

Comorbidity Among Multiple Pain Symptoms and Anxious Depression in a Dutch Population Sample

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Abstract: Most studies on pain focus on specific disorders, which makes it difficult to compare characteristics across different types of pain symptoms. In this large population-based study, we examine the prevalence and comorbidity patterns among pain symptoms across a wide range of anatomic sites (back, neck, head, abdomen, joints, chest, face, teeth, and "other") in relation to anxious depression and a range of demographic, health, and lifestyle variables. Self-report data were collected in 11,787 adult participants of The Netherlands Twin Registry (mean age 44.5 years, 62% female), including twins and relatives of twins. Headache and abdominal pain were strongly associated with female sex, whereas chest pain and toothache were not. Joint pain strongly increased with age, whereas headache and abdominal pain decreased with age. Most other pain sites were only weakly associated with age. A highly consistent pattern of comorbidity was observed: All pain symptoms were correlated with all other pain symptoms, as well as with anxious depression. Frequent and widespread pain (ie, pain at multiple sites) was most strongly associated with anxious depression. These observations reflect important differences between specific pain symptoms, suggesting partly separate etiologies, but also highlight the importance of shared mechanisms underlying pain symptoms in general.

Perspective: The association of pain with sex and age strongly depends on pain location. However, all pain sites are consistently associated with other pain sites as well as with anxious depression. This provides important clues with respect to both similarities and differences in the mechanisms underlying different types of pain.

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Some characteristics are shared by many pain disorders. For example, it is known that several pain disorders increase the risk of other pain disorders.¹¹ Patients with irritable bowel syndrome have increased

rates of fibromyalgia, back pain, and migraine²⁹; patients with chronic low back pain show higher rates of other musculoskeletal pain disorders as well as neuropathic pain disorders¹⁴; and patients with temporomandibular pain often suffer from neck pain as well.³⁶

Pain disorders not only tend to cluster among each other but also co-occur with psychiatric disorders, in particular with anxiety and depression.^{17,26} This seems to be relatively independent of the type of pain disorder. For example, we previously showed that more pain symptoms were reported in a clinical sample of patients with anxiety and/or depressive disorders than in controls, regardless of the location of the pain.²⁴ It is unknown whether this consistent comorbidity of anxiety,

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depression, and pain symptoms is also present at the general population level.

However, there are also some striking differences among pain disorders. Although pain tends to be more prevalent in females than in males, the strength of this relationship differs considerably depending on the disorder. Migraine has been found to be 2 to 3 times more prevalent in females,³³ but for low back pain the relationship with sex is much weaker.² And although migraine has a peak incidence in adolescence and decreases after menopause,³³ the prevalence of fibromyalgia is reported to increase steadily with age.⁸

Thus, although different pain disorders appear to share characteristics, suggesting a general susceptibility to pain disorders, the observed differences among pain conditions may provide important clues as to how the underlying mechanisms may differ. However, a good overview of the patterns in prevalence and comorbidity across different pain conditions is largely lacking, because most studies have focused on specific pain conditions. Studies assessing a wider range of pain symptoms simultaneously are rare and often restricted to a certain type of symptom, for example, musculoskeletal pain only.^{4,18} This prevents a good comparison across different conditions because of inevitable methodologic differences among studies.

In this study, we first evaluate the extent to which pain symptoms differ as a function of sex, age, and other demographic, health, and lifestyle variables, as this may reflect differences in the mechanisms underlying these pain symptoms. Then we test the following 2 hypotheses: 1) pain symptoms consistently co-occur with other pain symptoms, irrespective of anatomic site, and 2) pain symptoms consistently co-occur with anxiety and depression. For this purpose, we conducted an extensive data collection on pain and anxious depression in 11,787 participants of the Netherlands Twin Registry (NTR).⁴⁰ This allowed us to obtain an overview of the patterns in prevalence and comorbidity among pain symptoms in a wide range of anatomic sites (back, neck, head, abdomen, joints, chest, teeth, face, and "other") in a general population sample.

Methods

The data described in this study were collected in participants of the NTR. The NTR conducts longitudinal questionnaire research, with a focus on health, personality, and lifestyle variables.^{6,7,40} Adult NTR participants receive invitations to participate in questionnaire research approximately every 2 to 3 years. This study is based on data from the ninth wave of questionnaire research (survey 9). Data were collected in 2011 to 2012.

Participants

The participants in this study were twins (49.1%) and relatives of twins (parents, 33.6%; siblings, 10.6%; partners, 5.1%; children of twins, 1.3%; and children of siblings, .4%). Invited participants were aged 18 or older

Pain Prevalence and Comorbidity in The Netherlands and came from families in which at least 1 person had completed the previous survey (survey 8).

Data Collection

An invitation letter with a personal log-in code and a link to an online questionnaire was mailed to the participants. A hard copy version of the questionnaire was available on request. Invitations for participation in the study were mailed to a total of 27,892 participants in January, April, and September 2011 and February 2012. Participants who had not yet completed the questionnaire received a reminder by mail within a few months after the first invitation. Additional reminders were sent to targeted groups, such as twins whose co-twin had already completed the questionnaire, to maximize the number of complete twin pairs. These efforts resulted in 11,948 completed questionnaires, which equals a total response rate of 43%, comparable to previous studies in the adult NTR sample.⁴⁰ Of these individuals, 11,565 completed the questionnaire online and 383 on paper. For the present study, 6 individuals were excluded because they were younger than age 18 years and 155 because they did not complete the pain questionnaire, resulting in a sample of 11,787 individuals for analysis. Of these, 10,783 had already participated in previous surveys (mean number of surveys 2.9, standard deviation = 2.0); 1,004 participated for the first time. The study was approved by the Medical Ethics Committee of the VU University Medical Center Amsterdam.

Measures

Pain

The pain inventory addressed pain in 9 different anatomic sites, experienced during the last year. The pain locations assessed were back, neck, head (headache or migraine, collectively referred to as headache throughout this paper), abdomen, joint, chest, tooth, face, and somewhere else (referred to as "other" throughout this paper). Participants who reported having pain somewhere else were asked to report the location of this pain (open-ended question). In some cases, this pain matched one of the other existing categories, in which case the participant was reclassified accordingly.

For each pain location, participants were asked how often they experienced pain (no pain, occasionally, a lot of the time). We refer to pain that was present occasionally in the last year as "occasional pain" and pain that was present a lot of the time in the last year as "frequent pain." Participants were asked whether there was a known cause for the pain (open-ended question). The pain that bothered the participant the most was further assessed with the Graded Chronic Pain Scale.³⁸ This is a validated scale that assesses pain intensity and pain-related disability. From the Graded Chronic Pain Scale, a "characteristic pain intensity" and a "disability score" can be derived, both of which range from 0 to 100. The characteristic pain intensity score reflects the intensity of the current, worst, and average pain, whereas the disability score reflects how much the pain interferes

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