

Urinary Neurotransmitter Analysis

The following includes summaries of studies that used urinary neurotransmitter analysis as a biomarker for the examination of various disorders including depression, anxiety and post-traumatic stress disorder.

1. **Hughes JW, Watkins L, Blumenthal JA, Kuhn C, Sherwood A. Depression and anxiety symptoms are related to increased 24-hour urinary norepinephrine excretion among healthy middle-aged women. *J Psychosom Res* 2004; 57(4): 353-8.**

In this study conducted by Hughes et al at the Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, the researchers examined the relationship between depression and anxiety and urinary neurotransmitter and cortisol excretion. Ninety-one women were evaluated for depression (using the Beck Depression Inventory) and anxiety (using the Spielberger State-Trait Anxiety Inventory). Twenty-four hour urine collections were assayed for each participant measuring norepinephrine, epinephrine and cortisol production. The results of this study showed that higher levels of depressed symptoms in women were associated with higher levels of urinary norepinephrine excretion. Higher levels of anxiety were associated with higher urinary norepinephrine and cortisol excretion. This research suggests that exacerbated symptoms of depression and anxiety may be associated with increased sympathetic nervous system (SNS) activity. These results are consistent with the possibility that increased SNS activity may play a role in increased mortality associated depression in older adults.

2. **Yehuda R, Southwick S, Giller EL, Ma X Mason JW. Urinary catecholamine excretion and severity of PTSD symptoms in Vietnam combat veterans. *J Nerv Ment Dis* 1992; 180(5): 321-5.**

In this study, conducted at the Department of Psychiatry, Mount Sinai Medical School by Yehuda et al, urinary measurements of the neurotransmitters dopamine, norepinephrine

and epinephrine were used as biomarkers to measure the severity of posttraumatic stress disorder (PTSD) in Vietnam combat veterans. Twenty-two male patients (14 inpatients and eight outpatients) with PTSD, as well as 16 nonpsychiatric normal males participated in this study. This study found that urinary dopamine and norepinephrine levels were significantly correlated with the severity of PTSD symptoms. The researchers concluded that these findings supported the theory that enhanced sympathetic nervous system (SNS) activation plays a major role in PTSD and that increased SNS arousal may be closely linked to the severity of certain PTSD clusters.

3. Hernandez-Reif M, Ironson G, Field T, Hurley J, et al. Breast cancer patients have improved immune and neuroendocrine functions following massage therapy. *J Psychosom Res.* 2004; 57(1): 45-52.

This study was conducted at the University of Miami School of Medicine by Hernandez-Reif et al. Cancer patients are at an increased risk of suffering from depression and anxiety. Depression and anxiety can compromise immunological function in Cancer patients, including natural killer (NK) cell activity. Stress has been linked to increased tumor development by decreasing NK cell activity. In this study, the researchers examined the use of massage therapy as a treatment option for stress reduction and mood enhancement using urinary neurotransmitter measurements (Norepinephrine, Epinephrine, Dopamine and Serotonin) as biological markers. Blood measurements were also drawn to study the effects of stress reduction and mood on the immune system. Thirty- four women diagnosed with Stage 1 or 2 breast cancer were randomly assigned to the massage therapy or a control group. The massage therapy group received 30 minute massages three times per week for 5 weeks. The long-term massage effects included a reduction in depression and hostility along with increased urinary dopamine and serotonin values, NK cell number, and lymphocytes. The researchers concluded that massage therapy for cancer patients may provide benefits for mood enhancement and immune system support.

4. Delahanty DL, Nugent NR, Christopher NC, Walsh M. Initial urinary epinephrine and cortisol levels predict acute PTSD symptoms in child trauma victims. *Psychoneuroendocrinology* 2005; (2): 121-8.

Previous research has suggested that children with posttraumatic stress disorder (PTSD) have altered levels of catecholamines (Dopamine, Norepinephrine, and Epinephrine) as compared to children that have suffered from trauma that do not have PTSD. The researchers in this study want to again examine whether a significant variance in urinary cortisol and neurotransmitter excretion following a traumatic event in children may be associated with an increased risk for the development of PTSD. Urinary catecholamine and cortisol measurements were conducted on 82 children aged 8-18 that were admitted to a Level 1 trauma center. The urine samples were immediately collected upon admission. Additional

assessments included PTSD and depressive symptomatology for 6 weeks following the initial traumatic event. The results of this study indicated that elevated initial urinary cortisol and epinephrine levels immediately following a traumatic event continued to predict the development of acute PTSD symptoms, particularly in boys.

5. **Tripodianakis J, Markianos M, Sarantidis D, Agouridaki M. Biogenic amine turnover and serum cholesterol in suicide attempt. Eur Arch Psychiatry Clin Neurosci 2002; 252(1): 38-43.**

In this study, the researchers investigated the correlation between suicidal behavior and changes in neuronal activity. The researchers examined the urinary neurotransmitter turnover in one hundred eleven subjects that were admitted to a hospital following suicide attempt. The urine metabolites of the neurotransmitters serotonin, dopamine and norepinephrine (5-HIAA, HVA, MHPG respectively) were collected within 24 hours of admission. These urine samples were compared to urine neurotransmitter metabolite turnover in a group of 62 healthy controls. According to psychiatric diagnosis made, according to DSM-III-R criteria, 54 subjects in the suicide attempt group were diagnosed with adjustment disorder, 25 were diagnosed with depression, 16 with schizophrenia, and 16 with personality disorder. Within all subgroups of patients diagnosed with various disorders following suicide attempt, a significant increase in the urinary norepinephrine metabolite MHPG was found, versus normal controls.

6. **Lykouras L, Markianos, Hatzimanolis J, Malliaras D, Stefanis C. Association of biogenic amine metabolites with symptomatology in delusional (psychotic) nondelusional depressed patients. Prog Neuropsychopharmacol Biol Psychiatry 1995; 19(5): 877-887.**

In this study, the urine metabolites of the neurotransmitters norepinephrine, serotonin, and dopamine (MHPG, 5HIAA and HVA respectively) were examined in 84 patients diagnosed with major depressive disorder. Fifty of the 84 patients were nondelusional, 34 were diagnosed delusional (psychotic) per DSM-III-R criteria. In the delusional group, norepinephrine metabolite excretion was positively related to scores of depressed mood and insomnia. Serotonin metabolite excretion was negatively associated with insomnia, work and interests. In both the delusional and nondelusional groups Dopamine metabolite was positively related to agitation.

7. **Takahashi S, Takahashi R, Masumura I, Miike A. Measurement of 5-hydroxyindole compounds during L- 5-HTP treatment in depressed patients. Folia Psychiatr Neurol Jpn 1976; 30(4): 461-73.**

In an open clinical trial, 5-hydroxytryptophan (5-HTP), an immediate precursor to serotonin was given to hospitalized patients suffering from depression. The

patients received 150 mg of 5-HTP for seven days. Seven of 14 patients (50%) responded to the small dose of 5-HTP with mild to moderate improvement of their depression. Urinary excretion levels and plasma concentrations of three 5-hydroxyindole compounds, 5-HTP, 5-HT and 5-HIAA, were measured during the treatment. In this study, the researchers found that patients that did not have positive improvement in their symptoms of depression, following oral treatment with 5-HTP, exhibited significantly lower excretion levels of the serotonin metabolite 5-HIAA in urine. The researchers concluded that 5-HTP may not have been fully utilized in the depressed patients who did not react positively to the agent.