

Osteoarthritis and Cartilage



Acute resistance exercise and pressure pain sensitivity in knee osteoarthritis: a randomised crossover trial



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SUMMARY

Objective: To determine whether a single bout of resistance exercise produces an analgesic effect in individuals with knee osteoarthritis (OA).

Design: Eleven participants with knee OA (65.9 ± 10.4 yrs), and 11 old (61.3 ± 8.2 yrs) and 11 young (25.0 ± 4.9 yrs) healthy adults performed separate bouts of upper and lower body resistance exercise. Baseline and post-exercise pressure pain thresholds were measured at eight sites across the body and pressure pain tolerance was measured at the knee.

Results: Pressure pain thresholds increased following exercise for all three groups, indicating reduced pain sensitivity. For the young and old healthy groups this exercise-induced analgesia (EIA) occurred following upper or lower body resistance exercise. In contrast, only upper body exercise significantly raised pain thresholds in the knee OA group, with variable non-significant effects following lower body exercise. Pressure pain tolerance was unchanged in all groups following either upper or lower body exercise.

Conclusion: An acute bout of upper or lower body exercise evoked a systemic decrease in pain sensitivity in healthy individuals irrespective of age. The decreased pain sensitivity following resistance exercise can be attributed to changes in pain thresholds, not pain tolerance. While individuals with knee OA experienced EIA, a systemic decrease in pain sensitivity was only evident following upper body exercise.

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Introduction

Exercise has long been regarded as a primary treatment modality for knee osteoarthritis (OA)^{1,2}. It improves both pain and function, but the underlying mechanisms have not been clearly identified³. One proposed mechanism is modulation of joint loading and stability, with a number of studies having demonstrated individuals with knee OA display reduced quadriceps strength^{4–6}. Therefore, research to date has focused predominantly on neuromechanical factors by exploring the notion that increased leg strength improves joint loading, leading to symptom reduction^{7–9}. While this hypothesis has been investigated in human and animal studies it remains speculative³. Moreover, recent studies have demonstrated that strength training interventions for knee OA

may improve symptoms with no accompanying change in joint moments or loads^{10–12}. These findings suggest that mechanisms other than neuromuscular changes might contribute to symptom reduction following strength training.

Sensitisation, both peripherally and centrally, has been implicated in the pain experience of knee OA^{13–15}. Exercise has been shown to transiently decrease pain sensitivity in healthy populations, which is termed 'exercise-induced analgesia' (EIA)^{16,17}. With EIA, the threshold at which a stimulus, such as mechanical, thermal or electrical stimulus, is deemed to be painful is typically elevated following a bout of exercise; hence pain sensitivity is reduced. The most accepted mechanism underlying EIA is the release of endogenous opioids^{16,18}, although multiple factors have been implicated in this phenomenon^{19–21}. The majority of research to date has focused on healthy populations, but there is growing evidence that EIA may occur in some chronic pain conditions yet be absent in others^{21,22}.

Aerobic exercise, the most commonly studied modality with respect to EIA, has been shown to cause an analgesic response lasting up to 30 min, whilst the analgesic response to resistance training has been shown to last up to 20 min^{16,17}. Although the

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duration of EIA is only relatively brief, understanding the way in which acute exercise influences the pain sensation in OA may provide insight into the means by which exercise can reduce pain in the longer term. There is also evidence, though less conclusive, that chronic exercise^{23,24} or even generally elevated levels of physical activity^{25,26} can reduce pain sensitivity. It is difficult to ascertain from existing studies of people with OA whether observed reductions in pain after chronic exercise were mediated by a direct influence on pain sensitivity or via other adaptations to exercise. If EIA does occur in people with OA, it would provide evidence that exercise can influence pain sensitivity directly.

The most common method for assessing EIA is via quantitative sensory testing^{20,27,28}. This involves experimentally exposing an individual to a quantifiable noxious stimulus and recording a response, such as pain threshold or intensity. Whilst there is some conjecture as to whether quantitative sensory testing reflects clinical pain, studies have shown that quantitative sensory testing is reliable in people with knee OA²⁹ and can differentiate between people with OA and healthy controls^{13,14,30}. Imamura *et al.* demonstrated that pressure pain thresholds both at the knee and at non-affected sites had a significant correlation with the Western Ontario and McMaster Osteoarthritis Index (WOMAC)³¹ pain and physical activity scores ($r^2 > 0.6$, $P < 0.001$)³². Quantitative sensory testing is being increasingly used in studies of knee OA^{17,21,33,34} and is more suitable than existing questionnaires for detecting transient changes in pain in response to acute interventions, such as exercise.

The primary aim of this investigation was to determine whether resistance exercise increased the threshold and tolerance of pressure pain in individuals with knee OA and, if so, whether this effect was systemic or confined to the exercising limbs. A secondary aim was to determine if this effect was similar in apparently healthy individuals of the same age, as well as a young healthy cohort, to examine potential age-related differences in EIA.

Method

Participants

Three groups of 11 participants were recruited: (1) a knee OA group; (2) an old healthy comparison group; and (3) a young healthy comparison group. The inclusion criterion for the OA group was a diagnosis of OA in one or both knees by a GP or rheumatologist. The healthy group participants were reportedly pain free. The WOMAC was used to assess knee pain and function³¹. WOMAC scores indicated that the OA group had mild to moderate symptoms. As a result, radiographic data were not collected given the discordance between radiographic damage and pain in this population³⁵. Exclusion criteria included: any current severe musculo-skeletal or neuromuscular disorders; absolute or uncontrolled cardiovascular contraindications to exercise; any form of arthritis (other than OA for the knee OA group); and classification of 'distressed somatic' or 'distressed depressive', according to the Distress and Risk Assessment Method (DRAM) questionnaire³⁶. Recruitment was performed via posters, along with data collection, at two exercise clinics in Sydney, Australia, so the majority of the participants were currently undergoing resistance training.

Study design and protocol

This was a randomized crossover experimental study of the effects of upper and lower body resistance training on pressure pain threshold and tolerance. This study was approved by the University of New South Wales Human Research Ethics Committee and the trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613001224718). Written informed consent was

obtained from each participant prior to testing. Participants attended the research laboratory on 3 days, each separated by at least 1 week. During the first visit, participants underwent baseline measures of pressure pain threshold and tolerance. The one repetition maximum (1RM, the maximum amount of weight an individual can lift once) was determined for each of the six resistance exercises (three upper and three lower body exercises, described below). On the second visit, participants were randomised to undertake a bout of either upper or lower body exercises, followed immediately by the pain assessments. On the third visit, participants undertook the alternative bout of exercise, followed immediately by the pain assessments. Participants were asked to refrain from taking any pain medications for 24 h prior to the testing. Subjects were randomised using a table created with a random number generator in Microsoft Excel. The sequence was generated by the researchers who assigned participants as they were enrolled. Since participants performed both bouts of exercise it was not possible to blind them. It was not possible to blind the assessors since the researchers assessed the outcomes and instructed the participants in the exercise bouts.

Pressure pain threshold

A Wagner Force Ten FDX-25 pressure algometer (Wagner Instruments, Greenwich CT) was used to determine pressure pain threshold. This device had a 1-cm diameter rubber footplate and measured the pressure in kg/cm². Pressure pain thresholds were measured at eight sites; four upper and four lower limb. All sites were on the right side of the body, unless injury precluded it, however for the OA group the most affected lower limb was used. The sites were the upper trapezius, biceps brachii, extensor carpi radialis longus, first dorsal interosseous, rectus femoris, vastus lateralis and tibialis anterior muscles, and the medial compartment of the knee. The muscles were assessed at the muscle belly, with the exception of the vastus lateralis, which was measured at the distal musculo-tendinous junction. The medial compartment of the knee has been shown to be the most sensitive to OA pain¹⁴ and was probed at the joint line, 2–3 cm medial to the inferior-medial corner of the patella. The algometer was placed on each site and the pressure increased at approximately 1 kg/s until the participant indicated the pressure had turned to pain. The investigators cycled through each site three times, which resulted in approximately 2–3 min rest between measures at each site. An average of the three tests was determined as the individual's pressure pain threshold. Pressure pain thresholds have been shown to be reliable in individuals with knee OA^{13,29} and in young healthy adults in pilot testing for this study.

Pressure pain tolerance

Pain tolerance was assessed at the medial joint line of the knee (as described above) with a custom-built device incorporating a force transducer in series with a 1-cm diameter rubber footplate. Since contextual factors can play a role in the pain experience³⁷, the assessment was always performed in the same room, at the same time of day and with the same information and instruction provided. Before the pressure was applied, the participant was asked to give an initial 0–10 pain rating on a scale measuring from 0 (no pain) to 10 (worst possible pain). A constant pressure (90% of the individual's baseline pain threshold) was then applied and maintained for 5 min or until the participant indicated that they could no longer tolerate the pain. The participants were asked to rate their pain every 30 s. The majority of participants ($n = 30$) were able to tolerate the pressure for the full 5 min so the mean pain rating across the time was taken to represent pain tolerance. The three

participants unable to complete the full 5 min were from the healthy groups. Since these participants had registered a pain rating of 10 when they terminated the tolerance task, the remaining time points were all given a rating of 10 to reflect the maximal pain experienced and enable inclusion in data analyses. Pilot testing had revealed the mean pain rating across the 5 min captured more of the variability between individuals than the peak pain rating and reliability of the pressure pain tolerance measure was confirmed in young healthy individuals across three non-consecutive days (intra-class correlation coefficient of 0.86). Given the established reliability of pressure pain threshold testing in young healthy individuals and older people with OA, it was assumed that pressure pain tolerance would be reliable in the knee OA and old healthy groups.

Resistance exercise

Each exercise bout consisted of three upper or lower body exercises on Nautilus-style machines. The upper body exercises were lat pulldown, seated row and chest press. The lower body exercises were leg press, leg curl and calf raise. For each exercise, three sets of 10 repetitions were performed at 60% of the individuals' 1RM. One-minute rest was given between sets. The basis for this modest volume and intensity of exercise was the low tolerance for exercise often accompanying knee OA³⁸. Following each set of exercise, participants were asked to rate their effort using a Borg Rating of Perceived Exertion (RPE) scale ranging from 6 (no exertion at all) to 20 (maximal exertion)³⁹. 1RMs were obtained on resistance machines under the supervision of an experienced clinician and standardised encouragement was given.

Statistical analysis and sample size

Repeated measures ANOVAs were performed using IBM Statistical Package for Social Sciences (SPSS, version 20) to assess an effect of exercise condition (within subjects: baseline, post lower-body exercise, post upper-body exercise) and group (between subjects: OA, old healthy, young healthy) at the level of $P = 0.05$. These analyses were performed for pain tolerance and the mean pressure pain threshold across eight sites. The location of pressure pain threshold measures (upper and lower body) was included in separate ANOVA models as an additional within subject factor, using the mean of the four lower limb or four upper limb measures. *T* tests were used to assess group differences at baseline (unpaired) as well as within-participant differences between baseline and post-exercise (paired) for pressure pain threshold and pressure pain tolerance.

To date there have been two studies examining pressure pain thresholds following dynamic resistance exercise^{18,27}, but both of these studies used a constant pressure and the time at which this became painful as their threshold measure. Studies that had examined the influence of exercise on pressure pain thresholds in units of pressure had been performed only for aerobic exercise and for isometric contractions⁴⁰. With this limited information, we estimated a mean change of 1 kg/cm² with a standard deviation of 0.5–1.0 kg/cm². On this basis a sample size of ≥ 10 was required to detect EIA with a paired sample *T* test (two tailed), 80% power and alpha of 0.05. A pressure of 1 kg/cm² approximates reported differences in pressure pain threshold distinguishing people with knee OA from healthy controls¹⁴. Hence, the study was powered to detect a magnitude of EIA consistent with, or slightly less than, previous reports for young healthy adults as well as a change in pressure pain threshold of possible clinical significance.

Results

Participant characteristics are presented in Table I. There were no dropouts or exclusions following randomisation, nor were any harm or unintended outcomes reported. Recruitment and assessments occurred between September 2011 and September 2012 and concluded when the planned sample size was reached. The OA and the old healthy groups were similar in age, BMI and mean 1RM ($P > 0.19$). The OA group reported a significantly higher WOMAC score than both healthy groups indicating worse knee pain and function ($P < 0.001$). Leg press provided a measure of lower limb strength involving the knee joint. The OA group had significantly lower leg press 1RM compared with the young healthy group ($P = 0.016$). The OA group had a lower leg press 1RM than the old healthy group but this was not significant ($P = 0.098$). The mean load used for each exercise (60% of the individuals' 1RM) and mean RPE are presented in Table II. The RPE for each exercise bout was not significantly different across all three groups ($P > 0.14$).

Baseline pain measures

The mean (SD) baseline pressure pain thresholds across all eight sites were: OA: 4.50 (1.34) kg/cm², old healthy: 4.64 (2.22) kg/cm² and young healthy: 5.95 (2.57) kg/cm². The mean (SD) baseline 0–10 ratings for the pressure pain tolerance test were: OA: 6.6 (1.9), old healthy: 5.6 (1.7), young healthy: 5.1 (2.0). While these threshold and tolerance data at baseline suggest increased pain sensitivity in the knee OA group, these differences were not statistically significant ($P > 0.13$).

Pain thresholds post-exercise

The mean pressure pain threshold following exercise was significantly increased across all three groups (main effect of exercise condition $P < 0.001$); pairwise comparisons revealed higher thresholds following the lower body and the upper body exercise, compared with baseline conditions ($P \leq 0.001$), and no difference between the two exercise conditions ($P = 0.605$). There was no group by exercise condition interaction ($P = 0.337$), suggesting pressure pain thresholds increased similarly for all groups after exercise when quantified as the mean across eight sites. Following upper-body exercise, the mean (SD) increases in pressure pain threshold (kg/cm²) were 0.87 for OA (1.18, $P = 0.018$), 0.57 for old healthy (0.84, $P = 0.007$) and 0.57 for young healthy (1.64, $P = 0.057$). Following lower-body exercise, the mean (SD) increases in pressure pain threshold (kg/cm²) were 0.61 (0.92, $P = 0.050$) for the old healthy group and 0.84 (1.64, $P = 0.012$) for the young healthy. However, for the OA group there was no clear increase for the pressure pain thresholds across eight sites after lower body exercise: 0.38 (1.19, $P = 0.304$). The effect sizes for the increase in pressure pain thresholds following lower and upper body exercise

Table I

Participant characteristics for the knee OA, old healthy and young healthy groups, presented as mean (SD). Mean 1RM is the maximum weight lifted averaged across six upper and lower body exercises

	OA (<i>n</i> = 11, 6♀ 5♂)	Old healthy (<i>n</i> = 11, 6♀ 5♂)	Young healthy (<i>n</i> = 11, 7♀ 4♂)
Age (yrs)	65.9 (10.4)	61.3 (8.2)	25.0 (4.9)*
Height (kg)	1.66 (0.10)	1.67 (0.11)	1.67 (0.11)
BMI	25.5 (3.2)	26.7 (4.2)	22.1 (3.0)*
Mean 1RM (kg)	44.8 (21.5)	49.7 (27.5)	62.9 (16.3)
Leg press 1RM (kg)	63.6 (39.0)	76.6 (48.5)	103.2 (26.7)*
WOMAC score	16.3 (6.4)	1.2 (2.2)*	0.8 (2.0)*

* Indicates significant difference relative to the OA group at the $P = 0.05$ level.

Table II

Mean (SD) loads in kg used for each resistance training exercise and mean (SD) RPE for each exercise bout for the knee OA, old healthy and young healthy groups

		OA	Old healthy	Young healthy
Lower body	Leg press	38.1 (18.8)	46.0 (28.4)	61.9 (16.5)
	Leg curl	19.4 (10.8)	21.5 (12.0)	18.3 (4.9)
	Calf raise	41.2 (18.0)	43.8 (24.8)	58.4 (12.7)
	Mean RPE	13.3 (1.5)	14.0 (2.1)	14.0 (1.9)
Upper body	Lat pulldown	24.9 (7.1)	27.8 (14.9)	32.6 (10.5)
	Seated row	24.5 (7.7)	26.8 (15.5)	30.7 (10.1)
	Chest press	19.1 (11.7)	17.6 (13.9)	24.7 (9.4)
	Mean RPE	13.0 (1.0)	13.9 (2.0)	13.7 (1.5)

for the OA group were 0.32 and 0.84, respectively. The corresponding effect sizes for the old healthy group (0.67 and 1.01) and young healthy group (0.93 and 0.64) showed less disparity between lower body and upper body exercise.

For subsequent analyses, pressure pain threshold data for the upper and lower limbs were separated and averaged across four sites, respectively, in order to investigate local and systemic effects of the exercise (Table III). For the young healthy and old healthy groups, upper-body and lower-body exercise resulted in a similar elevation of pressure pain thresholds for the lower body (Fig. 1) and the upper body (Fig. 2). For the OA group, upper body exercise resulted in significantly elevated pain thresholds at upper and lower body measures ($P \leq 0.029$), while lower body exercise had no effect on pain thresholds in the upper or lower body measures ($P > 0.30$).

Pain tolerance post-exercise

Pressure pain tolerance ratings are presented in Fig. 3 and Table IV. There was no significant change in mean pain tolerance ratings following upper or lower body exercise for any of the groups (Fig. 3) when assessed with paired sample *T* tests ($P \geq 0.064$). ANOVA did identify a significant main effect of exercise condition across groups ($P = 0.025$), with pairwise comparisons revealing a difference between baseline and the lower-body exercise ($P = 0.033$), but there was no group by exercise condition interaction ($P = 0.949$). However, when this ANOVA was repeated with the change in pressure pain threshold at the medial compartment of the knee as a covariate, to account for the use of the baseline PPT at the medial knee joint for all test conditions, the main effect of exercise condition disappeared ($P = 0.214$).

Discussion

This study examined the effects of a single bout of exercise on pressure pain threshold and pain tolerance in individuals with knee OA and young and old healthy adults. An acute bout of resistance

Table III

Mean (SD) pressure pain thresholds (PPT, kg/cm²) for the upper and lower limbs at baseline and following upper or lower body exercise for the knee OA, old healthy and young healthy groups

		Baseline	Post lower body exercise	Post upper body exercise
OA	Lower limb PPT	5.68 (1.92)	6.19 (2.20)	6.71 (2.25)*
	Upper limb PPT	3.32 (0.94)	3.59 (1.36)	4.04 (1.36)*
Old healthy	Lower limb PPT	5.87 (2.56)	6.59 (2.35)	6.46 (2.51)*
	Upper limb PPT	3.41 (1.99)	3.92 (1.82)	3.96 (1.81)*
Young healthy	Lower limb PPT	7.74 (3.67)	8.66 (4.18)*	8.32 (4.11)
	Upper limb PPT	4.07 (1.62)	4.82 (2.36)*	4.63 (2.25)*

* Indicates significant difference relative to baseline measures at the $P < 0.05$ level.

exercise significantly increased mean pressure pain thresholds in individuals with knee OA and young and old healthy adults. These results provide evidence of EIA in individuals with knee OA following resistance exercise.

The EIA in the knee OA group occurred after upper body exercise only, with no apparent change in pressure pain threshold in the knee OA group following lower body exercise. This may be explained by the large degree of variability in the individual pain thresholds in the knee OA group following the bout of lower body exercise. In some participants, pressure pain thresholds increased, whilst in others these decreased (+81% to -12%). This variability may be associated with symptom exacerbation in some individuals despite the modest intensity of the exercise. While the absence of a statistically significant difference in pressure pain thresholds may be attributed to the small sample size of this study, the magnitude of the effect of lower body exercise on pressure pain thresholds was notably smaller for people with knee OA. The comparatively smaller effect size for lower body exercise in the people with knee OA is indicative of the large variability in the response and suggests that the mechanisms underlying EIA were disrupted by individual-specific factors.

Notably, lower body pressure pain thresholds increased following a single bout of upper body resistance exercise. Likewise, upper body pressure pain thresholds increased following a bout of lower body resistance exercise, though not for the knee OA group. These results suggest that exercise produced an immediate reduction in pain sensitivity, even in non-exercised limbs and supports previous research showing a systemic analgesic effect using isometric contractions^{20,33,34,41}. The evidence of a systemic analgesic effect of exercise is, to our knowledge, the first such demonstration following traditional, dynamic resistance exercise in any population.

A systemic analgesic effect post-exercise suggests that the mechanisms underlying EIA are in part, centrally mediated. Pain processing is highly complex and occurs at peripheral, spinal and supraspinal levels and is modulated by descending inhibitory and facilitatory pain pathways⁴². It is believed that EIA is the result of increased activity in the descending inhibitory pathways mediated by neurotransmitters thought to include endogenous opioids, primarily, and possibly cannabinoids and neurotransmitters such as serotonin and norepinephrine among others^{17,21}. However in chronic pain conditions such as fibromyalgia, shoulder myalgia, chronic fatigue syndrome and chronic whiplash associated disorders, an analgesic effect has been shown to be absent when exercising painful muscles^{40,43}. Consistent with this, neither upper nor lower body pressure pain thresholds were increased for the knee OA group after performing lower body exercise. The absence of EIA in chronic pain patients may be associated with central sensitisation, a common phenomenon accompanying many chronic pain conditions⁴⁴.

One way in which central sensitisation may disrupt EIA in people with chronic pain is via an interaction between the inhibitory and facilitatory pain mechanisms. For example, when the knee is exercised in individuals with knee OA the already sensitised nociceptors increase the facilitatory drive more than the accompanying inhibitory drive. This results in a net increase in pain sensation, which several participants in the knee OA group in the present study experienced. In contrast exercising the non-affected limbs, such as the upper body or indeed any muscle of the healthy group, does not facilitate the pain pathways to the same extent as the concurrent inhibition, resulting in an analgesic response. Another possible explanation for the absence of the analgesic effect in chronic pain conditions is that the noxious input associated with performing a resistance exercise at the knee, acts to shut down or decrease the inhibitory inputs, thereby diminishing

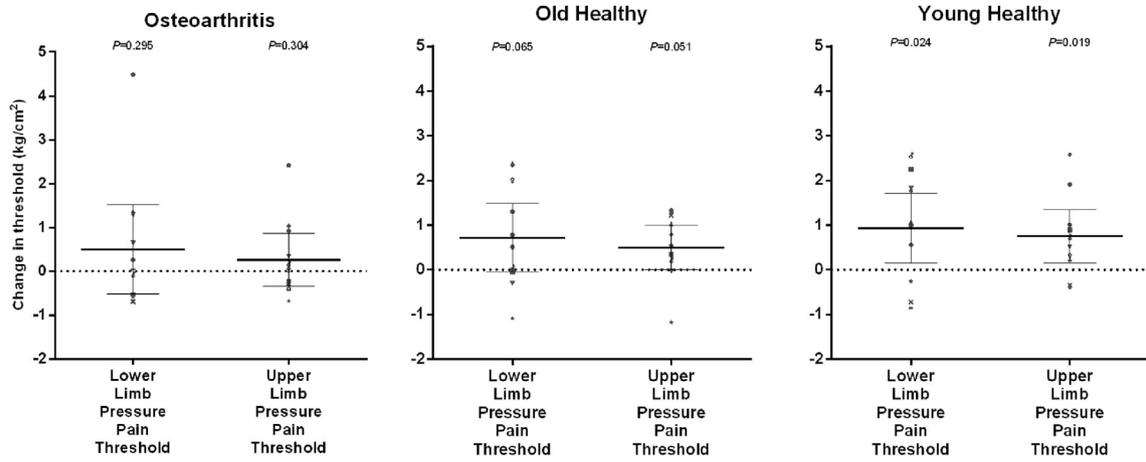


Fig. 1. Change in pressure pain thresholds following a single bout of *lower body resistance exercise* in knee OA, old healthy and young healthy groups. Pressure pain threshold (kg/cm²) is averaged across four lower limb or four upper limb sites. Individual data (symbols), and group mean and 95% confidence intervals (bold line with error bars) are displayed. *P* values are from paired sample *T* tests.

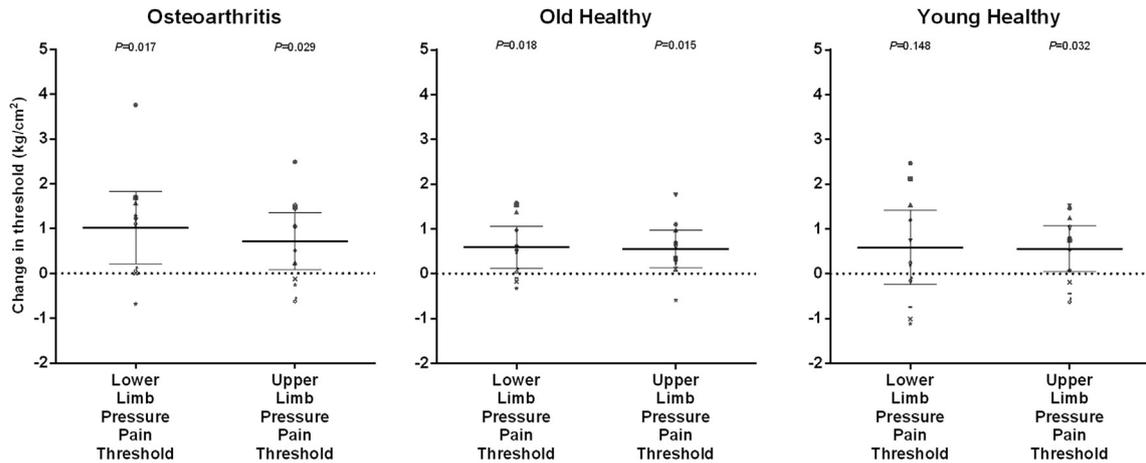


Fig. 2. Change in pressure pain thresholds following a single bout of *upper body resistance exercise* in knee OA, old healthy and young healthy groups. Pressure pain threshold (kg/cm²) is averaged across four lower limb or four upper limb sites. Individual data (symbols), and group mean and 95% confidence intervals (bold line with error bars) are displayed. *P* values are from paired sample *T* tests.

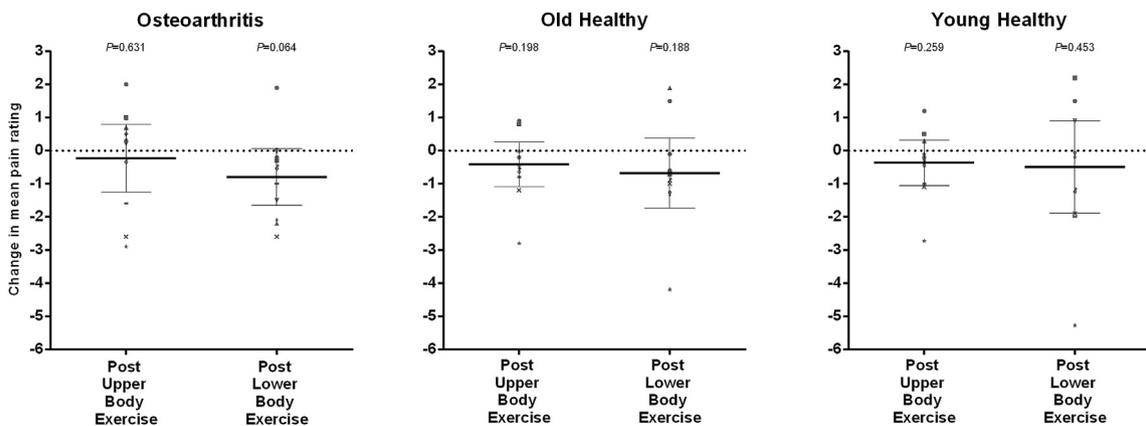


Fig. 3. Change in pain tolerance at the knee joint following a single bout of lower or upper body resistance exercise in knee OA, old healthy and young healthy groups. Pain ratings were reported on a 0–10 scale every 30 s throughout the 5-minute test and the mean of these ratings were used. Individual data (symbols), and group mean and 95% confidence intervals (bold line with error bars) are displayed. *P* values are from paired sample *T* tests.

Table IV

Mean (SD) pain ratings averaged over the 5 min test of pressure pain tolerance for the knee OA, old healthy and young healthy groups at baseline and post-exercise

	Baseline	Post lower body exercise	Post upper body exercise
OA	6.6 (1.9)	5.8 (1.9)	6.4 (2.2)
Old healthy	5.6 (1.7)	5.0 (2.5)	5.2 (2.0)
Young healthy	5.1 (2.2)	4.6 (1.5)	4.7 (1.7)

the analgesic response. Regardless of the cause, the EIA or lack thereof in knee OA (or other conditions) appears to be highly individualised. As seen in the present study, there was a wide variance in response of the OA group to the lower body exercise.

Following the bouts of exercise, *pressure pain tolerance* was unchanged in the OA, old healthy and young healthy groups (Fig. 3). Our measure of pain tolerance was conducted over a 5 min period during which participants were asked to rate their pain every 30 s. This task required a greater degree of cognitive processing than the threshold testing, due to constant monitoring and rating of the pain over an extended time period. Many factors including context, attention, expectation, fear, anxiety and past pain experiences can influence pain processing and may have influenced our pain tolerance results. For example, attention to a painful stimulus influences pain perception⁴⁵, while distraction from a painful stimulus can attenuate pain perception⁴⁶. Reporting the pain ratings every 30 s in the absence of any distraction may have increased the participants' attention to the painful stimulus, augmenting pain perception. Threat expectancy during the 5 min pressure pain test may have influenced the participants' perception of the pain³⁷. Other highly individualised cognitive processes associated with fear, anxiety and previous pain experiences may also have contributed to the pain tolerance results⁴⁷. It appears that a test of pain sensitivity under greater influence of higher processing is less sensitive to exercise than simple measures of pain threshold.

Although the pain experience of people with knee OA can involve psychological factors, such as fear and anxiety⁴⁸, the pain tolerance measure was still unaffected in this group. Studies that have shown global self-reported pain to decrease with exercise training in individuals with OA^{1,2} have not assessed which aspect of the pain experience is affected. Somewhat in contrast to our results are previous findings that in healthy individuals chronic training increases pain tolerance but not pain threshold²⁴. It may be that long-term training increases an individual's pain tolerance, whilst the immediate effects of a single exercise bout modulate pain thresholds. Regardless, the demonstration that acute exercise can reduce pain sensitivity in people with knee OA hints at the possibility that a reduction in pain sensitivity may be part of the adaptive response to chronic exercise.

A limitation of this study is uncertainty regarding the duration of the analgesic response to exercise. It has been shown that analgesia following aerobic exercise can last as long as 30 min, while the effect following resistance exercise is of shorter duration^{16,17}. In this study, pain was measured immediately following exercise, with no follow up measures. It would be of interest to measure how long the analgesic response lasted with repeated measures after exercise. A further limitation was the small sample size, which may have contributed to the lack of between-group differences¹³ and some within-group effects lying on the margin of statistical significance.

The findings of this study may have clinical implications. Firstly, individualised prescription should be recommended for knee OA since exercising the affected limb at 60% 1RM reduced pain sensitivity in some of the knee OA group yet increased sensitivity in others. For knee OA patients with a low tolerance for lower-body

exercise, conservative individualised exercise prescription is likely to reduce the risk of symptom exacerbation. Secondly, and a key finding of this study, exercising unaffected limbs may produce a systemic analgesic response without the risk of symptom flare up, though the duration of this effect is unclear and the analgesic response was measured for experimentally induced pain rather than specific clinical symptoms of knee OA. As noted in the introduction, quantitative sensory testing is reliable in individuals with knee OA²⁹, can distinguish between individuals with knee OA and healthy controls^{13,14,30} and also correlates with WOMAC scores³². Despite this evidence, caution should be taken when inferring clinical significance from a change in experimentally induced pain. Notwithstanding these limitations, for those individuals with a poor tolerance of lower-body exercise, such as people just commencing an exercise intervention, upper-body exercise may be prescribed to evoke an analgesic response. It remains to be determined if and how this acute effect of resistance exercise on pain sensation may manifest as an adaptation to chronic exercise.

Registration

This trial has been registered with the Australian and New Zealand Clinical Trials Registry, registration number ACTRN12613001224718. The universal trial number (UTN) with the World Health Organisation (WHO) is U1111-1149-9258.

Contributions

Author contributions are as follows:

- Nick Burrows (n.burrows@unsw.edu.au)
 - Conception and design
 - Analysis and interpretation of the data
 - Drafting of the article
 - Final approval of the article
 - Collection and assembly of the data
- John Booth (john.booth@unsw.edu.au)
 - Conception and design
 - Analysis and interpretation of the data
 - Critical revision of the article for important intellectual content
 - Final approval of the article
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 - Analysis and interpretation of the data
 - Critical revision of the article for important intellectual content
 - Final approval of the article
 - Statistical expertise
 - Administrative, technical or logistic support

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Competing interests

There are no competing interests to declare.

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