PAIN® 155 (2014) 53–59

PAIN®

www.elsevier.com/locate/pain

Pain and the onset of depressive and anxiety disorders

Marloes M.J.G. Gerrits [a,b,*], Patricia van Oppen [a,b], Harm W.J. van Marwijk [b], Brenda W.J.H. Penninx [a,c,d], Henriëtte E. van der Horst [b]

[a] Department of Psychiatry, EMGO Institute for Health and Care Research, VU University Medical Center and Academic Outpatient Clinic for Affective Disorders, GGZ inGeest, Amsterdam, The Netherlands
[b] Department of General Practice and Elderly Care Medicine, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands
[c] Department of Psychiatry, Leiden University Medical Center, The Netherlands
[d] Department of Psychiatry, University Medical Center Groningen, The Netherlands

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 25 April 2013
Received in revised form 23 August 2013
Accepted 3 September 2013

Keywords:
Anxiety disorder
Depressive disorder
Incidence
Pain
Self-report

ABSTRACT

Patients with pain may be at increased risk of developing a first episode of depressive or anxiety disorder. Insight into possible associations between specific pain characteristics and such a development could help clinicians to improve prevention and treatment strategies. The objectives of this study were to examine the impact of pain symptomatology on depression and anxiety onset and to determine whether these associations are independent of subthreshold depressive and anxiety symptoms. Data from the Netherlands Study of Depression and Anxiety, collected between 2004 and 2011, were used. A total of 614 participants with no previous history and no current depression or anxiety at baseline were followed up for 4 years. Onset of depressive or anxiety disorder was assessed at 2- and 4-year follow-up by Composite International Diagnostic Interview. Baseline pain characteristics were location, duration, and severity, as assessed by chronic pain grade. Onset of depressive or anxiety disorder occurred in 15.5% of participants. Using Cox survival analyses, onset of depression and anxiety was associated with 6 pain locations (neck, back, head, orofacial area, abdomen, and joints; hazard ratio [HR] = 1.96 to 4.02; $P < .05$), increasing number of pain locations (HR = 1.29; $P < .001$), and higher severity of pain (HR = 1.57; $P < .001$). By contrast, there was no association with duration of pain symptoms (HR = 1.47; $P = .12$). Independent of subthreshold affective symptoms, only joint pain and increasing number of pain locations were still significantly associated with depression and anxiety onset. Clinicians should be aware that regardless of affective symptoms, pain, particularly at multiple locations, is a risk indicator for developing depressive and anxiety disorders.

1. Introduction

Pain is usually defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [43]. Pain is associated with functional impairment, (social) disability [44], pain-related anxiety, and even anxiety sensitivity, the tendency to catastrophically misinterpret anxiety sensations [38], which have all been linked to an increased development of depressive as well as anxiety disorders [12]. Data from epidemiological studies also suggest that pain could be a risk indicator for depressive and anxiety disorder onset [5,18,24], but we know little about the specifics of such a relationship. The emotional, economic, and societal burden of pain and depressive and anxiety disorders, separately and conjointly, is high [6,8,21,54]. An estimate of the contribution of pain to the onset of depressive and anxiety disorders could support the development of new management strategies in clinical practice.

There are several methodological issues that hamper a sound estimation of this relationship. Firstly, most current studies are based on the onset of depressive or anxiety symptoms [4,13,22,24,33,34], but not all individuals with symptoms will ultimately develop a disorder [2,15,26]. Pain was found to be associated with increased risk of depressive and anxiety symptom onset in these studies, with 1 exception [33]. Secondly, most of these studies use a single determinant of pain, such as location (joints [34], neck, back [13], unspecified [22]) or interference with daily life [4,24], to examine the impact on depression and anxiety onset. Two studies showed that having pain at a particu-

* Corresponding author. Address: Department of General Practice, VU University Medical Center and EMGO+ Institute for Health and Care Research, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands. Tel.: +31 20 4446116; fax: +31 20 4448361.
E-mail addresses: m.gerrits@ggzingeest.nl, mj.gerrits@vumc.nl (M.M.J.G. Gerrits).

0304-3959/$36.00
http://dx.doi.org/10.1016/j.pain.2013.09.005

lar location (bladder, migraine, back) was associated with increased risk of incident major depressive disorder [28,39]. We did not find comparable studies for anxiety disorder onset. Thirdly, some studies include depression only, but the associations between pain and depression and anxiety should be studied in concert due to the high comorbidity of these disorders [29,32]. Moreover, the variation in pain characteristics associated with anxiety onset could be different than for depressive disorders [16]. Fourth, some of the abovementioned studies did not exclude participants with a depression or anxiety history [4,13] or did not specifically report on this [24,28,33]. The findings of these studies are more difficult to interpret because the associations could have been driven by a previous episode, which is an acknowledged predictor of recurrence [10,14]. Lastly, to our knowledge there are no studies examining the relationship between pain and depressive or anxiety disorder onset that also consider the important role of subthreshold depressive and anxiety symptoms. We already know that such symptoms often are associated with disorder onset [15,47]. Estimating the effect of pain over and beyond such subthreshold symptoms can help to determine whether pain is an independent risk indicator for depression and anxiety onset. If pain is indeed a risk indicator, independent of subthreshold symptoms, then adequate pain management (which is now frequently lacking [37,52]) could, aside from improving pain symptoms, potentially also reduce depression and anxiety risk. Using a longitudinal study design, we examined the following questions: Which specific pain characteristics—location, severity, duration—are associated with onset of depressive and anxiety disorders? Is pain associated with depressive and/or anxiety disorder onset directly or indirectly through elevated subthreshold depressive and anxiety levels?

2. Methods

2.1. Sample design

The Netherlands Study of Depression and Anxiety (NESDA) is a longitudinal ongoing cohort study comprising 2981 participants (18 to 65 years) and is aimed at describing the course of depressive and anxiety disorders. Participants were recruited from the general population (n = 564), primary care (n = 1610), and secondary mental health care (n = 807). Nonresponse was higher among men and younger persons (<40 years). Neither psychiatric nor somatic health problems had any significant impact on willingness to participate [49]. Exclusion criteria were not being fluent in Dutch and having a primary diagnosis of psychotic, obsessive-compulsive, bipolar, or severe addiction disorder. A detailed description of the NESDA study design and sampling procedures has been provided [40]. The ethics committees of participating universities approved the research protocol, and written informed consent was obtained from all individuals. Specially trained research staff conducted the interviews. All 2981 participants were screened for depressive and anxiety disorder at baseline using the Composite International Diagnostic Interview (CIDI, version 2.1). CIDI is a *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV)–based reliable and valid instrument for assessing depressive and anxiety disorders [53,55]. Included disorders were major depressive disorder, dysthymia, social phobia, generalized anxiety disorder, panic disorder, and agoraphobia. Participants either had no prior history, a prior history, or a current depressive and/or anxiety disorder. Baseline data collection took place between 2004 and 2007, with follow-up assessments, including the CIDI, 2 and 4 years later.

We studied 652 participants who reported never to have had a depressive or anxiety disorder during their lifetime. Of these, 38 (5.8%) did not undergo an assessment at both 2- and 4-year follow-up. Consequently, a total of 614 participants were followed up for 4 years.

2.2. Onset of depressive and/or anxiety disorder

Onset of a depressive or anxiety disorder (yes/no) was defined by a DSM-IV–based CIDI diagnosis of depression or anxiety at 2- or 4-year follow-up. We calculated the time to onset of a depressive or anxiety disorder in months, with a maximum of 48 months, from the moment the participants were assessed at baseline until the moment a participant was diagnosed with a depressive or anxiety disorder at one of the follow-up assessments according to the CIDI. Participants who were diagnosed with a depressive and/or anxiety disorder at the 2- or 4-year follow-up assessment were asked to indicate the recency of disorder onset: less than 1 month ago, between 1 and 6 months ago, between 6 and 12 months ago, 12 months ago, and between 12 and 24 months ago. We used this information and calculated the median of a time interval to assign time of onset. For instance, if a participant reported a recency of disorder onset between 1 and 6 months ago (median 3 months ago) at the 4-year follow up interview (and no disorder was diagnosed at 2-year follow up), the time from baseline to be used in the analyses was (48 − 3 =) 45 months. For participants not having a depressive or anxiety disorder during follow-up, time was censored as the time from the baseline assessment until the end of the follow-up period (48 months).

2.3. Measurements

2.3.1. Pain

To assess baseline pain over the last 6 months in various ways, the baseline interview contained 4 different measures: (1) 7 specific common pain locations (neck, back, head, orofacial area, abdomen, chest, and joints); (2) the number of pain locations; (3) duration of pain; and (4) chronic pain severity, all determined by the Chronic Pain Grade (CPG) [51]. First, the number of pain locations (0 to 7) in the last 6 months was assessed. Next, the participant was asked to choose the most painful of the specific locations, to which all subsequent questions applied. Then, duration of pain in the last 6 months was dichotomized as $\geqslant$90 days versus <90 days, based on the most frequently used definition of chronic pain as lasting at least 3 months [1]. Last, chronic pain severity was based on the reported pain intensity and pain disability. Pain intensity is a scale of 0 to 100 derived from the mean score of current pain, worst pain, and average pain over the past 6 months, and classified as low pain intensity <50 and high pain intensity $\geqslant$50. The pain disability score, also a scale of 0 to 100, was based on the mean of disability in daily activities, social activities, and work activities. Disability points (0 to 6) were given for the number of days with experienced pain disability (0 to 3 points) and the disability score (0 to 3 points). The CPG scale developed by Von Korff et al. [51] separated the following pain grades: grade 1, low intensity–low disability (intensity < 50, <3 disability points); grade 2, high intensity–low disability (intensity $\geqslant$ 50, <3 points); grade 3, high disability–moderately limiting (3 to 4 points, regardless of intensity); grade 4, high disability–severely limiting (5 to 6 points, regardless of intensity).

Patients with no pain in the past 6 months are included in grade 1. To exclude pain symptoms that were very mild or occurred only sporadically in the past 6 months, we chose to adjust the pain location variables. The specific pain locations and the number of pain locations were only taken into account if at least grade 2 on the CPG was reported, so that the more severe locations of pain were measured.