Nordic Laboratories

PATIENT: XXXXXXXXXXXXXXXXX
TEST NUMBER: T-NL-XXXXX (XXXXXXXXXX)
GENDER: XYZ
AGE: XX

COLLECTED: XX/XX/XXXX
RECEIVED: XX/XX/XXXX
TESTED: XX/XX/XXXX

TEST REF: TST-NL-XXXX
PRACTITIONER:
XXXXXXXXXXXXX
XXXXXXXXXXXXXXXXXXXX

TEST NAME: NeuroAdvanced

TEST NAME	RESULTS | 03/15/21	RANGE
Urinary Inhibitory Neurotransmitters		
Tryptophan	3774	2633-12688 µg/g Cr (Optimal 3970-8450)
Serotonin	32 L	47.6-140.3 µg/g Cr (Optimal 61.0-103.2)
5-HIAA	11800	2205-11816 µg/g Cr (Optimal 2988-5850)
GABA	142 L	167-463 µg/g Cr (Optimal 193-367)
Glycine	124	41-295 mg/g Cr (Optimal 61-159)
Taurine	16.1	7.1-293.1 mg/g Cr (24.5-134.1)
Urinary Excitatory Neurotransmitters		
Glutamate	5000 H	1213-4246 µg/g Cr (Optimal 1515-2710)
Glutamine	95	27-106 mg/g Cr (Optimal 37-71)
Histidine	22.9	10.8-98.9 mg/g Cr (Optimal 19.7-58.4)
Histamine	23	3.6-44.3 µg/g Cr (Optimal 5.2-15.3)

TEST NAME: NeuroAdvanced

TEST REPORT | Results *continued*

NeuroAdvanced w Saliva Hormones
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TEST NAME	RESULTS | 03/15/21	RANGE
Urinary Excitatory Neurotransmitters		
N-Methylhistamine	138	59-195 µg/g Cr (Optimal 79-140)
PEA	40 H	3.6-38.8 µg/g Cr (Optimal 5.3-16.1)
Tyrosine	4795	3128-15548 µg/g Cr (Optimal 4790-10278)
Tyramine	1046 H	187-910 µg/g Cr (Optimal 279-588)
Dopamine	60 L	103-282 µg/g Cr (Optimal 144-240)
DOPAC	370 L	495-2456 µg/g Cr (Optimal 658-1449)
HVA	3000 L	3025-9654 µg/g Cr (Optimal 3737-7048)
Norepinephrine (pooled)	8 L	10.0-35.7 µg/g Cr (Optimal 15.0-28.1)
Normetanephrine	15	13.4-44.8 µg/g Cr (Optimal 17.9-31.7)
Epinephrine (pooled)	1	0.8-6.2 µg/g Cr (Optimal 1.4-4.2)
Ratio: Norepi/Epi	8	2.9-25.2 (Optimal 5.2-13.7)
VMA	2500	1996-5939 µg/g Cr (Optimal 2580-4766)
Urinary Inflammatory Markers		
Kynurenine	1195	108-1641 µg/g Cr (Optimal 257-960)
Kynurenic Acid	1759 H	437-1719 µg/g Cr (Optimal 639-1200)
3-Hydroxykynurenine	1568 H	80-822 µg/g Cr (Optimal 147-467)
Xanthurenic Acid	3417 H	450-2175 µg/g Cr (694-1510)
Urinary Creatinine		
Creatinine (pooled)	0.92	0.3-2.0 mg/mL

*<dl = Less than the detectable limit of the lab. **N/A** = Not applicable; 1 or more values used in this calculation is less than the detectable limit. **H** = High. **L** = Low.*

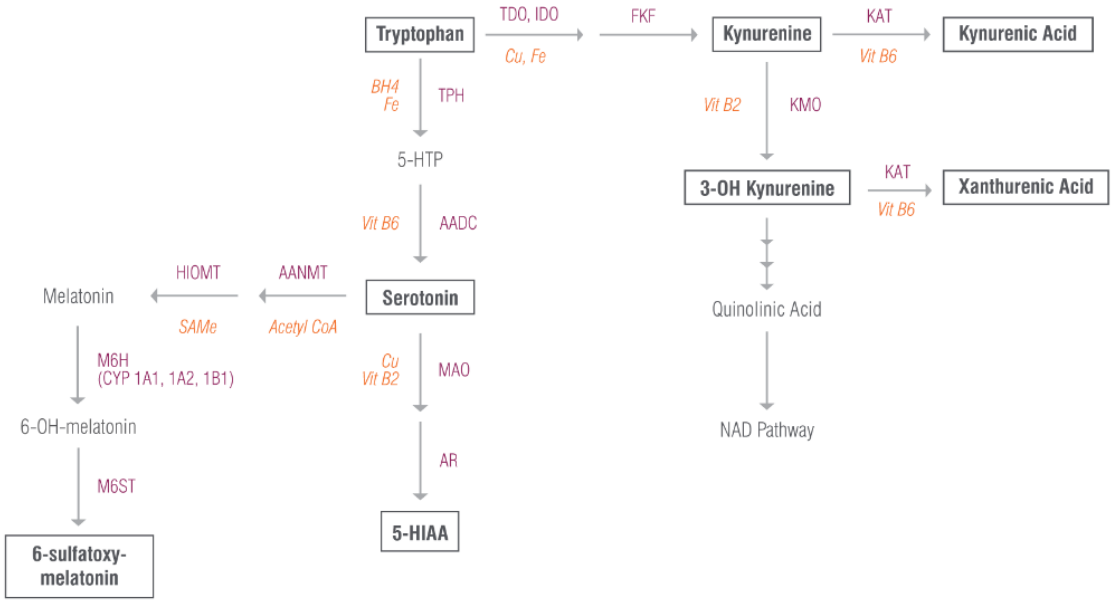
Therapies

Vitex

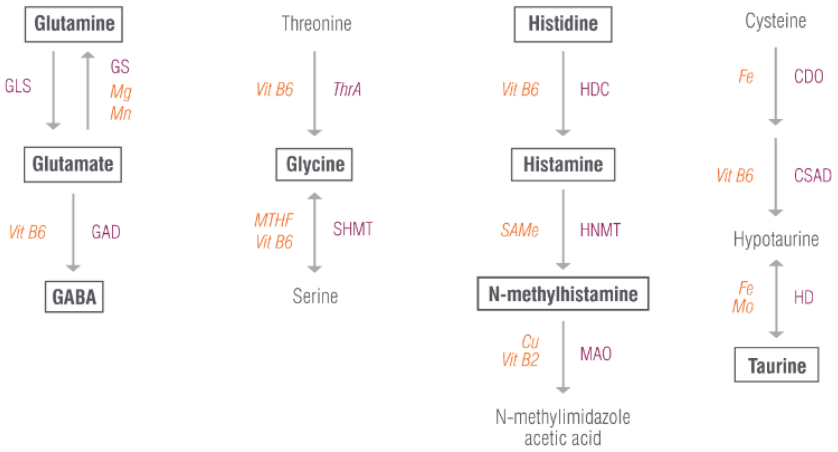
TEST NAME: NeuroAdvanced

Neurotransmitter Cascades

Tryptophan & Metabolites



Glutamate/GABA, Glycine, Histamine & Taurine

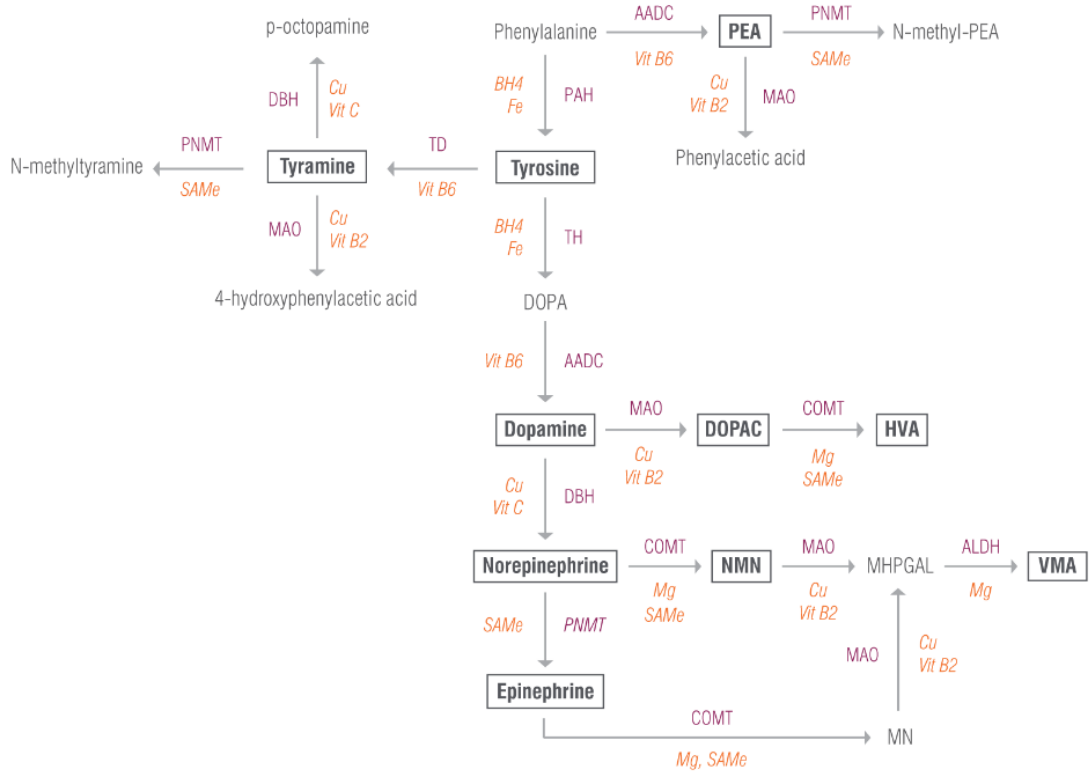


Nordic Laboratories

PATIENT: XXXXXXXXXXXXXXXXX			TEST REF: TST-NL-XXXX
TEST NUMBER: T-NL-XXXXX (XXXXXXXXXX)	COLLECTED: XX/XX/XXXX		PRACTITIONER: XXXXXXXXXXXXX
GENDER: XYZ	RECEIVED: XX/XX/XXXX		
AGE: XX	TESTED: XX/XX/XXXX		XXXXXXXXXXXXXXXXXXXX

TEST NAME: NeuroAdvanced

Catecholamines & Metabolites



Abbreviations & Key

Neurotransmitters & Metabolites:

HVA	homovanillic acid
NMN	normetanephrine
PEA	phenethylamine
VMA	vanillylmandelic acid
5-HIAA	5-hydroxyindole 3-acetic acid

Cofactors:

BH4	tetrahydrobiopterin
Cu	copper
Fe	iron
Mg	magnesium
Mn	manganese
Mo	molybdenum
MTHF	methyltetrahydrofolate
SAMe	S-adenosyl methionine

Enzymes:

AADC	aromatic L-amino acid decarboxylase
AANMT	arylalkylamine N-methyltransferase
ALDH	aldehyde dehydrogenase
AR	aldehyde reductase
CDO	cysteine dioxygenase
COMT	catechol-O-methyltransferase
CSAD	cysteinesulfinic acid decarboxylase
DBH	dopamine beta hydroxylase
FKF	N-Formyl kynurenine formamidase
GAD	glutamate decarboxylase
GLS	glutaminase
GS	glutamine synthetase
HD	hypotaurine dehydrogenase
HDC	histidine decarboxylase
HIOMT	hydroxyindole-O-methyltransferase
HNMT	histamine N-methyltransferase
IDO	indoleamine 2,3-dioxygenase
KAT	kynurenine aminotransferase
KMO	kynurenine hydroxylase/monooxygenase
MAO	monoamine oxidase
M6H	melatonin 6 hydroxylase
M6ST	melatonin 6 sulfotransferase
PAH	phenylalanine hydroxylase
PNMT	phenylethanolamine N-methyltransferase
SHMT	serine hydroxymethyltransferase
TD	tyrosine decarboxylase
TDO	tryptophan 2,3-dioxygenase
TH	tyrosine hydroxylase
ThrA	threonine aldolase
TPH	tryptophan hydroxylase

TEST NAME: NeuroAdvanced

TEST REPORT | Comments *continued*

INHIBITORY NEUROTRANSMITTERS

TRYPTOPHAN
Tryptophan is low-normal (<20th percentile). The essential amino acid tryptophan originates in diet and serves as a constituent of proteins and a precursor to neurotransmitters. Only a fraction of tryptophan is used by the GI tract, the vast majority of this amino acid enters portal circulation and undergoes liver metabolism. The remaining tryptophan pool, together with its liver degradation products, is distributed to peripheral circulation and transported to tissues such as the brain, heart, and skeletal muscle. Tryptophan not taken up by the upper GI tract is metabolized by resident microbiota.
Tryptophan is a substrate for two important biosynthetic pathways relevant to the inflammatory neuropsychiatric interface: the generation of the neurotransmitter serotonin and therefore hormone melatonin, and the formation of kynurenine derivatives and therefore niacin (vitamin B3). Tryptophan hydroxylase initiates the two-step conversion to serotonin, a process that requires tetrahydrobiopterin (BH4), iron and vitamin B6. Approximately 5-10% of tryptophan is converted to serotonin. Tryptophan dioxygenase and indoleamine 2,3-dioxygenase are the enzymes responsible for tryptophan's conversion to kynurenine in a copper and iron-dependent manner. In fact, upward of 90-95% of tryptophan is metabolized to the kynurenine pathway, and upregulation of this pathway may be a hallmark of neuroinflammation.
Research shows that tryptophan excretion is low in patients with autism spectrum disorder (Kaluzna-Czaplinska, Michalska et al. 2010), and in some individuals with a low protein diet (Poesen, Mutsaers et al. 2015). Clinically, low tryptophan is associated with aggression (Comai, Bertazzo et al. 2016), depression (Maes, Wauters et al. 1996, Messaoud, Mensi et al. 2019), impulsivity (Walderhaug, Lunde et al. 2002), with fructose malabsorption (Ledochowski, Widner et al. 2001), Alzheimer's disease (Gulaj, Pawlak et al. 2010), Crohn's disease (Gupta, Thaker et al. 2012), multiple sclerosis (Monaco, Fumero et al. 1979), pain disorders like fibromyalgia (Yunus, Dailey et al. 1992), and glucose imbalance like diabetes (Herrera, Manjarrez et al. 2003).

TREATMENT CONSIDERATIONS: Increasing protein intake may help increase tryptophan to a normal range. High tryptophan foods include chocolate, meat, tofu, fish, beans, milk, nuts, seeds, oatmeal, and eggs. The recommended daily intake for tryptophan is 4 mg per kilogram of body weight or 1.8 mg per pound.

SEROTONIN AND 5-HIAA
Serotonin is lower than the optimal range, whereas 5-hydroxyindoleacetic acid (5HIAA) is higher than the optimal range. This indicates that monoamine oxidase (MAO) activity may be high. Increased MAO activity has been reported in patients with mood disorders, such as depression, anxiety and sleep disturbances which are also symptoms of low serotonin and were self-reported by the patient (Zeb, et. al. 2017; Aleksovski, et. al. 2017; Audhya, et. al. 2012). MAO is modulated by estrogens (which slow down MAO) and cortisol (which speed up MAO), so when if estrogen is low and/or cortisol is high, MAO activity increases, accelerating conversion of serotonin to its inert metabolite 5-HIAA.

THERAPEUTIC CONSIDERATIONS: When serotonin is low, testing for estrogen and cortisol is worth considering. In addition, supplementation with cofactors to promote serotonin biosynthesis (e.g. vitamin B6) and precursors (such as 5-HTP) to help raise serotonin are often helpful. L-theanine, and probiotics may be beneficial (Patterson et al., 2014; Pamela Wartian Smith, 2008; Strasser et al., 2016). Botanical MAO inhibitors may also be helpful in slowing down MAO activity, these include but are not limited to curcumin and passionflower. Additionally, lifestyle modifications, such as regular exposure to bright light, healthy diet, sufficient exercise, and positive self-talk are all effective strategies that result in increased serotonin levels (Young, 2007). If dysbiosis is suspect, introducing digestive support may be beneficial.

GABA
GABA is below the optimal range. The brain's major inhibitory neurotransmitter, GABA functions as the "off" switch in the brain. GABA is essential to limiting brain neuron excitation so that input signals are balanced and not overdone. Appropriate levels of GABA prevent anxiety, improve mood, promote sleep, lower blood pressure, act as a muscle relaxant, aid in formation and storage of fear memories, increase insulin secretion and decrease blood glucose levels.
Research on urinary levels of GABA is scarce, however in individuals with anxiety and depression, GABA levels are low in the blood, in cerebrospinal fluid and in the brain (Mann, et. al. 2014; Goddard, 2016). The inhibitory and excitatory balance between GABA and glutamate is very important for healthy brain function, and imbalance in these systems may contribute, in part, to the pathology of anxiety and depression, but we have yet to understand the mechanism.

THERAPEUTIC CONSIDERATIONS: with low GABA, supplementation with GABA, L-theanine, cofactor support (e.g. B6), growth hormone-releasing hormone, Ginko biloba, Ashwagandha, Kava, Valerian root, Melissa off. (lemon balm), Scutellaria sinensis (skullcap), Gotu Cola, Magnolia and Phellodendron bark, and probiotics may be helpful (Alramadhan et al., 2012; Awad et al., 2007; Alexeev et al., 2012; Dhakal et al., 2012). Additionally, yoga (Streeter et al., 2012) and meditation (Guglietti et al., 2013) increase brain GABA levels.

GLYCINE
Glycine is within normal range. Glycine is a simple, nonessential (can be made in the body) amino acid that plays a role in the production of DNA, phospholipids, collagen, creatine, heme and glutathione. Glycine serves as a neurotransmitter that modulates excitatory signals in the brain, and as an anti-inflammatory agent that calms aggression, improves sleep quality, stabilizes blood sugar, and improves metabolic parameters.

TAURINE
Taurine is low-normal (<20th percentile). Taurine is a semi-essential or conditionally essential sulfur-containing amino acid and an inhibitory

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TEST REPORT | Comments *continued*

(calming) neurotransmitter. Taurine improves sleep, relieves anxiety, alleviates fatigue, aids with metabolism and digestion, and promotes glucose control and electrolyte balance.
The main source of taurine is diet (highest in shellfish and poultry (dark meat)). Taurine protects healthy cells and tissues, functions as a potent antioxidant to reduce oxidative stress, mitigates mitochondrial and endoplasmic reticulum stress, inhibits lipid peroxidation, improves energy metabolism, regulates gene expression, and participates in detoxification, calcium homeostasis and osmoregulation processes. By fulfilling all these functions, taurine is therefore protective in cardiovascular health, improves lean body mass and exercise performance. With regard to brain health, taurine serves a neuroprotective role, promotes neural development in embryonic and adult brain tissues, and is an important factor in neurogenesis.
Research shows that taurine excretion is low specifically with vegetarian or vegan diets (Rana and Sanders 1986) and with low protein diets in general (Turner, Brum et al. 1964). Low taurine levels are implicated in diabetes (Sak, Erdenen et al. 2019), hypertension (Sak, Erdenen et al. 2019) and breast cancer (El Agouza, Eissa et al. 2011).

THERAPEUTIC CONSIDERATIONS: taurine is found in most types of meat, shellfish, and fish - increasing intake of these foods may help restore normal taurine levels. Additionally, taurine supplementation is considered safe and can be tolerated up to 3 g per day without adverse effects.

EXCITATORY NEUROTRANSMITTERS

GLUTAMATE
Glutamate is above the optimal range. Research shows that in depressed individuals (self-reported), glutamate is elevated in urine (Jones, et. al. 2005), in blood (Ogawa, et. al. 2018), and in the brain (Sanacora, et. al. 2005). Elevated glutamate levels in depression are thought to be related to higher levels of inflammation (Muller, 2007) and inadequate mitochondrial function to properly metabolize glutamate (Abdallah, et. al. 2014).
The brain's major excitatory neurotransmitter glutamate (also known as glutamic acid) functions as the "on" switch in the brain. Glutamate regulates appetite, thinking, increases gut motility, optimizes learning, modulates memory, mood and perception of pain, improves libido, and decreases sleep. Symptoms of high glutamate may include anxiety, depression, impulsivity, decreased focus, and insomnia. Additional studies on urinary glutamate levels report higher levels in patients with celiac disease (Marko, et. al. 1960), hyperthyroidism (Belanger, et. al. 1972), and rheumatoid arthritis (Jones, et. al. 2005).

THERAPEUTIC CONSIDERATIONS: Therapies such as GABA, L-theanine, lithium orotate and taurine may be beneficial to counter glutamate actions. NAC and Vitamin E can help reduce oxidative stress and co-factor supplementation (B3 and B6, magnesium, NAC) can aid in glutamate metabolism.

GLUTAMINE
Glutamine is high-normal (>80th percentile), likely due to supplementation or recent dietary intake. Glutamine is an essential and the most abundant free amino acid in the human body. Glutamine provides fuel for rapidly dividing cells (lymphocytes, enterocytes and epithelial cells of the intestines), helps balance ammonia levels in the body, improves immune system function, contributes to biosynthesis of proteins, amino acids, nucleic acids and glutathione, and protects intestinal lining. Additionally, glutamine increases glutamate and GABA levels in the brain and in the body.
Research on urinary high glutamine levels is scarce, however high circulating levels of glutamine are associated with bipolar depression (Pålsson, Jakobsson et al. 2015).

TREATMENT CONSIDERATIONS: evaluation of supplementation may be warranted. Glutamine is also high in chicken, fish, cabbage, spinach, diary, tofu and lentils among many over foods.

HISTIDINE
Histidine is within range. Histidine is a semi-essential amino acid that gives rise to the neurotransmitter histamine. Histidine protects neurons, assists with making new blood cells, reduces inflammation and oxidative stress, helps with tissue repair and growth. Histidine also helps ameliorate fatigue, promotes clear thinking and concentration, reduces appetite, decreases anxiety, improves sleep and glucose homeostasis.

HISTAMINE
Histamine is above the optimal range, which may be due to allergies (self-reported). Research shows that individuals with gastrointestinal food allergies have higher urinary histamine levels (Raithel, et. al. 2015). This study showed that histamine was elevated in both IgE- and non-IgE food allergy types during consumption of offending foods, but not during the hypoallergenic diet.

Histamine plays a dual role in the body as a neurotransmitter and a modulator of the immune system that has anti-pain properties, plays a neuroprotective role in the brain, and contributes to optimal maintenance of cognition and memory. Histamine stimulates wakefulness and decreases sleep, stimulates gastric acid production, increases metabolism, suppresses appetite, and prevents weight gain. Histamine is a potent vasodilator and a pro-inflammatory agent. Additional research studies show that urinary histamine is elevated in patients with flushing disorder (Myers et al., 1981), cystitis (el-Mansoury et al., 1994), polycythemia (Horakova et al., 1977), and pregnancy (Harrison et al., 1974). Clinically, high histamine levels are implicated in depression, headaches, sensitivity to chemicals, and sleep difficulties.

THERAPEUTIC CONSIDERATIONS: Beneficial therapeutic strategies to reduce histamine levels may involve antihistamines and/or a low histamine diet. High histamine foods include but are not limited to beer, champagne, aged cheeses, eggplant, canned fish, fermented meat, red and white wine, sauerkraut, and spinach (Maintz and Novak, 2007), however individual food sensitivities ought to be considered as well.

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Additionally, flavonoids (green tea extract, quercetin, grape seed extract, gingko biloba, citrus bioflavonoids, bilberry extract, hawthorn extract) may be beneficial to ease the symptoms of high histamine (Murray et al., 2005).

N-METHYLHISTAMINE
N-Methylhistamine is within range. N-Methylhistamine is a major metabolite of the neurotransmitter histamine.

PEA
PEA is elevated. PEA, also known as phenethylamine, promotes energy, elevates mood, and regulates attention. PEA also contributes to aggression, serves as a biomarker for ADHD, and prolongs the signaling of dopamine, norepinephrine, and serotonin. Urinary PEA levels increase after amphetamine use (Kusaga et al., 2002;Zametkin et al., 1984), exercise (Szabo et al., 2001), and in the following disorders: bipolar disorder (Karoum et al., 1982), phenylketonuria (Reynolds et al., 1978), schizophrenia (O'Reilly and Davis, 1994), postpartum period (Taylor et al., 1996), and in severe anxiety and insomnia (DeLisi et al., 1984). High PEA is suspected in the etiology of anxiety, inflammation, inability to focus (racing thoughts), sleep difficulties, and toxicity.
PEA is preferentially inactivated to phenylacetic acid by monoamine oxidase b (MAOb). Inhibitors of MAOb can result in increased levels of PEA and have beneficial effects but also precipitate symptoms of excess PEA. Irreversible pharmaceutical inhibitors of MAOb include selegiline-eldepryl and rasagiline. The antifungal medication Lamisil-Terbinafine, widely used for treating athlete's foot, is also a MAOb inhibitor, as are herbs commonly used in foods (tumeric, nutmeg) and natural medications (Syrian Rue, Passionflower, Kava).

THERAPEUTIC CONSIDERATIONS: Consideration of eliminating, reducing, or changing medications/herbs that may inhibit MAOb and increase PEA to high levels associated with side effects.

TYROSINE
Tyrosine is within range. Tyrosine is obtained from diet (sesame seeds, cheese, soy, meat, nuts and fish) or synthesized in the body from the amino acid phenylalanine. Tyrosine serves as a constituent of proteins and gives rise to neurotransmitters, like dopamine, norepinephrine and epinephrine; and the trace-amine tyramine. Additionally, in the thyroid gland, tyrosine can also be iodinated to give rise to thyroid hormones. Tyrosine enhances cognitive performance, energy, and alertness, and improves memory after sleep deprivation. Tyrosine also prevents the depletion of central and peripheral catecholamines (dopamine, norepinephrine, epinephrine) induced by acute stress, thereby eliciting protective effects on behavioral and cardiovascular parameters in the body.

TYRAMINE
Tyramine is high which is usually due to eating foods high in this trace amine (protein). Specifically, tyramine is found in aged, fermented cured or spoiled food where microbes with decarboxylase enzymes convert tyrosine to tyramine. These foods include aged cheeses, smoked fish, cured meats, wine, and some types of beer. In sensitive individuals, high tyramine ingestion can trigger migraines by causing blood vessel restriction and then rebound vasodilation (Burns and Kidron 2020). Additionally, tyramine can trigger norepinephrine release, thereby stimulating sympathetic nervous system and consequently increase blood pressure. Because of this sympathetic mechanism, symptoms of agitation, anxiety, rapid heartbeat, and headaches may be noted.

THERAPEUTIC CONSIDERATIONS: avoid tyramine high foods (https://headaches.org/wp-content/uploads/2018/02/TyramineDiet.pdf) and calm the sympathetic nervous system. Supplements such as SAMe, magnesium, vitamin B2 may aid with promoting norepinephrine metabolism. Additionally, nervines, adaptogens, L-theanine, biofeedback and meditation may help quiet down the overactive sympathetic response.

DOPAMINE
Dopamine is lower than the reference range. Dopamine improves attention, focus, and motivation, helps with decision making, modulates movement control, promotes lactation, increases blood pressure, urine output and sodium excretion, and allows for feelings of reward and pleasure. Additionally, the quest for dopamine stimulation plays a central role in the etiology of addiction. Dopamine also serves as the parent precursor to norepinephrine and epinephrine. Research shows that urinary dopamine levels are reduced in patients with Alzheimer's disease (Liu et al., 2011), anorexia nervosa (Van Binsbergen et al., 1991), anxiety with depression (Field et al., 2010), fibromyalgia (Riva et al., 2012), and periodic limb movement disorder (Cohrs et al., 2004). Clinically, low dopamine is implicated in addiction, apathy, cravings, depression, fatigue, impulse control issues, increased sensitivity to pain, low libido, low mood, memory issues, sleep disturbances, and weight control issues.

THERAPEUTIC CONSIDERATIONS: Supplementation with precursors (tyrosine or L-DOPA) and/or cofactors (iron, vitamin B6, tetrahydrofolate) to promote biosynthesis may be beneficial.

DOPAC
DOPAC is lower than the reference range. DOPAC is the primary metabolite of dopamine formed via the actions of monoamine oxidase. Research shows that DOPAC is reduced in the urine of patients with Alzheimer's disease (Liu et al., 2011).

HVA
Homovanillic acid (HVA) is lower than the reference range. HVA is a dopamine metabolite formed through the actions of the monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT) enzyme. Research shows that HVA is reduced in the urine of patients with monoamine oxidase enzyme deficiency (Sims et al., 1989), polycystic ovarian syndrome (Shoupe and Lobo, 1984), and periodic limb movement disorder (Cohrs et al., 2004).

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NOREPINEPHRINE
Norepinephrine is lower than the reference range. Norepinephrine functions both as a neurotransmitter and a hormone, participating in the body's fight or flight response. Norepinephrine increases alertness, focuses attention, fine-tunes vigilance, increases blood pressure, heart rate, and blood glucose, reduces digestive activity, pain and sleep, prevents bladder emptying, and regulates body temperature. The adrenal gland produces approximately 20% of norepinephrine with 80% produced by the sympathetic nerve fibers. Research shows that urinary norepinephrine is reduced in patients with Alzheimer's disease. Clinically, low norepinephrine is implicated in anorexia, attention impairment, depression, fatigue, hypotension, lack of motivation, lethargy, low mood, memory issues, slow pulse rate, and weight issues.

THERAPEUTIC CONSIDERATIONS: Precursor supplementation with tyrosine or phenylalanine, or cofactor support with ascorbic acid, iron, tetrahydrofolate, and vitamin B6 may be beneficial.

NORMETANEPHRINE
Normetanephrine is low-normal (<20th percentile). Lower normetanephrine levels may be reflective of insufficient norepinephrine levels in the adrenal glands.

EPINEPHRINE
Epinephrine is low-normal (<20th percentile). Epinephrine functions both as a neurotransmitter and a hormone, participating in the body's "fight or flight" response. Approximately 80% of peripheral catecholamine output by the adrenal glands is epinephrine. Research shows that urine epinephrine is decreased in Alzheimer's disease (Liu et al., 2011), metabolic syndrome (Landsberg et al., 1991), and obesity (Landsberg et al., 1991). Clinically, low epinephrine is implicated in attention impairment, chronic stress, depression, cold body temperature, dizziness, chronic fatigue, hypotension, low mood and libido, and memory issues.

THERAPEUTIC CONSIDERATIONS:Adrenal support may be beneficial to increase epinephrine levels.

VMA
Vanillylmandelic acid (VMA) is low-normal (<20th percentile). VMA is a norepinephrine and epinephrine metabolite formed via the actions of monoamine oxidase (MAO), catechol-O-methyl transferase (COMT), and aldehyde dehydrogenase. Research shows that in rare cases, VMA is reduced in patients with MAO deficiency (Sims et al., 1989) or on SSRI and SNRI combination therapy (Chalon et al., 2003).

INFLAMMATORY MARKERS

KYNURENINE
Kynurenine is high-normal (>80th percentile). Kynurenine is a central metabolite of the amino acid tryptophan with vasodilatory properties. Kynurenine is utilized by the body in the production of niacin (vitamin B3), eventually leading to the formation of NAD+, which plays a pivotal role in energy metabolism, gene expression, cell death and regulation of calcium homeostasis. More than 90% of the body's tryptophan is metabolized to the kynurenine pathway.
Kynurenine is synthesized by the enzyme tryptophan dioxygenase, which is expressed primarily but not exclusively in the liver, and indoleamine 2,3-dioxygenase, which is made in many tissues in response to immune activation by interferons and cytokines, or free radicals. In the brain, approximately ~40% of kynurenine is produced locally, whereas the rest is absorbed from the blood.
Kynurenine degradation generates a series of neuroprotective and neurotoxic compounds that can activate or inhibit N-methyl-d-aspartate (NMDA) glutamate receptors (see kynurenic acid and 3-OH kynurenine). Upregulation of this pathway may be a hallmark of neuroinflammation and is associated with certain disorders.
Research shows that kynurenine is high in high with tryptophan administration (Michael, Drummond et al. 1964), hydrocortisone treatment (Rose and Braidman 1971), metabolic syndrome (Oh, Seo et al. 2017), with major coronary events (Pedersen, Svingen et al. 9/2013), and in women in pregnancy (Rose and Braidman 1971). High kynurenine levels have been implicated in disorders like Irritable Bowel Syndrome (Fitzgerald, Cassidy Eugene et al. 2008), lupus (Akesson, Pettersson et al. 2018), Crohn's disease (Gupta, Thaker et al. 2012), and Alzheimer's Disease (Chatterjee, Goozee et al. 2018). Additionally, caffeine (Orlikov and Ryzov 1991) and regular black tea (Gostner, Becker et al. 2015) consumption can elevate kynurenine levels as well.

TREATMENT CONSIDERATIONS: reduction of inflammation through diet and supplementation may be beneficial. Glutathione support and modulation of the NMDA receptor (e.g. magnesium) may help reduce symptoms.

KYNURENIC ACID
Kynurenic acid is high. Kynurenic acid is a neuroactive metabolite produced from kynurenine. Kynurenine is formed from tryptophan via the enzyme tryptophan dioxygenase and indoleamine 2,3-dioxygenase; and metabolized along two independent pathways to produce kynurenic acid via aminotransferases and 3-OH kynurenine.
Kynurenic acid (unless in excess amounts) is regarded to have a neuroprotective role because it inhibits the N-methyl-d-aspartate (NMDA) glutamate receptor, reduces the neurotransmitter glutamate release and thereby prevents excitotoxicity.
Research shows that urinary kynurenic acid levels are high with tryptophan administration (Michael, Drummond et al. 1964) and metabolic syndrome (Oh, Seo et al. 2017). High kynurenic acid levels are implicated in schizophrenia (Fazio, Lionetto et al. 2015).

TREATMENT CONSIDERATIONS: evaluate tryptophan supplementation and blood sugar regulation. Consider anti-inflammatory diet and supplements to reduce neuroinflammation.

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3-HYDROXYKYNURENINE
3-Hydroxykynurenine is high. 3-Hydroxy Kynurenine (3-OH Kynurenine) is a metabolic intermediate of the kynurenine pathway, one of the major metabolites of tryptophan degradation. Kynurenine is transformed into 3-OH Kynurenine, which acts as a N-methyl-d-aspartate (NMDA) glutamate receptor agonist and has been demonstrated to exert neurotoxic effects.
Neurotoxicity elicited by 3-OH Kynurenine appears to be also related to generation of oxidative stress produced by reactive radical species, formed as a result of auto-oxidation. Additionally, 3-OH Kynurenine gives rise to neurotoxic metabolites, such as quinolinic acid, which activate the NMDA receptor, induce lipid peroxidation and promote oxidative stress.
Research shows that urinary levels of 3-OH Kynurenine are high with hydrocortisone treatment (Rose and Braidman 1971) and in women in pregnancy (Rose and Braidman 1971). High 3-OH Kynurenine is implicated in vitamin B6 deficiency (Theofylaktopoulou, Ulvik et al. 2014) and Alzheimer's disease (Schwarz, Guillemin et al. 2013).

TREATMENT CONSIDERATIONS: consider glutathione support and antioxidant support to prevent the oxidative stress produced by 3-hydroxyhynurenine. Consider B6 supplementation (under 200 mg/day for safety).

XANTHURENIC ACID
Xanthurenic acid is high. Xanthurenic acid is a metabolite of the kynurenine pathway, formed directly from 3-OH Kynurenine, and serves as an indirect marker of vitamin B6 status. Vitamin B6 insufficiency leads to elevated levels of xanthurenic acid in urine. Increased excretion of xanthurenic acid following tryptophan ingestion has been used a measure of vitamin B6 deficiency, which in scientific literature is called the tryptophan loading test (oral 2 g challenge). If xanthurenic acid levels are elevated in the absence of tryptophan administration, vitamin B6 deficiency is considered to be significant.
Vitamin B6 deficiency that contributes to elevated xanthurenic acid levels can also increase oxidative stress in the body. The hydroxylated quinone structure of xanthurenic acid can bind iron and increase DNA oxidative damage. Therefore, elevated xanthurenic acid levels may suggest antioxidant insufficiency.
Research shows that xanthurenic acid is high with vitamin B6 deficiency (Chiang, Selhub et al. 2005), with hydrocortisone treatment (Rose and Braidman 1971), rheumatoid arthritis (Chiang, Selhub et al. 2005), metabolic syndrome (Oh, Seo et al. 2017), autism spectrum disorder (Gevi, Zolla et al. 2016), and in women in pregnancy (Rose and Braidman 1971).

THERAPEUTIC CONSIDERATIONS: vitamin B6 supplementation with antioxidant support may be warranted.

Creatinine levels reflect urine concentration.
Low values suggest overly dilute urine; High values suggest overly concentrated urine.
Extreme low or high values may be induced by kidney or other metabolic disorders, but most values will be due to inadequate hydration (high creatinine) or excessive water intake in the several hours prior to testing (low creatinine). Creatinine is used to adjust the lab results for kidney function. No samples were refused due to quality issues.

Estradiol is lower than the observed range for a postmenopausal woman, which contributes to symptoms of estrogen deficiency. Progesterone is within expected low range for a postmenopausal woman. Consider estrogen therapy (assuming no contraindications) in combination with bio-identical progesterone to help resolve estrogen deficiency symptoms.

Progesterone is within range. Reported symptoms suggest estrogen deficiency (i.e. hot flashes, night sweats). It would be worthwhile to consider progesterone supplementation, as it often helps balance symptoms of both estrogen dominance and estrogen deficiency.

Testosterone is within normal range but symptoms of androgen deficiency persist. This may be due to other hormonal imbalances with symptom profiles similar to low androgens, which include low thyroid or low cortisol caused by excessive stressors. Note that symptoms of both low thyroid and low cortisol are self-reported as problematic.

DHEAS is within low-normal expected age range. Chronic low DHEAS may suggest HPA axis dysfunction, particularly if cortisol is also low and symptoms are indicative of low adrenal function. DHEAS is highest during the late teens to early twenties (10-20 ng/ml) and drops steadily with age to the lower end of range by age 70-80. Consider adrenal adaptogens or DHEA supplements if symptoms of androgen deficiency are problematic.

Cortisol is within the expected range in the morning but symptoms of both high and low cortisol indicate adrenal gland stressors. Under stress situations the adrenal glands respond by increasing cortisol output. When cortisol levels are within normal range under situations of excessive stress this is not suggestive of normal adrenal function and more likely indicates that the adrenal glands are fatigued and not meeting the demands of the stressors. Since cortisol was only tested in the morning, it is possible that levels dropped to lower levels (adrenal fatigue) or increased throughout the remainder of the day. Additional testing of cortisol, minimally as an am/pm sample, but preferably 4x throughout the day to determine the circadian profile is recommended to help guide treatment strategy. HPA axis dysfunction is most commonly caused by chronic unresolved stress (mental/emotional/physical), and usually leads to symptoms such as fatigue, allergies (immune dysfunction), chemical sensitivities, cold body temperature, and sugar cravings. Adequate sleep, gentle exercise, meditation, a healthful diet, natural progesterone, adrenal gland extracts, as well as nutritional (vitamins C and B5) and botanical supplements are some of the natural ways to help support adrenal function. For additional information and for strategies to manage stress and to support adrenal health, the following books are worth reading: "Adrenal Fatigue: The 21st Century Stress Syndrome" by James L. Wilson, ND, DC, PhD; "The Cortisol Connection" by Shawn Talbott, PhD; "The End of Stress As We Know It" by Bruce McEwen, PhD.

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INHIBITORY NEUROTRANSMITTERS

TRYPTOPHAN
Tryptophan is low-normal (<20th percentile). The essential amino acid tryptophan originates in diet and serves as a constituent of proteins and a precursor to neurotransmitters. Only a fraction of tryptophan is used by the GI tract, the vast majority of this amino acid enters portal circulation and undergoes liver metabolism. The remaining tryptophan pool, together with its liver degradation products, is distributed to peripheral circulation and transported to tissues such as the brain, heart, and skeletal muscle. Tryptophan not taken up by the upper GI tract is metabolized by resident microbiota.
Tryptophan is a substrate for two important biosynthetic pathways relevant to the inflammatory neuropsychiatric interface: the generation of the neurotransmitter serotonin and therefore hormone melatonin, and the formation of kynurenine derivatives and therefore niacin (vitamin B3). Tryptophan hydroxylase initiates the two-step conversion to serotonin, a process that requires tetrahydrobiopterin (BH4), iron and vitamin B6. Approximately 5-10% of tryptophan is converted to serotonin. Tryptophan dioxygenase and indoleamine 2,3-dioxygenase are the enzymes responsible for tryptophan's conversion to kynurenine in a copper and iron-dependent manner. In fact, upward of 90-95% of tryptophan is metabolized to the kynurenine pathway, and upregulation of this pathway may be a hallmark of neuroinflammation.
Research shows that tryptophan excretion is low in patients with autism spectrum disorder (Kaluzna-Czaplinska, Michalska et al. 2010), and in some individuals with a low protein diet (Poesen, Mutsaers et al. 2015). Clinically, low tryptophan is associated with aggression (Comai, Bertazzo et al. 2016), depression (Maes, Wauters et al. 1996, Messaoud, Mensi et al. 2019), impulsivity (Walderhaug, Lunde et al. 2002), with fructose malabsorption (Ledochowski, Widner et al. 2001), Alzheimer's disease (Gulaj, Pawlak et al. 2010), Crohn's disease (Gupta, Thaker et al. 2012), multiple sclerosis (Monaco, Fumero et al. 1979), pain disorders like fibromyalgia (Yunus, Dailey et al. 1992), and glucose imbalance like diabetes (Herrera, Manjarrez et al. 2003).

TREATMENT CONSIDERATIONS: Increasing protein intake may help increase tryptophan to a normal range. High tryptophan foods include chocolate, meat, tofu, fish, beans, milk, nuts, seeds, oatmeal, and eggs. The recommended daily intake for tryptophan is 4 mg per kilogram of body weight or 1.8 mg per pound.

SEROTONIN AND 5-HIAA
Serotonin is lower than the optimal range, whereas 5-hydroxyindoleacetic acid (5HIAA) is higher than the optimal range. This indicates that monoamine oxidase (MAO) activity may be high. Increased MAO activity has been reported in patients with mood disorders, such as depression, anxiety and sleep disturbances which are also symptoms of low serotonin and were self-reported by the patient (Zeb, et. al. 2017; Aleksovski, et. al. 2017; Audhya, et. al. 2012). MAO is modulated by estrogens (which slow down MAO) and cortisol (which speed up MAO), so when if estrogen is low and/or cortisol is high, MAO activity increases, accelerating conversion of serotonin to its inert metabolite 5-HIAA.

THERAPEUTIC CONSIDERATIONS: When serotonin is low, testing for estrogen and cortisol is worth considering. In addition, supplementation with cofactors to promote serotonin biosynthesis (e.g. vitamin B6) and precursors (such as 5-HTP) to help raise serotonin are often helpful. L-theanine, and probiotics may be beneficial (Patterson et al., 2014; Pamela Wartian Smith, 2008; Strasser et al., 2016). Botanical MAO inhibitors may also be helpful in slowing down MAO activity, these include but are not limited to curcumin and passionflower. Additionally, lifestyle modifications, such as regular exposure to bright light, healthy diet, sufficient exercise, and positive self-talk are all effective strategies that result in increased serotonin levels (Young, 2007). If dysbiosis is suspect, introducing digestive support may be beneficial.

GABA
GABA is below the optimal range. The brain's major inhibitory neurotransmitter, GABA functions as the "off" switch in the brain. GABA is essential to limiting brain neuron excitation so that input signals are balanced and not overdone. Appropriate levels of GABA prevent anxiety, improve mood, promote sleep, lower blood pressure, act as a muscle relaxant, aid in formation and storage of fear memories, increase insulin secretion and decrease blood glucose levels.
Research on urinary levels of GABA is scarce, however in individuals with anxiety and depression, GABA levels are low in the blood, in cerebrospinal fluid and in the brain (Mann, et. al. 2014; Goddard, 2016). The inhibitory and excitatory balance between GABA and glutamate is very important for healthy brain function, and imbalance in these systems may contribute, in part, to the pathology of anxiety and depression, but we have yet to understand the mechanism.

THERAPEUTIC CONSIDERATIONS: with low GABA, supplementation with GABA, L-theanine, cofactor support (e.g. B6), growth hormone-releasing hormone, Ginko biloba, Ashwagandha, Kava, Valerian root, Melissa off. (lemon balm), Scutellaria sinensis (skullcap), Gotu Cola, Magnolia and Phellodendron bark, and probiotics may be helpful (Alramadhan et al., 2012; Awad et al., 2007; Alexeev et al., 2012; Dhakal et al., 2012). Additionally, yoga (Streeter et al., 2012) and meditation (Guglietti et al., 2013) increase brain GABA levels.

GLYCINE
Glycine is lower than the optimal range, which may be due to depression (self-reported). Although research on urinary levels of glycine is scarce, levels of glycine in blood are lower in depressed individuals than in controls (Altamura, et. al. 1995). Sleep disturbance symptom is also self-reported by this individual. Supplementation with glycine has been shown to improve sleep quality (Yamadera, et. al. 2007) and help with daytime sleepiness and fatigue associated with interrupted sleep (Bannai, et. al. 2012). Research shows that glycine crosses the blood-brain barrier, induces vasodilation throughout the body, decreases core body temperature and promotes sleep by stabilizing sleep state and shortening latency to slow-wave sleep without any alterations to sleep architecture (Kawai, et. al. 2015).
Glycine is a neurotransmitter and a simple, nonessential (can be made in the body) amino acid that plays a role in the production of DNA, phospholipids, collagen, creatine, heme and glutathione. Glycine serves as an anti-inflammatory agent, calms aggression, improves sleep quality, stabilizes blood sugar, improves metabolic parameters and modulates excitatory signals in the brain. Low levels may be indicative of

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chronically increased demand for tetrahydrofolate (active folic acid) production, for which glycine serves as a precursor.
Additional research studies show that urinary glycine levels are reduced after intense exercise (Corsetti, et. al. 2016), and in patients with rheumatoid arthritis (Jones, et. al. 2005), or hypometabolic disorders, such as hypothyroidism (Friedrich, et. al. 2017), obesity (Ahmad, et. al. 2016), and diabetes (Sasaki, et. al. 1988).

THERAPEUTIC CONSIDERATIONS: Glycine supplementation, vitamin B6, serine and MTHF may all support optimal glycine levels.

TAURINE
Taurine is lower than the reference range. Taurine is a semi-essential or conditionally essential sulfur-containing amino acid and an inhibitory (calming) neurotransmitter. Taurine improves sleep, relieves anxiety, alleviates fatigue, aids with metabolism and digestion, and promotes glucose control and electrolyte balance.
The main source of taurine is diet (highest in shellfish and poultry (dark meat)). Taurine protects healthy cells and tissues, functions as a potent antioxidant to reduce oxidative stress, mitigates mitochondrial and endoplasmic reticulum stress, inhibits lipid peroxidation, improves energy metabolism, regulates gene expression, and participates in detoxification, calcium homeostasis and osmoregulation processes. By fulfilling all these functions, taurine is therefore protective in cardiovascular health, improves lean body mass and exercise performance. With regard to brain health, taurine serves a neuroprotective role, promotes neural development in embryonic and adult brain tissues, and is an important factor in neurogenesis.
Research shows that taurine excretion is low specifically with vegetarian or vegan diets (Rana and Sanders 1986) and with low protein diets in general (Turner, Brum et al. 1964). Low taurine levels are implicated in diabetes (Sak, Erdenen et al. 2019), hypertension (Sak, Erdenen et al. 2019) and breast cancer (El Agouza, Eissa et al. 2011).

THERAPEUTIC CONSIDERATIONS: taurine is found in most types of meat, shellfish, and fish - increasing intake of these foods may help restore normal taurine levels. Additionally, taurine supplementation is considered safe and can be tolerated up to 3 g per day without adverse effects.

EXCITATORY NEUROTRANSMITTERS

GLUTAMATE
Glutamate is above the optimal range. Research shows that in depressed individuals (self-reported), glutamate is elevated in urine (Jones, et. al. 2005), in blood (Ogawa, et. al. 2018), and in the brain (Sanacora, et. al. 2005). Elevated glutamate levels in depression are thought to be related to higher levels of inflammation (Muller, 2007) and inadequate mitochondrial function to properly metabolize glutamate (Abdallah, et. al. 2014).
The brain's major excitatory neurotransmitter glutamate (also known as glutamic acid) functions as the "on" switch in the brain. Glutamate regulates appetite, thinking, increases gut motility, optimizes learning, modulates memory, mood and perception of pain, improves libido, and decreases sleep. Symptoms of high glutamate may include anxiety, depression, impulsivity, decreased focus, and insomnia. Additional studies on urinary glutamate levels report higher levels in patients with celiac disease (Marko, et. al. 1960), hyperthyroidism (Belanger, et. al. 1972), and rheumatoid arthritis (Jones, et. al. 2005).

THERAPEUTIC CONSIDERATIONS: Therapies such as GABA, L-theanine, lithium orotate and taurine may be beneficial to counter glutamate actions. NAC and Vitamin E can help reduce oxidative stress and co-factor supplementation (B3 and B6, magnesium, NAC) can aid in glutamate metabolism.

GLUTAMINE
Glutamine is lower than the reference range. Glutamine is an essential and should be the most abundant free amino acid in the human body. Glutamine provides fuel for rapidly dividing cells (lymphocytes, enterocytes and epithelial cells of the intestines), helps balance ammonia levels in the body, improves immune system function, contributes to biosynthesis of proteins, amino acids, nucleic acids and glutathione, and protects intestinal lining. Additionally, glutamine increases glutamate and GABA levels in the brain and in the body.
Although the body usually makes enough glutamine to meet all its needs, extreme stress (e.g., strenuous exercise, persistent stress, or injury) can increase the demand for glutamine beyond the amount naturally manufactured. Research on urinary low glutamine levels is scarce, however low circulating glutamine levels are reported after intense exercise (Keast, Arstein et al. 1995), in overtraining syndrome (Rowbottom, Keast et al. 1996), in diabetes (Liu, Zheng et al. 2019), depression (Umehara, Numata et al. 2017), and in autism spectrum disorder (Rolf, Haarmann et al. 1993, Moreno-Fuenmayor, Borjas et al. 1996). Low glutamine levels are associated with high oxidative stress (Pietzner, Kaul et al. 2017).

THERAPEUTIC CONSIDERATIONS: consider supplementation with glutamine which comes in capsules or powder. Glutamine is a fairly bland tasting amino acid and easily goes into smoothies. Glutamine is also high in chicken, fish, cabbage, spinach, diary, tofu and lentils among many over foods.

HISTIDINE
Histidine is low. Histidine is a semi-essential amino acid that gives rise to the neurotransmitter histamine. Histidine protects neurons, assists with making new blood cells, reduces inflammation and oxidative stress, helps with tissue repair and growth. Histidine also helps ameliorate fatigue, promotes clear thinking and concentration, reduces appetite, decreases anxiety, improves sleep and glucose homeostasis.
Research shows that urinary levels of histidine are low in in folate deficiency (Cooperman and Lopez 2002). Low histidine levels are also implicated in obesity (Niu, Feng et al. 2012), fatigue with MS (Loy, Fling et al. 2019), rheumatoid arthritis (Gerber 1975), obstructive pulmonary disease (Diao, Labaki et al. 2019), and chronic kidney disease (Watanabe, Suliman et al. 2008).

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THERAPEUTIC CONSIDERATIONS: dosages of histidine up to 4 g/day have shown no negative side effects and have been associated with general improvements. Meat, fish, eggs, soy, and beans are all high in histidine.

HISTAMINE
Histamine is above the optimal range, which may be due to allergies (self-reported). Research shows that individuals with gastrointestinal food allergies have higher urinary histamine levels (Raithel, et. al. 2015). This study showed that histamine was elevated in both IgE- and non-IgE food allergy types during consumption of offending foods, but not during the hypoallergenic diet.

Histamine plays a dual role in the body as a neurotransmitter and a modulator of the immune system that has anti-pain properties, plays a neuroprotective role in the brain, and contributes to optimal maintenance of cognition and memory. Histamine stimulates wakefulness and decreases sleep, stimulates gastric acid production, increases metabolism, suppresses appetite, and prevents weight gain. Histamine is a potent vasodilator and a pro-inflammatory agent. Additional research studies show that urinary histamine is elevated in patients with flushing disorder (Myers et al., 1981), cystitis (el-Mansoury et al., 1994), polycythemia (Horakova et al., 1977), and pregnancy (Harrison et al., 1974). Clinically, high histamine levels are implicated in depression, headaches, sensitivity to chemicals, and sleep difficulties.

THERAPEUTIC CONSIDERATIONS: Beneficial therapeutic strategies to reduce histamine levels may involve antihistamines and/or a low histamine diet. High histamine foods include but are not limited to beer, champagne, aged cheeses, eggplant, canned fish, fermented meat, red and white wine, sauerkraut, and spinach (Maintz and Novak, 2007), however individual food sensitivities ought to be considered as well. Additionally, flavonoids (green tea extract, quercetin, grape seed extract, gingko biloba, citrus bioflavonoids, bilberry extract, hawthorn extract) may be beneficial to ease the symptoms of high histamine (Murray et al., 2005).

N-METHYLHISTAMINE
N-Methylhistamine is within range. N-Methylhistamine is a major metabolite of the neurotransmitter histamine.

PEA
PEA is elevated. PEA, also known as phenethylamine, promotes energy, elevates mood, and regulates attention. PEA also contributes to aggression, serves as a biomarker for ADHD, and prolongs the signaling of dopamine, norepinephrine, and serotonin. Urinary PEA levels increase after amphetamine use (Kusaga et al., 2002;Zametkin et al., 1984), exercise (Szabo et al., 2001), and in the following disorders: bipolar disorder (Karoum et al., 1982), phenylketonuria (Reynolds et al., 1978), schizophrenia (O'Reilly and Davis, 1994), postpartum period (Taylor et al., 1996), and in severe anxiety and insomnia (DeLisi et al., 1984). High PEA is suspected in the etiology of anxiety, inflammation, inability to focus (racing thoughts), sleep difficulties, and toxicity.
PEA is preferentially inactivated to phenylacetic acid by monoamine oxidase b (MAOb). Inhibitors of MAOb can result in increased levels of PEA and have beneficial effects but also precipitate symptoms of excess PEA. Irreversible pharmaceutical inhibitors of MAOb include selegiline-eldepryl and rasagiline. The antifungal medication Lamisil-Terbinafine, widely used for treating athlete's foot, is also a MAOb inhibitor, as are herbs commonly used in foods (tumeric, nutmeg) and natural medications (Syrian Rue, Passionflower, Kava).

THERAPEUTIC CONSIDERATIONS: Consideration of eliminating, reducing, or changing medications/herbs that may inhibit MAOb and increase PEA to high levels associated with side effects.

TYROSINE
Tyrosine is within range. Tyrosine is obtained from diet (sesame seeds, cheese, soy, meat, nuts and fish) or synthesized in the body from the amino acid phenylalanine. Tyrosine serves as a constituent of proteins and gives rise to neurotransmitters, like dopamine, norepinephrine and epinephrine; and the trace-amine tyramine. Additionally, in the thyroid gland, tyrosine can also be iodinated to give rise to thyroid hormones. Tyrosine enhances cognitive performance, energy, and alertness, and improves memory after sleep deprivation. Tyrosine also prevents the depletion of central and peripheral catecholamines (dopamine, norepinephrine, epinephrine) induced by acute stress, thereby eliciting protective effects on behavioral and cardiovascular parameters in the body.

TYRAMINE
Tyramine is high which is usually due to eating foods high in this trace amine (protein). Specifically, tyramine is found in aged, fermented cured or spoiled food where microbes with decarboxylase enzymes convert tyrosine to tyramine. These foods include aged cheeses, smoked fish, cured meats, wine, and some types of beer. In sensitive individuals, high tyramine ingestion can trigger migraines by causing blood vessel restriction and then rebound vasodilation (Burns and Kidron 2020). Additionally, tyramine can trigger norepinephrine release, thereby stimulating sympathetic nervous system and consequently increase blood pressure. Because of this sympathetic mechanism, symptoms of agitation, anxiety, rapid heartbeat, and headaches may be noted.

THERAPEUTIC CONSIDERATIONS: avoid tyramine high foods (https://headaches.org/wp-content/uploads/2018/02/TyramineDiet.pdf) and calm the sympathetic nervous system. Supplements such as SAMe, magnesium, vitamin B2 may aid with promoting norepinephrine metabolism. Additionally, nervines, adaptogens, L-theanine, biofeedback and meditation may help quiet down the overactive sympathetic response.

DOPAMINE
Dopamine is lower than the reference range. Dopamine improves attention, focus, and motivation, helps with decision making, modulates movement control, promotes lactation, increases blood pressure, urine output and sodium excretion, and allows for feelings of reward and pleasure. Additionally, the quest for dopamine stimulation plays a central role in the etiology of addiction. Dopamine also serves as the parent

precursor to norepinephrine and epinephrine. Research shows that urinary dopamine levels are reduced in patients with Alzheimer's disease (Liu et al., 2011), anorexia nervosa (Van Binsbergen et al., 1991), anxiety with depression (Field et al., 2010), fibromyalgia (Riva et al., 2012), and periodic limb movement disorder (Cohrs et al., 2004). Clinically, low dopamine is implicated in addiction, apathy, cravings, depression, fatigue, impulse control issues, increased sensitivity to pain, low libido, low mood, memory issues, sleep disturbances, and weight control issues.

THERAPEUTIC CONSIDERATIONS: Supplementation with precursors (tyrosine or L-DOPA) and/or cofactors (iron, vitamin B6, tetrahydrofolate) to promote biosynthesis may be beneficial.

DOPAC
DOPAC is lower than the reference range. DOPAC is the primary metabolite of dopamine formed via the actions of monoamine oxidase. Research shows that DOPAC is reduced in the urine of patients with Alzheimer's disease (Liu et al., 2011).

HVA
Homovanillic acid (HVA) is lower than the reference range. HVA is a dopamine metabolite formed through the actions of the monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT) enzyme. Research shows that HVA is reduced in the urine of patients with monoamine oxidase enzyme deficiency (Sims et al., 1989), polycystic ovarian syndrome (Shoupe and Lobo, 1984), and periodic limb movement disorder (Cohrs et al., 2004).

NOREPINEPHRINE
Norepinephrine is lower than the reference range. Norepinephrine functions both as a neurotransmitter and a hormone, participating in the body's fight or flight response. Norepinephrine increases alertness, focuses attention, fine-tunes vigilance, increases blood pressure, heart rate, and blood glucose, reduces digestive activity, pain and sleep, prevents bladder emptying, and regulates body temperature. The adrenal gland produces approximately 20% of norepinephrine with 80% produced by the sympathetic nerve fibers. Research shows that urinary norepinephrine is reduced in patients with Alzheimer's disease. Clinically, low norepinephrine is implicated in anorexia, attention impairment, depression, fatigue, hypotension, lack of motivation, lethargy, low mood, memory issues, slow pulse rate, and weight issues.

THERAPEUTIC CONSIDERATIONS: Precursor supplementation with tyrosine or phenylalanine, or cofactor support with ascorbic acid, iron, tetrahydrofolate, and vitamin B6 may be beneficial.

NORMETANEPHRINE
Normetanephrine is low-normal (<20th percentile). Lower normetanephrine levels may be reflective of insufficient norepinephrine levels in the adrenal glands.

EPINEPHRINE
Epinephrine is low-normal (<20th percentile). Epinephrine functions both as a neurotransmitter and a hormone, participating in the body's "fight or flight" response. Approximately 80% of peripheral catecholamine output by the adrenal glands is epinephrine. Research shows that urine epinephrine is decreased in Alzheimer's disease (Liu et al., 2011), metabolic syndrome (Landsberg et al., 1991), and obesity (Landsberg et al., 1991). Clinically, low epinephrine is implicated in attention impairment, chronic stress, depression, cold body temperature, dizziness, chronic fatigue, hypotension, low mood and libido, and memory issues.

THERAPEUTIC CONSIDERATIONS:Adrenal support may be beneficial to increase epinephrine levels.

VMA
Vanillylmandelic acid (VMA) is low-normal (<20th percentile). VMA is a norepinephrine and epinephrine metabolite formed via the actions of monoamine oxidase (MAO), catechol-O-methyl transferase (COMT), and aldehyde dehydrogenase. Research shows that in rare cases, VMA is reduced in patients with MAO deficiency (Sims et al., 1989) or on SSRI and SNRI combination therapy (Chalon et al., 2003).

INFLAMMATORY MARKERS

KYNURENINE
Kynurenine is high-normal (>80th percentile). Kynurenine is a central metabolite of the amino acid tryptophan with vasodilatory properties. Kynurenine is utilized by the body in the production of niacin (vitamin B3), eventually leading to the formation of NAD+, which plays a pivotal role in energy metabolism, gene expression, cell death and regulation of calcium homeostasis. More than 90% of the body's tryptophan is metabolized to the kynurenine pathway.
Kynurenine is synthesized by the enzyme tryptophan dioxygenase, which is expressed primarily but not exclusively in the liver, and indoleamine 2,3-dioxygenase, which is made in many tissues in response to immune activation by interferons and cytokines, or free radicals. In the brain, approximately ~40% of kynurenine is produced locally, whereas the rest is absorbed from the blood.
Kynurenine degradation generates a series of neuroprotective and neurotoxic compounds that can activate or inhibit N-methyl-d-aspartate (NMDA) glutamate receptors (see kynurenic acid and 3-OH kynurenine). Upregulation of this pathway may be a hallmark of neuroinflammation and is associated with certain disorders.
Research shows that kynurenine is high with tryptophan administration (Michael, Drummond et al. 1964), hydrocortisone treatment (Rose and Braidman 1971), metabolic syndrome (Oh, Seo et al. 2017), with major coronary events (Pedersen, Svingen et al. 9/2013), and in women in pregnancy (Rose and Braidman 1971). High kynurenine levels have been implicated in disorders like Irritable Bowel Syndrome (Fitzgerald,

Cassidy Eugene et al. 2008), lupus (Akesson, Pettersson et al. 2018), Crohn's disease (Gupta, Thaker et al. 2012), and Alzheimer's Disease (Chatterjee, Goozee et al. 2018). Additionally, caffeine (Orlikov and Ryzov 1991) and regular black tea (Gostner, Becker et al. 2015) consumption can elevate kynurenine levels as well.

TREATMENT CONSIDERATIONS: reduction of inflammation through diet and supplementation may be beneficial. Glutathione support and modulation of the NMDA receptor (e.g. magnesium) may help reduce symptoms.

KYNURENIC ACID
Kynurenic acid is high. Kynurenic acid is a neuroactive metabolite produced from kynurenine. Kynurenine is formed from tryptophan via the enzyme tryptophan dioxygenase and indoleamine 2,3-dioxygenase; and metabolized along two independent pathways to produce kynurenic acid via aminotransferases and 3-OH kynurenine.
Kynurenic acid (unless in excess amounts) is regarded to have a neuroprotective role because it inhibits the N-methyl-d-aspartate (NMDA) glutamate receptor, reduces the neurotransmitter glutamate release and thereby prevents excitotoxicity.
Research shows that urinary kynurenic acid levels are high with tryptophan administration (Michael, Drummond et al. 1964) and metabolic syndrome (Oh, Seo et al. 2017). High kynurenic acid levels are implicated in schizophrenia (Fazio, Lionetto et al. 2015).

TREATMENT CONSIDERATIONS: evaluate tryptophan supplementation and blood sugar regulation. Consider anti-inflammatory diet and supplements to reduce neuroinflammation.

3-HYDROXYKYNURENINE
3-Hydroxykynurenine is high. 3-Hydroxy Kynurenine (3-OH Kynurenine) is a metabolic intermediate of the kynurenine pathway, one of the major metabolites of tryptophan degradation. Kynurenine is transformed into 3-OH Kynurenine, which acts as a N-methyl-d-aspartate (NMDA) glutamate receptor agonist and has been demonstrated to exert neurotoxic effects.
Neurotoxicity elicited by 3-OH Kynurenine appears to be also related to generation of oxidative stress produced by reactive radical species, formed as a result of auto-oxidation. Additionally, 3-OH Kynurenine gives rise to neurotoxic metabolites, such as quinolinic acid, which activate the NMDA receptor, induce lipid peroxidation and promote oxidative stress.
Research shows that urinary levels of 3-OH Kynurenine are high with hydrocortisone treatment (Rose and Braidman 1971) and in women in pregnancy (Rose and Braidman 1971). High 3-OH Kynurenine is implicated in vitamin B6 deficiency (Theofylaktopoulou, Ulvik et al. 2014) and Alzheimer's disease (Schwarz, Guillemin et al. 2013).

TREATMENT CONSIDERATIONS: consider glutathione support and antioxidant support to prevent the oxidative stress produced by 3-hydroxyhynurenine. Consider B6 supplementation (under 200 mg/day for safety).

XANTHURENIC ACID
Xanthurenic acid is high. Xanthurenic acid is a metabolite of the kynurenine pathway, formed directly from 3-OH Kynurenine, and serves as an indirect marker of vitamin B6 status. Vitamin B6 insufficiency leads to elevated levels of xanthurenic acid in urine. Increased excretion of xanthurenic acid following tryptophan ingestion has been used a measure of vitamin B6 deficiency, which in scientific literature is called the tryptophan loading test (oral 2 g challenge). If xanthurenic acid levels are elevated in the absence of tryptophan administration, vitamin B6 deficiency is considered to be significant.
Vitamin B6 deficiency that contributes to elevated xanthurenic acid levels can also increase oxidative stress in the body. The hydroxylated quinone structure of xanthurenic acid can bind iron and increase DNA oxidative damage. Therefore, elevated xanthurenic acid levels may suggest antioxidant insufficiency.
Research shows that xanthurenic acid is high with vitamin B6 deficiency (Chiang, Selhub et al. 2005), with hydrocortisone treatment (Rose and Braidman 1971), rheumatoid arthritis (Chiang, Selhub et al. 2005), metabolic syndrome (Oh, Seo et al. 2017), autism spectrum disorder (Gevi, Zolla et al. 2016), and in women in pregnancy (Rose and Braidman 1971).

THERAPEUTIC CONSIDERATIONS: vitamin B6 supplementation with antioxidant support may be warranted.

Creatinine levels reflect urine concentration.
Low values suggest overly dilute urine; High values suggest overly concentrated urine.
Extreme low or high values may be induced by kidney or other metabolic disorders, but most values will be due to inadequate hydration (high creatinine) or excessive water intake in the several hours prior to testing (low creatinine). Creatinine is used to adjust the lab results for kidney function. No samples were refused due to quality issues.