Randomized Controlled Trial

Central Adaptation of Pain Perception in Response to Rehabilitation of Musculoskeletal Pain: Randomized Controlled Trial

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Background: Understanding the mechanisms of long-standing musculoskeletal pain and adaptations in response to physical rehabilitation is important for developing optimal treatment strategies. The influence of central adaptations of pain perception in response to rehabilitation of musculoskeletal pain remains unclear.

Objectives: To investigate the effect of neck/shoulder resistance training on pressure pain threshold (PPT) of the painful neck/shoulder muscles (upper trapezius) and a non-painful reference muscle of the leg (tibialis anterior) in adults with neck/shoulder pain.

Study Design: Examiner-blinded, parallel-group randomized controlled trial with allocation concealment. Trial registration: ISRCTN60264809

Setting: Office workplaces in the capital of Denmark

Methods: The study contained 198 adults with frequent neck/shoulder pain (174 women and 24 men, mean: age 43 years, duration of pain 186 days during the previous year, computer use 93% of work time) were randomly allocated to 10 weeks of specific resistance training for the neck/shoulder muscles for 2 or 12 minutes per day 5 times a week, or weekly information on general health (control group). Primary outcomes were changes in PPT of the painful neck/shoulder muscles (upper trapezius) and a distant non-painful reference muscle (tibialis anterior) at 10 weeks.

Results: PPT of both the trained painful trapezius and the non-trained reference muscle of the leg increased more in the training groups compared with the control group ($P < 0.05$), providing evidence of central adaptations. The change in PPT of the reference muscle was of similar magnitude to that of the painful muscle. Compared with the control group, the change in PPT of the trapezius and tibialis anterior was 31 (95% CI 3 to 60) kPa and 36 (8 to 65) kPa in the 2 min group, respectively, and 29 (1 to 58) kPa and 36 (7 to 64) kPa in the 12 min group.

Limitations: Blinding of participants is not possible in behavioural interventions.

Conclusion: Central adaptations of pain perception occur in response to rehabilitation of musculoskeletal pain. Thus, treating pain in one region of the body reduces sensitivity to pressure in other regions of the body. Clinicians and researchers may use this knowledge to better understand adaptations of pain perception in patients with musculoskeletal pain.

Key words: Hyperalgesia, neck pain, trapezius myalgia, pressure pain threshold, physical exercise

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Musculoskeletal disorders are a major cause of disability and sickness (1-5). Approximately one third of working-age adults experience neck/shoulder pain to a significant degree (6). Neck/shoulder pain is highly prevalent among office workers (7), with tenderness of the upper trapezius muscle being the most common complaint (8). Continuous activation of low threshold motor units of the upper trapezius muscle during computer work is believed to result in repetitive strain injury and consequently muscle tenderness (9).

In intervention studies, reporting of perceived pain is influenced by outcome expectations (10). By contrast, pressure algometry provides objective information on muscle tenderness in musculoskeletal pain conditions (11,12). Because blinding of participants is not possible in behavioral interventions, objective measures such as pressure algometry should be the preferred method of evaluating effects of interventions treating musculoskeletal pain. Adults with neck/shoulder pain commonly experience hyperalgesia of the upper trapezius muscle as evidenced by reduced pressure pain threshold (PPT) (12,13). Although local muscle cellular mechanisms may partly explain the pain and tenderness (9,14), central mechanisms are involved in many types of chronic pain. Thus, generalized hyperalgesia exists in patients with carpal tunnel syndrome (15), whiplash (16), fibromyalgia (17,18), chronic low back pain (19) osteoarthritis (20), repetitive strain injury (21), and trapezius myalgia (22). Because local pain in one part of the body may lead to generalized hyperalgesia (19), treating pain may regulate general pain perception.

Longitudinal studies have shown the effectiveness of resistance training for relieving neck/shoulder pain and improving physical functioning in adults (23-27). Some studies used pressure algometry for evaluating muscle tenderness, and reported significant effects of physical exercise on pressure pain threshold of painful muscles (11,22,28). Two of these studies included algometry measurements at a non-painful reference site. While one of these studies -- a high-quality randomized controlled trial – found no change in PPT of the reference site, the sternum bone (11), a small-scale study with weaker methods observed increased PPT of a non-trained reference muscle (22). Thus, the influence of central adaptations of pain perception in response to rehabilitation of musculoskeletal pain remains unclear.

We hypothesize that specific training of painful neck/shoulder muscles evokes a generalized increase in PPT. We use the painful trapezius muscle and a non-painful reference muscle (tibialis anterior) of adults with frequent neck/shoulder pain to test this hypothesis.

Methods

Study Design and Flow of Participants

We performed an examiner-blinded randomized controlled trial in Copenhagen, Denmark, from August to December 2009, and have previously reported the study design and results on changes in perceived neck/shoulder pain (29). Figure 1 shows the flow of participants. A screening questionnaire went out to 1,094 employees from 2 large office companies, and 653 replied (60%). We defined a set of criteria to locate generally healthy adults with frequent neck/shoulder muscle pain, but without competing diseases or disorders that could give rise to hyperalgesia. Exclusion criteria were a medical history of cardiovascular or cerebrovascular events, fibromyalgia, rheumatoid arthritis, cervical disc herniation, whiplash or other significant traumatic injuries of the neck or shoulder, major chronic diseases, pregnancy, working less than 30 hours per week, or performing more than 2 hours per week of vigorous physical exercise. Eligible adults with a neck/shoulder pain intensity of at least 2 on a scale of 0-10 during the last 3 months, at least 30 days with pain during the last year, and self-reported tenderness of the neck/shoulder muscles were invited for a clinical neck/shoulder examination (n = 305) (47% of those who replied to the questionnaire).

Clinical Examination and Pressure Algometry

During the clinical examination additional exclusion criteria were blood pressure above 160/100, a positive foramen compression test, subacromial impingement syndrome, or severe joint pain of the shoulder, elbow, or wrist during resisted shoulder abduction. Finally, we included those with a history of frequent neck/shoulder pain during the last year and examiner-verified palpable tenderness in the neck/shoulder muscles in the trial (n=198) (65% of those who were invited for the examination).

The last part of the clinical examination included pressure algometry. Using an electronic pressure algometer (Wagner Instruments, Greenwich, CT, USA), an examiner blinded to group allocation measured PPT of the painful muscle (upper trapezius) and a non-painful reference muscle (tibialis anterior). The contact area of the circular probe was 1 cm^2. Pressure was applied perpendicular to the skin at the mid-belly of the muscle at a rate of 30 $kPa.s^{-1}$. For the upper trapezius,

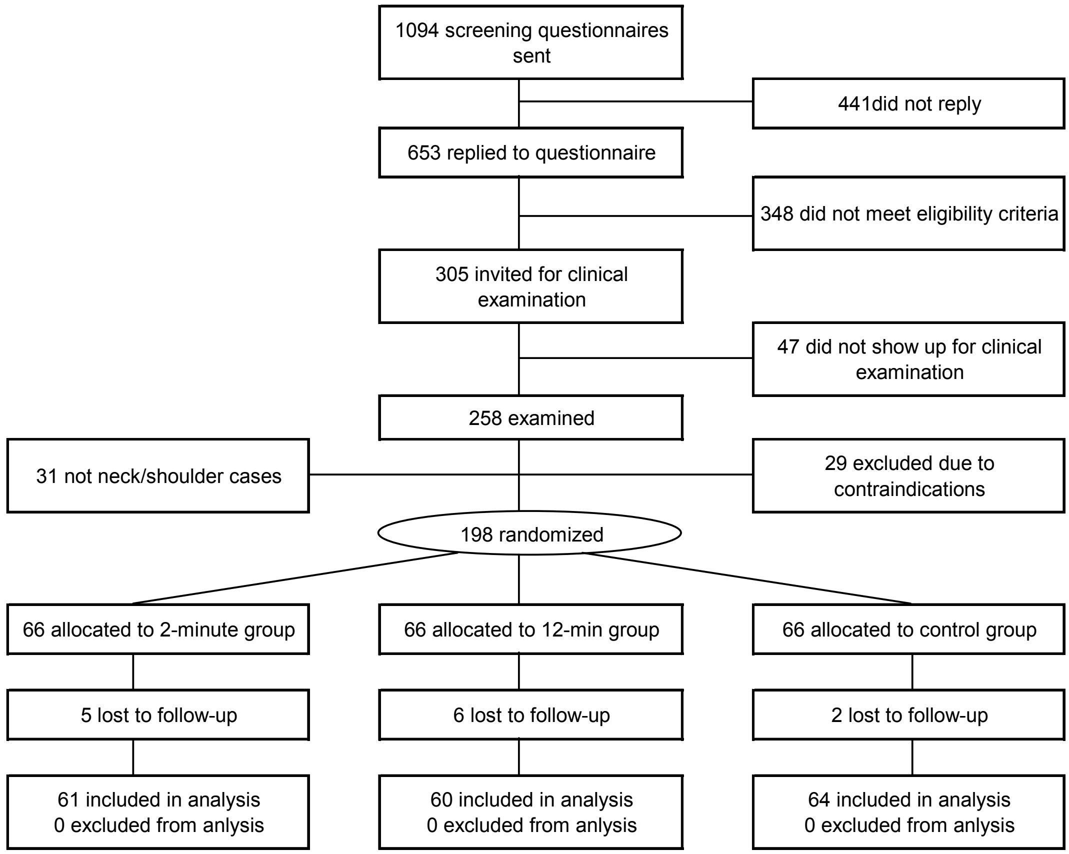

Fig. 1. *Flow of participants through the intervention*

the mid-belly was determined as midway between the acromion to the seventh cervical vertebrae, and for the tibialis anterior as midway between the lateral condyle of the tibia and the lateral malleolus of the fibula. The participant was not aware of the reading of PPT on the display, and was instructed to clearly state when the sensation of "pressure" changed to "pain." After a few habituation attempts on the hand of the participant, PPT was measured 4 times at the trapezius and tibialis anterior with 1½ min between each measurement alternating between the 2 muscles. PPT for each muscle was subsequently expressed as the average value of the 4 measurements. Previous studies have shown satisfactory to good test-retest reliability of PPT (30,31).

Ethics and Trial Registration

Participants were informed about the main objective and content of the project and gave written informed consent to participate in the study which conformed to The Declaration of Helsinki, and was approved by the Local Ethical Committee (HC2008103). Prior to enrolment of participants, the study was registered in the International Standard Randomised Controlled Trial Number Register: ISRCTN60264809.

Interventions

This study has 3 arms; 2 or 12 minutes of specific resistance training performed 5 times a week, and a control group receiving weekly information on general health. Concealed random allocation to one of the 3 intervention groups was performed after clinical examination of all participants. All 3 interventions were initiated simultaneously and lasted 10 weeks. The intervention activities have been described in detail previously (29). In brief, the 2 and 12 minute groups performed the resistance exercise "lateral raise" with elastic tubing (Thera-Band, Akron, Ohio) to specifically target the neck/shoulder muscles (27,33). The participant was standing erect on the middle of the elastic tubing holding the handles to the side and abducted the shoulders in a controlled manner to approximately 90 degree shoulder abduction and 30 degrees horizontal flexion, and then lowered the arms again. The 12-minute group performed 5-6 sets of 8-12 repetitions in a progressive manner for a total of 25-30 sets per week, equivalent to the effective amount of specific resistance training for treating trapezius myalgia (25). The 2-minute group performed a single set of exercise with as many consecutive repetitions as possible to fatigue. The control group was encouraged to continue ordinary physical activities and received e-mail based information once a week during the 10 week intervention period on various aspects of general health (e.g., diet, smoking, alcohol, physical exercise, stress management, workplace ergonomics, and indoor climate).

Statistics

We analyzed the variables in accordance with the intention-to-treat principle, and invited dropouts to the follow-up clinical examination to avoid selection bias. Using the Mixed Procedure of SAS (SAS Institute, Cary, NC, version 9.2), we performed a 2-way analysis of variance to model the change in PPT from baseline to follow-up. Group (2-minute, 12-minute, and control group) and muscle (trapezius and tibialis anterior) were categorical independent variables.

A priori power analysis was based on neck/shoulder pain intensity, and showed that 48 participants of each group were adequate to reject the null hypothesis of equality of treatment (minimal relevant difference = 1 (scale 0-10), β=0.95, α=0.05). An alpha level of 5% was accepted as statistically significant. We report baseline values as means (SD) and changes from baseline to follow-up as differences in least square means (95% confidence intervals) between the groups.

Results

Table 1 shows baseline characteristics of the participants. At baseline PPT of the trapezius was significantly higher in the 12-minute group compared with the control group (P = 0.04). We controlled for this difference in the ANOVA by including baseline PPT as a covariate. Table 1 shows that at baseline there were no significant differences among the groups for the remainder of the variables. PPT was higher in tibialis anterior than in trapezius in all 3 groups (P < 0.001)

Table 1. *Descriptive baseline characteristics of the 3 intervention groups. Values are group mean (SD) or percentage of participants (%).*

	2-minute	12-minute	Control
Demographics			
Age, year	44 (11)	42 (11)	43 (10)
Height, cm	171 (8)	170 (8)	169 (7)
Weight, kg	72 (14)	68 (15)	67 (11)
Body Mass Index, $kg.m^{-2}$	25 (5)	24 (5)	23 (4)
Number of women/men	58/8	58/8	58/8
Clinical			
Days with neck/shoulder pain previous year	176 (112)	209 (134)	180 (117)
Neck/shoulder pain intensity previous 3 months, scale 0-10	5.2 (1.9)	5.2 (2.1)	4.5 (1.9)
PPT Trapezius, kPa	239 (92)	260 (108)	219 (73)
PPT Tibialis anterior, kPa	329 (124)	331 (127)	309 (120)
Work-related			
Computer use, percentage of worktime	93 (14)	96 (10)	91 (16)
Weekly working hours	39 (5)	38 (5)	37 (3)
Duration of office work, years	11 (9)	10 (10)	13 (11)
Higher education	92%	85%	89%

Five, 6 and 2 of the participants in the 2-minute, 12-minute and control groups did not present for the follow-up examination, corresponding to a total loss to follow-up of 7% for the PPT measurements (Fig. 1).

At baseline a significant correlation between PPT of the painful trapezius muscle and the non-painful reference muscle existed (Pearson's r = 0.60, *P* <0.0001) (Fig. 2a). Likewise, a significant correlation between changes from baseline to follow-up in PPT of the painful trapezius muscle and the non-painful reference muscle existed (Pearson's r = 0.56, *P* < 0.0001) (Fig. 2b).

Figure 3 shows baseline and follow-up PPT values

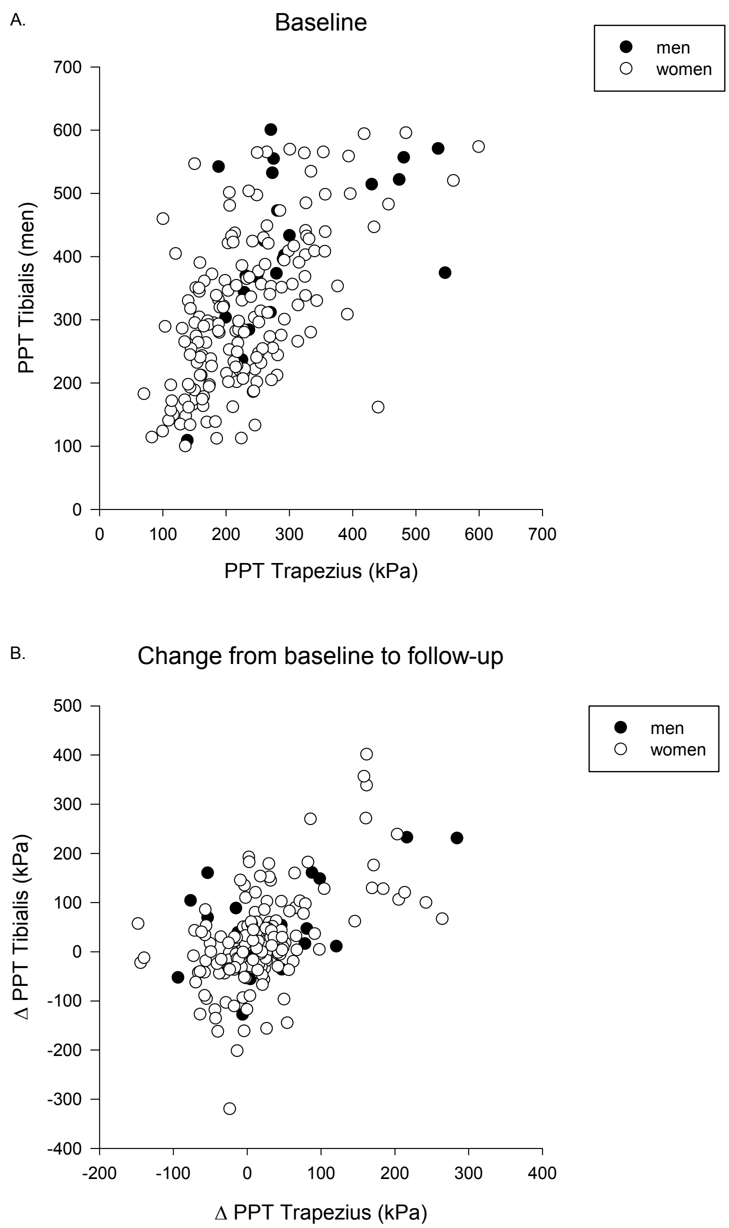

Fig. 2. *a) Correlation between pressure pain threshold (PPT) of the trapezius and tibialis at baseline (Pearson's r = 0.60, P < 0.0001), and b) the correlation between changes from baseline to follow-up of PPT in the trapezius and tibialis (Pearson's r = 0.56, P < 0.0001). Filled and open circles indicates men and women, respectively.*

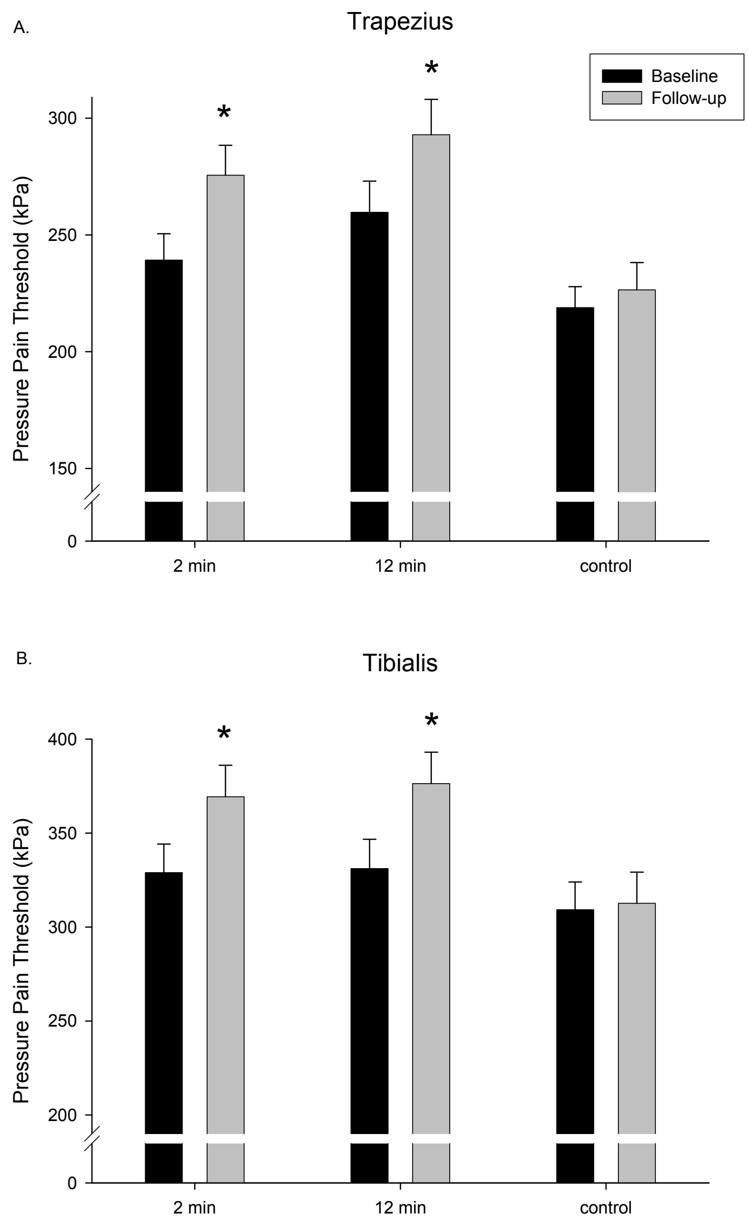

Fig. 3. ***Pressure pain threshold (PPT) at baseline and follow-up in the 2-minute, 12-minute and control groups in the a) trapezius and b) tibialis anterior. *) change from baseline to follow-up $P < 0.05$.***

for each group. A priori hypothesis testing of main effects showed that PPT increased significantly more in both training groups compared with the control group ($P < 0.05$). Compared with the control group the change from baseline to follow-up in the trapezius and tibialis anterior was 31 (3 to 60) and 36 (8 to 65) kPa in the 2 minute group, respectively, and 29 (1 to 58) and 36 (7 to 64) kPa in the 12 min group. There was no significant group by muscle interaction for the change in PPT with the intervention ($P = 0.89$), i.e. the change in PPT of the painful trapezius was not significantly different from that of the non-painful tibialis anterior.

Discussion

Ten weeks of specific neck/shoulder resistance training among adults with frequent neck/shoulder pain increased PPT of the painful trapezius and the non-painful tibialis anterior muscle. Thus, our study provides evidence of central adaptations of pain perception in response to rehabilitation of specific musculoskeletal pain.

At baseline, the participants had values of trapezius and tibialis anterior PPT similar to that of women with trapezius myalgia and lower than those of healthy controls (22). Although PPT in the tibialis was higher than in the trapezius, the relatively low PPT of the non-painful tibialis anterior reflects a certain degree of generalized hyperalgesia. Other studies have also reported generalized hyperalgesia among patients with specific musculoskeletal disorders (15,16,19-22). The mechanism has been suggested to involve opening of latent collateral synaptic connections facilitating neighbouring neurons, which can lead to central sensitization (32).

In our study, specific training of the painful neck/shoulder muscles increased PPT of the distant non-painful reference muscle. This suggests that reducing pain in one region of the body evokes central desensitization. The exercise used specifically targets the neck/shoulder muscles (33), and is therefore unlikely to induce a training effect of the tibialis anterior. More likely, central adaptations of pain perception occurred. Interestingly, Niddam and coworkers (34) showed that acute supraspinal adaptation of pain perception is possible in response to electrostimulation of painful triggerpoints in the trapezius muscle. A small-scale study observed that bicycling and resistance training increased PPT of the tibialis anterior although this muscle was not trained directly (22). Ylinen and coworkers (11) reported increased PPT of the painful neck/shoulder muscles in response to resistance training and endurance training in women with chronic neck pain, but no change in PPT of the reference site – the sternum bone. By contrast, we used a non-trained distant muscle as reference – the tibialis anterior. This suggests that central adaptations of pain perception are transferable to soft tissues of the musculoskeletal system.

Our study is the first to investigate the effect of a minimal resistance training program on PPT of painful muscles. In response to the 10-week intervention PPT of the painful trapezius muscle increased approximately 11-13% in the training groups compared with the control group. Thus, as little as 2 minutes of daily resistance training can modulate mechanical pain perception of painful muscles. Ylinen and coworkers (24) found a more marked improvement of 50% in PPT of the trapezius muscle in response to a one-year comprehensive program with initial institutional rehabilitation. Our simple program with a single exercise was not designed to induce the individually largest effect, but a program that would be digestible for the majority of adults with neck/shoulder pain. The high training adherence of more than 3 times per week confirms that this succeeded.

Strengths of our study include the concealed random allocation of participants, blinding of clinical examiners, a low loss to follow-up of participants, inclusion of dropouts in the intention-to-treat analysis, and the high adherence to the training program. These factors protected against systematic bias and allowed us to test the actual effect of the intended intervention. Further, the objective nature of the PPT measurements protects against recall bias of and influence of reporting bias on subjective pain symptoms. Using only a single reference site – the tibialis anterior – may be a limitation. On the other hand, nociceptive responses to different types of painful stimuli largely converge (35).

Conclusion

In conclusion, 10 weeks of specific resistance training in adults with neck/shoulder pain increased PPT of the painful trapezius as well as the non-painful tibialis anterior muscle. Thus, our study provides evidence of central adaptations of pain perception in response to rehabilitation of musculoskeletal pain.

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