Bilateral experimental neck pain reorganize axioscapular muscle coordination and pain sensitivity

Christensen, Steffan Wittrup; Hirata, Rogerio Pessoto; Graven-Nielsen, Thomas

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BILATERAL EXPERIMENTAL NECK PAIN REORGANISE AXIOSCAPULAR MUSCLE COORDINATION AND PAIN SENSITIVITY

SW Christensen, RP Hirata & T Graven-Nielsen

Center for Neuroplasticity and Pain (CNAP),

SMI, Department of Health Science and Technology,

Aalborg University, Denmark

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What's known about the topic and what does this study add?

- Bilateral clinical neck pain alters axioscapular muscle coordination but only effects of unilateral experimental neck pain has been investigated.
- Bilateral experimental neck pain causes task-dependent reorganised axioscapular and trunk muscle activity in addition to widespread decrease in pressure pain sensitivity.

Conflict of interest: The authors have no conflicts of interests.

Corresponding author:
Professor Thomas Graven-Nielsen, DMSc, Ph.D.
Center for Neuroplasticity and Pain (CNAP)
SMI. Department of Health Science and Technology
Faculty of Medicine
Aalborg University,
Fredrik Bajers Vej 7D-3
9220 Aalborg E, Denmark
Phone: +45 9940 9832
Fax: +45 9815 4008
http://www.smi.hst.aau.dk/~tgn
E-mail: tgn@hst.aau.dk

ABSTRACT

Background Neck pain is a large clinical problem where reorganised trunk and axioscapular muscle activities have been hypothesised contributing to pain persistence and pain hypersensitivity. This study investigated the effects of bilateral experimental neck pain on trunk and axioscapular muscle function and pain sensitivity.

Methods In 25 healthy volunteers, bilateral experimental neck pain was induced in the splenius capitis muscles by hypertonic saline injections. Isotonic saline was used as control. In sitting, subjects performed slow, fast, and slow-resisted unilateral arm movements before, during, and after injections. Electromyography (EMG) was recorded from eight shoulder and trunk muscles bilaterally. Pressure pain thresholds (PPTs) were assessed bilaterally at the neck, head, and arm. Data was normalised to the before-measures.

Results Compared with control and post measurements, experimental neck pain caused (i) decreased EMG activity of the ipsilateral upper trapezius muscles during all but slow-resisted down movements ($P<0.001$), and (ii) increased EMG activity in the ipsilateral erector spinae muscle during slow and fast movements ($P<0.02$), and in the contralateral erector spinae muscle during all but fast-up and slow-resisted down movements ($P<0.007$). The PPTs in the painful condition increased at the head and arm compared with post measurements and the control condition ($P<0.001$). In the post-pain condition, the neck PPT was decreased compared with the control condition ($P<0.001$).

Conclusion Acute bilateral neck pain reorganised axioscapular and trunk muscle activity together with local hyperalgesia and widespread hypoalgesia indicating that acute neck pain immediately affects trunk and axioscapular function which may affect both assessment and treatment.

INTRODUCTION

Neck pain is a major problem in the general population (Fejer et al., 2006) with multiple symptoms and involved structures (Bogduk 2011). Developing effective treatment strategies requests an improved understanding of the mechanisms behind neck pain (Michaleff et al., 2014). So far, the main focus has been directed towards the painful neck area.

Based on abnormal axioscapular muscle function in neck pain patients, dysfunctional shoulder girdles have been suggested as an important factor in persistent neck pain (Behrsin and Maguire 1986; O'Leary et al., 2009) although it is not known if it is an effect of neck pain or a causal factor for neck pain. Emerging studies show altered alignment of the shoulder girdle in neck pain patients, displaying protracted shoulders and a forward head posture in rest (Helgadottir et al., 2011b) and during functional tasks (Helgadottir et al., 2010). Although electromyographic studies during upper limb tasks reported reorganised axioscapular muscle activity in neck pain patients compared with healthy controls, the results are conflicting. In neck pain patients one study found reduced activity of the upper trapezius muscle during arm movement (Falla et al., 2004) whereas another study found no change in activity of the upper trapezius muscle but a task dependent increase in the lower trapezius muscle during isometric contractions (Zakharova-Luneva et al., 2012). Wegner et al. (2010) found reduced activity in the lower trapezius muscle and increased activity of the middle trapezius muscle during a typing task in neck pain patients compared with controls while others reported no changes for the trapezius muscle but delayed onset and reduced duration of the serratus anterior muscle activity during arm movement (Helgadottir et al., 2011a). Different tasks or heterogeneous patient groups may explain the previous contrasting findings. Clinical confounding factors have been eliminated in studies using experimental neck pain where saline-induced neck pain in healthy subjects demonstrate reduced upper trapezius muscle activity during arm movement (Christensen et al., 2015; Falla et al., 2007) and increased trunk muscle activity (Christensen et al., 2015). Since neck pain patients often present with bilateral pain (Fernandez-de-las-Penas et al., 2008) the unilateral experimental pain models may not be sufficient.

Hyperalgesia to pressure in the neck region has been reported for acute and chronic neck pain compared with healthy controls (La Touche et al., 2010; Scott et al., 2005) while widespread hyperalgesia were only reported for chronic neck pain (Javanshir et al., 2010). Experimental neck pain did not cause local hyperalgesia after a unilateral injection of hypertonic saline into the trapezius muscles (Ge et al., 2003; Schmidt-Hansen et al., 2006) but after bilateral injections, hypoalgesia due to descending pain modulation were observed outside the injected areas (Ge et al., 2003).

This study aimed to investigate the effects of bilateral experimental neck pain on axioscapular muscles coordination during standardised arm movements as well as the pressure pain sensitivity.

Experimental neck pain was expected to reorganise axioscapular and trunk muscle activity and cause hypoalgesia to pressure away from the painful area.

MATERIALS AND METHODS

Subjects

Twenty-five healthy volunteers were recruited from a university setting (13 women, one left-handed). Women had a mean age of 24.4 ± 3.4 years (± standard deviation) and a mean body mass index (BMI) of 21.3 ± 2.1 kg/m^2. For men, the mean age was 24.3 ± 3.0 years and mean BMI was 23.6 ± 2.5 kg/m^2. Exclusion criterions were persistent or recurring neck or shoulder pain within the past year, deviations in spinal posture such as significant scoliosis, kyphosis, or forward head posture. In addition, any signs or symptoms indicating rheumatologic or neurological disorders that may influence the outcome of the study, use of pain medication, or pregnancy were cause of exclusion. Subjects were given written and verbal information about the study after which informed consent was obtained. The study was approved by the local ethics committee (N20120018) and performed according with the Helsinki declaration.

Experimental protocol

The study used a single blinded randomised crossover design (Fig. 1) with data collection performed in a single session. The muscle activity was assessed by electromyography (EMG) recorded during arm movements where subjects were seated in an upright position (Fig.2) while the pressure pain thresholds (PPTs) were measured with subjects leaning over a bench. All measurements were performed bilaterally, starting with the EMG measurements, and were done before (baseline), during (immediately after experimental neck pain was induced by bilateral injections of hypertonic saline into the splenius capitis muscles or the control injections by isotonic saline), and after (i.e. 5 min after any potential pain had vanished). A 10 min. pause was included between the post measurements after the first series of injections (e.g. hypertonic saline) and the baseline before the second series of injections (e.g. isotonic saline). The sequence of experimental pain and control sessions was randomised in a balanced way with participants a priori blinded to the sequence.

Experimental neck pain

The splenius capitis muscle was identified between the posterior border of the sternocleidomastoid muscle and the lateral border of the upper trapezius muscle using ultrasonography (Logiq S7 Expert mounted with a ML6-15L transducer; GE Medical Systems, Milwaukee, Wisconsin, USA). A

hypodermic needle was inserted into the splenius capitis muscle and the initial injection of hypertonic saline (5.8%, 0.75 ml) was injected. The time between the bilateral injections was approximately 45 s and to compensate for this delay the pain duration of the first injection was prolonged by a larger volume (Graven-Nielsen et al., 1997) than the subsequent injection (0.5 ml). This novel approach ensured that bilateral pain was kept during the experimental session and avoided that pain in one side would be fading away before the other during the recordings. For the control condition, isotonic saline (0.9%) was used with volumes of 0.75 ml and 0.5 ml for the two sequential injections. The side of the initial injection was randomised in a balanced way for both injection types.

The pain intensity profile was recorded using a 10 cm electronic visual analogue scale (VAS) labelled with "no pain" (0 cm) and "maximum pain" (10 cm). Participants were continuously reminded to update the VAS throughout the experiment. Peak, duration and area under the VAS-time curve were extracted for further analysis. The duration of pain was defined as the time difference between the first and last VAS score exceeding 0.1 cm and was defined as 0 s if the VAS remained zero. Subjects drew areas of perceived pain on a body chart and the pain areas were extracted (VistaMetrix v.1.38.0, SkillCrest, LLC) in arbitrary units (a.u.).

Standardised arm movements

To ensure a standardised arm movement, subjects sat on a custom built chair, supporting only the sacrum. The starting position was an upright sitting position with arms hanging relaxed by the side and feet flat on the floor. Adjustable walls, angled 30° from the frontal plane, allowing movement in the scapular plane (scaption), were placed on the side of the chair; Subjects were asked to keep the back of their hand in contact with the wall at all times during movements. Movements were done with outstretched arm and thumbs pointing up. A physical upper marker was placed on the vertical surface allowing for abduction to 140°. Arm movements were performed bilaterally, alternating between sides, with a 6 s break in-between. To guide when the movement should 1) start, 2) be at the upper marker, and 3) returned to the resting position, a custom made program (Aalborg University, DK) was set to make 3 beep cues separated by 3 s thereby giving a 3 s window for both up and down movement without any breaks at the upper marker. Each movement series was initiated with 3 slow movements in each side, followed by 3 fast movements in each side. During fast movements, subjects were instructed to move the arm as fast as possible from the starting position to the upper marker. The down movements for the fast movements were not recorded. Immediately after the fast movements another slow resisted movement series (3 in each side) was conducted with the addition of a 1 kg wrist cuff attached to each arm. The total movement

series, consisting of slow, fast and resisted movements in both side, lasted 3.5 min. Subjects were reminded to keep an upright posture and this was visually inspected throughout the study.

Accelerometers (ACC; EVAL-ADXL327Z; Analog Devices, Norwood, Massachusetts, USA) placed over the lateral epicondyle of each arm were used to monitor the timing of each movement. For the slow movements, time parameters were extracted showing the time from the first cue (i.e. start) to maximum angle and from maximum angle to the third cue (i.e. return position) while for the fast movements only the time from the first cue to maximum angle was recorded. For the accelerometer analysis an average of the 3 movements for each movement type (slow up, slow down, fast up, resisted slow up, resisted slow down) was used.

Participants rated the perceived difficultness of the arm movements on a 6-point Likert scale after each movement series (0: "no problems", 1: "minimally difficult", 2: "somewhat difficult", 3: "fairly difficult", 4: "very difficult" 5: "unable to perform").

Electromyography recordings

Eight muscles were assessed bilaterally with surface EMG: Serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), obliqus externus (OE), and erector spinae (ES) muscles. Adhesive bipolar surface electrodes (Neuroline 72001-k; AMBU, Denmark) were mounted pairwise on the skin which had been prepared according to the SENIAM recommendations (Hermens et al., 2000). A ground electrode (OT Bioelettronica, Italy) was mounted on the right wrist. The EMG recordings were amplified (gain 500) and sampled at 2048 Hz (OT Bioelettronica, Italy). The raw EMG signal was rectified and filtered (Butterworth 2nd order, band pass 25-450Hz) in matlab (R2012a; The MathWorks Inc., Natick, MA). Root mean square (RMS) EMG values from 2 epochs of 3 seconds (i.e. between cues), representing slow up and down movements were extracted for further analysis. For the fast up movements the epochs were defined as the time from the first cue to the maximum angle (based on the accelerometer data). The average RMS-EMG values from the 3 movement repetitions from the respective series were used for further analysis and normalised to baseline (100%).

Pressure algometry

A 1-cm^2 probe enclosed by a disposable latex sheet was mounted on a handheld pressure algometer (Somedic, Hörby, Sweden). A steady increasing pressure was applied at a rate of 30 kPa/s. The pressure pain threshold (PPT) was defined, as the time point where the pressure was first perceived as painful. When the PPT was reached, participants were instructed to push a button in order to record the specific pressure at the time point.

Bilateral PPTs (six in total) were measured above 1) the injection site, over the splenius capitis muscle (neck), 2) over the middle part of the temporalis muscle (head) (Kasch et al., 2001), and 3) above the extensor carpi radialis brevis (arm) muscle (Slater et al., 2005). The PPT was always assessed first at the side of the first injection, starting proximal and moving distal before assessing the contralateral side. This was done three times, giving an interval of approximately 25 s before re-assessing the same site again. An average of the three values for each site was used for further analysis and normalised to baseline (100%).

Statistics

Data are presented as mean and standard error of the mean (SEM). A Wilcoxon test was used to compare pain areas,VAS parameters and Likert scores after the two injections. Accelerometer, PPT and EMG data was inspected using QQ plots and log-transformed (log10) if not normally distributed (RMS-EMG) before two steps were taken to analyse data: i) a comparison of baselines (one before each injection) before data was normalised to baseline ii) analysis of the normalised data.

For accelerometer, PPT, and RMS-EMG the baseline recordings were compared separately for each movement type using a repeated-measure analysis of variance (RM-ANOVA) with *session* (baseline recordings before hypertonic and isotonic saline injections) along with *site* (PPT sites [3]; EMG recording sites [16 muscles]) where relevant. Data was then normalised to baseline (100%) and analysed using a RM-ANOVA with *time* (during, after) and *saline* (hypertonic or isotonic) along with *side* (left or right) as within factors for each movement type in order to investigate saline*time*side or saline*time interactions. To compensate for the use of multiple ANOVAs in the analysis of EMG data (16 muscles) the P-value for ANOVA effects was Bonferroni corrected to $P<0.0031$ (i.e. 0.05/16). The Newman-Keuls post-hoc test adjusting for multiple comparisons was applied if a significant interaction was detected in the RM-ANOVA or ANOVA. Significance level was set at a P-value of 0.05. Analysis was carried out using STATISTICA 10 (StatSoft Inc., Tulsa, USA).

RESULTS

Experimental neck pain

Injection of hypertonic saline compared with isotonic saline caused higher VAS peaks (5.7 ± 0.4 cm vs. 0.6 ± 0.2 cm, $P<0.001$), longer duration (597.6 ± 53.4 s vs. 52.3 ± 14.7 s, $P<0.001$), and larger area under the VAS-time curve (1524.4 ± 188.8 cm·s vs. 65.6 ± 19.8 cm·s, $P<0.001$). One subject indicated higher pain intensity on the side of the initial injection of hypertonic saline while the

remaining subjects felt no difference. The hypertonic saline also caused larger perceived area of pain in posterior (1.149 a.u. vs. 0.113 a.u., P<0.001) and side view (0.204 a.u. vs. 0.001 a.u., P=0.011). The saline-induced pain generally covered an area extending from the level of the external occipital protuberance and down to the level of the spinous process of Th3 (Fig. 3). For the upper pain area, it extended to the side of the neck while one subject felt it extending to the temporal region. For the lower pain area, the lateral border reached the level of the acromio-clavicular joint.

Performance of arm movements

Due to technical problems, accelerometer data from two participants were discarded. Average timings for slow movements in the two baseline recordings from the first cue signal to maximum angle and from maximum angle to the last cue signal were 3.16 ± 0.02 s and 2.84 s ± 0.02 s for up and down movements, respectively. For the resisted slow movements the same parameters were 3.07 ± 0.02 s and 2.93 ± 0.02 s. During the fast movements the time recorded from the cue signal to the maximum angle was on average 1.04 ± 0.02 s. No significant timing differences were found between baseline recordings or between the normalised data for the isotonic/hypertonic conditions and post measurements.

During the painful session, 24% of the participants felt an increase in the perceived difficultness of lifting the arm indicated by a Likert score of 1 or above whereas all subjects scored 0 for the non-painful session (P=0.027).

Muscle activity during baseline measurements

Average RMS-EMG for the two baseline recordings during fast, slow, and slow-resisted movements are presented in supplementary material (Fig. S6). Comparing RMS-EMG in the two baseline sessions (before each injection) for the different movement types (slow up & down, fast up, and slow-resisted up & down movements) found one significant interaction between sessions and side when lowering the arm during slow movements (RM-ANOVA: F[15,73] = 1.7, P=0.032); post-hoc test revealed that the baseline RMS-EMG for the lower trapezius muscle contralateral to arm movement for the control condition was increased (by 15.8 ± 1.9%) compared with the baseline for the painful condition (NK: P<0.001).

Muscle activity during painful slow movements

The interactions between saline, time and side in the RM-ANOVAs of RMS-EMG were all non-significant whereas Table S1 presents all saline*time interactions. Significant interactions for the normalised RMS-EMG is shown in Fig. 4.

For the upper trapezius muscle on the side of movement (ipsilateral) an interaction between saline and time was found with the post-hoc test revealing decreased RMS-EMG activity during the painful condition when compared with both post and control conditions (NK: $P<0.001$, Fig. 4a). On the side of movement an increased RMS-EMG was found in the anterior deltoid muscle during the painful condition when compared to the post and control conditions (NK: $P<0.001$). For the ipsilateral middle deltoid muscle, the post-hoc test revealed a reduction in the post painful condition (NK: $P<0.001$) compared with both immediately after the injection and the control condition. However, for the control condition an increase was seen when compared with immediately after the isotonic saline injection (NK: $P=0.039$). In the trunk muscles, the bilateral erector spinae muscles showed an increase during the painful condition when compared with post and control conditions (NK: $P<0.003$). In addition, an increase in the ipsilateral erector spinae muscles was observed for the post measurement in the control condition compared with the immediately after recordings in the control condition and with the post recording after the painful condition (NK: $P<0.03$).

In the slow, down movement a decreased RMS-EMG activity of the upper trapezius muscle during the painful condition was found when compared with post and control conditions (Fig. 4b, NK: $P<0.001$). A similar pattern, although with a smaller RMS-EMG reduction during the painful condition, was seen for the middle trapezius muscle (NK: $P<0.001$). The bilateral erector spinae muscles showed an increase in RMS-EMG during the painful condition compared to the post recording and control condition (NK: $P<0.002$).

Muscle activity during painful fast up movements

Reduced RMS-EMG was found in the side of movements during the painful condition when compared with the post and control condition for the upper and middle trapezius muscles (Fig. 4e NK: $P<0.001$). A decrease in RMS-EMG was also found during the painful condition for the contralateral upper trapezius muscle when comparing this to the post recording and control condition (Fig. 4c, NK: $P<0.001$). The ipsilateral erector spinae muscle showed an increase in RMS-EMG during the painful condition compared with post and control conditions in addition to an increase in the post measurement after the control injections of isotonic saline (NK: $P<0.02$).

Muscle activity during slow resisted movements

Data from one participant for the upper trapezius had to be discarded due to technical problems. For the slow, resisted up movement a decreased RMS-EMG was found for the ipsilateral upper trapezius muscles during the painful condition compared with post and control measurements (Fig. 4c; NK: $P<0.001$). For the erector spinae muscle a bilateral increased RMS-EMG was found during the painful condition compared with the post measurement (NK: $P<0.002$) although only

significantly different from the control condition in the contralateral side (NK: P<0.001). However for the ipsilateral side the post RMS-EMG measurement in the erector spinae muscle was decreased compared with the post measurement of the control condition (NK: P=0.010).

For the slow, resisted down movements no significant differences were detected.

Pressure algometry

The PPT at the neck site was higher (RM-ANOVA: F[2,98] = 5.6, P=0.004; NK: P=0.018) in the baseline recordings before the hypertonic injection (214 ± 8 kPa) compared with the baseline before the isotonic injections (199 ± 11 kPa). For the head (356 ± 8 kPa) and arm (371± 9 kPa) sites such differences were not found.

No interactions was found for the saline, time and side analysis for the normalised PPTs however, a saline and time interaction (Fig. 5) was found for the neck site (RM-ANOVA: F[1,48] = 53.0, P<0.001) with post-hoc testing revealing a drop in PPTs in the post-pain condition compared with all other recordings for this site (NK: P<0.001). Increased PPT was observed during experimental pain compared with post and control measurements for both the head (RM-ANOVA F[1,48] = 7.2, P=0.009; NK: P<0.001) and arm sites (ANOVA: F[1,48] = 11.1, P=0.001; NK: P<0.001).

DISCUSSION

This study demonstrated that acute bilateral experimental neck pain reorganised the activity of axioscapular and trunk muscles simultaneously with increased perceived difficultness of lifting the arm. Additionally, the painful condition caused widespread hypoalgesia as well as localized hyperalgesia.

Performance of arm movements

No timing differences were found between the different movement types although performance of movements were perceived as more difficult during the painful condition, indicating that the observed RMS-EMG changes may cause the altered perception. However, the RMS-EMG for the contralateral lower trapezius, during the slow unresisted down movements, was 15.8% lower during baseline before the painful condition compared to the baseline before the control condition. Although significant, this difference was not thought to have influenced the results since data was normalized to baseline and therefor adjusting for this discrepancy. Although one subject felt more pain in the side of the first injection, the injection sequence did probably not affect the current results since the side of first injection with respect to arm movement was randomized.

Axioscapular muscle activity during neck pain

During experimental neck pain a consistent reduction in muscle activity was found for the ipsilateral upper trapezius muscle, which was present during all but the slow resisted down movement. Based on a similar protocol, unilateral experimental pain reduced activity of approximately 12% in the upper trapezius muscle activity (Christensen et al., 2015) whereas the present study, bilateral pain caused a drop of approximately 20%. Another finding supporting a larger impact on the motor system by bilateral neck pain is the significant adaptations seen for the trapezius and erector spinae muscles during the fast movements (Fig. 4e) in the present study which was not found in the study by Christensen et al. (2015). In line with the present study, only bilateral, and not unilateral knee-related pain, caused alterations in the EMG activity of leg muscles during standing (Hirata et al., 2012). Interestingly, when assessing the different movements, the amount of reduced EMG activity for the ipsilateral upper trapezius muscle varied, with the resisted movement showing the least decrease in muscle activity, indicating that changes may be task dependent (Wegner et al., 2010). The activity in the other muscles during both slow resisted and fast up movements (Fig. 4c & e) were less effected by pain, displaying smaller increase or decrease in activity, compared with the slow unresisted up movements (Fig. 4a). A similar pattern, with less effect of pain, was found when comparing the slow resisted down movements with the unresisted down movements (Fig. 4b & d). The added weight for the resisted movements or faster speed probably caused recruitment of additional motor units with higher thresholds to produce the force needed and may have caused less pronounced pain-adaptation effects (Hodges et al., 2008). Such additional recruitment during more demanding movements, may explain the stable motor performance observed in both resisted and fast movements compared to the slow unresisted movements (Fig. 4). A final explanation for less reductions of axioscapular muscle activity during fast or resisted painful movements may indicate that an optimal strategy for these movements had already been obtained during the baseline movements and therefore a pain-related adjustment to optimise or compensate the movement strategy was not possible without compromising the performance.

A factor unaccounted for in this study is the possible internal redistribution of activity within a muscle, which previously have been shown for the upper trapezius during experimental pain (Falla et al., 2009; Madeleine et al., 2006). Furthermore, knowledge of the activity of the deeper layers of axioscapular muscles such as levator scapula and pectorals minor muscles are warranted in order to understand the complex relationship between the reorganised muscle activities while moving the arm during a painful condition. The changes in axioscapular muscle activity in this study and the different motor performance during different movement types may explain some of

the contrasting findings in patient studies studying the axioscapular muscle activity during different tasks. For instance, the upper trapezius activity have been studied during different tasks where some find a reduction (Falla et al., 2004) while others do not (Helgadottir et al., 2011a; Wegner et al., 2010) even though similar patient groups were included. Different strategies for motor adaptations of axioscapular muscle activity due to neck pain have been identified in experimental and clinical studies. Although it may serve as a protective strategy, the long-term effect of such adaptations could be detrimental (Hodges and Tucker 2011).

Trunk muscle activity during neck pain

The erector spinae muscles showed increased activity bilaterally during all but the fast up painful and slow resisted down movements, with the maximal mean increases of approximately 25% during the painful condition. If the increased trunk muscle activity was only found contralateral it could be argued that participants used a strategy with lateral flexion of the trunk to help lifting the arm. However, the additional increased ipsilateral erector spinae muscle activity would counteract such approach and it therefore seems as an unlikely strategy. Nonetheless, altered trunk movement during pain cannot be ruled out without movement analysis, which was not used in the present study. The bilateral increased activity may serve as a protective strategy by increasing the overall stiffness of the spine to protect from further harm (Hodges et al., 2013; Hodges and Tucker 2011). A recent study also found increased activity of a trunk muscle, the contralateral external oblique muscle, while lowering the arm during experimental neck pain (Christensen et al., 2015). The increased activity for erector spinae muscle in the present study and not the external oblique muscle as previously seen is unclear. However, the increased muscle activity distant to the painful area, could indicate a disrupted motor planning, causing an overestimation of the force needed to accomplish the task (Palsson et al., 2015).

Although the results of the present study indicates that pain may cause an increase in muscle activity for the erector spinae muscles, a similar increase is seen for in the post measurement after the control injection, particularly during the fast up movements for which explanations remain elusive. Despite the observation of increased activity in the erector spinae muscle during a condition that should not be painful, the remaining findings from the present study, in combination with previous experimental findings and observations of altered trunk muscle activity in clinical neck pain (Moseley 2004), it seems likely that a link between neck pain and alter motor control of trunk muscles exist.

In general this study shows that experimental neck pain reorganizes axioscapular and trunk muscle activity, but it is unknown if people experiencing an acute episode of clinical neck pain, causing

various acute changes and adaptations, will be predisposed for later development of on-going neck pain.

Pressure pain sensitivity

A small difference in PPTs between baselines (14.8 kPa) at the neck site was found but not believed to influence the results since data was normalised to baseline and thereby adjusting for this. Hyperalgesia in the post measurements at the neck site is contrasting finding to that made in a previous study using unilateral experimental pain (Christensen et al., 2015) and other studies on experimental pain in the neck/shoulder area (Ge et al., 2003; Schmidt-Hansen et al., 2006). Nonetheless, in another study on experimental pelvic girdle pain a similar response with hyperalgesia at the injection site was observed in the post-pain condition (Palsson and Graven-Nielsen 2012).

For the head and arm sites, increased PPTs were found during the painful condition when compared to the post and control conditions. Such hypoalgesia away from the injection site are in line with a previous study using bilateral experimental pain (Ge et al., 2003) and could indicate the importance of the spatial summation (bilateral versus unilateral pain) in triggering a conditioned pain modulation. The local hyperalgesia is similar to clinical neck pain where reduced PPT has been observed in some subgroups of neck pain patients while the hypoalgesia away from the neck site is a contrasting finding to those done in patients (La Touche et al., 2010; Sterling et al., 2002) most likely due to impaired mechanisms for conditioning pain modulation in patients due to the persistent pain condition (Yarnitsky 2010).

Conclusion

Bilateral experimental neck pain in healthy subjects reorganised the activity of axioscapular and some trunk muscles with adaptations being linked to the type of arm movement. In addition, experimental neck pain caused localised hyperalgesia along with widespread hypoalgesia. Together, these results demonstrate complex adaptations of the sensory and motor systems, which could be a protective mechanism. Although this study only shows the immediate effect of bilateral experimental neck pain on healthy subjects, the findings may help clinicians making mechanism-based decisions by supporting the inclusion of the shoulder girdle and trunk muscles in the examination and rehabilitation of clinical neck pain.

AUTHOR CONTRIBUTION

Steffan Wittrup Christensen was in charge of planning and executing data collection, statistical analyses, and writing the first draft of the manuscript. Rogerio Pessoto Hirata and Thomas Graven-Nielsen contributed to the planning of the study, statistical analyses and development of the final version of the manuscript. All authors discussed the results, commented on the manuscript and agreed on the final version.

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FIGURE LEGENDS

Figure 1. Study design: Electromyographic (EMG) recordings were followed by pressure pain threshold (PPT) measurements at Baseline, During (i.e. immediately after the injection), and Post (i.e. 5 min after any potential pain had vanished). The order of saline injections was randomised in a balanced way.

Figure 2. Photographic depiction of a subject performing the standardized arm movements from an upright sitting position.

Figure 3. Superimposed body chart drawings (N = 25) after the hypertonic saline (a) and isotonic saline injections (b). Transparency in colours indicates that these were less frequently marked by the subjects.

Figure 4. Mean normalised RMS-EMG (+ SEM, N = 25 for slow & slow resisted movements; N = 23 for fast movements) recorded immediately after injection of hypertonic (Hyp) or isotonic (Iso) saline and in a post session 5 min after any potential pain had vanished. RMS-EMG was extracted from the arm movements during the slow up (a), down (b), slow resisted up (c), down (d) and fast up (e) phases. EMG recordings from ipsilateral (Ipsi) and contralateral (Contra) muscles: Upper trapezius (UT), middle trapezius (MT), anterior deltoid (AD), middle deltoid (MD), and erector spinae (ES). Significantly different RMS-EMG from post recordings following either the painful or the control condition (*, NK: $P<0.05$) or compared with the same time (immediately after injection or post) for the control condition (#, NK: $P<0.05$) is illustrated.

Figure 5. Mean (averaged for both sides) normalized pressure pain thresholds (PPTs; +SEM, N=25) for the Neck (injection site), Head (m. temporalis muscle), and the Arm (m. extensor carpi radialis brevis) immediately after the injection of hypertonic (Hyp) or isotonic (Iso) saline and in a post measurement 5 min after any potential pain had gone. Significantly different PPT from post recordings following either the painful or the control condition (*, NK: $P<0.05$) or compared to the same time (immediately after injection or post) for the control condition (#, NK: $P<0.05$) is illustrated.

Figure 1

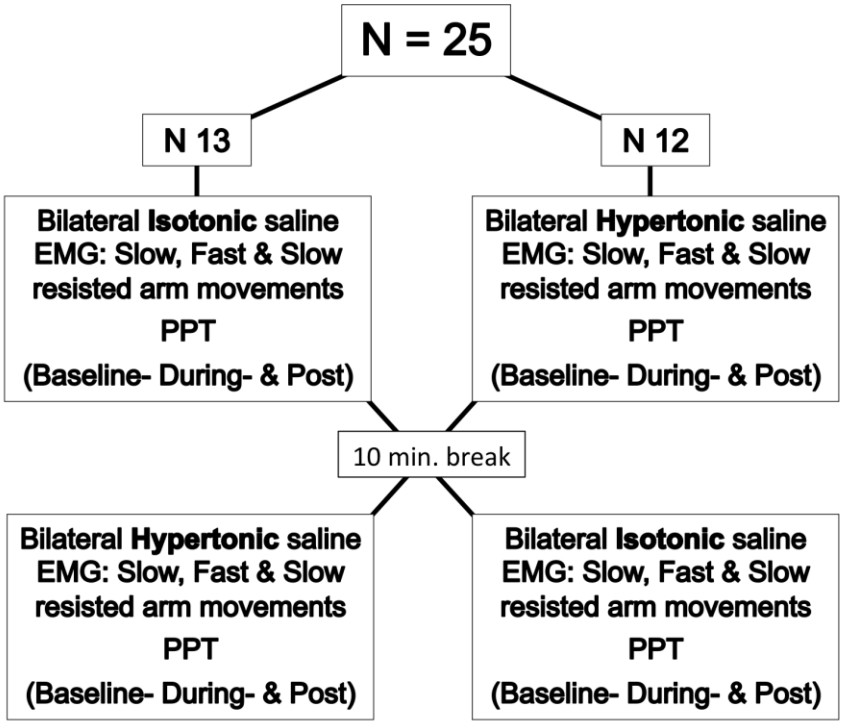


Figure 2

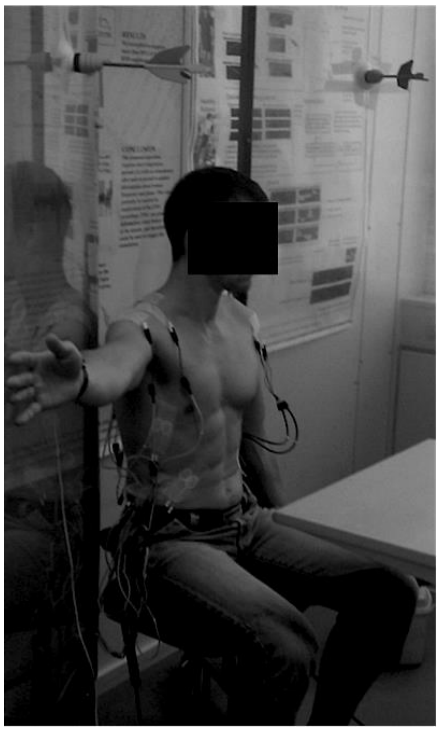
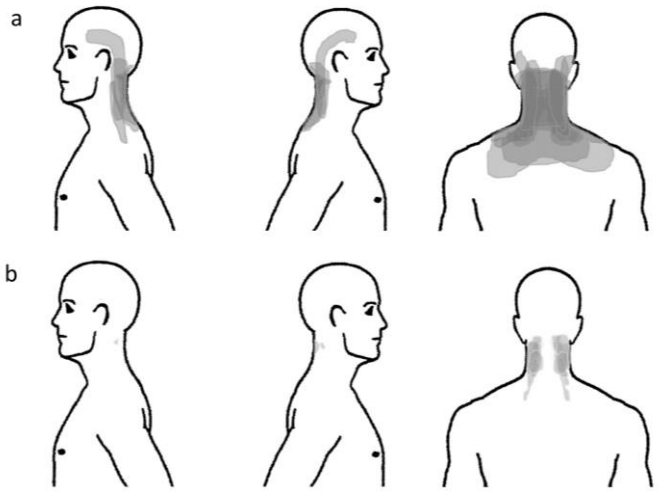


Figure 3



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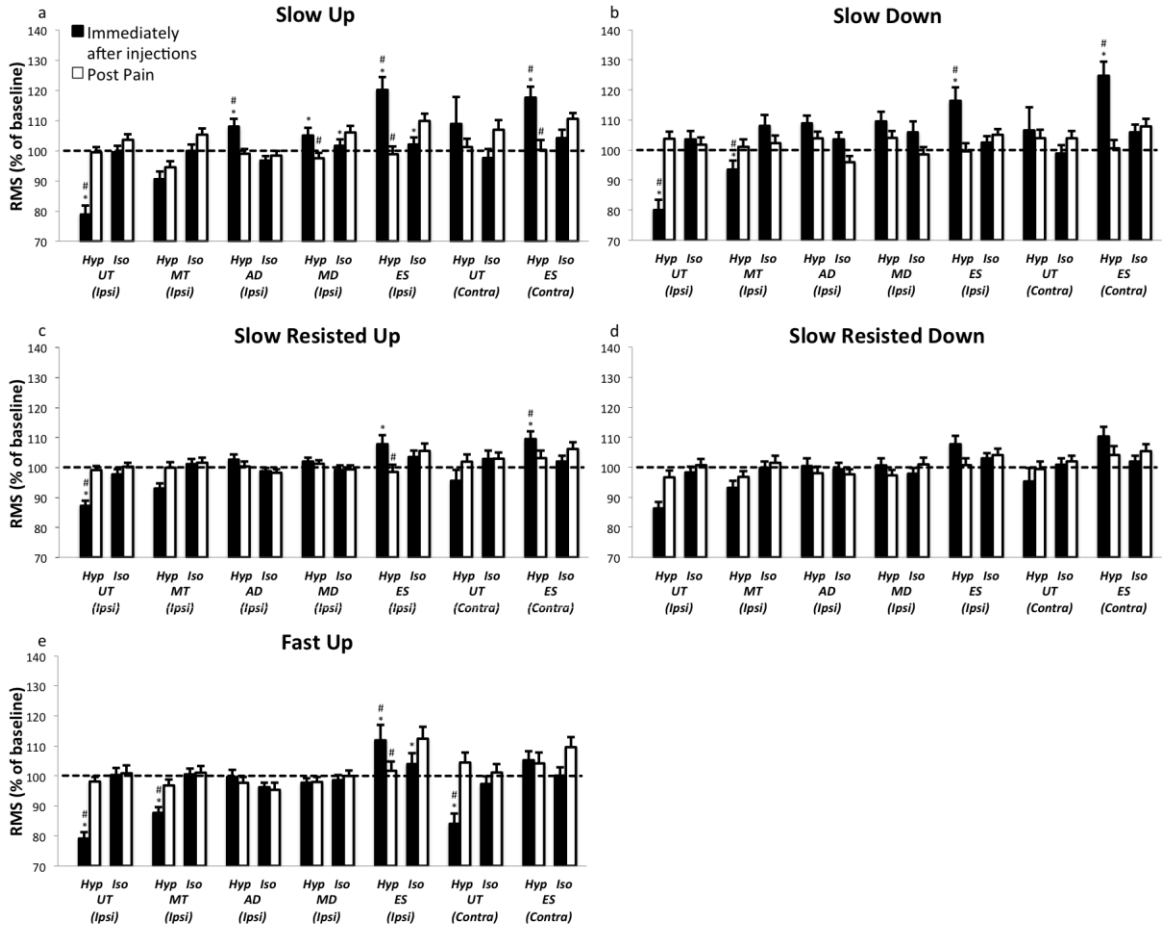

Figure 5

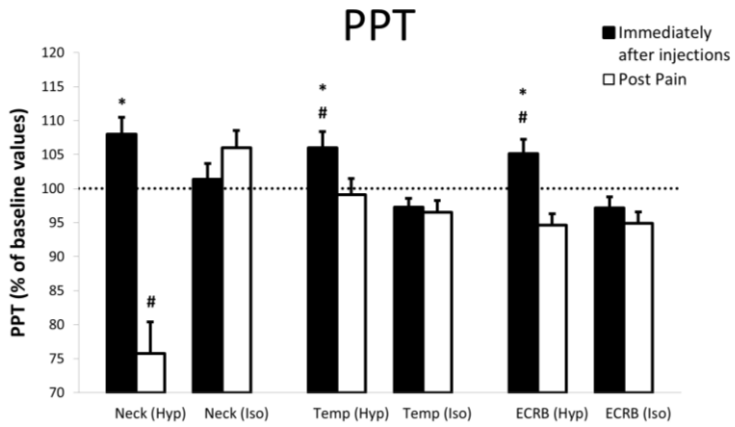

Figure S6

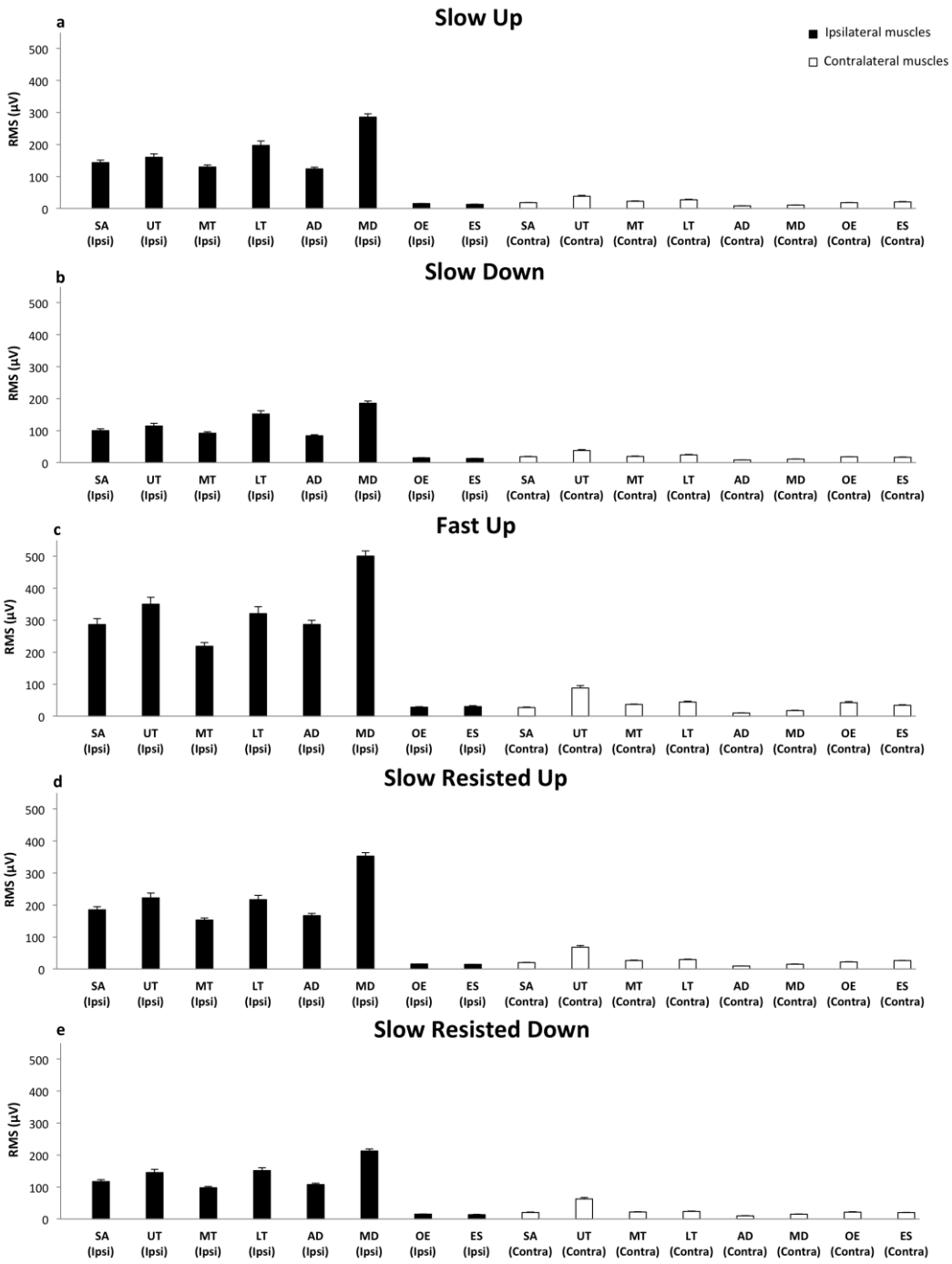

Figure S6: Mean RMS-EMG values (+ SEM, N = 25 for slow & slow resisted movements; N = 23 for fast movements) of baseline recordings (mean of right and left movements) for slow up (a), slow down (b), fast up (c), slow resisted up (d) and slow resisted down (e). Root-mean-square electromyographic (RMS-EMG) parameters from ipsilateral (Ipsi) and contralateral (Contra) muscles: Serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), external oblique (OE), and erector spinae (ES).”

Table S1: The RM ANOVA interactions between saline and time for RMS-EMG recordings for all muscles and all movements. Ipsilateral (Ipsi) and contralateral (Contra) muscles with respect to the movement: Serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), external oblique (OE), and erector spinae (ES). Significant ANOVA interactions (P<0.003, Bonferroni corrected due to multiple ANOVAs) followed by significant post-hoc testing is indicated (**, P<0.05).

Table S1	**Movement Type**				
Muscle:	**Slow Up**	**Slow Down**	**Fast Up**	**Resisted up**	**Resisted down**
SA, Ipsi	F[1,48] = 0.1 P=0.713	F[1,48] = 2.8 P=0.100	F[1,44] = 6.7 P=0.012	F[1,48] = 0.4 P=0.485	F[1,48] = 0.6 P=0.418
UT, Ipsi	**F[1,48] = 37.9 P<0.001	**F[1,48] = 40.3 P<0.001	**F[1,44] = 56.1 P<0.001	**F[1,47] = 21.3 P<0.001	F[1,48] = 7.3 P=0.009
MT, Ipsi	F[1,48] = 0.004 P=0.948	**F[1,48] = 14.9 P<0.001	**F[1,44] = 11.1 P=0.001	F[1,48] = 8.5 P=0.005	F[1,48] = 0.8 P=0.356
LT, Ipsi	F[1,48] = 1.4 P=0.229	F[1,48] = 3.6 P=0.061	F[1,44] = 7.3 P=0.009	F[1,48] = 1.1 P=0.261	F[1,48] = 0.1 P=0.665
AD, Ipsi	**F[1,48] = 10.6 P=0.002	F[1,48] = 0.8 P=0.350	F[1,44] = 0.009 P=0.921	F[1,48] = 0.3 P=0.570	F[1,48] = 0.01 P=0.888
MD, Ipsi	**F[1,48] = 22.1 P<0.001	F[1,48] = 0.3 P=0.557	F[1,44] = 0.1 P=0.706	F[1,48] = 0.2 P=0.605	F[1,48] = 3.4 P=0.070
OE, Ipsi	F[1,48] = 0.1 P=0.669	F[1,48] = 0.01 P=0.889	F[1,44] = 0.6 P=0.438	F[1,48] = 1.5 P=0.220	F[1,48] = 0.08 P=0.778
ES, Ipsi	**F[1,48] = 34.3 P<0.001	**F[1,48] = 16.0 P<0.001	**F[1,44] = 18.0 P<0.001	**F[1,48] = 11.9 P=0.001	F[1,48] = 7.5 P=0.008
SA, Contra	F[1,48] = 2.3 P=0.134	F[1,48] = 0.01 P=0.908	F[1,44] = 1.0 P=0.319	F[1,48] = 2.6 P=0.113	F[1,48] = 2.59 P=0.113
UT, Contra	F[1,48] = 3.6 P=0.061	F[1,48] = 0.6 P=0.419	**F[1,44] = 32.6 P<0.001	F[1,48] = 4.7 P=0.034	F[1,48] = 0.9 P=0.332
MT, Contra	F[1,48] = 2.7 P=0.102	F[1,48] = 0.1 P=0.752	F[1,44] = 0.2 P=0.622	F[1,48] = 0.01 P=0.896	F[1,48] = 3.7 P=0.058
LT, Contra	F[1,48] = 3.7 P=0.057	F[1,48] = 0.09 P=0.761	F[1,44] = 0.8 P=0.370	F[1,48] = 4.7 P=0.033	F[1,48] = 0.4 P=0.521
AD, Contra	F[1,48] = 3.5 P=0.067	F[1,48] = 0.1 P=0.730	F[1,44] = 0.002 P=0.963	F[1,48] = 0.1 P=0.707	F[1,48] = 0.6 P=0.412
MD, Contra	F[1,48] = 0.03 P=0.858	F[1,48] = 0.1 P=0.667	F[1,44] = 0.3 P=0.531	F[1,48] = 6.0 P=0.017	F[1,48] = 4.3 P=0.043
OE, Contra	F[1,48] = 1.2 P=0.273	F[1,48] = 0.1 P=0.722	F[1,44] = 0.7 P=0.400	F[1,48] = 0.001 P=0.964	F[1,48] = 0.6 P=0.793
ES, Contra	**F[1,48] = 24.7 P<0.001	**F[1,48] = 22.3 P<0.001	F[1,44] = 5.8 P=0.019	**F[1,48] = 18.1 P<0.001	F[1,48] = 9.5 P=0.003