NEUROTRANSMITTER TESTING IN DRIED URINE

NeuroAdvanced Profile

Tests included:
GABA, Glutamate, Dopamine, Epinephrine, Norepinephrine, Serotonin, PEA (Phenethylamine), Glycine, Histamine, DOPAC, HVA (Homovanillic Acid), VMA (Vanillylmadelic Acid), 5-HIAA, Normetanephrine

Provides an overall view of neurotransmitter function, the body's inflammatory response, and neurotransmitter metabolism.

Optional add-ons:

Saliva Hormones

Urine Hormone Metabolites

Diurnal Cortisol

Diurnal Cortisone

Diurnal Melatonin

Diurnal Epinephrine

Diurnal Norepinephrine

For a more comprehensive picture when there may be sex hormone imbalances or sleep or adrenal issues.

Neurotransmitter Testing – Giving a Diagnostic Edge in Treating Mood Disorders

Mental health disorders affect millions of people in the United States and profoundly contribute to the burden of disease in society. The National Alliance of Mental Illness reports that nearly 7% of American adults live with major depression and approximately 18% live with anxiety disorders such as panic disorder, obsessive compulsive disorder, posttraumatic stress disorder, generalized anxiety disorder, and phobias[1]. Mood disorders are the third most common cause of hospitalization in the U.S. for individuals aged 18 to 44[1]. The top-prescribed and top-selling prescription drugs in the U.S. in 2014 included antipsychotics, antidepressants, and attention-deficit disorder drugs[2].

The current treatment paradigm in addressing poor brain health relies on diagnostic tools that encompass the evaluation of clinical signs and symptoms. Despite the lack of testable biomarkers for mood disorders, for many patients treatments can generally be effective. However, even after treatment frequent relapse episodes can still occur. Furthermore, a large number of patients suffer from treatment-resistant depression[3]. Therefore, selection of the best therapeutic regimen for each patient remains a challenge, and is often discovered through a time-consuming process of trial and error. Also, no single approach works for everyone with any one disorder.

Targeted neurotransmitter testing can help health care practitioners achieve a diagnostic edge beyond the traditional psychological inventory by identifying specific imbalances in neurotransmitter levels. Based on neurotransmitter test results, practitioners can identify specific biochemical heterogeneities for each particular patient, and objectively monitor therapeutic responses during and after intervention. Neurotransmitter testing objectively enhances medical assessment and represents a major advance in the personalization of the treatment of mood disorders.

How Neurotransmitters Relay Information within the Body

The brain orchestrates the delicate interplay between the body and the mind. Structural brain units, the neurons, discharge neurotransmitters. These neurotransmitters provide a communication platform for the brain to fuel internal systems with information. Anything the body senses, feels, hears, smells, touches, or ingests serves as an input that prompts an astoundingly fast response. In the

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central and peripheral nervous system, neurotransmitters operate as chemical messengers that relay the signal and receive feedback via electrochemical impulses to regulate cognition, memory, emotions, respiration, heart rate and contractility, digestion, metabolism, blood flow and pressure, and hormonal responses. When released from peripheral organs, neurotransmitters can also behave as hormones by diffusing to distant sites via the circulation.

Clinical Utility of Urinary Neurotransmitter Analysis

The etiology of mood disorders is profoundly complex and likely encompasses many different types of neurotransmitters, how they achieve balance in the brain and in the gut axis, and how they each interplay with other hormone systems throughout the body. Appropriate balancing of neurotransmitter signals allows the body to maintain equilibrium. When brain and peripheral neurochemistry become unbalanced, the body will struggle to re-establish physiological integrity, which may present in the form of suboptimal psychological well-being. Excessive or deficient levels of certain neurotransmitters in both the brain and in the periphery are associated with a spectrum of neurobiological disorders, such as depression and anxiety. The measurement of specific imbalances may be a very effective neurobiological tool in guiding targeted intervention, aimed at addressing the individual excess or deficiency in question.

Clinical Validity of Urinary Neurotransmitter Assessment

The importance of effectively assessing and treating mood disorders cannot be overstated. Objectivity is a key element to the therapeutic approach to mood disorders. Currently, the standard of care dictates a trial and error pharmaceutical approach is taken with each patient based on both self and clinician assessments. However, without information yielded from objective clinical testing, selection of the most effective treatment for each particular patient with a mood disorder continues to be a challenge. While this may prove effective for some patients, the potential for harm during those interim treatment failures is a real concern for clinicians and patients alike. Urinary neurotransmitter analysis has a breadth of data to support the efficacy of the test in clinical practice. Evaluation of neurotransmitter levels in urine provides valuable information about the heterogeneity of patient biochemistry, epigenetics, and how the body functions as a whole.

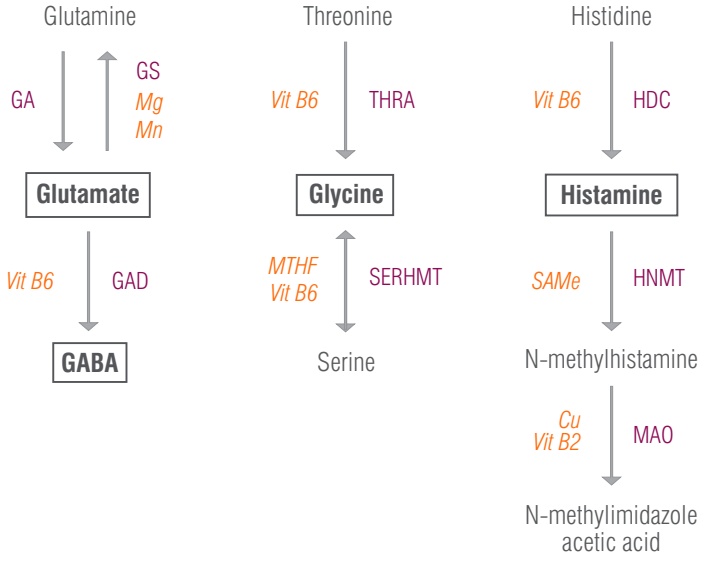
A common misconception is that urinary neurotransmitter measurements cannot be used to assess individual neurochemical imbalances. The degree of significance of neurotransmitter activity in the periphery is sometimes overlooked. In addition to executing vital roles in the brain, neurotransmitters are biosynthesized in the periphery to regulate essential biological processes. Urinary neurotransmitter evaluation provides information regarding the state of a physiological condition, function of enzymes on biosynthesis and breakdown, and allows monitoring the progress of therapeutic interventions. Therefore, in reality, the test provides a means to glean a functional systemic perspective regarding each neurotransmitter.

How do neurotransmitters end up in urine? Some neurotransmitters are produced in the brain and transported across the blood-brain barrier into blood, and others are produced in the periphery (e.g., norepinephrine and epinephrine). Nephrons, the functional units of the kidney, filter circulating neurotransmitters or their precursors from the blood into urine[36]. For some neurotransmitters, urinary measurements correlate with levels in the central nervous system (e.g., glutamate, PEA), and for others, what ends up in urine is only reflective of peripheral biosynthesis (e.g., serotonin, dopamine). Regardless of production origin, neurotransmitter excretion reflects the overall systemic neurotransmitter tone, dysregulation of which may contribute to disease states. The ability to identify abnormality across specific areas of the catecholamine and PEA, GABA/glutamate, serotonin, histamine, and glycine pathways allows healthcare providers to develop a tailored treatment plan to the specific areas associated with imbalance.

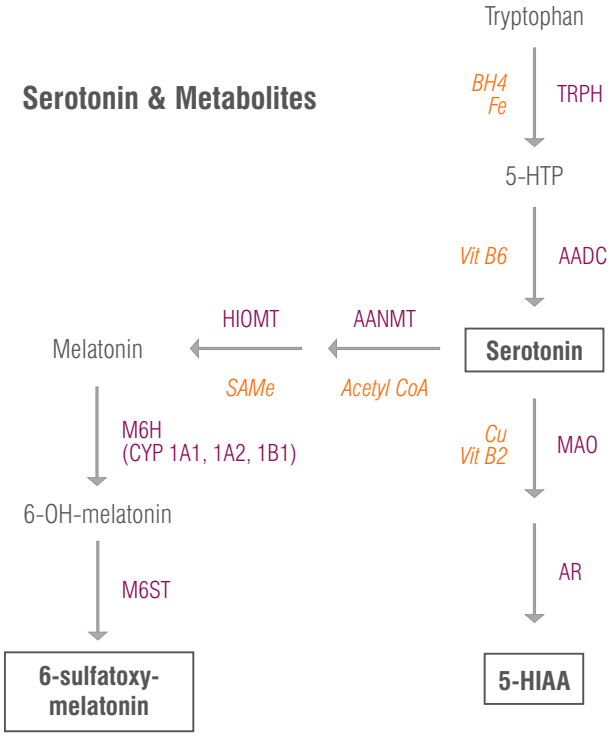
NEUROTRANSMITTER FUNCTIONS & IMBALANCES

Neurotransmitter	High Levels in Urine	Low Levels in Urine
Glutamate functions as the brain's major excitatory neurotransmitter.	Glutamate is high in celiac disease[4] and hyperthyroidism[5]. Clinically, high glutamate is suspected in anxiety, autism, bipolar disorder, depression, panic attacks, and sleep issues.	Glutamate is low in patients with migraines[6]. Clinically, low glutamate is implicated in agitation, depression, chronic fatigue, lack of concentration, low energy levels, and sleep disturbance.
PEA serves as a biomarker for ADHD.	PEA is elevated in individuals with bipolar major affective disorder[7] and severe anxiety[8].	PEA is low in patients with autism[9], ADHD[9-11], depression[12], and inattentiveness[13].
Histamine is a neurotransmitter and immuno-modulator.	High histamine may implicate allergies, depression, headaches, migraines, OCD, and sleep difficulties.	Low histamine is associated with fatigue, low libido, low productivity, mild depression, tension headaches, and weight gain.
Dopamine serves as the reward and pleasure center in the brain. **DOPAC** and **HVA** are dopamine metabolites.	High dopamine is reported in patients with high in anxiety[14], stress[15], PTSD[16], and mercury toxicity[17].	Dopamine is low in Alzheimer's disease[18], anorexia nervosa[19], fibromyalgia[20], periodic limb movement disorder[21], sleep disturbances[22].
Epinephrine (adrenalin) and **norepinephrine** regulate the "fight or flight" response. **Normetanephrine** is a norepinephrine metabolite, and **VMA** is a norepinephrine and epinephrine metabolite.	Epinephrine and norepinephrine levels are high in patients with anxiety[23,24], ADHD[13,25], bipolar disorder[26], depression[27], sleep apnea[28], PTSD[16], and stress[29,30].	Epinephrine and norepinephrine levels are low in Alzheimer's disease[18], metabolic syndrome[31], and obesity[32].
GABA functions as the brain's major inhibitory neurotransmitter.	GABA is elevated in ovarian cancer patients[33], and is suspected in anxiety, excessive need for sleep, foggy thinking, and lethargy.	Low GABA is implicated in anxiety, sleep difficulties, adrenal distress and hypothalamic pituitary adrenal axis feedback dysfunction. Low GABA levels are associated with disorders like ADHD and Tourette syndrome[34].
Serotonin contributes to the feelings of happiness and well-being. **5-HIAA** is a serotonin metabolite.	Increased serotonin is implicated in anxiety, high blood pressure, irritability, and low libido.	Serotonin is decreased in depression[35], and may be associated with heightened sensitivity to pain, hot flashes, hunger, low mood, migraines, OCD, panic disorder, sleep disturbances, and worsened PMS.
Glycine plays a dual role as a neurotransmitter and an amino acid that serves as a building block to proteins.	Clinically, high glycine levels are suspected in anxiety and sleep difficulties.	Clinically, low glycine levels are suspected in anxiety.

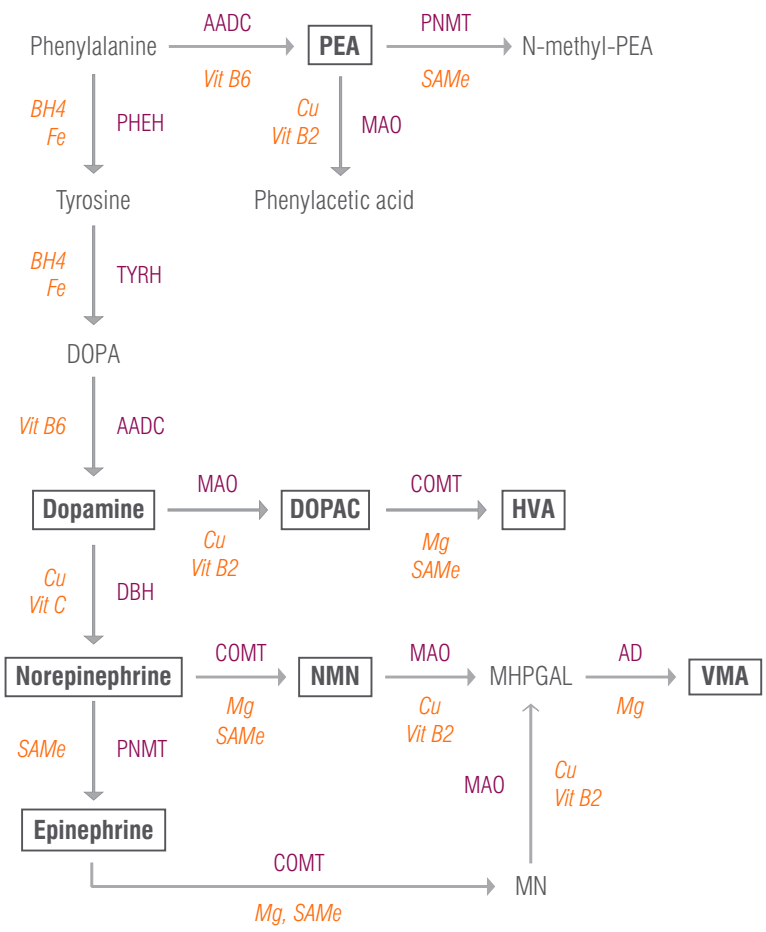
Glutamate/GABA, Glycine & Histidine



Serotonin & Metabolites



Catecholamines & Metabolites



Neurotransmitters & Metabolites:

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

Enzymes:

AADC	aromatic L-amino acid decarboxylase
AANMT	arylalkylamine N-methyltransferase
AD	aldehyde dehydrogenase
AR	aldehyde reductase
COMT	catechol-O-methyltransferase
DBH	dopamine beta hydroxylase
GA	glutaminase
GAD	glutamate decarboxylase
GS	glutamine synthetase
HDC	histidine decarboxylase
HIOMT	hydroxyindole-O-methyltransferase
HNMT	histamine N-methyltransferase
MAO	monoamine oxidase
M6H	melatonin 6 hydroxylase
M6ST	melatonin 6 sulfotransferase
PHEH	phenylalanine hydroxylase
PNMT	phenylethanolamine N-methyltransferase
SERHMT	serine hydroxymethyltransferase
THRA	threonine aldolase
TRPH	tryptophan hydroxylase
TYRH	tyrosine hydroxylase

Cofactors:

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

Dried Urine – A Convenient Testing Option

The nature of urine collection is non-invasive and preferable over the traditional invasive collection approaches such as measurement of cerebrospinal fluid. Even with liquid urine collection the patient experiences the enormous hassle of collecting all urine voids over a 24-hr period into a large jug. To circumvent this inconvenience some labs have settled for collecting only the 2nd void limiting neurotransmitter results to a single morning time point snapshot. ZRT Laboratory offers alternative to the liquid urine collection method by offering a simple and convenient collection of four separate urine samples at specific time points throughout the day – 1st morning, 2nd morning (approximately 2 hours after the first collection), early evening, and bedtime. Urine is collected onto filter strips by urinating directly on the strip, or by dipping the filter card in a cup containing the collected urine. The urine cards are then allowed to dry overnight, and sent to ZRT for testing. The convenience of the collection method warrants patient compliance and ease of incorporation into clinical practice.

Considerations

- The neurotransmitter test assumes proper kidney function. Neurotransmitter levels are reported in μg/g creatinine, where creatinine is measured from the same sample. This test should not be used in individuals with compromised renal function.
- The sample can become very dilute due to increased fluid consumption during the day. Therefore, on the day of testing, individuals should restrict their liquid intake to normal consumption.
- On the day before and the day of testing, individuals are advised to avoid avocados, bananas, pineapple, nuts and nut butters, as well as alcohol and nicotine, because they may interfere with testing.

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