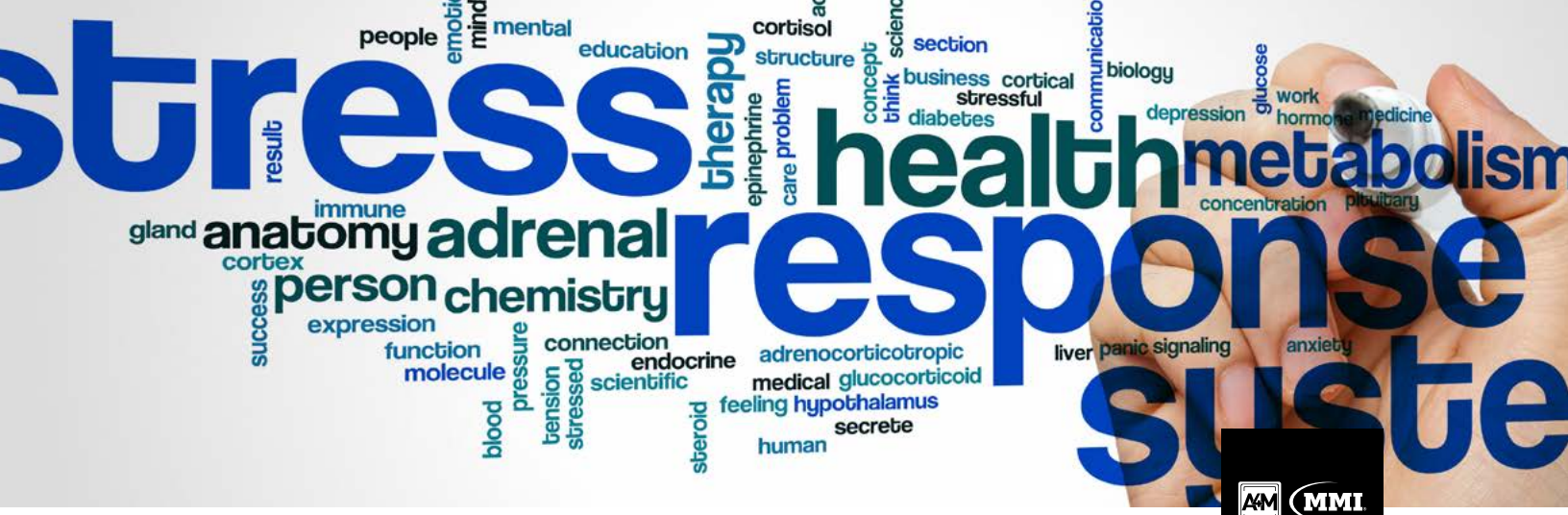

How Stress Affects the Body

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The importance of the hypothalamic-pituitary-adrenal axis (HPA) in mediating the stress response and maintaining physiologic homeostasis has long been described. It is well established that chronic stress propagates a systemic cascade of dysfunctional metabolic events initially intended to be adaptive. Dysfunction of the HPA axis appears to be a major initiating and contributing factor to this process, ultimately giving rise to disruption of the normal diurnal cortisol release pattern.

Maladaptive cortisol release patterns can be characterized as hypercortisol, which is an overly exaggerated response to stress, or hypocortisol, which is an underproduction of cortisol under stressful circumstances. While the latter has been often characterized as 'Adrenal Fatigue,' this notion does not fully appreciate the complex, multi-step process that results in low cortisol states, or the body of literature that characterizes hypocortisolism as an adaptive response to stress.

This paper reviews the components of the stress response, mechanisms of alterations in cortisol production, and common botanical therapies utilized in mitigating the stress response and protecting the health of the individual.

Physiologic Adaptation to Stress

Physiologic stress is a "state of disharmony or threatened homeostasis" that occurs in the central nervous system (CNS) and surrounding tissues and organs.[1] It triggers an intricate series of metabolic responses collectively called the "adaptive stress response" that is intrinsically designed to help the body reestablish equilibrium to counteract a perceived extrinsic or intrinsic "stressor."[1-4]

Lifestyle behaviors along with stress duration, intensity, and frequency can add to dysregulation of the stress system and result in a myriad of health problems and ultimately, disease, thus affecting an individual's ongoing resiliency or "successful adaption to change."[1-6] The brain's ability, in particular, to resist the effects of a stressor plays a central role in determining the integrity of the stress response itself, and whether it remains intact or develops abnormal patterns of reaction over time. [1,2,5]

Allostasis: Balance in the Stress Response

The ability to achieve stability through change or "Allostasis" within the stress response is reliant upon a system of healthy interactions across the neuroendocrine, cellular, and molecular components of the stress system, including the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS), central nervous system (CNS) and periphery, in addition to the cardiopulmonary, endocrine, immune and gastrointestinal tract.[1-4] When these systems remain resilient and produce a positively coordinated reaction to stress, resiliency and metabolic reserve is maintained and the health of the individual protected.

Allostatic Load: Overwhelming the Stress Response

Chronic activation of the stress system contributes to the "Allostatic load" as coined by McEwen and Stellar, which reflects the total strain on the stress response.[1] Contributors to allostatic load include major life events, trauma, abuse, work, home, community, as well as day-to-day lifestyle behaviors including sufficient rest, diet, nutrition, exercise, toxins, and substance abuse.[1-8]

If allostatic load overwhelms the body's ability to compensate, thus degrading allostasis, a number of emotional and physiological manifestations can arise including: [1-9]

Mood	Depression, Anxiety and Sleep Disorders; Altered perception, behavior and social interactions
Cognition	Memory loss, word finding difficulties, decreased executive function
Endocrine	Obesity, Insulin resistance, Diabetes, decreased leptin, increased grehlin,
Cardiovascular	Abnormal heart rate, hypertension, hyperlipidemia, elevated fibrinogen, myocardial infarction, stroke
Immune	Poor immune defense, Increased pro-inflammatory cytokines, cancers, auto-immune diseases, Atopic illnesses
Neurologic	Headaches, decreased heart rate variability (HRV), increased SNS activity (12-hour urinary norepinephrine and epinephrine)
Reproductive	Infertility, hormone imbalances
Gastrointestinal	GERD, peptic ulcers, Irritable Bowel Syndrome, Ulcerative Colitis
Skin	Rashes, hives, atopic dermatitis

McEwen categorizes these into primary, secondary and tertiary markers of allostatic load. Primary mediators that have a direct response from stress and predictive validity in the context of longitudinal behavioral assessments include cortisol, adrenaline, sympathetic and parasympathetic activity, pro- and anti-inflammatory cytokines, metabolic hormones and neurotransmitters and neuromodulators.[10]

Secondary markers are indirect measures of immune system efficacy and a result of the aggregate impact of primary mediators including WHR, BP, cholesterol/HDL ratio, HDL cholesterol, glycosylated hemoglobin, inflammatory markers mentioned above (IL-6, C-reactive protein, and fibrinogen), and telomere length and telomerase activity.[1-10]

Individuals who experience early life adversity are likely to experience higher levels of oxidative and inflammatory stress (primary mediators) resulting in telomere shortening (secondary outcome) or obesity (secondary outcome), and are at increased risk for depression, diabetes, CVD or substance abuse.1-10 Tertiary mediators or outcomes such as CVD, decreased physical activity, severe cognitive decline, Alzheimer's disease, vascular dementia, or cancer are the diseases or disorders that result from the extreme values of secondary outcomes due to increased allostatic load.[10]

The Stress Response: It All Begins in the Brain

The stress response begins in the paraventricular nucleus (PVN) of the hypothalamus, the anterior lobe of the pituitary gland, and the adrenal gland, otherwise known as the hypothalamic-pituitary-adrenal (HPA) axis.[1-9] Neurons in the medial parvocelluar subdivision of the PVN synthesize and secrete corticotropin-releasing factor (CRF), the principle regulator of the HPA axis and automonic nervous system (learning, memory, feeding, reproduction), and vasopressin (AVP).[9]

In response to stress, CRF is released and binds to the CRF type 1 receptor (CRFR1) on pituitary corticotropes which activate the cyclic adenosine monophosphate (cAMP) pathway and release of adrenocoriticotrophic hormone (ACTH) into systemic circulation.[1,3,4,9] Circulating ACTH binds to the melanocortin type 2 receptors (MC2-R) in the adreno-cortical zona fasciculata, causing steroidogenesis and glucocorticoid, mineralocorticoid (MR), and androgenic steroid synthesis and secretion.[1,3,4,9]

Stress-receptive neurons in the brain stem, relay sensory information from cranial nerves to the PVN that excite large areas of thoracic and abdominal viscera.[9] Projections from the prefrontal cortex and amygdala limbic structures regulate the behavioral responses to stress by releasing catecholamines.[9] The anterior cingulate and prelimbic cortex increase ACTH and glucocorticoid responses to stress.[1,2,9]

Medial (MeA) nuclei of the amygdala are activated following exposure to "emotional" stressors while central (CeA) nuclei are activated by "physiological" stressors and regulate the HPA axis through intermediary brain stem neurons.[1,9,10] The amygdala is a target for circulating glucocorticoids and the CeA and MeA express both GR and mineralocorticoid receptors (MR). In contrast to the effects on hippocampal and cortical neurons, glucocorticoids increase expression of CRF in the CeA and potentiate autonomic responses to chronic stress.[1-10]

Activation of brain stem noradrenergic neurons and sympathetic and renomedullary circuits further contribute to the body's response to stressful stimuli including emotion, vigilance, memory, and resiliency.[1,3,9,10] Stressful stimuli alter neuronal electrophysiological activity and induce release of norepinephrine, ACTH release, anxiogenic-like activity, and immune suppresion.[1-10]

Metabolic Response to Stress

The extra-CNS metabolic response to acute stress includes rapid and strong elevation of plasma concentrations of glucose, insulin, glycerol, and ketone bodies, stimulation of adipose tissue lipase by circulating catecholamines, activation of the autonomic nervous system via glucagon secretion, and decrease in triacylglycerol levels.[1,4,9]

Several neuropeptide systems in the brain are substantially affected by stress including norepinephrine, epinephrine, serotonin, dopamine, glutamate, taurine, GABA, glycine, phenylethylamine (PEA), and histamine.[1-10] Ongoing disruption of neurotransmission can potentially lead to neuropsychiatric symptom manifestation and acceleration of neurotransmitter depletion, with the mesoprefrontal pathway being particularly at-risk, thus impacting reward-mediating neurotransmitters possibly leading to addictive behaviors.[1,9,10]

Activation of cerebral cholinergic transmission impacts arousal, motivation, and cognition.[1,4,9,10] Extracellular levels of glutamate, the major excitatory amino acid transmitter, increases in numerous regions of the brain, while changes in GABA receptor properties can also impact the stress response.[4,9,10]

However, several aspects of GABA-ergic neurotransmission may be obscured by endogenous steroid hormone derivatives whose synthesis is increased following stress.[4,9,10] These compounds influence several aspects of the behavioral and neuroendocrine response to stress.9-10 Alterations in the endogenous opioid neurotransmission are implicated in stress-related endocrine and autonomic responses.[9,10]

Alterations in the Stress Response

Stress can induce changes in CRH and AVP expression in the PVN, and increased concentrations of ACTH in the systemic circulation, result in desensitization of pituitary CRH receptors and blunted ACTH release.[1-10] This dissociation between CRH hyperactivity and refractory corticotrophin responsiveness is a pathognomonic feature of stress-associated neuroendocrine dysregulation.[10]

Beyond this, stress drastically affects growth hormone secretion, thyroid axis function, and reproductive function via decreased gonadotropin levels, suppressed gonadal steroids, increased circulating prolactin, disruption of the ovarian cycle, and decreased libido.[1-10]

Hypocortisolism: A Protective Mechanism?

While elevated cortisol patterns are well recognized and understood, the process through which hypocortisolism evolves remains ill defined. Although reduced availability of cortisol may be due to primary dysfunction of the adrenal glands, controversially labeled as "adrenal fatigue", reductions in biosynthesis of hormones at different levels of the HPA axis likely play a greater role.

Since integrity of HPA axis function and predictable patterns of diurnal cortisol release are essential for maintaining homeostasis during periods of chronic stress, much of the available research on hypocortisolism and stress induced disease has focused on disturbances in these latter mechanisms.

Hellhammer and Wade postulated a developmental model whereby hypocortisolism may develop via hypoactivity of the HPA axis after prolonged periods of chronic stress. After an initial period of HPA axis hyperactivity and hypercortisolism, *hypocortisolism* may ultimately develop as a type of maladaptive "over compensation" of the self preservation mechanisms designed to protect metabolic machinery, and particular the brain, from the deleterious effects of persistent cortisol elevation.[12]

An increase in hypothalamic release of CRF with subsequent adaptive down-regulation of CRF receptors at the level of the pituitary gland has also been proposed. Although this has been demonstrated in animal studies, replication of such a process in human subjects has been difficult but may be indirectly implied. Yehuda et al. and others have postulated that an *increase in the sensitivity of the HPA axis* to hypercortisolism induces negative feedback control on further release of stimulating hormones thereby causing hypocortisolism.[13]

McEwen identifies a central mechanism for low cortisol states via alterations in the CA1 and CA3 regions of the hippocampus. Known as the 'Neurodegenerative Model of Hypocortisolism,' in which the hippocampus plays a central role in the regulating the entirety of the stress response. While a primary purpose of this critical brain structure is to consolidate memories, and assign importance to those memories, it also maintains the highest concentration of cortisol receptors in the brain.[14]

The hippocampus is therefore exquisitely vulnerable to high stress states, with cortisol potentially playing a catabolic or damaging role that can lead to alterations in both function and structure of this brain center. It should be noted that the hippocampus serves a regulatory role to the HPA axis, and once injured, can lead to low cortisol states. The neuroinflammation and neurodegeneration associated with the damaging effects of cortisol in the brain argues for therapeutic strategies that limit injury of cortisol to key brain areas, reduce inflammation and induce neurogenesis.

Intrinsic dysfunction of the adrenal gland has also been proposed as well, but overall limited data exists in comparison to other mechanisms that lead to hypocortisolism. Heim and colleagues have reviewed studies on the effects of chronic stress on the adrenal glands and have concluded, "There is a considerable body of evidence of reduced adrenal gland activity and reactivity in human subjects living under conditions of chronic stress."[15]

Scott and colleagues found patients with CFS and abnormal endocrine parameters to have a significant reduction in adrenal gland volume compared to control subjects.[16] Another study by Cleare et al. found CFS patients to have impaired adrenal cortical function as evidenced by not only decreased basal cortisol levels but also blunted cortisol responses to stimulation testing.[17]

Regardless of the underlying process, some believe the maladaptive physiological changes induced by hypocortisolism may actually be protective to ensure survival. As postulated by Fries et al, "Hypocortisolism is a protective response dampening chronic HPA axis activity and thereby reducing the damaging effects of the glucocorticoid response to daily hassles at the expense of symptoms such as high stress sensitivity, pain, and fatigue".[18]

In further support of this theory, Fries and colleagues have observed comparable groups of pregnant women and found those with lower morning cortisol levels had higher daily stress compared to their counterparts experiencing normal or low daily stress loads. The authors speculate that the hypocortisolism may be a counterregulatory protective mechanism designed to protect placental CRF from maternal cortisol.[18]

Raison and Miller suggest that hypocortisolism enhanced stimulation of the immune system may be protective as well. In individuals suffering from recurrent or ongoing infectious assaults, reduced

glucocorticoid signaling impairs the normally adaptive inhibitory mechanisms thereby promoting the body's ability to mount adequate retaliatory defenses. Other authors have coined the term "sickness response" to describe the anorexia, fatigue, anhedonia, hyperesthesia, and concentration difficulties often accompanying the body's response to infection via elevated immune activity.[19]

In his 1988 paper, Hart wrote that the sickness response results from the body's adaptive attempts to ration and prioritize its defenses to better eliminate the pathogen.[20] Many symptoms of the sickness response mimic those of stress related bodily disorders, and an association between hypocortisolism induced FMS and the sickness response has been observed. The notion that hypocortisolism is actually protective is intriguing.

Hypocortisolism, has been linked to fibromyalgia (FMS), post-traumatic stress disorder (PTSD), irritable bowel syndrome (IBS), low back pain (LBP), burn-out, atypical depression, chronic pelvic pain (CPP), chronic fatigue syndrome (CFS), insomnia, and degenerative neurological diseases.[2-7] Damaging effects on the immune system occur due to increased levels of pro-inflammatory cytokines and natural killer cells (NK) and T-lymphocytes which lower resistance to inflammatory and infectious disease.[1-7]

Breast cancer patients demonstrate significant post-treatment exhaustion and have been shown to have significantly altered HPA axis activity in combination with elevated IL-6 levels, flattened cortisol curves, increased mortality, and metastases. Furthermore, the more flattened the cortisol curve the worse the prognosis and the earlier the mortality.

Additional studies have found elevations in interleukin-1ß, natural killer cells, antinuclear autoantibodies, thyroid antibodies, and prostaglandins in patients with PTSD, in patients with intrusive traumatic memories, in sexually abused girls, and in patients with CFS, FMS, and chronic pelvic pain respectively.

The hypocortisol state also permissively allows an increase in sympathetic nervous system and catecholamine activity since normal cortisol-mediated suppression is lacking. Increased levels of catecholamines have been observed in patients with both PTSD and FMS.

Furthermore, exaggerations in sympathetic tone, in conjunction with underlying hypocortisolism, further fuels the production of pro-inflammatory cytokines. Associations between insulin resistance, obesity, diabetes, osteoporosis, mood disorders, and chronic pain have been described in patients with elevated levels of cytokines, particularly interleukin-6.

Alterations in rhythmicity of cortisol release have been associated with various negative outcomes, including tumor growth, early mortality in cancer, obesity and disrupted glucose metabolism. Increased coronary artery calcification and metabolic syndrome have also been linked to circadian abnormalities in cortisol, particularly flattened cortisol curves.

Measuring the Stress Response

Emerging metabolic measures of stress or "biomarkers" assist in evaluating the complex multi-system brain-body biological interactions that occur and predict the risk of disease and response to proposed interventions that can impact mental and thereby physical wellness for a lifetime.[10]

One of the key features of the HPA axis is its circadian rhythm that results in a predictable diurnal cortisol secretion pattern, whereby cortisol levels are naturally highest just before awakening, and decline over the course of the day.[2]

The preferred method for measuring the stress response is a single-day, four-point cortisol test, with the most important measurements being the first morning cortisol or cortisol awakening response (CAR) measured 30-40 minutes after awakening, and last sample prior to bedtime.[2]

Clinicians may ask patients to refrain from exercise on day of testing to avoid mis-diagnosis of hypercortisolism or diurnal dysrhythmia.[2] CAR is used significantly more than the overall diurnal salivary cortisol to define stress-induced HPA axis abnormality as a mini "stress test" as it is influenced by overall HPA reactivity and a person's anticipation of stress.[2] A blunted cortisol response upon wakening is a sign of burnout or chronic fatigue, while higher CAR is can be indicative of depression.[2] Testing should be done on a "normal" day of anticipated stress, but if an abnormal stressor is encountered, they can rinse out the collection tubes and repeat the test on a "normal" day.[2]

Additionally, common abnormal diurnal patterns include persistently elevated cortisol throughout the day, 'hypercortisolism,' and conversely abnormally low cortisol, or 'hypocortisolism.' Each has been associated with a variety of symptomatic and clinical states, but hypocortisolism is thought to represent a more 'injured' stress response and higher risk for morbidity and mortality overall, likely due to releasing of the immune response yielding higher baseline levels of inflammation.

Botanicals for Stress

'Adaptogens' are a diverse group of herbs that restore overall balance and functioning of the body as a whole through stimulating, relaxing, helping to improve focus or immune function, or normalizing unbalanced physiological processes. They have been shown to clinically reduce self-reported stress, improve mood and energy, and strengthen the immune system.

They are often particularly helpful in stress-related conditions due to their shielding effects on the brain, immune and cardiopulmonary systems. Some, such as ginseng, ashwagandha, and rhodiola, are specifically neuroprotective by blunting the impact of cortisol within the CNS by reducing neuroinflammation and even encouraging repair.

Name	Uses	Dosage
Astragaluls (Astragalus membranaceus)	Enhances mental and physical performance, learning ability, stress, fatigue, resistance to cancer and diabetes, immune function, chemoprotective, increase oxygen to tissues	250-500mg, 3-4 times daily of a standardized extract (at least 0.4% 4'-hydroxy-3'-methoxyisoflavone 7-sug.); 3 weeks on, 2 weeks off cycle
Ashwagandha (Indian ginseng, Poison gooseberry, Winter cherry)	Strengthen immunity to colds and infections, improve physical and athletic ability, increase vitality, male fertility and libido, regulate blood sugar, antioxidant, antibiotic, anti-inflammatory, rejuvenating, astringent, anti-anxiety, anti-tumor, diuretic, insomnia, reduce cholesterol, arthritis, tuberculosis, asthma, leukoderma, bronchitis, backache, fibromyalgia,menstrual problems, hiccups, chronic liver disease, balances cortisol, supports HPA axis, boosts thyroid hormones	400-900 mg daily of a standardized extract (at least 2.5% withanolides); 3 weeks on, 2 weeks off cycle
Bacopa (Bacopa monniera)	Cognitive function, concentration, fatigue, antioxidant, anxiety, epilepsy	50-100g, 1-4 times a day of a standardized extract (20% bacosides A&B)
Chaga mushroom	Strongest anti-cancer mushroom with an epochal effect in breast, liver, uterine and gastric cancer, hypertension, diabetes, tuberculosis (TB) of the bones, strengthen immune system, anti-inflammatory, anti-ulcer, anti-tumor, DNA Repair, anti-mutagenic	

Cordyceps (Cordyceps sinensis)	Immunosuppresive, anti-aging, antioxidant, decreases pro-inflammatory monoamine oxidase and lipid peroxidation activity, liver and lung protection (increase oxygenation), asthma, bronchitis, chemoprotective, anti-cancer, chronic renal failure, atherosclerosis, antiarrhythmic effects	1050mg, 2-3 times per day of a standardized extract (0.14% adenosine and 5% mannitol)
Eleuthero root or Siberian ginseng (*Eleutherococcus senticosus*)	Invigorate qi (chi or energy) or endurance, strengthen immune system, memory, chemoprotective, DNA repair, anti-inflammatory, normalize body function, particularly kidney, spleen and heart meridians, radiological protection, anti-cholesterolemic, anti-oxidant, angina, headache, insomnia, poor appetite, stress, fatigue, HPA-axis dysfunction	
Glycyrrhiza Glabra (Licorice)	Adrenal stress, expectorant, phytoestrogen effects, food sweetener, reduces cholesterol manufacturing, antiviral	250-500mg, 3 times daily standardized to contain 20% glycyrrhizinic acid or 15-30 drops of liquid extract, 3 times daily in juice or beverage
Holy basil (Tulsi, Ocimum tenuiflorum or Ocimum sanctum)	Enhance body's natural response to physical and emotional stress, reduce bloating and gas, antioxidant, support healthy adrenal function, cortisol release and immunity, radiation protection, lipid balance, blood sugar regulation, anti-inflammatory (COX-2 inhibitor), cancer prevention, slow age-related memory impairment, lower cholesterol	400-800mg daily of a standardized extract (1.0 - 2.5% ursolic acid; supercritical extracts 7-11% eugenol & 4% caryophyllene; hydroethanolic extracts 0.7-4.0% triterpenoic acids, ursolic and oleanolic acids; steam distilled extracts 40% eugenol & 15% caryophyllene
L-theanine	Found in green tea, induces relaxation through increased dopamine and serotonin, and improves sleep quality	100 mg-200mg, 1-3 times daily
Mastic (Pistacia lentiscus)	Adrenal stress, expectorant, food sweetener, H.pylori infections, oral health/cancer, phytoestrogen effects,	Oleoresin: 500mg, 2-4 times daily
Mucuna pruriens (Cowhage, Velvet bean)	Lower stress as a source of L-DOPA the precursor for dopamine, neuroprotective, Parkinson's disease, antioxidant, blood sugar, weight loss, metabolic syndrome, male infertility	100-200 mg of a standardized extract (20-95% L-Dopa) once daily in the morning, 30 minutes before breakfast
Muira puama (Ptychopetalum olacoides)	Neuroprotective, stress, libido, depression, mood	500mg up to 3 times daily
Panax ginseng	Mood, cognition, immunity, antifatigue, protection against mental, physical and environmental stress	
Phenyl-GABA		200mg BID
Phosphatidylserine (PS)	Decrease symptoms of mild depression in mood disorders	

Relora Plus	Proprietary blend of plant extracts from Magnolia officianalis, Phellodendron amurense, and B-vitamins that normalizes cortisol levels, stress-related eating, decreases weight gain, and anxiety	250mg, 3 times daily
Rosa Majalis	Anti-cancer, anti-oxidant, source for Vitamins A,C,E	
Reishi or Lingzhi (Ganoderma lucidum)	Adaptogen (mental, physical performance, learning, decrease stress and fatigue), blood pressure stabilizer, antioxidant, analgesic, kidney and nerve tonic, strengthen immune system, anti-inflammatory, anti-viral, anti-tumor, anti-parisitic, liver protectant, blood glucose regulation, chemoprotective	150-300mg, 3-4 times daily of standardized extract (4% triterpenes and 10% polysaccharides (ß-1, 3-glucans))
Rhaponticum	Strength or endurance or reduce fatigue, impotence or aphrodisiac	
Rhodiola rosea (Golden root, Roseroot, Western roseroot, Aaron's rod, Arctic root, King's crown, Lignum Rhodium, Orpin Rose)	Adaptogen, strength or endurance, reduce fatigue, mental and physical performance, decrease recovery time, antioxidant, learning, adrenal stress, depression, improve immunity, sleep patterns, mood stability, and motivation, resistance to cancer, type 2 diabetes, cardio-protective	150-300mg, 1-3 times daily, standardized (3-5% rosavins and less than 1% salidrosides)
Schisandra or Magnolia vine	Antioxidant, infection-resistant, increase skin health, liver protectant, stress/fatigue, enhance mental and physical performance, learning, adaptogen, improve resistance to cancer and diabetes, improve immune function, chemoprotective	100-200mg, twice daily with food standardized (9% schisandrans), taken 3 weeks on, 2 weeks off
Shiitake (Lentinus edodes)	Enhances mental and physical performance, increases learning ability, and decreases stress and fatigue, may improve resistance to cancer and diabetes, immune function, antiviral, chemoprotective	100-400mg 3 times daily of a standardized extract
Tongkat Ali (Eurycoma longifolia)	Stress and cortisol balance, energy/ fatigue, weight loss, erectile dysfunction, testosterone balance, infertility, athletic performance, antioxidant, anti-inflammatory	200-400mg daily of a standardized water extract of the root (50:1 to 200:1 water extraction; 200:1 standardized to 1% eurycomanone, 22% protein, 30% polysaccharides, 35% glycosaponins; LJ100 = 100:1 water extraction; contains 40% glycosaponins and 22% eurypeptides)
Valerian (Valeriana officianalis)	Insomnia, anxiety, sedation, stress/sleep disorders	200-500mg of standardized extract (0.4-1% valerenic acids), or 30-60 drops of liquid extract (1:4 w/v) in water 1-2 hours before bedtime or as needed

Nervines Tonics

Nervines are a class of botanicals that reduce sympathetic overdrive, anxiety, and irritability by sedating the autonomic nervous system and inducing a sense of calm or relaxation. They can be used during the day to blunt a hyperaroused state, or in the evening for sleep induction.

Avena sativa (Oats)	Antidepressant, anxiolytic, nervous system tonic & trophorestorative, nutritional, hypolipidemic (as food), cardiotonic, demulcent, emollient, vulnerary, antispasmodic	Infusion: 1 heaped Tbsp (approx. 3 g) to 1 cup Water; steep until at room temperature. Drink throughout the day. Tincture: (1:5, 25%), 1-5 ml TID. Bath: Add 1 heaping cup to bath water, enjoy!
Bacopa monniera (Brahmi)	Cognition & memory enhancer, nerve and brain tonic, mild anti-convulsant, antioxidant, anti-inflammatory, cardiotonic, vasocontrictor, bitter, emetic, laxative & diuretic (leaf), aphrodisiac	Powdered herb: 5-10g, QD. Extract: 300mg, QD. Capsule: 3000mg BID. Skin rub: skin mixed with oil applied prn. Tincture: (1:2, 25%), 5-13ml QD
Borago officinalis (Borage)	Leaf: Diuretic, demulcent, emollient, refrigerant, adrenal restorative, galactagogue, expectorant. Oil: inflammatory modulating, anti-atheroslcerotic, anti-platelet, hypolipidemic, atopic dermatitis, dysmenorrhea, PMS, cyclic mastalgia, hypertension and diabetic neuropathy.	2 tsp dried herb/cup; 1 cup BID. Tincture: (1:5, 60%), 1-10 ml BID. Juice pulp from fresh leaves, 10 ml BID. Seed oil: 500 mg capsule: 1-4 capsules daily.
Centella asiatica (Gotu kola)	Strengthens nervous system, function, memory, relaxant, detoxifer, diuretic, topical antibiotic, peripheral vasodilator, anti-rheumatic, vulnerary, venotonic, keratolytic, anti-mycobacerial, bitter, digestive, anti-inflammatory, laxative, dermatological builder, connective tissue builder, cellulite, cirrhosis of the liver, keloids and hypertrophic scars, leprosy, scleroderma, varicose veins and venous insufficiency, and wound repair.	Tincture: (1:2, 45%), 3-6ml QD. Dried leaves: 0.6g TID. Infusion: 1 tbsp/cup, infuse 10 min, TID. Poultice. Extract: standardized to contain asiaticoside (40%), 60-120mg QD.
Hypericum perforatum (St. John's wort)	Anti-depressant, anti-inflammatory, antimicrobial, astringent, nervine tonic, topical wound healing (burns)	Infusion: 2-4 g / cup QD to TID Tincture (1:5, 40%), 1-4 ml TID Standardized extract: 500 to 1000 mg divided daily of extract standardized to 0.3% hypericin for mild-moderate depression.
Verbena officinalis (Blue vervain)	Digestive tonic that increases intestinal motility, parasympathomimetic, anti-spasmodic, mild analgesic, nervous system tonic, hepatic stimulant, depression, melancholy	Infusion: 1 tsp/cup water, 1 cup QD – TID (fresh 3x dried). Tincture: (1:5, 25%), 2-5 ml TID. Fluid extract: (1:1, 25%), 1-3 ml TID.
Vinca major/minor (Periwinkle)	Astringent, cerebral circulatory stimulant, cytotoxic (anti-cancer), diabetes, glaucoma, stroke, brain trauma, poor memory, disordered thinking	Tincture: (1:5, 60%), 1-5 ml TID. 100 ml weekly max.

Nervines Tonics

Lavendula off. (Lavender)	Carminative, nervous system relaxant, sedative, antispasmodic, anti-depressant, anti-septic, aromatic, uterine stimulant, emmenagogue, diuretic, hypotensive, anti-rheumatic	Tincture: (1:2, 60%), 2-5ml QD. Dried flowers: 1-2g, TID. Capsules: 500mg, BID. Infusion: 1 tsp/cup, infuse 15 min, TID. Essential oil: 1-4ggt inhalations, chest rub, massage oil, pillow, douche. Bath: 100g infused and strained, added to bath.
Humulus lupulus (Hops)	Sedative, hypnotic, diuretic, analgesic, topical antibacterial, astringent, antispasmodic, premature ejaculation, restlessness, nervous tension, headache, indigestion, restless leg syndrome, anxiety, phytoestrogen (PMS or menopause-related hormonal imbalances)	100 mg 2 times a day of standardized product (5.2% bitter acids & 4% flavonoids)
Melissa off. (Lemon Balm)	Nervous system tonic and relaxant, carminative, sedative, diaphoretic, antidepressant, anti-viral, anti-microbial, hyperthyroidism choleretic, antispasmodic, anti-histamine, mild analgesic, cardiotonic, hepatic, gout, herpes, rheumatism, neuralgias	Capsules: 2-4 g QD. Infusion: 2 tsp/cup, BID. Tincture: (1:2, 45%), 3-6 ml TID (maximum of 100 ml per week). Topically: poultice, compress, Herpelieve: apply 2 – 4 times daily.
Matricaria recutita (Chamomile)	Nervous system sedative, antispasmodic, analgesic, anti-inflammatory, antiseptic, carminative, anti-microbial, anti-allergic, anti-uler, wound healing, neuralgia, rheumatic and muscular pains	Infusion: 1-2 tsp/cup water; steep 3-5 min. covered; 1 cup TID. Tincture (1:5, 45%), 1-4 ml TID; max. weely dose 100 ml. Baths, Steams, Enemas. Note: Matricaria is best dosed on the low end of its dosage range over a long period of time.
Stachys offincialis (Betony)	Sedative, mild diuretic, carminative, aromatic, skeletal muscle relaxant, astringent, alterative, circulatory tonic	Infusion: 1 tsp/cup TID. Tincture: (1:5, 45%), 2-6ml TID. Dried herb: 2-4g, TID. Poultice, mouth wash/ gargle.
Scutellaria laterifolia (Skullcap)	Sedative, nervous system relaxant, antispasmodic, anticonvulsant, hypotensive	Powdered herb: 1-2 g QD. Infusion: 1 tbsp/cup, TID. Tincture: (1:2, 45%), 2-4 ml TID (weekly max. = 100 ml).
Passiflora incarnata (Passionflower)	Antispasmodic, sedative, hypnotic, vasodilator, cardiotonic, analgesic, anxiolytic, relaxant, diuretic, anti-depressant, insomnia	Anxiety: 100-250mg, 2 times daily standardized (3.5-4% isovitexin); Insomnia/sedation: 200-500mg at bedtime standardized ((3.5-4% isovitexin)
Tilia europa (Lime flower, Linden tree)	Anxiolytic, hypotensive, sedative, diaphoretic, anti-spasmodic, diuretic, emollient, immunomodulator, anti-inflammatory, expectorant, anti-coagulant, mild astringent, peripheral vasodilator	Infusion: 1tsp/cup, 3-5 times QD. Tincture: (1:5, 40%), 3-5ml TID. Dried flowers: 2-4g, TID.

Lactuca virosa (Wild Lettuce)	Nervous system relaxant, sedative, analgesic, hypnotic, narcotic, antispasmodic, whooping cough, rheumatism, aphrodisiac	Dried leaves: 0.5-3g TID. Infusion: 1 tsp/cup, infuse 15 min, TID. Tincture: (1:1, 25%), 0.5-3ml TID.
Piper methysticum (Kava-kava)	Sedative, nervous system, anticonvulsant, local anesthetic, analgesic, anti-fungal, anti-spasmodic, stimulant, anti-depressant, muscle relaxant, euphoric, anti-inflammatory, diaphroretic, carminative, diuretic, interstitial cystitis, restless leg syndrome, anxiety, cognition	100-300mg, 1-3 times daily (for no more than 3 months) standardized to contain 30-70% kavalactones

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