Neurotransmitter Testing in Dried Urine

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 i mbalances i n n eurotransmitter l evels. B ased o n n eurotransmitter 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.

Available Tests

NeuroAdvanced Profile

Tests: GABA, Glu, Gly, DA, Epi, NE, HIST, 5-HT, PEA, DOPAC, HVA, 5-HIAA, NMN, VMA, Crtn (dried urine)

Testing neurotransmitters in patients with a suspected neurochemical imbalance can help assess individual biochemistry and get to the root of persistent issues such as mood/affective disorders, adrenal dysfunction, addictive behaviors, ADD or OCD, or PMS or PMDD.

Add-On Options (dried urine, unless noted)

- Saliva Hormones: E2, Pg, T, DS, C
- Urine Hormones: E2, Pregnanediol, Allopregnanolone, Androstenedione, T, Epi-T, DHT, DHEA, 5α,3α-Androstanediol
- Diurnal Cortisol: Free Cortisol x 4, Free Cortisone x 4
- Diurnal Cortisol & Melatonin: Free Cortisol x 4, Free Cortisone x 4, Melatonin (MT6s) x 4
- Diurnal Cortisol, Norepinephrine & Epinephrine: Free Cortisol x 4, Free Cortisone x 4, NE x 4, Epi x 4
- Diurnal Cortisol, Melatonin, Norepinephrine & Epinephrine: Free Cortisol x 4, Free Cortisone x 4, Melatonin (MT6s) x 4, NE x 4, Epi x 4
- Urine Elements: Iodine, Selenium, Bromine, Lithium, Arsenic, Cadmium, Mercury

Neurotransmitter Testing

Non-invasive home test kit

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 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 testing is performed with the goal that therapeutic interventions may be introduced to address, alleviate, and improve a patient's well-being and has a breadth of data to support the efficacy of the test in clinical practice (see Table on next page). Evaluation of neurotransmitter levels in urine provides valuable information about the heterogeneity of patient biochemistry, epigenetics, and how the body functions as a whole.

Although the urine test is not a direct measure of brain neurotransmitter levels, it provides relevant information with respect to neurotransmitter regulation in the brain, which can be altered by treatment. The levels in urine often parallel levels in the central nervous system, and the test may therefore assist in the selection of patients with mood issues who might respond to specific pharmaceutical or over-the-counter treatment interventions[58,59]. In other words, the test provides a means to glean a functional systemic perspective regarding each neurotransmitter in the periphery, which ultimately operates under the control of the brain.

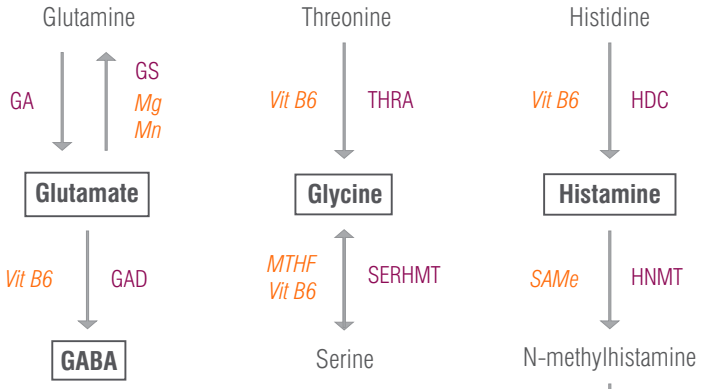
How do neurotransmitters end up in urine? Some neuro-transmitters are produced in the brain and transported across

NEUROTRANSMITTER FUNCTIONS & IMBALANCES

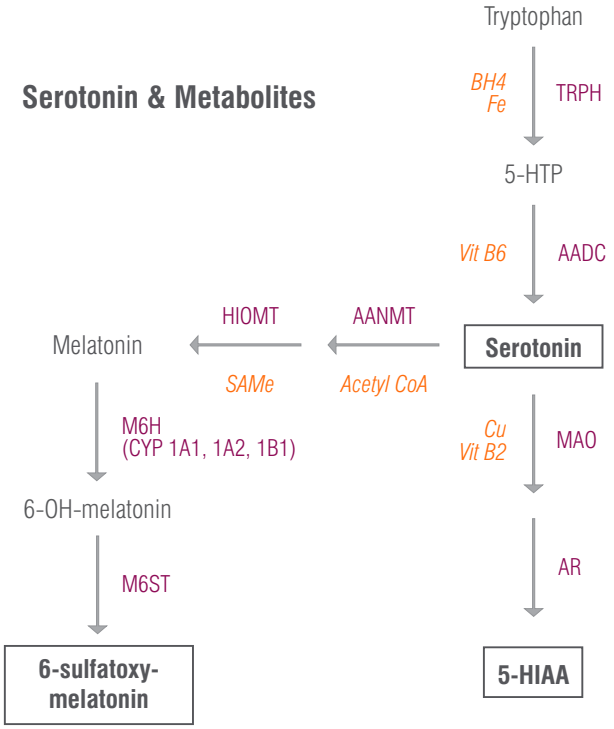
Neurotransmitter	High Levels in Urine	Low Levels in Urine
Serotonin is the "housekeeping" molecule – promotes healthy sleep, regulates appetite, improves mood, supports healthy digestive function and so much more. 5-HIAA is a metabolite.	Serotonin is high in depression[4,5] and with 5HTP use[6], and is implicated in anxiety, dysbiosis, irritability, and low libido.	Serotonin is decreased in autism spectrum disorder[7], depression[8], with oral contraceptives[9,10] and may be associated with anxiety, low mood, irritability, and sleep disturbances.
GABA functions as the major inhibitory neurotransmitter, induces relaxation and reduces anxiety.	GABA is elevated in sleep apnea[11], ovarian cancer[12], 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[13].
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 may be associated with insufficient vitamin B status and/or methylation events.	Glycine levels are low in diabetes[14], hypothyroidism[15], obesity[16], and after intense exercise[17], Clinically, low glycine levels are suspected in depression.
Glutamate functions as the major excitatory neurotransmitter and metabolic fuel throughout the body.	Glutamate is high in celiac disease[18] and hyperthyroidism[19]. Clinically, high glutamate is suspected in anxiety, autism spectrum disorder, depression and sleep issues.	Glutamate is low in patients with migraines[20]. Clinically, low glutamate is implicated in depression, chronic fatigue, lack of concentration, low energy levels, and sleep disturbances.
Histamine is a neurotransmitter and immuno-modulator.	Histamine is high in cystitis[21], flushing disorder[22], food allergies[23], polycythemia[24] and pregnancy[25]. 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.
PEA serves as a biomarker for ADHD.	PEA is elevated in individuals with bipolar major affective disorder[26], anxiety and insomnia[27], phenylketonuria[28] and with methylphenidate treatment[29].	PEA is low in patients with autistic spectrum disorder[30], ADHD[29,31,32], depression[33], and inattentiveness[34,35].
Dopamine serves as the reward and pleasure center in the brain, and messenger of the sympathetic nervous system in the periphery. DOPAC and HVA are metabolites.	High dopamine is reported in patients with high in anxiety[36], stress[37], paroxysmal hypertension[38], primary aldosteronism[39], PTSD40, and mercury toxicity[41].	Dopamine is low in Alzheimer's disease[42], anorexia nervosa[43], fibromyalgia[44], hypertension[45], periodic limb movement disorder[46], sleep disturbances[47], hypoadrenergic orthostatic hypotension[48].
Epinephrine 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[49,50], ADHD[34,35], bipolar disorder[51], depression[52], hyperglycemia[53], sleep apnea[11], PTSD[40], and stress[54,55].	Epinephrine and norepinephrine levels are low in Alzheimer's disease[42], metabolic syndrome[56], and obesity[57].

NEUROTRANSMITTER CASCADE

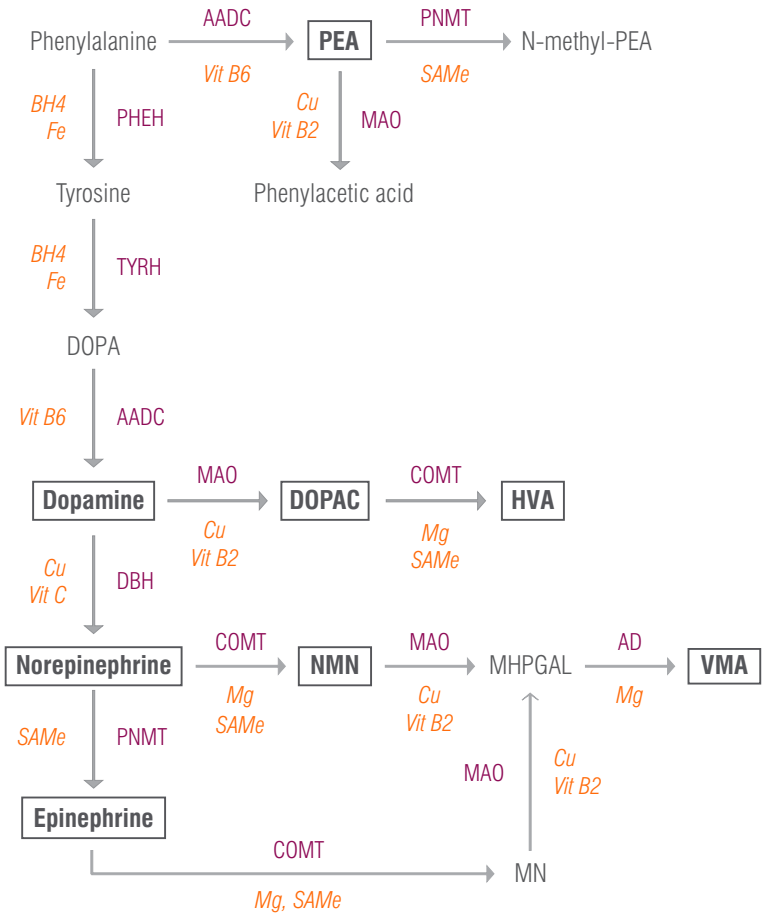
Glutamate/GABA, Glycine & Histamine



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

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[60]. 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, GABA, dopamine, norepinephrine, epinephrine). 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.

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-hour 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 an 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 of testing, individuals are advised to refrain from consuming alcohol, nicotine, bananas, pineapple, and walnuts as they may interfere with testing.

HORMONE ADD-ON OPTIONS

Both hormones and neurotransmitters serve as key modulators of psychological wellbeing. The targeted neuroendocrine assessment including hormones as well as neurotransmitters provides clinicians with a focused individualized biochemical platform to guide treatment interventions.

Saliva Hormones

The saliva hormones add-on includes estradiol, progesterone, testosterone, DHEA-S, and cortisol, and is an excellent way to assess the initial “big picture” of overall sex and adrenal hormone status in female and male patients. The test provides clinical information regarding the bioavailable fraction of hormones. For those Individuals who produce very little saliva or who use supplementary troche/sublingual hormones, this test is not suitable. It can be used with oral, topical, vaginal, patch, injectable, and pellet forms of hormone administration.

Urine Hormones

The hormonal profile in dried urine features 2 main progesterone metabolites and 6 major androgens, along with estradiol. Assessment of these hormones in dried urine is a convenient option for those patients who are unable to collect sufficient saliva for the salivary test. While the salivary hormones add-on provides an overall glance at the major hormones, the metabolites add-on expands the evaluation to the major sex steroid metabolites and is specifically geared to those patients who present with low or high androgen symptoms or symptoms of estrogen dominance. Urine hormone testing is only suitable for oral, topical, patch, injectable, and pellet forms of hormone administration, but not for vaginal supplementation as vaginal hormones can contaminate the sample.

When to Test Neurotransmitters Alone	When to Combine Neurotransmitters with Diurnal Urinary Hormones	When to Combine Neurotransmitters with Saliva Hormones	When to Combine Neurotransmitters with Urine Hormone Metabolites
• Managing psychiatric interventions • Establish a baseline • Patients unable to use HRT • Children and Adolescents • Hormone levels recently tested	• Suspected HPA axis dysfunction • Sleep problems • PCOS • Pre-menopause & menopause • Andropause • ADHD	• PMS/PMDD • Symptoms of estrogen dominance • High or low androgen symptoms • Pre-menopause & menopause • Irregular cycles • PCOS • Suspected HPA axis dysfunction	• Low androgen symptoms: fatigue, foggy thinking, decreased stamina • High androgen symptoms: acne, scalp hair loss, facial hair growth • PCOS • Symptoms of estrogen dominance • Suspected HPA axis dysfunction

Diurnal Urinary Hormones

Diurnal rhythms of cortisol, cortisone, norepinephrine, and epinephrine reflect HPA axis function; the addition of diurnal melatonin provides a useful measure of circadian rhythm regulation. Detailed characterization of these biochemical parameters may aid in identifying specific imbalances in an individual's response to stress.

Elements Add-on Option

We are exposed to both nutritional and toxic elements through diet, drinking water, supplements, and even the air we breathe. Elements have a variety of effects on brain health. Seven elements are tested in the urine elements profile to give an assessment of deficiencies in essential elements or excessive exposure to toxic heavy metals.

Iodine is essential for healthy thyroid function, and a healthy thyroid is essential to a healthy brain. Thyroid hormone is neuroprotective and plays an important role in regulating the major enzyme involved in methylation in the brain and the body.

Selenium combats mercury and cadmium toxicity. Selenium's effects are antioxidant, anti-inflammatory and neuroprotective in nature through its integration with selenoproteins. Selenoproteins play an essential role in the activation of thyroid hormones as well as integration with glutathione production.

Bromine, in high amounts through exposure to environmental pollutants (e.g., brominated flame retardants), can induce neurotoxicity by inappropriately modifying glycine, glutamate and GABA signaling. Neurological abnormalities from excessive bromine exposure can include detrimental changes in cognition and mood.

Lithium, in trace amounts, has been shown to improve mood and slow the progression of dementia. Overall, lithium's effects on the brain are neuroprotective, antioxidant and regenerative. Lithium can modulate monoamine oxidase activity to appropriately break down serotonin, dopamine, and phenethylamine.

Arsenic disrupts serotonin and dopamine metabolism, thus compromising neuronal health. Even at low-level exposure, arsenic predisposes to cognitive dysfunction and susceptibility to mood disorders. Additionally, arsenic can induce neuronal death by stimulating processes implicated in Alzheimer's disease.

Cadmium upsets the delicate balance between glycine, glutamate and GABA to negatively impact memory and cognition by being especially destructive to white matter in the brain. Cadmium exposure has detrimental effects on neurocognitive development in children, and is associated with learning disabilities, lower IQ, attention deficits, behavioral problems, and hearing loss.

Mercury is a potent neurotoxin, which increases oxidative stress by permanently inhibiting glutathione function, thereby stripping neurons of their defensive mechanisms. Mercury radically skews neurotransmission – it stimulates excitatory signaling (e.g., glutamate, dopamine) and decreases inhibitory signaling (e.g., GABA). Mercury exposure can cause a variety of neurological symptoms, including irritability, concentration and memory difficulties, and sleep disturbances.

References

1. National Alliance on Mental Illness. Mental Illness. Facts and Numbers. 2013.
2. Brooks M. Top 100 Most Prescribed, Top-Selling Drugs. Medscape 2014.
3. Eby GA, III, Eby KL. Magnesium for treatment-resistant depression: a review and hypothesis. Med Hypotheses 2010;74:649-60.
4. Mitani H, Shirayama Y, Yamada T, Kawahara R. Plasma levels of homovanillic acid, 5-hydroxyindoleacetic acid and cortisol, and serotonin turnover in depressed patients. Prog Neuropsychopharmacol Biol Psychiatry. 2006;30:531-4.
5. Audhya T, Adams JB, Johansen L. Correlation of serotonin levels in CSF, platelets, plasma, and urine. Biochim Biophys Acta. 2012;1820:1496-501.
6. Joy T, Walsh G, Tokmakejian S, Van Uum SH. Increase of urinary 5-hydroxyindoleacetic acid excretion but not serum chromogranin A following over-the-counter 5-hydroxytryptophan intake. Can J Gastroenterol. 2008;22:49-53.
7. Gevi F, Zolla L, Gabriele S, Persico AM. Urinary metabolomics of young Italian autistic children supports abnormal tryptophan and purine metabolism. Mol Autism. 2016;7:47.
8. Nichkova MI, Huisman H, Wynveen PM, et al. Evaluation of a novel ELISA for serotonin: urinary serotonin as a potential biomarker for depression. Anal Bioanal Chem 2012;402:1593-600.
9. Shaarawy M, Fayad M, Nagui AR, Abdel-Azim S. Serotonin metabolism and depression in oral contraceptive users. Contraception. 1982;26:193-204.
10. Var C, Keller S, Tung R, et al. Supplementation with vitamin B6 reduces side effects in Cambodian women using oral contraception. Nutrients. 2014;6:3353-62.
11. Kheirandish-Gozal L, McManus CJ, Kellermann GH, et al. Urinary neurotransmitters are selectively altered in children with obstructive sleep apnea and predict cognitive morbidity. Chest 2013;143:1576-83.
12. Nicholson-Guthrie CS, Guthrie GD, Sutton GP, Baenziger JC. Urine GABA levels in ovarian cancer patients: elevated GABA in malignancy. Cancer Lett 2001;162:27-30.
13. Perlmutter D, Loberg K. Brain Maker. The Power of Gut Microbes to Heal and Protect Your Brain - for Life. Little, Brown and Company, Hachette Book Group, 2015.
14. Sasaki M, Sato K, Maruhama Y. Rapid changes in urinary serine and branched-chain amino acid excretion among diabetic patients during insulin treatment. Diabetes Res Clin Pract. 1988;5:219-24.
15. Friedrich N, Pietzner M, Cannet C, et al. Urinary metabolomics reveals glycemic and coffee associated signatures of thyroid function in two population-based cohorts. PLoS One. 2017;12:e0173078.
16. Ahmad MS, Alsaleh M, Kimhofer T, et al. Metabolic Phenotype of Obesity in a Saudi Population. J Proteome Res. 2017;16:635-44.
17. Corsetti R, Barassi A, Perego S, et al. Changes in urinary amino acids excretion in relationship with muscle activity markers over a professional cycling stage race: in search of fatigue markers. Amino Acids. 2016;48:183-92.
18. Marko AM, Gerrard JW, Buchan DJ. Glutamic acid derivatives in adult celiac disease. II. Urinary total glutamic acid excretion. Can Med Assoc J 1960;83:1324-5.
19. Belanger R, Chandramohan N, Misbin R, Rivlin RS. Tyrosine and glutamic acid in plasma and urine of patients with altered thyroid function. Metabolism 1972;21:855-65.
20. Ragginer C, Lechner A, Bernecker C, et al. Reduced urinary glutamate levels are associated with the frequency of migraine attacks in females. Eur J Neurol 2012;19:1146-50.
21. el-Mansoury M, Boucher W, Sant GR, Theoharides TC. Increased urine histamine and methylhistamine in interstitial cystitis. J Urol. 1994;152:350-3.
22. Myers G, Donlon M, Kaliner M. Measurement of urinary histamine: development of methodology and normal values. J Allergy Clin Immunol. 1981;67:305-11.
23. Raithel M, Hagel A, Albrecht H, et al. Excretion of urinary histamine and N-tele methylhistamine in patients with gastrointestinal food allergy compared to non-allergic controls during an unrestricted diet and a hypoallergenic diet. BMC Gastroenterol. 2015;15:41.
24. Horakova Z, Keiser HR, Beaven MA. Blood and urine histamine levels in normal and pathological states as measured by a radiochemical assay. Clin Chim Acta. 1977;79:447-56.
25. Harrison VC, Peat G, de Heese HV. Fetal growth in relation to histamine concentration in urine. J Obstet Gynaecol Br Commonw. 1974;81:686-90.
26. Karoum F, Linnoila M, Potter WZ, et al. Fluctuating high urinary phenylethylamine excretion rates in some bipolar affective disorder patients. Psychiatry Res 1982;6:215-22.
27. DeLisi LE, Murphy DL, Karoum F, et al. Phenylethylamine excretion in depression. Psychiatry Res 1984;13:193-201.
28. Reynolds GP, Seakins JW, Gray DO. The urinary excretion of 2-phenylethylamine in phenylketonuria. Clin Chim Acta. 1978;83:33-9.
29. Kusaga A, Yamashita Y, Koeda T, et al. Increased urine phenylethylamine after methylphenidate treatment in children with ADHD. Ann Neurol 2002;52:372-4.
30. Kusaga A. [Decreased beta-phenylethylamine in urine of children with attention deficit hyperactivity disorder and autistic disorder]. No To Hattatsu. 2002;34:243-8.
31. Baker GB, Bornstein RA, Rouget AC, et al. Phenylethylaminergic mechanisms in attention-deficit disorder. Biol Psychiatry 1991;29:15-22.
32. Irsfeld M, Spadafore M, Pruss BM: Beta-phenylethylamine, a small molecule with a large impact. Webmedcentral 2013;4:pii 4409.
33. Sabelli HC, Fawcett J, Gusovsky F, et al. Urinary phenyl acetate: a diagnostic test for depression? Science. 1983;220:1187-8.
34. Faraone SV, Bonvicini C, Scassellati C. Biomarkers in the diagnosis of ADHD--promising directions. Curr Psychiatry Rep 2014;16:497.
35. Scassellati C, Bonvicini C, Faraone SV, Gennarelli M: Biomarkers and attention-deficit/hyperactivity disorder: a systematic review

References (cont'd.)

and meta-analyses. J Am Acad Child Adolesc Psychiatry 2012;51:1003-19.

36. Field T, Diego M, Hernandez-Reif M, et al. Prenatal dopamine and neonatal behavior and biochemistry. Infant Behav Dev. 2008;31:590-3.
37. Ghaddar A, Omar KH, Dokmak M, et al. Work-related stress and urinary catecholamines among laboratory technicians. J Occup Health 2014;55:398-404.
38. Kuchel O, Buu NT, Larochelle P, et al. Episodic dopamine discharge in paroxysmal hypertension. Page's syndrome revisited. Arch Intern Med. 1986;146:1315-20.
39. Ishiguro T, Shimamoto K, Sakamoto T, et al. Renal dopaminergic activity in patients with primary aldosteronism. Hypertens Res. 1995;18 Suppl 1:S193-S5.
40. Yehuda R, Southwick S, Giller EL, et al. Urinary catecholamine excretion and severity of PTSD symptoms in Vietnam combat veterans. J Nerv Ment Dis 1992;180:321-5.
41. Houston MC. Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. J Clin Hypertens (Greenwich) 2011;13:621-7.
42. Liu L, Li Q, Li N, et al. Simultaneous determination of catecholamines and their metabolites related to Alzheimer's disease in human urine. J Sep Sci 2011;34:1198-204.
43. Van Binsbergen CJ, Odink J, Van der Beek EJ, et al. Biogenic amines in anorexia nervosa: circadian rhythm in urinary excretion and influence of posture and physical task load on plasma catecholamines. Psychosom Med 1991;53:440-52.
44. Riva R, Mork PJ, Westgaard RH, et al. Catecholamines and heart rate in female fibromyalgia patients. J Psychosom Res 2012;72:51-7.
45. Gill JR, Jr., Grossman E, Goldstein DS. High urinary dopa and low urinary dopamine-to-dopa ratio in salt-sensitive hypertension. Hypertension. 1991;18:614-21.
46. Cohrs S, Guan Z, Pohlmann K, et al. Nocturnal urinary dopamine excretion is reduced in otherwise healthy subjects with periodic leg movements in sleep. Neurosci Lett 2004;360:161-4.
47. Seay JS, McIntosh R, Fekete EM, et al. Self-reported sleep disturbance is associated with lower CD4 count and 24-h urinary dopamine levels in ethnic minority women living with HIV. Psychoneuroendocrinology 2013;38:2647-53.
48. Kuchel O, Buu NT, Hamet P, et al. Orthostatic hypotension: a posture-induced hyperdopaminergic state. Am J Med Sci. 1985;289:3-11.
49. Paine NJ, Watkins LL, Blumenthal JA, et al. Association of depressive and anxiety symptoms with 24-hour urinary catecholamines in individuals with untreated high blood pressure. Psychosom Med 2015;77:136-44.
50. Hughes JW, Watkins L, Blumenthal JA, et al. Depression and anxiety symptoms are related to increased 24-hour urinary norepinephrine excretion among healthy middle-aged women. J Psychosom Res 2004;57:353-8.
51. Koslow SH, Maas JW, Bowden CL, et al. CSF and urinary biogenic amines and metabolites in depression and mania. A controlled, univariate analysis. Arch Gen Psychiatry 1983;40:999-1010.
52. Grossman F, Potter WZ. Catecholamines in depression: a cumulative study of urinary norepinephrine and its major metabolites in unipolar and bipolar depressed patients versus healthy volunteers at the NIMH. Psychiatry Res 1999;87:21-7.
53. Troisi RJ, Weiss ST, Parker DR, et al. Relation of obesity and diet to sympathetic nervous system activity. Hypertension. 1991;17:669-77.
54. Holzman C, Senagore P, Tian Y, et al. Maternal catecholamine levels in midpregnancy and risk of preterm delivery. Am J Epidemiol 2009;170:1014-24.
55. Fujiwara K, Tsukishima E, Kasai S, et al. Urinary catecholamines and salivary cortisol on workdays and days off in relation to job strain among female health care providers. Scand J Work Environ Health 2004;30:129-38.
56. Lee ZS, Critchley JA, Tomlinson B, et al. Urinary epinephrine and norepinephrine interrelations with obesity, insulin, and the metabolic syndrome in Hong Kong Chinese. Metabolism 2001;50:135-43.
57. Landsberg L, Troisi R, Parker D, et al. Obesity, blood pressure, and the sympathetic nervous system. Ann Epidemiol 1991;1:295-303.
58. Ravindran AV, Bialik RJ, Brown GM, Lapierre YD. Primary early onset dysthymia, biochemical correlates of the therapeutic response to fluoxetine: II. Urinary metabolites of serotonin, norepinephrine, epinephrine and melatonin. J Affect Disord. 1994;31:119-23.
59. Maas JW, Koslow SH, Katz MM, et al. Pretreatment neurotransmitter metabolite levels and response to tricyclic antidepressant drugs. Am J Psychiatry. 1984;141:1159-71.
60. Pestana M, Jardim H, Correia F, et al. Renal dopaminergic mechanisms in renal parenchymal diseases and hypertension. Nephrol Dial Transplant. 2001;16 Suppl 1:53-9.