MRI study of the cross-sectional area for the cervical extensor musculature in patients with persistent whiplash associated disorders (WAD)

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Abstract

Cervical muscle function is disturbed in patients with persistent pain related to a whiplash associated disorder (WAD) but little is known about neck extensor muscle morphometry in this group. This study used magnetic resonance imaging to measure relative cross-sectional area (rCSA) of the rectus capitis posterior minor and major, multifidus, semispinalis cervicis and capitis, splenius capitis and upper trapezius muscles bilaterally at each cervical segment. In total, 113 female subjects (79 WAD, 34 healthy control; 18–45 years, 3 months–3 years post-injury) were recruited for the study.

Significant main effects for differences in muscle and segmental level were found between the two groups ($P<0.0001$) as well as a significant group * muscle * level interaction ($P<0.0001$). The cervical multifidus muscle in the WAD group had significantly larger rCSA at all spinal levels and in contrast, there were variable differences in rCSA measures across levels in the intermediate and superficial extensor muscles when compared to the healthy controls ($P<0.0001$). There were occasional weak, although statistically significant relationships between age, body mass index (BMI), duration of symptoms and the size of some muscles in both healthy control and WAD subjects ($P<0.01$).

It is possible that the consistent pattern of larger rCSA in multifidus at all levels and the variable pattern of rCSA values in the intermediate and superficial muscles in patients with WAD may reflect morphometric change due to fatty infiltrate in the WAD muscles. Future clinical studies are required to investigate the relationships between muscular morphometry, symptoms and function in patients with persistent WAD.

Keywords: MRI; Cervical; Muscle; CSA; Whiplash

1. Introduction

Morphometric alterations are common in paraspinal muscles in patients with low back pain (Hides et al., 1994; Kader et al., 2000) and there are qualitative data supporting similar changes in the cervical paraspinal muscles of patients with chronic neck pain (McPartland et al., 1997; Kristjansson, 2004). Quantitative measurements of paraspinal muscle size can be obtained with both real-time ultrasonography and magnetic resonance imaging (MRI) and there is growing support for their use in investigations of patients with spinal pain (Kristjansson, 2004; Elliott et al., 2005; Rankin et al., 2005). While these studies have offered valuable reference data for measurable differences in paraspinal muscle size in both asymptomatic and symptomatic subjects, the value of diagnostic muscular imaging in patients with traumatic neck pain (whiplash associated...
disorders (WAD)) has yet to be determined. Since MRI can be regarded as the gold-standard for muscle imaging, it can be used to accurately determine if muscle size in patients with WAD varies significantly from normative data. Such knowledge may assist the understanding of muscle changes in neck disorders as well as serve as an outcome measure in rehabilitation.

The purpose of this cross-sectional study was to (1) measure the cross-sectional area (CSA) of cervical extensor muscles, (2) determine whether there was a difference in CSA between WAD and healthy control subjects within a defined age-range (18–45 years), and (3) determine if age, neck disability index (NDI) scores, duration of symptoms and body mass index (BMI) had an influence on extensor muscle size. It was hypothesized that CSA alterations in the cervical extensor musculature would be greater in patients with persistent WAD than healthy control subjects.

2. Methods

2.1. Subjects

Volunteer subjects with persistent WAD were gained upon referral from physical therapy and medical centers in both Denver (USA) and Brisbane (Australia). Healthy control subjects were recruited through university advertisement campaigns.

Whiplash subjects were included provided they suffered from persistent neck pain and disability (duration from 3 months to 3 years) resulting from a motor vehicle crash (MVC) and were classified as Grade (duration from 3 months to 3 years) resulting from a MVC-related loss of consciousness (2). One healthy control subject was excluded following reports that she had suffered from intermittent neck pain with symptoms of vague dizziness for the past 5 years. Thus, the study population consisted of 79 WAD subjects (78 Americans and 1 Australian) and 34 healthy controls (16 Americans and 18 Australians). Ethical approval was granted by local and Institutional Ethics Committees. Written informed consent was obtained from all subjects prior to their inclusion into the study.

2.2. Procedure of MRI acquisition

In the USA, all subjects were scanned using a conventional spin-echo pulse sequence (656 ms TR and 14 ms TE) with a Horizon LX General Electric 1.5 T scanner (Milwaukee, WI, USA). In Australia a SONATA 1.5 T magnet (448 ms TR and 14 ms TE) (Siemens, Erlangen, Germany) was used using the same measurement methodology. There was no systematic difference found between images acquired in the USA and those acquired in Australia. Axial images of the cervical spine were obtained from the mid point of the cerebellum through to the T1 segmental level, thus ensuring proper capture of the paraspinal musculature. Fig. 1 illustrates the cervical extensor musculature on T1-weighted axial MRI scan at the C6 segmental level (healthy control). The suboccipital muscles (rectus capitis posterior minor (RCPmin) and major (RCPmaj)) were measured at the C1 and C2 segments and the cervical extensor muscles (multifidus, semispinalis cervicis and capitis, splenius capitis and upper trapezius) were measured at each segment (C3–7). T1-weighted MR parameters were chosen in order to provide images of reasonable tissue contrast between fat and skeletal muscle (Murphy et al., 1986).

2.3. Procedure of image analysis

The images were analyzed post hoc with MRICro software (www.mricro.com) (Rorden and Brett, 2000) and securely stored on a laptop computer. Analysis was accomplished by manually tracing defined regions of interest (ROI) within the fascial borders of the suboccipital and cervical extensor muscles bilaterally on the axial T1-weighted images. The most cephalad portion of each vertebral body (C3–C7) was the landmark used for measurement of the cervical extensors, multifidus, semispinalis cervicis, capitis, splenius capitis and upper trapezius at each level. The axial MR slices were positioned parallel to the C2/3 intervertebral disk, which produced a slight measurement error for the CSA measures of muscles above and below. This was consistent for the muscles bilaterally at each vertebral segment and between each subject. As a result, relative CSAs (rCSA) are reported. The rCSA of cervical extensor musculature were calculated by the number of pixels under each ROI in the x and y axes (mm $\times$ mm = mm$^2$) with MRICro software. The rCSA measures for the RCPmin muscle were measured after
identifying the odontoid process and occipital condyles at the C1 segmental level on the MR axial scan. The rCSA measures for the RCPmaj muscle were measured from the most cephalad portion of the C2 segmental level on the MR axial scan. The rCSA measures for the bilateral segmental extensor muscles (C3–C7) were measured after identifying the individual muscle at the most cephalad portion of each particular vertebral level on the MR axial scan. This process ensured consistent representation of rCSA measures for each muscle at each level between the subjects and has been previously reported in detail (Elliott et al., 2005).

The examiner (JE) was not blinded to the status of the subjects. To determine the fidelity of the measures (as well as inter-examiner reliability), a second researcher undertook the rCSA measures for the right side multifidus, semispinalis cervicis, capitis, and splenius capitis muscles at the 5 segments (C3–C7 levels) on 5 subjects (100 measures).

2.4. Data analysis

Data were analyzed with SPSS 13.0. Intraclass correlational coefficients (ICC) were performed to examine inter-examiner reliability and the ICCs and standard error of the measure (SEM) were calculated for each muscle at each segmental level. Analysis of the main data was performed through several steps. In justifying the assumption of common distribution for the two groups, a Q–Q plot was graphed and revealed that the distribution of errors for the rCSA measures was skewed positively. As a result, raw data values (mm²) for rCSA were transformed and analyzed as logged values. A multi-factorial repeated measures analysis of variance was used to investigate whether there were any differences between the whiplash and control groups in measures of rCSA of the cervical extensor muscles across muscle, side and segmental levels. Group differences between WAD and control subjects for rCSA measures in the RCPmin and RCPmaj muscles were compared using independent sample t-tests. The Spearman correlations were also performed to determine if the score on the NDI (Vernon and Mior, 1991) age, BMI and length of history from date of injury had an influence on muscle size. Significance was set conservatively at $P<0.01$.

3. Results

Table 1 presents the demographic characteristics for the two groups. The WAD group were marginally (albeit significantly) older and had a higher BMI than the control group, although there were no significant differences in height and weight between groups.

In the reliability study, the measures of muscle rCSA ranged from 74.7–215.1 mm². The ICCs for the inter-rater agreement of the rCSA measures of the right sided cervical extensors at the C3–C7 segmental levels ranged from 0.96 to 0.99 (SEM 0.96–4.87), indicating the measure to have acceptable accuracy.

3.1. rCSA of cervical extensor muscles

The ANOVA revealed significant main effects for muscle and segmental level ($P<0.0001$) with a significant interaction for group * muscle * level, indicating
that differences in rCSA between the two groups varied by muscle and level ($P<0.0001$). There was no significant interaction between group * side * muscle and as a result, we have averaged the rCSA values for right and left sides for post hoc analysis.

Fig. 2 presents the logged rCSA measures for each muscle of the cervical extensor group at each cervical level (C3–C7) for the WAD and control groups. Post hoc analysis revealed that there was a significantly larger rCSA in the multifidii at all levels (C3–C7) in the WAD compared to control subjects ($P<0.0001$). In contrast, the other intermediate to superficial musculature (semispinalis cervicis, semispinalis capitis, splenius capitis and upper trapezius) yielded variable differences with regards to muscle size. Specifically, the rCSA measures were smaller in the WAD subjects for the semispinalis cervicis and the difference was significant for C3 ($P = 0.005$), C5 and C6 levels ($P<0.001$). A mixed pattern of muscle size was noted for the semispinalis capitis and splenius capitis muscles. In particular, rCSA values were significantly larger in the WAD group for semispinalis capitis at C3 ($P<0.001$); and splenius capitis at the C3 level ($P<0.001$). However, at the C6 level the semispinalis capitis was larger in the healthy control group ($P=0.001$). No significant differences were noted in rCSA of the upper trapezii musculature between the two groups ($P = 0.5678$). Appendix A presents raw data for rCSA values (mm$^2$) of the cervical extensor musculature * side * level * group. Appendix B presents raw data for rCSA values (mm$^2$) of the sub-occipital musculature * side * group.

### 3.2. rCSA of the suboccipital musculature

The independent samples $t$-test revealed no significant between-group differences in rCSA (averaged between sides) for the RCPmin ($P = 0.07$) and for the RCPmaj ($P = 0.02$). The general trend was for larger rCSA in the WAD RCPmin and RCPmaj musculature.
3.3. $rCSA$ and NDI, duration of symptoms, BMI and age

The Spearman’s $\rho$ correlation analyses indicated that there were no significant associations between the rCSA measures in the WAD group extensor muscles (averaged between sides) and NDI scores or duration of symptoms. However, there were weak (albeit significant) positive correlations between the rCSA measures in some of the extensor muscles for both groups and BMI scores ($r^2$ range from 0.06 (semispinalis capitis—C7) to 0.14 (splenius capitis—C3)) and for age ($r^2 = 0.05$ (semispinalis cervicis—C5)) ($P<0.01$). Even though the correlations differed significantly from zero, the amount of variation captured in the associations of age and BMI was very small and only explained between 5% and 14% of the variance (age: semispinalis cervicis—C5; BMI: splenius capitis—C3, respectively).

4. Discussion

This study has identified changes in the MRI measure for rCSA in the cervical extensor musculature in patients with persistent WAD compared to healthy control subjects. Specifically, significantly larger rCSAs were identified in the deep multifidus muscle at the C3–C7 levels in the WAD group and a varying pattern in rCSA was found in the more intermediate musculature. Smaller rCSAs were found in the WAD group for the semispinalis cervicis (C3, C5 C6) while larger rCSAs were found in the more superficial muscles; semispinalis capitis (C3) and splenius capitis (C3). The semispinalis capitis had a greater rCSA in the healthy control group at the C6 level only. No significant differences were found in the upper trapezius or in the suboccipital muscles (RCpmin and RCpmaj). There was a weak correlation between rCSA, age and BMI (both groups) for some muscles. However, the muscle changes were independent of self-reported levels of pain and disability (NDI) and duration of symptoms in the WAD subjects. NDI scores (/100) in the WAD group ranged from 16 to 82 (mean 45.5 ± 15.9) indicating self-reported levels of pain and disability in this whiplash group ranged from mild to severe.

4.1. Increased rCSA in multifidus

A consistent pattern of larger rCSA was observed in the WAD group in the multifidus muscle at each segment (C3–7) and this contrasted to a less-consistent pattern in rCSA measures in the other more intermediate and superficial muscles; semispinalis cervicis and capitis and splenius capitis. It is possible that fatty infiltrate is responsible for these findings in the multifidus. We have previously established that the WAD subjects from this study also demonstrate widespread fatty infiltrate in all cervical extensor muscles (Elliott et al., 2006). However, the highest fat indices were consistently found in the deep multifidii at all segmental levels (C3–C7) and lesser fatty infiltrate was present in the other paraspinal muscles. This may help to explain the reversed pattern of larger rCSA in the multifidii musculature compared to the other muscles in this study. Higher fat content is likely to alter and expand the musculofascial borders thereby creating larger rCSA values with MRI measures. This suggests that measures of rCSA of the cervical extensor musculature have to be interpreted with caution at least in persons with persistent WAD. Increased fat content has also been found in the lumbar paraspinal muscles in patients with persistent low back pain (Alaranta et al., 1993; Kader et al., 2000) and observed in the suboccipital muscles in patients suffering from persistent neck pain (Hallgren et al., 1994; McPartland et al., 1997). It is possible that the measures of MR fatty infiltration may be more sensitive markers than CSA for changes in these muscles in patients with persistent WAD, or both measures should be taken concurrently.

The involvement of multifidus at all segments in the cervical region in this chronic whiplash group is notable as multifidus has substantial muscle insertions into the cervical facet capsule (Winkelstein et al., 2001). Numerous reports have implicated the facet joint in neck pain and injury (Lord et al., 1996; Panjabi et al., 1998; Winkelstein et al., 2000; Siegmund et al., 2001). Anderson et al. (2002) have further substantiated that the cervical multifidus is architecturally complex with deep and superficial fascicular subgroups attaching directly to the facet capsules. Based on the location of the cervical multifidus, any morphometrical changes may compromise its ability to play a role in controlling cervical segmental motion. These muscular changes may therefore be a contributing factor to ongoing neck pain and disability.

4.2. Altered rCSA in the other neck extensor muscles

The consistent finding of reduced rCSA in the semispinalis cervicis may reflect general wasting, without the large volumetric influence of higher levels of fatty infiltrate as was noted to occur in the deep WAD multifidus. The changes in the semispinalis capitis and splenius capitis were not as marked through the spine with the exception of the C3 level where paradoxically the rCSAs were larger in the WAD group. This cannot be explained by fatty infiltrate as these muscles were found to have less fat within muscle than the semispinalis cervicis (Elliott et al., 2006). The increased rCSA in semispinalis capitis and splenius capitis at the C3 level could represent a function adaptation in response to the changes in multifidus and semispinalis cervicis at this level. Nevertheless, at the C6 level, the rCSA of semispinalis capitis was significantly smaller in the WAD group, which might question this proposal. Further research is required to replicate this finding.
before more definitive explanations can be provided. No significant changes in rCSA were observed in the upper trapezius musculature; a muscle that largely influences the shoulder girdle and upper limb mechanics rather than the neck (Johnson et al., 1994).

It is known that a whiplash injury can damage any number of structures at any segment in the cervical spine (Grauer et al., 1997; Panjabi et al., 1998; Pearson et al., 2004). Nevertheless, Lord et al. (1996) examined the prevalence of cervical zygapophysial joint pain in patients with persistent WAD using diagnostic anesthetic blocks and found the highest incidence at the C2–3 and C5–6 cervical zygapophysial joints. While we found significant rCSA differences existed throughout the cervical spine segments, the C3 level featured significant rCSA changes in all four of the cervical muscles measured and the C6 level had changes in three of the four muscles (multifidus, semispinalis cervicis and capitis). The findings of most altered muscular morphometry at the C3 (C2–3) and C6 (C5–6) levels in our WAD group are consistent with those of Lord et al. (1996). However, the level of symptoms was not determined clinically in this study. Future research is warranted to determine the relationship of segmental muscle size and symptoms.

4.3. rCSA in the sub-occipital muscles

We found no significant differences in rCSA in the sub-occipital musculature. This was surprising as we have previously reported higher amounts of fatty infiltration in these muscles in those subjects suffering from persistent WAD (Elliott et al., 2006). Our proposal for the multifidus muscle, that MRI markers of fat infiltration provide a more sensitive measure than CSA may thus apply to the analysis of sub-occipital muscle morphology of patients with possible upper cervical injury.

4.4. rCSA and NDI, BMI, age and duration of symptoms.

The finding that rCSA changes in the WAD group were not associated with NDI scores was unexpected as injury severity is usually related to higher levels of pain and disability (Gargan and Bannister, 1990). BMI and age appeared to impact on some of the rCSA measures for the cervical extensor muscles in both the control and WAD subjects (18–45 years) and this was surprising as age-related reductions in lean body mass are reported not to commence until the fifth or sixth decade of life (Forbes and Reina, 1970). However, future research is required to better understand the potential cultural influences, if any, on muscle size and BMI. Nevertheless, the relationships were weak and without a consistent pattern of muscle involvement. While the clinical relevance of these findings is not clear, it does indicate BMI and age should be included for consideration in future research of muscle measurements in the cervical region. The correlation analysis investigating the association between duration of symptoms and rCSA in the WAD subjects did not yield significant findings. Our findings of muscle size changes indicate that they were established by 3 months following injury and it is currently unknown how quickly these changes occur after injury. Further longitudinal study involving acute WAD subjects is warranted to better answer that question.

Regardless of the prevailing mechanisms for the observed muscle changes in this study, these morphometrical alterations in the deep muscles may provide valuable insight into the common functional impairments observed in patients with persistent WAD. The deep cervical muscles are predominantly comprised of Type I fibers (Boyd-Clark et al., 2002) and have high muscle spindle density (Liu et al., 2003) suggestive of muscle-specific differences in the precise control of movement and proprioceptive function (Bakker et al., 1984; Edney and Porter, 1986; Porter, 1986). Disturbances in cervical kinesthetic sense (Treleaven et al., 2005) are also common in patients suffering from persistent WAD and these kinesthetic deficits may relate to abnormal cervical afferent input due to alterations within the deep musculature.

5. Conclusion

This is the first MRI study to demonstrate that female patients (18–45 years) with persistent WAD (grade II) show quantifiable alterations in rCSA of the cervical paraspinal musculature that differ significantly from subjects with no history of neck pain. In particular, this study demonstrated larger rCSA in all of the segmental levels (C3–C7) of the deep multifidus muscle in the WAD group which is different from the pattern of variable segmental alterations in rCSA found in the other extensor muscles. The origin behind these findings is not completely understood and further work is warranted to investigate potential mechanisms contributing to these differences and their relevance to function and symptomatology. Finally, the muscle changes found in this study relate to persistent WAD. It is unknown if such changes are associated with chronic neck pain of idiopathic or a nontraumatic origin and this is to be investigated.

Acknowledgments

We wish to sincerely thank Dr. Ross Darnell, Statistician; John Finnesy and Dorinda Gill, Radiology Technicians; Bao Nguyen, MD, Radiologist, Kathy Francis and Candice Valdez, research assistants, for their assistance with conducting this study.
Appendix A

The raw data for rCSA values (mm²) of the cervical extensor musculature * side * level * group are shown in Table A1.

Table A.1
rCSA values (mm²) of the cervical extensor musculature * side * level * group

<table>
<thead>
<tr>
<th>Group</th>
<th>Multifidus</th>
<th>Semispinalis cervicis</th>
<th>Semispinalis capitis</th>
<th>Splenius capitis</th>
<th>Upper trapezius</th>
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<tbody>
<tr>
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<td>R</td>
<td>L</td>
<td>R</td>
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<td>R</td>
</tr>
<tr>
<td>WAD C3</td>
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<td>70.8</td>
<td>113.9</td>
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Data reported as mean (SD) (muscle size is reported as relative cross-sectional area (mm²)).

Appendix B

The raw data for rCSA values (mm²) of the sub-occipital musculature * side * group are shown in Table B1.

Table B.1
rCSA values (mm²) of the sub-occipital musculature * side * group

<table>
<thead>
<tr>
<th>Group</th>
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<tr>
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<tr>
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<td>(34.0)</td>
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</table>

Data reported as mean (SD) (muscle size is reported as relative cross-sectional area (mm²)).

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