# **Urinary Neurotransmitter Testing**

The nervous system serves as the central control mechanism for nearly every bodily process. The brain maintains homeostasis within the body through the use of neurotransmitters, which act as chemical messengers for the trillions of connections between the brain and all other organs. Disruption of communication within the nervous system, due to neurotransmitter imbalances, may lead to the manifestation of psychological, somatic and mood disorders, and related clinical complaints. Additionally, neurotransmitters are released through immune activity and can therefore provide insight into the immune system.

#### Which neurotransmitters could be involved in your patient's health concerns?

	Epi	NE	Dop	Ser	Gly	Tau	GABA	Glu	PEA	НА
Poor Sleep	Х	Х		Х		Х	Х	Х	Х	Х
Fatigue	Х	Х						Х		Х
Anxiousness	Х	Х			Х	Х	Х	Х	Х	
Low Mood		Х	X	Х	Х			Х	Х	
Attention Difficulties		Х	Х					Х	Х	
Excess Energy	Х	Х				Х	Х			
Cravings			Х	Х				Х		
Intestinal Complaints				Х						
Poor Cognitive Function			Х					Х	Х	
Weight Management Difficulties	Х			Х						
Excess Stress	Х	Х		Х	Х					
Headaches				Х						Х
Immune Issues		Х	Х	Х	Х			Х		Х

## **Neurotransmitter Imbalances**

#### Commonly seen in:

- Depression
- Insomnia
- Fatigue
- Anxiety
- Focus/attention issues

#### Affect sympathetic function:

- Metabolism
- Cardiac issues
- Weight gain
- Insulin resistance
- Hormone imbalances

#### Influenced by other factors:

- Immune activation
- Inflammation
- Oxidative stress
- Microbial challenges
- Environmental exposures
- Mental/emotional issues
- Lifestyle

## **Pre-configured Panels**

Test	ltem	Biomarkers	Specimen requirement
NeuroScreen Essential	9074	Epinephrine, Norepinephrine, Dopamine, Serotonin, GABA, Glutamate, PEA	2 Urine
NeuroScreen Basic	9023	Epinephrine, Norepinephrine, Dopamine, Serotonin, Glycine, GABA, Glutamate, PEA, Histamine	2 Urine
NeuroScreen Expanded	9123	Epinephrine, Norepinephrine, Dopamine, DOPAC, Serotonin, 5-HIAA, Glycine, Taurine, GABA, Glutamate, PEA, Histamine	2 Urine

### Individual Tests (Build Your Own) 9900

- 5-HIAA
- DOPAC
- Dopamine (Dop)
- Epinephrine (Epi)
- GABA
- Glutamate (Glu)
- Glycine (Gly)
- Histamine (HA)

- Kynurenic Acid (KA)
- Norepinephrine (NE)
- Phenylethylamine (PEA)
- Serotonin (Ser)
- Taurine (Tau)
- Tryptamine (Tryp)
- Tyramine (Tyr)



## Sample report (NeuroScreen Expanded)

	2.5%	20%	80%	97.5%	Result	Collected	Reference Range	U
Serotonin			1		162.0	04/04/2012 (6:30AM)	57 - 306	hð
5-HIAA					4,927.0	04/04/2012 (6:30AM)	800 - 13000	μg
GABA					5.5	04/04/2012 (6:30AM)	2.4 - 12.7	µMol.
Taurine					143.7 (L)	04/04/2012 (6:30AM)	52 - 1025	µMol.
Glycine					266.0 (L)	04/04/2012 (6:30AM)	182 - 2225	µMol.
Glutamate		-			37.9 (H)	04/04/2012 (6:30AM)	6.9 - 71.8	µMol.
Histamine					17.7	04/04/2012 (6:30AM)	4 - 71	рg
PEA		-			143.8 (H)	04/04/2012 (6:30AM)	15 - 167	nMol.
Dopamine					138.0	04/04/2012 (6:30AM)	64 - 261	hð
DOPAC					442.0	04/04/2012 (6:30AM)	100 - 2100	μg
Norepinephrine					27.1 (L)	04/04/2012 (6:30AM)	19 - 76	μg
Epinephrine					11.8	04/04/2012 (6:30AM)	4.7 - 20.8	μg

Ranges were established based on the 95% confidence interval for apparently healthy adult subjects.

## **Biomarkers**

Serotonin	A neuromodulator with pleiotropic activity depending upon receptor type and location. It serves as the precursor to the sleep hormone melatonin. Low levels of serotonin have been linked to sleep disorders, migraines, anxiety, and depression. <sup>4</sup>
5-HIAA	A metabolite of serotonin. The activity of serotonergic neurons in the brain can be associated with the assessment of serotonin and 5-HIAA levels. Imbalances in 5-HIAA have been connected with depression, migraines, and intestinal issues. Imbalances may also be associated with insomnia, cravings, and addictions. <sup>1,2,3</sup>
GABA	The primary inhibitory neurotransmitter in the brain and is important for regulating the activity of excitatory neurotransmission. Research has shown that GABA is a modulator of the stress response, and is associated with complaints such as insomnia, anxiety, and hyperactivity. <sup>11</sup>
Taurine	Both an inhibitory neurotransmitter and a neuromodulator. As a neuromodulator, taurine promotes the effects of GABA. Taurine has been shown to be neuroprotective and beneficial for heart function, while imbalances have been associated with insomnia, anxiety, and hyperactivity! <sup>6,17</sup>
Glycine	The principal inhibitory amino acid in the brainstem and spinal cord that regulates excitatory neurotransmission. Glycine, like GABA and taurine, may increase to compensate for elevations in excitatory neurotransmitters, primarily glutamate and aspartic acid. <sup>3</sup>
Glutamate	The primary excitatory neurotransmitter in the brain and is important in the promotion of wakefulness. The presence of light stimulates the release of glutamate, activating wake-promoting centers of the brain <sup>12</sup> Glutamate is also released in large quantities by an activated immune system.
Histamine	An excitatory neurotransmitter involved in the sleep/wake cycle and immune processes. A review of literature illustrates that histamine is intimately involved in insomnia, allergies, active infections, and may be involved in cognitive functions and neuropsychiatric disorders. <sup>14</sup>
Phenylethylamine (PEA)	An excitatory neurotransmitter involved in attention, focus, and mood. Imbalances in PEA may be associated with anxiety, insomnia, and altered moods. Studies have confirmed that PEA plays a role in hyperactivity and focus/concentration disorders. <sup>6</sup>
Dopamine	Responsible for feelings of pleasure, satisfaction, muscle control and function, GI issues, and modulating immune responses.
DOPAC	A metabolite of dopamine. The combination of DOPAC and dopamine measurements can assist in the assessment of the activity of dopaminergic neurons. DOPAC imbalances have been associated with anorexia, untreated Parkinson's disease, polycystic ovaries, and compulsive/addictive behaviors. <sup>4,5,6</sup>
Norepinephrine	A key neurotransmitter important for energy, mental focus, and sympathetic function. In relation to the sleep/wake cycle, it is mainly found in wake-promoting regions of the brain. <sup>15</sup> Low levels of norepinephrine have been associated with focus issues, while higher levels have been associated with anxiety issues.
Epinephrine	An excitatory neurotransmitter released in response to stress. Epinephrine is important for motivation and energy, but it also has been associated with restlessness. <sup>8</sup> Low levels are commonly seen with weight gain, whereas elevated levels of epinephrine have been correlated with sleep disturbances. <sup>9,10</sup>
Tryptamine	A neuromodulator and a trace amine formed from tryptophan decarboxylase activity. Altered tryptamine levels have been reported in psychiatric conditions including depression and schizophrenia. <sup>18</sup>
Tyramine	A neuromodulator. Elevated tyramine levels can increase the release of neurotransmitters, such as dopamine, norepinephrine, and epinephrine. <sup>9</sup> Elevated levels of catecholamines and neuromodulators in turn, have been associated with such things as migraine headaches. <sup>20</sup>
Kynurenic Acid	Kynurenic acid is a metabolite of tryptophan that may act as a marker of inflammation. During an inflammatory reaction, the enzyme indoleamine decarboxylase (IDO) is up-regulated. Increased IDO activity shifts tryptophan metabolism away from serotonin and favors kynurenic acid.

#### References

1. Celada, P. and Artigas, F. Plasma (1993) J.Neurochem. 61(6): 2191-2198.

2. Linnoila, V. M. and Virkkunen, M. (1992) J.Clin.Psychiatry. 53 Suppl46-51.

3. Bousser, M. G., Elghozi, J. L., Laude, D., and Soisson, T. (1986) Cephalalgia. 6(4): 205-209.

4. Delgado, P.L. (2000). J. Clin Psychiatry, 61(6): 7-11.

5. Simonneaux, V. and Ribelayga, C. (2003) Pharmacol.Rev. 55(2): 325-395.

6. Kusaga, A., Yamashita, Y., Koeda, T., Hiratani, M., Kaneko, M., Yamada, S., and Matsuishi, T. (2002) Ann. Neurol. 52(3): 372-374.

7. Black, J. MD and Scammell, T. MD. Neurophysiologic Pathways and Pharmacologic Targets (1-17-2005) 4-20.

8. Hanna, G. L., Ornitz, E. M., and Hariharan, M. (1996) J.Child Adolesc. Psychopharmacol. 6(1): 63-73.

9. Nishihara, K. and Mori, K. (1991) J.Hum. Ergol.(Tokyo). 20(1): 7-12.

10. Nishihara, K. and Mori, K. (1992) Physiol Behav. 52(2): 397-400.

11. Eisenhofer, G., Kopin, I. J., and Goldstein, D. S. (2004) Pharmacol. Rev. 56(3): 331-349.

12. Simonneaux, V. and Ribelayga, C. (2003) Pharmacol. Rev. 55(2): 325-395.

13. Kirsch, J. (2006). Cell Tissue Res. 326(2): 535-40.

14. Schwartz, J. C. and Arrang, J. M. Histamine. (2002) 5(14): 179-190.

15. Eldrup, E., Mogensen, P., Jacobsen, J., Pakkenberg, H., and Christensen, N. J. (1995) Acta Neurol.Scand. 92(2): 116-121.

16. Huxtable, R. J. (1992) Physiol Rev. 72(1): 101-163.

17. El, Idrissi A., Messing, J., Scalia, J., and Trenkner, E. (2003) Adv.Exp.Med.Biol. 526515-525.

18. Ruddick, J.P., Evans, A.K., Nutt, D.J., Lightman, S.L., Rook, G.A., and Lowry, C.A. Tryptophan metabolism in the central nervous system: medical implications. (2006). Exp Rev. Mol. Med. 8(20): 1-27.

 Burchett, S.A. and Hicks, T.P. The mysterious trace amines: Protein neuromodulators of synaptic transmission in mammalian brain.
(2006). Prog. Neurobiol. 79(5-6): 223-46.

20. D'Andrea, G., Nordera, G.P., Perini, F., Allais, G., Granella, F. Biochemistry of neuromodulation in primary headaches: focus on abnormalities of tyrosine metabolism. (2007) Neurol Sci. 28(2);S94-6.



373 280th Street, Osceola, WI 54020 Phone 1-715-294-1705 Toll-free 1-888-342-7272

Testing performed by Pharmasan Labs is available through NeuroScience, Inc. CLIA certified ID# 52D0914898. New York State Department of Health PFI #7426.