The power of longitudinal population-based studies for investigating the etiology of chronic widespread pain

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Published in:
Pain

DOI:
10.1016/j.pain.2012.09.001

Publication date:
2012

PAIN® 153 (2012) 2305–2306

PAIN®

www.elsevier.com/locate/pain

Commentary

The power of longitudinal population-based studies for investigating the etiology of chronic widespread pain

In this issue of Pain, Gale et al. show that lower childhood intelligence is associated with increased risk of chronic widespread pain (CWP) later in life [2]. Although an association between chronic pain and cognitive ability has been shown before, the Gale et al. report is the first longitudinal study in a large general population cohort. Two important characteristics stand out in their study.

First, its longitudinal design enabled the researchers to study causal direction as well as interesting explanatory mechanisms in the association between intelligence and pain. A previous cross-sectional study interpreted this association as an effect of pain on cognitive function [8]. Gale et al., however, show that the reverse might also occur. Specifically, the authors found that lower intelligence predicted the development of CWP many years later. They suggest several interesting mechanisms to explain their findings, including inappropriate coping styles and suboptimal health literacy. These suggestions imply important roles for health seeking behavior and dealing with symptoms or symptom related information, and will inspire further research in this area.

The second key feature of the Gale et al. study is that it used a population-based design, which contrasts with many previous etiological studies that compared patients to healthy controls. This approach is especially relevant because of the nature of CWP, which is the core symptom of fibromyalgia, one of the most prevalent functional somatic disorders (FSD). CWP was defined according to the American College of Rheumatology criteria for fibromyalgia. The definition is based on questions on symptom diversity and chronicity, which is preferable to identifying cases based on self-report of fibromyalgia. Not all persons fulfilling the criteria for an FSD present with a formal diagnosis [4,10]; one of the factors increasing the chance of an FSD diagnosis in persons with persistent functional somatic symptoms (FSS) was high intelligence [5]. This increased chance of an FSD diagnosis in highly intelligent people might mask the fact that the FSS on which the FSD diagnosis is based are less prevalent in this group [7]. The strategy used by Gale et al., which is based on the assessment of the core symptom CWP and not on the self-reported diagnosis of fibromyalgia, avoids this problem.

This study is consistent with previous studies that associated lower intelligence with a large variety of somatic and psychiatric health problems as well as mortality. These health problems include various types of FSS in both adults [1,3,7] and adolescents [6]. The results suggest that lower intelligence may be a generic risk factor for morbidity and mortality that deserves further study, especially with regard to the mechanisms responsible for the intelligence-ill health association.

Several large population-based cohort studies and biobanks have been initiated in the previous years, often consisting of multiple assessments and usually quantifying multiple disease outcomes. These cohorts could potentially facilitate research into the specific mechanisms that relate intelligence to a variety of health outcomes. However, the Public Population Project in Genomics (P3G) observatory website, which provides an overview of the data collected in large cohorts, reveals that only a small minority of these studies includes a measure of intelligence. A lack of data on intelligence might be related to the difficulties and costs associated with assessments of intelligence in large groups of participants from the general population. Some studies used substitute data for intelligence level, such as educational level, but this is not adequate. This limitation is confirmed in the present study, which demonstrated that intelligence can predict health outcomes independent of educational level. To unravel the mechanisms that underlie the association of intelligence and health problems, there is clearly a need for short, validated instruments that measure intelligence in large representative longitudinal population-based cohorts. With regard to the outcome, validated pain questionnaires are missing from the majority of current large cohort studies, despite the availability of multiple instruments that can assess severity, diversity and chronicity of pain symptoms. The Phenotype and Exposure (PhenX) initiative, which aims to select high-quality, relatively low-burden measures for inclusion in large-scale research efforts, recommends use of the short form of the Brief Pain Inventory [9].

Symptoms such as pain are more than reflections of disease. As these symptoms are not only prevalent but are also very disabling, a better understanding of their etiology is urgently needed. We wish to stress the importance of including validated pain and other somatic symptom questionnaires in the large population-based cohorts that are currently being initiated and followed-up. Including these questionnaires will enable the definition of trajectories leading to chronic pain, as well as their genetic underpinnings and their functional consequences. These questionnaires will also make it possible to study in what ways trajectories to pain differ from those to other somatic symptoms. The use of gold standard symptom measures allows combining multiple cohorts, thereby obtaining the very large sample sizes needed to investigate current questions with regard to the complex etiology of chronic pain.

☆ DOI of original article: http://dx.doi.org/10.1016/j.pain.2012.07.027

http://dx.doi.org/10.1016/j.pain.2012.09.001

Conflict of interest statement

The authors have no conflict of interest to declare.

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