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Exercise Increases Pressure Pain Tolerance but Not Pressure and Heat Pain Thresholds in Healthy Young Men

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Abstract

Background: Exercise causes an acute decrease in the pain sensitivity known as exercise-induced hypoalgesia (EIH), but the specificity to certain pain modalities remains unknown. This study aimed to compare the effect of isometric exercise on the heat and pressure pain sensitivity.

Methods: On three different days, 20 healthy young men performed two submaximal isometric knee extensions (30% maximal voluntary contraction in 3 min) and a control condition (quiet rest). Before and immediately after exercise and rest, the sensitivity to heat pain and pressure pain was assessed in randomized and counterbalanced order. Cuff pressure pain threshold (cPPT) and pain tolerance (cPTT) were assessed on the ipsilateral lower leg by computer-controlled cuff algometry. Heat pain threshold (HPT) was recorded on the ipsilateral foot by a computer-controlled thermal stimulator.

Results: Cuff pressure pain tolerance was significantly increased after exercise compared with baseline and rest ($p < 0.05$). Compared with rest, cPPT and HPT were not significantly increased by exercise. No significant correlation between exercise-induced changes in HPT and cPPT was found. Test–retest reliability before and after the rest condition was better for cPPT and CPTT (intraclass correlation > 0.77) compared with HPT (intraclass correlation = 0.54).

Conclusions: The results indicate that hypoalgesia after submaximal isometric exercise is primarily affecting tolerance of pressure pain compared with the pain threshold. These data contribute to the understanding of how isometric exercise influences pain perception, which is necessary to optimize the clinical utility of exercise in management of chronic pain.

Significance: The effect of isometric exercise on pain tolerance may be relevant for patients in chronic musculoskeletal pain as a pain-coping strategy.

What does this study add?

- The results indicate that hypoalgesia after submaximal isometric exercise is primarily affecting tolerance of pressure pain compared with the heat and pressure pain threshold.
- These data contribute to the understanding of how isometric exercise influences pain perception, which is necessary to optimize the clinical utility of exercise in management of chronic pain.

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1 Introduction

Efficiency of the endogenous pain inhibitory pathways can be assessed by paradigms of exercise-induced hypoalgesia (EIH) (Lannersten and Kosek, 2010) with recordings of pain sensitivity before and after an exercise condition. Isometric muscle exercises have been linked to modulation of pain sensitivity in healthy subjects (Hoeger Bement et al., 2008, 2014; Vaegter et al., 2014) and in patients with chronic pain (Hoeger Bement et al., 2011; Vaegter et al., 2016). Moreover, it has been hypothesized that impaired EIH may be indicative of a dysfunction of the pain inhibitory systems (Lannersten and Kosek, 2010). In healthy subjects, EIH after isometric exercises are often demonstrated as an increase in pressure pain thresholds (Koltyn et al., 2001; Kosek and Lundberg, 2003; Koltyn and Umeda, 2007; Hoeger Bement et al., 2008, 2009, 2014; Umeda et al., 2010; Lemley et al., 2014, 2015; Vaegter et al., 2014) or a decrease in heat pain ratings (Koltyn et al., 2014; Misra et al., 2014; Naugle et al., 2014).

Few studies on EIH have assessed both heat pain and pressure pain sensitivity modalities (Cook et al., 2010; Kodesh and Weissman-Fogel, 2014; Naugle et al., 2014), and no studies have directly compared these modalities at the same time. Furthermore, heat pain thresholds and pain tolerance are rarely assessed, and no studies have compared the effect of isometric exercise on different aspects of pain sensitivity. Such a comparison will significantly contribute to the understanding of how physical activity influences pain perception, which is necessary to optimize the clinical utility of physical activity as a method of pain management. The potential effect of exercise on pain tolerance could be relevant for patients in chronic pain as a pain-coping strategy. In addition, it has been recommended to include a range of stimulus intensities in the assessment of experimental pain sensitivity to reveal potential effects that are manifest with more painful stimuli (Greenspan et al., 2007). Moreover, different nociceptive pathways in skin and muscles are evoked by varying stimulation modalities, and responses to different experimental pain modalities should be assessed in combination to improve understanding of the pain experience (Neziri et al., 2011).

Previously, it has been demonstrated that input to dorsal horn neurons from muscle nociceptors is subject to stronger descending inhibition compared with input from cutaneous nociceptors (Yu and Mense, 1990), and it may be hypothesized that the magnitude of EIH would be greater for assessment in the deeper musculoskeletal structures compared with assessment on the skin.

The primary aim of this study was to compare heat pain threshold, pressure pain threshold and pressure pain tolerance before and after isometric exercise and quiet rest in healthy young men. It was hypothesized that (1) isometric exercise would increase pressure pain thresholds as well as pressure pain tolerance compared with quiet rest, (2) the hypoalgesic response to exercise would be greater in the deeper tissues compared with the skin and (3) the exercise-induced changes in heat and pressure pain thresholds would not be correlated.

2 Methods

2.1 Subjects

In this study 20 healthy young men (age: 24.4 ± 2.0 years; body mass index: 24.8 ± 2.1 kg/m^2; 18 with right side dominance) were included. Due to potential gender-related differences in pain modulation capacity (Popescu et al., 2010) and EIH (Koltyn et al., 2001), only young men between 18 and 30 years of age were included in the study. Subjects were recruited by advertisement at the local university and the local physiotherapy school. All subjects were naive to experimental pain testing. None of the included subjects suffered from neurological, psychological, cardiovascular diseases, had any pain or used any pain medication during the weeks prior to participation. All subjects were asked to refrain from physical exercises, coffee and nicotine on the days of participation. The study was conducted in accordance with the Declaration of Helsinki, approved by the local ethical committee (S-20140203) and all subjects provided written informed consent.

2.2 Procedure

Each subject was assessed at the same time of day on three different days separated by 1 week (Fig. 1). In the first session, subjects were thoroughly introduced to the procedures for the pain sensitivity assessments by drawings as well as verbal instructions. All pain sensitivity assessments were performed with the subject seated on a plinth without foot support. In the beginning of each of the three sessions all subjects completed 1–2 practise trial with assessment of heat and pressure pain sensitivity on the leg not used for assessment of EIH to ensure that all participants understood the procedures. Each session lasted approximately 30 min. All assessments were performed by a male experimenter.

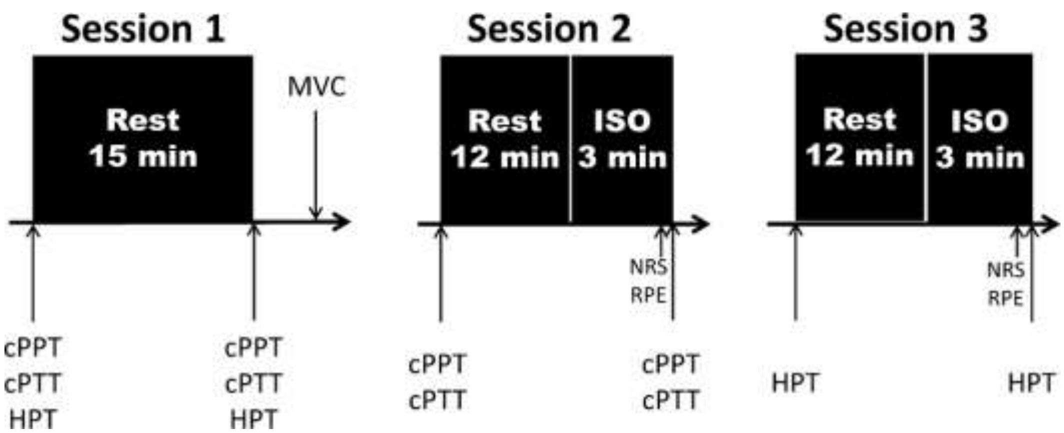

Figure 1. Illustration of the experimental procedure performed on the three testing days. Session 1: The sensitivity to heat pain and pressure pain was assessed before and immediately after a 15 min control condition (quiet rest). The sequence between assessment of heat and pressure pain sensitivity was randomized and counterbalanced. Following rest the maximal voluntary contraction (MVC) for isometric knee extension was determined. Sessions 2 and 3: Before and immediately after a 15 min active condition (a 3 min submaximal isometric knee extension at 30% of MVC with the dominant leg preceded by 12 min rest) the sensitivity to either heat pain or pressure pain was assessed. The sequence between sessions 2 and 3 was randomized and counterbalanced. MVC, maximal voluntary contraction; NRS, numerical rating scale; RPE, rating of perceived exertion; cPPT, cuff pressure pain threshold; cPTT, cuff pressure pain tolerance; HPT, heat pain threshold.

2.2.1 Session 1

Before and immediately after a 15 min control condition (quiet rest), the sensitivity to heat pain and pressure pain was assessed. The sequence between assessment of heat and pressure pain sensitivity was randomized and counterbalanced. Subjects were instructed to relax comfortably in a supine position on a plinth for 15 min in a temperate and undisturbed room with the light subdued. Following the control condition, the maximal voluntary contraction (MVC) for an isometric knee extension with the dominant leg was determined. Subjects were seated on a table with full support of the whole thigh. The dominant leg was strapped above the ankle to the force transducer (Commander Muscle Tester, Powertrack II; JTECH Medical, Midvale, UT, USA). The MVC during isometric knee extension was determined in a position of ninety degrees of knee flexion. Three maximal contractions separated by one min between contractions were performed and the average MVC was used to determine the submaximal value.

2.2.2 Sessions 2 and 3

Before and immediately after a 15 min active condition (initiated with 12 min rest followed by a 3 min submaximal isometric knee extension at 30% of MVC with the dominant leg), the sensitivity to either heat pain or pressure pain was assessed on the exercised leg. The intensity and duration of contraction was chosen based on previous studies in healthy subjects, which have shown robust EIH at this intensity (Kosek and Ekholm, 1995; Vaegter et al., 2014). During the sustained sub-maximal isometric contractions, subjects were required to match the target force as displayed on the monitor of the force transducer. The subjects were verbally encouraged to sustain the force throughout the 3 min. The sequence between sessions 2 and 3 was randomized and counterbalanced. Rating of perceived exertion (RPE; Borg Scale: 6-20) and rating of perceived pain (0–10 numerical rating scale, NRS) during isometric knee extension were assessed just before completion of the knee extension.

2.3 Assessment of heat pain sensitivity

Heat pain threshold (HPT) was assessed by a computer-controlled surface thermode (MSA Thermal Stimulator; SENSELab, Somedic Sales AB, HÖrby, Sweden) covering a 25 × 50 mm skin area on the dorsum of the dominant foot. The method of limit was used where the temperature started at baseline of 32 °C and increased by 1.0 °C/s with a maximum of 50 °C. As soon as the heat sensation was defined as first sensation of pain, the subjects were instructed to press a handheld switch. The peak temperature was stored and the thermode instantly decreased its temperature (3.0 °C/s) to the baseline of 32 °C. The thermal stimulus was repeated three times and the average heat pain thresholds were calculated.

2.4 Assessment of pressure pain sensitivity

Pressure pain thresholds (cPPT) and pressure pain tolerance (cPTT) were assessed by computer-controlled cuff algometry (Nocitech, Denmark and Aalborg University, Denmark). A 13-cm-wide silicone tourniquet cuff (VBM, Sulz, Germany) with an equal-sized proximal and distal chamber was wrapped around the dominant lower leg. The cuff was mounted with a 5 cm distance between its upper rim and the tibial tuberosity. The cuff pressure was increased with a rate of 1 kPa/s in both chambers and the maximal pressure limit was 100 kPa. The maximal pressure limit was based on the maximum capacity of the system. Air was supplied from a 200 L external air tank to avoid loud noises from the cuff system during assessment. The participants used an electronic visual analogue scale (VAS) to rate their pressure-induced pain intensity and a button to release the pressure. The electronic VAS was sampled at 10 Hz. Zero and 10 cm extremes on the VAS were defined as 'no pain' and as 'maximal pain', respectively. The participants were instructed to rate the pain intensity continuously on the electronic VAS from when the pressure was defined as first sensation of pain and to press the pressure release button when the pain was intolerable. The pressure value, when the subject rated the sensation of pain as 1 cm on the VAS, was defined as the pain threshold (cPPT) and when the subject terminated the pressure inflation was defined as the tolerance (cPTT). In case the maximum pressure stimulation was achieved before reaching the cPTT, 100 kPa was used for further analysis as a conservative estimate of the cPTT.

2.5 Statistics

The distribution of HPT, cPPT, cPTT, pain intensity scores (NRS) and the ratings of perceived exertion (RPE) during isometric contractions did not deviate significantly from normality (Shapiro–

Wilks test: $p > 0.06$). The effect of sequence between assessment of heat pain and pressure pain sensitivity on HPT, cPPT, and cPTT prior to rest was analysed with paired *t*-tests. The effects of exercise and rest on heat pain and pressure pain sensitivity were analysed with mixed-model repeated-measures analysis of variances (RM-ANOVAs) with time (before and after) as repeated measure and condition (active and control) as group factor. Effect sizes between active and control conditions were determined using partial eta squared. Due to significant difference in HPT before rest and exercise conditions, the percentage change in heat and pressure pain sensitivity before and after isometric exercise and rest was calculated. The distribution of percentage change after isometric exercise deviated from normality (Shapiro–Wilks test: $p < 0.001$) and the percentage differences were compared with non-parametric Wilcoxon Signed Rank test. The Friedman test was used to analyse the percentage change in heat and pressure pain sensitivity after exercise with the factor *modality* (heat pain threshold, pressure pain threshold, pressure pain tolerance). In case of significant factors or interactions in ANOVAs or Friedman test, Bonferroni corrected *post-hoc* tests were used for comparisons incorporating correction for the multiple comparisons. Paired *t*-tests were used to compare the pain intensity scores (NRS) and the ratings of perceived exertion (RPE) during isometric contractions in sessions 2 and 3. Furthermore, Pearson product–moment correlations were calculated to determine associations between exercise-induced percentage change in cPPT, cPTT and HPT and between NRS and RPE scores during exercise and exercise-induced percentage change in cPPT, cPTT and HPT. *p*-values <0.05 were considered significant. Finally, intraclass correlations (ICCs) based on a single rating, consistency, two-way mixed-effect model ($ICC_{3,1}$) and Bland–Altman methods were used for analysis of test–retest reliability of cPPT, cPTT and HPT before and after rest. An ICC above 0.75 was taken as excellent reliability, 0.40–0.75 was fair to good reliability and <0.40 defined poor reliability (Fleiss, 1986). Data were analysed using SPSS Statistics, version 21 (IBM, Armonk, NY, USA).

3 Results

3.1 Heat pain and pressure pain sensitivity test–retest repeatability

Repeatability between tests of HPT was fair with ICC of 0.54 (Table 1). Results from Bland–Altman demonstrated reasonable agreement for HPT reflected in the 95% CI of the mean difference, where zero lies within the interval. Repeatability between tests of cPPT and cPTT was excellent with ICCs of 0.86 and 0.77, respectively, and results from Bland–Altman analysis demonstrated no systematic bias between assessments.

Table 1. Intraclass correlations (ICCs) and Bland/Altman analyses for assessment of pain sensitivity parameters before and after the resting condition in session 1

Pain sensitivity parameter	ICC			Bland and Altman		
	Before resting Mean ± SD	After resting Mean ± SD	$ICC_{3,1}$ (95% CI)	Mean difference (95% CI)	SD diff (kPa)	95% Limits of agreement
HPT (°C)	46.6 ± 2.1	46.9 ± 2.2	0.54 (0.14–0.79)	0.4 (−0.6–1.3)	2.1	−3.7–4.5
cPPT (kPa)	20.6 ± 8.5	21.7 ± 8.9	0.86 (0.67–0.94)	1.2 (−1.0–3.4)	4.7	−8.0–10.4
cPTT (kPa)	63.7 ± 18.4	64.2 ± 18.3	0.77 (0.50–0.90)	0.5 (−5.4–6.4)	12.6	−0.24.2–25.2

1. HPT, heat pain threshold; cPPT, cuff pressure pain threshold; cPTT, cuff pressure pain tolerance.

3.2 Isometric contractions

The average MVC was 455.0 ± 86.7 N. The pain intensity and rated perceived exertion reported during the submaximal isometric contractions in the session with assessment of pressure pain sensitivity (NRS: 6.1 ± 1.4; RPE: 15.2 ± 1.6) and heat pain sensitivity (NRS: 6.3 ± 1.5; RPE: 15.2 ± 1.5) were not significantly different (t-test: $p > 0.49$).

3.3 Heat pain sensitivity after quiet rest and isometric contraction

There was no significant effect of assessment sequence on HPT prior to the resting condition (*t*-test: $p > 0.4$). Baseline HPTs were significantly different during the quiet rest (46.6 ± 2.1 °C) and isometric contraction sessions (45.4 ± 2.9 °C; *t*-test: $p < 0.023$). The RM-ANOVA of HPT demonstrated a significant main effect of time ($F(1,38) = 7.09$, $p < 0.011$, $\eta_p^2 = 0.16$). *Post-hoc* test showed that HPT increased during quiet rest (before: 46.6 ± 2.1 °C; after: 46.9 ± 2.2 °C) and during isometric contraction (before: 45.4 ± 2.9 °C; after: 46.8 ± 2.0 °C). The interaction between condition and time in the RM-ANOVA approached significance ($F(1,38) = 2.39$, $p < 0.13$, $\eta_p^2 = 0.06$). In addition, the difference in percentage change in HPT after rest (0.9 ± 4.5%) and isometric contraction (3.4 ± 5.9%) approached significance (Wilcoxon: $p = 0.08$).

3.4 Pressure pain threshold during quiet rest and isometric contraction

There was no significant effect of assessment sequence on cPPT prior to the resting condition (*t*-test: $p = 0.94$). Baseline cPPTs during the quiet rest (20.6 ± 8.5 kPa) were not significantly different compared with the isometric contraction sessions (24.4 ± 11.2 kPa; *t*-test: $p = 0.08$). Pressure pain threshold (cPPT) increased during quiet rest (before: 20.6 ± 8.5 kPa; after: 21.7 ± 9.0 kPa) and during isometric contraction (before: 24.4 ± 11.2 kPa; after: 26.3 ± 11.7 kPa). In the RM-ANOVA of cPPT, a main effect of time approached significance (Fig. 2A; $F(1,38) = 3.56$, $p = 0.07$, $\eta_p^2 = 0.09$). There was no significant interaction between condition and time ($F(1,38) = 0.19$, $p = 0.67$, $\eta_p^2 = 0.005$). There was no significant difference in percentage change in cPPT after rest (6.8 ± 22.9%) and isometric contraction (11.9 ± 23.7%; Wilcoxon: $p > 0.3$).

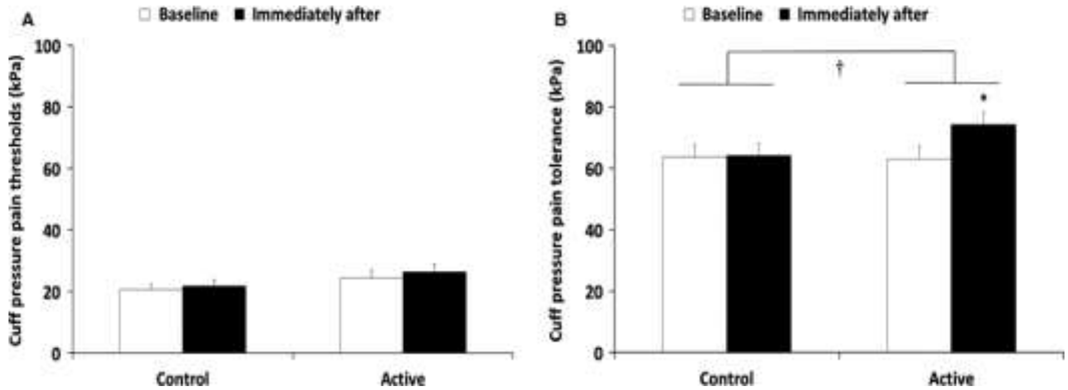

Figure 2. Mean (±SEM, n = 20) cuff pressure pain threshold (A) and cuff pressure pain tolerance (B) assessed before and after a submaximal isometric knee extension (Active) and quiet rest (Control). The cuff pressure pain sensitivity was assessed at the dominant lower leg. Significantly different compared with baseline (*$p < 0.05$) and significantly different compared with the control condition (†$p < 0.05$).

3.5 Pressure pain tolerance during quiet rest and isometric contraction

There was no significant effect of assessment sequence on cPTT prior to the resting condition (t-test: $p = 0.81$). Baseline cPTTs were similar during the quiet rest (63.7 ± 18.4 kPa) and isometric contraction sessions (63.11 ± 18.3 kPa; t-test: $p = 0.84$). Pressure pain tolerance (cPTT) increased during quiet rest (before: 63.7 ± 18.4 kPa; after: 64.2 ± 18.3 kPa) and during isometric contraction (before: 63.1 ± 18.3 kPa; after: 74.2 ± 18.3 kPa). The RM-ANOVA of cPTT demonstrated a significant interaction between condition and time (Fig. 2B; $F(1,38) = 10.15$, $p < 0.003$, $\eta_p^2 = 0.21$). *Post-hoc* test showed that cPTT did not change during quiet rest, but increased during isometric contraction. There was a significant difference in percentage change in cPTT after rest (2.9 ± 18.1%) and isometric contraction (20.2 ± 19.1%; Wilcoxon: $p < 0.01$).

3.6 Comparisons of EIH on HPT, cPPT and cPTT

There was a statistically significant difference in EIH depending on the noxious stimulus used to assess EIH ($X^2(2) = 6.7$, $p = 0.035$; Fig. 3). *Post-hoc* test showed a significant percentage increase in cPTT compared with cPPT and HPT (Wilcoxon: $p < 0.05$).

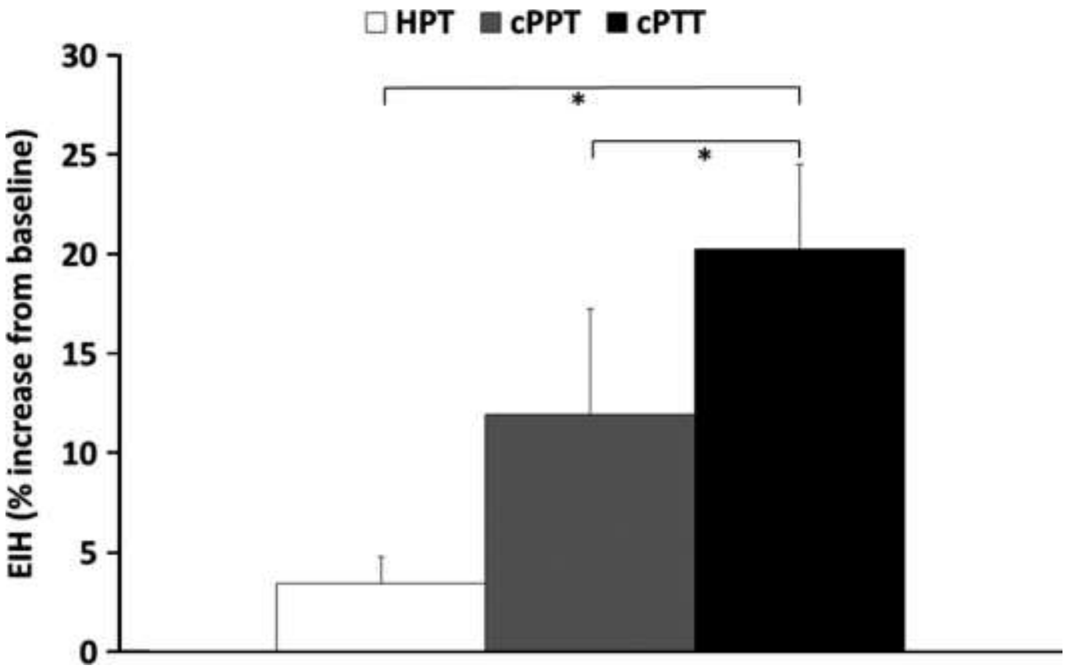

Figure 3. Mean (±SEM, n = 20) percentage increase in heat pain threshold (HPT), cuff pressure pain threshold (cPPT) and cuff pressure pain tolerance (cPTT) after submaximal isometric exercise. Significantly different compared with other assessment parameters (*$p < 0.05$).

3.7 Associations between exercise-induced changes in heat and pressure pain sensitivity

There was a significant positive correlation between the exercise-induced percentage change in cPPT and the change in cPTT ($r(18) = 0.50$, $p < 0.026$). There was no significant correlation between the exercise-induced percentage change in heat pain sensitivity and the percentage change in pressure pain sensitivity ($r(18) < 0.13$, $p > 0.59$). No significant correlations were found between ratings of pain intensity and perceived exertion during the submaximal isometric contractions and the exercise-induced changes in heat pain and pressure pain sensitivity ($r(18) < 0.42$, $p > 0.07$).

4 Discussion

This is the first study to compare the effects of a submaximal isometric exercise condition on heat and pressure pain sensitivity in healthy young men. As hypothesized, an increase in pressure pain tolerance was found after exercise compared with baseline and the control condition. In contrast with the hypothesis, no significant effects were found for pressure pain and heat pain thresholds. The results indicate that hypoalgesia after submaximal isometric exercise is primarily affecting tolerance of pain compared with the pain threshold. Furthermore, no significant correlations between exercise-induced changes in heat pain and pressure pain sensitivity were found. Pressure pain sensitivity was not significantly affected by quiet rest and assessments of pressure pain sensitivity were more reliable than assessment of heat pain sensitivity. These findings have clinical implications as the deeper tissues play an important role in many musculoskeletal pain conditions (Graven-Nielsen and Arendt-Nielsen, 2010) where exercise often is an essential part of treatment and rehabilitation (Mannerkorpi and Henriksson, 2007). Furthermore, the effect of exercise on pain tolerance could be relevant for patients in chronic pain.

4.1 Exercise-induced hypoalgesia

This findings are in agreement with a recent study demonstrating an increase in pressure pain tolerance after submaximal isometric exercise (Vaegter et al., 2015), indicating that the hypoalgesia after isometric exercise manifests with more intensely painful stimuli. However, the results are in contrast to previous studies demonstrating increases in pressure pain thresholds (Kosek and Ekholm, 1995; Koltyn et al., 2001; Kosek and Lundberg, 2003; Koltyn and Umeda, 2007; Hoeger Bement et al., 2008, 2009; Umeda et al., 2010; Naugle et al., 2014, Hoeger Bement et al., 2014; Lemley et al., 2014; Koltyn et al., 2014; Vaegter et al., 2014) after submaximal isometric exercise. In the previous studies demonstrating increase in pressure pain thresholds after isometric exercise pressure pain thresholds is often assessed with manual algometry. The contrast in findings with manual pressure and cuff algometry may suggest that the spatial integration is a major determinant for the hypoalgesic response after isometric exercise. In contrast to manual pressure algometry, computer-controlled cuff algometry stimulates a larger tissue volume (Polianskis et al., 2001). Moreover, cuff algometry is less likely to be influenced by local variations in pain sensitivity and is also an examiner-independent technique reducing the potential measurement bias. This results are in agreement with a previous study demonstrating no hypoalgesic response after isometric hand exercises when compared with a rest condition (Umeda et al., 2009). In addition, Bartholomew et al. (1996) found that pressure pain tolerance but not pressure pain threshold increased after an exercise session with mixed types of exercises. Although multisegmental increase in PPT after isometric exercise has been demonstrated (Kosek and Lundberg, 2003; Hoeger Bement et al., 2008; Vaegter et al., 2014), the increase in pressure pain thresholds is larger in the exercising body part compared with non-exercising body parts (Vaegter et al., 2014), indicating that local mechanisms play an important role in the EIH response after isometric exercise. Moreover, pronounced EIH responses at the contracting thigh muscle compared with the contralateral non-contracting thigh muscle has previously been demonstrated (Kosek and Lundberg, 2003). This could influence the results in this study as heat and pressure pain sensitivity was assessed on the foot and lower leg, respectively, and not on the thigh.

Although heat pain threshold increased compared with baseline, no significant difference was found compared with quiet rest, indicating that isometric exercise does not influence pain perception to pressure or heat stimulus near the threshold when compared with quiet rest. The effect of isometric exercise on heat pain threshold has not previously been investigated, but the results are in agreement with previous studies demonstrating no effect on heat pain threshold after aerobic exercise (Cook et al., 2010; Kodesh and Weissman-Fogel, 2014). However, previous studies have demonstrated reduced pain intensity to heat pain (Misra et al., 2014) and reduced temporal summation of heat pain (Koltyn et al., 2013) after isometric exercise indicating that isometric exercise can influence pain perception to heat stimulus above the pain threshold. Furthermore, the study by Misra et al. (2014) demonstrated a progressive increase in the hypoalgesic effect with an increase in exercise intensity and it is currently unknown whether higher intensity exercise (e.g. 60% MVC) would have influenced pain perception to pressure or heat stimulus near the pain threshold. Isometric exercise was the only exercise stimulus used in this study; thus, the results cannot be generalized to other modes of exercise.

Using other paradigms for assessment of endogenous pain modulation, such as conditioning pain modulation, similar differences in modality-specific findings have been demonstrated. In line with this results, Kosek and Hansson (1997) and Tuveson et al. (2006) showed that pressure pain threshold but not heat pain threshold increased in healthy subjects after a tourniquet test used to assess the conditioning pain modulation. However, Leffler et al. (2002) demonstrated an increase in pressure pain and heat pain thresholds in healthy subjects during a cold pressor test and Oono et al. (2013) showed an increase in pressure pain thresholds and pain tolerance in healthy subjects when a compression device around the head was used to assess conditioning pain modulation. Although conflicting results, different mechanisms may underlie endogenous pain modulation for various types of noxious stimulation and further research in this area is warranted.

The non-significant correlation between heat pain thresholds and pressure pain thresholds indicates that heat stimulation and cuff algometry assess different mechanisms. Similar findings have been reported for pain thresholds assessed by electrical, thermal and mechanical modalities (Neziri et al., 2011).

4.2 Test–retest reliability

Cuff pressure pain threshold and tolerance demonstrated excellent ICCs and acceptable agreement between tests with no systematic mean difference before and after the resting condition in healthy young men. Previous studies on cuff pressure algometry have demonstrated high levels of reliability with ICC values above 0.7 for test–retest data in healthy subjects (Graven-Nielsen et al., 2015) and in patients with chronic musculoskeletal pain (Vaegter et al., 2016). Previous studies demonstrating good test–retest reliability have based the pressure algometry pain thresholds on the average of at least two trials (Ohrbach and Gale, 1989; Nussbaum and Downes, 1998). However, this study showed high ICC and acceptable agreement based on just one repetition with computer-controlled cuff algometry.

Heat pain threshold demonstrated lower ICC compared with cuff algometry, but acceptable agreement between tests with no systematic mean difference between the two sessions. A previous systematic review on the test–retest reliability of quantitative sensory testing including heat pain threshold demonstrated that the reliability of heat pain threshold ranged from fair to excellent. A possible explanation of the lower ICC for heat pain threshold compared to cuff algometry is that heat pain threshold is more easily affected by environmental factors, such as ambient temperature and noise; methodological factors, such as test protocol, test application and test instructions; and the cooperation and attention of the individual being tested (Chong and Cros, 2004). This may also explain the differences in baseline HPT found in the two sessions. Furthermore, heat pain and pressure pain sensitivity was assessed at different sites (dorsum of foot vs. circumference around lower extremity). It is possible that the difference in test–retest reliability is related to whether the tests are applied at bony or more muscular body sites.

4.3 Limitations

Pain tolerance was only assessed with pressure stimulus and the effect of isometric exercise on heat pain tolerance remains unclear in this sample. Heat pain tolerance was not assessed in this study due to ethical considerations. Previous research has shown that heat pain stimulation may influence subsequent responses to mechanical stimulation (Grone et al., 2012) causing a risk of carry-over effect in the experimental design in session 1. However, such carry-over effect is unlike in this study as no significant order effect was found on heat pain or pressure pain sensitivity. Finally, the results from this study can only be generalized to healthy young men and it remains unclear whether women, older subjects and individuals with chronic pain would experience similar results. Further research on gender differences in EIH after isometric exercises is warranted as previous studies have demonstrated mixed results (Koltyn et al., 2001; Kosek and Lundberg, 2003).

5 Conclusion

Isometric exercise significantly increased cuff pressure pain tolerance compared with baseline and the control condition. Although not known if related with the exercise dose, the findings suggest that hypoalgesia after isometric exercise is primarily affecting tolerance of pain compared with the pain threshold. These findings indicate that mechanisms underlying exercise-induced hypoalgesia after isometric exercise are targeting pain perception above the threshold and contribute to the understanding of how isometric exercise influences pain perception, which is necessary to optimize the clinical utility of exercise in management of chronic pain.

Author contributions

All authors contributed to the conception and design of the study as well as making intellectual contributions to its content. Henrik Bjarke Vaegter, Anders Bjarke Madsen, Jakob Fridriksson and Marcus Dasa collected data; and Henrik Bjarke Vaegter, Thomas Graven-Nielsen and Marie Hoeger Bement contributed to the analysis and interpretation. Henrik Bjarke Vaegter drafted the manuscript. All authors discussed the results, commented on and approved the final manuscript.

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