Isometric exercise above but not below an individual's pain threshold influences pain perception in people with lateral epicondylalgia.

Brooke Kaye Coombes (PhD)¹; Matheus Wiebusch (B.Phty,Hons)²; Luke Heales (PhD)³; Aoife Stephenson (MSc)³; Bill Vicenzino(PhD)³

¹ The University of Queensland, School of Biomedical Sciences, Brisbane, Australia.

² Universidade Federal de Ciências da Saúde de Porto Alegre, Faculdade de Fisioterapia, Porto Alegre, Brasil.

³ The University of Queensland, School of Health and Rehabilitation Sciences, Division of Physiotherapy, Brisbane, Australia.

Address for correspondence:

Bill Vicenzino
School of Health and Rehabilitation Sciences: Physiotherapy
The University of Queensland
Building 84A
St Lucia QLD 4072
Phone: + 617 3365 2781
Fax: + 617 3365 1622
Email: b.vicenzino@uq.edu.au

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ABSTRACT

OBJECTIVE: To examine the acute effects of isometric exercise of different intensities on pain perception in individuals with chronic lateral epicondylalgia.

METHODS: Participants performed three experimental tasks completed in a randomised order on separate days: control (no exercise) and isometric wrist extension (10 x 15 sec) at load 20% below (infra-threshold) and 20% above (supra-threshold) an individual's pain threshold. Self-reported pain intensity (11-point numeric rating scales (NRS)), pressure pain threshold and pain free grip were assessed by a blinded examiner before, immediately after and 30min after task performance.

Correlation between pain ratings and clinical variables, including pain and disability and kinesiophobia was performed.

RESULTS: 24 individuals with unilateral lateral epicondylalgia of median 3-month duration participated. Pain intensity during contraction was significantly higher during supra-threshold exercise than infra-threshold exercise (Mean difference in NRS 1.0, 95%CI 0.4, 1.5, $p = 0.002$). Pain intensity during supra-threshold exercise was significantly correlated with pain and disability ($R=0.435$; $p=0.034$) and kinesiophobia ($R=0.556$, $p=0.005$). Pain intensity was significantly higher immediately after performance of supra-threshold exercise, compared to infra-threshold exercise ($p=0.01$) and control ($p<0.001$) conditions, while infra-threshold exercise and control conditions were comparable. Thirty minutes later, pain levels remained significantly higher for supra-threshold exercise compared to infra-threshold exercise ($p=0.043$). Pressure pain threshold and pain free grip showed no significant effects of time, condition, or time by condition ($p>0.05$).

DISCUSSION: Individuals with lateral epicondylalgia demonstrated increased pain intensity following an acute bout of isometric exercise performed at an intensity above, but not below, their individual pain threshold. Further investigation is needed to determine whether measurement of an individual's exercise induced pain threshold may be important in reducing symptom flares associated with exercise.

Key words: lateral epicondylalgia, isometric exercise, pain, hyperalgesia

INTRODUCTION

Lateral epicondylalgia, commonly known as tennis elbow, is an overuse tendinopathy affecting males and females predominantly between the ages of 35 and 54, with prevalence rates of 1-3% in the general population¹ and higher in high risk activities, such as tennis² or the fish processing industry.³ The dominant clinical features are pain over the lateral elbow aggravated by loading of the wrist extensors and reduced pain-free grip. Patients also display significant mechanical hyperalgesia at both local and remote sites.^{4,5} This finding, along with evidence of increased nociceptive withdrawal reflex⁶, and bilateral cold hyperalgesia in severe cases of lateral epicondylalgia⁴, implicate involvement of central sensitization mechanisms.

Exercise is an important component in the treatment and rehabilitation of patients with chronic pain. Although the therapeutic benefits of exercise for treatment of lateral epicondylalgia have been established,⁷⁻⁹ the immediate effects of exercise on pain perception are not known. Numerous studies show that in healthy individuals, acute exercise reduces sensitivity to painful stimuli, a phenomenon known as exercise-induced analgesia (EIA). Recent meta-analysis¹⁰ found isometric contractions of varying intensities produced moderate to large hypoalgesic effects during and immediately following contraction, with effects attenuating over 15-30 minutes. Similar effects were observed for both areas local and remote to the exercise body part, indicating isometric exercise exerts a generalised or central pain inhibitory response. Much less is known about the responses to acute exercise in adults with chronic pain, with some studies finding reduced pain perception (hypoalgesia)^{11, 12} and others finding increased pain perception (hyperalgesia).^{12, 13} The high variability suggests that dysfunctional EIA is not characteristic for all chronic pain patients, but may be limited to those with clear evidence of central sensitization (e.g. chronic whiplash, fibromyalgia or chronic fatigue syndrome).¹⁰

Exercise prescription for lateral epicondylalgia has been traditionally aimed at improving muscular strength and tendon remodelling,¹⁴ while its utility as a method of acute pain management is unclear. There is a paucity of research regarding the individual pain modulatory responses to exercise, as well as the optimal type and dose of exercise that is needed to modulate pain. The current study evaluated the effects of an acute bout of isometric exercise of the wrist extensor muscles on pain threshold and pain intensity in patients with unilateral lateral epicondylalgia. Our objectives were (1) to determine whether in comparison to a control condition, EIA occurs in the exercised elbow and non-exercised, contralateral elbow; (2) investigate whether EIA response differs when performed at an intensity above, or below, an individual's pain-free threshold.

MATERIALS AND METHODS

A blinded repeated-measures study with control comparison was used to compare the immediate effects of isometric exercise performed at an intensity above or below an individual's pain threshold on pain perception in patients with chronic unilateral lateral epicondylalgia. Participants were naïve to the experimental hypotheses. All participants attended the laboratory on 4 occasions: one screening session and 3 experimental sessions (two exercise and one control sessions). A washout period of approximately 48 hours separated each of the experimental sessions, which occurred at the same period of the day in a randomised order. The order of the experimental conditions was randomised by a research officer not involved in testing, using a computer-generated randomisation sequence. Allocation was concealed using sealed, opaque envelopes. Ethical approval was granted by the Medical Research Ethics Committee of The University of Queensland. All participants provided written consent at the commencement of first experimental session.

Participants

Between November of 2013 and May of 2014, residents of Brisbane, Australia, were recruited via advertisements in local press media, e-mails to academic community and social networking website. By accessing a link provided in the advertisement notices, participants could respond to an online survey with information regarding aspects of pain and injury history and the following validated questionnaires. The Patient Rated Tennis Elbow evaluation (PRTEE) was used as a condition-specific measure of pain and disability,¹⁷ with total scores ranging from 0 (no pain or disability) to 100 (significant pain and functional disability). The 11-item Tampa Scale of Kinesiophobia (TSK-11)¹⁸ was used as a measure of fear of movement or re-injury, with total scores ranging from 11 to 44, and higher scores indicating greater fear.

Potentially eligible individuals were invited to attend the laboratory for physical screening. To be included in this study, participants were required to be aged over 18 years, have experienced unilateral symptoms of lateral epicondylalgia for longer than six weeks, rate their worst pain during the past week as greater than 3 out of 10 on a numeric rating scale (NRS: 0 being no pain and 10 being worst pain imaginable), with a positive response to at least two of the following tests: pain on palpation of affected elbow, resisted wrist or middle finger extension, or while stretching the forearm muscles; and at least 30% deficit of pain free grip compared to the unaffected side.

Participants were excluded if they met at least one of the following criteria: symptoms over the contralateral side within the preceding 6 months; symptoms suggesting radicular, neurological or systemic arthritis conditions; other elbow pathologies, such as fracture, bursitis, medial epicondylalgia; history of conservative intervention(s), including exercise or physical therapy, within 3 months or injection within 6 months; occurrence of cervical or other arm pain which needed treatment or restricted participation in work or recreational activities within the preceding 6

months; pregnancy or breastfeeding. Participants were asked to avoid consumption of pain relieving medication in the 24 hours prior to testing sessions.

Outcome measures

Three measures with established reliability¹⁹ were used to quantify changes in pain perception: pain intensity (NRS), pressure pain threshold and pain-free grip force. A researcher blinded to the exercise condition collected the measures before, immediately after and 30 minutes after each experimental condition. Resting pain intensity was measured using NRS with endpoints 0 (no pain) and 10 (worst imaginable pain). Pain during contraction was also collected during each of the ten isometric contractions using the same scale.

Pressure pain threshold was measured with a digital algometer (probe size of 1cm²) (Somedic AB, Farsta, Sweden) using a standardised protocol¹⁹. Participants were positioned in supine lying, with the elbow in flexion and hand resting on the abdomen. Pressure was applied at a rate of 40kPa/s to the unaffected, followed by affected lateral epicondyle. Participants were instructed to press a button at the moment sensation changed from pressure to pressure and pain. Three measures with a 30 second interval were taken, with mean values used in analysis.

Pain-free grip force of the affected arm was measured with an electronic digital dynamometer (MIE Medical Research Ltd, United Kingdom) using a standardised protocol.²⁰ Participants were lying in supine, with the assessed limb by the side of the body, positioned in full elbow extension and forearm pronation. Participants were instructed to cease gripping the moment they felt the first sensation of pain. Maximal grip strength of the unaffected arm was tested first. This was used to generate a pain-free grip ratio (affected/unaffected%). Testing was repeated three times with an interval of 30 seconds.

Experimental conditions

One control condition and two exercise conditions were performed in a randomised order on separate days with a minimum 48 hour washout period. Instruction was provided by a researcher blinded to both outcome measurement and injury history.

A custom-made apparatus consisting of a digital force gauge (Chatillon® DFX-200, United States of America) and fixation for the wrist and forearm was designed for the exercise conditions (Figure 1). Participants were seated, with the tested limb in slight shoulder abduction, elbow flexed at approximately 90°, forearm in neutral pronation/supination and wrist in approximately 30° of extension. The dynamometer force gauge was positioned perpendicular to the distal metacarpal bones of the 2nd to 5th digits, allowing measurement of isometric wrist extension force (N). Participants were encouraged to avoid compensatory actions at other joints during testing. Prior to the commencement of each experimental session, maximal isometric wrist extension of the unaffected wrist and pain-free isometric extension of the affected wrist were measured three times with 30 second rest intervals. For testing of the affected arm, the participant was instructed cease applying force at the first onset of pain. The exercise load was determined from these pre-session measurements. Reliability testing in 12 healthy, pain-free young adults showed excellent test-retest reliability (ICC 0.98) for this measure.

For both exercise conditions, participants performed 10 isometric wrist extension contractions, each held for 15 seconds, with resting intervals of 15 seconds between contractions. Participants were able to monitor the force generated by visualising the gauge's display. For the "supra-threshold" exercise condition, they were asked to perform isometric contractions at a target intensity of 120% of their pain-free threshold. For the "infra-threshold" exercise condition, the target intensity was set

at 80% of their pain-free threshold. These intensities (at 20% above and below an individual's pain threshold) were chosen a-priori to explore whether pain experienced during exercise affects pain perception. Although the effects of intermittent isometric exercise are unclear, intermittent dynamic exercise, and not just continuous exercise, has been shown to be capable of producing EIA.¹⁰ An intermittent exercise protocol was adopted based on a previous study finding a hypoalgesic effect of therapeutic neck exercise (10second isometric holds x 10 contractions) in patients with chronic neck pain.²¹ For the control (no-exercise) condition, participants remained seated with the affected arm resting within the apparatus for an equivalent period of 4-minutes.

Statistical analysis

Tests for assumption of normality were performed before statistical analysis using IBM SPSS Statistics software (version 20.0) (SPSS Inc, Chicago, IL, USA). Pressure pain threshold and pain-free grip force were normally distributed and are reported as means and standard deviations. Analysis for each arm was performed using repeated-measures Analysis of Variance (ANOVA) with condition (control/supra-threshold exercise/infra-threshold exercise) and time (pre/0 minutes post/30 minutes post) considered within-subject effects. Pain intensity scores were non-normally distributed and are reported as median and interquartile range (IQR [1st – 3rd quartiles]). Wilcoxon signed-rank tests were used to evaluate differences between experimental conditions at each time point.

Pearson correlation was used to explore the relationship between pain during contraction and pain and disability (PRTEE) and kinesiophobia (TSK). Significance was set as $p < 0.05$. The sample size of 24 was assumed on the basis that a previous study of 24 individuals with lateral epicondylalgia showed statistically significant initial effects of a manual therapy treatment.²²

RESULTS

Twenty four individuals (13 males and 11 females) with a mean (SD) age of 52.0 (9.7) years consented to participate in this study (Figure 2). The median (IQR) duration of their symptoms was 3.0 (2.0 – 5.0) months and 79% involved the dominant arm. Worst pain during the previous week averaged 5.4 /10 (SD 1.6). Mean (SD) scores for pain and disability (PRTEE) and kinesiophobia (TSK-11) were 36.6 (13.0) and 23.1 (5.6) respectively.

Mean (SD) pain-free wrist extension measured 62.7N (29.1) for the affected arm and 131.6N (29.7) for the unaffected arm (MD 63.9N, 95% CI 51.0, 76.7, $p < 0.001$). Consequently, the infra-threshold exercise condition was performed at a mean (SD) load of 51.0N (25.7), while the supra-threshold exercise was performed with a mean (SD) load of 71.7N (30.4). These forces represented an average 38% and 55% of maximum strength of the unaffected side, respectively. All participants completed the exercise tasks and no adverse responses occurred.

Numerical ratings of pain intensity during each of the ten isometric contractions showed no effect of time ($p = 0.82$), indicating no significant temporal pattern during exercise (figure 3). Participants reported significantly greater pain during performance of supra-threshold exercise compared to infra-threshold exercise (MD 1.0/10 NRS, 95%CI 0.4, 1.5, $p = 0.002$). Average pain ratings during supra-threshold exercise were significantly correlated with both PRTEE ($R = 0.435$, $p = 0.034$) and TSK-11 ($R = 0.556$, $p = 0.005$) (figures 4a & 4b), indicating higher exercise-induced pain ratings in participants with higher pain and disability or greater kinesiophobia. No such correlations were seen for pain ratings during infra-threshold exercise.

Pain intensity experienced at rest prior to, immediately after and 30 minutes after the experimental conditions are illustrated in Figure 5. Prior to each of the experimental conditions, no significant differences in pain intensity between conditions were found ($p > 0.4$), demonstrating an effective washout period. Non-parametric (Wilcoxon Rank) tests showed significantly higher pain scores

immediately after supra-threshold exercise, compared with both infra-threshold exercise ($p = 0.01$) and control ($p < 0.001$) conditions. Thirty minutes after the tasks were performed, pain intensity remained higher for the supra-threshold exercise than infra-threshold exercise ($p = 0.043$).

Mean (SD) values for pressure pain threshold and pain-free grip force measured in the affected and unaffected arm are shown in the Table 1. Compared to the unaffected arm, the affected arm showed significantly lower pain-free grip force (MD 153.1N, 95% CI 127.2, 179.1, $p < 0.001$) and pressure pain threshold (MD 45.9KPa, 95% CI 3.9, 88.0, $P = 0.034$), indicating significant mechanical hyperalgesia. However, ANOVA showed no significant effects of time, condition or an interaction for either outcome.

DISCUSSION

To our knowledge, this is the first experimental study of the immediate effects of isometric exercise on pain perception in chronic lateral epicondylalgia. Our key findings were that isometric wrist extension exercise at an intensity 20% above an individual's pain threshold increased self-reported resting pain intensity immediately after exercise, while an identical exercise protocol at 20% below their pain threshold did not. Pain intensity remained significantly higher 30 minutes after supra-threshold exercise than infra-threshold exercise. Pressure pain threshold and pain-free grip force were not significantly altered by either supra-threshold or infra-threshold exercise. A secondary finding was that participants with greater self-reported pain and disability or with greater fear of movement or re-injury reported greater pain intensity during supra-threshold exercise, despite exercising at individually matched target loads.

Meta-analysis of experimental studies conducted in healthy individuals shows isometric exercise at similar intensities (40-50% maximum) and similar total durations (2-3 minutes) to this study produces large (standardised mean differences of >0.8) hypoalgesic effects across a range of stimulus modalities, as well as reduction in patient rated pain intensity.¹⁰ In the five studies that assessed pain measures at contracting and remote body areas in healthy individuals, an almost identical reduction in mechanical hypersensitivity was found at each site, suggesting isometric exercise exerts a generalised inhibitory response. Previous study in patients with fibromyalgia and myalgia demonstrated increased pain ratings and increased sensitivity to pressure pain stimuli following low load exercise compared to healthy controls¹². In our study of patients with unilateral lateral epicondylalgia, no changes in mechanical sensitivity were found for either the contracting or contralateral arm. Smaller sample size and a lack of healthy control reference group may underlie different results between studies.

A number of theories have been developed to explain why exercise produces contrary effects in chronic pain patients and healthy individuals. The exercise-induced resting lateral elbow pain found in our participants with lateral epicondylalgia, as well as other chronic pain populations, may be caused by an imbalance between endogenous pain inhibitory and facilitatory mechanisms.

Lannersten and Kosek¹² speculated that the lack of hypoalgesic response in patients with fibromyalgia and shoulder myalgia may occur because of an incapacity for additional recruitment of pain inhibitory mechanisms that are already activated by ongoing pain at baseline. Alternatively, excessive activation of muscle or tendon nociceptive afferents during painful, supra-threshold exercise may explain our findings of greater resting pain when compared to infra-threshold exercise and control. Long term pain stimulation in patients with chronic pain may lead to central neuroplastic changes favouring augmentation of spinal sensitivity and/or descending pain facilitation. Recent research using transcranial magnetic stimulation demonstrated altered cortical representation in patients with lateral epicondylalgia compared to healthy controls and changes

were correlated with resting pain intensity.²³ Another possible explanation for greater resting pain after the suprathreshold exercise is the participant attending more to the elbow during the painful exercise. This explanation ought to be tempered by an understanding that both isometric tasks required considerable attention by participants to match the target force during repeated contractions, and second, that the pain experienced during exercise was not of a very high level (Figure 3).

The strengths of this study include the blinded collection of outcome measures and comparison to a control condition, features which are often lacking in studies of pain perception¹⁰. We adopted a clinical measure of pain intensity, rather than experimentally induced pain stimulation, which may have affected the variability in this measure. In addition, we used novel assessment of each individual's pain threshold to determine the intensity of prescribed isometric wrist extension. While previous authors have confirmed the reliability of maximal wrist extension force using a handheld dynamometer and 'break' test,²⁴ we are the first to report excellent test-retest reliability for measuring pain free isometric wrist extension force. Although we did not set out to measure changes in pain-free wrist extension force over time, our reliability data indicates that differences of 18.7N or greater would be needed to be 95% confident of a difference.

There are three considerations which should be acknowledged. First, we did not test healthy individuals, hence we cannot be certain that the intermittent exercise protocol (ten sustained contractions, equivalent to 2.5minutes) adopted in this study produces hypoalgesia. Second, grip strength testing might be capable of inducing an analgesic response, but it was performed prior to each testing session and hence would be anticipated to have influenced outcome measures equally between sessions. Third, infra-threshold and supra-threshold exercise conditions differed in volume. This is probably not a major issue, as previous studies in healthy individuals suggests that EIA is a relatively robust response observed across a range of isometric exercise intensities and durations.¹⁰

Future studies should consider standardising the volume when comparing responses to different exercise protocols.

The results of this study provide a basis for a more systematic approach to understanding pain during exercise in managing chronic pain conditions, such as lateral epicondylalgia. An area in need of further exploration is the relationship between acute perception of pain during exercise and long term response to exercise. We concur with others,²⁵ that an absence of EIA does not imply that exercise is an ineffective therapy for chronic pain. On the contrary, response to acute exercise may in part explain the varied response to exercise observed in clinical studies.²⁶ Our findings suggest that severity of pain and disability or kinesiophobia may influence responses to acute exercise. Further research is needed to establish whether testing of EIA can help identify patients at risk of chronic pain and secondly whether exercise prescribed at 80% of an individual's pain threshold for at risk individuals leads to more optimal recovery. Further investigation is needed to determine whether measurement of an individual's exercise related pain threshold is a factor in optimal management of chronic pain conditions, including the reduction of symptom flares associated with exercise.

CONCLUSION

In patients with lateral epicondylalgia, increased self-reported resting pain intensity lasting beyond 30 minutes was found following acute isometric exercise, but only when contractions exceeded an individual's pain threshold.

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Figure 1: Digital force gauge and custom-made apparatus used for measuring and monitoring wrist extension force. A perpendicular force against the gauge's pad was applied during isometric contractions of the extensor muscles of the wrist at an angle of 30 degrees wrist extension.

Figure 2: Inclusion and exclusion eligibility flowchart.

Figure 3: Mean pain intensity ratings during each of the ten isometric wrist extension contractions performed at 20% below (infra-threshold exercise) and 20% above (supra-threshold exercise) individual pain threshold. NRS – numerical rating scale (0-10).

Figure 4: Average pain intensity during supra-threshold exercise: Relationships with self-reported pain and disability and kinesiophobia. Pearson correlation coefficient provided. PRTEE- Patient Rated Tennis Elbow Evaluation; TSK – Tampa scale of Kinesiophobia.

Figure 5: Pain intensity measured at rest on a numeric rating scale (NRS) before, immediately after and 30-minutes after the three experimental conditions: Data represents individual scores (closed markers) and how many times that particular score was rated; median (open markers) and 1st – 3rd quartiles (error bars). Control condition (circle), infra-threshold exercise (square), supra-threshold exercise (triangle).

Table 1: Pressure pain threshold (PPT) and pain-free grip (PFG) measurement prior to, immediately after and 30minutes after each experimental condition. Data represented by mean (SD).