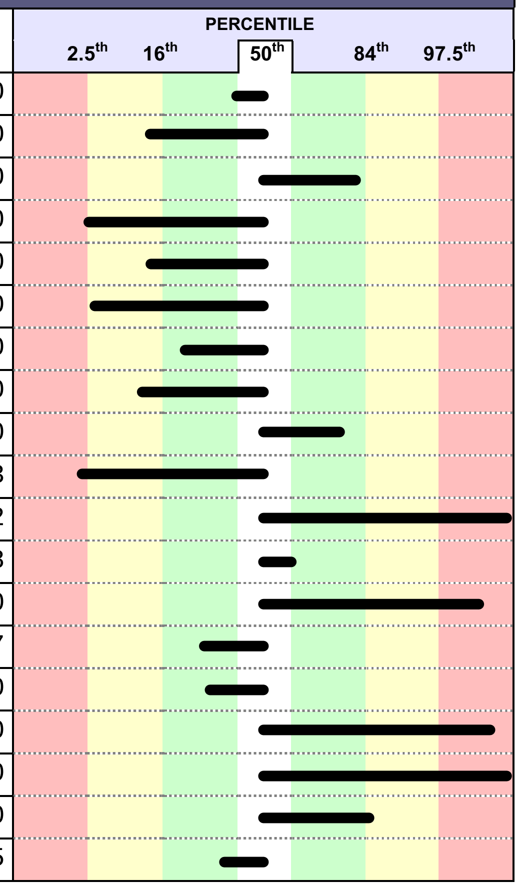
LAB #: U00000-0000-0
PATIENT: Sample Patient
ID: P0000000000
SEX: Female
DOB: AGE: 49

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Neuro-Biogenic Amines, Comprehensive; urine *first morning void*

	RESULT/UNIT per g creatinine		REFERENCE INTERVAL
Dopamine, free	182	µg	65- 400
3,4-Dihydroxyphenylacetic acid (DOPAC)	709	µg	450- 2400
3-Methoxytyramine (3-MT)	158	nmol	30- 250
Norepinephrine, free	14.5	µg	15- 80
Normetanephrine	160	µg	80- 500
Epinephrine, free	1.6	µg	1.5- 20
Metanephrine	66	µg	35- 220
Serotonin	94	µg	50- 250
5-Hydroxyindolacetic acid (5-HIAA)	5994	µg	1000- 9000
Tryptamine	0.17	µmol	0.2- 1.3
Glutamate	120	µmol	6- 52
Gamma-aminobutyrate (GABA)	2.9	µmol	1- 8
Tyrosine	148	µmol	28- 120
Tyramine	2.6	µmol	1.5- 7
Phenethylamine (PEA)	61	nmol	16- 160
Taurine	1573	µmol	220- 1300
Glycine	5491	µmol	350- 3500
Histamine	34	µg	6- 60
Creatinine	109	mg	35- 225



SPECIMEN DATA

Comments:

Date Collected: 03/07/2015
Date Received: 03/16/2015
Date Completed: 03/19/2015
Methodology: LCMS QQQ, Creatinine by Jaffe Method

Time Collected:
Collection Period: first morning void
Volume:

<dl: less than detection limit
Body Surface Area: 1.63

Introduction

For the analysis of neuro-biogenic amines excreted in urine, the method employed by Doctor's Data is designed to detect and measure the free, unconjugated forms of these components. The exception is made for Metanephrine and Normetanephrine, for which the standard of care is based upon reference intervals established for the total metanephrines, which includes both the free and sulfur-conjugated forms of these components. Analysis is performed using tandem LC-MS, using calibrators prepared from certified sources.

"A Comprehensive Guide to Functional Assessment of Urinary Neuro-Biogenic Amines" is available online at www.doctorsdata.com to assist in the interpretation of neurotransmitter test results. The Guide covers neurotransmitter biochemistry, nutritional therapy options, and physiological and environmental conditions that may contribute to neurological and behavioral symptoms. Please refer to the Guide for additional information not included in these abridged interpretive paragraphs.

Urinary neuro-biogenic amines provide an overall assessment of a patient's ability to synthesize and metabolize neurotransmitters, both in the periphery and, for some enzymes, behind the blood brain barrier as well. Alterations in urinary neurotransmitter status may be associated with a variety of conditions including metabolic disorders, mood/behavioral disorders, and in rare occasions the presence of certain tumors. Associations between urinary neurotransmitter levels and health conditions have been documented in scientific literature and may provide valuable insights as part of a comprehensive health assessment.

The activities of many enzymes are expressed differently in specific cells and organs, therefore circulating levels of their metabolites may have distinctive sources. For example, dopamine and serotonin synthesis in the body occurs primarily in the gastrointestinal tract (GIT). Urinary levels of neurotransmitters primarily reflect the activity of the peripheral and GIT enteric nervous systems. Up to 20% of urinary neurotransmitters are estimated as originating in the CNS.

Enzymes and receptors involved in neurotransmitter metabolism may be subject to mutations and single nucleotide polymorphisms (SNPs). A lack of nutritional cofactors (vitamins, minerals) required for normal enzyme function may also decrease enzymatic activity and neurotransmitter levels. Enzymatic defects in synthesis or metabolism may affect levels of neurotransmitters, and normal neurotransmitter receptor function is necessary for normal neurotransmitter activity. Neurotransmitter levels may also be influenced by diet, ifestyle and other health conditions such as high sodium diet, age, gender, body mass index, kidney function, environmental exposures, infection and tobacco use.

References:

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Norepinephrine LOW

The level of norepinephrine is lower than expected in this sample. Norepinephrine is a catecholamine hormone and neurotransmitter secreted by the adrenal gland. It is the principal neurotransmitter in sympathetic nerve endings. Norepinephrine may help regulate vigilant attention, cognition and sleep. Studies indicate that the brain contributes at most 20% of circulating norepinephrine levels.

Low levels of norepinephrine may be associated with conditions such as orthostatic hypotension, dopamine beta-hydroxylase (DBH) enzyme deficiency and Menke’s disease. Alpha-2 agonistic pharmaceuticals decrease sympathetic nerve outflow and norepinephrine levels. Metyrosine therapy may decrease norepinephrine levels. Surgical sympathectomy or medical conditions that disrupt autonomic nerve functions may also decrease norepinephrine levels. Low levels of precursor amino acids phenylalanine or tyrosine, or low levels of the precursor neurotransmitter dopamine may result in low norepinephrine levels.

The synthesis of norepinephrine from dopamine requires Vitamin C and copper. About half of all norepinephrine is produced in the gastrointestinal tract, pancreas and spleen. Most of the norepinephrine produced by these mesenteric organs is removed from portal vein blood by the liver and converted to vanillylmandelic acid (VMA) for excretion.

References:

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Glutamate HIGH

Glutamate is a non-essential amino acid that acts as an excitatory neurotransmitter for metabolic signaling pathways. Glutamate signaling affects neuronal maturation, plasticity and higher cognitive functions.

Excess glutamate signaling, and its effects, has been termed ”excitotoxicity” and is considered a contributing factor in the neurodegeneration seen in HuntingtonÆs disease, Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis, stroke and fibromyalgia. Animal studies indicate that acute stressors may cause transient elevations in extracellular glutamate. Glutamate signaling may occur through a variety of glutamate receptors. N-methyl-D-aspartate (NMDA) receptor signals are the most complex, requiring both glutamate and glycine to function.

The blood-brain barrier prevents the passage of glutamate. Astroglial cells are the primary source of glutamate in the CNS. Any glutamate released into the synapse is cleared by excitatory amino acid transporters (EAAT) found on the astroglia. EEATs, unless damaged or defective, keep extracellular glutamate levels low and insufficient for glutamate receptor signaling. EAAT functions are inhibited by oxidative stress. Extracellular glutamate may alter activity by binding with extra-synaptic high affinity glutamate receptors. Extracellular glutamate levels may also accumulate due to defects in the glutamate-glutamine cycle which removes ammonia from the CNS.

Enteric glial cells in the gastrointestinal tract may be important in glutamate signaling within the gut as neurotransmitter receptors and glial cells respond to dietary L-glutamate and monosodium glutamate (MSG). Gastrointestinal microbes may also affect glutamate levels.

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Glycine High

The level of glycine is higher than expected in this sample. Glycine is a non-essential amino acid that acts as a neurotransmitter in the central nervous system (CNS). Glycine is inhibitory when bound to glycine receptors in the spinal cord, brain or retina, and is considered inhibitory in the CNS. The presence of glycine transporters on glial cells suggests that glycine may also have neuromodulatory effects. Glycine is an essential ligand with glutamate for N-methyl-D-aspartate (NDMA) receptor excitatory signaling.

Animal studies indicate that elevated glycine levels may severely impair energy use in the CNS. Genetic defects may result in glycine encephalopathy. Elevated levels of glycine in the CNS may result in intellectual disability, poor muscle tone, chorea, and respiratory or feeding difficulties (infants). This condition is characterized by non-ketotic hyperglycinemia (NHK) and elevated urinary glycine. Most cases are diagnosed during infancy, although occasionally a patient will have a milder, atypical form of NHK with onset from late infancy to adulthood. Genetic variation in the glycine receptor may contribute to seizure disorders, and may also affect neuronal excitability and plasticity. Mutations of glycine receptor subunits have been associated with hereditary hyperekplexia (startle disease). Glycine supplements may be used in conjunction with pharmaceutical supports for schizophrenia or psychosis, and may result in elevated urinary glycine.

The glycine cleavage complex (GCC) metabolizes glycine and is comprised of four different proteins. GCC requires vitamin B6 and tetrahydrofolate as cofactors. Alternately, glycine may be converted to serine by serine hydroxymethyltransferase, which also requires vitamin B6.

High levels of glycine may interact with clozapine and decrease the drug’s effect.

References:

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Taurine (2-aminoethane- sulfonic acid) HIGH

The level of taurine in this sample is higher than expected. Taurine acts as a neuromodulator and exerts, in vitro, an inhibitory effect on the firing rate of neurons in the central nervous system (CNS). Taurine has been shown in human and animal studies to have mild anti-convulsive effects. Taurine promotes neural development in both the embryonic brain and the adult brain.

High plasma taurine may be associated with stress reactions, depression and psychosis. Patients with Cushing’s disease may have elevated urinary taurine levels, but low plasma levels. Patients with autism may have elevated urine taurine, glycine and alanine with low glutamate. Elevated urinary taurine levels may result from inherited renal defects, liver disease, heart disease or radiation injury. Gastrointestinal dybiosis with associated excess beta-alanine can cause taurine wasting in the urine (high). Oral supplementation may raise urinary taurine levels. Taurine is an ingredient in many ”energy drinks” and taurine supplements are used by some athletes.

Taurine is excreted via urine and bile. A renal wasting condition may result in elevated urine taurine with a low plasma taurine level. The amount of taurine excreted daily is affected by various factors including genetics, age, gender, diet, renal function and medical conditions.

References:

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Tryptamine LOW

The level of tryptamine is lower than expected in this sample. Tryptamine is derived from the essential amino acid tryptophan. Tryptamine levels may affect arterial resistance (vasoconstriction) and serotonin signaling.

Low tryptamine levels or deficient trace amine functions may be associated with some depressive disorders. Low plasma tryptamine levels have been associated with chronic migraine and chronic tension headaches. Tryptamine may act as a neuromodulater for serotonin signaling; serotonin affects mood, sleep and appetite. Urinary tryptamine levels seem to correlate with symptom severity in schizophrenia. Tryptamine levels may affect arterial resistance (vasoconstriction) and serotonin signaling. Methylated tryptamines may also play a role in the development of schizophrenia.

Aromatic L-amino acid decarboxylase (AADC) is the rate-limiting enzyme in the conversion of tryptophan to tryptamine. Altered AADC activity may affect trace amine levels without affecting the levels of monoamine neurotransmitters (catecholamines, histamine, serotonin, etc.). Reserpine decreases AADC activity and trace amine levels.

References:

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Tyrosine HIGH

The level of tyrosine in this sample is higher than expected. Tyrosine is the precursor for the catecholamine neurotransmitters dopamine, epinephrine and norepinephrine. Brain tyrosine levels control the rate of synthesis for the catecholamine neurotransmitters. Tyrosine is also a precursor for thyroid hormone.

Elevated plasma tyrosine levels may result in seizures or developmental delays. Migraine headaches and hyperthyroid conditions may be exacerbated by elevated tyrosine levels. Tyrosine may interfere with medications such as MAO inhibitors, thyroid hormone replacement and L-dopa replacement. Human studies indicate that tyrosine supplementation may improve cognition and performance under stressful conditions.

Tyrosine is also synthesized in the liver from dietary phenylalanine, an essential amino acid. The proportion of dietary tyrosine that enters systemic circulation is controlled by the enzyme tyrosine aminotransferase (TAT) in liver and kidney. TAT requires vitamin B6 and alpha-ketoglutarate as cofactors. Oxidative stress has been shown to lower TAT activity (in vitro). Tyrosine levels may be elevated due to heritable enzyme defects (tyrosinemia), liver disease, or supplementation.

References:

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Creatinine

The urinary creatinine concentration (CC) presented in this report represents the actual creatinine concentration in the specimen that was submitted. Under normal conditions, the rate of excretion of creatinine is quite constant and highly correlated with lean body mass (muscle). However, the CC can vary significantly as a function of urine volume. An unusually high CC most likely indicates poor hydration of the patient at the time of the urine collection. A very low CC most likely indicates unusually high fluid consumption, or perhaps the influence of diuretics. If the urine specimen is very dilute (extremely low CC), the accuracy of the neurotransmitter analysis may be compromised due to analytical detection limits. It is emphasized that the CC in this specimen should not be utilized to assess renal function or glomerular filtration. For that purpose, one should perform a bona fide creatinine clearance test.

For a given age and gender, intra-individual variability in daily creatinine excretion can vary by as much as two-fold. Therefore, to more accurately assess neurotransmitter status using a random collection, the reported values for each analyte are expressed per gram ”normalized” creatinine.