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Longitudinal association between pain, and depression and anxiety over four years

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ABSTRACT

Objective: Many patients with depression and/or anxiety (D/A) persistently report pain. However, it is not clear how the course of D/A is associated with pain over time. The present study assessed longitudinal associations between D/A and pain, and compared pain over time between D/A and healthy controls.
Methods: 2676 participants of the Netherlands Study of Depression and Anxiety were followed-up for four years. At three waves (baseline, 2, 4 years) we assessed depressive and anxiety symptom severity. Using DSM-IV criteria, we also assessed four different D/A disorder courses over time (n = 2093): incident, remitted, chronic, and no D/A (reference group). Pain was assessed at the three waves by severity and number of locations.
Results: Change in D/A symptoms was positively associated with change in pain symptoms. Compared to healthy controls (n = 519), D/A subjects – incident (n = 333), remitted (n = 548) or chronic (n = 693) – reported more severe pain (b = 0.4–0.7, p < 0.001) and more pain locations (b = 0.8–1.4, p < .001) at all waves, with the highest ratings in chronic D/A. Remission of D/A during follow-up was associated with a significant decline in pain (severity; p = 0.002, number of locations; p < .001), but pain levels remained significantly higher compared to healthy controls. Findings were similar for separate depression or anxiety course.
Conclusions: This study largely confirms synchrony of change between depression, anxiety and pain. However, even after depression and anxiety remission, subjects report higher pain ratings over time. Individuals with D/A (history) seem to be at increased risk of chronic pain.

Introduction

Pain is a major global health care problem which is often persistent over time [1,2]. Insight into factors that may influence the course of pain could help to optimize treatment strategies. Previously, we already found that pain is a risk indicator for developing D/A when we analyzed the impact of pain on the first onset of D/A in 614 adults, but it may also be expected that – reversely – D/A may exert an influence on the longitudinal course of pain [3]. Depressive and/or anxiety disorders (D/A) are highly prevalent in those with pain [4–12] and the combination of D/A and pain leads to reduced quality of life, major societal costs and even increased numbers of suicide death [13–16]. Furthermore, D/A are associated with reduced psychosocial functioning and inadequate coping strategies which could result in increased pain ratings over time [17,18]. D/A may also lead to changes in the insular cortex and abnormalities in the hypothalamic–pituitary–adrenal axis and autonomic nervous system that could subsequently lead to or aggravate pain [17,19–24]. With these psychosocial and biological changes it is questionable whether D/A recovery will also result in decreasing pain levels. As the course of D/A is known to be diverse, ranging from a single short episode to chronically persistent [25–28], the trajectory of D/A may be associated with pain course.

There are only a few short-term studies examining how change in D/A is related to the course of pain over time. When depressive symptoms improved in 103 primary care patients, pain also improved over 6 months [29]. A clinical trial showed that the increase of depressive symptoms was associated with more severe pain after 1 year, whereas depression relief was associated with less pain [30]. In another study with neurology outpatients, depression severity predicted pain over one year [31]. In patients with serious burn injuries, more depressive and anxiety symptoms were associated with greater pain at the subsequent time point [32]. Finally, in 529 older patients with osteoarthritis, depressive symptoms did not predict pain during follow-up [33]. Most of these findings from relatively small and specific samples point to a synchrony of change over a short period of time, such that if depressive and anxiety symptoms change then pain symptoms will change in a

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similar direction. Of the above mentioned studies, four focused on depressive symptoms and only one on anxiety. In daily practice, disorders (such as D/A) guide clinical decisions more than symptom levels. Therefore, rather than solely measuring symptom severity we also considered it interesting to examine whether temporary versus more chronic states of psychiatrically defined depressive and anxiety disorders compared to a mentally healthy state impact on pain over time. Our objectives were to determine how different courses of depressive and/or anxious symptoms and disorders (incident, remitted and chronic D/A versus healthy controls) are associated with pain over a four-year period in a large sample.

Methods

Sample

Data of the current study are derived from the Netherlands Study of Depression and Anxiety (NESDA). This is a longitudinal cohort study among 2981 participants (18 to 65 years) who were recruited from community, general practice and specialized mental health care. An extensive description of the NESDA study design has been provided by Penninx et al. [34]. Participants were assessed for D/A using the DSM-IV based Composite International Diagnostic Interview at baseline and the 2- and 4-year follow-up assessments (CIDI, version 2.1). The CIDI is a structured interview with acceptable reliability and validity for assessing depressive (major depressive disorder, dysthymia) and anxiety (social phobia, generalized anxiety disorder, panic disorder, agoraphobia) disorders [35,36]. Exclusion criteria were not being fluent in Dutch and having a primary diagnosis of psychotic, obsessive compulsive, bipolar or severe addiction disorder. Willingness to participate did not depend on somatic or mental health problems but was slightly lower in younger men [37]. Data were gathered in three waves: at baseline in 2004–2007 (T0), after 2 years (T1, 2006–2009) and after 4 years (T2, 2008–2011). In the present study, we included NESDA participants who participated in at least one of the two follow-up assessments (n = 2676). At baseline, the 305 non-responders more often had a depressive and/or anxiety disorder and more pain symptoms.

Depression and/or anxiety (D/A) course

To examine depression and/or anxiety course over four years, we used two different indicators. The first was based on change in depressive and anxiety symptoms and the second was based on the presence or absence of CIDI-based DSM-IV depressive and/or anxiety disorders over time.

Change in D/A symptoms

Depressive and anxiety symptoms were assessed at the baseline interview (T0) and at the two- and four-year follow-up (T1, T2) covering symptomatology experienced in the past week. Depressive symptoms were measured using the Quick Inventory of Depressive Symptomatology-self-report (QIDS), a reliable and valid instrument consisting of 16 items, none of which covering pain symptomatology (0–27 score) [38,39]. Self-reported anxiety symptoms were measured using the reliable and valid Beck Anxiety Inventory (BAI), consisting of 21 items (0–63 score) measuring severity of mainly arousal-related symptoms of anxiety [40]. Next to the BAI, we also used the Fear questionnaire (FQ) measuring mainly avoidance symptoms, consisting of 15 items (0–120 score) with good reliability and validity [41,42]. To describe the change in depressive and anxiety symptoms, we calculated two change scores for the QIDS, BAI and FQ symptoms separately: change between T0 and T1 (T1 − T0) and between T1 and T2 (T2 − T1).

Course of D/A disorders

We were interested in examining how clinically relevant distinct courses of D/A – incident, remitted, and chronic – compared to healthy controls are associated with pain over time. We defined these four trajectories as outlined below:

1. Healthy controls: participants who did not have a D/A diagnosis at all three waves and who did not have a D/A lifetime history. The healthy controls were regarded as the reference group.
2. Incident D/A: participants who did not have a D/A diagnosis at baseline but who developed a D/A diagnosis during follow-up.
3. Remitted D/A: participants who had a baseline D/A diagnosis (six-month prevalence) but who remitted during follow-up.
4. Chronic D/A: participants who had a baseline D/A diagnosis (six-month prevalence) and a D/A diagnosis at one of the two follow-up assessments with at least 24 months out of the 48 months of follow-up having reported symptoms. The latter was based on the Life Chart Interview (LCI) [43] included in each follow-up assessment. The LCI uses a calendar approach to recall life events to refresh memory, after which depressive and anxiety symptoms were determined for each month during follow-up.

Since depression and anxiety are often comorbid (in the NESDA sample in 67% of all cases [44]) we assessed the association of depressive and anxiety disorders with pain over time conjointly. However, compared to depression, the link between anxiety and pain is less investigated [4]. Consequently, we additionally explored whether the longitudinal pain associations were comparable for depression and anxiety course trajectories by examining depression and anxiety disorders separately.

Pain

During the baseline interview and at the two- and four-year follow-up, participants were systematically questioned about pain symptoms in the last six months using the Chronic Pain Grade Questionnaire by von Korff et al. [45]. An inventory was made of pain symptoms of joints in the extremities, back, neck, abdomen, chest, head and orofacial area. Next, the participant was asked to choose the most painful location, for which pain intensity and pain-related disability were assessed. Pain intensity was based on the mean of present pain, average and worst pain over the past six months on a 0–100 scale. Pain-related disability was calculated from the mean interference of pain with usual activities, work/housework activities and social activities in the prior six months (0–100 scale) and disability days in the prior 6 months (score 0–180). Of all mentioned pain locations, the number of pain locations was calculated (0–7).

We used two different outcome measures for pain to cover several relevant aspects of pain symptomatology:

a. Pain severity: We combined the continuous scales for intensity and disability into one measure of pain severity, in line with the original concept of the Chronic Pain Grade Questionnaire. These concepts were shown to be highly correlated (r = 0.69) and led to an adequate internal consistency (Cronbach's alpha = 0.89). We transformed pain intensity and disability into standardized Z-scores. The pain severity measure was the mean of the intensity and disability Z-scores.
b. Number of pain locations: based on the number of pain locations (0–7) the participant reported (for the LMM analyses standardized Z-scores were used).

Also, we calculated change scores for both measures (change between T0 and T1 (T1 − T0) and between T1 and T2 (T2 − T1)).

Covariates

Socio-demographic covariates were selected a priori on the basis of previously reported associations between both pain and D/A. Baseline characteristics included age, sex and years of education [9,46,47]. Baseline chronic disease status was based on self-reported diagnoses of the following disease categories: cardiometabolic, respiratory, digestive,