Detection of peripheral and central sensitisation at acupoints in patients with unilateral shoulder pain in Beijing: a cross-sectional matched case–control study

Chao-Qun Yan, Shuai Zhang, Qian-Qian Li, Li-Wen Zhang, Xue-Rui Wang, Qing-Nan Fu, Guang-Xia Shi, Cun-Zhi Liu

ABSTRACT

Objective To investigate the pattern of experimental pain responses at acupoints in patients with unilateral shoulder pain.

Design A cross-sectional matched study.

Setting Acupuncture and Moxibustion Department, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University.

Participants Volunteer samples of 60 participants (30 patients with unilateral shoulder pain, 30 healthy controls).

Interventions Not applicable.

Main outcome measures Pressure pain thresholds (PPTs) were measured at four acupoints—namely, Tianzong (SI 11), Jianliao (SI 14), Jianyu (LI 15) and Jianzhen (SI 9), on the painful/non-painful side in patients with unilateral shoulder pain or healthy controls, respectively. The correlations between the Peripheral Sensitisation Index (PSI) and Central Sensitisation Index (CSI) were compared.

Results Analysis showed significantly lower PPT values at acupoints on the painful side compared with the non-painful side in patients with shoulder pain (p<0.025). Meanwhile, PPTs on the non-painful side of these patients were lower than those on the ipsilateral side of healthy controls (p<0.025). No significant differences in PPT values were found between the non-acupoint of the painful/non-painful side in patients with shoulder pain and the ipsilateral side of healthy controls (p>0.05). Additionally, it was observed that the pressure pain assessment acupoints have a strong association with PSI and CSI; three acupoints, in particular, SJ 14, LI 15 and SI 9, showed a correlation with PSI and CSI.

Conclusion The results suggest the presence of peripheral and central sensitisation at acupoints in participants with unilateral shoulder pain. There exists an obvious relationship among the three acupoints SJ 14, LI 15 and SI 9, which are usually chosen to treat shoulder pain. The results provide evidence for the selection of acupoints to treat shoulder pain by acupuncture.

INTRODUCTION

Acupuncture is one of the most widely used forms of complementary and alternative medicine. According to a survey conducted by the World Federation of Acupuncture and Moxibustion Societies in 2013 about 183 countries use acupuncture treatment.1 WHO reports that acupuncture treatment can be beneficial for more than 40 disorders.2 Pain is particularly amenable to acupuncture. Evidence in reviews demonstrates that acupuncture treatment can effectively reduce various types of clinical pain in multiple clinical trials.3–5 One meta-analysis reported that shoulder pain, low back pain, neck pain, osteoarthritis and chronic headache was significantly alleviated after acupuncture treatment.6 Shoulder pain is the third most common musculoskeletal disorder, with a prevalence ranging from 6.9% to 26% for point prevalence and increasing to 66.7% for lifetime prevalence in the general population.7 8 In our previous study, we showed that acupuncture can alleviate shoulder pain, particularly in particular acupoints (unpublished data).

Acupoints are special sites at precise locations and lie on ‘meridians’ without a physical...
sensitive than other areas. Nevertheless, whether ulcer or gastritis and found that
imental pain-sensitive points in patients with gastric
ments, which typically would be not painful. Central
nociception in pain perception during activities or move-
Peripheral sensitisation is defined as the broadening of
on the painful side would have a
healthy controls. Specifically, we suggested that acupoints
lower PPT than that
in patients with musculo-
skeletal pain has not been described in detail in previous
Sensitisation is a nervous system phenomenon that can
occur in conjunction with pain. When sensitisation is
present, two types of hypersensitivity occur, including
peripheral sensitisation and central sensitisation, which
are important mechanisms in musculoskeletal pain. Peripheral sensitisation is defined as the broadening of
nociception in pain perception during activities or move-
ments, which typically would be not painful. Central
sensitisation refers to an amplification of neural signal-
ing within the central nervous system that elicits pain
hypersensitivity. It reflects increased activity of pain facilit-
ation pathways and malfunctioning of descending pain
inhibitory pathways.

We performed a multicentre, single blind, factorial
randomised controlled clinical trial previously (Number
Register: ISRCTN61861069). In that study, we found that
the decrease in the pain threshold at related acupoints
in patients with unilateral shoulder pain was widespread.
Therefore, we chose some patients from the trial to
detect whether acupoints are hypersensitive in musculo-
skeletal pain disease. We hypothesised that the patients
with unilateral shoulder pain would present peripheral
or central sensitisation at acupoints as shown by pres-
ure pain threshold (PPT) detection, in comparison with
healthy controls. Specifically, we suggested that acupoints
on the painful side would have a lower PPT than that on
the non-painful side of patients. Also, acupoints on the
non-painful side of patients would be hypersensitive, as
assessed by PPTs, with respect to the ipsilateral side of
healthy controls. If the results confirm these hypothe-
eses, then they provide evidence that acupoints exist
for the peripheral sensitisation and central sensitisation
phenomena in patients with unilateral shoulder pain.

METHODS AND ANALYSIS
Study design
This cross-sectional matched case–control study was
conducted at the Department of Acupuncture and Moxi-
bustion, Beijing Hospital of Traditional Chinese Medicine
affiliated to Capital Medical University.

Participants
Clinical patients—Thirty patients with shoulder pain
were chosen from a total of 164 patients with shoulder
pain recruited from three centres to a randomised trial
between January 2014 and September 2014. We enrolled
the final 30 patients from 76 patients who had been
screened at the Beijing Hospital of Traditional Chinese
Medicine centre before any treatments were dispensed.
The research ethical committee of Beijing Hospital of
Traditional Chinese Medicine affiliated to Capital Medical
University approved the trial (reference: 201315).

The inclusion criteria were presenting with unilat-
eral shoulder pain for at least 6 weeks and up to 2 years;
reporting the pain intensity as >50 mm on a Visual
Analogue Scale (VAS); being right hand dominant
and not having received acupuncture or other analgesic
treatments in the preceding month.

The exclusion criteria were as follows: pain in both
shoulders; referred pain from the cervical spine; previous
history of shoulder surgery, pectoral muscle pain,
thoracic outlet syndrome, stroke or ipsilateral breast
surgery; heart diseases and severe hypertension; osteo-
arthritis of the glenohumeral joint or systemic bone and
joint disorder (rheumatoid arthritis); endocrine diseases
such as hyperthyroidism; severe infection; undergoing
current treatment involving analgesics and especially,
major illness depression.

Healthy controls—The healthy controls were matched
to the patients with shoulder pain individually. Each healthy
control was matched for gender, age (±1 year), ethnicity
and dominant hand to one patient. Healthy controls
were recruited from the community via posted flyers and
general advertisements between May 2014 and September
2014. Healthy controls were eligible if they were not
currently performing resistance exercise for the upper
extremity. They were excluded based on the following
criteria: had received acupuncture or other analgesic
treatments in the preceding month; experiencing neck
or shoulder pain; had a history of shoulder surgery or
neurological impairments of the upper extremity; had a
shoulder skin infection, had difficulty in understanding
instructions and were currently taking any pain medica-
tion.

Protocol
All participants completed a number of questionnaires,
including demographic data (age, sex, race, dominant
hand) and psychological information, before informed
consent was obtained. The patients were initially examined by a researcher who assessed compliance using the inclusion and exclusion criteria. The Beck Depression Inventory (BDI), a multiple choice self-reported inventory for measuring the severity of depression, was used.\(^{18}\) If the BDI outcome was >4, possible participants were excluded.\(^{19}\) Clinical pain intensity was assessed by a Visual Analogue Scale (VAS), in which consists of a 0–100 mm line, with 0 representing ‘no pain at all’ and 100 mm representing ‘the most intense pain imaginable’.

After completing the questionnaires, both shoulders of participants were exposed and the measuring sites were marked. The participants were not told which site was the non-acupoint. An expert acupuncturist was responsible for the procedure. Five points were marked in this study as shown in figure 1 and Supplementary appendix table 1. To assess the pain sensitivity of acupoints, four acupoints Jianliao (SJ 14), Jianyu (LI 15), Jianzhen (SI 9) and Tianzong (SI 11), were shown bilaterally by a circle drawn with a marker pen (figure 1A,B). To assess the pain sensitivity in the non-acupoint, a point 2 cm down from Tianzong (SI 11) was marked bilaterally in participants (figure 1B).

**Measurement of PPTs**

Both shoulders were exposed for examination by an operator. The participants were asked to take a prone position on the examination bed with a suitable pillow under the chest when Jianzhen (SI 9), Tianzong (SI 11) and the non-acupoint were measured. Then participants were required to sit on a chair with a researcher helping to keep the arm and shoulder in parallel when Tianzong (SI 11) was marked bilaterally. The participants were instructed to indicate when the pressure became painful; at that time the pressure was immediately stopped and the dights were recorded. PPT was calculated as the mean of three trials on each point. The operator was not told which side was the painful shoulder or whether the subject was a patient or a healthy controls. Additionally, the operator had no basic knowledge of acupoints and did not know whether the measuring sites were acupoints or not during testing.

**Data analysis**

The data were double entered with an adequate check in EpiData. SPSS 17.0 software (SPSS Inc, Chicago, Illinois, USA) was used for analysis. Discrete variables were summarised as frequencies and percentages. Distributed data were summarised using mean±SD or median and IQR. The distributed data were analysed using a parametric statistical test (paired t-test) if it agreed with normal distribution. Otherwise, the data were analysed using a non-parametric (Wilcoxon’s signed rank test) statistical test. A Shapiro–Wilk test and observation of histograms and normal probability plots were used for all study variables to determine whether they followed a normal distribution. To adjust for multiple comparisons, an \(\alpha\) level of 0.025 was used for all pairwise comparisons.

Peripheral and Central Sensitisation Indexes were used to determine whether pain sensitivity existed at the pressure pain assessment sites. Peripheral sensitisation referred to a patient’s response for PPT on the painful side that fell below the 25th centile compared with the non-painful side.\(^{22}\) The PPT value of the 25th centile is determined by the average value of seventh and eighth lowest observations on the non-painful side. We examined a patient’s proportional response for PPT on the painful side if it fell below the 25th centile. Each response PPT is considered for the Peripheral Sensitisation Index (PSI).

Central sensitisation indicates that a patient’s response for the PPT on the non-painful side fell below the 25th centile (the average value of the seventh and eighth

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with shoulder pain (n=30)</th>
<th>Healthy controls (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.60±12.19</td>
<td>50.63±12.20</td>
</tr>
<tr>
<td>Sex (female), n (%)</td>
<td>19 (63.3)</td>
<td>19 (63.3)</td>
</tr>
<tr>
<td>Race (number of Han), n (%)</td>
<td>30 (100)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Pain duration (weeks)</td>
<td>19.07±16.99</td>
<td>–</td>
</tr>
<tr>
<td>VAS (median, IQR)</td>
<td>70 (50–80)</td>
<td>–</td>
</tr>
<tr>
<td>BDI (median, IQR)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>BMI</td>
<td>25.27±4.17</td>
<td>24.91±3.77</td>
</tr>
<tr>
<td>Normal (≤23.9), n</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Overweight (24–27.9), n</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Obese (≥28), n</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory; BMI, Body Mass Index; VAS, Visual Analogue Scale.
lowest observations) among the ipsilateral side of healthy controls. We computed the proportional responses for PPT on the non-painful side if it fell below the 25th centile among the ipsilateral side of healthy controls. Each response PPT is considered for the Central Sensitisation Index (CSI). The 25th centile was suggested as a lower limit reference value for enhanced sensitivity.23 Each index was examined by Pearson’s correlation.

We determined whether patients with shoulder pain demonstrated peripheral, central, a mixed-pattern or no sensitisation, and analysed the association between sensitisation subgroups and the relevant baseline characteristics, including demographic and clinical variables. Comparisons among the variables were examined using one-way analysis of variance or χ² and assessment of 95% confidence intervals (CIs). A p value <0.05 was defined as statistically significant.

RESULTS

Recruitment and baseline characteristics

Between January 2014 and September 2014, 30 patients with shoulder pain (11 male, 19 female) were enrolled in this study. The average age of the 30 patients was 50.60±12.19 years (table 1). The healthy controls included 11 male and 19 female subjects with a mean age of 50.63±12.20 years. All participants were right-hand dominant.

PPT comparison of related acupoints

For the patients with shoulder pain, lower PPT levels were detected at acupoints on the painful side compared with the non-painful side (table 2). The differences were 94.90 (95% CI 53.47 to 136.33; p<0.001) at Tianzong (SI 11), 102.91 (95% CI 79.85 to 125.97; p<0.001) at Jianliao (SJ 14), 91.19 (95% CI 44.82 to 137.56; p<0.001) at Jianyu (LI 15) and 86.79 (95% CI 56.30 to 117.28; p<0.001) at Jianzhen (SI 9), respectively.

Table 2

<table>
<thead>
<tr>
<th>Patients with shoulder pain</th>
<th>Painful versus non-painful side</th>
<th>Healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (95% CI) p Value</td>
<td>Mean (95% CI) p Value</td>
<td></td>
</tr>
<tr>
<td>Non-painful side</td>
<td>Ipsilateral side</td>
<td>Non-painful side</td>
</tr>
<tr>
<td>Tianzong (SI 11)</td>
<td>414.83±135.61</td>
<td>509.73±168.05</td>
</tr>
<tr>
<td>Jianliao (SJ 14)</td>
<td>469.70±181.07</td>
<td>572.61±196.71</td>
</tr>
<tr>
<td>Jianyu (LI 15)</td>
<td>434.79±140.39</td>
<td>525.98±160.16</td>
</tr>
<tr>
<td>Jianzhen (SI 9)</td>
<td>453.08±154.54</td>
<td>539.87±167.59</td>
</tr>
<tr>
<td>Non-acupoints</td>
<td>521.34±147.02</td>
<td>538.67±163.89</td>
</tr>
</tbody>
</table>

Values are shown as mean±SD in kPa units.

![Figure 2](http://bmjopen.bmj.com/) Values (mean±SD) of the pressure pain threshold (PPT) at the non-acupoint.
The PPT value difference between the non-painful side of the patients and the ipsilateral side of healthy controls was also compared. PPTs at the acupoints on non-painful side of the patients were lower than those on the ipsilateral side of healthy controls. The differences were 57.71 (95% CI 24.72 to 90.70; p=0.001) at Tianzong (SI 11), 81.03 (95% CI 41.40 to 120.67; p<0.001) at Jianliao (SJ 14), 72.20 (95% CI 10.90 to 133.50; p=0.02) at Jianyu (LI 15) and 88.09 (95% CI 39.88 to 136.30; p=0.001) at Jianzhen (SI 9), respectively.

**PPT comparison of non-acupoint**

Figure 2 shows PPT at the non-acupoint. For patients, the analysis revealed no marked difference in PPT value (17.33 (95% CI −36.99 to 2.34; p=0.08) on the painful side compared with the non-painful side. Similarly, no significant difference of PPT level 10.51 was found between the non-painful side of the patients and the ipsilateral side of healthy controls (95% CI −18.87 to 39.89; p=0.47).

**Peripheral sensitisation index**

All measured acupoints demonstrated side-to-side difference in the patients. They were used to compute a peripheral sensitisation index (PSI). PPT values at acupoints on the painful side below the 25th centile of the non-painful side indicated peripheral sensitisation. The proportion of the patients with peripheral sensitisation was 77% at Tianzong (SI 11), 37% at Jianliao (SJ 14), 43% at Jianyu (LI 15) and 60% at Jianzhen (SI 9) (table 3). Significant correlation (Supplementary appendix table 2) was observed in PSI among Jianliao (SJ 14), Jianyu (LI 15) and Jianzhen (SI 9) (p<0.01). There was no significant association between PSI and other baseline variables (p>0.05) (Supplementary appendix table 3).

**Central Sensitisation Index**

The four measured acupoints demonstrated a difference between the non-painful side of patients and the ipsilateral side of healthy controls. Therefore, they were used to compute the central sensitisation index (CSI). The proportion of the patients with central sensitisation was 43% at Tianzong (SI 11), 57% at Jianliao (SJ 14), 63% at Jianyu (LI 15) and 60% at Jianzhen (SI 9) (table 3). A distinct and significant association (Supplementary appendix table 4) was observed between Jianliao (SJ 14) and Jianyu (LI 15) (p<0.01), Jianyu (LI 15) and Jianzhen (SI 9) (p<0.01) in CSI. Supplementary appendix table 5 showed no statistical significance correlations between CSI and relevant baseline characteristics (p>0.05).

**Comparison of peripheral and central sensitisation index**

The frequencies of the patients who had both PSI and CSI were 43% at Tianzong (SI 11), 30% at Jianliao (SJ 14), 40% at Jianyu (LI 15) and 50% at Jianzhen (SI 9), respectively (table 3). Significant correlation was observed between PSI and CSI in measured acupoints (p<0.05) (Supplementary appendix table 6). Table 4 shows that association between subgroups and gender approached statistical significance at the assessment acupoints (p<0.001). No significant association was observed between subgroups and other baseline variables (p>0.05).

**DISCUSSION**

Our results are in agreement with a peripherally sensitised state at acupoints which is determined by a difference of PPT values between the sides in patients with unilateral shoulder pain. Central sensitisation at acupoints was conducted by comparing pressure sensitivity in patients with that in age- and sex-matched healthy controls. No clear difference in PPT values was found at the non-acupoint among the painful side, non-painful side and ipsilateral side. To advance this line of research, association between peripheral and central sensitisation at acupoints was examined. We found that the patients had a significant association between peripheral and central sensitisation at measured acupoints. This finding demonstrates that there are two patterns of sensitisation at acupoints. In addition, three acupoints Jianliao (SJ 14), Jianyu (LI 15) and Jianzhen (SI 9) that are normally used for treating shoulder pain correlated with CSI and PSI.

Previous investigations reported that splanchnic diseases can induce mechanical hyperalgesia on the corresponding acupoints when pressed.21 Acupoints became activated or sensitised in pathological conditions. This phenomenon is called ‘acupoint sensitisation’. At some acupoints there appeared to be hypersensitivity towards temperature (heat sensitisation) or pain threshold (pain-sensitisation) under visceral pain.9 25 But unlike those studies, we examined acupoints in patients with musculoskeletal pain in this study.

Central sensitisation is challenging clinically, since no standard assessment exists. Some studies recommended the use of various modalities for pain sensitivity at local and distal locations.22 26 However, other research shows reduced PPTs at the painful and non-painful shoulder, but not at the muscle tibialis anterior.27–29 According to the ‘Criteria for the Classification of Central Sensitisation Pain’, patients with diffuse pain distribution, allodynia, and hyperalgesia are more likely to present with central sensitisation. One of the patterns of pain distribution is that patients have bilateral pain/mirror pain.17 In patients with shoulder pain, the increased sensitivity to mechanical

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**Table 3** Frequencies meeting the Peripheral Sensitisation Index (PSI) and Central Sensitisation Index (CSI) based on pressure pain threshold response

<table>
<thead>
<tr>
<th>Sites</th>
<th>PSI</th>
<th>CSI</th>
<th>PSI+CSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tianzong (SI 11)</td>
<td>23 (77)</td>
<td>13 (43)</td>
<td>13 (43)</td>
</tr>
<tr>
<td>Jianliao (SJ 14)</td>
<td>11 (37)</td>
<td>17 (57)</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Jianyu (LI 15)</td>
<td>13 (43)</td>
<td>19 (63)</td>
<td>12 (40)</td>
</tr>
<tr>
<td>Jianzhen (SI 9)</td>
<td>18 (60)</td>
<td>18 (60)</td>
<td>15 (50)</td>
</tr>
</tbody>
</table>

Values are individual counts (percentages).
### Table 4  Demographic, clinical and psychological characteristics of the sensitisation groups

<table>
<thead>
<tr>
<th></th>
<th>Peripheral sensitisation</th>
<th>Central sensitisation</th>
<th>Peripheral and central sensitisation</th>
<th>No sensitisation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tianzong</strong> (SI 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.78 (43.45 to 54.21)</td>
<td>50.38 (44.02 to 56.75)</td>
<td>50.38 (44.02 to 56.75)</td>
<td>56.57 (48.00 to 65.15)</td>
<td>0.47</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>78.28 (56.14 to 92.52)</td>
<td>76.92 (46.16 to 94.89)</td>
<td>76.92 (46.16 to 94.89)</td>
<td>14.29 (3.68 to 57.62)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain duration (weeks)</td>
<td>21.04 (12.91 to 29.17)</td>
<td>24.31 (10.23 to 38.38)</td>
<td>24.31 (10.23 to 38.38)</td>
<td>12.57 (7.16 to 17.99)</td>
<td>0.60</td>
</tr>
<tr>
<td>VAS</td>
<td>68.04 (61.25 to 74.84)</td>
<td>71.15 (62.77 to 79.53)</td>
<td>71.15 (62.77 to 79.53)</td>
<td>60.00 (52.45 to 67.55)</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>Jianliao</strong> (SJ 14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.09 (38.47 to 57.71)</td>
<td>49.59 (43.35 to 55.82)</td>
<td>48.89 (38.97 to 58.81)</td>
<td>53.27 (46.22 to 60.33)</td>
<td>0.78</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>100</td>
<td>82.35 (56.42 to 96.62)</td>
<td>100</td>
<td>27.27 (6.01 to 60.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain duration (weeks)</td>
<td>22.55 (10.81 to 34.28)</td>
<td>23.29 (12.80 to 33.79)</td>
<td>22.22 (7.96 to 36.49)</td>
<td>11.64 (7.07 to 16.21)</td>
<td>0.32</td>
</tr>
<tr>
<td>VAS</td>
<td>70.00 (59.17 to 80.83)</td>
<td>68.82 (61.14 to 76.51)</td>
<td>72.22 (59.60 to 84.84)</td>
<td>63.18 (53.41 to 72.95)</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>Jianyu</strong> (LI 15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.92 (38.29 to 55.56)</td>
<td>47.47 (41.20 to 53.75)</td>
<td>45.42 (36.64 to 54.19)</td>
<td>55.10 (48.95 to 61.25)</td>
<td>0.32</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>92.31 (63.76 to 99.81)</td>
<td>89.47 (66.90 to 98.70)</td>
<td>100</td>
<td>20.00 (2.54 to 55.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain duration (weeks)</td>
<td>19.69 (9.51 to 29.87)</td>
<td>21.89 (12.14 to 31.65)</td>
<td>20.67 (9.73 to 31.60)</td>
<td>14.80 (9.23 to 20.37)</td>
<td>0.76</td>
</tr>
<tr>
<td>VAS</td>
<td>68.46 (59.62 to 77.30)</td>
<td>66.84 (59.65 to 74.04)</td>
<td>66.67 (57.96 to 75.38)</td>
<td>62.50 (53.38 to 71.62)</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>Jianzhen</strong> (SI 9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.22 (41.53 to 54.91)</td>
<td>48.00 (41.35 to 54.65)</td>
<td>46.27 (38.65 to 53.88)</td>
<td>53.33 (45.49 to 61.17)</td>
<td>0.64</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>83.33 (58.57 to 96.44)</td>
<td>83.33 (58.57 to 96.44)</td>
<td>93.33 (67.97 to 99.83)</td>
<td>33.33 (7.45 to 70.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain duration (weeks)</td>
<td>17.11 (9.58 to 24.64)</td>
<td>18.22 (10.77 to 25.67)</td>
<td>18.67 (9.70 to 27.63)</td>
<td>24.00 (6.74 to 41.26)</td>
<td>0.78</td>
</tr>
<tr>
<td>VAS</td>
<td>67.78 (60.43 to 75.13)</td>
<td>66.67 (58.85 to 74.48)</td>
<td>68.00 (59.32 to 76.68)</td>
<td>65.00 (53.79 to 76.21)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Values presented as % (for sex) or mean with (95% CI).

VAS, Visual Analogue Scale.
input in the contralateral shoulder would be interpreted as central sensitisation. A large number of studies define central sensitisation as pain sensitivity at local and distal locations. We chose bilateral pain to define central sensitisation, unlike earlier studies, and to determine whether there existed patterns of experimental pain responses at shoulder acupoints.

Collectively, the findings of the study support the alteration in both peripheral and central sensitisation at acupoints in patients with musculoskeletal pain. We determined whether peripheral and central sensitisation were more likely to occur together or alone. Table 3 shows that 19 patients had central sensitisation and 13 patients had peripheral sensitisation in Jianyu (LI 15). A previous study showed that long-term peripheral sensitisation can lead to central nervous system changes, resulting in central sensitisation. However, six patients had central sensitisation only, without peripheral sensitisation. This result indicates that peripheral sensitisation is not a prerequisite for the presence of central sensitisation at acupoints. In PSI or CSI, a strong association was found at three acupoints—namely, Jianliao (SJ 14), Jianyu (LI 15) and Jianzheng (SI 9). Jianliao (SJ 14), Jianyu (LI 15) and Jianzheng (SI 9) are frequently chosen to treat shoulder pain in clinical practice, and have been called the ‘shoulder three acupoints’ by acupuncturists. They are highly refined acupoints used to treat shoulder pain in the clinic, and have been proved to effectively regulate muscle strength and tension of the shoulder joint. The strong association among Jianliao (SJ 14), Jianyu (LI 15) and Jianzheng (SI 9) is consistent with the concept of traditional Chinese medicine.

To our knowledge, this is the first study to research peripheral and central sensitisation at acupoints in patients with shoulder pain. One of the advantages of the study is that the measured acupoints and non-acupoint were marked by an acupuncturist with 24 years of experience in clinical acupuncture treatment. The evaluator who measured PPTs also had extensive experience with using an algometer and had no basic knowledge of acupoints. The internal validity was increased by blinding the evaluator, who did not know whether or not the measured sites were acupoints or whether the test participant was a patient or a healthy control. The participants were asked to take different positions when different acupoints were measured. For example, the participants were required to take a prone position on the examination bed with a suitable pillow under the chest and the arms close to the body when Jianzheng (SI 9) was measured as this increases the reliability of testing PPT over a soft area.

Specifically, the results indicate that peripheral and central sensitisation at acupoints is not relevant to pain duration. Moreover, there is no obvious evidence that the pattern of sensitisation is related to the degree of severity of the clinical condition as measured by a VAS. These changes are consistent with the idea of traditional Chinese medicine that acupoints are the crucial reflex points of body lesions under pathological circumstances. Hyperalgesia and skin sensitisation can occur at the corresponding acupoints in the presence of some diseases. Morphological structure studies have reported that the nervous system and blood vessels might have a close relationship with acupoints. For example, abundant microvessels existed at the acupoints of Zhongji (RN3) and Zusanli (ST36) in contrast to the surrounding tissues. The acupoints also have a high density of nerve endings including A- and C-afferent fibres. Those characteristics of higher concentration of neural, vascular elements and mast cells could make pain perception more sensitive, and might contribute to peripheral sensitivity.

To confirm the specificity of acupoints, we selected a non-acupoint in the infraspinatus muscle. No significant difference was found in PPT values among the painful/non-painful side of patients and the ipsilateral side of healthy controls. The finding proved that acupoints are the specific reflex points that respond to the presence of musculoskeletal pain. Our study provides evidence that there is an association between sensitisation of acupoints and gender. Pain difference in men and women has been increasingly studied in recent years, and lower PPT values in women than those in men were found both in healthy subjects and in clinical patients. But, the significant difference we found might be due to the fact that the majority of patients in the study (63.3%) were female.

This study has some limitations. First, pain perception is multidimensional. PPT measurements are a mechanical and standardised stimulation and are inadequate to describe the complexity of pain perception. A multimodal approach should be used to provide details of the pain system in both normal and pathophysiological situations, such as different stimulus modalities and quantitative assessment of various pain mechanisms. Second, the non-acupoint was chosen as 2 cm down from Tianzong (SI 11) because the shoulder blade is relatively flat and may reduce measurement errors between acupoints and non-acupoints. In a clinical trial published recently, the distance was one cun (2–3 cm) between the non-acupoints and acupoints, and clinical outcome showed that treatment of acupoints provided greater alleviation of symptoms than treatment of non-acupoints. In some studies including measurement of PPT the measured sites are adjacent. In our study the distance between the non-acupoint and Tianzong (SI 11) was 2 cm, which is acceptable. To reduce the stimulation effect, there is an approximately 2 min interval between the repetitions. The probability of stimulation by an acupoint that is too close is low but cannot be ruled out completely. In addition, ashi points, also called reflexing points or tender spots, are temporary acupoints, which are dissimilar from acupoints of the 14 meridians or extraordinary points. In general, ashi points have no specific names and definite locations, and will vanish after recovery from the disease. The aim of our study was to investigate the pattern of experimental pain responses at acupoints, which have specific names and definite locations and therefore the ashi points were not taken into account in this study. This
study was conducted in a single institution with a small sample size, so the external validity is unclear. Finally, this was a cross-sectional study, and it is not known whether the sensitisation experienced at acupuncture changes as the disease progresses. Further studies are needed to confirm the phenomena observed here.

CONCLUSIONS
In conclusion, mixed sensitisation patterns occur at acupuncture points in patients with unilateral shoulder pain and a strong correlation among Jianliao (SI 14), Jianyu (LI 15) and Jianzhen (SI 9). Future research using a multimodal pain approach should be conducted, as such suprathreshold heat pain response, to determine various sensitivity mechanisms.

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