The relationship between sensory and sympathetic nervous system changes and posttraumatic stress reaction following whiplash injury—a prospective study

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Abstract

Objective: To investigate differences in sensory and sympathetic nervous system (SNS) function between whiplash-injured persons with and without a posttraumatic stress reaction (PTSR). To explore associations between sensory, SNS function, and persistent PTSR at 6 months postinjury. Methods: Seventy-six acutely (<1 month) whiplash-injured persons (10 with PTSR persisting to 6 months postinjury, 14 with early PTSR that resolved, and 52 with no PTSR) were prospectively investigated. Results: Those with persistent PTSR showed sensory hypersensitivity and impaired peripheral vasoconstriction compared to those whose PTSR resolved and those without PTSR ($P<.05$). The early presence of sensory hypersensitivity was associated with PTSR at 6 months, but this relationship was mediated by pain and disability levels. Impaired vasoconstriction and higher pain and disability levels were associated with PTSR at 6 months. Conclusion: Sensory disturbances following whiplash injury are associated with persistent PTSR but may be mediated by levels of pain and disability. © 2006 Elsevier Inc. All rights reserved.

Keywords: Whiplash injury; Acute posttraumatic stress reaction; Sensory hypersensitivity

Introduction

Whiplash injuries from motor-vehicle crashes are costly in terms of both economic and social costs associated with the significant numbers of individuals who fail to fully recover from the injury [1]. It is emerging that whiplash-associated disorders (WADs) are a complex condition involving, to varying extents, both physical and psychological impairments that are present from soon after injury [2] and persist into the chronic phase of the condition [3–5]. In the acute stage of injury, the presence of generalized psychological distress is common and appears to occur irrespective of reported levels of pain and disability [5]. However, those individuals with greater levels of pain and disability show a unique psychological reaction in the form of elevated levels of acute posttraumatic stress as measured with the Impact of Events Scale (IES) [2]. This posttraumatic stress reaction (PTSR) seen soon after the injury has been shown to be associated with poor functional recovery at both 6 and 12 months [6,7].

Some whiplash-injured individuals also show widespread (local and remote to the site of injury) sensory changes including both mechanical and thermal hyperalgesia and impaired peripheral sympathetic vasoconstrictor responses [3,8]. In a subgroup of whiplash patients (22.5% of this cohort), such sensory changes occurred soon after injury and persisted unchanged to the chronic stage of the condition [3]. Some of the sensory changes in addition to sympathetic nervous system (SNS) dysfunction and elevated levels of PTSR are significant predictors of higher levels of pain and disability at 6 months postinjury [7].

The co-occurrence of a PTSR, profound sensory disturbances, and higher self-reported levels of pain and
disability in both acute and chronic stages of whiplash injury is interesting. People with chronic posttraumatic stress disorder have been shown to have elevated physiological reactivity [9] that may indicate neuronal sensitization and heightened reactivity to stimuli [10]. Features of hyperarousal such as sleep disturbance and concentration difficulties are also features of posttraumatic stress [11] as well as WAD [1]. We have demonstrated a relationship between sensory hypersensitivity, SNS disturbance, and prolonged pain and disability following whiplash injury [3], but the relationship between these factors and persistent PTSR is not known.

The aims of this study were twofold: Firstly, to investigate the differences in sensory and SNS function between those with a PTSR within a month of whiplash injury that persisted to 6 months postinjury, those with an initial PTSR that had resolved by 6 months, and those who never experienced a PTSR. The second aim of the study was to test the hypothesis that sensory hypersensitivity and SNS disturbances in the acute stage of whiplash injury would be associated with persistent posttraumatic stress at 6 months postinjury, but that this relationship may be mediated by higher initial self-reported levels of pain and disability.

Methods

This study was part of a prospective longitudinal investigation of whiplash injury. Previous papers have reported on other findings from this cohort with pain and disability levels as outcomes [3–5,7].

Participants

Eighty volunteers (24 males, 56 females, mean age 33.5 ± 14.7 years) reporting neck pain as a result of a motor vehicle crash participated in the study. The whiplash subjects were recruited within 1 month of injury via hospital accident and emergency departments, primary care practices (medical and physiotherapy), and from advertisement within radio and print media. They were eligible if they met the Quebec Task Force Classification of WAD I, II, or III [12]. Subjects were excluded if they were WAD IV, experienced concussion, loss of consciousness, or head injury as a result of the accident, and if they reported a previous history of whiplash, neck pain, headaches, or psychiatric condition that required treatment.

Ethical clearance for this study was granted from the Medical Research Ethics Committee of The University of Queensland.

Measures of sensory function

Pressure pain thresholds

Pressure pain thresholds (PPTs) were measured using a pressure algometer (Somedic, Farsta, Sweden) at two bilateral cervical spine sites (over the articular pillars of C2/3 and C5/6), at three bilateral upper limb sites (over the three peripheral nerve trunks), and at a bilateral remote site (tibialis anterior). The upper limb nerve trunk sites were as follows: median nerve at the anteromedial aspect of the elbow, radial nerve over the radial groove of the upper arm, and ulnar nerve over the ulnar groove at the medial aspect of the elbow. The probe size used was 1 cm², and the rate of application was set at 40 kPa/s. These sites have been previously used in investigation of WAD [3]. Participants were requested to push a button when the sensation changed from one of pressure alone to one of pressure and pain [13]. Triplicate recordings were taken at each site, and the mean value for each site was used in the analysis.

Thermal pain thresholds

Thermal pain thresholds were measured bilaterally over the cervical spine using the Thermotest system (Somedic). The thermode was placed over the skin of the mid cervical region and preset to 30°C with the rate of temperature change being 1°C/s. To identify cold pain thresholds (CPTs) and heat pain thresholds (HPTs), subjects were asked to push a patient-controlled switch when the cold or warm sensation first became painful. Triplicate recordings were taken at each site, and the mean value for each site was used in the analysis.

Sympathetic vasoconstrictor reflex

The sympathetic vasoconstrictor reflex (SVR) was used as an indication of SNS activity [14,15]. Using laser Doppler flowmetry (FloLAB Monitor, Moor Instruments, Devon, England), we measured the skin blood flow in the fingertips of both hands. Data were sampled at 20 Hz. A provocation maneuver (inspiratory gasp), which is known to cause a short sympathetic reaction and cutaneous vasoconstriction, was performed [15]. A program using Labview software was written which calculated two quotients that represented the change in blood flow following the inspiratory gasp. These were taken after Schurmann et al. [15] and included the sympathetic reflex (SRF) parameter, which represents the relative drop in the curve after provocation, and the quotient of integrals (QI), which also takes into account the duration of perfusion decrease. A high QI and low SRF are indicative of an impaired vasoconstrictor response.

Questionnaires

Participants’ acute PTSR was measured using the IES [16]. The IES scale consists of 15 items, seven of which measure intrusive symptoms (intrusive thoughts, nightmares, intrusive feelings, and imagery), eight measure avoidance symptoms (numbing of responsiveness, avoidance of feelings, situations, ideas), and, combined, provide a total subjective stress score. The IES has been validated in studies of the acute emotional response to trauma [17] and has shown good reliability and sensitivity [16].
Self-reported pain and disability were measured using the Neck Disability Index (NDI). The NDI consists of 10 items addressing functional activities such as personal care, lifting, reading, work, driving, sleeping, and recreational activities as well as pain intensity, concentration, and headache [18]. There are six potential responses for each item ranging 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 two. A higher score indicates greater pain and disability. The NDI has been shown to be reliable and valid [19].

Procedure

The whiplash subjects first completed the NDI and IES questionnaires. After completion of the questionnaires, the subjects lay supine, and the laser Doppler blood flow sensors were attached to the tips of the middle fingers using double-sided adhesive discs. Subjects rested their hands on their abdomen, and an electric heating pad was placed over the hands to obtain a uniform increase in blood flow of the fingertips. Subjects rested in this position for 10 to 15 min. After this time and as soon as a stable blood flow baseline was obtained for at least 30 s, the provocation maneuver of inspiratory gasp was performed. Subjects were requested to inspire as deeply as possible and then to expire with a deep sigh. The moment of full inspiration was marked with an electronic footswitch. Recording of blood flow continued for another 30 s. The SVR testing was performed in a temperature-controlled laboratory. The temperature was set at 20°C, lights were dimmed, and ambient noise was kept low.

Pressure pain thresholds were then measured in the following order: tibialis anterior, median, radial and ulnar nerves, C5/6 and C2/3. At all sites, the left side was measured first followed by the right side. Thermal pain thresholds were then measured over the cervical spine; CPTs followed by HPTs. In both instances, the left side was measured first.

The same examiner (MS) performed all tests. This examiner remained blind to the subjects’ responses on all questionnaires. For all tests, no verbal cues/feedback were given to the subjects about their performance.

Statistical analysis

The whiplash participants were classified into one of three groups based on their IES scores at the initial and final assessment points. The groups were:

- Participants with an initial moderate PTSR (IES score 26 and above) [32] that did not resolve (remained above 26) (PTSR group)
- Participants with an initial moderate PTSR (IES score 26 and above) that did resolve (decreased to below 26) (resolved PTSR group)
- Participants without a significant PTSR (IES score below 26) at any time during the study (non-PTSR group).

A repeated measures mixed model analysis of covariance with a between-subjects factor of group (three levels: PTSR, resolved PTSR, and non-PTSR) and a within-subjects factor of time (four levels: <1 month, 2, 3, and 6 months postinjury). Age and gender were used as covariates in the analysis. Planned comparisons were used to evaluate differences between the group with persistent PTSR compared to the other two groups.

Mediational hypotheses were tested for associations involving persistent PTSR (6 months postinjury) and those variables that were shown to be significantly different between the three whiplash groups based on the MANCOVA analysis [20].

For all analyses, significance was set at $P < .05$.

Results

Participant classification based on IES scores

Of the 80 subjects who entered the study, four withdrew during the study period, all after the initial assessment point. At entry into the study, 24 (31.5%) of the 76 whiplash-injured participants demonstrated an IES score of 26 or above, thereby manifesting a moderate PTSR. The acute PTSR resolved in 14 (18.4% of the total cohort), leaving 10 (13% of the cohort) with an acute PTSR that persisted

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>QTF classification</th>
<th>Age (year) (mean±S.D.)</th>
<th>Gender (% female)</th>
<th>NDI (mean±S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent PTSR</td>
<td>10</td>
<td>WAD II: 8, WAD III: 2</td>
<td>40.1 (12.2)</td>
<td>70</td>
<td>47.9 (20.1)</td>
</tr>
<tr>
<td>Resolved PTSR</td>
<td>14</td>
<td>WAD II: 13, WAD III: 1</td>
<td>31.2 (11.6)</td>
<td>79</td>
<td>28.2 (16.9)</td>
</tr>
<tr>
<td>Non-PTSR</td>
<td>52</td>
<td>WAD II: 2, WAD II: 50</td>
<td>35.2 (12.8)</td>
<td>66.5</td>
<td>17.4 (7.2)</td>
</tr>
</tbody>
</table>

Persistent PTSR, whiplash-injured participants with IES scores of 26 and greater that persisted throughout the 6-month study period; resolved PTSR whiplash-injured participants with IES scores of 26 or greater at initial assessment but resolved over the study period; non-PTSR, whiplash-injured participants whose IES scores were always below 26.
throughout the study period. Fifty-two (68.4%) participants never experienced posttraumatic stress. The reported pain and disability levels (NDI) were greater in the group with a persistent moderate PTSR ($P<.001$) than both the resolved PTSR and non-PTSR groups with no difference between the latter two groups ($P=.098$). The NDI scores, age, and gender distribution of the three groups are shown in Table 1.

This study did not aim to investigate the effect of treatment. Subjects were free to pursue any form of treatment. Fifty-five percent ($n=42$) of participants sought treatment, the majority being physiotherapy treatment (85.7% of all treatments received). Forty-two percent ($n=32$) of all participants received medication that was mostly in the form of simple analgesics and nonsteroidal anti-inflammatories (88% of all medication) with codeine (15.6% of all medication) and antidepressants (9% of all medication) also being prescribed. No participant saw a psychologist during the study period.

**Pressure and thermal pain thresholds**

There was no difference between right and left sides for any sensory or SNS measure at any site ($P>.05$); therefore, for all analyses the mean values for both sides were used in further analysis.

![Heat pain threshold](#)

![Cold pain threshold](#)

Fig. 1. Cold and heat pain thresholds (mean±SD) for each whiplash group (PTSR, resolved PTSR, non-PTSR) at each time point.

There was a significant main effect for group for PPT at the median nerve site, HPT, and CPT ($P<.001$). There was no effect of time or interaction between group and time for any of the PPT or TPT measures ($P>.14$), indicating that these measures remained stable in all groups over the study period. The group with persistent PTSR showed lower PPTs at the median nerve ($t=-5.4$, $P=.001$) and lower heat ($t=-5.7$, $P=.001$) and CPTs ($t=-3.2$, $P=.01$) when compared to the resolved PTSR and the non-PTSR groups (median nerve $t=-5.2$, $P=.001$; HPT $t=-5.6$, $P=.001$; CPT $t=-3.3$, $P=.01$). Cold and heat pain thresholds and PPTs at the median nerve for each group at each assessment point are illustrated in Figs. 1 and 2.

As we have previously reported, there was no effect of age ($P>.3$) but a significant effect of gender ($P<.01$) on all PPT and TPT measures [3].

**Sympathetic vasoconstrictor response**

There was a significant group effect for both quotients of the SVR (both $P<.01$) with no time effect ($P>.65$) for either quotient of the SVR, indicating that these measures remained stable over the study period.

The group with persistent PTSR demonstrated a higher QI ($t=-3.8$, $P=.01$) and a lower SRF ($t=-3.5$, $P=.01$), indicating impaired peripheral vasoconstriction, compared to the group with resolved PTSR which demonstrated a higher QI ($t=-3.2$, $P=.02$) and lower SRF ($t=-3.5$, $P=.01$) when compared to the non-PTSR group (Fig. 3).

**Mediational analyses**

Mediational analyses were performed on the variables that demonstrated significant group differences in the above analyses. These were PPTs over the median nerve, HPTs and CPTs, as well as the QI and SRF quotients of the sympathetic vasoconstrictor response.
Two models were tested. The first model hypothesized that initial sensory hypersensitivity (mechanical hyperalgesia over the median nerve, heat and cold hyperalgesia) would be associated with moderate PTSR at 6 months postinjury but would be mediated by initial pain and disability levels (NDI scores). The second model was similar except that initial sympathetic disturbances (QI and SRF quotients of the sympathetic vasoconstrictor response) replaced the sensory measures as the independent variable.

In the first model, consistent with the requirements demonstrating mediation [20], the sensory measures (PPT median nerve, HPTs and CPTs) were associated with both PTSR ($b=0.28$, $P=0.02$) and initial NDI scores ($b=0.42$, $P<0.001$). To examine whether the effects of the sensory measures on PTSR were mediated by initial NDI, initial NDI was entered into the regression analysis together with the sensory measures. The effect of the sensory measures on PTSR was no longer significant ($b=0.07$, $P=0.54$).

The second model failed to reach the requirements for testing mediational associations. The SNS quotients (QI and SRF) were associated with PTSR ($b=0.24$, $P=0.04$), but there was no significant association between the SNS quotients and initial NDI scores ($b=0.2$, $P=0.1$).

**Discussion**

Thirty-two percent of acutely injured whiplash participants in this study demonstrated a PTSR within 4 weeks of their motor-vehicle crash. These findings support those of Drottning et al. [21] who found elevated scores on the IES in whiplash subjects with higher levels of pain both within hours of the accident and at 4 weeks postaccident. The acute PTSR decreased in just over half of those individuals with initial moderate levels of distress by 2 to 3 months postinjury, until at 6 months 13% of participants continued to manifest a moderate reaction. These data corroborate those of studies specifically investigating posttraumatic stress disorder, where the number of individuals with posttraumatic symptoms substantially decreases as time increases after the precipitating event [22].

Evidence of profound sensory disturbances in both acute and chronic WAD is accumulating and has been postulated to occur as a consequence of sensitization of central nervous system nociceptive pathways or changes in endogenous descending pain modulation mechanisms [3,23–25]. We have previously shown that widespread sensory hypersensitivity occurs soon after whiplash injury, is associated with poor recovery, and is independent of general psychological distress [3]. However, posttraumatic stress disorder has also been shown to be associated with increased sensitivity to stimuli [10]. In this study, the whiplash-injured group with persistent PTSR demonstrated mechanical hyperalgesia in the upper limb (median nerve trunk, heat and cold hyperalgesia) when compared to those whose PTSR resolved and those never affected by PTSR. The values for these measures in the group with persistent PTSR were outside the 95% confidence intervals for values of healthy asymptomatic individuals [26]. There was no difference between the groups for other sensory measures including PPTs at other upper limb sites and over the lower limb site (tibialis anterior). This finding is in contrast to our previous studies where marked group differences were seen in all sensory measures when the subgroupings were based on reported pain and disability levels with those reporting higher levels of pain and disability, demonstrating greater sensory hypersensitivity on all measures [3]. This indicates a stronger relationship between sensory disturbance and pain and disability than sensory disturbance and posttraumatic stress symptoms.

Although there was an association between mechanical and thermal hyperalgesia in the acute stage of injury (<1 month) and PTSR at 6 months, this relationship was mediated by the levels of pain and disability reported. As such, this suggests that it is the severity of pain and disability experienced by the whiplash injured that is a driver of PTSR present in the chronic stage of the condition. Although previous investigations suggest that injury severity itself may not be related to the development of posttraumatic stress disorder [11], few studies have incorporated measures of pain despite some evidence that current pain levels may predict the severity of an acute stress reaction [27]. Smith et al. [28] have shown that persons infected with human immunodeficiency virus who were also diagnosed with PTSD reported significantly higher pain intensity and greater pain-related functional impairment. It has been frequently
shown that initial levels of pain are predictive of functional outcome following whiplash injury [7,29], and this further relationship of initial pain to the development of PTSR indicates that valid assessment of pain and disability levels in the acute stage of injury will be important in the assessment and management of this condition.

The whiplash-injured group with a persistent PTSR also showed diminished peripheral vasoconstriction following a sympathetic provocation maneuver when compared to those whose PTSR resolved and those without PTSR at all assessment points (i.e., both the acute and chronic stages of the whiplash condition). Values for the quotients of the sympathetic vasoconstrictor response in this group were outside 95% confidence interval data of healthy asymptomatic subjects that we have previously identified and similar to those seen in patients with complex regional pain syndrome [15], although it should be acknowledged that our control data were from only 20 subjects [3]. It would appear that those with persistent PTSR have significantly impaired SNS function leading to diminished vasoconstrictor activity. The presence of excessive autonomic nervous system arousal in the form of higher levels of basal cardiovascular activity in individuals with PTSD is recognized [30]. Our findings of decreased peripheral sympathetic reactivity appear at odds to these findings where increased not decreased SNS activity has been mainly found. However, it should be noted that the SVR used in our study does not measure basal sympathetic activity but peripheral SNS reactivity to a provocative stimulus. In view of this discrepancy, it may be difficult to compare findings across studies. Furthermore, the involvement of peripheral sympathetic responses in posttraumatic psychological states has not been determined. It is of interest to note that a recent preliminary case report demonstrated the development of complex regional pain syndrome that arose in a patient following exacerbation of posttraumatic stress [31]. These authors suggest the involvement of supraspinal mechanisms to explain this phenomenon. It is feasible that the presence of a PTSR following whiplash injury may induce sympathetic disturbances.

However, the results of our mediational analysis attest that the relationship between SNS disturbance and PTSR may occur in the opposite direction. The presence of sympathetic disturbances in the acute stage of injury was associated with moderate PTSR at 6 months postinjury. Interestingly, there was no relationship between early diminished vasoconstrictor activity and initial reported pain and disability levels. Contrary to our findings on mediational analysis of mechanical and thermal pain threshold data, where initial NDI scores mediated the association between these measures, no such mediation occurred for the association between early SNS changes and persistent PTSR. Although speculative, this may be an indication of an atypical biological response in some with acute whiplash injury which could be a trigger for PTSR seen in the chronic stage of the condition. This warrants further investigation.

The findings of this study indicate that widespread sensory sensitivity associated with whiplash injury mostly occurs independently of PTSR and may reflect underlying physiological changes in central pain processing mechanisms. In contrast, diminished sympathetic vasoconstriction appears related to persistent PTSR. Further investigation of the relationship between SNS function and the development of PTSR following whiplash injury is warranted.

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References


