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The role of central sensitization in shoulder pain: A systematic literature review

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ABSTRACT

Introduction: Hyperexcitability of the central nervous system has been suggested to play an important role in pain experienced by patients with unilateral shoulder pain. A systematic literature review following the PRISMA guidelines was performed to evaluate the existing evidence related to the presence of central sensitization in patients with unilateral shoulder pain of different etiologies including those with chronic subacromial impingement syndrome. Studies addressing neuropathic pain (e.g., post-stroke shoulder pain) were not considered.

Methods: Electronic databases PubMed, EBSCO, and Web of Science were searched to identify relevant articles using predefined keywords regarding central sensitization and shoulder pain. Articles were included till September 2013. Full-text clinical reports addressing studies of central sensitization in human adults with unilateral shoulder complaints including those diagnosed with subacromial impingement syndrome were included and screened for methodological quality by two independent reviewers.

Results: A total of 10 articles were retrieved for quality assessment and data extraction. All studies were cross-sectional (case–control) or longitudinal in nature. Different subjective and objective parameters, considered manifestations of central sensitization, were established in subjects with unilateral shoulder pain of different etiologies, including those receiving a diagnosis of subacromial impingement syndrome. Overall results suggest that, although peripheral mechanisms are involved, hypersensitivity of the central nervous system plays a role in a subgroup within the shoulder pain population.

Conclusions: Although the majority of the literature reviewed provides emerging evidence for the presence of central sensitization in unilateral shoulder pain (including those diagnosed with subacromial impingement syndrome), our understanding of the role central sensitization plays in the shoulder pain population is still in its infancy. Future studies with high methodical quality are therefore required to investigate this further.

Introduction

Shoulder pain is the third most common musculoskeletal disorder, with prevalence rates varying from 6.9% to 26% for point prevalence and up to 66.7% for lifetime prevalence in the general population [1,2]. Although many patients completely recover within a few months after injury, a large patient group reports persisting shoulder pain that contributes to more than 80% of the total economic cost due to shoulder pain [3–5].

Within the unilateral shoulder pain population, subacromial impingement syndrome (SIS) is a common diagnosis. SIS is a disabling and costly disorder affecting the general population, which leads to important expenditures for the public health care system [6,7]. Over the past years, research findings point to the possibility that central sensitization (CS) is present in (some)

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patients with unilateral shoulder pain (including those with SIS) [8]. CS is defined as an "amplification of neural signaling within the central nervous system (CNS) that elicits pain hypersensitivity" [9]. CS is a broad term that encompasses distorted sensory processing in the CNS [10], malfunctioning of descending pain-inhibitory mechanisms [11], enhanced activity of pain-facilitatory mechanisms [12], and long-term potentiation of the neural synapses in the anterior cingulated cortex [13]. Indeed, if the CNS is sensitized, minimal tissue damage or sensory input without tissue damage could be sufficient to trigger pain perception. This may explain the mismatch between the pain experienced by patients and the extent of injury at the subacromial space commonly found in patients with SIS [14].

Different modalities of quantitative sensory testing (QST) have been used to assess central pain dysregulation [15]. QST is based on standardized (painful) stimuli applied to cutaneous and musculoskeletal structures that aim at assessing the sensitivity of these structures to specific stimuli modalities. Those stimuli can be applied locally (i.e., in the proximity of or at the affected joint or tissue) or at distant sites (i.e., remote from the affected joint or tissue), providing a better understanding of peripheral and central nervous system sensitization, respectively. Various QST responses have been associated with CS in patients with unilateral shoulder pain, including alteration of descending pain-inhibitory mechanisms [16] or remote areas of hyperalgesia [8,14]. All these changes are considered different pain biomarkers evaluating the same construct (i.e., CS) [15,17,18].

Currently, it remains unclear whether enough consistent evidence is available regarding CS in unilateral shoulder pain, including those patients diagnosed with SIS. Recent systematic literature reviews have demonstrated that CS plays an important role in other chronic pain conditions such as whiplash [19], osteoarthritis [20], chronic fatigue syndrome [21], and (to a much lesser extend) rheumatoid arthritis [22]. In addition, some studies claim for a role of the CNS in pain experienced by people with unilateral shoulder pain, such as those with rotator cuff tendinopathy [23], frozen shoulder [24], and chronic hemiplegic shoulder pain [25,26]. The latter group of patients addresses neuropathic pain, as stroke is a typical example of objective evidence of (central) nervous system "damage," as required for complying with the diagnostic criteria for neuropathic pain [27]. As CS has been well established as the underlying mechanism of neuropathic pain [17,28,29], neuropathic shoulder pain will not be the focus of the present systematic review. Here, we focus on non-neuropathic shoulder pain patients, including those with SIS, for examining whether CS plays a role in these types of shoulder pain.

Although preliminary evidence seems to support the role that CS plays in subjects with unilateral shoulder pain, there is currently no systematic literature review available regarding CS in these patients. Hence, the aim of this study was to systematically review and evaluate the existing evidence from the literature, in order to establish if there are enough arguments to either support or refute a role for CS in unilateral shoulder pain, including those with SIS. Any type of association between CS and unilateral shoulder pain was explored, such as the merely presence of CS (i.e., epidemiologic studies), any cause–effect relationship, or the effect of treatments focusing on CS in unilateral shoulder pain patients. Studies related to neuropathic shoulder pain (e.g., post-stroke shoulder pain) were not considered.

Methods

Search strategy

To identify relevant articles regarding central pain processing in patients with SIS, a systematic search of the literature using the PRISMA statement guidelines [30] was performed in databases such as PubMed (http://www.ncbi.nlm.nih.gov/sites/entrez), EBSCO (http://search.ebscohost.com), and Web of Science (http://apps.isiknowledge.com) until September 2013. The results for every database and combination of keywords and MeSH terms used in the search strategy are represented in Supplementary Table S1. In addition, the reference lists from relevant articles were checked to obtain as complete information as possible.

Study selection

An article had to meet all the following inclusion criteria to be included in this review: (I) it had to be reported in a peer-review academic journal; (II) it had to study the phenomenon of CS in human adults (18 years or older) with unilateral shoulder pain, including those with SIS; (III) it had to be a full-text original research report; and (IV) it had to be written in English. If any of these inclusion criteria were not fulfilled, the article was excluded from the literature search. No limitation regarding year of publication was used, and all clinical study designs were eligible. Although review articles were not eligible for inclusion, their reference lists were screened to collect relevant articles, which were not initially retrieved by the systematic search. Articles related to neuropathic shoulder pain (e.g., pain post-stroke shoulder pain) were excluded.

Study process

After performing the literature search, duplicate articles were removed. Eligibility assessment was performed based on the title and the abstract. Initially, all titles and abstracts of the retrieved articles were screened to identify relevant articles related to CS in unilateral shoulder pain (including those with SIS) using the predefined inclusion criteria. In case of uncertainty regarding appropriateness of the article after reading the title and the abstract, the full version of the text was retrieved and checked for fulfillment of the inclusion criteria. Screening was done independently by two researchers (M.N.S. and M.K.). A consensus meeting was organized to discuss potential disagreements. When consensus could not be reached, a third opinion was provided by another researcher (E.L.L.).

The full-text version of all the articles that met the inclusion criteria were retrieved, and methodological quality assessment and data extraction were performed.

Quality assessment

Methodological quality assessment of the full-text articles was evaluated using the PEDro scale, which is based on the Delphi list developed by Verhagen et al. [31]. The inter-rater reliability of the PEDro scale reported a generalized Kappa static ranging between 0.40 and 0.75 [32]. This scale is considered to provide a measure of internal validity and ability to predict bias [33,34]. The PEDro scale is composed of 11 items, where the first relates to external validity (and it is not considered part of the total score) and the remaining 10 determine the internal quality and indicate whether the trial includes enough data to make it interpretable [35]. The PEDro scale grades articles getting 6/10 or more points from moderate to high quality, and it was originally designed to assess the risk of bias in Randomized Control Trials (RCTs) [32]. For non-RCTs, the PEDro scale was accommodated to the number of items that were applicable for each experimental design. For instance, criteria number 2, 3, 6, 8, and 9 were not scored for cross-sectional and