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Altered pain sensitivity and axioscapular muscle activity in neck pain patients compared to healthy controls

--Manuscript Draft--

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Abstract:	<p>Background Previous studies have indicated that neck pain patients feel increased symptoms following upper limb activities and altered axioscapular muscle function have been proposed as a contributing factor.</p> <p>Methods Pain sensitivity and muscle activity, during arm movements, were assessed in neck pain patients and controls. Patients with ongoing insidious onset neck pain (IONP, N=16) and whiplash associated disorders (WAD, N=9) were included along with sex- and age-matched controls (N=25). Six series of repeated arm abductions were performed during electromyographic (EMG) recordings from eight bilateral muscles. The first and last three series were separated by 8-min and 42-s, respectively. Each series consisted of three slow and three fast movements. Pressure pain thresholds (PPTs) were recorded bilaterally from neck, head, and arm at baseline, after the third and sixth movement series. Pain intensity was recorded on a electronic visual analogue scale (VAS).</p> <p>Results Larger pain areas and higher VAS scores were found in patients compared with controls ($P<0.001$), and in patients the VAS scores increased in the course of movements ($P<0.02$). PPTs were lower in patients compared with controls at all sites ($P<0.03$) and these decreased during arm movements in the IONP group ($P<0.03$) while increasing at head and neck sites in controls ($P<0.04$). During the slow movements, increasing serratus anterior EMG activity was found in the series with short breaks in-between for the WAD group compared with IONP and controls ($P<0.001$).</p> <p>Conclusion Axioscapular movement caused different responses in pain sensitivity and muscle activity between neck-pain patient groups and compared with controls.</p>

ABSTRACT

Background Previous studies have indicated that neck pain patients feel increased symptoms following upper limb activities and altered axioscapular muscle function have been proposed as a contributing factor.

Methods Pain sensitivity and muscle activity, during arm movements, were assessed in neck pain patients and controls. Patients with ongoing insidious onset neck pain (IONP, N=16) and whiplash associated disorders (WAD, N=9) were included along with sex- and age-matched controls (N=25). Six series of repeated arm abductions were performed during electromyographic (EMG) recordings from eight bilateral muscles. The first and last three series were separated by 8-min and 42-s, respectively. Each series consisted of three slow and three fast movements. Pressure pain thresholds (PPTs) were recorded bilaterally from neck, head, and arm at baseline, after the third and sixth movement series. Pain intensity was recorded on a electronic visual analogue scale (VAS).

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ALTERED PAIN SENSITIVITY AND AXIOSCAPULAR MUSCLE ACTIVITY IN NECK PAIN PATIENTS COMPARED TO HEALTHY CONTROLS

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Significance

Neck pain patient's reports increased symptoms following upper limb activities. This study shows that repeated arm movements caused differentiated responses in pain sensitivity and muscle activity between subgroups of neck pain patient and asymptomatic controls. Such findings may be of great clinical significance when planning rehabilitation for this patient population.

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1 **ABSTRACT**

2 *Background* Previous studies have indicated that neck pain patients feel increased symptoms
3 following upper limb activities and altered axioscapular muscle function have been proposed
4 as a contributing factor.

5 *Methods* Pain sensitivity and muscle activity, during arm movements, were assessed in neck
6 pain patients and controls. Patients with ongoing insidious onset neck pain (IONP, N=16) and
7 whiplash associated disorders (WAD, N=9) were included along with sex- and age-matched
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19 EMG activity was found in the series with short breaks in-between for the WAD group
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21 *Conclusion* Axioscapular movement caused different responses in pain sensitivity and muscle
22 activity between neck-pain patient groups and compared with controls.

1 INTRODUCTION

2 Neck pain is a common musculoskeletal condition (Flachs et al., 2015; Hoy et al., 2014) but
3 despite vast amounts of research, no superior treatment strategies have been identified. While
4 several studies have shown positive effect of exercise on both pain intensity, disability (Jull et
5 al., 2007; Ylinen et al., 2003) and pain sensitivity (Andersen et al., 2012; Ylinen et al., 2005)
6 Michaleff et al., (2014) showed simple advice to be as effective as a comprehensive exercise
7 program for treating patients suffering from whiplash associated disorders (WAD).

8 In recent years, there has been a growing focus on strategies including the axio­scapular
9 muscles and shoulder girdle in examination and rehabilitation of neck pain patients (Cagnie
10 et al., 2014; Cools et al., 2014; O'Leary et al., 2009). Particularly the force couple around the
11 scapula (serratus anterior, upper and lower trapezius muscles) has been of interest due to their
12 ability to upwardly rotate the scapula. Especially the serratus anterior and the lower trapezius
13 muscles may be crucial for upward rotation (Kibler 1998; Kibler and McMullen 2003) and
14 neck pain patients have impaired activity of these muscles compared with asymptomatic
15 controls (Helgadottir et al., 2011; Wegner et al., 2010), potentially increasing the load on the
16 cervical spine (Behrsin and Maguire 1986). This is supported by reports claiming up to 80%
17 of neck pain patients experience symptom aggravation with upper limb activity (Osborn and
18 Jull 2013), and studies showing reorganized muscle coordination (Helgadottir et al., 2011)
19 and activity (Castelein et al., 2015; Wegner et al., 2010; Zakharova-Luneva et al., 2012)
20 during arm movements. Interestingly, subgroups differences in axio­scapular muscle activity
21 may exist in neck pain patients (Castelein et al., 2015). During an upper limb task, the upper
22 trapezius muscle activity was reduced in patients with insidious onset of neck pain (IONP)
23 but not in patients suffering from whiplash associated disorders (WAD) although they
24 showed increased activity after completing the task (Falla et al., 2004). So far, it is not know
25 if repeated series of arm movements have a perpetuating effect on muscle function.

26 Increased pain sensitivity is a frequent finding in ongoing neck pain and several studies
27 have shown reduced pressure pain thresholds (PPT) in both WAD (Scott et al., 2005; Sterling
28 et al., 2004; Sterling et al., 2002) and IONP patients (Javanshir et al., 2010; La Touche et al.,
29 2010; Scott et al., 2005). One study, investigating the relationship between a cycling task and
30 pressure pain sensitivity, indicated that higher but not lower cycling intensities caused
31 reduced PPTs in neck pain patients, which was not the case for healthy controls (Van
32 Oosterwijck et al., 2012). So far, it is not clear if or how repeated arm movements affect pain
33 and pain sensitivity in neck pain patients compared with healthy controls.

1 This study set out to investigate activity and coordination between axioscapular
2 muscles during repeated arm movements in groups of IONP, WAD and healthy controls as
3 well as the effects on pain sensitivity and pain perception. It was hypothesized that repeated
4 arm movements **would** cause reorganized axioscapular muscle activity, increased pain
5 intensity, and hyperalgesia in WAD and IONP patients compared with controls.

6 7 8 **METHODS**

9 *Participants*

10 Participants were recruited through advertisements in local newspapers, educational facilities,
11 and social media. The inclusion criteria for patients were neck pain classified as IONP or
12 WAD lasting more than 3 months. Additionally, they had to have neck pain during active
13 cervical range of motion and palpation soreness of posterior neck muscles, which both were
14 exclusion criteria for the control group if present within the past 6 months. Neck pain patients
15 were excluded if they had referred or radiating pain down the arms. All participants were
16 required to have pain-free shoulder active range of motion. Furthermore, exclusion criteria
17 for all participants were signs or symptoms of neurological, rheumatological or other
18 disorders that could influence the results of the study along with pregnancy. An experienced
19 **musculoskeletal** physiotherapist examined all participants before inclusion. During a 2-year
20 period, 122 possible participants reported with neck pain. 66 fulfilled the inclusion criteria
21 while 31 did not wish to participate after receiving information about the study (Fig. **S1**). In
22 total, 25 neck pain patients with bilateral neck pain and 25 healthy age- and sex-matched
23 controls were enrolled in the study. Sixteen of the 25 neck pain patients had neck pain of
24 insidious onset (IONP) and 9 were due to whiplash-associated disorder (WAD).

25 Demographics of participant can be seen in Table 1. Informed consent was collected from all
26 participants prior to the test session. The study followed the Helsinki declaration and was
27 approved by the local ethics committee (N20120018).

28 29 *Protocol*

30 This study was designed as a cross-sectional study and conducted in a single session, using a
31 setup similar to that used in a previous **studies** on experimental neck pain (Christensen et al.,
32 2015; **2017**). Pressure pain thresholds (PPT) were recorded with participants in a sitting
33 position leaning over a table. Electromyography (EMG) was used to quantify muscle activity
34 during series of standardized repeated arm abduction movements performed from an upright-

1 seated position. PPT and EMG were assessed bilaterally throughout the study. A total of six
2 series of arm movements were performed where the first three series (Bout-I) of arm
3 movements were separated by approximately 8-min and the last three series (Bout-II) of arm
4 movements were separated by approximately 42-s (Fig. 1). Bout-I and Bout-II were separated
5 by a 10-min break. PPTs were assessed at baseline, after Bout-I, and after Bout-II.
6 Participants scored the intensity of perceived pain on a visual analogue scale (VAS) and drew
7 the perceived pain area on a body map at baseline, after each of the first three series of arm
8 movements (Bout-I), and again after the final movement series (Bout-II). Additionally, all
9 participants were asked describe the quality of their pain using a McGill pain questionnaire
10 after Bout-II (Drewes et al., 1993; Melzack 1975).

11

12 *Repeated arm movements and perceived pain*

13 To allow for comparability with previous studies a standardized arm movement was adopted
14 from previous experimental and clinical neck pain studies (Christensen et al., 2015; 2017;
15 Helgadottir et al., 2011). Participants were seated in a comfortable position, on a chair
16 supporting the sacrum, with arms hanging by their side. From this position, participants were
17 asked to perform an abduction in the scapular plane, 30° to the frontal plane (scaption), to a
18 140° angle with stretched arm. One movement series consisted of three slow movements
19 consisting of a 3-s up and 3-s down phase followed by three fast movements where only the
20 fast up movement was recorded. Each movement was separated by a 6-s break before moving
21 the contralateral arm. A detailed description of the precautions taken to ensure standardized
22 movements can be seen in Methods S1

23 During the break between arm movements, participants were asked to score their
24 perceived pain on an electronic visual analogue scale (VAS) anchored with ‘no pain’ at 0-cm
25 and ‘maximum pain’ at 10-cm. A mean of VAS scores during series 1-3 (Bout-I) and series
26 4-6 (Bout-II) was extracted for analysis. Pain areas were quantified (VistaMetrix, v.1.38.0,
27 SkillCrest, LLC) and reported in arbitrary units (a.u.) for baseline, Bout-I (averaged across
28 movement series 1-3), and Bout-II (after the last movement series).

29 After Bout-II participants were asked to rate the difficultness of performing the arm
30 movements on a 6 point Likert scale going from 0 = ‘no problems’, 1 = ‘minimally difficult’,
31 2 = ‘somewhat difficult’, 3 = ‘fairly difficult’, 4 = ‘very difficult’, to 5 = ‘unable to perform’.

32

33 *Kinematic recordings*

1 Arm movements were quantified with an accelerometer (ACC; EVAL-ADXL327Z; Analog
2 Devices, Norwood, Massachusetts, USA) mounted over the lateral humeral epicondyle and
3 data was extracted for the slow-up, -down, and fast-up movements (see Method S1). An
4 average of the ACC data for the three trials for each movement type was extracted separately
5 for the six movement series and averaged across Bout-I and Bout-II for further analysis.

6 *Muscle activity*

7 Adhesive surface EMG electrodes (Neuroline 72001-k; AMBU, Denmark) were placed over
8 eight muscles bilaterally: Serratus anterior (SA), upper trapezius (UT), middle trapezius
9 (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), obliquus externus
10 (OE), and erector spinae (ES) muscles. A reference electrode (OT Bioelettronica, Italy) was
11 mounted at the right wrist. Details on electrode position have been described in detail
12 elsewhere (Christensen et al., 2015).

13
14 The EMG signal was amplified (gain 500) and sampled at 2048 Hz (OT Bioelettronica,
15 Italy). The EMG signal was subsequently rectified and filtered (Butterworth 2nd order, band
16 pass 25-450Hz). Root mean square (RMS) value of the rectified and filtered EMG signal was
17 extracted for the slow up and slow down movement (3-s epochs). ACC data for the fast-up
18 movement was used to determine the time used for the fast movement and RMS-EMG data
19 was then extracted in this epoch. The mean RMS-EMG (for each movement type: slow-up,
20 slow-down, and fast-up) across the three movement trials in each movement series was
21 extracted. In order to compare RMS-EMG across groups, the RMS-EMG from the last two
22 movement series in each Bout was averaged and then normalized to the RMS-EMG from the
23 first movement series and used for further analysis. Thus, the RMS-EMG in each Bout
24 reflected the progression of EMG activity in the course of three movement series.

25 For the fast movements, the muscle activity onset (EMG onset) was automatically
26 identified using a technique successfully used in other studies (Christensen et al., 2015;
27 Santello and McDonagh 1998). A detailed description of the onset detection can be seen in
28 Methods S1. To ensure data quality, a visual inspection was conducted and errors in onset
29 detection were manually corrected. Data was arranged with onsets relative to the onset of the
30 anterior deltoid muscle and the mean onsets across the three fast-up trials were calculated.
31 Since EMG onsets of contralateral muscles are generally weakly defined, only EMG onsets
32 of ipsilateral muscles were used for further analysis. Finally, EMG onset was averaged across
33 movement series in Bout-I and Bout-II, respectively.

34

1 *Pressure pain sensitivity*

2 The PPT was recorded using a handheld pressure algometer (Somedic, Hörby, Sweden)
3 mounted with a 1-cm² probe covered by a single-use latex cover. A continuously increasing
4 pressure at a rate of 30 kPa/s was used. The algometer was wired with a stop-button, which
5 the participant was asked to push when the pressure first was perceived as painful.
6 Assessment of PPTs were collected at 1) over the splenius capitis muscle (NECK), 2) over
7 the temporalis muscle (TEMP) and 3) over the extensor radialis brevis muscle (ECRB). A
8 detailed description of assessment sites and procedure can be seen in Method S1.

9

10 *Statistics*

11 Data are presented as mean and standard error of the mean (SEM) in text and figures. Data
12 distribution was inspected using QQ plots. Demographic data (table 1) and Likert scores
13 (after Bout-II) were compared across groups using the Kruskal-Wallis (KW) analysis of
14 variance, followed by the Mann-Whitney post-hoc test including Bonferroni corrections
15 when needed. For VAS scores and pain areas non-parametric analysis was needed. For each
16 group across time (baseline, Bout-I, Bout-II) a Friedman analysis was used and if significant
17 followed by a Wilcoxon test including Bonferroni correction. For each time point (baseline,
18 Bout-I, Bout-II) across groups, the Kruskal-Wallis (KW) analysis was used, followed by the
19 Mann-Whitney U post-hoc test including Bonferroni corrections.

20 RMS-EMG data was log transformed (Log10) before ACC, PPT (3 sites), RMS-EMG
21 (16 muscles), and EMG onset (7 muscles) were compared between groups and sides, using a
22 three-way mixed-model analysis of variance (ANOVA) with *time* (PPT: baseline, Bout-I &
23 Bout-II; ACC, RMS-EMG, EMG-onset: Bout-I & Bout-II) and *side* (dominant & non-
24 dominant arm) as within factor and *group* (WAD, IONP & Control) as between factor. This
25 was done for each muscle (EMG-Onset, RMS-EMG) or site (PPT), and separate for each
26 movement type (slow-up, slow-down, fast-up), in order to investigate for potential
27 time*group*side interactions. Due to the multiple ANOVA's, a Bonferroni correction was
28 used to adjust the P-value for ANOVA significance (i.e. for PPTs, the ANOVA was
29 significant for $P < 0.05/3$; for RMS-EMG $P < 0.05/16$; for EMG-Onset $P < 0.05/7$). In case of
30 a significant ANOVA, the Newman-Keuls (NK) post-hoc test was used to assess significant
31 factors or interactions. A significance level of 0.05 was accepted.

32

33 **RESULTS**

34 *Performance of arm movements*

1 During arm movements 67% of the WAD group scored ≥ 1 on the Likert scale reflecting the
2 perceived difficultness of performing the movement while this was only the case for 25% of
3 the IONP group, and none from the control group. Only the WAD group was significantly
4 different from controls (KW: $H(2)=18.3$, $P<0.001$; Mann-Whitney U: $P=0.002$).

5 Analysis of accelerometer data did not reveal any significant difference during slow up,
6 down and fast up movements between groups or sides. Mean values for each group and
7 movement type can be seen in Table S1.

8

9 *Intensity, area and quality of pain during movement*

10 For both neck pain groups the mean VAS score was significantly higher at baseline, during
11 Bout-I and Bout-II compared with pain free controls (Fig. 2A; KW: $H(2)>42.0$, $P<0.001$;
12 Mann-Whitney U: $P<0.001$). The Friedman ANOVA indicated a difference over time for
13 both IONP ($\chi^2(2)=6.2$, $P=0.046$) and WAD ($\chi^2(2)=10.8$, $P=0.004$). The post-hoc test revealed
14 increasing VAS score throughout the study for IONP when comparing baseline to Bout-I
15 (Wilcoxon: $P = 0.013$) and for both neck pain groups when this was compared to Bout-II
16 (Wilcoxon: IONP $P=0.008$; WAD $P=0.015$). A significant increase during Bout-II compared
17 to Bout-I was seen for both neck pain groups (Wilcoxon: IONP $P=0.007$; WAD $P=0.015$).

18 Neck pain patients perceived bilateral neck pain expanding in the course of movements
19 (Fig. 2B). After baseline, Bout-I and Bout-II both neck pain groups showed significantly
20 larger pain areas compared with the control group (Fig. 3B; KW: $H(2)>42.2$, $P<0.001$; Mann-
21 Whitney U: $P<0.001$). The pain areas for IONP participants increased over time with the pain
22 area after Bout-II being larger than after Bout-I (Friedman: $\chi^2(2)=7.1$, $P=0.02$; Wilcoxon:
23 $P=0.008$).

24 For the IONP group the pain was most commonly described as ‘taut’ (81% of
25 participants) while 44% indicating ‘tugging’ and ‘tiring’ being descriptive for their pain. For
26 the WAD group the most commonly used words was ‘nagging’ (67%) followed by
27 ‘throbbing’, ‘tiring’ and ‘radiating’ (56%).

28

29 *Pressure pain sensitivity*

30 No difference between sides was detected for any of the sites. For the NECK site, a time and
31 group interaction was found (Fig. 3; ANOVA: $F[4,18]=15.0$; $P<0.001$). Decreased PPT at all
32 time points was found when comparing both the IONP (NK: $P<0.03$) and WAD (NK:
33 $P<0.001$) with controls. In WAD, compared with IONP, the PPT was decreased at baseline
34 (NK: $P=0.041$). For controls the PPTs were progressively increasing and different between

1 all time points (NK: $P < 0.04$), while for the IONP group the post-hoc test showed decreased
2 PPT after Bout-I and Bout-II compared with baseline (NK: $P < 0.001$).

3 For the TEMP site, an interaction (ANOVA: $F[4,18]=9.8$; $P < 0.001$) showed that both
4 neck pain groups had decreased PPTs compared with controls at all time points (NK:
5 $P < 0.001$). Furthermore, for the IONP group the PPT was decreased after Bout-I and Bout-II
6 compared with baseline (NK: $P < 0.03$). For controls, an increase in PPTs was found after
7 Bout-II when compared with baseline and Bout-I (NK: $P < 0.002$).

8 For the ECRB site, an interaction (ANOVA: $F[4,18]=6.9$; $P < 0.001$) demonstrated that
9 both neck pain groups displayed decreased PPT at all time points when compared with the
10 control group (NK: $P < 0.001$). For the IONP group, the post-hoc test revealed decreased PPT
11 at Bout-I and Bout-II compared with baseline (NK: $P < 0.002$).

12

13

14 *EMG onset during fast movement series*

15 For some participants it was not possible to detect EMG onsets for all muscles, which is
16 reflected in the F statistics (Table S2) Mean EMG onsets during Bout-I and Bout-II can be
17 seen on figure S2A&B. No significant interactions between time and group were found for
18 Bout-I and Bout-II.

19

20 *Muscle activity during arm movements*

21 Due to technical problems during the fast up movement in Bout-II, it was not possible to
22 obtain data from the ipsilateral middle trapezius in one person. Figure S3 shows raw RMS-
23 EMG (mean of both arms) during Bout-I and Bout-II for slow-up, slow-down and fast-up
24 movements. All ANOVA results are based on percentages changes relative to the first arm
25 movement series in each Bout (Table S3) A significant difference was found for the serratus
26 anterior muscle for the slow up movement (Fig. 4; ANOVA: $F[2,97] = 8.8$; $P < 0.001$), with
27 the post-hoc test revealing an increased activity for the WAD group during Bout-II compared
28 with Bout-I, as well as when compared to both IONP and control groups (NK: $P < 0.001$).

29

30

31 **DISCUSSION**

32 These findings demonstrate widespread hyperalgesia for neck pain patients compared with
33 controls. Repeated arm movements in controls were non-painful and showed pressure

1 hypoalgesia in the neck and head site, while IONP developed hyperalgesia. For the serratus
2 anterior muscle, increased activity was found for the WAD group when pauses between
3 movement series were reduced, while the IONP group responded similarly to controls.

4 5 *Hyperalgesia caused by repeated movements*

6 Findings of hyperalgesia in both IONP and WAD groups, not only locally in the neck, but
7 also on the temporalis muscle and on the arm, is contrasting to most previous studies where
8 mostly WAD patients seem to have widespread hyperalgesic changes (La Touche et al.,
9 2010; Scott et al., 2005; Sterling et al., 2002) although there have been similar findings in
10 some IONP patients (Javanshir et al., 2010). Levels of pain and disability may be of
11 importance for these sensory manifestations, which is supported by a study showing that only
12 WAD patients with moderate to severe but not mild symptoms had reduced pain sensitivity,
13 when compared to controls (Sterling et al., 2004). Pain duration may also be important
14 because chronic and not acute IONP groups had widespread hyperalgesia when compared
15 with controls (Javanshir et al., 2010). Taken together, this could explain why some
16 similarities are found in the present study when comparing IONP and WAD to controls, since
17 they have similar levels of pain intensity, pain duration, and area of pain. However,
18 differences between patient groups were found in the progressively changing PPTs during
19 repeated arm movements, where controls displayed hypoalgesia, while hyperalgesia was
20 found for the IONP group. Such response, with increased PPT in controls while decreased in
21 painful populations, as a response to exercise, have previously been demonstrated in both
22 WAD (Van Oosterwijck et al., 2012) and fibromyalgia patients (Staud et al., 2005), and have
23 been interpreted as a sign of abnormal or reduced descending endogenous pain inhibition
24 (Staud et al., 2005; Van Oosterwijck et al., 2012). Interestingly, such an effect was only
25 observed for IONP and not WAD, but WAD had in general the lowest PPTs, and the lack of
26 change over time could indicate a floor effect. A previous study showed that WAD patients
27 displayed a dose-response relationship with a self-paced cycling task causing increased PPT
28 at the calf muscle, while the opposite was the case after a submaximal cycling task (Van
29 Oosterwijck et al., 2012). Potentially, self-paced arm movements compared to the ones used
30 in this study could have caused a different response. Nonetheless, compared with controls
31 and IONP patients, the highest frequency of patients perceiving difficulties in the movement
32 was found for WAD, suggesting that this was likely to be at a submaximal intensity.
33 Previously Andersen et al., (2012) found increased PPTs in neck/shoulder pain patients after

1 a 10 week training program and future studies comparing the long-term training effects
2 between WAD and IONP are needed.

3

4 *Muscle coordination*

5 With upper limb activity aggravating symptoms in neck pain patients, as seen in the current
6 study, and suggestions of this being caused by altered axioscapular muscle function (Osborn
7 and Jull 2013) it would be expected to find altered EMG onsets of axioscapular muscles
8 when comparing neck pain patients to controls. Interestingly, in the current study no
9 significant differences in EMG onset between neck pain patients and controls was found
10 which is in contrast to a previous study showing delayed EMG onset of the serratus anterior
11 muscle in neck pain patients compared with controls (Helgadottir et al., 2011). The
12 discrepancy between the current and previous study could simply be due to the fast
13 movements investigated in this study compared to slow movement in the previous study
14 (Helgadottir et al., 2011). The current EMG onset is reported relative to that of the anterior
15 deltoid muscle, which was not the case in the previous study (Helgadottir et al., 2011). No
16 other studies have assessed EMG onset of axioscapular muscles in clinical neck pain during
17 arm movements and further studies are needed to clarify the effects on the muscle onset.

18 Although no group differences were detected for the EMG onset of the serratus anterior
19 muscle, an increased activity was found in the WAD group when compared to both the IONP
20 and control group. This group difference was however only present during Bout-II, where
21 rest between movements was short and pain intensity was increased compared to Bout-I. The
22 increase in pain could potentially cause increased muscle activity in an agonistic muscle
23 which have previously been found for neck movements during experimental pain (Falla et al.,
24 2007). However, in the present study, the VAS score increased similarly in both the WAD
25 and IONP group during movements, although the muscle activity increase was different. The
26 increased muscle activity may be interpreted as a component of the physiological fatigue
27 response (Oberg 1995) with recruitment of additional high threshold motor units in order
28 maintain force output (Hodges et al., 2008; Oberg 1995). Surprisingly, none of the other
29 axioscapular muscles demonstrated significant changes, in contrast to previous studies in
30 clinical neck pain populations. Falla et al. showed reduced upper trapezius muscle activity in
31 IONP but not WAD patients while doing a cyclic arm movement in front of the body (Falla et
32 al., 2004). For the lower trapezius muscle, Zakharova-Luneva et al. found increased activity
33 during isometric abduction and external rotation (Zakharova-Luneva et al., 2012), while
34 another study found decreased activity during a typing task (Wegner et al., 2010) even

1 though both include IONP patients. These variable findings in different studies could be
2 explained by the different tasks and patient populations investigated (Castelein et al., 2015).
3 However, when considering all the studies and conflicting evidence on axioscapular muscle
4 activity in neck pain patients (Castelein et al., 2015) there seems to be a wide ‘natural’
5 diversity, which could explain different findings in different cohorts. Such natural diversity is
6 supported by a study on experimental low back pain where healthy participants displayed a
7 variety of different patterns of muscle activity following a painful stimulus (Hodges et al.,
8 2013), indicating that there is no ‘universal’ pattern that fits all. The purpose of altered
9 muscle activity in the presence of pain has been suggested to serve as a protective strategy,
10 by redistributing activity or altering behavior to modify movement and stiffness (Hodges and
11 Tucker 2011). Such modified strategy is likely to be different between subjects (Hodges et
12 al., 2013) thereby indicating that an individual tailored rehabilitation strategy might be
13 needed for optimal results.

14

15 *Limitations*

16 The sample size of the neck pain groups may have influenced the results, especially for **EMG**
17 where only the WAD group demonstrated **a difference in** RMS-EMG. Secondly, the current
18 study investigates RMS-EMG changes over time and does not account for differences
19 between groups at baseline since EMG recordings cannot be compared between subjects (van
20 Dieen et al., 2003). Furthermore, movement patterns are unaccounted for in this study, and
21 because altered scapula orientation during arm movements have been identified in neck pain
22 patients (Helgadottir et al., 2010) future studies using 3-dimensional movement analysis
23 along with EMG recordings are warranted (Castelein et al., 2015). Lastly, there could be
24 limitations when measuring PPT since it was impossible to blind participants to the fact that
25 the effect of movements on PPTs were investigated. **However,** this influence **was** minimized
26 since participants could not see the PPT values when they indicated the pain threshold.

27

28 *Conclusion*

29 Hyperalgesia and pain evoked by arm abduction was found in IONP patients, compared with
30 asymptomatic controls where the arm movements were pain-free and a hypoalgesic response
31 was found. Increased muscle activity was found for the serratus anterior muscle during
32 slow arm movements for the WAD group compared to the IONP and control groups. Taken
33 together, these results indicate that not all neck pain patients are alike, underpinning the

1 necessity of identifying specific, individual contributing factors for neck pain in order to
2 tailor rehabilitation rather than applying ‘one size fits all’ strategy based on **pain** location.

3

4

5

6

7 **AUTHOR CONTRIBUTION**

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

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15

1 **FIGURE LEGENDS**

2 **Figure 1**

3 Study design overview. Measurement of pressure pain threshold (PPT). Movement Series
4 during Bout-I and Bout-II indicate recordings of muscle activity during standardized and
5 repeated arm movements.

6

7 **Figure 2**

8 Mean VAS scores (A) and perceived area of pain (a.u.) from body chart drawings (B; + SEM,
9 N = 50; 16 IONP, 9 WAD, 25 Control) recorded at baseline, during/after Bout-I and Bout-II.
10 Significant difference within group (#, Wilcoxon: $P < 0.016$) and compared with control (*:
11 Mann-Whitney U: $P < 0.016$).

12

13 **Figure 3**

14 Mean PPT (+ SEM, N = 50; 16 IONP, 9 WAD, 25 Control) recorded over the m. splenius
15 capitis (NECK), m. temporalis (TEMP), m. extensor carpi radialis brevis (ECRB) at baseline,
16 after Bout-I and Bout-II. Significant difference compared with controls (*), or within (#) and
17 between (⊗) groups (NK: $P < 0.05$).

18

19 **Figure 4**

20 Mean (+ SEM, N = 50; 16 IONP, 9 WAD, 25 Control) normalized RMS-EMG for the
21 ipsilateral (Ipsi) serratus anterior (SA) muscle during slow up movement in Bout-I and Bout-
22 II. Significant difference between (⊗) and within (#) groups (NK: $P < 0.05$).

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1 **TABLE LEGENDS**

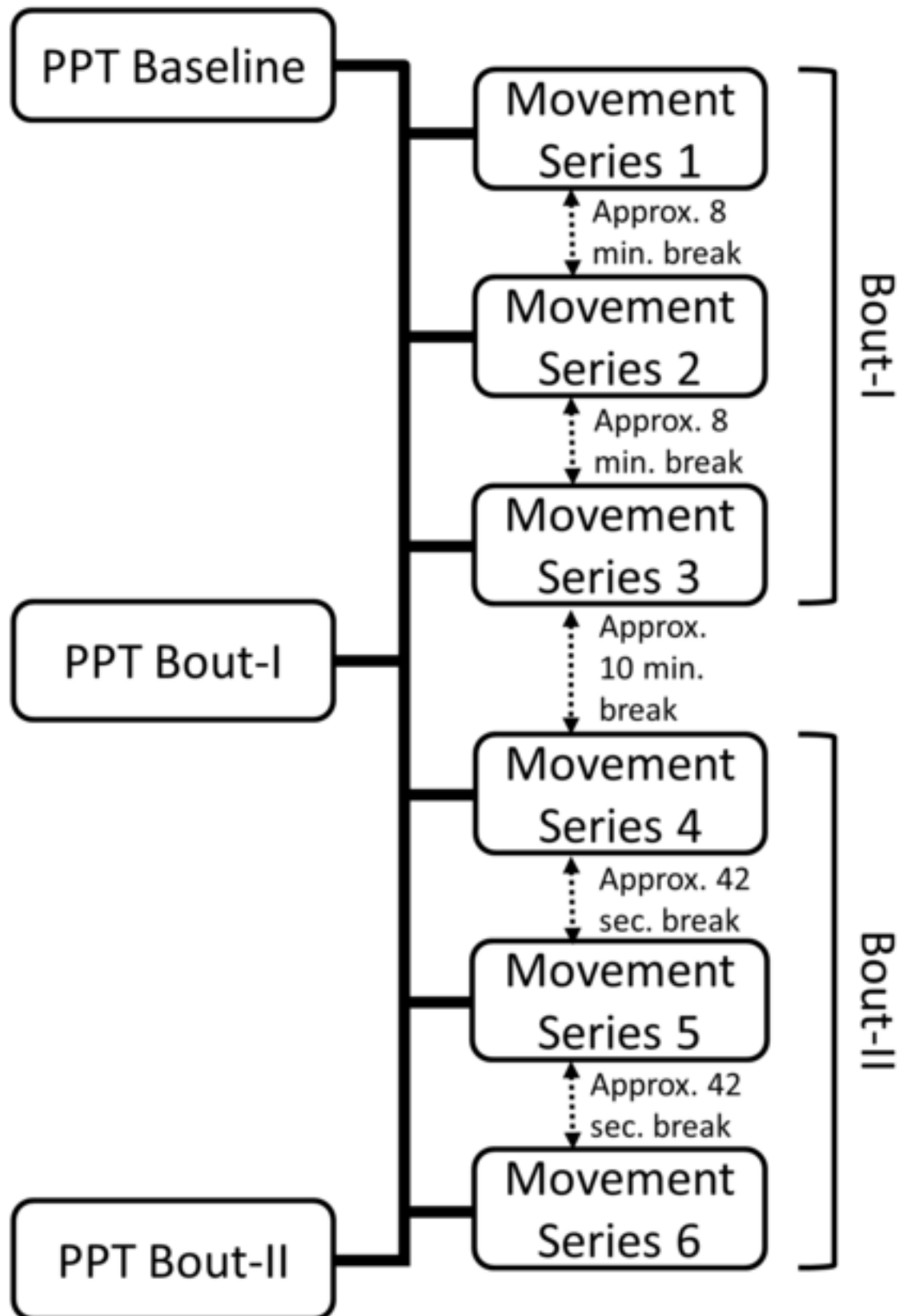
2 **Table 1**

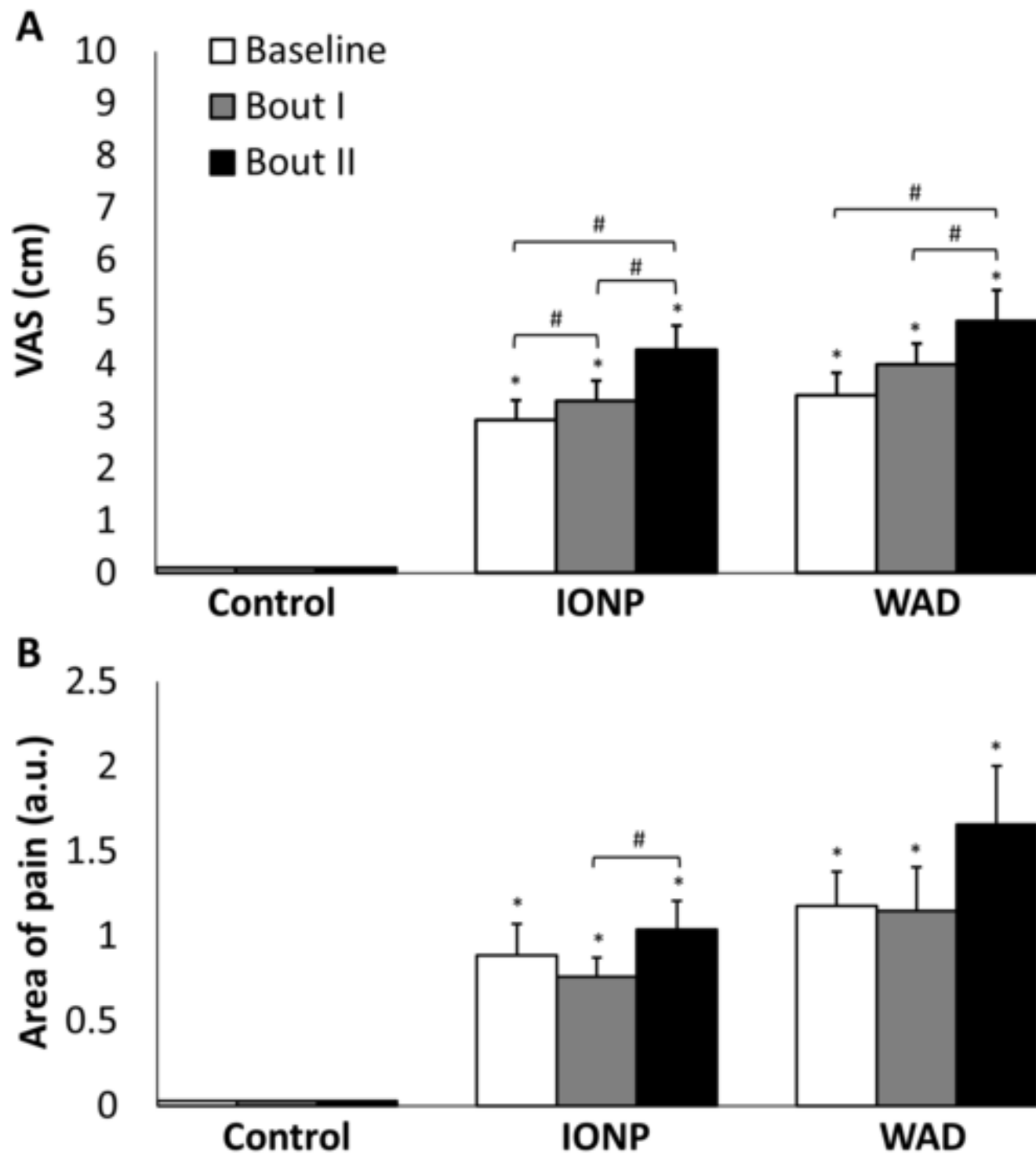
3 Demographic parameters of participants. Significantly different compared with controls (*)
4 or between neck pain groups (α ; Mann-Whitney U: $P < 0.016$; Bonferroni corrected due to
5 multiple comparisons). BMI: Body Mass Index. NDI: Neck Disability Index.

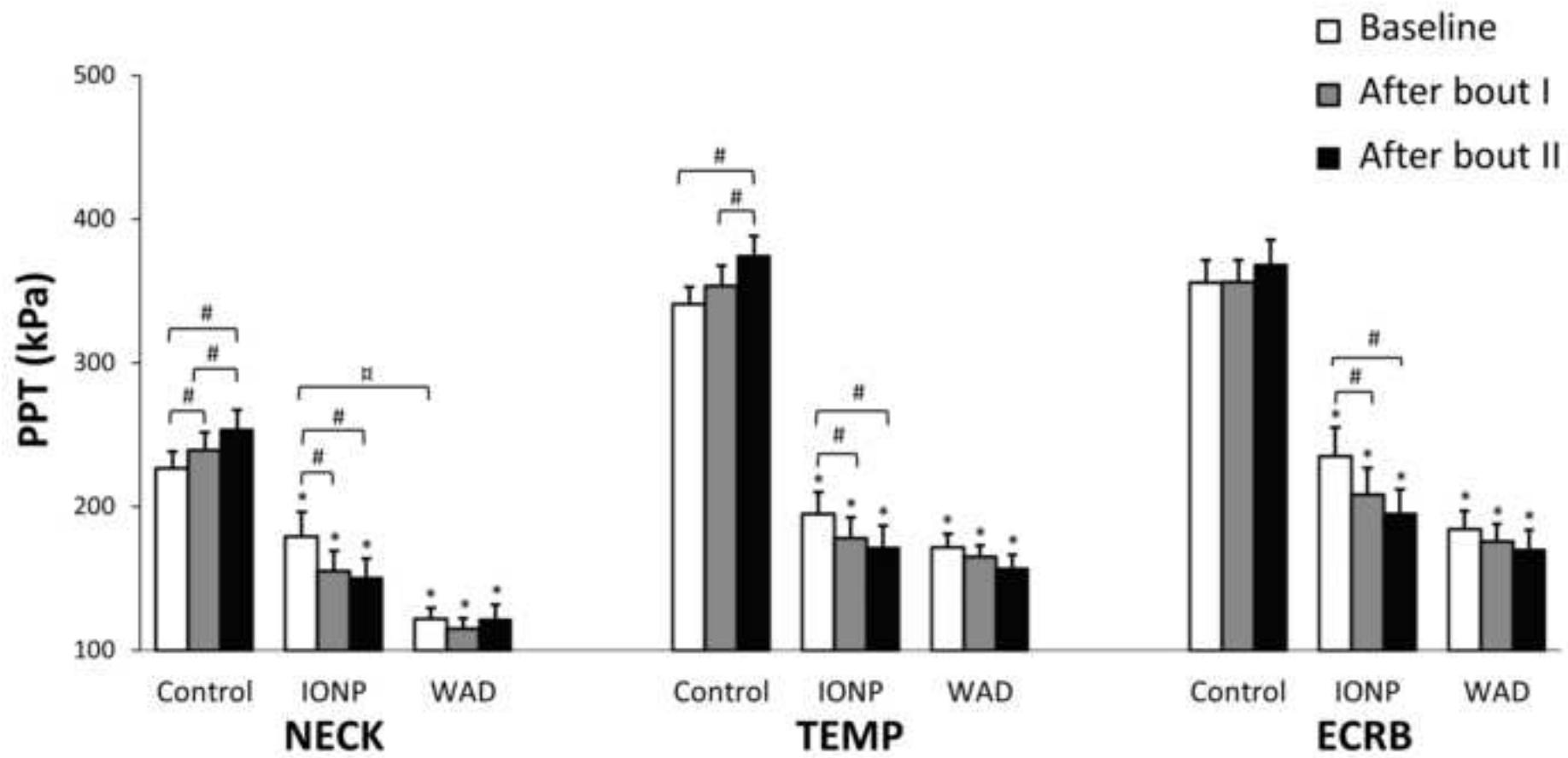
Table1

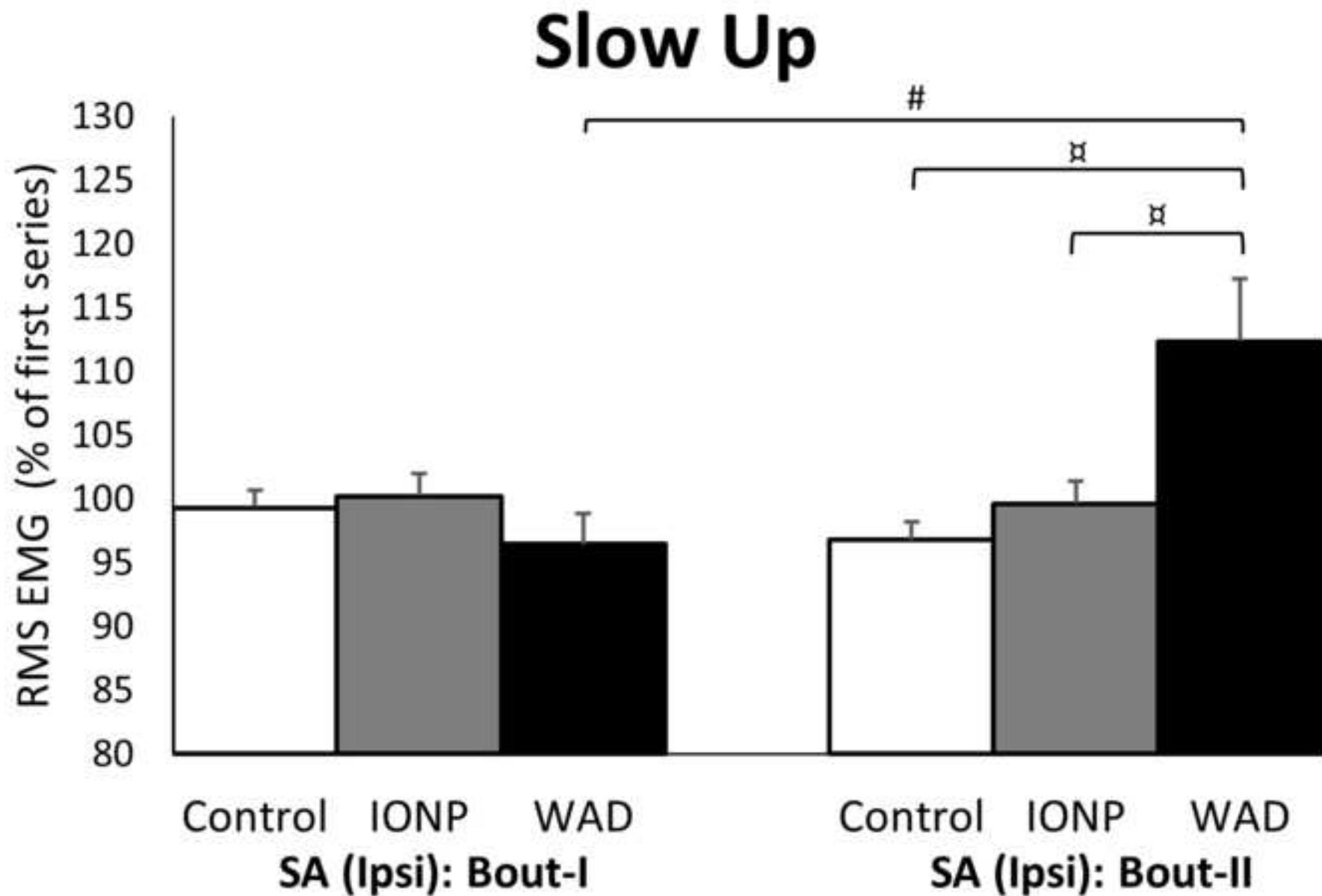
	IONP	WAD	Controls
Number of participants (females)	16 (10♀)	9 (7♀)	25 (17♀)
Mean age (SEM, years)	27.6 ± 1.8	33.8 ± 2.5	29.9 ± 1.6
Mean BMI (SEM, kg/ m ²)	24.4 ± 0.8*	26.2 ± 1.3*	22.9 ± 0.6
Years with neck pain (SEM)	5.5 ± 1.1*	4.5 ± 1.1*	0.0 ± 0.0
NDI (% of max score, SEM)	18.8 ± 1.9* [‡]	41.3 ± 3.8*	1.4 ± 0.4
Average pain VAS in the past week (SEM, cm)	3.3 ± 0.9*	4.4 ± 0.4*	0.0 ± 0.0

Study Design









Methods S1

Repeated arm movements

The movement plane was standardized by placing a Plexiglas wall behind the participants so the back of the hand would be in contact with this during the entire movement and an upper mark was placed at the top level. Each slow movement consisted of a 3-s up movement followed by a 3-s down movement without a break at the top level. A custom made program (Aalborg University, Denmark) was used to cue the movements by three 'beep' cues separated by 3-s: 1) to start, 2) when the arm should be at maximum height, and thereby indicating the start of the downward movement and 3) when the arm should be back at the 'start' position, after which there was a 6-s break before next movement was conducted with the opposite arm. After three slow arm movements on each side, three fast arm movements were performed on each side following a similar pattern. During these fast movements only the up movement was of interest with participants instructed to move the arm as fast as possible to the top level. Throughout the movement series participants were reminded to keep an upright posture.

Kinematic recordings

For the slow arm movements ACC data was extracted from the first 'beep' to max angle and from max angle to the last 'beep', representing the slow up and down movement. For the fast-up movement, only the data from the first 'beep' to maximum angle was extracted.

Muscle activity - Onset

The time points for muscle activity onsets were automatically detected for the fast up movements using a method previously described in details by Santello et al. (1998) where RMS-EMG data was represented as a continuously integrated value over time (IEMG). The IEMG at the end of the task along with time was then set to 1. The plotted line for the IEMG was then compared to a line with the slope of 1, representing a 1:1 association between time and RMS-EMG. The EMG onset was defined as the time point with the greatest distance between the two lines followed by a continuously increased activity (curve with a slope greater than 1).

Pressure pain sensitivity

A detailed description of the three bilateral PPT sites: 1) a local neck site (NECK), over the splenius capitis muscle at the level of C3, between the posterior border of the sternocleidomastoid muscle and the anterior border of the upper trapezius muscle was used (Christensen et al., 2015; 2017), 2) a segmental site over the temporalis muscle (TEMP) above the base of the ear (Christensen et al., 2015; 2017; Kasch et al., 2001), with innervation (trigeminal nerve) converging with that of the splenius capitis (C2-C3) at the spinal cord (Bogduk 2001), and 3) the proximal part of

the extensor radialis brevis muscle (ECRB)(Christensen et al., 2015; 2017; Slater et al., 2005) was used as a distal site. Assessments always started at the NECK, then TEMP and finished with the ECRB site before moving on to the contralateral site. The side of the first measurement was randomized in a balanced way. An average of the three trials was used for further analysis.

Figure S1

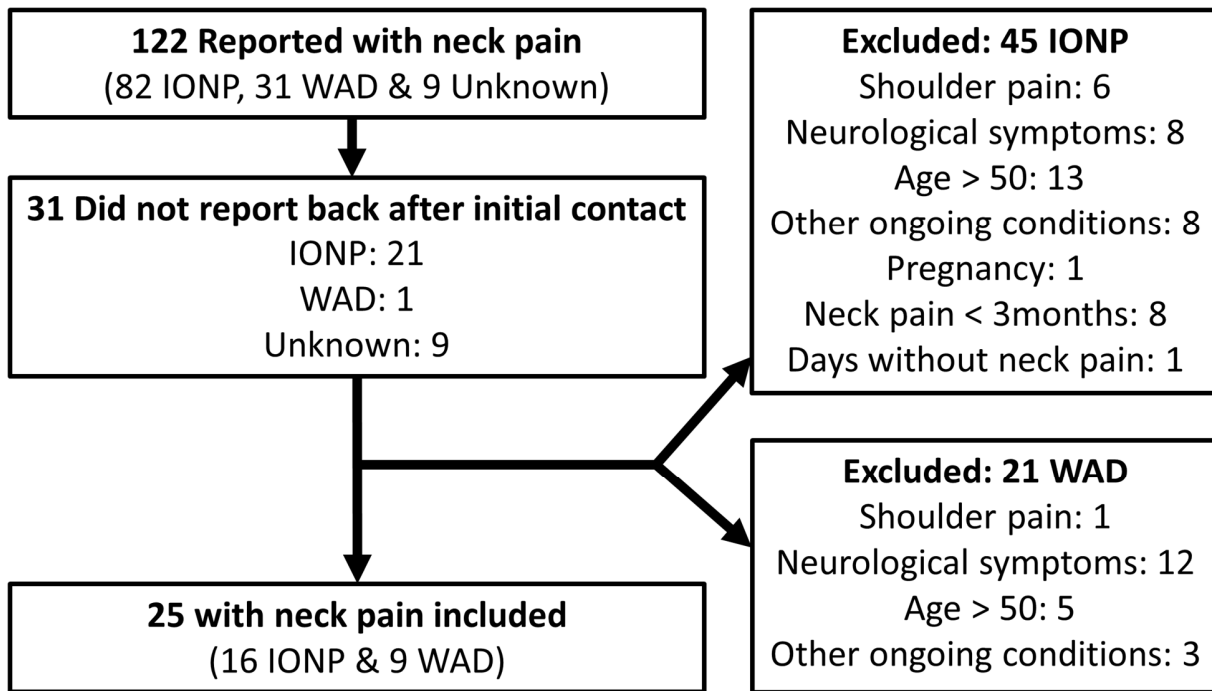


Figure S1 Inclusion and exclusion of neck pain patients: Insidious onset of neck pain (IONP) and Whiplash associated disorders (WAD).

Figure S2

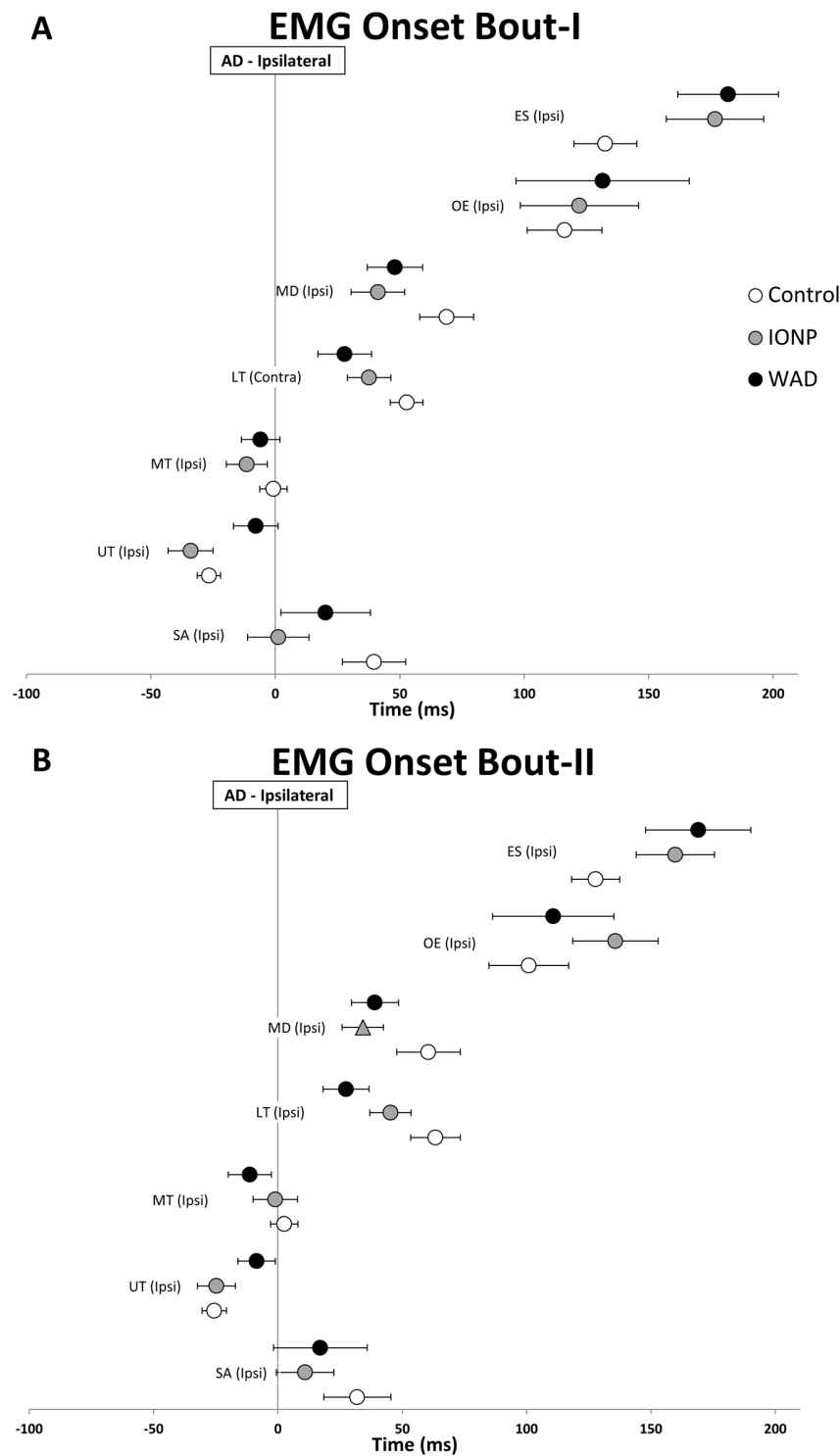


Figure S2 Mean EMG onset values of fast movements (+ SEM, N = 50; 16 IONP, 9 WAD, 25 Control). Onsets for movements in Bout-I (A) and Bout-II (B) from the serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), middle deltoid (MD), external oblique (OE), and erector spinae (ES) muscles on the ipsilateral (Ipsi) side to movement are presented relative to the onset of the anterior deltoid (AD) muscle.

Figure S3

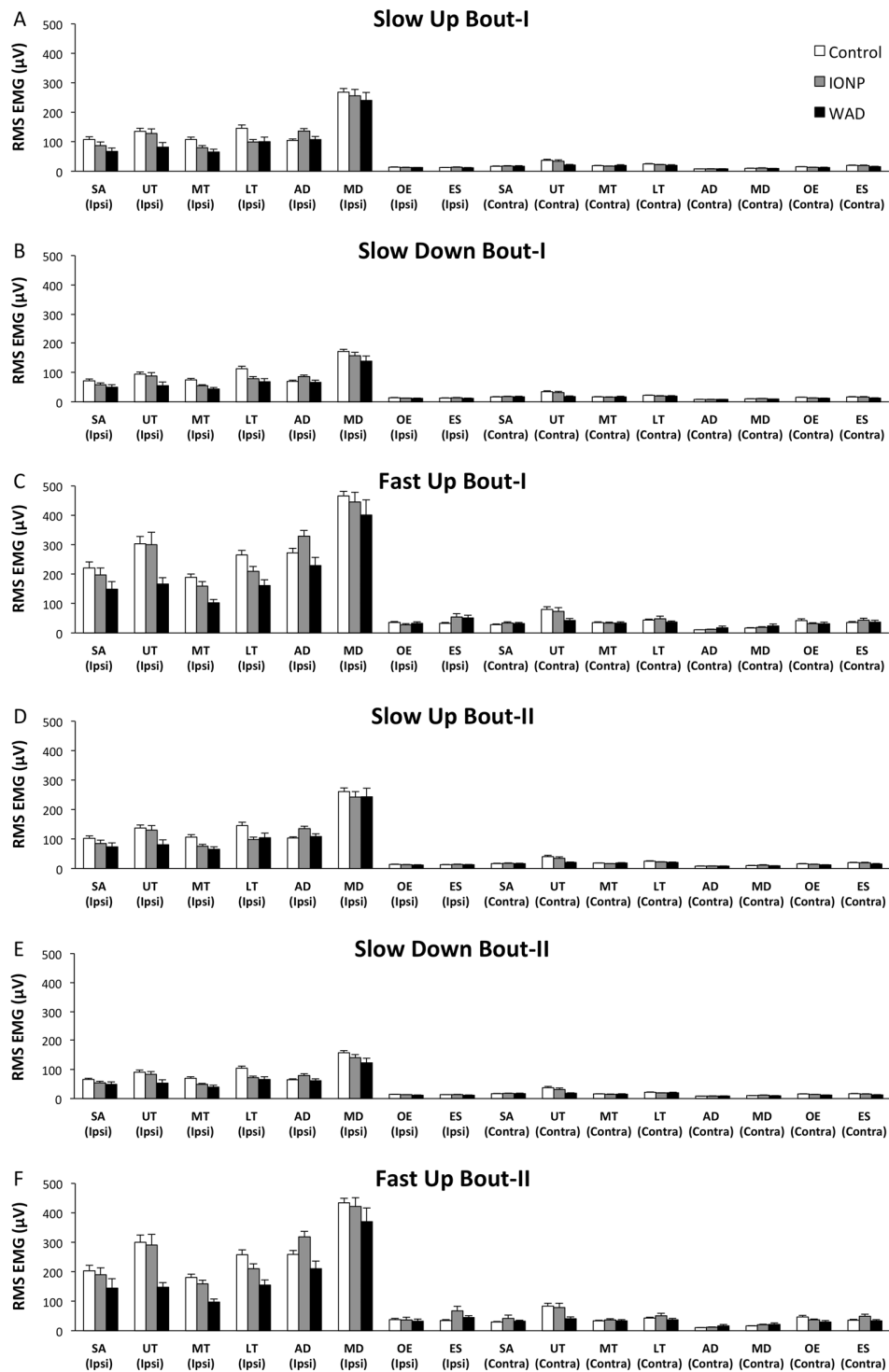


Figure S3 Mean RMS-EMG for Bout-I and Bout-II (+ SEM, N = 50; 16 IONP, 9 WAD, 25 Control). RMS-EMG was extracted separately for the slow up (A, D), down (B, E), and fast up (C, F) arm movement from 8 bilateral muscles: Serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), external oblique (OE), and erector spinae (ES). Ipsilateral (Ipsi), contralateral (Contra).

Table S1

	Slow Up		Slow Down		Fast Up	
Group:	Bout-I	Bout-II	Bout-I	Bout-II	Bout-I	Bout-II
Controls	3.2 ± 0.02	3.1 ± 0.02	2.8 ± 0.02	2.9 ± 0.02	0.9 ± 0.01	0.9 ± 0.01
IONP	3.1 ± 0.03	3.1 ± 0.03	2.9 ± 0.03	2.9 ± 0.03	0.9 ± 0.01	0.8 ± 0.02
WAD	3.1 ± 0.03	3.0 ± 0.03	2.9 ± 0.03	3.0 ± 0.03	0.9 ± 0.03	0.9 ± 0.03

Table S1

Mean accelerometer data (s; ± SEM) for Bout-I and Bout-II for all groups and movement types.

Table S2

EMG ONSET		
Muscle	Time*Group*Side	Time*Group
SA, Ipsi	F[2,93]=1.5, P=0.221	F[2,93]=1.0, P=0.358
UT, Ipsi	F[2,93]=0.3, P=0.740	F[2,93]=0.8, P=0.439
MT, Ipsi	F[2,93]=0.3, P=0.693	F[2,93]=1.0, P=0.351
LT, Ipsi	F[2,93]=0.1, P=0.866	F[2,93]=0.3, P=0.681
MD, Ipsi	F[2,93]=1.8, P=0.169	F[2,93]=0.009, P=0.991
OE, Ipsi	F[2,87]=3.1, P=0.049	F[2,87]=0.3, P=0.681
ES, Ipsi	F[2,83]=0.3, P=0.674	F[2,83]=0.2, P=0.779

Table S1 ANOVA for EMG Onsets for all ipsilateral muscles during fast movements in Bout-I and Bout-II: Serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), middle deltoid (MD), external oblique (OE), and erector spinae (ES).

Table S3

Muscle	RMS-EMG					
	Slow Up		Slow Down		Fast Up	
	Time*Side*Group	Time*Group	Time*Side*Group	Time*Group	Time*Side*Group	Time*Group
SA, Ipsi	F[2,94]=4.2, P=0.017	**F[2,94]= 8.7, P<0.001	F[2,94]=0.07, P=0.926	F[2,94]=3.3, P=0.040	F[2,94]=1.2, P=0.299	F[2,94]=2.4, P=0.088
UT, Ipsi	F[2,94]=1.1, P=0.320	F[2,94]=0.6, P=0.513	F[2,94]=0.3, P=0.703	F[2,94]=1.3, P=0.254	F[2,94]=1.3, P=0.254	F[2,94]=0.4, P=0.659
MT, Ipsi	F[2,94]=2.4, P=0.091	F[2,94]=5.4, P=0.005	F[2,94]=2.6, P=0.077	F[2,94]=0.9, P=0.406	F[2,93]=0.4, P=0.670	F[2,93]=0.2, P=0.748
LT, Ipsi	F[2,94]=0.6, P=0.511	F[2,94]=1.9, P=0.146	F[2,94]=0.8, P=0.432	F[2,94]=0.3, P=0.734	F[2,94]=0.5, P=0.560	F[2,94]=1.4, P=0.243
AD, Ipsi	F[2,94]=0.8, P=0.448	F[2,94]=1.6, P=0.198	F[2,94]=1.2, P=0.297	F[2,94]=0.1, P=0.830	F[2,94]=0.06, P=0.932	F[2,94]=3.0, P=0.054
MD, Ipsi	F[2,94]=0.4, P=0.658	F[2,94]=1.4, P=0.251	F[2,94]=2.6, P=0.073	F[2,94]=0.09, P=0.913	F[2,94]=0.08, P=0.921	F[2,94]=1.9, P=0.142
OE, Ipsi	F[2,94]=0.5, P=0.594	F[2,94]=0.3, P=0.672	F[2,94]=0.4, P=0.646	F[2,94]=1.1, P=0.309	F[2,94]=0.2, P=0.780	F[2,94]=0.8, P=0.422
ES, Ipsi	F[2,94]=0.04, P=0.954	F[2,94]=3.5, P=0.031	F[2,94]=1.4, P=0.248	F[2,94]=1.3, P=0.260	F[2,94]=0.5, P=0.564	F[2,94]=0.3, P=0.705
SA, Contra	F[2,94]=0.1, P=0.866	F[2,94]=1.6, P=0.193	F[2,94]=0.1, P=0.880	F[2,94]=0.1, P=0.848	F[2,94]=2.4, P=0.089	F[2,94]=0.6, P=0.499
UT, Contra	F[2,94]=0.09, P=0.908	F[2,94]=2.1, P=0.116	F[2,94]=0.4, P=0.647	F[2,94]=2.7, P=0.069	F[2,94]=0.08, P=0.919	F[2,94]=0.3, P=0.683
MT, Contra	F[2,94]=0.1, P=0.832	F[2,94]=0.5, P=0.579	F[2,94]=0.5, P=0.552	F[2,94]=0.7, P=0.483	F[2,94]=0.004, P=0.995	F[2,94]=0.7, P=0.471
LT, Contra	F[2,94]=0.8, P=0.447	F[2,94]=3.3, P=0.039	F[2,94]=0.03, P=0.967	F[2,94]=0.08, P=0.916	F[2,94]=0.1, P=0.852	F[2,94]=0.7, P=0.477
AD, Contra	F[2,94]=0.7, P=0.491	F[2,94]=0.2, P=0.772	F[2,94]=0.9, P=0.402	F[2,94]=0.08, P=0.921	F[2,94]=2.0, P=0.128	F[2,94]=0.3, P=0.701
MD, Contra	F[2,94]=0.007, P=0.992	F[2,94]=0.3, P=0.717	F[2,94]=0.2, P=0.745	F[2,94]=0.7, P=0.468	F[2,94]=0.5, P=0.598	F[2,94]=0.4, P=0.640
OE, Contra	F[2,94]=0.3, P=0.739	F[2,94]=2.9, P=0.058	F[2,94]=0.05, P=0.949	F[2,94]=0.3, P=0.702	F[2,94]=1.1, P=0.312	F[2,94]=2.0, P=0.139
ES, Contra	F[2,94]=1.1, P=0.310	F[2,94]=1.0, P=0.365	F[2,94]=0.1, P=0.842	F[2,94]=1.2, P=0.304	F[2,94]=0.05, P=0.949	F[2,94]=5.4, P=0.005

Table S2: ANOVA results for the normalized RMS EMG recordings during Bout-I and Bout-II. 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). Significant ANOVA interactions (P<0.0031, Bonferroni corrected due to multiple ANOVAs) followed by significant post-hoc testing is indicated (**, NK: P<0.05).