Journal of Affective Disorders 205 (2016) 112–118

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

The impact of somatic symptoms on the course of major depressive disorder

Ella Bekhuis *, Lynn Boschloo, Judith G.M. Rosmalen, Marrit K. de Boer, Robert A. Schoevers

University of Groningen, University Medical Center Groningen, Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion Regulation (ICPE), Groningen, The Netherlands

ARTICLE INFO

Article history:
Received 1 March 2016
Received in revised form
10 June 2016
Accepted 11 June 2016
Available online 14 June 2016

Keywords:
Depressive disorder
Somatic symptoms
Course
Psychiatric characteristics
Somatic characteristics
Disability

ABSTRACT

Objective: Somatic symptoms have been suggested to negatively affect the course of major depressive disorder (MDD). Mechanisms behind this association, however, remain elusive. This study examines the impact of somatic symptoms on MDD prognosis and aims to determine whether this effect can be explained by psychiatric characteristics, somatic diseases, lifestyle factors, and disability.

Methods: In 463 MDD patients (mean age=44.9 years, 69.8% female) from the Netherlands Study of Depression and Anxiety (NESDA), we examined whether the type and number of somatic symptom clusters predicted the two-year persistence of MDD. Diagnoses of MDD were established with the Composite International Diagnostic Interview (CIDI) and somatic symptom clusters were assessed with the Four-Dimensional Symptom Questionnaire (4DSQ) somatization scale. Psychiatric characteristics, somatic diseases, lifestyle factors, and disability were taken into account as factors potentially underlying the association.

Results: The cardiopulmonary, gastrointestinal, and general cluster significantly predicted the two-year persistence of MDD, but only when two or more of these clusters were present (OR=2.32, 95% CI=1.51–3.57, p=<0.001). Although the association was partly explained by MDD severity, the presence of multiple somatic symptom clusters remained a significant predictor after considering all potentially underlying factors (OR=1.69, 95%CI=1.07–2.68, p=0.03).

Conclusions: Somatic symptoms are predictors of a worse prognosis of MDD independent of psychiatric characteristics, somatic diseases, lifestyle factors, and disability. These results stress the importance of considering somatic symptoms in the diagnostic and treatment trajectory of patients with MDD. Future research should focus on identifying treatment modalities targeting depressive as well as somatic symptoms.

1. Introduction

Major depressive disorder (MDD) is highly prevalent in the general population (Hasin et al., 2005; Kessler et al., 2005) and has a substantial impact on physical, occupational, and social functioning (Judd et al., 2000; Wittchen et al., 2011). The course of MDD varies widely across individual patients. Although the majority of patients achieve remission within the six months following disorder onset, 20% of patients develop a chronic disorder that lasts for two years or longer (Satyanarayana et al., 2009; Spijker et al., 2002). It is important to identify the factors that predict such an unfavorable course as more insight into their effects is essential for optimizing treatment strategies.

Somatic symptoms are often reported by patients with MDD (Bekhuis et al., 2015; Simon et al., 1999). Kroenke et al., for example, showed that patients with the mental disorder experienced an average of six somatic symptoms during the past month (Kroenke et al., 1997). Several studies have shown that somatic symptoms are associated with a poor prognosis of MDD (Gerrits et al., 2012; Novick et al., 2013; Stegenga et al., 2012). A study among patients with incident MDD, for example, demonstrated that remission rates were twice as low in patients with severe somatic symptoms as in patients without those symptoms (Novick et al., 2013). In addition, a primary care study showed that somatic symptoms were related to chronicity of MDD (Stegenga et al., 2012). Despite extensive research on the association between somatic symptoms and outcome of MDD, however, little is known about the specificity of this association. Somatic symptoms are, for example, a heterogeneous group of symptoms and specific symptoms may, therefore, show differential associations with the course of MDD (Kroenke and Price, 1993). Similarly, as somatic symptoms often co-occur (Kroenke et al., 1994), their association

* Corresponding author.
E-mail address: e.bekhuis@umcg.nl (E. Bekhuis).

http://dx.doi.org/10.1016/j.jad.2016.06.030
0165-0327/

with the course of MDD could be conditional on the number of these symptoms. More insight into the specific characteristics of somatic symptoms that affect the course of MDD may contribute to better recognition of MDD patients at risk for a worse prognosis.

In addition, although the physical inconvenience of somatic symptoms may directly maintain feelings of depression, other mechanisms have also been hypothesized to underlie the association of these symptoms with the course of MDD. For example, somatic symptoms are associated with specific *psychiatric characteristics* such as more severe depressive symptoms and comorbid mental disorders (Gerrits et al., 2012; Haug et al., 2004), which are also well-known predictors of a poor course of MDD (Penninx et al., 2011). Similarly, depressed patients with somatic symptoms receive less optimal psychiatric treatment than patients without those symptoms (Huijbregts et al., 2010), and this could also worsen the course of MDD (Akerblad et al., 2006). Somatic diseases have also been shown to be associated with MDD prognosis (Wells et al., 1993) and have, therefore, been suggested to underlie somatic symptoms that affect the course of MDD. Furthermore, an unhealthy lifestyle (e.g., heavy alcohol use and lack of physical activity) could cause and/or result from somatic symptoms (Janssens et al., 2014), and these factors are also predictors of an unfavorable course of MDD (Boschloo et al., 2014). Finally, researchers have hypothesized that *disability* resulting from somatic symptoms may affect the course of MDD (Gerrits et al., 2012). To our knowledge, no previous study has simultaneously considered such a wide range of factors (i.e., psychiatric characteristics, somatic diseases, lifestyle factors, and disability) and has examined whether they explain the effect of somatic symptoms on MDD prognosis.

In this study, we aim to examine the impact of specific types and numbers of somatic symptoms on the two-year course of MDD in a large sample of MDD patients (N=463). Second, we investigate potential mechanisms underlying this association by focusing on psychiatric characteristics, somatic diseases, lifestyle factors, and disability.

2. Methods

2.1. Study sample

Data were derived from the Netherlands Study of Depression and Anxiety (NESDA), a large scale longitudinal cohort study aimed at studying the long-term course of depressive and anxiety disorders. A total of 2981 adults (18–65 years) were initially included, consisting of a healthy control group, people with a history of depressive or anxiety disorder and people with a current depressive and/or anxiety disorder. Participants were recruited from community (19%), primary care (54%) and outpatient mental health care services (27%) to represent various settings and stages of psychopathology. Community-based participants had previously been identified in a population-based study, and primary care participants were selected from a random sample of consulting patients of 65 general practitioners through a three-stage screening procedure (involving the Kessler 10 scale (Kessler 10 scale; Kessler et al., 2002; as screening questionnaire and the short-form Composite International Diagnostic Interview [CIDI] as phone-screen interview). Mental health care participants were recruited when newly enrolled at one of the 17 participating mental health organization locations. Patients were excluded when they had insufficient command of the Dutch language or a primary clinical diagnosis of bipolar disorder, obsessive compulsive disorder, severe substance use disorder, psychotic disorder, or organic psychiatric disorder. The research protocol was approved by the Ethical Committee of the three participating universities and all participants gave written informed consent. A detailed account of the rationale, objectives, and methods of NESDA can be found elsewhere (Penninx et al., 2008). Interviews took place in 2004–2007 (first interview), two years later (second interview; response N=2596 [87.1%]; Lamers et al., 2012), and four years later (third interview; response N=2402 [80.6%]), and included a face-to-face assessment as well as paper-and-pencil questionnaires.

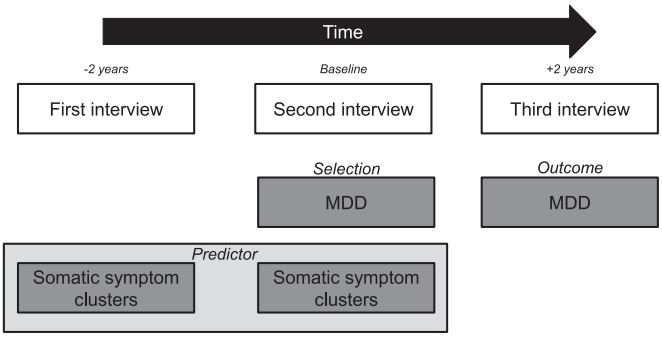

Fig. 1. Study design.

For the current study, we selected all participants with a diagnosis of MDD in the six months prior to the second interview with valid data on somatic symptoms (N=526; see Fig. 1 for a schematic representation of the study design). Compared to non-selected participants, the selected participants received education for a shorter time period (12.6 versus 11.9 years, $p < 0.001$), but no differences were found with respect to sex (65.4% versus 68.8% female, $p=0.15$) or age (43.8 versus 44.9 years, $p=0.09$). Of all selected persons, those with incomplete data on MDD at the follow-up assessment were excluded from the analyses (N=63 [12.0%]). Excluded persons received less education (10.5 versus 12.1 years, $p < 0.001$) than persons with complete data; however, age (44.4 versus 44.9 years, $p=0.74$), sex (61.9% versus 69.8% female, $p=0.25$), and the number of somatic symptom clusters (1.8 versus 1.5, $p=0.06$) were not associated with non-response.

2.2. The two-year persistence of MDD

Diagnoses of MDD were established with the CIDI (version 2.1; Wittchen et al., 1991) according to the DSM-IV criteria (American Psychiatric Association, 1994), administered by especially trained research staff. The CIDI has shown high interrater and test-retest reliability and high validity (Wittchen et al., 1991). MDD was considered persistent when a person also met the DSM-IV criteria for MDD in the six months before the third interview (i.e., after two years).

2.3. Somatic symptom clusters

The self-report somatization scale of the Four-Dimensional Symptom Questionnaire (4DSQ; Terluin et al., 2006) was used to score the frequency of 16 somatic symptoms (scoring 1='never' to 5='often') in the past week. In line with a previous study by our group (Bekhuis et al., 2015), four clusters of somatic symptoms were distinguished: cardiopulmonary symptoms (i.e., excessive perspiration, pain in chest, palpitations, pressure or tight feeling in chest, and shortness of breath), musculoskeletal symptoms (i.e., back pain, neck pain, muscle pain, and tingling in fingers), gastrointestinal symptoms (i.e., bloated feeling in abdomen, nausea or upset stomach, and pain in abdomen or stomach area), and general symptoms (i.e., dizziness or feeling lightheaded, fainting, and headache). A cluster was considered present when at least one of the symptoms included in that cluster was scored with 3 ('regularly') to 5 ('often') (see also Bekhuis et al., 2015). A weakness of