Evidence that central sensitisation is present in patients with shoulder impingement syndrome and influences the outcome after surgery

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Impingement syndrome in the shoulder has generally been considered to be a clinical condition of mechanical origin. However, anomalies exist between the pathology seen in the subacromial space and the degree of pain experienced. These may be explained by variations in the processing of nociceptive inputs between different patients. We investigated the evidence for augmented pain transmission (central sensitisation) in patients with impingement syndrome, and the relationship between the presence of pre-operative central sensitisation and the outcomes following arthroscopic subacromial decompression.

We recruited 17 patients with unilateral impingement syndrome of the shoulder and 20 age- and gender-matched controls, all of whom underwent pre-treatment quantitative sensory testing, to detect thresholds for mechanical stimuli, distinctions between sharp and blunt punctate stimuli, and heat pain. Additionally Oxford Shoulder Scores to assess pain and function, and PainDETECT questionnaires to identify ‘neuropathic’ and referred symptoms were completed. Patients also completed these questionnaires three months after surgery.

A significant proportion of patients awaiting subacromial decompression experienced referred pain radiating down the arm and had significant hyperalgesia to punctate stimulus of the skin compared to controls (unpaired t-test, p < 0.0001). These are felt to represent peripheral manifestations of augmented central pain processing (central sensitisation).

The presence of either hyperalgesia or referred pain pre-operatively resulted in a significantly worse outcome from subacromial decompression three months after surgery (unpaired t-test, p = 0.04 and p = 0.005, respectively).

These observations confirm the presence of central sensitisation in a proportion of patients with shoulder pain associated with impingement syndrome. Also, if patients had evidence of relatively high levels of central sensitisation present pre-operatively, as indicated by higher levels of punctate hyperalgesia and/or complaints of referred pain, the outcome three months after subacromial decompression was significantly worse.

Shoulder pain is common and frequently disabling. The exact source of subacromial pain is unknown, but free
nerve endings containing substance P and calcitonin gene-related peptides are known to populate the subacromial space,¹ and it is hypothesised that they are the origin of nociception in impingement syndrome.

As with other musculoskeletal pain conditions, shoulder pain attributed to impingement syndrome is often associated with pain that is referred to sites remote from the site of the presumed primary pathology.² A recent study³ suggests that over half of patients with impingement syndrome experience paraesthesia that radiates into the forearm and which resolves following successful surgery. Similarly, experimental models of induced shoulder pain have shown a high incidence of pain referred into the arm.⁴,⁵

Associated with documented phenomena of referred pain, patients with painful musculoskeletal conditions have also been found to display increased sensitivity to painful stimuli within the referred pain area.⁵⁻⁷ Features of referred pain, hypersensitivity to peripheral stimuli and reports of ‘neuropathic’ pain symptoms are felt to represent peripheral manifestations of augmented central pain processing. This phenomenon is termed central sensitisation,²,⁸ which may be induced by long-term bombardment from peripheral nociceptors⁹ and may be mediated by alterations in the endogenous facilitatory/inhibitory systems.¹⁰,¹¹

To date, no attempt has been made to identify the sensory disturbances associated with radiating pain secondary to shoulder impingement syndrome. Also, the prevalence of neuropathic-like symptoms has not been reported in this population.

This study aimed to quantify the presence of somatosensory disturbances and neuropathic-like symptoms in a population of patients due to undergo subacromial decompression for impingement syndrome. It also aimed to correlate pre-operative psychophysical test findings and neuropathic-like symptoms with the post-operative outcome.

Patients and Methods
From the outpatient department of our institution we recruited 20 patients who were listed for arthroscopic subacromial decompression. All potential subjects met the following entry criteria: unilateral shoulder pain, with a contralateral Oxford Shoulder Score (OSS) ≥ 42; pain attributed to impingement, either primary or secondary to acromioclavicular joint pathology, and listed for an arthroscopic subacromial decompression procedure; absence of a full-thickness rotator cuff tear on high-definition ultrasound examination; absence of gleno-humeral osteoarthritis on plain radiography; no evidence of cervical radiculopathy. Each patient underwent high-definition ultrasound, and all but two were reported as normal, with those two having a suspicion of a partial-thickness tear.

One patient was excluded as they were subsequently found to have neck pain. Two were later excluded as they did not go on to have their operation at our institu-
tion. This left 17 patients remaining in the study for analysis. The pre-operative conditions of all 17 are summarised in Table I.

Additionally, 17 age- and gender-matched controls were recruited through local advertising, all of whom were free from shoulder pain with an OSS of 48.

The study was approved by the local research ethics committee and written informed consent was obtained. All participants underwent detailed quantitative sensory testing over both shoulders at the site overlying the deltoid insertion. Each site was tested for punctate sharpness threshold (the force at which punctate stimuli became painful/sharp) and sharpness of a 256 mN punctate stimulus (visual analogue scale (VAS) 0 to 10). Protocols for these tests were in line with those described previously.12 This process was repeated five times for each test site and a mean result was generated for analysis. All participants also completed questionnaires (OSS, PainDETECT, and the brief pain inventory) which was four weeks prior to their surgery for the patient group.

All patients underwent arthroscopic subacromial decompression at our institution, and three had an additional acromioclavicular joint excision. Two patients were found to have a full-thickness supraspinatus tear, and two had a partial-thickness tear. None of these were diagnosed pre-operatively on ultrasound, nor were they repaired. Each patient was found to have a normal glenohumeral joint. This information is summarised in Table II.

Post-operatively, participants underwent our standard rehabilitation regime, which involves early mobilisation from day one, once the nerve blocks have worn off, with scapular movements, pendular exercises, assisted active elevation and external rotation. Patients are then seen at four weeks in the extended-scope practitioner clinic, where emphasis is placed on scapular stability and regaining range of movement and rotator cuff control, provided that pain in the impingement range is reducing.

A longitudinal observational approach was used. Data from psychophysical assessment and self-completion questionnaires were collected. Patients were then contacted three months after their operation and asked to complete a new set of questionnaires.

Statistical analysis.

Results
There were approximately equal numbers of men and women in each of the two groups (M:F = 7:10) and there were no significant differences between their ages (mean age 55 for the patient group and 53 for control group; unpaired t-test, p < 0.001).

Pre-operatively, patients had a mean total OSS of 20 (sd 7.6) which improved to 34 (sd 7.1) three months after surgery (paired t-test, p < 0.001). The mean VAS for pain levels reduced significantly from 5.6 (sd 1.6) to 2.3 (sd 0.8) after surgery (paired t-test, p = < 0.001). No significant difference was found between the patients’
PainDETECT scores pre- and three-months post-operatively (paired $t$-test, $p = 0.517$), although the post-operative results were seen to be confounded by pain not arising from the shoulder. A total of 11 patients reported referred pain radiating down the arm, and six denied any referred pain. The results of the quantitative sensory testing are presented in Table III.

Analysis of pre-operative psychophysical testing. Patients’ affected shoulders had a lower detection threshold at which the mechanically induced pain from punctate stimuli were perceived as painful/sharp (Log data, paired $t$-test, $p < 0.001$). There were also significant differences in the perceived sharpness of a 256 mN probe applied over the shoulders ($p = 0.017$). The application of the stimulus to the affected shoulder resulted in significantly higher ‘sharpness’ ratings than to the unaffected shoulder. The results for these two modalities, both within the patient group (affected versus unaffected) and comparing controls with patients, are shown in Table III.

Between-group analysis. Analysis was made between the affected shoulder and the mean of the shoulders in the control group. The only difference in the sensitivity of the skin overlying the shoulder in the two groups was related to punctate stimuli. As shown in Table I, the affected shoulders in the patients group displayed a lower mechanical pain threshold than in the control group (unpaired $t$-test, $p < 0.001$); however, the VAS for pain when exposed to a 256 mN punctate stimulus was not significantly different (unpaired $t$-test, $p = 0.156$).

Analysis of post-operative psychophysical testing. There were no statistically significant relationships between pre-operative PainDETECT scores and mechanical pain thresholds with post-operative OSS.

Psychophysical tests as predictors of outcomes (correlation analysis). Pre-operative hyperalgesia, as measured by the mechanical pain threshold when dividing each variable into high/low groups by the median value, was found to have a significant role as a predictor of outcome of the post-operative OSS (Fig. 1). The presence or absence of referred pain pre-operatively was also found to have a significant role as a predictor of outcome of the post-operative score (Fig. 2).

Discussion

In line with other reports of outcome following arthroscopic decompression for impingement, our cohort was found to have a significant improvement in their OSS and mean pain scores three months after surgery.13

We found a significant difference in mechanical hyperalgesia to punctate stimuli between affected shoulders and between both contralateral shoulders and those of the control group. In line with the results reported here, the majority of previous authors have highlighted the mechanical hyperalgesia found at the site of musculoskeletal pain.4,6,14,15 These reports have used pressure devices to deduce the mechanical pain threshold,
although confirmatory data on punctate stimuli are available.\textsuperscript{16}

Pre-operative variables and their relationship to outcome. There was no significant relationship seen between total Pain-DETECT scores and the outcome of surgery. However, Figures 1 and 2 show that both the presence or absence of referred pain pre-operatively and relative hyperalgesia (as defined by dividing the responses in the patient group at the median value) have a significant relationship with the outcome after subacromial decompression three months after surgery. Specifically, the presence of referred pain, or higher levels of hyperalgesia, was associated with a worse outcome.

The process of quantitative sensory testing was liable to numerous potential confounders. In order to minimise these, in our study the tests were undertaken in the same air-conditioned room by a single investigator, using a single set of testing devices. However, other variables remained controlled such as variations in patient motivation, attention and reaction times.\textsuperscript{7}

In this study we could not establish a relationship between pre-operative and post-operative measures of absolute pain reported by VAS and PainDETECT, because many of the patients who completed post-operative PainDETECT scores referred to pains coming from sites away from the shoulder. These sources of pain had not been identified on the pre-operative questionnaires. The two possibilities are therefore that these pains not attributable to the shoulder are genuinely ‘new’ or have been unmasked since the shoulder pain was reduced. Regardless of the reasons, this observation highlights the importance of joint-specific outcome measures rather than general ‘pain’ assessments, owing to the possibility of confounding factors from joints not under investigation.

This is the first study to investigate the psychophysical alterations associated with referred pain in shoulder impingement syndrome. It has also identified that the presence of both relative hyperalgesia to punctate stimuli and referred pain pre-operatively results in a significantly worse outcome than if these two features are not present. This observation is the first indicator of heterogeneity within patients presenting with shoulder impingement syndrome, and suggests that the presence of CS\textsuperscript{2} negatively affects outcome.

Identifying the presence of CS\textsuperscript{2} in a proportion of patients with impingement syndrome has important consequences. First, it offers insights that might explain the observation that the amount of pain patients feel does not necessarily correlate with the pathology in the joint. Second, it may be appropriate, based on this finding, to subdivide patients entering clinical trials for impingement syndrome treatments into those with and without evidence of CS. This stratification may prevent the inappropriate abandonment of treatments that work in some patients and not in others when they present with the same apparent condition.
References


Fig. 1 Median split of the pre-operative mechanical pain threshold (Log). A significant difference is seen in the post-operative Oxford shoulder score between patients who were hyperalgesic before surgery and those who were not.

Fig. 2 When patients are separated into those with referred pain pre-operatively (n = 11) and those without (n = 6), a significant difference is seen between groups in terms of both pre-operative and post-operative Oxford shoulder score.
### Table I. Pre-operative conditions of the study subjects

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Diagnosis</th>
<th>Duration of pain (yrs)</th>
<th>Number of steroid injections</th>
<th>OSS*</th>
<th>Ultrasound of cuff</th>
<th>Radiography</th>
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<tr>
<td>1</td>
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<td>Normal</td>
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<td>3</td>
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<td>Normal</td>
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<td>2</td>
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<td>OA, ACJ</td>
</tr>
<tr>
<td>5</td>
<td>Impingement</td>
<td>2</td>
<td>5</td>
<td>13</td>
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<td>OA, ACJ</td>
</tr>
<tr>
<td>6</td>
<td>Impingement + ACJ† pain</td>
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<td>3</td>
<td>38</td>
<td>Intact</td>
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<td>Impingement</td>
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<td>4</td>
<td>25</td>
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<td>OA, ACJ</td>
</tr>
<tr>
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<td>3</td>
<td>37</td>
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<td>OA, ACJ</td>
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<td>34</td>
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<td>Normal</td>
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<td>Intact</td>
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<td>Impingement + ACJ† pain</td>
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<td>25</td>
<td>Intact</td>
<td>Normal</td>
</tr>
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<td>Impingement + ACJ† pain</td>
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<td>27</td>
<td>Intact</td>
<td>Normal</td>
</tr>
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<td>13</td>
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</tr>
</tbody>
</table>

* OSS, Oxford shoulder score  
† ACJ, acromioclavicular joint  
‡ OA, osteoarthritis  
§ PT, partial thickness tear suspected

### Table II. Procedures performed and intra-operative findings

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Procedure</th>
<th>Findings</th>
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<tbody>
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<tr>
<td>3</td>
<td>SAD</td>
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</tr>
<tr>
<td>4</td>
<td>SAD</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>SAD</td>
<td>Full-thickness tear supraspinatus</td>
</tr>
<tr>
<td>6</td>
<td>SAD</td>
<td>Partial-thickness tear supraspinatus</td>
</tr>
<tr>
<td>7</td>
<td>SAD</td>
<td>Nil</td>
</tr>
<tr>
<td>8</td>
<td>SAD + ACJ excision</td>
<td>Nil</td>
</tr>
<tr>
<td>9</td>
<td>SAD</td>
<td>Nil</td>
</tr>
<tr>
<td>10</td>
<td>SAD</td>
<td>Nil</td>
</tr>
<tr>
<td>11</td>
<td>SAD + ACJ excision</td>
<td>Nil</td>
</tr>
<tr>
<td>12</td>
<td>SAD + ACJ excision</td>
<td>Partial-thickness tear supraspinatus</td>
</tr>
<tr>
<td>13</td>
<td>SAD + ACJ excision</td>
<td>Nil</td>
</tr>
<tr>
<td>14</td>
<td>SAD</td>
<td>Full-thickness tear supraspinatus</td>
</tr>
<tr>
<td>15</td>
<td>SAD</td>
<td>Nil</td>
</tr>
<tr>
<td>16</td>
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<tr>
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</table>

* SAD, subacromial decompression, ACJ, acromioclavicular joint

### Table III. Results of quantitative sensory testing. All results are presented as means (SD). The raw data for mechanical pain threshold (Nm) was not initially normally distributed and are therefore reported as Log10[raw data] in line with previous reports12

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Patients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Right shoulder</td>
<td>Left shoulder</td>
</tr>
<tr>
<td>Log of mechanical pain threshold (Nm)</td>
<td>2.04 (0.346)</td>
<td>2.11 (0.248)</td>
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<tr>
<td>VAS rating of 256 stimulus (au)</td>
<td>4.3 (2.2)</td>
<td>4.1 (2.3)</td>
</tr>
</tbody>
</table>
Author queries

Page 1 Evidence: AQ - Reference 17 is not currently cited in the text. Please add it, or delete it.

Page 1 S. E. Gwilym: AQ - Please check all author names spelt correctly.

Page 1 NHS: AQ - Please provide the name of the institution where the research was carried out.

Page 1 S. E. Gwilym: AQ - Please provide the appointments, degrees, affiliations and full postal addresses for all authors.

Page 1 Med: AQ - Is this correct?

Page 2 Oxford Shoulder Score: AQ - Please provide a reference for the OSS.

Page 3 quantitative sensory testing: AQ - Is this the same as psychophysical testing?

Page 3 PainDETECT, and the brief pain inventory: AQ - Please give reference for each.

Page 3 psychophysical assessment: AQ - Please clarify what this includes.

Page 3 Statistical analysis: AQ - A section on statistical analysis is required reporting the figures used and why and the p-value for significance.

Page 3 approximately equal numbers: AQ - How many mean and women in each group? Both 7:10?

Page 3 mean age 55 for the patient group and 53 for control group: AQ - Please provide the ranges for each group.

Page 3 sd 7.1: AQ - Please give range, not SD.

Page 3 5.6 (sd 1.6): AQ - Please give range, not SD.

Page 3 2.3 (sd 0.8): AQ - Please give range, not SD.

Page 4 by pain not arising from the shoulder: AQ - Such as?

Page 4 256 mN: AQ - mN correct?

Page 4 no statistically significant: AQ - These results must be presented. Please add p-values.
Page 4 referred pain pre-operatively: AQ - This change ok? Otherwise not clear.

Page 5 single investigator: AQ - Author? Please give initials.

Page 5 CS: AQ - Meaning? Is it central sensitisation?

Page 5 CS: AQ - Meaning? Is it central sensitisation?

Page 5 CS: AQ - Meaning? Is it central sensitisation?

Page 6 No benefits: AQ - Is this statement correct?

Page 7 Table III: AQ - Please give range for all numbers in the table.

Page 7 Nm: AQ - Confirm these units should they be mN.

Page 7 Log10[raw data]: AQ - Do you mean 'log of the number 10' (Log10) or 'log of base 10' (log10)? Please clarify, as 10 must be either subscript or on the line here.

Page 7 0.348: AQ - Please give range.

Page 7 0.248: AQ - Please give range.

Page 7 0.341: AQ - Please give range.

Page 7 0.370: AQ - Please give range.

Page 7 256: AQ - Insert units.

Page 7 2.2: AQ - Please give range.

Page 7 2.3: AQ - Please give range.

Page 7 2.44: AQ - Please give range.

Page 7 1.61: AQ - Please give range.