FEATURES OF CENTRAL SENSITISATION IN PATIENTS WITH SHOULDER PAIN – A FEASIBILITY STUDY

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Abstract

Design. A case-control feasibility study, comparing people with unilateral shoulder pain and pain free controls. Background. Previous studies have suggested that central sensitisation (CS) may be present in people with shoulder pain, mostly based on testing of nociception rather than mechanosensitivity, both of which can change as part of CS. Changes in mechanosensitivity are important for physiotherapy, which often involves non-noxious mechanoreceptor stimulation. Objectives. This study tested sensitivity to a range of mechanical stimuli potentially associated with CS in people with shoulder pain, compared to asymptomatic individuals. It was hypothesised that if CS was present, the response to mechanoreceptor stimulation would be increased. Methods. Both shoulders in both groups were tested for sensitivity of static and dynamic touch, vibration and punctate stimulation, plus temporal summation and pressure pain threshold (PPT). Participants completed a demographic questionnaire, pain scales, PainDETECT for neuropathic pain, and QuickDASH for upper limb function. Results. PPT was found to be significantly lower in the affected compared to the unaffected shoulders ($p<0.003$), but no other statistically significant between-group differences were found. Conclusion. This study found a lowered PPT in people with unilateral shoulder pain compared with asymptomatic individuals, but no evidence of a heightened response to other forms of mechanoreceptor stimulation. The study protocol

was suitable for future studies and the required participant numbers were established. The variation in findings between studies suggests that a larger longitudinal study may be warranted.

Keywords: Central sensitisation, Shoulder pain, Sensory testing, Mechanosensitivity

Introduction

Central sensitisation (CS) is defined by the International Association for the Study of Pain (IASP) as an "increased responsiveness of nociceptive neurons in the central nervous system to their normal or sub threshold afferent input" [1]. It is not possible to establish CS or its exact mechanism in humans, so it is important to use the term only tentatively in clinical contexts [2]. That said, recent reviews have suggested that CS may play a role in persistent shoulder pain [3,4]. Studies included in these reviews found a range of painful shoulder issues to be associated with a reduced pressure pain threshold, a heightened sensitivity to punctate mechanical stimuli, a reduction in conditioned pain modulation (CPM) and a heightened response to noxious heat [5-9].

Neurophysiological research has demonstrated several segmental changes in the processing of nociceptive, as well as non-nociceptive, stimuli in the central nervous system. CS is thought to be associated with allodynia, mediated by low-threshold mechanoreceptors and Aß afferents [10, 11]. Another manifestation of CS is hyperalgesia, which occurs in response to noxious punctate or sharp stimuli, thought mainly to be mediated by nociceptive Aß afferents [11, 12]. Enhanced central processing may in addition facilitate temporal summation, a gradually increasing response to repeated stimulation [13].

Many physiotherapy treatments for pain involve non-noxious mechanical stimuli, which have not been investigated in detail in previous studies of CS in people with shoulder pain. It is important for healthcare professionals to know whether an apparent exaggerated response to mechanoreceptor stimulation could be the result of CS. This study therefore set out to investigate sensitivity to a number of mechanical stimuli that might be associated with CS: comparing individuals with unilateral shoulder pain with asymptomatic individuals. We hypothesised that if CS was present in patients with shoulder pain, the response to mechanoreceptor stimulation might be heightened. We also wanted to determine participant numbers required to establish between-group differences and to test the protocol for use in a larger investigation.

Materials and methods

Approvals

Ethics approval was obtained from the University of Hertfordshire Health and Human Sciences Ethics Committee with Delegated Authority, protocol number HSK/SF/UH/02716.

Participants

Participants had to have unilateral pain in the deltoid region of the shoulder of at least 3 months' duration, rated as 4/10 or more at least some of the time. The study's focus was on pain and sensory changes and most participants were a convenience sample of workers at the University of Hertfordshire rather than patients' attending a clinic, so no attempt was made to gather diagnostic information. The control group had to be asymptomatic at the shoulder. All participants had to be at least 18 years of age. Exclusion criteria were other pain problems present for more than 3 months, with pain rated as regularly greater than 4/10; scarring, lesions or numbness in the region to be tested; inability or unwillingness to bilaterally expose the deltoid region of the shoulder; concurrent neck pain.

All participants were recruited by emailing staff at the University of Hertfordshire in February 2017. Members of staff who expressed an interest in taking part in the study were sent information and a consent form. Some members of staff forwarded the email to relatives, who were sent the documents once they contacted the researcher. Following informed written consent, which permitted withdrawal at any time without the need to explain, participants were asked to complete a set of questionnaires and attend for sensory testing of both shoulders. As suggested by Hertzog [14], a minimum of 15 participants per group were recruited for this feasibility study.

Questionnaires

Participants were asked to complete a demographics questionnaire. The PainDETECT questionnaire was used to assess the likelihood of a neuropathic pain component[15]. Subjective pain and pain-related distress, both current and average, were assessed with numerical rating scales[16]. The QuickDASH questionnaire, an 11-item version of the longer 30 item Disabilities of the Arm, Shoulder and Hand questionnaire (DASH), was used to assess function of the upper limb[17].

Sensory testing

Sensitivity to a range of mechanical sensory stimuli were tested; specifically sensitivity to dynamic mechanical touch and punctate stimulation, as well as temporal summation. One nociceptive mechanical stimulus was included, pressure pain threshold (PPT), because it had been tested in several studies that suggested the presence of CS in people with shoulder pain. Perception threshold to static mechanical touch and vibration were also examined.

Sensory testing took place in a single room by the first author, using a single set of devices. The tests were applied as described by Rolke et al.[18] in the following standard order. Static mechanical perception threshold was tested using calibrated fibreglass Marstock Nervtest von Frey filaments. A wisp of cotton wool, a cotton wool bud on a light spring and a Somedic SENSELab Brush-05 were applied in this order to test pain sensitivity to dynamic light touch. Detection threshold for vibration was determined with a Rydell-Seiffer 64Hz calibrated tuning fork. A 256mN von Frey filament was used to determine sensitivity to punctate mechanical stimuli. Temporal summation was assessed by comparing the rating of a single 256mNvon Frey filament with the rating at the end of 10 repetitions of one per second. Finally, PPT was determined with a Wagner FPX pressure algometer with an applicator of 1cm2. In participants with shoulder pain, the non-painful side was tested first. Vibration was tested on the centre of the lateral border of the acromion; all other tests were applied over and around the centre of the deltoid region. Finally, time taken for the testing procedure was noted for future studies.

Statistical Analysis

Data were analysed using IBM SPSS version 25. Statistical analysis was undertaken using the independent t-test to compare the sensory characteristics between the participants with shoulder pain and the control group. The statistical significance threshold was set to $p=0.05$. Bonferroni p-value correction was applied because the control group data was used twice, with the adjusted $p<0.0167$ indicating statistical significance.

Results

Thirty-nine participants took part in the study. Eighteen had unilateral pain in the deltoid region of the shoulder and 21 did not have any shoulder symptoms. One participant was excluded from analysis because their pain was felt only over the medial border of the scapula. Table 1 details the demographic information.

TABLE 1. Age and gender distribution of participants

	Control n=21 Female=14; Male=7 All white All employed	Shoulder pain n=17 Female=15; Male=2 White; 1 mixed race female Employed; 1 pensioner
Age 30-39	8	2
Age 40-49	4	3
Age 50-59	7	7
Age 60+	2	3
Missing	-	2

No participants were found to have a definite neuropathic component to their pain based on their PainDETECT scores. Pain and pain-related distress, both average and current, showed wide variation in the group with shoulder pain (Table 2).

Mean QuickDASH scores were 0.36 (SD 0.89) for asymptomatic participants and 17.25 (SD 18.60) for participants with shoulder pain, with 2 scores missing from the pain group (Table 2). All participants allowed all tests to be performed, but equipment failure meant that PPT could not be tested in 2 participants with pain and 2 without pain.

TABLE 2. QuickDASH and pain scores (mean, SD)

	QuickDASH	Pain Current	Pain Average	Distress Current	Distress Average
Shoulder pain group	17.25 (18.6)	2.5 (2.34)	5 (2.56)	2.5 (2.00)	3.5 (2.18)
Control group	0.36 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)

Table 3 details the results of sensory testing of perception threshold for static light touch, sensitivity to vibration, PPT and temporal summation, comparing painful shoulders with all shoulders in the control group. Table 4 details the results for unaffected shoulders versus all shoulders in the control group. Results in both tables are presented as a mean (range). None of the raw data were normally distributed initially, so a Log10 transformation was applied to sensory perception threshold, vibration and PPT. A square root transformation was applied to temporal summation, in order not to negate zero difference. Independent t-tests compared the means between both groups for all tests except vibration, for which a Mann-Whitney test was performed because of non-normal distribution after transformation. For the feasibility aspect of the study, the sample size estimations were performed in G*Power (version 3.1.9.4) based on the calculated effect sizes, assuming a two-sided 80% power and a 5% significance level using the t-test.

No statistically significant differences between groups were established for sensitivity to static or dynamic touch, vibration, punctate stimulation or temporal summation. Only PPT in the painful shoulder was statistically significantly lower than PPT in the control group. Although PPT in unaffected shoulders in participants with shoulder pain was also lowered, this did not reach significance following Bonferroni correction. The study protocol was easy to apply in under 20 minutes.

Discussion

This study found that participants with unilateral shoulder pain had a significantly lower PPT over the deltoid muscle

TABLE 3. Results for painful shoulder vs both shoulders in control group

	Shoulder pain group-affected shoulder	Control group	Test statistic	p-value	Effect size	Power	Sample size required to differentiate (control group / pain group)
Log of sensory threshold mean	0.668 (0.41 to 0.97)	0.646 (0.36 to 0.87)	0.676	0.50	0.19	0.102	625 / 313
Log of vibration mean	0.861 (0.8 to 0.9)	0.876 (0.8 to 0.9)	0.992	0.321	0.453	0.328	123 / 61
Log of PPT mean	1.259 (0.98 to 1.65)	1.409 (1.07 to 1.70)	3.12	0.003*	0.963	0.867	28 / 14
Square root of temporal summation difference mean	2.605 (0 to 7.07)	1.917 (0 to 7.62)	1.156	0.248	0.343	0.328	211 / 105

* statistically significant

TABLE 4. Results for unaffected shoulder in shoulder pain group vs both shoulders in control group

	Shoulder pain group-affected shoulder	Control group	Test statistic	p-value	Effect size	Power	Sample size required to differentiate (power = 0.8) (control group / pain group)
Log of sensory threshold mean	0.6772 (0.53 to 1)	0.646 (0.36 to 0.87)	0.962	0.34	0.276	0.157	311 / 155
Log of vibration mean	0.866 (0.8 to 0.9)	0.876 (0.8 to 0.9)	0.983	0.326	0.322	0.19	240 / 120
Log of PPT mean	1.301 (1.15 to 1.56)	1.409 (1.07 to 1.70)	2.44	0.018	0.75	0.667	44 / 22
Square root of temporal summation difference mean	2.26 (0 to 5.2)	1.917 (0 to 7.62)	0.837	0.402	0.183	0.094	740 / 370

on the symptomatic side, compared with asymptomatic individuals. This is in line with findings by most previous authors, with the exception of one study which found a higher rather than a lower PPT threshold [19]. The current study tested for additional regional sensory changes associated with CS such as allodynia to stroking, sensitivity to punctate stimuli and temporal summation, and found no statistical difference between groups. Recent studies have failed to find temporal summation to repeated pinprick [19, 20], or a significantly lowered PPT [20], or vibration detection threshold [20]. Moreover, they found no evidence of changes in conditioned pain modulation or sensitivity at a distance from the shoulder [19, 20].

The feasibility aspect of this study established participant numbers required to establish differences in sensory modalities between participants with and without shoulder pain. The application time of under 20 minutes suggests that additional testing of sensitivity at distant sites may be feasible.

Diagnosis of shoulder pain

Diagnosing the source of shoulder pain is complex and may not always be possible with confidence, either clinically or radiologically [21-26]. In addition to clinical structural and radiological diagnoses, hyperexcitability of the CNS has been purported as an explanation for pain experienced by some individuals with unilateral shoulder pain, as well as poor surgical outcomes[8]. However, these outcomes may in part relate to the uncertainty of diagnostic labels such as subacromial impingement syndrome [24, 25], the appropriateness of certain surgical interventions [25, 27], and the small number of participants in the studies. We therefore recommend caution when interpreting published findings and translating them into clinical practice.

It is important for clinicians to appreciate that our understanding of the role of CS in a shoulder pain population is still in its infancy[4]. We agree with recent authors that it is important for clinicians to recognise signs of CS in their patients [28, 29], but to be mindful that CS cannot be demonstrated clinically [2]. Moreover, changes in sensory processing in patients with shoulder pain may be no more than a temporary adaptation to pain[31]. This would be entirely in line with the nervous system as a system for gathering and evaluating information, and generating appropriate responses [32, 33]. To improve the efficacy of physiotherapy, strategies designed to enhance central inhibitory mechanisms could be coupled with other therapeutic approaches[34, 35].

Terminology

It is possible that CS in people experiencing shoulder pain may have been over reported due to a confusion over the definition of the term. CS and its manifestations have been defined using various terminology, which differs from the IASP definition. One paper defines CS as *an amplification of neural signalling within the central nervous system (CNS) that elicits pain hypersensitivity*[4], citing an operational definition by Woolf [36], while Woolf himself has since endorsed the IASP definition [37]. Other authors refer to CS as *altered neural thresholds in the spinal cord and/or reduced cortical inhibition of pain*[3], or avoid the term in favour of the term *central hypersensitivity, an augmentation of the nociceptive pathways of the central nervous system*[5]. It may be necessary to reach a consensus on when to use the term CS and the terminology we use to define it. Most importantly, one should be aware that CS cannot be demonstrated in vivo, so clinical findings can be attributed to CS only hypothetically [2]. Respecting this uncertainty, we recommend cautious use of language when explaining the nature of symptoms to patients with shoulder pain. The variation in findings between studies and the fact that CS may be an adaptive mechanism, suggest that a larger longitudinal study may be warranted.

Limitations

This was a feasibility study involving only a small number of participants, nearly all of whom were white British or European, so results may not apply beyond these groups. Although participants with neck pain were excluded and no participants had neuropathic pain according to their PainDETECT scores, participants were not examined to exclude a potential cervical origin of their shoulder pain. We also acknowledge the limitations of using the PainDETECT questionnaire to rule out neuropathic pain in the upper limb. Symptoms may not have been as severe as in studies investigating people seeking treatment[5, 6, 8], which may have had implications for our findings. Demographic information and QuickDASH were missing for 2 participants and PPT could not be tested for 4 participants (2 with shoulder pain and 2 without), reducing the available datasets. It is possible that there is a time-dependent component to CS, which may be more pronounced as pain persists. One participant was made aware of the study by a relative who took part, with potential for bias. No tests were conducted for signs of altered sensitivity at sites remote from the shoulders. These issues must be addressed in a larger future study.

Conclusion

This feasibility study investigated the presence of a range of sensory changes associated with CS, comparing people with and without shoulder pain. Evidence of alterations in PPT were found on both sides in people with unilateral shoulder pain, which reached significance on the affected side. No other sensory differences were established. It is likely that CS is an adaptive phenomenon which changes over time. This and the fact that the findings of different researchers have varied, suggests that a larger longitudinal study investigating sensitisation in a larger group of participants with shoulder pain may be warranted. This study prepared the ground for such an investigation by testing the protocol and establishing the participant numbers required for detection of differences in PPT.

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