Urinary Biomarkers in the Diagnosis of Depression

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Abstract

Depression is a common psychological disorder and is frequently misdiagnosed. Currently, there is not an objective diagnostic tool for depression; clinicians must rely on symptoms of their patients in order to make a diagnosis. This study aimed to provide clinical values of key biomarkers to objectively differentiate between depressed and healthy controls. This study analyzed levels of Norepinephrine (NE), Brain-Derived Neurotrophic Factor (BDNF), and cortisol, found in participant urine. 63 adult men and women, currently living in the northern Utah area, comprised the sample of participants. The average age of participant was 25.3. Each participant submitted a first-morning-void urine sample and responded to the standardized demographic questionnaire and depression inventory. The Beck Depression Inventory (BDI) was used to classify participants along a continuum from healthy control to majorly depressed. Samples were tested for creatinine to assess kidney function and identify dilution factors for mathematical normalization. All analytes were measured using enzyme-linked immunosorbent assays (ELISA). All univariate linear regression analysis determined that there is no value in the analytes tested could reliably predict the BDI outcome.

RESULTS

Figure 1a. NE values across control, mild, and highly depressed groups
Figure 1b. Cortisol values across control, mild, and highly depressed groups
Figure 1c. BDNF values across control, mild, and highly depressed groups

Figure 2a. BDI vs. NE Linear Regression Multiple R²=0.014, p-value: 0.9415
Figure 2b. BDI vs. Cortisol Linear Regression Multiple R²=0.000274, p-value: 0.5437
Figure 2c. BDI vs. BDNF Linear Regression Multiple R²=0.01051, p-value: 0.4633

Figure 3a. Demographic findings of the participants based on BDI scores. Two groups were formed from the data: a control group (n=46) and a depressed group (n=14).
Figure 3b. Demographic findings of the participants based on BDI scores. Three groups were formed from the data: a control group (n=46), a mildly depressed group (n=12) and a highly depressed group (n=5).

Discussion

Testing showed no statistically significant correlation between each analyte and depression scores. The data in this study suggested that stress is not a primary cause of depression. Although this study did not find any correlation between depression severity and respective analyte levels, other analytes may provide opportunities for further research.

Data analysis is ongoing to further examine differences in BDI scores when compared to different demographic subsets. Women showed a higher mean BDI score than did men, so further analysis may show an association between the different demographics and the corresponding BDI scores. The analytes tested in this study were found in relatively low levels in urine samples; further research utilizing different sample types, such as cheek swabs or blood samples, may allow for better detection of analyte levels. More conclusive results may be discovered from a sample pool that contains a greater amount of participants with more severe depression.

Depression

Depression is a mood disorder in which feelings of sadness, loss, anger, or frustration interfere with everyday life for weeks or more. Characteristics of Depression are set forth in the Diagnostic and Statistical Manual of Mental Disorders, which include any five of the following during a two week period: sadness, loss of interest or pleasure in activities once enjoyed, change in appetite, difficulty sleeping, agitation, energy loss, feelings of worthlessness, difficulty concentrating, recurrent thoughts of death. In 2024, 15.3 million Americans suffered a major depressive episode. A study done in 2009 by Mitchell, Vaze, & Rao found that only 47.3% of 50,000 subjects had been correctly diagnosed with depression.

Norepinephrine

Norepinephrine is a hormone derived from dopamine. High levels of NE are found in cases of high stress, while low levels of NE have been correlated with sedation, low arousal, low alertness, and depression.

Cortisol

Cortisol is a hormone produced in the adrenal glands primarily in response to stress. Patients with clinical depression show increased levels of cortisol compared to individuals who are not depressed.

BDNF

Brain-Derived Neurotrophic Factor is a protein that promotes the survival and growth of neurons. BDNF has been shown to decrease in the presence of corticosterone that is released during psychological stress.

Methods

Participants collected a first-morning void and responded to the depression inventory without knowledge that the study was focusing on depression. This was done to ensure that the participants did not answer the questions under a preconceived notion of what was the “right” answer was. Upon completion of the depression inventory, participants were given full disclosure of the goals of the study and the opportunity to opt out. Urine samples were poured off into 3 sterile tubes and frozen at -20°C until testing.

Creatinine was tested in each participant urine to assess normal renal function and to standardize the concentration of each sample. Samples were diluted 1:21, and tested using colorimetric methods (Alere). Creatinine testing was performed on the first aliquot of all samples in order to mathematically normalize analyte values.

All analyte values were normalized according to the concentration of the most dilute sample. The second and third aliquots in their original concentration were tested using ELISA methods according to the specifications of the respective manufactures (BDNF - Boster Bio, NE - Eagle Biosciences, Cortisol - Rocky Mountain Diagnostics).

Before statistical analysis, the participants were separated into 2 different categories based on their BDI score. In one grouping, participants were divided based on healthy controls and depressed. The other grouping utilized healthy controls, mildly depressed, and severely depressed. The mean values of the 3 groups were analyzed in boxplots that compared the BDI score against the depression categories. A univariate linear regression was performed on each analyte to determine if there was an association between the analytes and their corresponding BDI score.

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