



## The predictive specificity of psychological vulnerability markers for the course of affective disorders

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### ABSTRACT

High scores on markers of psychological vulnerability have been associated with a worse course of affective disorders. However, little is known about the specificity of those associations in predicting the course of different depressive and anxiety disorders. We examined the impact of psychological vulnerability on the short- and long-term course of depressive and anxiety disorders. Participants from the Netherlands Study of Depression and Anxiety with a current diagnosis of depression or anxiety ( $n = 1256$ ) were reassessed after 2 and 6 years. Diagnostic status and chronic duration ( $> 85\%$  of the time) of symptoms were the outcomes. Predictors were neuroticism, extraversion, locus of control, cognitive reactivity (rumination and hopelessness reactivity), worry and anxiety sensitivity. High neuroticism, low extraversion and external locus of control predicted chronicity of various affective disorders. Rumination, however, predicted chronicity of depressive but not anxiety disorders. Worry specifically predicted chronicity of GAD and anxiety sensitivity predicted chronicity of panic disorder and social anxiety disorder. These patterns were present both at short-term and at long-term, without losing predictive accuracy. Psychological vulnerabilities that are theoretically specific to certain disorders indeed selectively predict the course of these disorders. General markers of vulnerability predicted the course of multiple affective disorders. This pattern of results supports the notion of specific as well as transdiagnostic predictors of the course of affective disorders and is consistent with hierarchical models of psychopathology.

### 1. Introduction

Psychological vulnerabilities are thought to play a role in the development of affective disorders (Hong, 2013; Hong and Cheung, 2015; Mathews and MacLeod, 2005). Some of these constructs are conceptualized as ‘general dispositions’ (Lahey et al., 2012; Starr et al., 2014), others as ‘specific cognitive vulnerabilities’ (Mathews and MacLeod, 2005). This idea fits nicely into hierarchical models of psychopathology, in which processes that are common to various diagnostic categories (i.e. transdiagnostic factors) are distinguished, as well as unique processes (Barlow, 2000; Clark and Watson, 1991; Kotov et al., 2017; Mineka et al., 1998). For example, in accordance with the tripartite model of anxiety and depression (Clark and Watson, 1991), these risk factors can be associated with either common or distinct components of anxiety and depression. General dispositions include a propensity to experience negative emotions (high neuroticism), a tendency to behave in a reserved and solitary fashion (low extraversion

(Kotov et al., 2010); and a low degree of perceived control in stressful situations (Chorpita and Barlow, 1998). Specific cognitive vulnerabilities for depression include a hopeless inferential style (Abramson et al., 1989) and a ruminative response style (Nolen-Hoeksema et al., 2008). Specific cognitive vulnerabilities for anxiety include danger expectancy leading to worry (Borkovec et al., 1983) and catastrophic misinterpretations of arousal (Reiss, 1991).

In line with this, prior cross-sectional research showed positive associations between several markers of general psychological vulnerabilities with both depression and anxiety such as high neuroticism and low extraversion (Kotov et al., 2010) and an external locus of control (Beekman et al., 1998; de Graaf et al., 2002; Hoehn-Saric and McLeod, 1985; Wiersma et al., 2011). Whereas markers of specific cognitive vulnerabilities are more strongly associated with either depression or anxiety, such as hopelessness and rumination (Aldao et al., 2010; Drost et al., 2012; Elgersma et al., 2015; Hendriks et al., 2014; Wiersma et al., 2011), worry (Drost et al., 2012; Feldman and Hayes, 2005; Hendriks

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et al., 2014; Muris et al., 2004; Olatunji et al., 2010; Segerstrom et al., 2000) and anxiety sensitivity (Drost et al., 2012; Hendriks et al., 2014; Olatunji and Wolitzky-Taylor, 2009). Multiple meta analyses indicate that these associations are robust (Aldao et al., 2010; Kotov et al., 2010; Olatunji and Wolitzky-Taylor, 2009; Olatunji et al., 2010). Longitudinal studies provided further evidence that these risk factors are involved in the onset and relapse of affective psychopathology (Acarturk et al., 2009; Batelaan et al., 2010; Calmes and Roberts, 2007; Drost et al., 2014; Ernst et al., 1992; Kopala-Sibley et al., 2016, 2017; Kruijt et al., 2013; Scholten et al., 2013; Segerstrom et al., 2000; Spinhoven et al., 2015a,b, 2016a,b; Spinhoven et al., 2015b; Spinhoven et al., 2016b; Struijs et al., 2013).

Fewer studies have looked at the associations of these risk factors with the chronicity of affective disorders. It was found that high neuroticism and low extraversion at baseline are associated with an increased risk of chronicity 2 years later in a sample of 1209 diagnosed depressed or and/or anxious participants (Spinhoven et al., 2011, 2013). External locus of control was associated with a lower likelihood of remission of affective disorders within 4 years in 1474 participants with a baseline diagnosis of a depressive or anxiety disorder (Hovens et al., 2016). Rumination and worry at baseline were associated with an increased risk of still being depressed 4 years later in a sample of 535 depressed participants (Spinhoven et al., 2016a). Anxiety sensitivity predicted percentage of time in panic disorder episode over a 1-year period in 136 participants with panic disorder (Benitez et al., 2009). Anxiety sensitivity also predicted chronicity of anxiety disorders over a 4-year period in 603 anxious participants (Spinhoven et al., 2017). A few studies exist that did not find an association between markers of psychological vulnerability and an unfavorable course of affective disorders (Boschloo et al., 2014; Lara et al., 2000; Rosellini et al., 2011; Wardenaar et al., 2015). However, these studies are heterogeneous in their predicting variables of psychological vulnerability, as well as in their outcome variables (symptoms, subtypes or disorders) and the duration of these outcomes.

A limitation of the studies that looked at the associations of risk factors with the chronicity of affective disorders is that they often focus on a single predictor and a single outcome variable. This is problematic, because comorbidity of depression and anxiety is the rule rather than the exception (Lamers et al., 2011; Penninx, 2015). Furthermore, psychological vulnerability markers of affective disorders are conceptually similar and highly correlated. Another limitation is that these studies often employ a relatively short follow-up period, while the examined associations may very well change over time.

The aim of the present study was to examine the predictive specificity of markers of psychological vulnerability for the course of depression and anxiety disorders. Based on theory, we expect that an external locus of control, high neuroticism and low extraversion will be associated with an unfavorable course of both depression and anxiety. Furthermore, we expect that hopelessness and rumination are specifically related to the course of depression, and that worry and anxiety sensitivity are specifically related to the course of anxiety disorders. We also explored the effect of psychological vulnerability on the course of affective disorders on a relatively short (2 year) and longer (6 year) term.

## 2. Methods

### 2.1. Sample

Data were derived from the baseline, 2-year and 6-year follow-up assessments of The Netherlands Study of Depression and Anxiety (NESDA), an ongoing longitudinal cohort study of the long term course and consequences of depression and anxiety. Participants were recruited from three different settings: the community, primary care and mental health care. Inclusion and exclusion criteria were: age 18 through 65; current (past six months) diagnosis of depressive or anxiety

disorder; proficiency in the Dutch language; no diagnosis of a psychotic disorder, obsessive compulsive disorder, bipolar disorder or severe addiction disorder. The study protocol was approved by the ethical review board of each participating centre. All participants signed written informed consent before participating in the study. The assessments were conducted from September 2004 until February 2013. A detailed description of the NESDA design and sampling procedure is provided elsewhere (Penninx et al., 2008). Baseline data were used as predictor variables and covariates; 2-year and 6-year follow-up data were used as outcome variables.

The baseline assessment (T0) was completed by 2981 participants, of whom 2596 (87%) completed T2 and 2256 (76%) completed T6. DSM-IV depressive [(Major Depressive Disorder (MDD) and dysthymia (DYS)] and anxiety disorders [(Panic Disorder (PD), Social Anxiety Disorder (SAD), Generalized Anxiety Disorder (GAD)] were assessed by means of the Composite International Diagnostic Interview (Wittchen, 1994). For the present study, participants were selected who had a current depressive and/or anxiety disorder at baseline, a valid outcome on the diagnostic interview at T2 or T6 and complete baseline data on all measures of psychological vulnerability. At baseline, 1701 participants were diagnosed with a 6-month recency depressive and/or anxiety disorder. Of those participants, 1419 completed the T2 assessment of whom 1256 had complete data on vulnerability variables. A total of 1187 participants completed the T6 assessment of whom 1059 had complete data on predicting variables.

### 2.2. Measures

#### 2.2.1. Course of psychopathology

Chronicity of diagnosis was defined as the existence of a 6-month recency DSM-IV diagnosis at T2 or T6. The duration of the core symptoms of depressive and anxiety disorders was measured via the Life Chart Interview (LCI): a calendar-based instrument that measured the number of months with symptoms between assessment points (Lyketsos et al., 1994) expressed as percentage of time with symptoms. Chronicity of symptoms was defined as the existence of a 6-month recency diagnosis at T2 or T6 plus at least 85% of time with symptoms between assessment periods. Two outcomes were created this way: chronicity of symptoms of depression (any depressive disorder plus chronic symptoms of depression) and chronicity of symptoms of anxiety (any anxiety disorder plus chronic symptoms of either arousal or avoidance). These variables could be calculated in 1245 participants with complete data at T2 and in 984 participants at T6.

#### 2.2.2. Constructs of psychological vulnerability

We used the subscales Neuroticism (NE) and Extraversion (EX) of the Dutch NEO five-factor inventory (Hoekstra et al., 1996). Both subscales contain twelve equally weighted items rated on a five-point scale (e.g. 'I often feel tense and jittery' (NE) or 'I don't consider myself especially light-hearted' (EX)). High NE indicates a propensity to experience negative emotions and low EX indicates a tendency to behave in a reserved and solitary fashion. The internal consistencies of the subscales in the present sample were good;  $\alpha = 0.82$  (NE) and  $\alpha = 0.80$  (EX).

The Mastery Scale (Pearlin and Schooler, 1978) was used to measure locus of control (LOC), i.e., the degree to which individuals believe that they have control over outcomes in their lives. This is a self-report questionnaire containing five equally weighted items rated on a five-point scale (e.g. 'I have little control over the things that happen to me'). The sum score indicates LOC, with lower scores indicating stronger personal control. Internal consistency was good ( $\alpha = 0.83$ ).

Rumination and hopelessness were assessed using the Rumination on Sadness and Hopelessness Reactivity subscales of the Leiden Index of Depression Sensitivity-Revised (LEIDS-R; Solis et al., 2017; Van der Does, 2002). The LEIDS-RUM and LEIDS-HOP subscales contain 6 and 5 equally weighted items rated on a five-point scale, respectively (e.g.

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