This research shows “more than 40 compounds have been isolated from kratom leaves. However, mitragynine (accounting for 66% of the total alkaloid content), and 7-hydroxymitragynine (accounting for an additional 2% of total alkaloid content) were found to be partial agonists at the μ -opioid receptor, and as antagonists at K- and δ opioid receptors Kratom has dose-dependent stimulant and opioid-like effects, such as mild euphoria and sedation (at higher doses) These are mediated by its interactions with opioid receptors, alpha-2 adrenergic receptors, and serotonin 5-HT₇ and 5-HT_{2C}-receptors” (Singh, Darshan,2018). This study done with rats “suggest a limited abuse liability of mitragynine and potential for mitragynine treatment to specifically reduce opioid abuse. With the current prevalence of opioid abuse and misuse, it appears currently that mitragynine is deserving of more extensive exploration for the its development or that of an analog as a medical treatment for opioid abuse”(Yue, K., Kopajtic, T. A., & Katz, J. L.,2018). This study suggests that the kratom alkaloid mitragynine has a low abuse potential and could help attenuate the current opioid problem. This next study looks at the effects of long term use of kratom in humans. “Overall, the performance of kratom users compared to control participants, and the performance of high (>3 glasses per day) as well as low (\leq 3 glasses per day) kratom using groups, were comparable on all neuropsychological domains. Higher intake of kratom juice (>3 glasses daily) did not appear to impair motor, memory, attention or executive function of regular kratom users”(Singh, Darshan,2018).

This study shows the lack of cognitive impairments in regular kratom users. Many users report enhanced cognitive functioning. These studies elucidate the potential of these plants to treat physical pain, next we will consider plants that could decrease emotional pain.

One important supplement in the treatment of depression is 5-HTP. 5-HTP is extracted from the *G. simplicifolia* plant of West Africa. Although there is no financial incentive to studying this supplement and available studies are lacking, the role of 5-HTP in serotonin synthesis can not be denied. “5-HTP is converted to serotonin by the enzyme aromatic L-amino acid decarboxylase (AADC), an enzyme that catalyzes the decarboxylation of a variety of aromatic L-amino acids; it converts L-DOPA to dopamine and 5-HTP to serotonin”(Turner, Erick H.,2006). As the main hypothesis of depression is based on a deficiency in serotonin, further research is suggested to evaluate the effectiveness of this supplement.

One study looked at the effects of 5-HTP on attention.“Our findings provide unique causal and mechanistic evidence suggesting that enhancing central serotonergic function results in categorically distinct changes in fundamental cognitive operations such as attention” (Weinberg-Wolf, Hannah,2018). This study shows how essential serotonin is to different cognitive functioning. Another study using l- theanine and 5-HTP to treat at risk children reported “Our results suggest that TAAT is a promising alternative to prescription drugs for children who are aggressive, anxious and/or depressed. Results include significant increases in urinary levels of the biomarkers for serotonin and gamma-aminobutyric acid, coupled with significant decreases in parent reports of the children’s behavior problems” (Cross, D. R., 2010). As predicted the use of this combination resulted in diminished behavioral problems that were associated with increases in serotonin and GABA. Another south African plant is *Sceletium tortuosum* known as Kanna. “The two major active alkaloids mesembrine and mesembrenone are still in the process of being more fully characterized pharmacologically. They are serotonin reuptake inhibitors, which provides a rationale for the plant's traditional use as an

antidepressant”(Krstenansky, John L.,2017). As serotonin reuptake inhibitors are the main class of drugs that are used to treat depression, Kanna as natural SRI warrants further research.

Another potential herbal remedy for depression is Rhodiola Rosea. This research shows that “R. rosea demonstrates multi-target effects on various levels of regulation of cell response to stress, affecting various components of the neuroendocrine, neurotransmitter receptor and molecular networks associated with possible beneficial effects on mood” (Amsterdam, Jay D., and Alexander G. Panossian.,2016). This review of the available studies focused on the many ways in which this plant can have an effect on mood. Another review article focused on the many ways that this plant could have an adaptogenic effect. “Studies on isolated organs, tissues, cells and enzymes have revealed that Rhodiola preparations exhibit adaptogenic effect including neuroprotective, cardioprotective, anti-fatigue, anti-depressive, anxiolytic, nootropic, life-span increasing effects and CNS stimulating activity” (Panossian, A.,2010). Evaluating the studies available allowed the researchers to elucidate the many effects of Rhodiola and their clinical applications.

Another plant that can increase serotonin as well as dopamine production is mucuna pruriens. “Mucuna pruriens(velvet bean or cowhage) is a leguminous plant that has been used for centuries in Ayurvedic medicine for the treatment of Parkinson’s disease. Mucuna pruriens contains levodopa as well as two components of the mitochondrial electron transport chain; coenzyme Q10 and nicotine adenine dinucleotide (NADH).In a single-dose, randomized controlled trial, a mucuna seed powder formulation had comparable efficacy to levodopa in reducing Parkinsonian symptoms. This formulation had a quicker onset and caused less dyskinesias than levodopa”(Simmons, A. D.,2018). This study demonstrated its potential to treat Parkinson's disease and its involvement in energy production. This next study demonstrates its efficacy in restoring neurotransmitter levels. “Unlike synthetic levodopa treatment, Mucuna pruriens cotyledon powder treatment significantly restored the endogenous levodopa, dopamine, norepinephrine and serotonin content in the substantia nigra.

(Manyam, B. V., Dhanasekaran, M., & Hare, T. A.,2004). These studies show the different content of mucuna and the difference in effects between mucuna and synthetic l-dopa based on their mechanisms of action. It suggested that mucuna can increase dopamine, norepinephrine and serotonin. This next study sheds light on how this happens. The study reported that “Dopamine is reported in 44 plant species and is synthesized in plants from tyrosine, either via tyramine or via l-DOPA. In *M. pruriens*, dopamine is synthesized by the enzyme dopa decarboxylase/tyrosine decarboxylase (DDC)” (Singh, S. K., Dhawan, S. S., Lal, R. K., Shanker, K., & Singh, M.2018). This enzyme is also involved in the synthesis of 5htp into serotonin. This displays how this bean can be used to increase serotonin as well as dopamine.

In this paper I have elucidated how one's neurochemistry works and how certain herbal supplements can be used to enhance cognitive functioning. There are many herbs which have not been studied and those which require more research. Unfortunately private funding for this research is lacking and there is not a lot of incentive to research them unless its to extract an active constituent and turn it into a drug for profit. As research continues, science is discovering that many active constituents of herbs work synergistically with other components of the herb and make up its medicinal effects. Also many herbs work synergistic with other herbs, vitamins and supplements. In this paper we focused on herbs and b vitamins and their effects on neurochemistry, in the follow up paper we will discuss more vitamins and supplements and how they work together with herbs to enhance brain functioning.

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