



Longitudinal associations of multiple physical symptoms with recurrence of depressive and anxiety disorders

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ABSTRACT

Objective: To examine longitudinal associations of multiple physical symptoms with recurrence of depressive and anxiety disorders.

Methods: Follow-up data of 584 participants with remitted depressive or anxiety disorders were used from the Netherlands Study of Depressive and Anxiety disorders. Multiple physical symptoms were measured at baseline (T1) and two-year follow-up (T2) by the Four-Dimensional Symptom Questionnaire (4DSQ) somatization subscale. Recurrence of depressive and anxiety disorders was assessed at two-year (T2) and four-year (T4) follow-up with the Composite International Diagnostic Interview. Logistic Generalized Estimating Equations were used to examine associations of multiple physical symptoms with recurrence of depressive and anxiety disorders. Depressive (IDS-SR) and anxiety symptoms (BAI), and other relevant covariates were taken into account.

Results: Multiple physical symptoms were significantly associated with recurrence of depression (OR = 1.04, 95%CI = 1.00–1.08), anxiety (OR = 1.07, 95%CI = 1.03–1.12), and depressive or anxiety disorders (OR = 1.06, 95%CI = 1.02–1.10), on average over time. Odds ratios did not change substantially when the IDS-SR mood-cognition and BAI subjective scale were included as covariates.

Conclusion: The presence of multiple physical symptoms was positively related to recurrence of depressive and anxiety disorders, independent of depressive and anxiety symptoms. Knowledge of risk factors for recurrence of depressive and anxiety disorders, such as the presence of multiple physical symptoms, could provide possibilities for better targeting interventions to prevent recurrence.

1. Introduction

Depressive and anxiety disorders are a leading cause of disease burden, mainly due to their recurrent nature [1–3]. The National Institute of Mental Health Collaborative Depression Study, reported recurrence rates of depression of 25–40% after two years and up to 85% after fifteen years [4,5]. Strategies to reduce the burden of depressive and anxiety disorders should not only focus on treatment of acute episodes but also on prevention of recurrence [6]. Knowledge of risk factors for recurrence of depressive and anxiety disorders could provide

a rationale for such preventive interventions or long-term treatment and allow possibilities for better targeting care [7].

Hardeveld et al. [8] found two main predictors of recurrence of depressive disorders in their systematic review: the number of previous depressive episodes and subclinical residual depressive symptoms after recovery from the last episode. However, they concluded that knowledge of predictors of recurrence of depressive disorders is still incomplete. They recommended more prospective research, particularly in the general population, to gain conclusive knowledge of predictors of recurrence of depressive disorders.

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Putative predictors of recurrence of depressive and anxiety disorders can be identified by looking at predictors of depressive and anxiety disorders in general. One of the factors related to co-occurrence, onset and course of depressive and anxiety disorders is the presence of multiple physical symptoms [9–14]. Despite these relationships, it is poorly understood how multiple physical symptoms impact the recurrence of depressive and anxiety disorders in remitted patients. A small study [15] concluded that a sustained high number of (medically unexplained) physical symptoms was predictive of subsequent recurrence in remitted, recurrently depressed patients. However, so far, little research has been performed on this association.

This study, therefore, examined the longitudinal association of multiple physical symptoms with recurrence of depressive and anxiety disorders in a prospective cohort study. Furthermore, as symptoms of depression and anxiety are a main predictor of recurrence of depressive and anxiety disorders, we took residual depressive and anxiety symptoms into account and examined whether excluding somatic features of residual depressive and anxiety symptoms altered our results.

2. Methods

2.1. Design

This study used four-year prospective data from the Netherlands Study of Depressive and Anxiety Disorders (NESDA) [16]. NESDA is an ongoing cohort study that aims to investigate the etiology, course and consequences of depressive and anxiety disorders. At baseline (2004–2007) 2981 participants aged 18 through 65 years were included, consisting of healthy controls; persons with a prior history of a depressive or anxiety disorder; persons with a high risk because of a family history or subthreshold depressive or anxiety symptoms; and persons with a current depressive or anxiety disorders. Participants were recruited in three settings: the community ($n = 564$), primary care ($n = 1610$), and mental health services ($n = 807$). Exclusion criteria were a primary diagnosis of obsessive compulsive disorder, bipolar disorder or severe addiction disorder, and not being fluent in Dutch. Assessments consisted of a diagnostic psychiatric interview, questionnaires, and a medical assessment. For the current analyses, we used the assessments at baseline (T0), two-year follow-up (T2), and four-year follow-up (T4). All participants provided written informed consent and the research protocol was approved by the ethical review boards of participating universities. The design and sampling procedure of NESDA have been described in more detail [16].

2.2. Study population

Participants who had a depressive (major depressive disorder or dysthymia) or anxiety (panic disorder, social phobia, generalized anxiety disorder or agoraphobia) episode in the past but were in remission at T0 for at least six months were selected for our study ($n = 628$). Current and lifetime depressive and anxiety disorders were examined using the DSM-IV based Composite International Diagnostic Interview (CIDI, version 2.1) [17].

Participants who did not participate in any of the follow-up measurements were excluded from analyses ($n = 40$). Additionally, participants without data on the main determinant (multiple physical symptoms) on any of the assessments were excluded ($n = 4$). This resulted in a study sample of 584 participants. Non-respondents ($n = 44$) were more often males (54.5%), compared to the study sample (28.9%, $p = 0.02$). No significant differences were found for any of the other study sample characteristics.

2.3. Measures

2.3.1. Recurrence of depressive and anxiety disorders

We defined recurrence of depressive and anxiety disorders as the

occurrence of a new depressive or anxiety disorder episode between T0 and T2, and between T2 and T4, respectively, according to CIDI diagnostic criteria.

2.3.2. Multiple physical symptoms

The presence of multiple physical symptoms was assessed at T0 and T2 by the somatization subscale of the Four-Dimensional Symptom Questionnaire [18,19]. Somatization is defined as “the tendency to experience and communicate somatic distress and symptoms unaccounted for by pathological findings, to attribute them to physical illness, and to seek medical help for them” [20]. The 4DSQ somatization subscale operationalizes somatization as a high number and frequency of physical symptoms and does not establish whether physical symptoms are medically unexplained or whether participants sought help for these symptoms. Therefore, in this study we used the 4DSQ somatization subscale to assess multiple physical symptoms, regardless of their being presented to a doctor or being explained.

The 16 items of the 4DSQ correspond to symptoms participants may have had in the past week (e.g. ‘during the past week did you suffer from dizziness; painful muscles; headache?’) and are scored on a five-point Likert scale (‘no’, ‘sometimes’, ‘regularly’, ‘often’, and ‘very often or constantly’). Item scores were recoded into a 3-point scale (‘no’, ‘sometimes’, and ‘regularly’ to ‘very often or constantly’) and summed to obtain a total score (0–32). An overall score of 11 or higher is indicative of an elevated level of somatization and risk of impaired functioning [18]. The 4DSQ somatization subscale has been validated against various measures (e.g. SCL-90 somatization subscale and GP’s diagnoses) in a variety of samples, including psychiatric, occupational, and primary care samples [18,21].

2.3.3. Covariates

2.3.3.1. Demographic characteristic. Age, gender and number of years of education were assessed at T0 by self-report questionnaires.

2.3.3.2. Chronic somatic diseases. Chronic somatic diseases may be related to the reporting of physical symptoms and the occurrence of depressive and anxiety disorders. Therefore, we took the number of chronic somatic diseases into account in our analyses. At T0, participants were asked whether they suffered from any of the chronic somatic diseases mentioned in the interview and whether they received medication or treatment for these diseases. The following diseases were surveyed: lung disease, heart diseases or infarction, diabetes, stroke, osteoarthritis, cancer, ulcer, intestinal disorders, liver disease, epilepsy and thyroid gland disease. Answers were categorized as ‘no chronic somatic disease’, ‘one chronic somatic disease’ or ‘two or more chronic somatic disease’.

2.3.3.3. Psychosocial characteristics. As several studies have indicated that neuroticism, mastery and childhood trauma may be associated with the presence of multiple physical symptoms as well as with (recurrence of) depressive and anxiety disorders, these variables were taken into account as covariates [7,8,22–24].

Neuroticism was measured by the Neuroticism domain of the NEO-FFI [25]. This domain consists of 12 items (e.g. “I am not a worrier”), which are scored on a five-point Likert scale. Item scores were summed to obtain a total score, ranging from 12 to 60.

Mastery, the extent to which a person perceives himself to be in control of events or ongoing situations, was measured by the Pearlin Mastery scale [26]. Participants rated their agreement with five statements on a five-point Likert scale. A sum score was calculated (5–25), with a higher score indicating more feelings of mastery.

Childhood trauma was assessed retrospectively at T0 by the Nemes Childhood Trauma Interview [27,28]. In this interview, questions were asked about the frequency of emotional neglect, psychological abuse, physical abuse, and sexual abuse before the age of 16. First, answers were recoded into three categories for each question (0 = never;

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