



**AALBORG UNIVERSITY**  
DENMARK

**Aalborg Universitet**

## **Origin of neck pain and direction of movement influence dynamic cervical joint motion and pressure pain sensitivity**

Qu, Ning; Lindstrøm, Rene; Hirata, Rogerio Pessoto; Graven-Nielsen, Thomas

*Published in:*  
Clinical Biomechanics

*DOI (link to publication from Publisher):*  
[10.1016/j.clinbiomech.2018.12.002](https://doi.org/10.1016/j.clinbiomech.2018.12.002)

*Creative Commons License*  
CC BY-NC-ND 4.0

*Publication date:*  
2019

*Document Version*  
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*

Qu, N., Lindstrøm, R., Hirata, R. P., & Graven-Nielsen, T. (2019). Origin of neck pain and direction of movement influence dynamic cervical joint motion and pressure pain sensitivity. *Clinical Biomechanics*, 61, 120-128. <https://doi.org/10.1016/j.clinbiomech.2018.12.002>

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

### **Take down policy**

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.

## Accepted Manuscript

Origin of neck pain and direction of movement influence dynamic cervical joint motion and pressure pain sensitivity

Ning Qu, Rene Lindstrøm, Rogerio Pessoto Hirata, Thomas Graven-Nielsen



PII: S0268-0033(18)30664-8

DOI: <https://doi.org/10.1016/j.clinbiomech.2018.12.002>

Reference: JCLB 4652

To appear in: *Clinical Biomechanics*

Received date: 8 August 2018

Accepted date: 4 December 2018

Please cite this article as: Ning Qu, Rene Lindstrøm, Rogerio Pessoto Hirata, Thomas Graven-Nielsen , Origin of neck pain and direction of movement influence dynamic cervical joint motion and pressure pain sensitivity. Jclb (2018), <https://doi.org/10.1016/j.clinbiomech.2018.12.002>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**ORIGIN OF NECK PAIN AND DIRECTION OF MOVEMENT INFLUENCE  
DYNAMIC CERVICAL JOINT MOTION AND PRESSURE PAIN SENSITIVITY**

Ning Qu<sup>a</sup>, Rene Lindstrøm<sup>a</sup>, Rogerio Pessoto Hirata<sup>a\*</sup>, Thomas Graven-Nielsen<sup>b</sup>

<sup>a</sup> *SMI, Department of Health and Science Technology, Faculty of Medicine, Aalborg University, Denmark*

<sup>b</sup> *Center for Neuroplasticity and Pain (CNAP), SMI, Department of Health and Science Technology, Faculty of Medicine, Aalborg University, Denmark*

**Original paper for:** Clinical Biomechanics

**Number of text pages:** 13

**Number of figures and tables:** 7

**Words of abstract:** 239

**Words of main text:** 3418

**\*Corresponding author:**

Rogerio Pessoto Hirata, Ph.D., Associate Professor

Center for Sensory Motor Interaction (SMI), Department of Health Science and Technology,  
Faculty of Medicine, Aalborg University

Fredrik Bajers Vej 7D-3

9220 Aalborg E, Denmark

E-mail: [rirata@hst.aau.dk](mailto:rirata@hst.aau.dk)

**Abstract**

*Background:* Patients with neck pain normally showed alterations in cervical motion and pressure pain sensitivity. Cervical joints show scattered motions opposite to (anti-directional) the primary motion direction (pro-directional) during dynamic cervical flexion and extension. This study aimed to assess dynamic cervical joint motion and pressure pain sensitivity when pain originated from different cervical muscles which may have clinical relevance in diagnosis of impairments related with neck pain.

*Methods:* Fluoroscopic video recordings of cervical flexion and extension were collected from fifteen healthy subjects before and during hypertonic saline-induced pain in right multifidus and trapezius muscles. Cervical flexion and extension motions were divided into 10 epochs with respect to time. Pro-directional, anti-directional, and total joint motion were extracted across epochs as well as joint motion variability. Pressure pain thresholds (PPTs) were assessed bilaterally over C2/C3 and C5/C6 facet joints.

*Findings:* Compared with baseline: 1) Multifidus muscle pain increased the C3/C4 anti-directional motion ( $P<0.01$ ), decreased the C6/C7 anti-directional motion ( $P<0.05$ ) during extension, and redistributed total joint motion between joints and between half ranges during flexion ( $P<0.05$ ). 2) Trapezius muscle pain decreased pro-directional motion ( $P<0.05$ ), anti-directional motion ( $P<0.05$ ), and joint motion variability ( $P<0.05$ ) during extension. 3) Trapezius and multifidus muscle pain increased the PPTs bilaterally over C2/C3 and on the left side of C5/C6 facet joints ( $P<0.05$ ).

*Interpretation:* The direction of motion influenced the effects of experimental muscle pain on dynamic cervical joint kinematics, and deep muscle pain showed local effects on individual joints while superficial muscle pain showed global effects spread to all joints.

**Key words:** Cervical Spine; Pro-directional Motion; Anti-directional Motion; Experimental Neck Pain; Video-fluoroscopy; Pressure Pain Thresholds

ACCEPTED MANUSCRIPT

## 1. INTRODUCTION

Neck pain is a worldwide disease with a mean of 37.2% one-year prevalence and ranked the fourth in leading causes of global disability<sup>1, 2</sup>. The underlying causes for neck pain are not clear and the majority of patients with neck pain is classified as non-specific neck pain without a clear etiology<sup>4</sup>. Therefore, neck pain is often described by subjective signs and symptoms. However, objective measures of neck pain has been used in previous studies such as reduced range of motion, decreased cervical muscle strength, lower movement velocity, increased neck reposition error, altered cervical joint motion and altered pressure pain sensitivity<sup>5-11</sup>.

Video fluoroscopy methods which could capture moving X-ray videos allows objective measurement of the motion of each cervical joint, and recently new evidence have been published on the variation of healthy cervical joint motion<sup>12-14</sup>. Patients with neck pain normally show altered cervical joint motion and altered pressure pain sensitivity of the neck<sup>6, 8, 15</sup>. Christensen et al assessed pressure pain sensitivity in neck pain patients before and after arm movements<sup>16</sup>. The understanding of links between joint motion and pressure pain sensitivity remain unclear. However, pressure pain thresholds (PPTs) through algometry does allow for objective assessment of pain sensitivity of structure overlaying cervical joints, and PPTs provide a method to examine pain sensitivity of tissues close to the cervical joints<sup>17</sup>. PPTs over bilateral C2/C3 and C5/C6 facet joints were demonstrated to be different between subgroups of patients with neck pain<sup>8, 15</sup>.

Individual cervical joint motion has been reported to be more important compared with total range of motion (ROM) in diagnosis and decision of surgery and postoperative assessments<sup>11, 18, 19</sup>. Anatomy dictates a difference in deep and superficial cervical muscles ability to influence single joint motion, as only the deep muscles such as the multifidus can directly control the motion of a single joint<sup>20</sup>. These anatomy evidence suggest that muscle

contraction as a result of pain in deep muscles would have local effects on the motion of cervical joints near to the site of pain, while pain in superficial cervical muscles may have a more global effects on motion of the multiple joint, which is between origin and insertion of the superficial muscles<sup>21</sup>. Traditional imaging examination of cervical joint kinematics in sagittal plane are based on static end-range radiographs of cervical flexion and extension movements, this imaging is severely limited measuring real time joint motion<sup>22</sup>. Quantitative video-fluoroscopy could capture moving X-ray videos of dynamic neck movement<sup>23</sup> and provides further insight and more details of cervical joint motion, which cannot be seen via visual inspections<sup>12-14, 24</sup>. Previous studies showed that individual cervical joint moved reversely to the primary motion direction during cervical flexion and extension in healthy subjects<sup>14</sup>. Joint motion opposite to the primary motion direction is defined as anti-directional motion and joint motion along with the primary motion direction is defined as pro-directional motion, the anti-directional motion is 40% of the pro-directional motion<sup>14</sup>. Changes in pro-directional motion and anti-directional motion under gravitational forces may reflect the fine neuromuscular control of individual joints related to a source of pain.

Experimental pain models provide the possibility to investigate pain from different cervical muscles on cervical motion and pressure pain sensitivity within subjects<sup>34</sup>. Therefore, the aim of the study was to investigate effects of experimental superficial (right trapezius) and deep (right multifidus) muscle pain on dynamic joint kinematics during flexion and extension and on PPTs over bilateral C2/C3 and C5/C6 facet joints. It was hypothesized that 1) experimental trapezius muscle pain will show global effect and experimental multifidus muscle pain will show local effect on dynamic joint kinematics, 2) PPTs over bilateral C2/C3 and C5/C6 facet joints will increase during superficial cervical experimental muscle pain but decrease during deep cervical experimental muscle pain.

## 2. METHODS

### 2.1 Subject

Fifteen healthy subjects without neck pain for the last 3 months were included (6 females) with mean age was 25.1 (SD 4.7) years, mean height was 172.7 cm (SD 11.6) and mean weight 70.0 kg (SD 13.6). Subjects were excluded if they had: (1) Cervical trauma or surgery, (2) Cervical musculoskeletal diseases, (3) Psychosocial profile that would affect responsiveness to pain, (4) inability to cooperate and (5) Possibility of pregnancy. The study was conducted according to the Declaration of Helsinki and approved by the local ethics committee (N20140004). All subjects provided written, informed consent after the study was explained.

### 2.2 Experimental protocol

The repeated-measures design was used that subjects attended two sessions separated by at least seven days. In the first session, either multifidus or trapezius muscle was randomly selected for injection of hypertonic sa-line to induce experimental neck pain. PPTs and cervical movements (cervical flexion and extension from the self-determined neutral position to the maximal end-range position) were assessed before and after injection. Pain intensity, pain duration and pain distribution was recorded after injections. In the second session, the same procedure was repeated with hypertonic saline injected in the previous non-injected muscle. The cervical flexion and extension records were performed after injections whenever the pain intensity was scored at least 3 cm on a 10-cm visual analogue scale (VAS) with “no pain” at 0 cm and “worst pain imaginable” at 10 cm.

### 2.3 Experimental muscle pain



The hypertonic saline-induced muscle pain model has been used extensively to investigate sensory and motor alterations associated with pain in previous studies for it comparably mimics clinical muscle pain without confounding factor usually found in chronic neck pain patients<sup>35</sup>. The experimental pain was induced by injecting a 0.5 ml bolus of sterile hypertonic saline (5.8%) in right cervical multifidus and right trapezius muscle with a randomized order across the two sessions. The right multifidus muscle was injected in the deepest layer at C4 level, which originates from the articular pillar of C5/C6 junction and inserts on the laminae of C3<sup>36</sup>. The right trapezius muscle was injected at the midpoint between the spinous process of C7 and the acromion<sup>37</sup>. All injections were ultrasound guided<sup>38</sup>.

The pain intensity was assessed on VAS. every minute after injections until the pain disappeared. The peak VAS score was extracted for analysis. The pain duration was calculated from the onset to the disappearance of the pain. Pain distribution was drawn on a body chart at the end of each session and were extracted (VistaMetrix v.1.38.0; SkillCrest, LLC, Tucson, AZ, USA) in arbitrary units (a.u.).

#### *2.4 Pressure pain thresholds*

Subjects lie on their stomach in a bed and totally relaxed the neck. The PPTs were measured bilaterally above C2/C3 and C5/C6 cervical facet joints<sup>15, 39</sup> by using a pressure algometer (Algometer, Somedic Production AB, Sollentuna, Sweden) with a round rubber tip (contact area 1 cm<sup>2</sup>). The pressure was delivered at a constant rate of 30kPa/s during measurements. Subjects were instructed to press a handheld button exactly at the moment when the pressure sensation became painful. Measurement at each site was repeated three times and the average of the three repetitions was used for further analysis.

### *2.5 Fluoroscopic recordings and extraction of kinematic data*

The study applied a method described previously (more details are in supplementary material)<sup>12-14</sup>. Video-fluoroscopy (Philips BV Libra, 2006, Netherland) was used to record videos of cervical flexion and extension (Fig. 1A). A custom Matlab (2015b) program was used to digitalize the images (frame-by-frame) obtained from the fluoroscopic videos. The program incorporated the approach of identifying the vertebral corners as landmarks developed by Frobin et al.<sup>40</sup> in addition to the external markers attached to the glasses, which were used to represent the occipital condyles (Fig. 1B). The reproducibility of the marking procedure has been published with good reliability and low average marking errors<sup>41</sup>. The markers of each cervical vertebra (C0-C7) were used to calculate vertebrae mid-planes. Joint angle was defined as the angle between two adjacent mid-planes and joint angles were positive during extension and negative during flexion. Joint motion was defined as angle difference of the same joint between different time points during neck movements (Fig.1C). Joint motion opposite to the primary motion direction was defined as anti-directional motion, while joint motion along with the primary motion direction was defined as pro-directional motion. Example of data extraction procedure was shown in Fig1D. The first and last frame of each flexion and extension motion were visually identified in videos to find the total number of frames. Eleven images in evenly divided intervals from the first frame to the last frame were selected. The eleven images separated each cervical flexion and extension motion into 10 epochs.. Joint motion during each epoch was obtained after marked the images, which includes both anti- and pro-directional motion. The sums of pro-directional and anti-directional motion across 10 epochs of individual cervical joint were extracted. Total joint motion is the sum of anti- and pro-directional motion. Joint motion variability was extracted by calculating the variance of joints motions across 10 epochs. Furthermore, the total joint

motion during the first half range (first 5 epochs) and the second half range (second 5 epochs) of flexion and extension motion were extracted.

## 2.6 Statistics

Mean and standard deviation (SD) were present in text, while mean and standard error (SE) were present in figures. Statistical analysis was performed in SPSS (IBM Statistics 24). Before statistical comparison, all data were tested for normal distribution by the Kolmogorov-Smirnov test, and the homogeneity of variance between paired conditions was tested by Mauchly's test. The normality and homogeneity were confirmed.

To assess if pain from deep and superficial cervical extensor show different pain characters, the pain distribution, peak VAS score and pain duration were compared between multifidus and trapezius muscle pain by paired t-test.

To assess if pain from deep and superficial cervical extensor show different effects on dynamic cervical joint kinematics, pro-directional motion, anti-directional motion, joint motion and joint motion variability across 10 epochs of individual cervical joint motion were analyzed separately for trapezius and multifidus muscle during cervical flexion and extension by two-way repeated-measures analysis of variance (RM-ANOVA) with factors: Joint (C0/C1, C2/C3, C3/C4, C4/C5, C5/C6 and C6/C7) and Time (before pain, during pain). Additionally, total joint motion during half ranges of flexion and extension motion were analyzed separately before and during trapezius and multifidus muscle pain by three-way RM-ANOVA with factors: Joint (C0/C1, C2/C3, C3/C4, C4/C5, C5/C6 and C6/C7), Time (before pain, during pain) and Range (first half, second half).

To assess if pain from deep and superficial cervical extensor show different effects on PPTs over bilateral C2/C3 and C5/C6 cervical facet joints, PPTs were analyzed separately for

trapezius and multifidus muscle by two-way RM-ANOVA with factors: Measurement site (right C2/C3, left C2/C3, right C5/C6 and left C5/C6) and Time (before pain, during pain).

All ANOVAs were corrected for family-wise error. If the significance remained, post hoc was performed with Bonferroni correction for multilevel comparison when appropriate. P-values < 0.05 were considered as significant.

### 3. RESULTS

#### 3.1 Pain intensity, duration and distribution

Multifidus and trapezius muscle pain showed non-significant difference in the pain distribution (Fig. 2A and Fig. 2B, Multifidus: 1.97 a.u. (SD 2.15), Trapezius: 1.10 a.u. (SD 0.86),  $t_{(14)} = 1.58$ ,  $P = 0.137$ ), the peak VAS score (Fig. 2C, Multifidus: 6.1 cm (SD 2.1), Trapezius: 5.5 cm (SD 2.2),  $t_{(14)} = -2.09$ ,  $P = 0.055$ ) and the pain duration (Fig. 2C, Multifidus: 8.3 mins (SD 1.7), Trapezius: 7.9 mins (SD 2.3),  $t_{(14)} = -1.07$ ,  $P = 0.30$ ).

#### 3.2 Pressure pain thresholds

The PPTs results before and during trapezius and multifidus muscle pain was presented in Fig. 3. One subject was excluded due to incomplete data. Main effect of time was significant before and during trapezius muscle pain (Fig. 2D,  $F_{(1,13)} = 7.647$ ,  $P = 0.032$ ). Post hoc analysis showed PPTs were higher during pain condition than before pain condition (during pain: 298 kPa (SD 22.7), before pain: 260 kPa (SD 20.5)).

Significant interaction of Measure site and Time was found before and during multifidus muscle pain condition (Fig. 2E,  $F_{(3,39)} = 4.496$ ,  $P = 0.016$ ). Post hoc analysis showed PPTs over bilateral C2/C3 facet joints (Bonferroni: Right:  $P = 0.035$ , Left:  $P = 0.010$ ) and over left C5/C6 facet joint (Bonferroni:  $P = 0.010$ ) were higher during pain condition than before pain condition.

### 3.3 Pro-directional motion and anti-directional motion

Pro-directional motion and anti-directional motion before and during multifidus muscle pain are shown in Fig. 3. Significant interaction between Joint and Time was found in anti-directional motion of cervical extension ( $F_{(6,84)} = 4.386, P = 0.008$ ). Post hoc analysis revealed that the C3/C4 anti-directional motion increased 1.7 degrees (SD 1.8) (Bonferroni:  $P = 0.002$ ) and C6/C7 anti-directional motion decreased 1.8 degrees (SD 2.4) (Bonferroni:  $P = 0.012$ ) compared to before pain condition.

Pro-directional motion and anti-directional motion before and during trapezius muscle pain are shown in Fig. 4. Main effect of Time was found in pro-directional motion ( $F_{(6,84)} = 14.410, P = 0.016$ ) and anti-directional motion ( $F_{(6,84)} = 10.463, P = 0.048$ ) of cervical extension. Post hoc analysis revealed that pro-directional motion decreased 6.7 degrees (SD 6.8) and anti-directional motion decreased 6.1 degrees (SD 7.3) compared to before pain condition.

### 3.4 Total joint motion

The two-way RM-ANOVA analysis does not provide any main effect or interaction effect. No significant difference was found for any total joint motion before and during trapezius and multifidus muscle pain (Supplementary Fig. 1).

### 3.5 Total joint motion during half ranges of flexion and extension

The total joint motion during half ranges of flexion and extension before and during pain was shown in Fig. 5. Significant interaction effect between Joint, Time and Epoch was found in cervical flexion before and during multifidus muscle pain ( $F_{(6,84)} = 4.186, P = 0.004$ ). Post hoc analysis revealed that multifidus muscle pain decreased the C3/C4 motion (Bonferroni:  $P$

= 0.003) and C5/C6 motion (Bonferroni:  $P = 0.004$ ) during first half range of flexion compared to before pain condition, and multifidus muscle pain increased the C1/C2 motion (Bonferroni:  $P = 0.038$ ) and C3/C4 motion (Bonferroni:  $P = 0.042$ ), but decreased C2/C3 motion (Bonferroni:  $P = 0.007$ ) during second half of flexion compared to before pain condition.

### *3.6 Joint motion variability*

Main effect of Time was found in cervical extension before and during trapezius muscle pain ( $F_{(6,84)} = 13.233$ ,  $P = 0.012$ ). Post hoc analysis revealed that joint motion variability decreased during pain compared to before pain condition (Fig. 6).

## **4. Discussion**

The results showed that experimental muscle pain had a varied effect on cervical joint motion, and the origin of pain and the direction of neck motion contributed to the variation. The variation included 1) altered proportions of anti-directional and pro-directional motion during an image sequence of a single joint; 2) redistributed motion of single joint between half ranges during cervical motion; and 3) redistributed the motion between multiple joints. The effects were only found when the painful muscles were agonist muscles for the overall pro-directional motion of the neck (i.e. extension), and the effects were often found in the anti-directional motion contributions.

The results confirmed our hypothesis that experimental trapezius muscle pain showed global effect on dynamic joint kinematics by decreasing pro-directional motion (on average 6.7 degrees), anti-directional motion (on average 6.1 degrees) and joint motion variability during cervical extension. Experimental multifidus muscle pain showed local effects indicated

as increased C3/4 anti-directional motion (on average 1.7 degrees) and decreased C6/C7 anti-directional motion (on average 1.8 degrees) during cervical extension.

The hypothesis of increased PPTs was not confirmed, as experimental trapezius and multifidus muscle pain increased the PPTs over bilateral C2/C3 and C5/C6 facet joints, except for the right C5/C6 facet joint. The right C5/C6 facet joint was near to the multifidus injection site.

#### *4.1 Pain intensity, duration and distribution*

The pain intensity, pain duration and pain distribution were not different between experimental multifidus and experimental trapezius muscle pain. This result is different from previous study with experimental low back pain in healthy subjects, where the deep low back muscles demonstrated higher pain intensity compared to superficial low back muscles<sup>33</sup>. The opposite finding may be explained by the intrinsic anatomical differences between neck region and low back region, that tissues of the neck region are more sensitive compared to the tissues of the low back region<sup>42</sup>. Furthermore, the difference in density and sensitivity of nociceptive afferents between deep and superficial cervical muscles may not be large enough to show significant difference in pain intensity<sup>43</sup>.

Pain evoked in the right trapezius muscle resulted in a unilateral and right distribution of neck pain<sup>37,44</sup>. The experimental pain in the right multifidus muscle distributed unilaterally to the right anterolateral neck and to the right shoulder. Different density of nerve innervations in these two muscles and different injection sites may explain the difference in pain distribution between multifidus and trapezius muscle pain<sup>45</sup>.

#### *4.2 Pressure pain sensitivity*

Trapezius and multifidus muscle pain showed increased PPTs over cervical facet joints. This result is in concordance with previous experimental pain studies that reduced response to painful stimuli was found at areas distant to the primary site of pain<sup>46,47</sup>. However, the finding from multifidus muscle pain is opposite to previous studies showing that experimental pain in deep tissues decreased PPTs at areas distant to the primary site of pain<sup>31,32</sup>. These differences may be explained by diverse stimulated tissues and the time between tonic painful stimuli and assessment of PPTs in studies<sup>31,44</sup>. Descending hypoalgesia is normally not found locally to the induced pain site<sup>48</sup>. Anatomically, injection site of the right multifidus muscle is closer to right C5/C6 facet joint than the trapezius muscle<sup>36</sup>, which may explain not increased PPTs over right C5/C6 facet joint during the multifidus pain.

#### *4.3 Dynamic joint kinematics*

The pro- and anti-directional motions reflect the fine neuromuscular control on individual cervical joints<sup>14</sup>. Larger pro- and anti-directional motion excursions indicate the movement of cervical joint is more fluctuant during cervical flexion and extension and vice versa<sup>14</sup>. Cervical joint motion patterns are characterized by alterations in pro- and anti-directional motion<sup>14</sup>.

Experimental pain from deep and superficial muscle showed different effects on cervical joint motion. Deep multifidus muscle pain during cervical extension demonstrated a local effect with increased C3/4 anti-directional motion and decrease C6/C7 anti-directional motion. The right multifidus muscle overlies the right C3/C4 facet joint<sup>36</sup>, and this may explain the less control on joint C3/C4 during pain. The redistribution of anti-directional motion could be explained by compensatory mechanisms between cervical joints, where decreased motion at one joint could be compensated by other joints<sup>18</sup>. These short-term local adaptive strategies



are assumed to protect the cervical spine from further damage, while the long-term influence of pain remains unclear<sup>49</sup>.

Superficial trapezius muscle pain globally decreased pro-directional motion, anti-directional motion and joint motion variability during cervical extension compared with before pain conditions. Although the anatomy of the trapezius muscle does not allow for control of single joints, pain in the superficial trapezius showed changes, which appears to arise from motor control of single joints. This result implies that pain in trapezius alter muscle activity of other deeper muscles, which can control single joints.

No alterations of pro- and/or anti-directional motion were found during cervical flexion. Both trapezius and multifidus muscle are extensors, and the result implied that the effect on joint motion of muscular pain may be more profound, when the muscles work as agonist<sup>50</sup>. Alternatively, anatomical difference between anterior and posterior osseous, muscular and ligament structures under the influence of gravity may account for different motion findings between cervical flexion and extension<sup>51</sup>. The results agree with previous studies, which showed that neck pain affected cervical motion differently between flexion and extension<sup>52</sup>.

Individual joint motion did not change significantly between before pain and during pain from trapezius and multifidus muscles. However, multifidus muscle pain redistributed motion between first and second half range of joint motion during cervical flexion. This study indicates that dynamic joint kinematics from real-time videos are more sensitive to detect effects of pain compared with joint motion measured from images with static upright and end positions<sup>53, 54</sup>.

#### *4.4. Clinical and scientific implications*

This study highlights the value of dynamic joint kinematics in detecting altered cervical joint motion in healthy subjects when experimental pain was induced in deep and superficial

cervical muscles. The study provides new background for the clinical value of training of deep and superficial neck muscles, and the study suggest that deep spinal stability is an integrated part of dynamic movement<sup>29</sup>.

The results suggest that pain from cervical muscles has a varied effect on single joint motion. Yet, is pain in clinical examination often perceived to have similar effect on joint motion instead of dissimilar effects. The clinical examination commits only descriptive attention to, the direction in which the patients are moved during examinations. This study suggests that many studies of neck motion such as the effects of surgical disc replacement on cervical motion may be confounded, as exclusion and inclusion criteria does not control for dissimilar effect of pain on joint motion.

#### *4.5 Limitation*

There are several limitations to the current study. First, the measurement error was a large source of errors in the present study. However, the reproducibility of the marking procedure has been published with good reliability and low average marking errors<sup>41</sup>. Second, pain effects on cervical joint motion and PPTs was investigated in cervical extensors instead of cervical flexor. Since the aim is to compare pain effects between two comparable deep and superficial agonist/antagonist muscles, the injection of deep cervical flexors was considered at potential risk. Third, the present study only investigated dynamic joint kinematics during cervical flexion and extension in the sagittal plane, while cervical joint motions in frontal and transversal planes may provide more information, which needs further researches.

#### *4.6 Further perspectives*

Cervical spine is a complex structure which includes many muscles, ligaments, bones and discs etc. Further studies may focus on how pain from cervical flexors, ligaments or other cervical structures affect dynamic joint kinematics and PPTs. The present results are from experimental pain in healthy subjects, which cannot directly apply to patients with neck pain.

Therefore, further studies are required to investigate dynamic joint kinematics and PPTs in different subgroups of patients with neck pain, for instance, acute neck pain, chronic neck pain, whiplash and non-specific neck pain etc.

## 5. Conclusion

The origin of pain and the direction of neck movement influenced the effects of experimental pain on neck motion, and the effects varied from no significant effects to a redistribution of joint motion within and between joints. Experimental pain in the deep multifidus muscle showed local effects while superficial trapezius muscle pain showed global effects on dynamic joint kinematics. Similar pain intensities from different cervical muscles appears to alter pressure pain sensitivity in the neck. The study provides new background for the clinical understanding of the value of training of deep and superficial neck muscles, and the study suggest that deep spinal stability is an integrated part of dynamic movement. Therefore, investigation of dynamic joint kinematics and pressure pain sensitivities may improve diagnosis and treatment of neck pain.

**Acknowledgement:** Danish Chiropractors Foundation awarded René Lindstrøm funds for design and execution of this study. Ning Qu has been awarded a scholarship provided by the China Scholarship Council (CSC NO.201506170031) to pursue his PhD study at Aalborg University. Thomas Graven-Nielsen is a part of Center for Neuroplasticity and Pain (CNAP) supported by the Danish National Research Foundation (DNRF121). The authors gratefully acknowledge Niels Peter Bak Carstens for his supply of experimental setting with fluoroscopy and staffs for data collection at Vejgaard Chiropractic, Aalborg, Denmark.

**REFERENCES**

1. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: A systematic critical review of the literature. *European spine journal*. 2006;15:834-848.
2. Hoy D, March L, Woolf A, et al. The global burden of low back pain: Estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. 2014;73:968-974.
3. Hogg-Johnson S, Van Der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population. *European Spine Journal*. 2008;17:39-51.
4. Guzman J, Hurwitz EL, Carroll LJ, et al. A new conceptual model of neck pain: Linking onset, course, and care: The bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther*. 2009;32:S17-28.
5. Bahat HS, Weiss PL, Laufer Y. The effect of neck pain on cervical kinematics, as assessed in a virtual environment. *Arch Phys Med Rehabil*. 2010;91:1884-1890.
6. Sjolander P, Michaelson P, Jaric S, Djupsjobacka M. Sensorimotor disturbances in chronic neck pain--range of motion, peak velocity, smoothness of movement, and repositioning acuity. *Man Ther*. 2008;13:122-131.
7. Tsang SM, Szeto GP, Lee RY. Movement coordination and differential kinematics of the cervical and thoracic spines in people with chronic neck pain. *Clin Biomech (Bristol, Avon)*. 2013;28:610-617.
8. Madrid A, López-de-Uralde-Villanueva I, La Salle C. Widespread pressure pain hyperalgesia in chronic nonspecific neck pain with neuropathic features: A descriptive cross-sectional study. *Pain physician*. 2016;19:77-87.

9. Dvir Z, Prushansky T. Cervical muscles strength testing: Methods and clinical implications. *J Manipulative Physiol Ther.* 2008;31:518-524.
10. Johnston V, Jull G, Souvlis T, Jimmieson NL. Neck movement and muscle activity characteristics in female office workers with neck pain. *Spine (Phila Pa 1976).* 2008;33:555-563.
11. Lan HH, Chen H, Kuo L, You J, Li W, Wu S. The shift of segmental contribution ratio in patients with herniated disc during cervical lateral bending. *BMC musculoskeletal disorders.* 2014;15:273.
12. Wang X, Lindstroem R, Plochanski M, Østergaard LR, Graven-Nielsen T. Repeatability of cervical joint flexion and extension within and between days. *Journal of Manipulative & Physiological Therapeutics.* 2018;41:10-18.
13. Wang X, Lindstroem R, Carstens NPB, Graven-Nielsen T. Cervical spine reposition errors after cervical flexion and extension. *BMC musculoskeletal disorders.* 2017;18:102.
14. Wang X, Lindstroem R, Plochanski M, Østergaard LR, Graven-Nielsen T. Cervical flexion and extension includes anti-directional cervical joint motion in healthy adults. *The Spine Journal.* 2017.
15. Scott D, Jull G, Sterling M. Widespread sensory hypersensitivity is a feature of chronic whiplash-associated disorder but not chronic idiopathic neck pain. *Clin J Pain.* 2005;21:175-181.
16. Christensen SW, Hirata RP, Graven-Nielsen T. Altered pain sensitivity and axioscapular muscle activity in neck pain patients compared with healthy controls. *European Journal of Pain.* 2017;21:1763-1771.

17. Walton D, MacDermid J, Nielson W, Teasell R, Nailor T, Maheu P. A descriptive study of pressure pain threshold at 2 standardized sites in people with acute or subacute neck pain. *Journal of orthopaedic & sports physical therapy*. 2011;41:651-657.
18. Schwab JS, Diangelo DJ, Foley KT. Motion compensation associated with single-level cervical fusion: Where does the lost motion go? *Spine (Phila Pa 1976)*. 2006;31:2439-2448.
19. Branney J, Breen AC. Does inter-vertebral range of motion increase after spinal manipulation? A prospective cohort study. *Chiropractic & manual therapies*. 2014;22:24.
20. Schomacher J, Falla D. Function and structure of the deep cervical extensor muscles in patients with neck pain. *Man Ther*. 2013;18:360-366.
21. Blouin JS, Siegmund GP, Carpenter MG, Inglis JT. Neural control of superficial and deep neck muscles in humans. *J Neurophysiol*. 2007;98:920-928.
22. Childs JD, Cleland JA, Elliott JM, et al. Neck pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the american physical therapy association. *Journal of Orthopaedic & Sports Physical Therapy*. 2008;38:A1-A34.
23. Bifulco P, Cesarelli M, Romano M, Fratini A, Sansone M. Measurement of intervertebral cervical motion by means of dynamic x-ray image processing and data interpolation. *Journal of Biomedical Imaging*. 2013;2013:21.
24. Wu SK, Kuo LC, Lan HC, Tsai SW, Su FC. Segmental percentage contributions of cervical spine during different motion ranges of flexion and extension. *J Spinal Disord Tech*. 2010;23:278-284.

25. Falla D, Farina D. Neuromuscular adaptation in experimental and clinical neck pain. *Journal of Electromyography and Kinesiology*. 2008;18:255-261.
26. Yoo W. Comparison of upper cervical flexion and cervical flexion angle of computer workers with upper trapezius and levator scapular pain. *Journal of physical therapy science*. 2014;26:269-270.
27. Du Rose A, Breen A. Relationships between paraspinal muscle activity and lumbar intervertebral range of motion. 2016;4:4.
28. Falla D, Farina D, Dahl MK, Graven-Nielsen T. Muscle pain induces task-dependent changes in cervical agonist/antagonist activity. *J Appl Physiol (1985)*. 2007;102:601-609.
29. Cholewicki J, Vanvliet Iv JJ. Relative contribution of trunk muscles to the stability of the lumbar spine during isometric exertions. *Clin Biomech*. 2002;17:99-105.
30. Rudolfsson T, Björklund M, Djupsjöbacka M. Range of motion in the upper and lower cervical spine in people with chronic neck pain. *Man Ther*. 2012;17:53-59.
31. Izumi M, Petersen KK, Arendt-Nielsen L, Graven-Nielsen T. Pain referral and regional deep tissue hyperalgesia in experimental human hip pain models. *PAIN®*. 2014;155:792-800.
32. Palsson TS, Graven-Nielsen T. Experimental pelvic pain facilitates pain provocation tests and causes regional hyperalgesia. *PAIN®*. 2012;153:2233-2240.
33. Tucker KJ, Fels M, Walker SR, Hodges PW. Comparison of location, depth, quality, and intensity of experimentally induced pain in 6 low back muscles. *Clin J Pain*. 2014;30:800-808.
34. Arendt-Nielsen L, Graven-Nielsen T. Muscle pain: Sensory implications and interaction with motor control. *Clin J Pain*. 2008;24:291-298.

35. Graven-Nielsen T. Fundamentals of muscle pain, referred pain, and deep tissue hyperalgesia. *Scand J Rheumatol*. 2006;35:1-43.
36. Anderson JS, Hsu AW, Vasavada AN. Morphology, architecture, and biomechanics of human cervical multifidus. *Spine*. 2005;30:E86-E91.
37. Falla D, Farina D, Graven-Nielsen T. Experimental muscle pain results in reorganization of coordination among trapezius muscle subdivisions during repetitive shoulder flexion. *Experimental Brain Research*. 2007;178:385-393.
38. Stokes M, Hides J, Elliott J, Kiesel K, Hodges P. Rehabilitative ultrasound imaging of the posterior paraspinal muscles. *journal of orthopaedic & sports physical therapy*. 2007;37:581-595.
39. Schomacher J, Boudreau SA, Petzke F, Falla D. Localized pressure pain sensitivity is associated with lower activation of the semispinalis cervicis muscle in patients with chronic neck pain. *Clin J Pain*. 2013;29:898-906.
40. Frobin W, Leivseth G, Biggemann M, Brinckmann P. Sagittal plane segmental motion of the cervical spine. A new precision measurement protocol and normal motion data of healthy adults. *Clin Biomech*. 2002;17:21-31.
41. Plocharski M, Lindstroem R, Lindstroem CF, Østergaard LR. Motion analysis of the cervical spine during extension and flexion: Reliability of the vertebral marking procedure. *Med Eng Phys*. 2018.
42. Keating L, Lubke C, Powell V, Young T, Souvlis T, Jull G. Mid-thoracic tenderness: A comparison of pressure pain threshold between spinal regions, in asymptomatic subjects. *Man Ther*. 2001;6:34-39.



43. Minaki Y, Yamashita T, Takebayashi T, Ishii S. Mechanosensitive afferent units in the shoulder and adjacent tissues. *Clinical Orthopaedics and Related Research*®. 1999;369:349-356.
44. Ge H, Madeleine P, Wang K, Arendt-Nielsen L. Hypoalgesia to pressure pain in referred pain areas triggered by spatial summation of experimental muscle pain from unilateral or bilateral trapezius muscles. *European Journal of Pain*. 2003;7:531-537.
45. La Touche R, Fernández-de-las-Peñas C, Fernández-Carnero J, Díaz-Parreño S, Paris-Alemany A, Arendt-Nielsen L. Bilateral mechanical-pain sensitivity over the trigeminal region in patients with chronic mechanical neck pain. *The Journal of Pain*. 2010;11:256-263.
46. Christensen SW, Hirata RP, Graven-Nielsen T. Bilateral experimental neck pain reorganize axioscapular muscle coordination and pain sensitivity. *European Journal of Pain*. 2017;21:681-691.
47. Graven-Nielsen T, Babenko V, Svensson P, Arendt-Nielsen L. Experimentally induced muscle pain induces hypoalgesia in heterotopic deep tissues, but not in homotopic deep tissues. *Brain Res*. 1998;787:203-210.
48. Gibson W, Arendt-Nielsen L, Graven-Nielsen T. Referred pain and hyperalgesia in human tendon and muscle belly tissue. *Pain*. 2006;120:113-123.
49. Hodges PW. Pain and motor control: From the laboratory to rehabilitation. *Journal of Electromyography and Kinesiology*. 2011;21:220-228.
50. Côté JN, Bement MKH. Update on the relation between pain and movement: Consequences for clinical practice. *Clin J Pain*. 2010;26:754-762.

51. Hsu WH, Chen YL, Lui TN, et al. Comparison of the kinematic features between the in vivo active and passive flexion-extension of the subaxial cervical spine and their biomechanical implications. *Spine (Phila Pa 1976)*. 2011;36:630-638.
52. Rudolfsson T, Björklund M, Djupsjöbacka M. Range of motion in the upper and lower cervical spine in people with chronic neck pain. *Man Ther*. 2012;17:53-59.
53. Anderst WJ, Donaldson WF, Lee JY, Kang JD. Cervical spine intervertebral kinematics with respect to the head are different during flexion and extension motions. *J Biomech*. 2013;46:1471-1475.
54. Anderst WJ, Donaldson WF, Lee JY, Kang JD. Cervical motion segment contributions to head motion during flexion\ extension, lateral bending, and axial rotation. *The Spine Journal*. 2015;15:2538-2543.

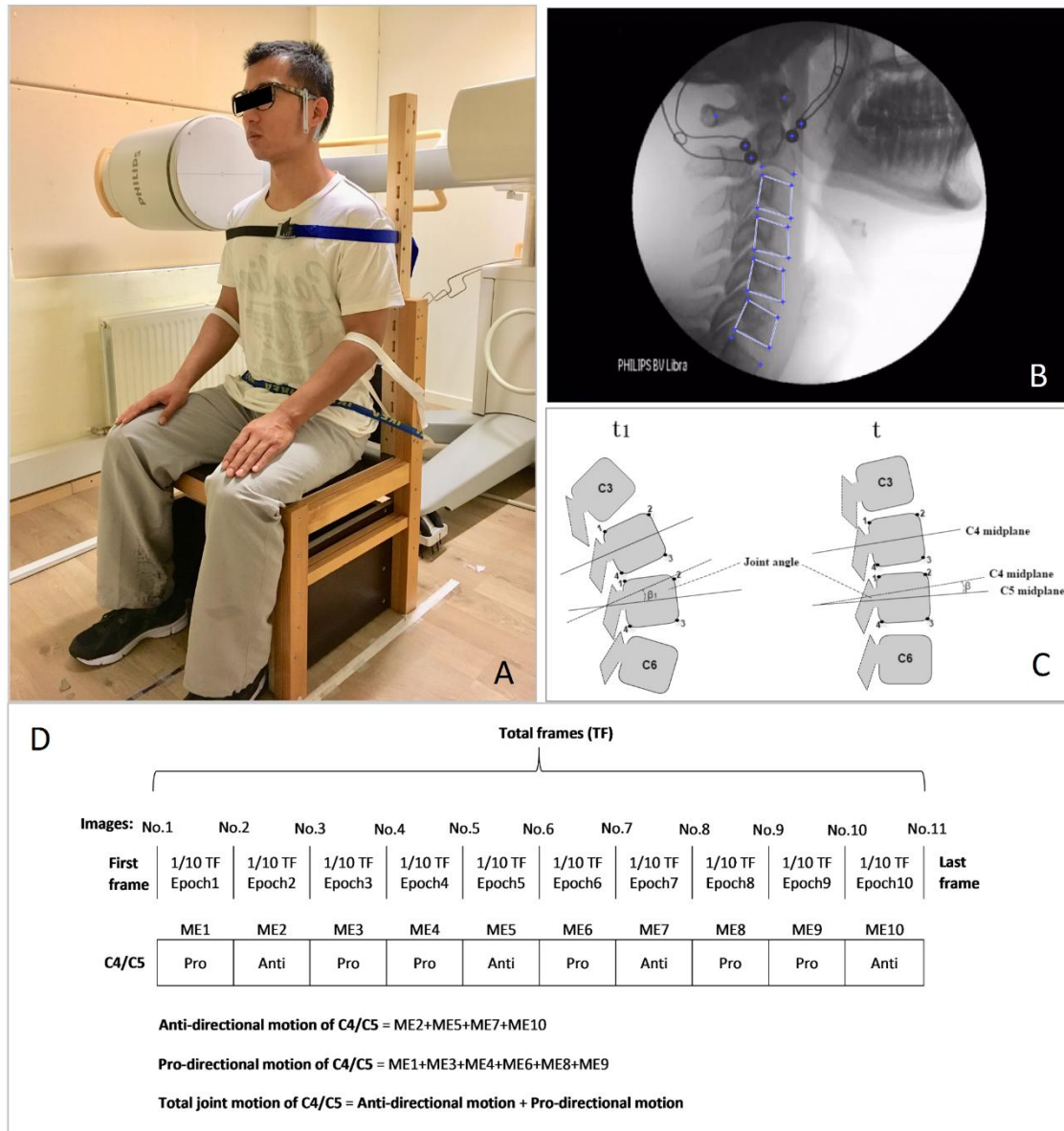


Fig.1. The setup of video-fluoroscopy to capture neck movements, the software and the algorithm to extract data of joint motions. **A**: Experimental chair between X-ray transmitter and screen, straps were used to lower shoulders and restrict the trunk movement. **B**: Illustration of markers on each cervical vertebra. **C**: Cervical vertebrae at two time points during cervical extension.  $\beta$  and  $\beta_1$  are joint angle of C4/C5. Joint motion of C4/C5 =  $\beta - \beta_1$ . **D**: Example of data extraction of C4/C5 joint motion from fluoroscopy videos of cervical flexion and extension. Eleven images (No.1, No.2, ... No.11) in evenly divided intervals (1/10 total frames) separate the motion into 10 even epochs. Joint motion during epochs includes both anti- and pro-directional motions. TF: total frames. ME: motion during epochs. Anti: anti-directional motion. Pro: pro-directional motion.

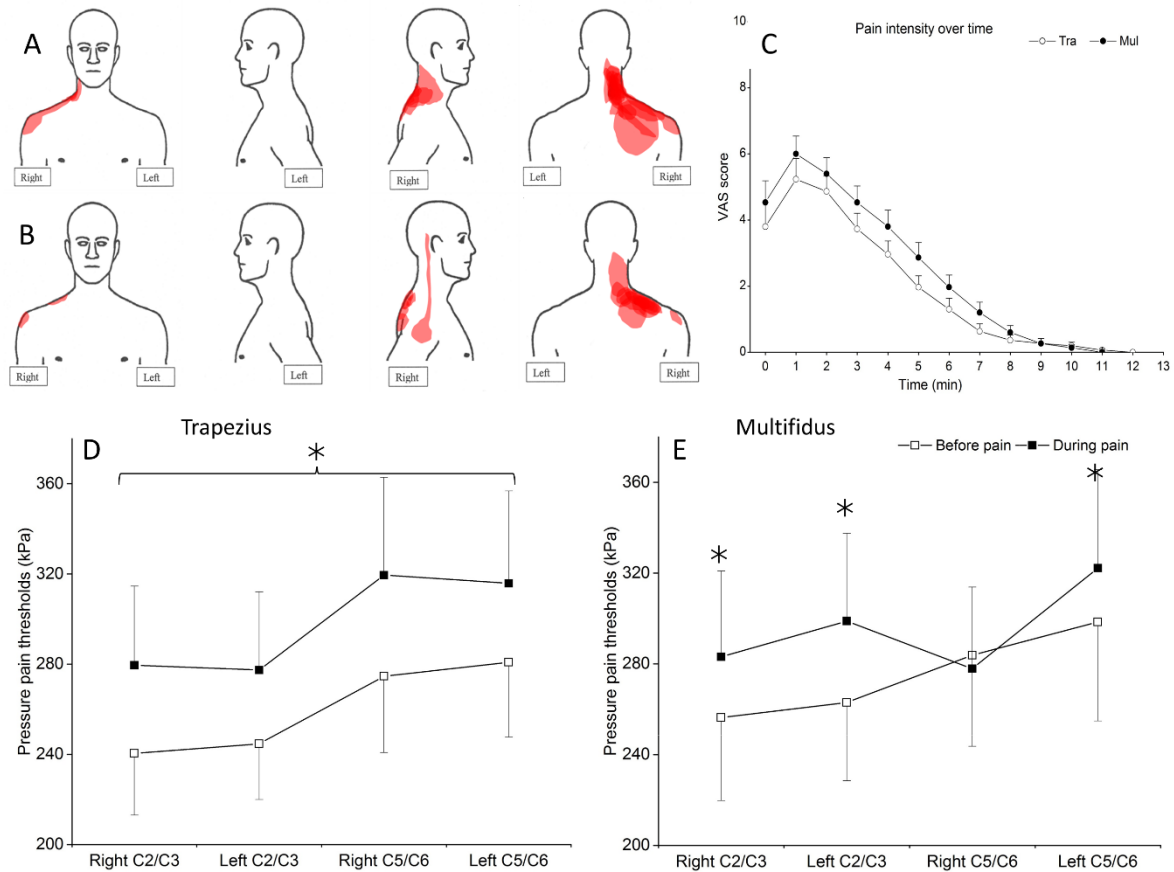


Fig.2. Pain distribution of 0.5 ml hypertonic saline (5.8%) in right multifidus (Mul) muscle at C4 level (**A**) and right upper trapezius (Tra) muscle (**B**). Low transparency in color indicates the area is less frequently marked by the subjects. **C**: Pain intensity over time followed injections of hypertonic saline in trapezius and multifidus muscles. Mean and SE of pressure pain thresholds above bilateral C2/C3 and C5/C6 facet joints before and during trapezius (**D**) and multifidus (**E**) muscle pain. Significant differences during pain compared with before pain: \*  $P < 0.05$ .

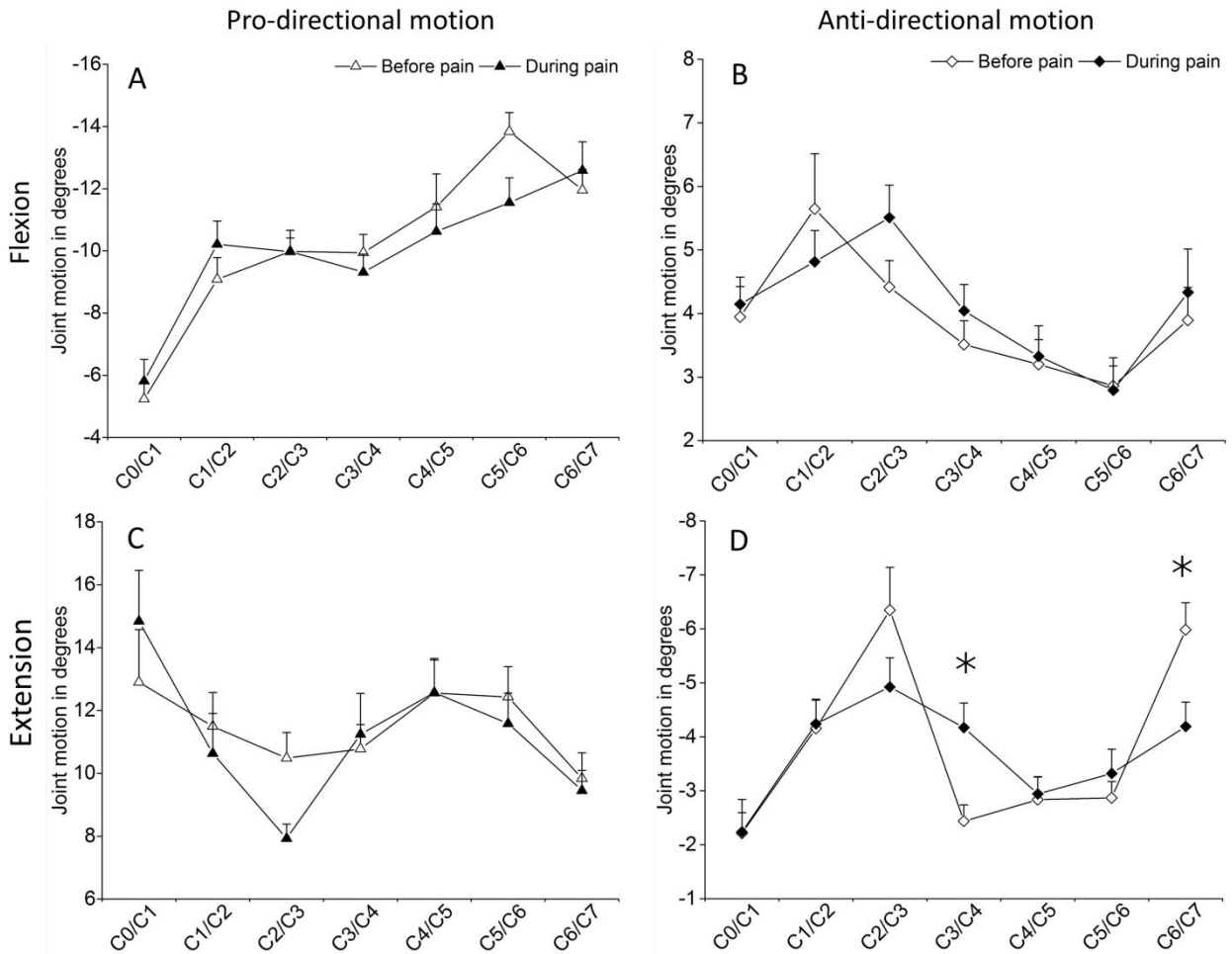


Fig.3. Mean and SE of pro-directional motion and anti-directional motion of cervical flexion and extension before and during multifidus muscle pain. **A:** Pro-directional motion during cervical flexion; **B:** Anti-directional motion during cervical flexion; **C:** Pro-directional motion during cervical extension; **D:** Anti-directional motion during cervical extension. Significant differences during pain compared with before pain: \*  $P < 0.05$ .

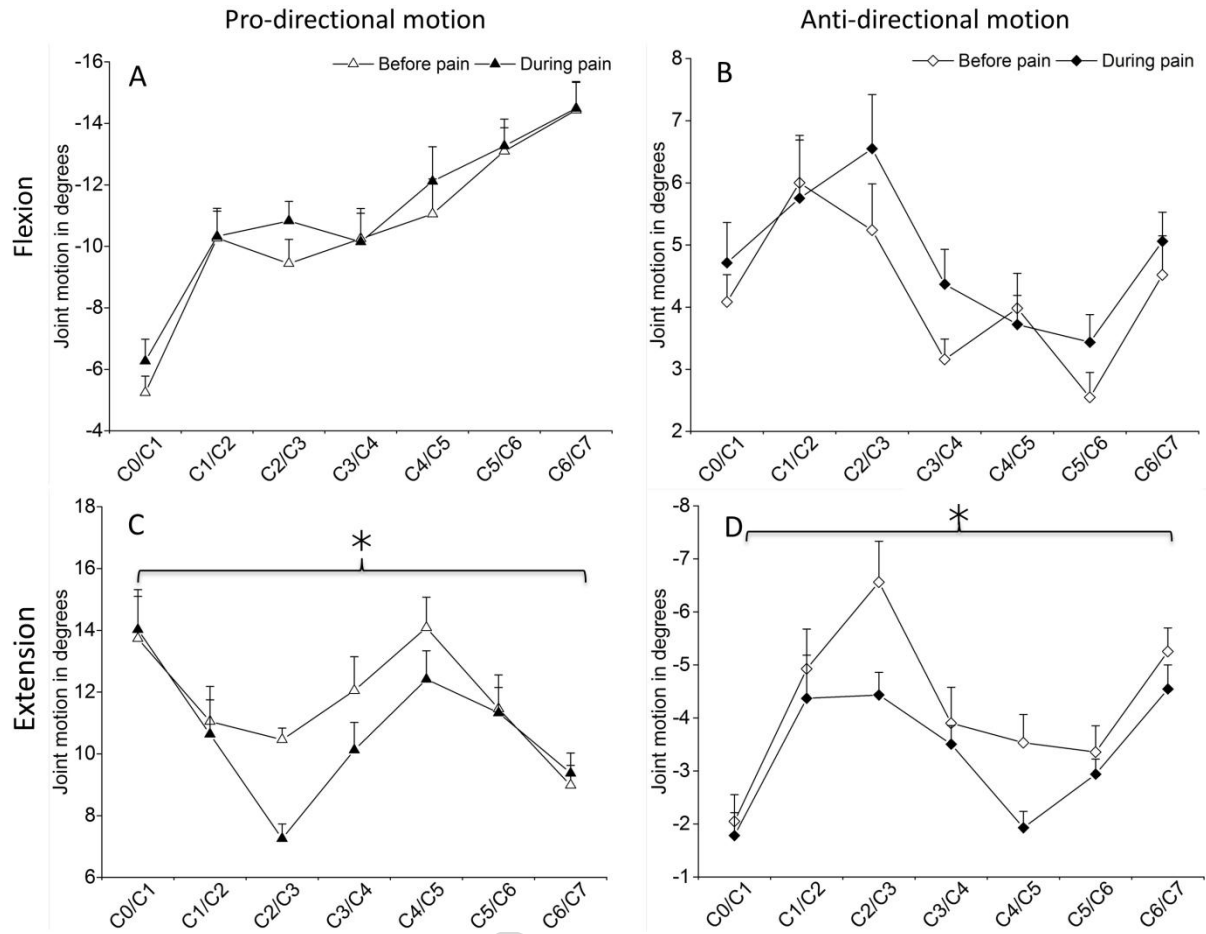


Fig.4. Mean and SE of pro-directional motion and anti-directional motion of cervical flexion and extension before and during trapezius muscle pain. **A**: Pro-directional motion during cervical flexion; **B**: Anti-directional motion during cervical flexion; **C**: Pro-directional motion during cervical extension; **D**: Anti-directional motion during cervical extension. Significant differences during pain compared with before pain: \*  $P < 0.05$ .

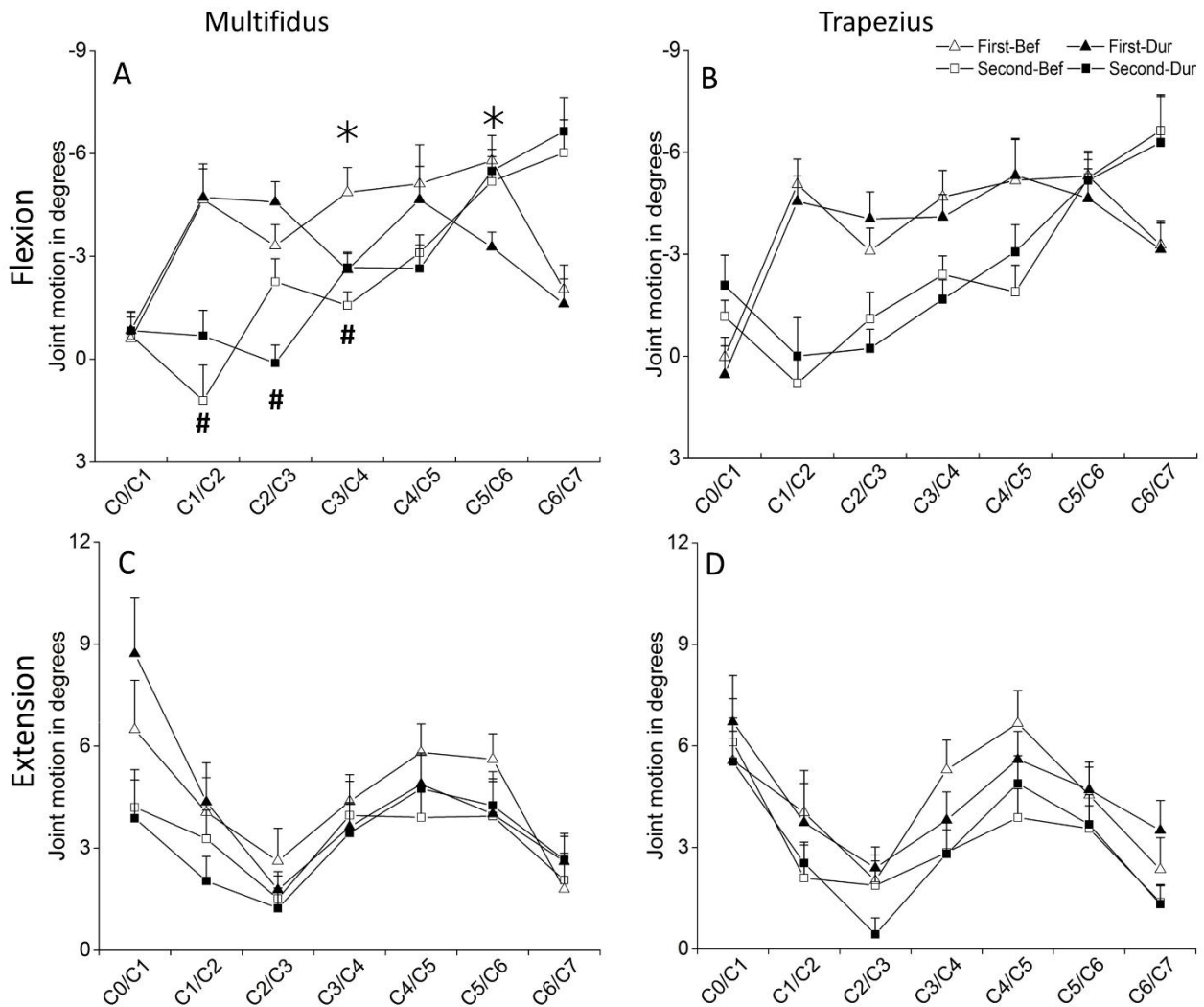


Fig.5. Joint motion during half ranges (first half, second half) of cervical flexion and extension before (Bef) and during (Dur) multifidus and trapezius muscle pain. **A:** Flexion before and during the multifidus muscle pain; **B:** Flexion before and during the trapezius muscle pain; **C:** Extension before and during the multifidus muscle pain; **D:** Extension before and during the trapezius muscle pain. Significant differences during first half (\*  $P < 0.05$ ) and during second half (#  $P < 0.05$ ) are illustrated.

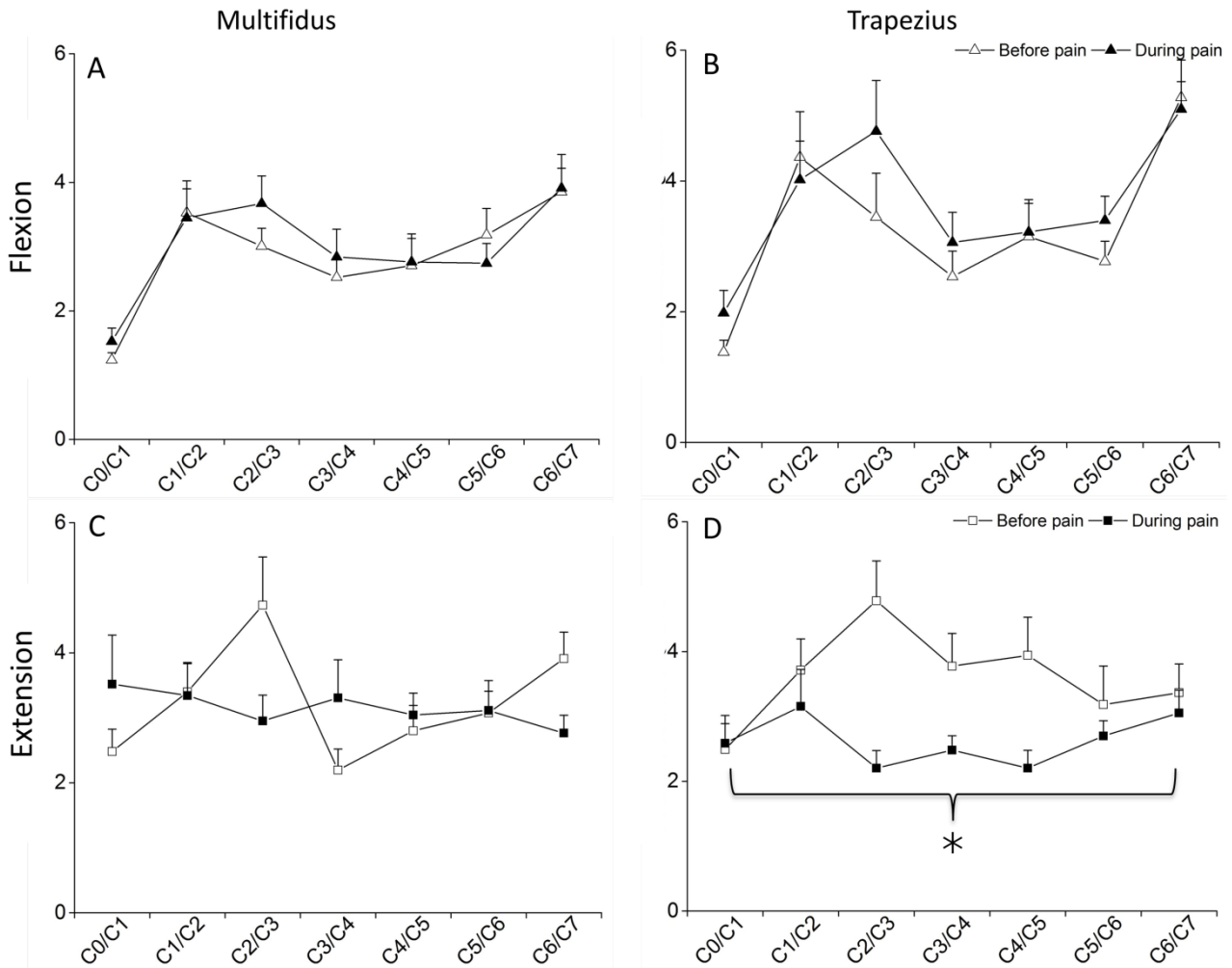


Fig.6. Mean and SE of joint motion variability of cervical flexion and extension before and during multifidus and trapezius muscle pain. **A:** Flexion before and during the multifidus muscle pain; **B:** Flexion before and during the trapezius muscle pain; **C:** Extension before and during the multifidus muscle pain; **D:** Extension before and during the trapezius muscle pain. Significant differences during pain compared with before pain: \*  $P < 0.05$ .



**Highlights:**

- Movement direction influenced cervical muscle pain effect on cervical joint motion
- Deep and superficial muscle pain has different effect on cervical joint motion
- Deep muscle pain affected individual joint motion during cervical extension
- Superficial muscle pain affected motion of the entire neck during cervical extension
- Deep and superficial muscle pain decreased pressure pain sensitivity in the neck