TEST REPORT

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ZRT LABORATORY

#

Ordering Provider:
Regenerus Laboratories, Ltd

Samples Received
11/15/2022

Report Date
11/22/2022

Samples Collected
Urine - 11/06/22 06:00
Urine - 11/06/22 08:00
Urine - 11/07/22 18:00
Urine - 11/08/22 22:00

Sample Report ZRT05

Gender	Last Menses	Height	Waist
Female	Unspecified	5 ft 8 in	Unspecified
DOB	**Menses Status**	**Weight**	**BMI**
10/25/1965 (57 yrs)	Postmenopausal	9 st	19.2

TEST NAME	RESULTS | 11/06/22	09/19/22	10/26/20	RANGE
Urinary Inhibitory Neurotransmitters				
Tryptophan	1756 L	2527 **L**		2633-12688 µg/g Cr (Optimal 3970-8450)
Serotonin	34.9 L	67.7	61.0	47.6-140.3 µg/g Cr (Optimal 61.0-103.2)
5-HIAA	3869	3317	4709	2205-11816 µg/g Cr (Optimal 2988-5850)
GABA	151 L	181	183	167-463 µg/g Cr (Optimal 193-367)
Glycine	46	80	76	41-295 mg/g Cr (Optimal 61-159)
Taurine	6.0 L	118.4		7.1-293.1 mg/g Cr (Optimal 24.5-134.1)
Urinary Excitatory Neurotransmitters				
Glutamate	1417	1186 **L**	2214	1213-4246 µg/g Cr (Optimal 1515-2710)
Glutamine	35	48		27-106 mg/g Cr (Optimal 37-71)
Histidine	7.0 L	20.5		10.8-98.9 mg/g Cr (Optimal 19.7-58.4)
Histamine	12.3	41.2	15.7	3.6-44.3 µg/g Cr (Optimal 5.2-15.3)
N-Methylhistamine	72	65		59-195 µg/g Cr (Optimal 79-140)
PEA	12.5	2076.4 **H**	869.7 **H**	3.6-38.8 µg/g Cr (Optimal 5.3-16.1)
Tyrosine	1794 L	3789		3128-15548 µg/g Cr (Optimal 4790-10278)
Tyramine	95 L	243		187-910 µg/g Cr (Optimal 279-588)
Dopamine	<14 L	135	94 **L**	103-282 µg/g Cr (Optimal 144-240)
DOPAC	104 L	971	461 **L**	495-2456 µg/g Cr (Optimal 658-1449)
HVA	2800 L	4708	4747	3025-9654 µg/g Cr (Optimal 3737-7048)

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Laboratory Director

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TEST NAME	RESULTS | 11/06/22	09/19/22	10/26/20	RANGE
Urinary Excitatory Neurotransmitters				
Norepinephrine (pooled)	1.5 L	11.1	11.9	10.0-35.7 µg/g Cr (Optimal 15.0-28.1)
Normetanephrine	11.8 L	18.3	23.3	13.4-44.8 µg/g Cr (Optimal 17.9-31.7)
Epinephrine (pooled)	0.4 L	1.2	0.8	0.8-6.2 µg/g Cr (Optimal 1.4-4.2)
Ratio: Norepi/Epi	3.8	9.3	14.9	2.9-25.2 (Optimal 5.2-13.7)
VMA	2291	2775	3634	1996-5939 µg/g Cr (Optimal 2580-4766)
Urinary Inflammatory Markers				
Kynurenine	154	160		108-1641 µg/g Cr (Optimal 257-960)
Kynurenic Acid	424 L	739		437-1719 µg/g Cr (Optimal 639-1200)
3-Hydroxykynurenine	47 L	88		80-822 µg/g Cr (Optimal 147-467)
Xanthurenic Acid	395 L	557		450-2175 µg/g Cr (Optimal 694-1510)
Urinary Creatinine				
Creatinine (pooled)	0.42	0.56	0.46	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

11/06/2022: None Indicated

09/19/2022: None

10/26/2020: topical Estrogen (type not indicated) (compounded) (1 Days Last Used); topical Testosterone (compounded) (1 Days Last Used)

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Disclaimer: Supplement type and dosage are for informational purposes only and are not recommendations for treatment. For a complete listing of reference ranges, go to www.zrtlab.com/reference-ranges.

TEST NAME	WOMEN
Urinary Inhibitory Neurotransmitters	
Tryptophan	2633-12688 µg/g Cr (Optimal 3970-8450)
Serotonin	47.6-140.3 µg/g Cr (Optimal 61.0-103.2); 75-2137 µg/g Cr (w/5-HTP tx); 137.7-215.8 µg/g Cr 10-14y/o; 182.2-366.8 µg/g Cr <10y/o
5-HIAA	2205-11816 µg/g Cr (Optimal 2988-5850); 4008-114,204 µg/g Cr (w/5-HTP tx); 3802-9879 µg/g Cr 10-14y/o; 6331-18834 µg/g Cr <10y/o
GABA	167-463 µg/g Cr (Optimal 193-367); 197-311 µg/g Cr 10-14y/o; 270-633 µg/g Cr <10y/o
Glycine	41-295 mg/g Cr (Optimal 61-159); 97-267 mg/gr Cr 10-14y/o; 99-330 mg/gr Cr <10y/o
Taurine	7.1-293.1 mg/g Cr (Optimal 24.5-134.1)
Urinary Excitatory Neurotransmitters	
Glutamate	1213-4246 µg/g Cr (Optimal 1515-2710); 1669-2651 µg/g Cr 10-14y/o; 2157-4735 µg/g Cr <10y/o
Glutamine	27-106 mg/g Cr (Optimal 37-71)
Histidine	10.8-98.9 mg/g Cr (Optimal 19.7-58.4)
Histamine	3.6-44.3 µg/g Cr (Optimal 5.2-15.3); 12.4-20.5 µg/g Cr 10-14y/o; 14.5-38.4 µg/g <10y/o
N-Methylhistamine	59-195 µg/g Cr (Optimal 79-140)
PEA	3.6-38.8 µg/g Cr (Optimal 5.3-16.1); 3.7-10.8 µg/g Cr 10-14y/o; 6.8-32.3 µg/g Cr <10y/o
Tyrosine	3128-15548 µg/g Cr (Optimal 4790-10278)
Tyramine	187-910 µg/g Cr (Optimal 279-588)
Dopamine	103-282 µg/g Cr (Optimal 144-240); 257-395 µg/g Cr 10-14y/o; 382-770 µg/g Cr <10y/o
DOPAC	495-2456 µg/g Cr (Optimal 658-1449); 700-1428 µg/g Cr 10-14y/o; 1090-5203 µg/g Cr <10y/o
HVA	3025-9654 µg/g Cr (Optimal 3737-7048); 5382-9753 µg/g Cr 10-14y/o; 7295-21939 µg/g Cr <10y/o
Norepinephrine (pooled)	10.0-35.7 µg/g Cr (Optimal 15.0-28.1); 16.7-30.6 µg/g Cr 10-14y/o; 23.9-61.1 µg/g Cr <10y/o
Normetanephrine	13.4-44.8 µg/g Cr (Optimal 17.9-31.7); 27.0-50.1 µg/g Cr 10-14y/o; 24.9-70.1 µg/g Cr <10y/o
Epinephrine (pooled)	0.8-6.2 µg/g Cr (Optimal 1.4-4.2); 2.3-5.4 µg/g Cr 10-14y/o; 2.8-13.0 µg/g Cr <10y/o
Ratio: Norepi/Epi	2.9-25.2 (Optimal 5.2-13.7); 2.4-10.9 <15y/o
VMA	1996-5939 µg/g Cr (Optimal 2580-4766); 3570-5373 µg/g Cr 10-14y/o; 4310-9207 µg/g <10y/o
Urinary Inflammatory Markers	
Kynurenine	108-1641 µg/g Cr (Optimal 257-960)
Kynurenic Acid	437-1719 µg/g Cr (Optimal 639-1200)
3-Hydroxykynurenine	80-822 µg/g Cr (Optimal 147-467)
Xanthurenic Acid	450-2175 µg/g Cr (Optimal 694-1510)
Urinary Creatinine	
Creatinine (pooled)	0.3-2.0 mg/mL

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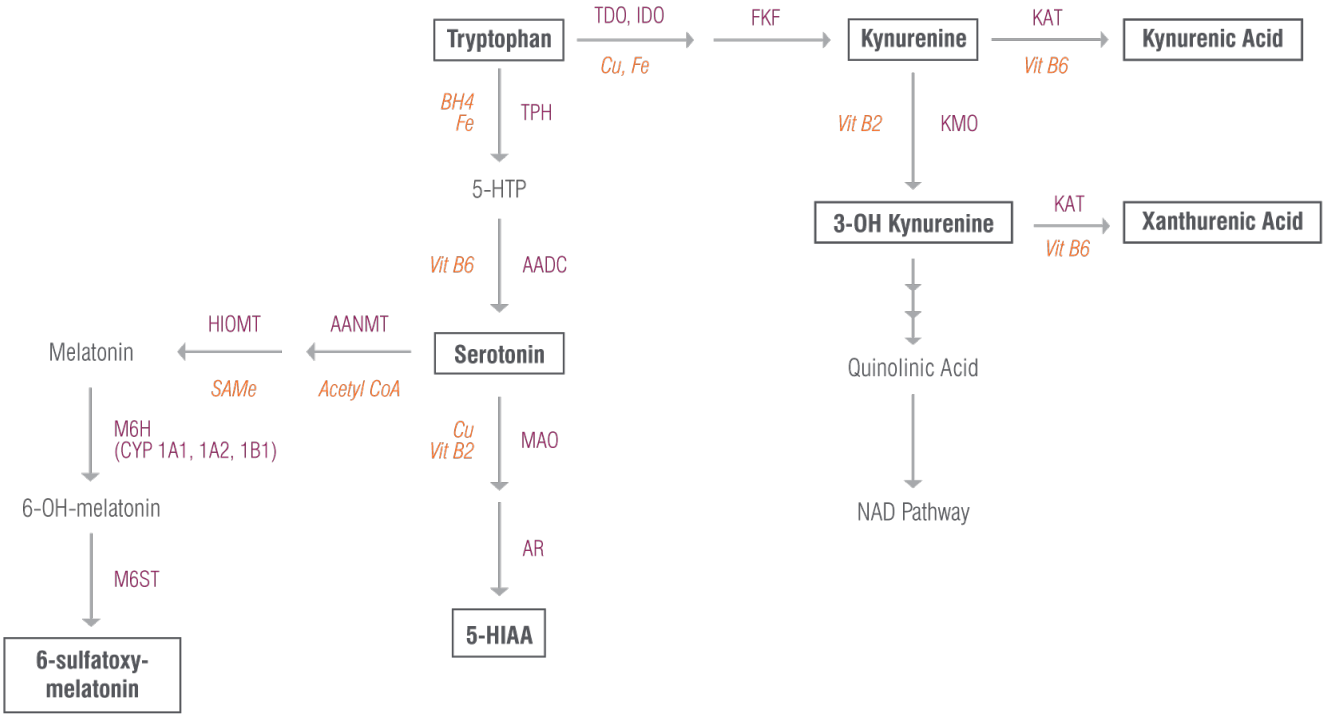
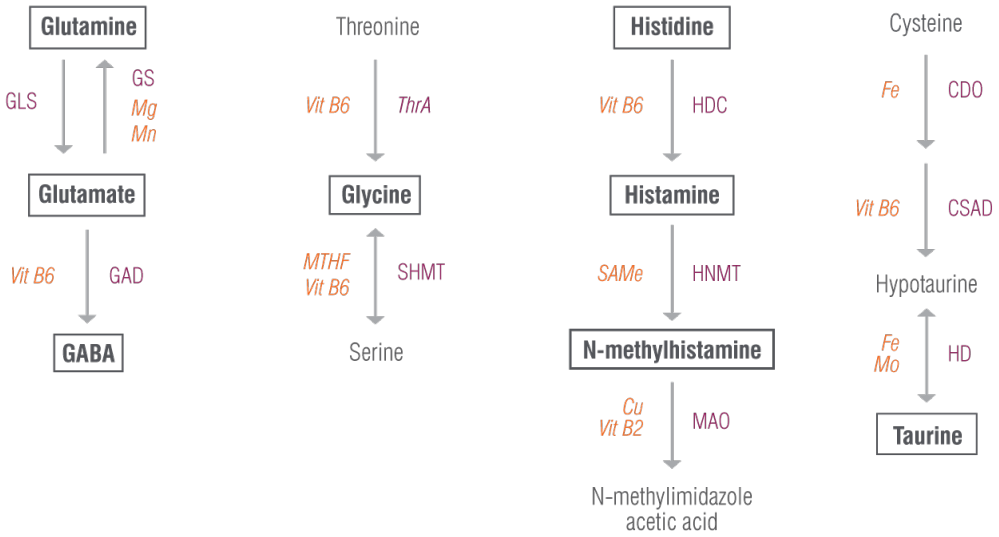
Neurotransmitter Cascades

Tryptophan & Metabolites



Glutamate/GABA, Glycine, Histamine & Taurine



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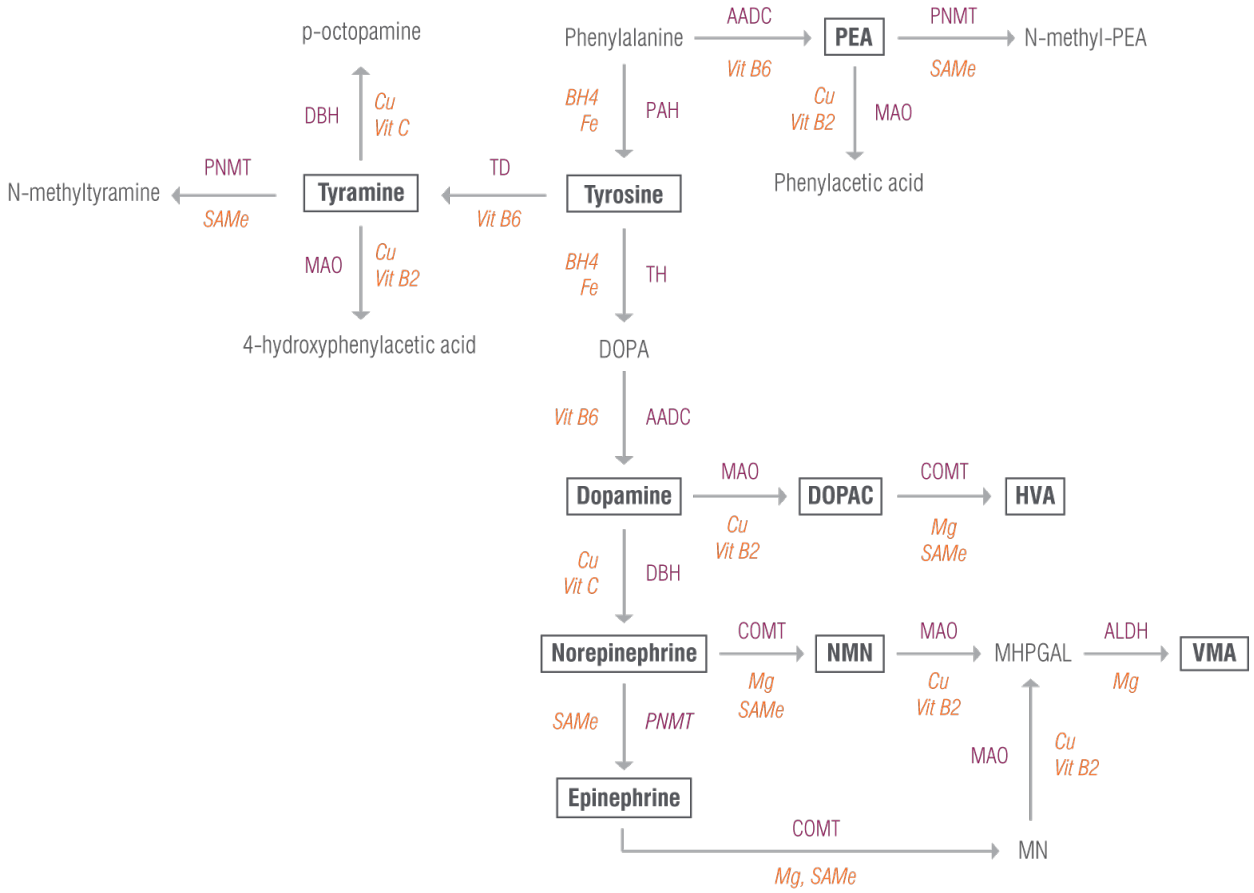
Catecholamines & Metabolites



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

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Disclaimer: Symptom Categories below show percent of symptoms self-reported by the patient compared to total available symptoms for each category. For detailed information on category breakdowns, go to www.zrtlab.com/patient-symptoms.

SYMPTOM CATEGORIES	RESULTS | 11/06/22	09/19/22	10/26/20
Estrogen / Progesterone Deficiency	25%	28%	0%
Estrogen Dominance / Progesterone Deficiency	6%	24%	0%
Low Androgens (DHEA/Testosterone)	39%	36%	0%
High Androgens (DHEA/Testosterone)	10%	27%	0%
Low Cortisol	34%	44%	0%
High Cortisol	19%	36%	0%
Hypometabolism	31%	43%	0%
Metabolic Syndrome	36%	33%	0%

SYMPTOM CHECKLIST (1 2 3)	RESULTS | 11/06/22	09/19/22	10/26/20
Aches and Pains			BLANK
Acne			BLANK
ADD/ADHD			BLANK
Addictive Behaviors			BLANK
Allergies		BLANK	BLANK
Anxious			BLANK
Autism Spectrum Disorder			BLANK
Bleeding Changes			BLANK
Blood Pressure High			BLANK
Blood Pressure Low			BLANK
Blood Sugar Low			BLANK
Body Temperature Cold			BLANK
Bone Loss		BLANK	BLANK
Breast Cancer			BLANK
Breasts - Fibrocystic			BLANK
Breasts - Tender			BLANK
Chemical Sensitivity			BLANK
Cholesterol High			BLANK
Constipation			BLANK
Depressed			BLANK
Developmental Delays			BLANK
Eating Disorders			BLANK
Fatigue - Evening			BLANK
Fatigue - Morning			BLANK
Fibromyalgia			BLANK
Foggy Thinking			BLANK
Goiter			BLANK
Hair - Dry or Brittle			BLANK
Hair - Increased Facial or Body			BLANK
Hair - Scalp Loss			BLANK
Headaches			BLANK
Hearing Loss			BLANK
Heart Palpitations			BLANK
Hoarseness			BLANK
Hot Flashes	BLANK		BLANK
Incontinence			BLANK
Infertility			BLANK
Irritable			BLANK
Libido Decreased			BLANK
Mania			BLANK

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SYMPTOM CHECKLIST	1	2	3							
Memory Lapse										BLANK
Mood Swings										BLANK
Muscle Size Decreased										BLANK
Nails Breaking or Brittle										BLANK
Nervous										BLANK
Night Sweats										BLANK
Numbness - Feet or Hands										BLANK
OCD										BLANK
Panic Attacks										BLANK
PreMenstrual Dysphoric Disorder										BLANK
Pulse Rate Slow										BLANK
Rapid Aging										BLANK
Rapid Heartbeat										BLANK
Skin Thinning										BLANK
Sleep Disturbed										BLANK
Stamina Decreased										BLANK
Stress										BLANK
Sugar Cravings										BLANK
Sweating Decreased										BLANK
Swelling or Puffy Eyes/Face										BLANK
Tearful										BLANK
Triglycerides Elevated	BLANK			BLANK						BLANK
Urinary Urge Increased										BLANK
Uterine Fibroids										BLANK
Vaginal Dryness										BLANK
Water Retention										BLANK
Weight Gain - Hips										BLANK
Weight Gain - Waist										BLANK

Lab Comments

INHIBITORY NEUROTRANSMITTERS

TRYPTOPHAN
Tryptophan is lower than the reference range. 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 + 5HIAA
Serotonin is lower than the reference range; however, its downstream metabolite 5-HIAA is within normal range. This suggests that monoamine

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oxidase (MAO) activity is high. MAO protein expression is inhibited by estrogens and stimulated by testosterone and cortisol. When levels of estrogens fall at the time of menopause, MAO activity increases, accelerating conversion of serotonin to its inert metabolite 5-HIAA. Overall lower serotonin contributes to some of the symptoms at menopause such as vasomotor symptoms (hot flashes and night sweats), memory lapses, depression, loss of libido, and increased appetite and sensitivity to pain.
Serotonin has calming effects and contributes to the feelings of well-being. Serotonin elevates mood, decreases anxiety, appetite, and libido, improves sleep and memory, eases depression, and helps regulate body temperature. Most of serotonin in the human body is produced in the gastrointestinal tract, where it stimulates gut motility. Research shows that urinary serotonin levels are reduced in patients with depression (Nichkova et al., 2012).

THERAPEUTIC CONSIDERATIONS: When serotonin is low, testing for estrogen and correction of low levels with estrogen replacement therapy in combination with bio-identical progesterone is worth considering. In addition, supplementation with cofactors to promote serotonin biosynthesis (e.g. vitamin B6) and with precursors (tryptophan/5-HTP) to help raise serotonin are often helpful. L-theanine, and probiotics may be helpful (Patterson et al., 2014;Pamela Wartian Smith, 2008;Strasser et al., 2016). In addition, natural MAO inhibitors may be beneficial including Curcumin, Berberine, Passiflora, and St Johns Wort. 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).

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 and regulating brain neuron excitation. 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 hypothyroid individuals GABA levels are low in the brain (Liu, et. al. 2017). Thyroid hormone regulates GABA production and signaling. 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 mood symptoms of hypothyroidism. Symptoms of thyroid deficiency are self-reported, which include fatigue, decreased stamina, depression, pain, sleep disturbances, cold intolerance, reduced body temperature, brittle nails, dry coarse hair, hair loss, infertility, low libido, puffy eyes and face, decreased sweating, menorrhagia, and/or constipation. It may be worthwhile to test thyroid hormone levels.

THERAPEUTIC CONSIDERATIONS: with low GABA, supplementation with GABA, L-theanine, cofactor support (e.g. B6), growth hormone-releasing hormone, thyroid replacement, 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 low-normal (<20th percentile). 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. Reduced levels may be suggestive of an increased demand for tetrahydrofolate (active folic acid) production, for which glycine serves as a precursor. Research shows that glycine levels are reduced after intense exercise (Corsetti, et. al. 2016) and in patients with rheumatoid arthritis (Jones, et. al. 2005), hypometabolism, such as hypothyroidism (Friedrich, et. al. 2017), obesity (Ahmad, et. al. 2016), and diabetes (Sasaki, et. al. 1988).

THERAPEUTIC CONSIDERATIONS: Glycine supplementation has been shown to improve metabolic response - such as cholesterol parameters and insulin sensitivity, reduce blood pressure, and aid with decreasing the levels of hemoglobin A1C and pro-inflammatory cytokines (Diaz-Flores, et. al. 2013; Perez-Torres, et. al. 2017). Additionally, vitamin B6, serine support, and MTHF may all support the production of glycine.

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

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effects.

EXCITATORY NEUROTRANSMITTERS

GLUTAMATE
Glutamate is low-normal (< 20th percentile). The brain's major excitatory neurotransmitter glutamate functions as the "on" switch in the brain. Glutamate regulates appetite, thinking, increases gut motility, optimizes learning, modulates memory, improves libido, and decreases sleep. Low urinary glutamate levels have been reported in patients with migraines (Ragginer et al., 2012). Clinically, lower glutamate levels may contribute to agitation, depression, chronic fatigue, lack of concentration, low energy levels, and sleep difficulties.

THERAPEUTIC CONSIDERATIONS: L-glutamine may be beneficial to restore glutamate to normal values.

GLUTAMINE
Glutamine is low-normal (<20th percentile). 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.
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).

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 within reference range. Histamine plays a dual role in the body as a neurotransmitter and a modulator of the immune system. Histamine 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.

N-METHYLHISTAMINE
N-Methylhistamine is low-normal (<20th percentile). N-Methylhistamine is a major metabolite of the neurotransmitter histamine. Research shows that N-methylhistamine in low in depression (Gagne, Wollin et al. 1982), in lupus (Trachtman, Tejani et al. 1987), in focal segmental glomerulosclerosis (Trachtman, Tejani et al. 1987), and in idiopathic nephrotic syndrome (Trachtman, Tejani et al. 1987). Additionally, N-Methylhistamine levels can be low in individuals with an alteration in the histamine N-methyltransferase gene.

THERAPEUTIC CONSIDERATIONS: evaluation of histidine levels is warranted as well as considering supplementation with methyl-donors.

PEA
PEA is within reference range. 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.

TYROSINE
Tyrosine is low. Tyrosine is obtained from the 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 is complexed with iodine to create thyroid hormones. Tyrosine enhances cognitive performance, energy and alertness, and improves memory after sleep deprivation, therefore fatigue and poor memory along with low thyroid symptoms may be noted in patients with low tyrosine levels. 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.
Research shows that tyrosine is low in depression (Zheng, Chen et al. 2016), in post-stroke depression (Xie, Han et al. 2020), and in in chronic kidney disease (Molnar, Wagner et al. 2005).

THERAPEUTIC CONSIDERATIONS: consider increasing dietary tyrosine from cheese, beans, meat, nuts, eggs, and whole grains. Tyrosine is available as a supplement with common dosages of 500-3000 mg per day in divided dosages.

TYRAMINE
Tyramine is low likely due to a diet low in processed or fermented foods and is of unknown significance. Tyramine is a trace amine derived from the amino acid tyrosine that is found naturally in food. 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 and some types of beer. In sensitive individuals, high tyramine ingestion can trigger migraines (Burns and Kidron 2020). Additionally, tyramine has vasoactive properties and can increase blood pressure. While supplementation of tyramine is not needed, for people who have low blood pressure or low sympathetic tone incorporating higher tyramine foods may actually have some beneficial impacts.

DOPAMINE
Dopamine is lower than the optimal range, consistent with research that shows low urinary dopamine in hypertension (Gill, et. al. 1991; Rudberg, et. al 1997). Dopamine is locally produced in the kidney and is one of the most important factors in regulating sodium excretion and blood pressure. In high blood pressure (self-reported), the impaired production of dopamine is one of the underlying factors that contributes to decreased sodium excretion, thus contributing to hypertension. Research shows that abnormalities in renal dopamine production may be related to dopamine receptor dysregulation in the kidney (Harris and Zhang, 2012).
Low dopamine tone in the body can also result from insufficient tyrosine intake from diet, insufficient levels of cofactors necessary for dopamine formation (iron, vitamin B6), and genetic polymorphisms (SNPs). Additionally, low dopamine levels have been reported in Alzheimer's disease (Liu, et. al. 2011), anorexia nervosa (Van Binsbergen, et. al. 1991), diabetes (Champaneri, et. al. 2012), fibromyalgia (Riva, et. al. 2012), hypertension (Gill, et. al. 1991), periodic limb movement disorder (Cohrs, et. al. 2004), sleep disturbances (Seay, et. al. 2013), hypoadrenergic orthostatic hypotension (Kuchel, et. al. 1985).

THERAPEUTIC CONSIDERATIONS: Consider evaluation of current diet to reduce sodium intake. 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 lower than the reference range. Normetanephrine is a norepinephrine metabolite formed via the actions of catechol-O-methyl transferase enzyme in response to stress and low levels may be indicative of overall lower norepinephrine levels.

EPINEPHRINE
Epinephrine is lower than the reference range. Epinephrine functions both as a neurotransmitter and a hormone, participating in the body's fight or flight response. Epinephrine 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. Approximately 80% of peripheral catecholamine output by the adrenal glands accounts for 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, dizziness, chronic fatigue, hypotension, low mood and libido, and memory issues.

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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 low-normal (<20th 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 made 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 urinary kynurenine levels are low in autism spectrum disorder (Gevi, Zolla et al. 2016). Low kynurenine levels have been implicated in aggression (Comai, Bertazzo et al. 2016), depression (Umehara, Numata et al. 2017) and headaches (Curto, Lionetto et al. 2015).

TREATMENT CONSIDERATIONS: low kynurenine may be a sign of low tryptophan levels or low co-factors for the enzymatic metabolism.

KYNURENIC ACID
Kynurenic acid is low. 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.
Mounting evidence suggests that kynurenic acid may be implicated in the pathophysiology of mood disorders. As a result, kynurenic acid has been considered for use in therapy in certain neurobiological disorders. Research shows that kynurenic acid is low with a low protein diet (Poesen, Mutsaers et al. 2015) and in Autism Spectrum Disorder (Gevi, Zolla et al. 2016). Low kynurenic acid is implicated in depression (Baranyi, Amouzadeh-Ghadikolai et al. 2017), headaches (Curto, Lionetto et al. 2015), bipolar disorder (Birner, Platzer et al. 2017) and Alzheimer's disease (Gulaj, Pawlak et al. 2010).

TREATMENT CONSIDERATIONS: consider increasing amino acids in the diet and improving inflammatory pathways.

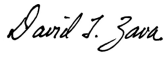
3-HYDROXYKYNURENINE
3-Hydroxykynurenine is low. 3-Hydroxy Kynurenine (3-OH Kynurenine) is a metabolic intermediate of the kynurenine pathway, one of the major metabolites of tryptophan degradation. Kynurenine is transformed into 3-OH Kynurenine, which acts as a N-methyl-d-aspartate (NMDA) glutamate receptor 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.
Low 3-OH Kynurenine levels are implicated in headaches (Curto, Lionetto et al. 2015), in males in Alzheimer's disease (Chatterjee, Goozee et al. 2018) and schizophrenia (Fazio, Lionetto et al. 2015).

TREATMENT CONSIDERATIONS: consider tryptophan levels to assure there is enough upstream amino acids as well as B6 supplementation and magnesium to allow for ideal co-factors for enzyme conversions.

XANTHURENIC ACID
Xanthurenic acid is low. 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. Patients with Down syndrome have been found to have a lower tryptophan metabolism and therefore lower xanthurenic acid levels.

THERAPEUTIC CONSIDERATIONS: evaluation of tryptophan levels and B vitamins may be beneficial.

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.



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Professional Comments

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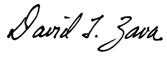

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