Association of BDNF genotype (ValVal) and neuroticism phenotype on mood and risk for depression in healthy adults across the lifespan

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Introduction

• Many factors contribute to depressive mood such as individual differences in genetic heritability and personality traits (Sen et al., 2002)
• Neuroticism is a personality trait that increases an individual’s tendency to experience negative emotions (Terracciano et al., 2011), especially feelings of threat, frustration, or loss (Pereira-Morales et al., 2017).
• Individuals who are high in neuroticism are more likely to be diagnosed with anxiety, depressive, and substance use disorders (Pereira-Morales et al., 2017).
• Brain-derived neurotrophic factor (BDNF) is a protein responsible for the regulation of growth, maturation, and maintenance of nerve cells, and there are three genotype polymorphisms: Val/Val, Val/Met, and Met/Met.
• Met-allele carriers have gray matter volume deficits in the temporal, frontal areas and thalamus, while Val-allele carriers lower white matter integrity of fiber tracts in the frontal, temporal, and occipital areas (Park et al., 2017).
• Research shows that variation of the BDNF gene plays a role in depression-related traits, particularly in Met-allele carriers that have a lower expression of the BDNF, which has been associated with Major Depressive Disorder (Mata et al., 2010)
• Previous studies indicate that lower BDNF concentration in plasma with higher neuroticism scores is linked to greater depressive symptoms (Terracciano et al., 2011)
• The current study examined whether individuals with BDNF Met/Met genotype and higher levels of neuroticism have more depressive symptoms, as indicated by the CES-D scale.

Methods

Participants

• N = 210 cognitively normal adults (age range) with no history of cardiovascular, neurologic, psychiatric or metabolic problems, head trauma with loss of consciousness, or substance abuse.
• Subsample who received saliva test/genotyping for BDNF, neuroticism scale (NEO-PI) and depression scale (CES-D) were included in the final analysis.

<table>
<thead>
<tr>
<th>Age Range</th>
<th>n(Val/Val)</th>
<th>n(Val/Met)</th>
<th>n(Met/Met)</th>
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<tr>
<td>20-34</td>
<td>141</td>
<td>63</td>
<td>12</td>
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Measures

Neuroticism

Neuroticism, Extraversion, Openness Personality Inventory (NEO-PI) is a 240-item self-reported questionnaire that is grouped in 30 facets, when then are narrowed into one of the Big Five personality trait: neuroticism, extraversion, openness to experience, agreeableness. Each item is scored on a 5-point scale and has a self-carbon page of the answer sheet which contains item values for rapid computation of scale raw scores (Costa & McCrae, 1992). Internal consistency coefficients for both Forms R and S range from .86-.95 for domain scales and from .56-.90 for facet scales (Costa & McCrae, 1992).

Brain Derived Neurotrophic Factor (BDNF) (rs6265)

Saliva samples were collected for DNA extraction in 2mL tubes and sent to the University of Texas Southwestern Medical Center Genomics and Microarray Core Facility. Participants with Val/Val polymorphism were coded as 1. Because of the small sample size, Val/Met and Met/Met are coded as 0.

Depression

Depression was measured using the Center for Epidemiology Studies Depression (CES-D) Scale. Contains a 20-item questionnaire that asks participants to rate how often they experienced depressive symptoms, such as feeling lonely and poor appetite. Response ranges from 0 to 3, with 3 being most or almost all the time. Scores range from 0 to 60. Because only healthy participants were selected, the highest level of depression went to 16 (American Psychological Association, 2011).

Statistical Analyses

General linear models were conducted in JASP with CES-D as a dependent variable. Neuroticism, BDNF (Val/Val, Val/Met, Met/Met), and neuroticism x BDNF interactions were added as independent predictors. Non-significant interaction terms (p>0.17) were removed, and the models were re-run to conserve statistical power.

Results

Neuroticism Effects on Depression

We found significant main effects of neurotic personality trait on depression. There is a proportional relationship in that, the higher the neurotic score, the more depressed the individual.

BDNF genotype Effects on Depression

The Val/Val genotype (1) has shown significant effects on depression compared to Val/Met and Met/Met (0).

No Effects of Neuroticism x BDNF Effects on Depression

To demonstrate the effects of neurotic personality combined with the BDNF gene, we show no significant effects on depression.

Discussion

• The results indicated a significant effect of neuroticism and BDNF (Val/Val) genotype on level of depression (Neuroticism: F= 25.46, MS= 297.25, p<0.001; BDNF: F= 4.72, MS= 55.09, p=0.032)
• No interaction effect on depression (F=. 0.76, MS= 8.98, p=0.39)
• Specifically, those who were higher on neuroticism were more likely to score higher on the depression scale.
• This parallels with other studies that showed that depressive disorders are associated with neuroticism, due to individuals experiencing an increase in negative emotions (Lahey 2009; Adan et al. 2016)
• Higher neuroticism levels can be attributed to stress levels, which creates a high risk for depression (Pereira-Morales et al., 2017).
• Stress can play a significant role in this personality trait which can lead to a poor quality of life (Diehr et al. 2006; Quilty et al. 2003)
• Literature demonstrates that individuals who scored high in neuroticism reported more daily problems, tended to react with more severe emotions and exhibited stronger reactions to recurring problems. As a result, it can potentially create a greater predisposition to depression and anxiety (Griffith et al., 2010; Suls & Martin 2005).
• Genetics can also play a role in depression as presented with BDNF. Our hypothesis stating that BDNFmet increases risk for depression was not supported (p=0.153). Our results indicate Val/Val is linked to higher CES-D scores.
• Previous studies showed that Val/Val polymorphism is linked to poorer response to antidepressant treatment, unlike those with the Met-allele (Zou et al., 2010).
• Further longitudinal studies is needed to evaluate within-subject effects of BDNF and neuroticism on longitudinal change in CESD. Due to inconsistent results within the literature, a study with specific BDNF polymorphism (whether it be Val/Val, Val/Met, or Met/Met) is required to signify its association to depression. Once the specific polymorphism is confirmed, we can conduct larger studies to find the interaction between that genotype and neuroticism on depression.
• Limitations include a small sample with Met-allele, and limit the generalizability of current findings.
• Future research should consider examining the effect of neuroticism and BDNF on depression in individuals with clinical depression.