Perceived stress as a mediator of the relationship between neuroticism and depression and anxiety symptoms

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ABSTRACT

Although major depressive disorder (MDD) is one of the main causes of global disease burden, there is little evidence for the association between personality traits and depressive symptoms in Latin America. The aim of this study was to examine the possibility that perceived stress is a mediator of the association between neuroticism and depressive and anxious symptoms. Two hundred seventy four Colombian subjects (mean age 21.3 years) were evaluated with the short version of the Big Five Inventory (BFI-S), the Center for Epidemiologic Studies Depression Scale (CES-D), the Hospital Anxiety and Depression Scale (HADS), the Zung Self-Rating Anxiety Scale (ZSAS) and the Perceived Stress Scale-10. Both the neuroticism and perceived stress were significantly correlated with higher scores in depressive and anxious symptoms: HADS, CES-D and ZSAS ($p<0.01$). Perceived stress was a significant mediator of the relationship of neurotic trait and depressive and anxious symptoms. Our results are one of the first descriptions of the role of perceived stress as a mediator of the association between neuroticism and psychological distress. These findings are of particular importance, considering the little evidence available in Latin America about the psychosocial risk factors for MDD.

Keywords: Personality, Depression, Anxiety, Perceived stress, Latin America**.**

INTRODUCTION

Major depressive disorder (MDD) is defined as a psychiatric condition with a chronic outcome and an elevated risk of mortality (Kupfer et al. 2012). According to the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition (DSM-V), it is characterized by depressive mood and loss of interest in most activities, feelings of worthlessness and guilt, appetite and sleep disturbance, lack of concentration and suicidal thoughts and ideation (Association 2013). The first onset of MDD usually occurs in early adult life and shows co-morbidity with other psychiatric and medical disorders (e.g. anxiety and substance use disorders) (Kupfer et al. 2012; Derek Richards 2011). According to data from the Global Burden of Disease Study, MDD is one of the leading causes of years lived with disability, accounting for 8.2% and for 2.5% of global disability-adjusted life years; the estimated prevalence is high, with 298 million MDD cases in 2010 (Ferrari et al. 2013). The cost of MDD can be particularly high in young people (Ibrahim et al. 2013; Aalto-Setala et al. 2001), reducing the quality of life and productivity and leading to increased disability and health care costs (Vos et al. 2012).

The study of possible risk factors for depression has found an important role of personality traits (Johan Ormel et al. 2001). Specifically, the neurotic trait has been identified as the single most important personality factor associated with many forms of psychopathology, in particular for the common mental disorders, including anxiety, depressive, and substance use disorders (Lahey 2009; Adan et al. 2016). Neuroticism is widely defined as the tendency to experience negative affect, especially when a person is threatened, frustrated or facing loss and it is known to be relatively stable over time (J. Ormel et al. 2013; Barnhofer and Chittka 2010; Costa and McCrae 1980; Harenski et al. 2009).

The largest meta-analyses showed that patients with depressive disorders (MDD, unipolar depression, and dysthymic disorder) had higher levels of neuroticism, in comparison to healthy controls (Kotov et al. 2010; Hakulinen et al. 2015). Neuroticism has been associated with a poorer outcome of depression, increased risk of suicide and extensive use of treatment (Newton-Howes et al. 2014; Hakulinen et al. 2015).

On the other hand, the stress perception hypothesis suggests that the primary driver of perceived stress is neuroticism (Conard and Matthews 2008). In occupational research, the neuroticism-psychological strain relationship has been proposed as mediated by the perceived stress (Ebstrup et al. 2011). Among various stress vulnerability factors, high neuroticism levels are associated with episodic stress and depressive episodes in longitudinal studies (Kendler et al. 2004). The majority of depressive episodes are preceded by stressful life events and severe stressful experiences increase the risk of developing depression (Mohamadi Hasel et al. 2013).

Stress is often described as being associated with anxiety and depression and some studies have suggested that stress, anxiety, and depression are also related to poor quality of life (Diehr et al. 2006; Quilty et al. 2003). Other studies, including meta-analyses, showed that anxiety is more frequent in moderate stress levels and that depression and suicide risk are more associated to high stress levels (Bergdahl and Bergdahl 2002; Versluis et al. 2016). Currently, there is little evidence about the role of perceived stress in the relationship between neuroticism and psychological distress. Only the recent study of Kim et al (S. E. Kim et al. 2016) explored this possible association in a Korean sample, suggesting the importance of studying the interaction between the neuroticism and symptoms of depression in the context of perceived stress. In the study of Kim et al, multiple models were used to examine the mediation roles of personality traits (from the five-factor model) and perceived stress in the link between gender and depressive symptoms, in a large cohort of participants. Their main findings showed that only extraversion and neuroticism were directly and indirectly associated with depressive symptoms

via perceived stress; however, they did not include an internationally standardized measure for perceived stress.

We hypothesized that higher neuroticism may promote maladaptive reactivity to stress, which increases the predisposition to depressive and anxious symptoms. Our hypothesis is based on two aspects: first, on previous findings from the stress sensitivity model that show that neurotic individuals report higher levels of physiological, cognitive and emotional stress even after controlling for stressors (Conard and Matthews 2008; Ebstrup et al. 2011) and second, on previous data that suggest that neuroticism is heritable and relatively stable (Tellegen et al. 1988; Suls and Martin 2005).

Although cross-cultural differences have been reported in studies about stress and personal control (O'Connor and Shimizu 2002) and it has been emphasized the need to publish results of research in behavioral sciences in other populations, extending beyond the habitual western and over-researched populations (Henrich et al. 2010), almost all studies about the risk factors for MDD have been carried out in North America, Europe, and Asia and there is little available evidence about the psychosocial risk factors for depression in Latin American countries. These considerations are important as it has been found that ethnicity influences the somatic presentation of depression (Parker et al. 2001), in addition to other studies that have found specific determinants of depression in Latin American samples (Muñoz et al. 2005; Garcia-Alvarez 1986).

The aim of this study was to examine the possibility that perceived stress is a mediator of the association between depressive and anxious symptoms and neuroticism, in a sample of young Colombian participants.

METHODS

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Participants

Young subjects (N=274) were recruited from two private universities in Bogotá (the capital city of Colombia). Inclusion criteria used were: ages over 18 years, absence of neurological diseases and completion of all the scales. All participants signed a written informed consent and the study was approved by the Institutional Ethics Committee of the Antonio Nariño University.

The age range in the sample was between 18 and 57 years, with a mean of 21.3 (SD=3.8). 24.9% of the participants were men and 75.1% were women. The socioeconomic status of the sample (SES) was defined by the categorization of the different mean socioeconomic strata available for the Colombian cities (ranging from 1=very low to 6=very high), which are characterized by the mean socioeconomic level of the inhabitants. A large fraction of the subjects were from low and medium socioeconomic status (33.5 and 44.5 %, respectively), the education level was mainly secondary (78.8%) and the marital status was principally single (93% of the sample).

Measurements

Assessment of Depressive and Anxiety Symptoms

To assess the presence of depressive and anxious symptoms, we used the Hospital Anxiety and Depression Scale (HADS), the Center for Epidemiologic Studies Depression Scale (CES-D) and the Zung Self-Rating Anxiety Scale (ZSAS) (Zigmond and Snaith 1983; Radloff 1977; Zung 1971).

The HADS (Zigmond and Snaith 1983) is a self-report screening scale that was originally developed to indicate the possible presence of anxiety and depression states in the setting of a

medical non-psychiatric outpatient clinic. It includes 14 Likert items rated on a 4-point scale, the total scores are 0 to 42 and has two sub-factors: Depression (HADS-D) and anxiety (HADS-A), each with 7 items. It has been validated in Spanish by Herrero et al (Herrero et al. 2003) and they recommended the following cut-off points: ≥6 for depression, ≥8 for anxiety and ≥13 for the total test. It has been validated in Colombia (Hinz et al. 2014) and the Cronbach's alphas for the current study were 0.83 for the HADS total score and 0.77 and 0.65 for the anxiety and depression subscales, respectively.

The CES-D (Radloff 1977) has been shown to be useful for identifying individuals with depression in the general population and widely used in primary care settings and epidemiological studies. CES-D is a 20-item self-report scale for measuring the current levels of depressive symptoms trough a Likert scale of 4 points; the total score is 60. It has been validated in Spanish (Vazquez et al. 2007) and in Colombia (Campo-Arias et al. 2007), with a recommended cut-off of ≥20 points for the general population. In our sample, the Cronbach's α for the total CES-D score was 0.89.

The ZSAS (Zung 1971) provides a self-report of symptoms, based on characteristic signs of anxiety. The ZSAS scale is composed of 20 items with 4 possible responses: (1) never, (2) rarely/sometimes, (3) frequently and (4) always, and each item is scored from 1 to 4. This scale provides scores between 20 and 80 points; scores of 50 or more suggest symptoms of anxiety of clinical importance. It has been validated in Spanish (Hernández-Pozo et al. 2008) and in Colombia (De La Ossa et al. 2009). The Cronbach's alpha for the ZSAS was 0.85 in the current study.

Personality assessment

To assess personality dimensions, the Big Five Inventory (BFI-S), 15 items (Lang et al. 2011) was used. It is one of the main models to assess the most important dimensions of personality:

Factor O (Openness), Factor C (Conscientiousness), Factor E (Extraversion), Factor A (Agreeableness) and Factor N (Neuroticism). The short version (15 items) was validated by Lang et al (Lang et al. 2011) and in the BFI–S each one of the five personality factors is measured with 3 items on a 7-point Likert scale: from 1 (strongly disagree) to 7 (strongly agree). The BFI–S is a short instrument designed to measure the Big Five personality factors in large surveys (Rammstedt et al. 2010) and the validity and reliability of the German paper-and-pencil version of the BFI–S proved acceptable (Lang., et al, 2011). The inventory has been widely used in other countries (e.g. the United Kingdom and Spain) (Hakulinen et al. 2015; Chamorro-Premuzic et al. 2009). A similar short version has been used in Spanish, showing acceptable psychometric properties (Renau et al. 2013). The Cronbach's alpha for the current study was 0.73 for factor O, $\alpha = 0.62$ for factor N, $\alpha = 0.61$ for factor E, $\alpha = 0.47$ for factor A and $\alpha = 0.42$ for factor C. In the current study, only sub-scales with Cronbach's alphas higher than 0.60 were included in the final analyses.

Perceived stress assessment

General perceived stress was assessed using a 10-item version of the Cohen's Perceived Stress Scale (PSS) (S. Cohen et al. 1983). The PSS is a 10-item self-report scale that assesses individual's experience of perceived stress over the past month. Higher scores indicate higher levels of stress and scores range from 0 to 40 (Cohen, et al., 1983). It has been validated in Spanish (Remor 2006) and in Colombia (Campo-Arias et al. 2014). In our sample, the Cronbach's α for the total score was 0.85 and a two-factor model was identified: general distress and coping capacity, accounting for 56 percent of variance; it has been found in previous studies (Lee 2012; Wongpakaran and Wongpakaran 2010).

Data Analyses

The sample was stratified into two groups according to the depressive symptoms measured with two scales for screening of MDD: the HADS and the CES-D. The first group (healthy subjects) included 184 subjects, who did not score high in the screening scales, according to the established cut-off points (Mean age: 21.3 years, SD=4.0; Mean scores for HADS, CES-D and SZAS: 11.0, 13.1 and 35.1, respectively). The second group (probable cases) was composed by 90 subjects (Mean age: 21.3 years; SD=3.5; Mean scores for HADS, CES-D and SZAS: 17.4, 29.5 and 45.2, respectively), whom had high scores in the two screening scales. Normal distributions of the scores for the used scales were explored following published recommendations (H. Y. Kim 2013).

To investigate the associations between variables, bivariate correlations analyses were conducted for the total sample and stratified by sex and group. The association of neuroticism perceived stress and depression symptoms was examined using linear regression analyses, controlling for age, gender, and group using a stepwise multiple regression model. In all analyses, neuroticism, perceived stress, sex, age, and group were the independent variables, while depression symptoms were taken as the outcome variable. In all statistical analyses, only the neurotic personality trait was included because of its Cronbach´s alpha above 0.60 and the well-known association of this personality trait with the predisposition for MDD and stress reactivity.

PASW Statistics 18.0.3 software was used for all the statistical analyses. *p* values <0.05 were taken as statistically significant.

Mediation analysis

To know whether the perceived stress played a role as mediator between the relationship of personality neurotic trait with depressive and anxious symptoms, mediation-in-serial models using multiple regressions were carried out, following the procedures recommended by (Hayes

2013). The mediation effect is referred to as the indirect effect of the independent variable (IV) on the outcome variable (DV) through the intervening variables. The mediation effect occurs when the correlation between the IV and DV is eliminated (complete mediation) or reduced (partial mediation) when the mediator is introduced in the analysis (S. E. Kim et al. 2016; Morgan-Lopez and MacKinnon 2006).

Neuroticism was inserted as an independent variable (IV), depressive and anxious symptoms (measured by the HADS and the CES-D scales) were included separately as the outcome variables (DV) and perceived stress was inserted as the mediating variable (MV). Direct effects, indirect effects, and total effects, as well as bias-corrected bootstrapped standard errors (1000=repetitions) and 95% confidence intervals, were calculated using the model 4 of the PROCESS plugin (Hayes 2013) in the PASW Statistics 18.0.3 software. For each model, we showed the relevant unstandardized coefficients: the total effect of the mediation, the effect of the IV on MV, the effect of IV on DV, the effect of MV on DV and the direct and indirect effect of IV on DV; and a path diagram displaying serial mediation for CES-D and ZSAS.

Effect size in mediation analysis was assessed with indirect effects with the maximum possible indirect effect (k^2), which is the proportion of the value of a quantity to the maximum value it could have been. $k^2=0$ implied that there is no linear indirect effect and $k^2=1$ implies that the indirect effect is large (Preacher and Kelley 2011). According to available guidelines (J. Cohen 1992), effect sizes are interpreted as small (0.02), medium (0.15), and large (0.35). Cohen's *d* was calculated as an effect size for multiple and multiple partial correlations.

RESULTS

Correlation analyses

The bivariate correlations were highly significant (p<0.001) for neuroticism and perceived stress compared with depressive and anxiety symptoms in the total sample, in the sample divided by sex and in the sample stratified by group with high and low depressive symptoms (*Table 1*). In the total sample, the depressive and anxiety symptoms were positively correlated with neuroticism and perceived stress. In women, neuroticism showed a higher correlation with depressive symptoms (CES-D and HADS-D, p<0.01) and a slightly higher correlation of anxiety symptoms (ZSAS, p<0.01) with neuroticism was found in men. In addition, higher correlations between perceived stress and depressive symptoms were found in women (**Table 1**). An analysis of the two PSS subscales (general distress and coping capacity), we find similar correlations to the overall scale score.

Multiple regression analyses

The best regression model for depressive symptoms, controlled for sex, showed that the neurotic trait is a significant predictor of depressive symptoms measured with the CES-D ($\beta=$ 0.30, $p=$ 0.004) and HADS-D ($\beta=$ 0.30, $p=$ 0.005), in the group with depressive symptoms (probable cases). For the anxious symptoms, the neuroticism was a significant predictor in both groups, for HADS-A ($\beta=$ 0.50, $p=$ 6.253^{E-7}) and for ZSAS ($\beta=$ 0.27, $p=$ 0.008); however, it was slightly higher in the control group, for HADS-A ($\beta=$ 0.40, $p=$ 8.700^{E-9}) and for ZSAS ($\beta=$ 0.34, $p=$ 2.215^{E-6}).

Perceived stress was a significant predictor of depressive symptoms measured with CES-D ($\beta=$ 0.76, $p=$ 7.523^{E-12}) and with HADS-D ($\beta=$ 0.30, $p=$ 0.005) and it was also was a significant predictor of anxious symptoms measured with HADS-A ($\beta=$ 0.41, $p=$ 7.466^{E-5}) and with ZSAS ($\beta=$ 0.54, $p=$ 4.119^{E-8}), in the group of probable cases. In the group of controls, perceived stress was a significant predictor of depressive and anxious symptoms in a larger degree: HADS-D ($\beta=$ 0.44, $p=$4.465^{E-10}), HADS-A ($\beta=$ 0.50, $p=$ 2.975^{E-13}) and ZSAS ($\beta=$ 0.61, $p=$ 1.410^{E-20}),

except for the depressive symptoms measured with the CES-D (β= 0.54, p=6.431^{E-15}). For anxious symptoms measured with ZSAS, R^2 was similar in both groups, although it was slightly higher in the control group **(Table 2)**.

In the analyses for gender, the neurotic trait was a significant predictor of the depressive and anxious symptoms in larger degree in women (CES-D, β= 0.43, p= 1.053^{E-10} and HADS-A, β= 0.55, p= 5.629^{E-18}) than in men (CES-D, β= 0.35, p= 0.003 and HADS-A, β= 0.40 p= 5.810^{E-4}).

Perceived stress was a better significant predictor of anxious symptoms in men than in women (ZSAS: β= 0.78, p= 2.144^{E-15} and β= 0.66, p= 3.927^{E-28} respectively). The best multiple regression model for neuroticism and perceived stress was found for anxiety symptoms rather than for depressive symptoms (HADS-A: R^2 =0.44, ZSAS: R^2=0.53, p<0.001) **(Table 2)**.

Mediation analysis

For both depression and anxious symptoms, perceived stress was a significant mediator. This mediator effect was evident for depressive symptoms measured with the CES-D (Figure 1) and for anxiety symptoms measured with the ZSAS **(Figure 2)**. For the HADS total score and their subscales this mediation effect was also significant (p<0.001) (HADS: coefficient= 1.19, CI: 0.88-1.60) **(Table S1)**.

Neuroticism affected the depressive symptoms directly (CES-D, coefficient: 3.923, SE: 0.49, p<0.001; HADS-D, coefficient: 0.807, SE: 0.13, p<0.001), as well as indirectly for CES-D (coefficient: 0.942, SE: 0.43, p<0.05), but not for HADS-D (coefficient: 0.207, SE: 0.14, p>0.05) **(Table S1)**.

Similarly, neuroticism affected the anxiety symptoms directly (ZSAS Coefficient: 3.563, p<0.001 and HADS-A, coefficient: 1.496, p<0.001) as well as indirectly, for both scales of anxiety (p<0.001) **(Table S1)**.

We found that the indirect effect was higher for the depressive symptoms (measured with the CES-D) than for the anxiety symptoms (measured with the ZSAS), showing a complete mediation of perceived stress between neuroticism and depressive symptoms (**Table S1 and Figure 1**). For depressive and anxiety symptoms, measured with the HADS total score, we found a partial mediation (direct effect coefficient= 2.30, SE= 0.23, p<0.001 vs indirect effect coefficient= 1.11, SE=0.23, p<0.001). A partial mediation was also found for the anxiety symptoms (**Table S1 and Figure 2**). The effect was of medium size for all variables (Cohen's *d*: CES-D= 0.33; HADS-D=0.23; HADS-A= 0.22; ZSAS=0.32 and HADS= 0.26).

DISCUSSION

Perceived stress has been associated with depression and anxiety symptoms (Hamad et al. 2008; H. J. Kim and Abraham 2016) and neuroticism has been found as a predictor of depression and anxiety (Leach et al. 2008; Goodwin and Gotlib 2004) and being correlated with perceived stress (Roohafza et al. 2016; Abbasi 2016). In our study, we corroborated the presence of these associations which were more evident in women and in subjects with high scores of depressive symptoms.

Only the study of Kim et al, (S. E. Kim et al. 2016) have explored the role of perceived stress as mediating variable in the relationship between neuroticism and depression symptoms. Kim, et al., (2016) reported that neuroticism was a significant mediator, along with stress, on the relationship between gender and depressive symptoms. However, this study did not include an internationally validated scale for the measurement of perceived stress or the analysis of anxiety symptoms. Our results are novel by two main reasons: in our methodology design we included an internationally validated measure of perceived stress (in contrast to the Kim et al paper) and we proposed a mediation model with only one mediator.

Our findings suggest that subjects with high neuroticism levels were more sensitive to the effects of stress and this may increase the susceptibility to depression, as it has been suggested in previous studies (Kendler et al. 2004; Kendler et al. 1995). Most interestingly, our results support a model in which the relationship between neuroticism and depression and anxiety is partially (for anxiety symptoms) or fully (for depressive symptoms) mediated by perceived stress. Our findings add evidence to the hypothesis of the "neurotic cascade": individuals who scored high in neuroticism reported more daily problems, tended to react with more severe emotions, and exhibited stronger reactions to recurring problems; this may result in a greater predisposition to depression and anxiety (Suls and Martin 2005; Griffith et al. 2010).

A strength of our proposed model is the scale used for the measurement of perceived stress, since it includes items that refer directly to negative affective reactions, such as anger and nervousness, and items that reflect a perception of the ability to cope with extant stressors (Hewitt et al. 1992; S. Cohen et al. 1983). This suggests that the construct measured in the current study reflects not only the presence of negative responses to stressors, which are highly associated with neuroticism, but also a perception of the degree of coping ability in relation to existing stressors (Hewitt et al. 1992). Although perceived stress is expected to be strongly associated with (but not identical to) neuroticism, the latter reflects individual differences that are commonly pervasive across different situations, while perceived stress is explicitly linked to the demand from the environment as perceived by the individual (Bovier et al. 2004).

In Latin America, there is scarce evidence about the role of specific psychosocial risk factors for MDD. Some studies have reported high levels of depression, specifically in Colombian university students, confirming some known risk factors (D. Richards and Sanabria 2014; Arrivillaga Quintero et al. 2004; Perea et al. 2012). The relative lack of studies on psychosocial risk factors for depression and anxiety in Latin American subjects makes difficult to understand the etiology of these disorders in these countries. Given the particular characteristics of the

Colombian population, that has been exposed for decades to an internal armed conflict, a high rate of mental disorders in Colombia, included MDD and anxiety disorders has been found (Bromet et al. 2011). This rate of prevalence of common mental disorders in Colombia is higher than those found in countries such as Mexico, Spain, Japan and Nigeria (Demyttenaere et al. 2004).

It is important to highlight that our study is the first of this type performed in a Latin American population, taking into account the high rates of prevalence of affective disorders in the Colombian population (Kessler et al. 2007). This study has two limitations: sample size and a higher proportion of female participants. In future studies, it will be important to include subjects with diagnosis of MDD and anxiety disorders and to carry out an evaluation of possible genetic and epigenetic risk factors (Gonzalez-Giraldo et al. 2015; Hernandez et al. 2014; Galvez et al. 2014). In addition, our finding of higher scores of perceived stress in the group with low levels of depressive symptoms needs further investigation.

The high prevalence of mental disorders in Colombia reinforces the interest and the importance of the current study, where risk factors were assessed with instruments of easy application. A better knowledge of the psychosocial risk factors for mental disorders around the world will facilitate the development of preventive interventions, which could have an impact on reducing the prevalence and impact of common mental disorders in developing countries.

Conflict of interest:

None reported.

Ethical approval:

"All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent: "Informed consent was obtained from all individual participants included in the study."

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Table 1

Pearson's correlation coefficients between psychosocial scales

Group		CES-D	HADS-D	HADS-A	HADS	ZSAS	Neuroticism
Total sample **N=274**	Neuroticism	0.43**	0.33**	0.54**	0.50**	0.45**	
	PSS	0.71**	0.54**	0.59**	0.65**	0.70**	0.49**
Men **N=68**	Neuroticism	0.32**	0.26*	0.40**	0.38**	0.52**	
	PSS	0.61**	0.48**	0.55**	0.59**	0.78**	0.45**
Women **N=206**	Neuroticism	0.41**	0.34**	0.55**	0.52**	0.41**	
	PSS	0.71**	0.55**	0.57**	0.65**	0.66**	0.47**
Healthy subjects **N=184**	Neuroticism	0.19**	0.10	0.42**	0.34**	0.35**	
	PSS	0.51**	0.44**	0.51**	0.58**	0.62**	0.42**
Probable cases **N=90**	Neuroticism	0.31**	0.27**	0.52**	0.48**	0.32**	
	PSS	0.65**	0.26*	0.43**	0.43**	0.57**	0.33**

**p <0.01, *p<0.05.

CES-D: Center for Epidemiologic Studies Depression Scale; HADS-D: the Hospital Anxiety and Depression Scale-Depression subscale; HADS-A: the Hospital Anxiety and Depression Scale-Anxiety subscale; HADS: the Hospital Anxiety and Depression Scale; ZSAS: Zung self-rating Anxiety Scale; PSS: Perceived Stress Scale.

Table 2

Multiple regressions for depressive and anxiety symptoms, perceived stress and neuroticism

Variable	Model 1 DEPRESSIVE SYMPTOMS			Model 2 ANXIETY SYMPTOMS		
	β	SE	R^2	β	SE	R^2
CES-D[a]						
Perceived stress	0.71**	7.6	0.51			
Perceived stress *x* Group[b] *x* Neuroticism	0.48** *x* 0.45** *x* 0.03	6.3	0.66			
HADS-D[a]						
Perceived stress	0.55**	2.4	0.30			
Perceived stress *x* Group[b] *x* Neuroticism	0.37** *x* 0.35** *x* 0.03	2.2	0.40			
HADS-A[a]						
Perceived stress				0.65**	4.1	0.42
Perceived stress *x* Neuroticism				0.49** *x* 0.30**	3.9	0.49
Perceived stress *x* Neuroticism *x* Group[b]				0.41** *x* 0.27** *x* 0.20**	3.7	0.52
ZSAS[a]						
Perceived stress				0.70**	6.7	0.49
Perceived stress *x* Neuroticism				0.60** *x* 0.19**	6.5	0.52
Perceived stress *x* Neuroticism *x* Group[b]				0.55** *x* 0.17** *x* 0.11*	6.4	0.53

**p <0.001; *p<0.05
[a] Outcome variable
[b] Group: Stratification of the total sample in two groups (healthy subjects and possible cases), according to the cut-off points indicative of clinically relevant depressive symptoms.
SE: Standard error
CES-D: Center for Epidemiologic Studies Depression Scale; HADS-D: the Hospital Anxiety and Depression Scale-Depression subscale; HADS-A: the Hospital Anxiety and Depression Scale-Anxiety subscale; HADS: the Hospital Anxiety and Depression Scale total score; ZSAS: Zung self-rating Anxiety Scale.

Fig. 1

Simple mediation model for depression symptoms (measured with CES-D). Note. [a]The effect of independent variable (VI) on mediator variable (MV); [b]The effect of MV on outcome variable VD; [c]The effect of VI on VD; [d]The indirect effect of VI on VD, via VM. The total effect for the mediation model was 2.98 (p<0.001; CI: 2.28-3.83).
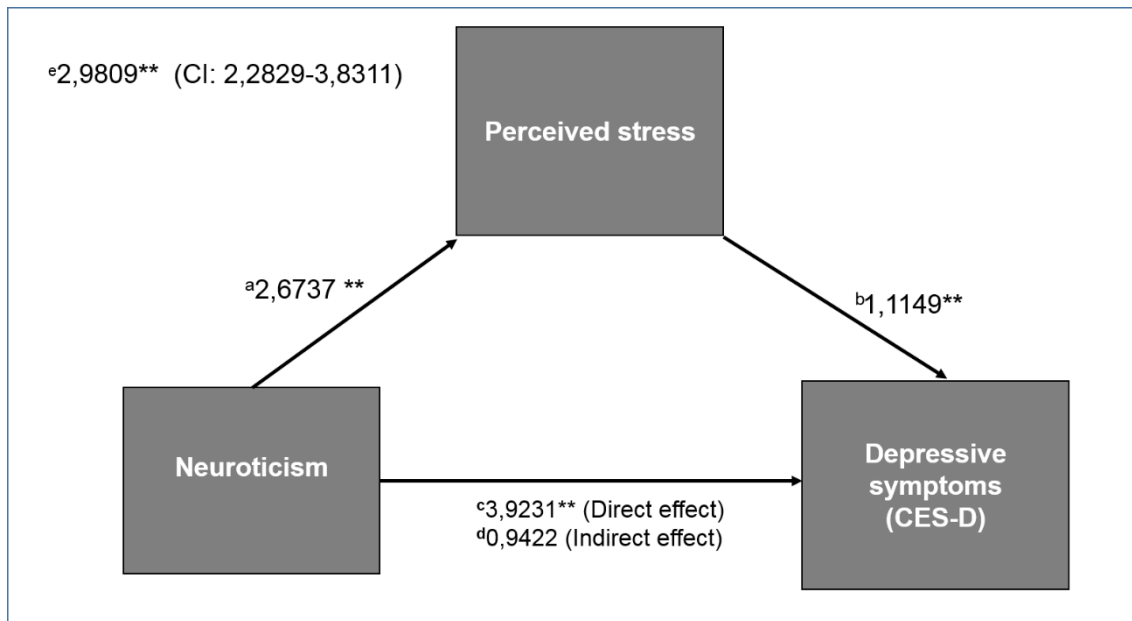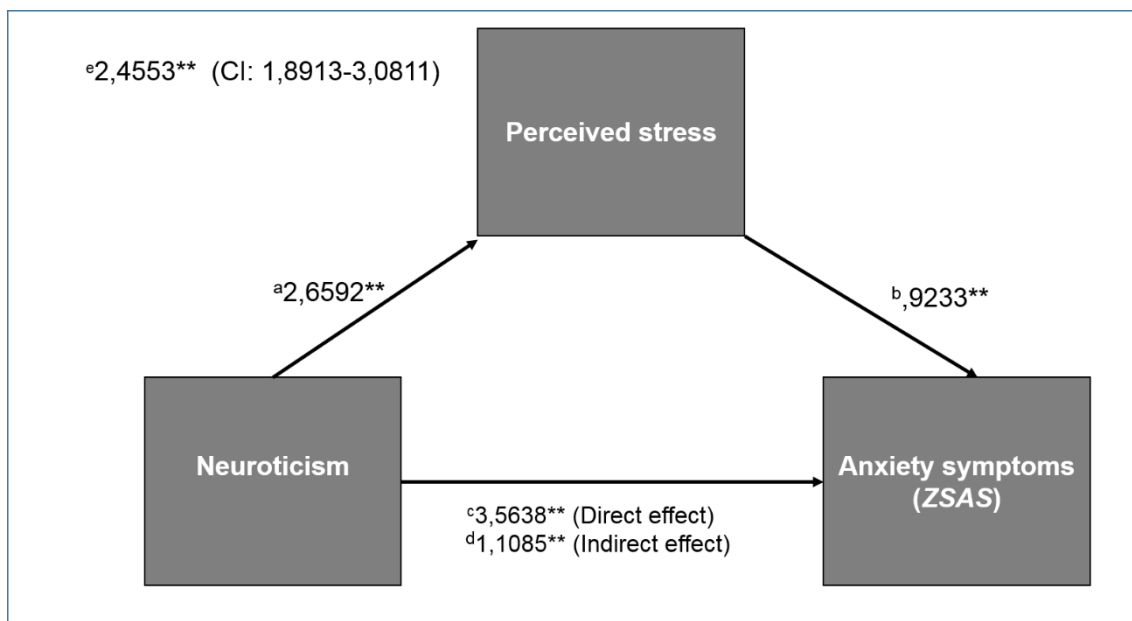
** p<0.001

Fig. 2

Simple mediation model for anxiety symptoms (measured with ZSAS). Note. [a]The effect of independent variable (VI) on mediator variable (MV); [b]The effect of MV on outcome variable VD; [c] The effect of VI on VD; [d] The indirect effect of VI on VD, via VM. The total effect for the mediation model was 2.45 (p<0.001; CI: 1.89-3.08).

** p<0.001

Table S1. Mediation effect for depressive and anxious symptoms

		Unstandardized coefficient	SE	Percentile 95% CI lower- upper	Effect size
Mediation model 1: Depressive symptoms	**Indirect effect via MV[a]**	0.942	0.43	0.077 - 1.807	
	Direct effect[b]	3.923	0.49	2.950 - 4.895	
	Total indirect effect	2.980	0.39	2.282 - 3.831	0.33
	Indirect effect via MV[c]	0.207	0.14	-0.071 - 0.485	
	Direct effect[d]	0.807	0.13	0.536 - 1.079	
	Total indirect effect	0.600	0.10	0.415 - 0.843	0.23
Mediation model 2: Anxiety symptoms	**Indirect effect via MV[e]**	1.108	0.38	0.355 - 1.862	
	Direct effect[f]	3.563	0.42	2.734 - 4.393	
	Total indirect effect	2.455	0.30	1.891 - 3.081	0.32
	Indirect effect via MV[g]	0.906	0.14	0.618 - 1.194	
	Direct effect[h]	1.496	0.14	1.219 - 1.774	
	Total indirect effect	0.590	0.11	0.385 - 0.835	0.22

MV= mediator vatiable (Perceived stress with PSS).

a: The indirect effect the Neuroticism via perceived stress on depressive symptoms measured with CES-D

b: The direct effect the Neuroticism on depressive symptoms measured with CES-D

c: The indirect effect the Neuroticism on depressive symptoms measured with HADS-D

d: The direct effect the Neuroticism on depressive symptoms measured with HADS-D

e: The indirect effect the Neuroticism via perceived stress on anxiety symptoms measured with ZSAS

f: The direct effect the Neuroticism on anxiety symptoms measured with ZSAS

g: : The indirect effect the Neuroticism via perceived stress on anxiety symptoms measured with HADS-A

h: The direct effect the Neuroticism on anxiety symptoms measured with HADS-A