Original Research Article

Cervical Radiofrequency Neurotomy Reduces Central Hyperexcitability and Improves Neck Movement in Individuals with Chronic Whiplash

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Abstract

Objective. This study aims to determine if cervical medial branch radiofrequency neurotomy reduces psychophysical indicators of augmented central pain processing and improves motor function in individuals with chronic whiplash symptoms.

Design. Prospective observational study of consecutive patients with healthy control comparison.

Setting. Tertiary spinal intervention centre in Calgary, Alberta, Canada.

Subjects. Fifty-three individuals with chronic whiplash associated disorder symptoms (Grade 2); 30 healthy controls.

Methods. Measures were made at four time points: two prior to radiofrequency neurotomy, and 1- and 3-months post-radiofrequency neurotomy. Measures included: comprehensive quantitative sensory testing (including brachial plexus provocation test), nociceptive flexion reflex, and motor function (cervical range of movement, superficial neck flexor activity during the craniocervical flexion test). Self-report pain and disability measures were also collected. One-way repeated measures analysis of variance and Friedman’s tests were performed to investigate the effect of time on the earlier measures. Differences between the whiplash and healthy control groups were investigated with two-tailed independent samples t-test or Mann–Whitney tests.

Results. Following cervical radiofrequency neurotomy, there were significant early (within 1 month) and sustained (3 months) improvements in pain, disability, local and widespread hyperalgesia to pressure and thermal stimuli, nociceptive flexor reflex threshold, and brachial plexus provocation test responses as well as increased neck range of motion (all \( P < 0.0001 \)). A nonsignificant trend for reduced muscle activity with the craniocervical flexion test (\( P > 0.13 \)) was measured.

Conclusions. Attenuation of psychophysical measures of augmented central pain processing and...
improved cervical movement imply that these processes are maintained by peripheral nociceptive input.

Key Words. Whiplash; Radiofrequency Neurotomy; Central Sensitization; Quantitative Sensory Testing; Peripheral Nociception

Introduction

Approximately 50% of individuals who sustain a whiplash injury will continue to report ongoing neck pain and disability 12 months later [1]. Chronic whiplash-associated disorder (WAD) is characterized by sensory disturbances (widespread hypersensitivity) [2–4] and heightened spinal cord flexor withdrawal responses [5,6], both indicative of augmented central nociceptive processing [7]. Changes in motor function are also evident with reduced neck range of movement and altered muscle recruitment patterns [8,9].

The processes underlying and contributing to these features are not clear. While it is generally accepted that sensory features result from augmented central nociceptive processing (central hyperexcitability) [10,11], there is much debate as to whether these are driven by an ongoing peripheral nociceptive source [12–14] or are self-maintaining due to neuroplastic changes in the central nervous system [7]. Previous studies of patients with painful hip or knee osteoarthritis demonstrated improved cervical movement imply that these processes are maintained by peripheral nociceptive input [15,16].

Similarly, persistence of motor changes following whiplash injury, such as morphometric muscular changes, local muscular weakness, and loss of range of movement, suggests the presence of ongoing peripheral mechanisms [17–21]. However, these changes cannot be separated from changes in central nervous system control, with neuromotor performance in individuals with neck pain associated with reorganization of control strategies [22–24].

While tissue damage usually cannot be detected in the patient with WAD with current imaging techniques, evidence to date suggests that a peripheral lesion of some kind is likely to be present [25–27]. Most available evidence would support the cervical facet joint as one source of nociception in individuals with chronic WAD [28–30]. Animal studies have demonstrated that cervical facet joint injury may be responsible for hypersensitivity and increased neuronal excitability [31–34]. Injury to the facet joint has also been implicated in local muscle responses in a cat model [35]. Modulating nociception from facet joints is possible via medial branch blocks (MBBs) or radiofrequency neurotomy (RFN). There are suggestions that MBB or RFN may attenuate sensory hypersensitivity [36–38]; although the evidence is weak, with studies involving limited subjects, measures or procedures; or only investigating immediate post-procedure effects. Thus, the role of the cervical facet joint in regard to sensory and motor changes in chronic WAD requires further investigation, with a wider range of measures of central hyperexcitability and inclusion of measures of motor function.

The aim of this study was to investigate changes in measures of central hyperexcitability following RFN of cervical spine facet joints in individuals with chronic WAD. We also investigated changes in motor function following the same procedure. The null hypothesis was that reducing nociception via RFN would not result in changes in psychophysical indicators of central hyperexcitability or changes in motor function.

Methods

Design

A prospective cohort study design was employed at a tertiary spinal intervention centre in Calgary, Alberta, Canada. Participants included individuals with chronic WAD who underwent RFN, following a successful response to cervical facet joint blockade. A healthy control (HC) cohort was also investigated to provide comparative data. Individuals with WAD attended the research laboratory at four time points: 1 month following cervical facet joint injections (double blockade procedure), immediately prior to receiving RFN, 1 month following RFN, and 3 months following RFN. HC individuals attended one session of laboratory testing.

Participants

Inclusion Criteria

Consecutive participants were recruited from individuals aged 18–65 years with WAD Grade II [39] of a duration greater than 6 months post-motor vehicle collision (MVC) following successful response (greater than 50% of neck pain relief) to cervical facet joint blockade (intra-articular block followed by confirmatory MBB) [40], who subsequently underwent RFN.

HC individuals with no previous history of neck pain, whiplash injury, or recent treatment for musculoskeletal pain (within previous 2 years) were recruited from advertisements placed around the spinal intervention centre.

Exclusion Criteria

Individuals were excluded from the study if they were classifiable as WAD Grade III (neurological deficit) or IV (fracture or dislocation) [39], sustained a concussion or loss of consciousness as a result of the trauma, or if they were not fluent in spoken or written English.

All the participants were unpaid volunteers. Ethical clearance for this study was granted from the institutional
medical research ethics committees (University of Calgary and University of Queensland) in 2009. All participants provided informed consent.

Outcome Measures

Quantitative Sensory Tests

Pressure Pain Thresholds. Pressure pain thresholds (PPTs) were measured using a pressure algometer (Somedic AB, Farsta, Sweden). The probe size was 1 cm², and the rate of application was 40 kPa/s. PPTs were measured over the articular pillars of C5/6 bilaterally (which is the most prevalent facet joint involved in neck pain [not involving headaches] following whiplash trauma) [30], over the median nerve trunk anterior to the elbow bilaterally, and at a bilateral remote site (upper one third of the muscle belly of tibialis anterior) as previously described in investigations of chronic WAD [4]. The participants were requested to push a button when the sensation of pressure first became painful. Three recordings were taken at each site and the mean value for each site used in the analysis.

Nociceptive Flexion Reflex. The nociceptive flexion reflex (NFR) is a polysynaptic spinal withdrawal reflex that is elicited following activation of nociceptive A-delta afferents [41]. It was performed via electrical stimulation through bipolar surface Ag/AgCl electrodes (interelectrode distance approximately 2 cm), which were placed just distal to the left lateral malleolus of the ankle (innervation area of the sural nerve). Electromyography (EMG) reflex responses to electrical stimulation were recorded from the middle of the biceps femoris muscle using Ag/AgCl electrodes. The participant lay prone, and a wedge was placed under the ankle to obtain 30 degrees knee flexion. The EMG signal was amplified and low-pass filtered 0–500 Hz by a multichannel EMG (Naroxon, Scottsdale, AZ, USA). Stimulation and recording was controlled and analyzed with custom software developed specifically for this test. A 25-millisecond, train-of-five, 1-millisecond, square-wave impulse (perceived as a single stimulus), was delivered by a computer-controlled constant current stimulator (Digitimer DS7A, Hertfordshire, England).

The current intensity was increased from 2 mA in steps of 2 mA until a reflex was elicited. The program delivered the impulses at random time intervals, so that the participants were not aware of when the stimulus was going to be applied. In this way, voluntary muscle contraction due to stimulus anticipation was avoided. A reflex response was defined using the standardized peak (NFR interval peak z score) EMG activity from biceps femoris as recommended [42]. The NFR interval peak z score is the NFR interval peak z score (EMG activity 90–150 milliseconds post-stimulation interval)—baseline mean (60 milliseconds before stimulation)/baseline standard deviation (SD). Rhudy and France [42] suggest an NFR interval peak z score of greater than 10.32 be used to define a reflex response. The 90- to 150-millisecond interval was chosen as it avoids possible contamination by low threshold cutaneous flexor reflex, startle reactions, and voluntary movements [43]. The current intensity required to elicit a reflex response was defined as the NFR threshold.

Thermal Pain Thresholds. Thermal pain thresholds were measured bilaterally over the cervical spine using the TSA II Neurosensory Analyzer (Medoc Advanced Medical Systems; Minneapolis, MN, USA). The thermode was placed over the skin of the mid-cervical region and preset to 32°C, with the rate of temperature change being 1°C/s. To identify cold pain thresholds (CPTs) and heat pain thresholds (HPTs), participants were asked to push a switch when the cold or warm sensation first became painful [44]. Triplicate recordings were taken at each site, and the mean value for each site was used in the analysis.

Brachial Plexus Provocation Test. The brachial plexus provocation test (BPPT) was performed in the following sequence: gentle shoulder girdle depression, glenohumeral abduction and external rotation in the coronal plane, forearm supination, wrist and finger extension, and elbow extension [45]. The range of elbow extension was measured at the participants’ pain threshold using a standard goniometer aligned along the mid-humeral shaft, medial epicondyle, and ulnar styloid [46]. If the participant did not experience pain, the test was continued until end of available range. Hypersensitive responses to this test have been demonstrated in chronic whiplash [47,48], and the test has excellent intratherapist reliability [49].

Motor Measures

Range of Motion. Active cervical range of motion (ROM) was measured using electromagnetic motion sensors (Fastrak, Polhemus, Colchester, VT, USA) [8]. One sensor was placed over the C7 spinous process and the other attached to the top of a light skull cap firmly fitted to the participant’s head, such that the second sensor sat on the vertex. Three trials were performed in each direction (flexion, extension, left and right rotation) and the means of the three trials were used in analysis. A computer program was developed to convert the Euler angles into degrees of freedom of motion of the vertex relative to C7. The Fastrak has previously been used in trials of neck pain and whiplash participants [50] and has shown to be accurate within ±0.2 degrees [51].

Cranio cervical Flexion Test. Surface EMG (Naroxon Tele Myo 900) was used to measure the activity of superficial neck flexor muscles (sternocleidomastoid, SCM) during the five incremental stages of the cranio cervical flexion test (CGFT) as described by Jull et al. [9]. The test was performed in supine and used a pressure biofeedback device (Stabilizer, Chattanooga, TN, USA) placed suboccipitally behind the neck to guide performance. It was inflated to a baseline of 20 mm Hg, and participants performed cranio cervical flexion to increase the pressure by five progressive increments of 2 mm Hg (22–30 mm Hg). Each pressure level was maintained for 10 seconds, and participants rested for 15 seconds between each stage. Myoelectric signals were collected from the SCM muscles
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using Ag–AgCl electrodes (Noraxon) in a bipolar configuration (interelectrode distance approximately 2 cm).

Electrodes were positioned along the lower one-third of the muscle bellies of the SCM [52]. Signals were amplified and filtered by a 500 Hz low pass filter (Noraxon TeleMyo 900) and sampled at 2,000 Hz (National Instruments DAQ PCI-6221). EMG data were analyzed as follows: The maximum root mean square (RMS) value was identified for each trace using a 1-second sliding window, incremented in 100-millisecond steps. RMS values were normalized for each participant, by dividing the 1 second maximum RMS from each level of the CCFT by the 1 second maximum RMS during a standardized head lift. The baseline EMG data (RMS value) obtained at rest (20 mm Hg) was subtracted from the measured EMG at each level of this test. The normalized RMS data for the left and right SCMs were averaged for analysis [9,50].

Questionnaires

Measures included a description of symptoms, symptom dominance (unilateral or bilateral), and severity, crash parameters, treatments since the crash, compensation status, list of medications, and demographic variables including gender, age, marital status, employment status, education level, and duration of neck pain as per a standard clinical examination.

A single item visual analog scale (VAS; 0–10 cm) was used to measure participants’ current pain intensity in the cervical spine (defined as the posterior region of the cervical spine from the superior nuchal line to the first thoracic spinous process) with (0) described as “No Pain” and (10) as “Worst Pain Imaginable.”

Self-reported pain and disability was measured in whiplash participants with the Neck Disability Index (NDI) [53]. The NDI consists of 10 items addressing functional activities such as personal care, lifting, reading, work, driving, sleeping, and recreational activities and also pain intensity, concentration, and headache, which are rated from no disability (0) to total disability (5). The overall score (out of 100) is calculated by totaling the responses of each individual item and multiplying by 2. A higher score indicates greater pain and disability. It is the questionnaire most utilized in WAD research [54].

Procedure

Participants were assessed on all outcome measures at the following time points: t(1) at a time period when their familiar baseline neck pain was present (when symptoms returned following successful cervical facet joint double blockade) [38]; t(2): immediately prior to receiving RFN; t(3): 1 month following RFN; and t(4): 3 months following RFN. Attendance at two time points prior to receiving RFN allowed us to determine if time alone (t(1) vs t(2)) resulted in improvements in measures prior to RFN being performed.

Participants first completed all questionnaires, after which a standard protocol was used for the order of tests [55]. The participants were seated, the Fastrak sensors applied, and ROM was measured. They were instructed to assume a comfortable position looking straight ahead, then to perform each movement three times, moving at a comfortable speed as far as possible and to return to the start position between each repetition. The order of movements assessed were flexion, extension, left rotation, and right rotation. The participants were then positioned supine, EMG electrodes were applied, and the CCFT was performed. For all of the following bilateral tests, the left side was measured first. PPTs were measured in the following order: tibialis anterior, median nerves, and C5/6. Thermal pain thresholds were then measured over the cervical spine, HPTs followed by CPTs. These were followed by the BPPT. The NFR was the final testing procedure. The same examiner tested all participants. No feedback or cues were given to the participants regarding their performance on any tests.

RFN Procedure

Details of the RFN procedure are provided in Appendix 1.

Data Analysis

Data were analyzed with Stata 9.0 statistical software. Based on our previous research [38], utilizing the SD of changes observed (in distal PPT pre-/post-interventional procedure), our statistical calculations indicated that this study required 26 participants (with 80% power at 5% level of significance) to adequately detect a minimally clinically important difference for the primary outcome measures (change in PPT in tibialis anterior, change in CPT, or change in NFR threshold). Extra participants were recruited in the whiplash group to power a further study.

Assumptions of normality, nonmulticollinearity, and homoscedasticity were tested through examination of histograms, box plot graphs, correlation matrices, and a plot of predicted to residual values, respectively. If the data were not normally distributed, transformation of the data was applied. PPT, BPPT, NFR threshold, and CCFT data required log transformation. Despite various transformations being attempted, normality for CPT and HPT was unable to be achieved (primarily due to floor and ceiling effects). A paired t-test was used to determine within participant side-to-side differences for all measures and followed by the exploratory analysis for all the measures. As no side-to-side differences were found (PPT, CPT, HPT, and BPPT), the data from each side were averaged and the mean data used for analysis.

All assumptions for repeated measures analysis of variance (ANOVA) were satisfied, except for HPT and CPT. One-way repeated measures ANOVA was performed to investigate the effect of time (four levels: 1 month following cervical facet blockade; 1 month prior to receiving RFN; 1 month following RFN, and 3 months following RFN) on the following log-transformed measures: PPT, BPPT, NFR, and CCFT, and normally distributed ROM. Nonparametric Friedman’s repeated measures test was used to analyze
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the effects of time on CPT and HPT. The baseline data for each dependent measure was entered into each ANOVA (but not Friedman's) analysis as a covariate. As this did not alter the significance of any of the results, further mention of baseline adjustment will not be made.

For ease of interpretation, results are presented using nontransformed data for medians and interquartile ranges, with probability estimates taken from analyses using transformed data. Where there was a significant difference over time, post-hoc tests of simple effects were performed to determine where these differences occurred. Significant level was set at 0.05 with Bonferroni adjustments used where appropriate. When the Friedman test was significant, multiple Wilcoxon signed-rank tests were performed with Bonferroni adjustment (P < 0.008) utilized to determine where those differences occurred. Differences between the whiplash and HC groups were investigated with two-tailed independent samples t-test or Mann–Whitney tests (for CPT and HPT, respectively).

The data were assessed for effect size using Cohen's \( d \) for normally distributed data and Cliff's Delta for nonparametric analyzed data [56]. The established convention rates were used. A Cohen's \( d \) effect size of 0 < 0.50 is small, a size of 0.50 to <0.80 is moderate, and >0.80 is large [57]. The corresponding effect sizes for Cliff's Delta are: <0.147 is small; between 0.148 and 0.33 is moderate, and >0.33 is large [58]. Effect size was calculated utilizing \( t(4) \), being the primary end point of this study; and \( t(2) \), the time period immediately prior to receiving RFN.

Results

Participants

Fifty-eight individuals had a successful response to the cervical facet joint blockade (intra-articular block followed by MBB) and agreed to participate in the study. Four individuals subsequently withdrew before undergoing RFN (three individuals declined to proceed with RFN, and one individual sustained other traumatic injuries from a skiing accident). Thus, 54 individuals underwent RFN.

At the 1 month review period following RFN \( t(3) \), one individual sustained neuritis (this was the only side effect noted for the duration of the study), and thus was unable to attend for further analysis. Thus, 53 individuals (36 female, 17 male; mean age = 44.7 ± 10.9 (SD) years) were included in the study. Three individuals were unable to attend the 3-month review (one pregnancy, two lost to follow-up), although all data until that point was included in the analysis.

The collision vectors reported were: rear-end impacts (51%), frontal impacts (23%), side impacts (21%), and combined (6%) vectors. Twenty-eight participants (53%) were involved in ongoing compensation claims, 30 (57%) reported the presence of other musculoskeletal symptoms (i.e., headaches [44%], low back pain [34%], thoracic spine pain [21%], shoulder/arm pain [21%], and jaw pain [8%]), 27 (51%) were university educated, 41 (77%) were fully employed throughout the course of the study, and 39 (74%) reported that they were married or in a long-term supportive relationship.

The median (range) duration of symptoms post-whiplash injury was 43 (9–195) months. Following the initial cervical facet double blockade procedure, there was a mean (±SD) wait of 10.4 (±4.5) months until RFN was performed. All participants received treatment following the MVC. Thirty-one participants (58%) were receiving conservative treatment at the time of participation in the study. Twenty-six participants (49%) had previously attended the local health authority multidisciplinary chronic pain centre.

The most common facet joint implicated was C2/3 (41%), followed by C6/7 (28%) and C5/6 (24%). C3/4 (11%) and C4/5 (4%) were less common. Bilateral facet joints were identified in 31% of individuals, while in 36%, both an upper cervical (C2–4) and lower cervical intervertebral segment (C4–7) were involved.

Following RFN, medication usage decreased as follows: anti-inflammatory medication (from 45% of individuals to 36%), simple over-the-counter analgesics (from 34% to 23%), various narcotic medications (from 26% to 19%), anticonvulsants (from 19% to 13%), selective serotonin reuptake inhibitors (from 13% to 8%), and tricyclic antidepressants (from 13% to 6%), with slight increase in usage of selective norepinephrine reuptake inhibitors (8–13%).

Table 1 presents the demographic, pain, and disability characteristics for the participants at the four measurement time points.

PPTs

There was a significant main effect of time for PPT at all sites (Table 2). PPTs at tibialis anterior and median nerve sites demonstrated early and sustained increases following RFN, with no difference in PPTs prior to or following RFN. Similar results (early and sustained increases following RFN with no differences prior to or following RFN) were demonstrated at the cervical spine site, with
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Table 1 Demographics of participants and changes in pain and disability over time in the WAD participants

<table>
<thead>
<tr>
<th>Gender (F/M)</th>
<th>Age (yrs ± SD)</th>
<th>Duration of Symptoms Months (median)</th>
<th>VAS (±SD) (0–100 mm)</th>
<th>NDI (±SD) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAD: 36/17</td>
<td>WAD: 44.7 (10.9)</td>
<td>43 (30–69)</td>
<td>t(1): 58 (19)^†</td>
<td>t(1): 42 (15)^†</td>
</tr>
<tr>
<td>HC: 21/9</td>
<td>HC: 44.2 (9.7)</td>
<td></td>
<td>t(2): 55 (19)</td>
<td>t(2): 43 (16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>t(3): 25 (20)^††</td>
<td>t(3): 29 (16)^††</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>t(4): 25 (21)^††</td>
<td>t(4): 27 (16)^††</td>
</tr>
</tbody>
</table>

* P < 0.0001 (between t(1) and t(x)); † P < 0.0001 (between t(2) and t(x)); ‡ P = 1.00 (between t(1 and 2), or t(3 and 4), or post-RFN).

HC = healthy control; NDI = Neck Disability Index; SD = standard deviation; t(1) = time-point 1 (admission to study following cervical facet joint injection double blockades); t(2) = time-point 2 (immediately prior to receiving radiofrequency neurotomy); t(3) = time-point 3 (1 month following radiofrequency neurotomy); t(4) = time-point 4 (3 months following radiofrequency neurotomy); VAS = visual analog scale; WAD = whiplash-associated disorder.

one slight difference, that being no significant difference measured between t(2) and t(3) (P = 0.27). The effect sizes were moderate for all sites measured (Table 2).

In comparison with the HC group, PPTs at all sites were lower in the whiplash group prior to undergoing RFN (81 df, P < 0.0001). Following RFN (t(4)), there were no differences between the WAD group and controls at the median nerve and tibialis anterior sites (78 df, P > 0.18), but PPT at the cervical spine remained lower in the WAD group (t(78) = 2.26, P = 0.013).

NFR

There was a significant main effect of time for NFR threshold (Table 2). Post-hoc tests showed that there was no significant difference in NFR thresholds before RFN. There was a significant increase in NFR thresholds between the time periods prior to RFN, and following RFN (except for t(2) to t(4); P = 0.056). There were no significant differences in NFR thresholds following RFN. The effect size was small: Cohen’s d = 0.40 (Table 2).

There was no significant difference between the HC group and the whiplash group at t(4): t(90) = 0.67, P = 0.51, but NFR threshold was lower in the WAD group prior to RFN (t(2): t(81) = 2.97, P = 0.004).

CPTs

There was a significant effect of time for CPT (Table 3). Post-hoc analyses revealed that significant reductions in cold hyperalgesia (lower CPTs) were measured post-RFN. There were no significant differences in CPTs measured before receiving RFN or following RFN. Effect sizes were large: Cliff’s Delta = 0.38.

Prior to undergoing RFN, the WAD group demonstrated a significantly elevated CPT (20.8°C) compared with the HCs (3.5°C, Table 2; Mann–Whitney U = −4.89, n_WAD = 53, n_HC = 30, P < 0.0001). At t(4), median CPTs in the whiplash group were significantly higher than those of controls (P = 0.003; Table 3).

HPTs

There was a significant time effect for HPT (Table 3). Post-hoc analysis revealed that significant increased HPTs followed RFN. There were no significant differences in HPTs measured in the time periods prior to or following RFN. The effect sizes were large: Cliff’s Delta = 0.41 (Table 3).

Prior to undergoing RFN, the WAD group showed lower HPT compared with controls (Mann–Whitney U = 4,43, n_WAD = 53, n_HC = 30, P < 0.0001; Table 2), but there was no difference between the groups following RFN (P = 0.17; Table 3).

BPPT

There was a significant main effect of time for elbow extension ROM with the BPPT (Table 2). Post-hoc analysis revealed that there were no significant differences measured prior to RFN. Elbow extension ROM increased following RFN, but there were no significant differences in the two time points following RFN. The effect size was large: Cohen’s d: 1.21 (Table 2).

The WAD group showed less elbow extension ROM compared with controls both prior to (t_81 = −8.2, P < 0.0001) and following RFN (t_77 = −2.61, P = 0.011; Table 2).

ROM

There were significant differences over time for cervical ROM (F_{3,153} = 104.4, P < 0.0001). Post-hoc analysis showed no change in cervical ROM between t(1) and t(2) (P = 1.00), but cervical ROM significantly improved following RFN (both early: t(3) [P < 0.0001]; and 3 months later: t(4); P < 0.0001). No significant differences in ROM were measured between t(3) and t(4) (P = 1.00). A large effect size was present: Cohen’s d: 1.78 (95% CI 1.52–2.04).
Table 2  Summary of sensory measures over time in WAD participants vs healthy controls

<table>
<thead>
<tr>
<th>Time (N)</th>
<th>t(1) (53)</th>
<th>t(2) (53)</th>
<th>t(3) (53)</th>
<th>t(4) (50)</th>
<th>Healthy Controls</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Effect Size</td>
<td>Cohen's d (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPT (kPa)</td>
<td>Cervical</td>
<td>186 (142–228)</td>
<td>199 (139–253)</td>
<td>236 (178–304)</td>
<td>293 (191–352)</td>
<td>344 (285–415)</td>
</tr>
<tr>
<td></td>
<td>Med N</td>
<td>242 (183–286)</td>
<td>253 (179–312)</td>
<td>307 (242–379)</td>
<td>338 (252–426)</td>
<td>371 (297–428)</td>
</tr>
<tr>
<td></td>
<td>Tib Ant</td>
<td>328 (282–398)</td>
<td>350 (285–436)</td>
<td>428 (363–549)</td>
<td>511 (360–657)</td>
<td>563 (462–728)</td>
</tr>
<tr>
<td>NFR (mA)</td>
<td>Median N</td>
<td>12 (6–18)</td>
<td>12 (6–20)</td>
<td>18 (10–30)</td>
<td>16 (8–38)</td>
<td>21 (10–38)</td>
</tr>
<tr>
<td></td>
<td>Tib Ant</td>
<td>29 (18–39)</td>
<td>31 (20–37)</td>
<td>12 (5–20)</td>
<td>10 (3–19)</td>
<td>3 (0–9)</td>
</tr>
</tbody>
</table>

Bolded P values denote statistical significance.

CI = confidence interval; BPPT = brachial plexus provocation test; °elb ext ROM = degrees of elbow extension range of motion; IQR = interquartile range; kPa = kilopascal; mA = milliamperes; Median N = median nerve; NFR = nociceptor flexor reflex; PPT = pressure pain threshold; Tib Ant = tibialis anterior; WAD = whiplash-associated disorder.
Both prior to and following RFN, the WAD group showed less cervical ROM compared with the HCs ($P < 0.0001$).

**CCFT**

There was a significant main effect of time for surface EMG at 24, 26, and 28 mm Hg levels of the CCFT (Table 4). No significant effect of time was found for the 22 and 30 mm Hg levels. Post-hoc tests of simple effects were not significant. Thus, a general trend for reduced EMG was evident at the 24, 26, and 28 mm Hg levels of the CCFT.

Prior to RFN, the WAD group demonstrated increased EMG levels compared with the controls at all levels of the CCFT ($P < 0.05$), except for 30 mm Hg ($P = 0.053$). Following RFN, there was no significant difference between the WAD and HC groups for any level of the CCFT ($P > 0.084$).

**Discussion**

The results of this study demonstrated that individuals with chronic WAD who underwent successful cervical RFN show significant and sustained reductions in sensory hypersensitivity (mechanical and thermal), spinal cord hyperexcitability, improved responses to the BPPT, and cervical ROM with trends toward improved cervical muscle control. Attenuation of widespread sensory hyperexcitability, spinal cord hyperexcitability and measures of motor function after RFN suggests that noiception from the cervical facet joint contributes to augmented central nociceptive processing and movement dysfunction in patients with chronic WAD.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Summary of thermal pain thresholds (median [IQR]) over time in WAD participants vs healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (N) t(1) (53) t(2) (53) t(3) (53) t(4) (50) Healthy Controls Effect Size Cliff’s Delta</td>
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<tr>
<td>CPT (°C) 19.6 (11.3–25.3) 20.8 (11.0–24.7) 12.6 (4.9–17.8) 9.7 (3.6–17.0) 3.5 (0–8.1) 0.38</td>
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<tr>
<td>$P$ values &lt;----------------- $P &lt; 0.0001$----------------&gt; &lt;----------------- $P &lt; 0.0001$----------------&gt;</td>
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<tr>
<td>HPT (°C) 42.6 (40.3–45.0) 43.5 (41.8–45.9) 46.7 (43.7–48.1) 46.6 (44.0–48.4) 47.5 (46.1–48.6) 0.41</td>
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<tr>
<td>$P$ values &lt;----------------- $P = 0.04$----------------- &lt;----------------- $P &lt; 0.0001$-----------------</td>
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</table>

**Table 4** CCFT RMS values (medians [IQR]) over time for WAD participants vs healthy controls

| Time (N), mm Hg t(1) t(2) t(3) t(4) ANOVA P value Healthy Controls |
|----------------|---------|---------|---------|---|---|---|
| 22 0.08 (0.03–0.26) 0.07 (0.04–0.15) 0.07 (0.03–0.16) 0.06 (0.02–0.15) 0.057 0.04 (0.02–0.08) |
| 24 0.13 (0.05–0.31) 0.16 (0.07–0.31) 0.10 (0.05–0.21) 0.12 (0.04–0.21) 0.044 0.06 (0.03–0.19) |
| 26 0.16 (0.07–0.42) 0.26 (0.14–0.66) 0.15 (0.06–0.39) 0.18 (0.05–0.28) 0.013 0.16 (0.06–0.23) |
| 28 0.30 (0.15–0.52) 0.34 (0.16–0.72) 0.29 (0.12–0.53) 0.27 (0.09–0.50) 0.015 0.21 (0.10–0.30) |
| 30 0.53 (0.17–0.82) 0.55 (0.21–0.86) 0.37 (0.16–0.69) 0.35 (0.10–0.71) 0.067 0.29 (0.10–0.46) |

**Bolded** $P$ values denote statistical significance.

ANOVA = analysis of variance; CCFT = craniocervical flexion test; IQR = interquartile range; mm Hg = millimeters mercury; RMS = root mean square; t(1) = time-point 1 = 1 month after receiving cervical facet joint blockade; t(2) = time-point 2 = immediately prior to receiving radiofrequency neurotomy; t(3) = time-point 3 = 1 month following radiofrequency neurotomy; t(4) = time-point 4 = 3 months following radiofrequency neurotomy; WAD = whiplash-associated disorders.
Post-mortem studies have previously demonstrated that cervical facet joints are injured in MVCs [59–62], with clinical studies confirming the facet joint as a candidate for ongoing nociception in patients with chronic WAD [28,30]. Biomechanical studies of cadavers and human volunteers have demonstrated how these injuries may occur [83–70]. Animal studies have shown that facet joint capsule stretch resulting from whiplash loading [71] has the potential to initiate physiological and behavioural responses including nociceptive afferent activation and after-discharge [31,71–75], release of inflammatory mediators resulting in peripheral sensitization [32], and alterations in neuronal excitability in the spinal cord [33,78,76–78]. The results of our study, where hyperalgesic responses were effectively modulated following the reduction of facet joint nociception, would support the results of these animal studies demonstrating a relationship between the facet joint and ongoing hyperalgesic responses in WAD.

Other studies in humans with chronic musculoskeletal pain have attempted to elucidate the relationship between peripheral mechanisms (persistent nociception) and augmented central processes. In studies of painful osteoarthritis, participants demonstrated central nervous system hyperexcitability prior to undergoing arthroplasty of the hip or knee that was reversed after arthroplasty surgery and subsequent pain relief [15,16], implicating the role of ongoing afferent nociception in augmentation of central pain processes. The influence of peripheral mechanisms driving central mechanisms was also demonstrated in a recent study involving individuals with chronic low back pain [79]. Following successful reduction in pain with surgery or facet joint injections, functional magnetic resonance imaging scans demonstrated a reversal of functional and structural brain abnormalities, which did not occur in those who did not respond to treatment [79]. Thus, it appears that successfully reducing nociception results in changes in central pain processing mechanisms.

Previous studies have investigated the effects of RFN on sensory measures in patients with WAD to some extent. Consistent with our findings, Chua et al. [37] and Chua et al. [36] demonstrated that PPTs measured over the cervical spine increased following RFN, and this may reflect local hypoalgesia related to the anesthetic procedure to the neck and decreased focal sensitization of peripheral structures. Our finding of decreased heat hyperalgesia may also support this proposal, as heat hyperalgesia is thought to reflect nociceptor sensitization and also be an indicator of peripheral sensitization [80,81]. Chua et al. [36] found no change in PPTs at remote sites. In contrast, we found that PPTs at sites remote to the neck also increased, indicating that RFN has the capacity to modulate central as well as peripheral nociceptive processing. This discrepancy in study findings could be explained by the low sample size (N = 9) of Chua’s study [36] in view of large variance in distal PPT measurements [38,82]. We previously demonstrated immediate (within hours) increases in PPTs at sites away from the site of injury (neck) in patients with chronic WAD [38]. The current study replicated these findings but demonstrated that these effects were sustained to at least 3 months post-procedure and exceeded published minimal detectable changes [83]. The current study findings also differed from those of our previous study. In the former study, PPT measures of the whiplash group remained lower than that of controls post-MBB, while in the current study, measures largely returned to those of the HC group. This may be due to the duration of pain relief in this study (3 months compared with 1–2 hours) or possibly due to participant variability in their health characteristics.

In addition to changes in PPT, we found sustained increases in NFR threshold following RFN, indicating reduced excitability of the spinal cord reflexes and reduced hyperalgesic response to the BPPT, together with decreased cold and heat hyperalgesia. Cold sensitivity has been postulated to occur as a result of sensitized afferent fibers or dorsal horn neurons, with possible underlying insular cortex dysfunction [84,85]. Dorsal horn sensitization has also been suggested as an underlying mechanism of heat hyperalgesia [16], while BPPT reactivity has been interpreted to reflect hyperalgesic motor and sensory responses as a consequence of central sensitization [86,87]. Thus, reduction of cold hyperalgesia, concomitant improvements in PPT at distal sites of uninjured tissues (tibialis anterior and median nerves), especially when combined with reduction of spinal cord hyperexcitability (increased NFR threshold) and improvement in BPPT hyperalgesia, would suggest that peripheral nociception contributes to these processes. Most of the sensory measures of the WAD group were no longer different from control data following RFN. The exceptions to this were CPT and BPPT responses, which remained more sensitive than the HCs at the follow-up time points, although the values for these two measures were within 95% CIs of published normative data [4,88].

Individuals with chronic WAD consistently demonstrate the presence of persistent motor dysfunction [8,17,50,89–91], most noticeable in those with increased levels of pain and disability [8,50]. In longitudinal studies, motor dysfunction has remained unchanged over time [50,92], with only modest improvements in ROM, pain and disability demonstrated following a course of multimodal physiotherapy [93]. The changes measured were not significantly different to a self-management group (advice booklet and exercise) [93]. In contrast, our study demonstrated a large and significant improvement in ROM following RFN with concurrent large reductions in pain and disability. There was also a trend toward improvement in performance of the CCFT, with changes not quite reaching statistical significance. However, following RFN, no significant difference in test performance was measured between the HC and WAD groups, indicating that the improvements measured were relevant. Hence, the reduction of nociception resulted in certain CCFT improvements occurring. Given that individuals continued to report ongoing mild levels of pain, further improvement could be postulated to occur if further pain reduction was possible. However, these results are also consistent with findings in previous research, where despite resolution of pain and disability in
Cervical Radiofrequency Neurotomy Reduces Central Hyperexcitability

some participants, deficits in performance of the CCFT remained [50]. Thus, the remaining motor impairment in this group with chronic neck pain probably reflects both local changes in muscle properties as well as changes in central neuromotor control [19,22–24].

Individuals in our study continued to present with mild-to-moderate levels of pain and disability, 1–3 months following RFN. These results are consistent with other studies, when comparing similar time periods post-RFN [37,94]. At first glance, these results may not seem as promising as Lord et al. [95], where complete relief of pain was reported in the days following the procedure. In our study, four patients reported complete relief of pain 1 month following RFN, and an additional 10 reported ≤1/10 pain. However, when comparing results at 3 months post-RFN, they are similar, with both studies finding that approximately 60% of participants reported relief of pain of at least 50% [95]. Pain reported at 1 and 3 months may be as a result of ongoing nociception from structures other than the facet joints influenced by RFN [96]. Additionally, ongoing disability found in our study could be related to factors such as persistent motor dysfunction (ongoing reduced ROM when compared with the HC participants and impaired motor control demonstrated via the CCFT) and persistent psychological distress [97].

There are some limitations in this study. We investigated 54 consecutive individuals undergoing RFN after successful response to facet joint double blockade. Selection of patients for and performance of RFN differed slightly from the stringent guidelines established by the International Spine Intervention Society [98,99]. Another limitation of the study was that it was not possible to blind the assessor to the status of the patient or the aims of the study. This may have introduced bias, thus indicating some caution with interpretation of study findings.

Conclusions

Cervical RFN resulted in increased NFR thresholds, increases in local (mechanical and thermal) and remote (mechanical) pain thresholds as well as improvement in cervical ROM. These results indicate that augmented central nociceptive processes, and movement loss are maintained by peripheral nociception arising from the cervical facet joints.

Acknowledgment

The authors would like to acknowledge Ms Meaghan Buisson for her assistance with participant recruitment.

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Applying the second IAB for individuals who reported greater than 50% relief of familiar neck pain following cervical facet joint blockade (intra-articular block [IAB] followed by confirmatory medial branch block [MBB]) were referred for RFN.

Clinically, this diagnostic pathway (IAB followed by MBB) is used prior to consideration for radiofrequency neurotomy. Although the scientific literature is varied, there is some evidence to suggest that a subset of individuals with suspected cervical facet joint pain might experience a therapeutic benefit from an intra-articular injection, with respect to a decrease in pain intensity over a period of 3 months or greater (Kim et al., 2005). As our publicly-funded center provides pain management services to a large catchment area, we possess a long (~6 month) waitlist for interventional techniques including diagnostic facet joint procedures. Historically, the clinic utilized a triple-injection procedure for the diagnosis of facet joint pain consisting of an intra-articular facet joint injection, followed by controlled, comparative MBB procedures when needed. Our unpublished data revealed that it was nearly universal, in that individuals that responded positively to both an intra-articular facet joint injection and the first MBB, responded positively to the second MBB. By eliminating the second MBB, we were able to reduce patient wait-time by approximately 15–20%, decrease the cost to the system, and manage select patients with IAB alone thereby decreasing the demand for RF neurotomies.

RFN Procedure:

Local anesthetic, fluoroscopic guidance, and sterile technique were utilized for placing 21 gauge RF cannulae to the expected location of the medial branches of the dorsal rami at the appropriate sites, depending on the levels to be treated. Cannulae were placed parallel to expected course of the nerves, along the lateral aspect of the articular pillars. A grounding pad was placed on the patient and connected to the RF lesion generator. Once the RF cannulae were in proper position based on the AP, oblique, and lateral fluoroscopic imaging, an RF probe was inserted into each cannula for determination of the tissue impedance and then motor stimulation. When it was determined that there was no motor nerve stimulation and the cannulae were considered in proper position, 2% lidocaine was injected through each cannula. After anesthetizing with lidocaine, RF thermocoagulation lesions were made at each site using an RF probe with a 5 mm active tip, heating to the tissue at the tip of the probe to 80 degrees centigrade for 75 seconds. For the C2–3 joint the third occipital nerve (TON) was included along with the medial branch at C3, making at least three lesions along the possible craniocaudal extent of the TON. For joints below C2–3, both medial branches that innervated the joint were targeted, with one to two lesions created at each site. A small amount (2 mg) of Celestone Soluspan was injected at each neurotomy site at the conclusion of the procedure to reduce the chance of a post-procedure neuritis. The patient was given post-procedure written instructions and phone numbers to reach the radiologist if necessary.

Appendix

Diagnostic Pathway:

Individuals who reported greater than 50% relief of familiar neck pain following cervical facet joint blockade

References


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