Brain or Strain? Symptoms Alone Do Not Distinguish Physiologic Concussion From Cervical/Vestibular Injury

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Objective: To compare symptoms in patients with physiologic postconcussion disorder (PCD) versus cervicogenic/vestibular PCD. We hypothesized that most symptoms would not be equivalent. In particular, we hypothesized that cognitive symptoms would be more often associated with physiologic PCD.

Design: Retrospective review of symptom reports from patients who completed a 22-item symptom questionnaire.

Setting: University-based concussion clinic.

Patients: Convenience sample of 128 patients who had symptoms after head injury for more than 3 weeks and who had provocative treadmill exercise testing.

Independent Variables: Subjects were classified as either physiologic PCD (abnormal treadmill performance and a normal cervical/vestibular physical examination) or cervicogenic/vestibular PCD (CGV, normal treadmill performance, and an abnormal cervical/vestibular physical examination).

Main Outcome Measures: Self-reported symptoms. Univariate and multivariate methods, including t tests, tests of equivalence, a logistic regression model, k-nearest neighbor analysis, multidimensional scaling, and principle components analysis were used to see whether symptoms could distinguish PCD from CGV.

Results: None of the statistical methods used to analyze self-reported symptoms was able to adequately distinguish patients with PCD from patients with CGV.

Conclusions: Symptoms after head injury, including cognitive symptoms, have traditionally been ascribed to brain injury, but they do not reliably discriminate between physiologic PCD and cervicogenic/vestibular PCD. Clinicians should consider specific testing of exercise tolerance and perform a physical examination of the cervical spine and the vestibular/ocular systems to determine the etiology of postconcussion symptoms.

Clinical Relevance: Symptoms after head injury, including cognitive symptoms, do not discriminate between concussion and cervical/vestibular injury.

Key Words: concussion, cervical, symptoms, vestibular, strain

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INTRODUCTION

Sport-related concussion (SRC) is defined by the 2012 Zurich Consensus Statement on Concussion in Sport as “a complex pathophysiological process affecting the brain, induced by biomechanical forces..., which may be caused either by a direct blow to the head, face, neck, or elsewhere on the body with an “impulsive” force transmitted to the head.” Rather than constituting a single entity, however, concussion is a heterogeneous disorder that can be modified by factors such as genetics, age, gender, premorbid illness, and symptom burden. Because there is no gold standard diagnostic test, concussion is a clinical diagnosis based on a combination of physical signs and subjective somatic, cognitive, and neurobehavioral symptoms that typically diminish over a matter of several days to weeks. Approximately 10% of concussed athletes, however, experience prolonged signs and symptoms of concussion for more than 2 weeks.

Symptoms after head injury may not be specific to the brain. Leslie and Craton recently hypothesized that concussion is really a syndrome that does not require brain involvement in all cases and that concussion symptoms can emanate from the cervical spine. Concomitant injury to the cervical spine resembling whiplash may occur as a result of the acceleration-deceleration forces sustained in concussive trauma. Structural and functional injury to the cervical spine can be associated with prolonged symptoms such as headache, dizziness, blurred vision, and vertigo. Cognitive complaints, including poor concentration and memory deficits, have also been reported after whiplash injury. Symptoms such as headache, dizziness, poor memory, and vertigo may therefore result either from a brain injury, from injury to the cervical spine, or from injury to both. As a brain injury, however, it would be reasonable to hypothesize that cognitive symptoms would reliably identify concussion from other potential symptom generators.
The pathophysiology of SRC is not fully understood. There are neurotransmitter and ion disturbances that persist for hours to days\textsuperscript{11} as well as altered autonomic nervous system function and control of cerebral blood flow that can persist for days to weeks.\textsuperscript{12,13} This metabolic and physiologic dysfunction produces symptoms that can be exacerbated by cognitive activity and by exercise.\textsuperscript{3,14} Exercise exacerbation of symptoms has been used systematically at our institution to define a homogeneous cohort of head-injured patients with “physiologic concussion” that, based on the response to exercise challenge and using physical examination findings, can be differentiated from patients with a cervical and/or vestibular source of symptoms after head injury.\textsuperscript{15} Thus, there are specific diagnostic groups within the larger array of concussed individuals, and it would be useful to clinicians if symptom patterns after head injury could be used to differentiate among these conditions since the treatment approach and prognosis differ.\textsuperscript{15}

The purpose of this study was to compare the symptom reports of a cohort of patients diagnosed with physiologic concussion with those diagnosed with a cervical/vestibular source of symptoms. We hypothesized that the presenting symptom reports of those with physiologic concussion would not be equivalent to the symptom reports of those with cervical/vestibular injury and that cognitive symptoms would be especially useful in discriminating between the 2 groups.

METHODS

Study Design

Retrospective review of symptom reports from patients who completed a 22-symptom Post-Concussion Symptom Scale (PCS) questionnaire, a validated instrument for assessing concussion symptoms with normative data in males, females, and athletes (see Appendix, Supplemental Digital Content 1, http://links.lww.com/JSM/A49, Symptom Evaluation Form).\textsuperscript{16} Each of the 22 symptoms are endorsed on a 0 to 6 scale with descriptors for “none” (0), “mild” (1-2), “moderate” (3-4), and “severe” (5-6). This questionnaire included 4 symptoms considered “cognitive” in a previous study (difficulty concentrating, difficulty remembering, feeling slowed down, and feeling mentally foggy).\textsuperscript{17} Subjects were diagnosed with postconcussion disorder (PCD) if their symptoms persisted for more than 3 weeks, which is consistent with expert opinion on when athletes are experiencing delayed recovery.\textsuperscript{18} The University at Buffalo Institutional Review Board approved the study without the requirement for obtaining consent because it was a retrospective review of clinical chart data.

Subjects

Subjects constituted a convenience sample of university-based concussion clinic patients who had symptoms after head injury that persisted for more than 3 weeks and who chose to undergo treadmill exercise testing to determine the etiology of their symptoms. This sample of 128 subjects represents 23\% (128/549) of all patients with concussion (acute and those with PCD) seen between July 2007 and April 2012. This sample of patients represents those who experienced prolonged symptoms (>3 weeks) that prevented return to play or work and who were judged safe for treadmill exercise. Patients with acute concussion having a typical recovery would not undergo treadmill testing unless they were not sure if they were really ready to return to sport. Other patients with PCS did not have treadmill testing because of comorbidities. See Table 1 for a description of the subjects. Subjects were classified as either physiologic PCD or cervicogenic/vestibular (CGV) PCD based on their response to a treadmill test, the Buffalo Concussion Treadmill Test (BCTT).\textsuperscript{14} Physiologic concussion was defined by a submaximal symptom-limited threshold on the BCTT, whereas CGV was defined by the ability to exercise to exhaustion without a submaximal symptom-limited threshold plus having abnormalities on the cervical physical examination (eg, tenderness, spasm, or reduced motion). Cervicogenic/vestibular subjects could also have had accompanying vestibular and/or ocular physical examination abnormalities such as abnormal tandem gait, abnormal ocular convergence, or abnormal signs/symptoms with smooth visual pursuits or saccades. Twelve subjects who were diagnosed with a combination of both physiologic and cervical/vestibular disorders, based on exercise intolerance on the BCTT plus cervical and vestibular physical examination abnormalities, were included in the PCD group because they had demonstrated a submaximal symptom-limited threshold on the treadmill test. We excluded patients who had recovered from concussion (n = 23) and those who had a primary diagnosis of migraine headache. The PCS symptom scale was administered on the same day but before the treadmill test.

Statistical Methods

Univariate and multivariate methods were used to ascertain the extent to which physiological (PCD) and CGV PCDs could be distinguished. Ten subjects had missing data for one or more of the 22 symptoms. Using the remaining 118 participants with complete data, a univariate analysis of each of the 22 symptoms involving formal tests of statistical difference and equivalence was conducted on a symptom by symptom basis. Tests of difference were conducted using Welch T test and independent sample t tests. Tests of equivalence were conducted using the two one-sided test approach with an epsilon value set equal to the estimated standard error.\textsuperscript{19} With 22 individual variables tested and using a P value of 0.05, we would expect that by chance alone, 1 to 2 variables would meet statistical significance for differences. Thus, a Bonferroni correction was used to adjust for multiple comparisons.

Joint analyses of all 22 questions were conducted using the 118 participants with complete data for all 22 symptoms. A logistic regression model was built using a stepwise Akaike Information Criterion modeling algorithm with both forward and backward admissible steps. Additionally, several “k-nearest neighbor” (knn) classifiers were implemented using the Euclidean distance metric. Patients were classified into groups based on each of these analyses, and the predictive ability of the models was examined.
Multidimensional scaling (MDS), using both Euclidean and Gower distance metrics, was used to visualize the 22-dimensional symptom space in only 2 dimensions, to test whether subjects could be classified into the 2 hypothesized diagnostic groups. A Principal Components Analysis was also conducted, and the data were projected into the 2-dimensional space defined by the first 2 principal components.

**RESULTS**

The t tests for differences between the PCD and CGV groups for each of the 22 individual symptoms reached significance (uncorrected for multiple comparisons) for “headache” and “sleep more than usual.” Fatigue approached significance. These differences were not, however, significant after correction for multiple comparisons using a Bonferroni-corrected familywise error rate of 0.05. Separate analysis of the group of 12 subjects with combined PCD/CGV using independent sample t tests did not reveal any significant differences from the larger PCD group.

The tests of equivalence conducted using the two one-sided test approach did not reach significance. The results of the t tests and the tests of equivalence are summarized in Table 2. Cognitive symptoms (difficulty concentrating, difficulty remembering, feeling slowed down, feeling mentally foggy) were considered indeterminate.

The stepwise logistic regression analysis misclassified 24 of 33 participants with a PCD diagnosis, or 73%. One of the 85 participants with a diagnosis of CGV was misclassified. The logistic model was unable to adequately distinguish patients with PCD from those with CGV. Similarly, the k-nearest neighbor analysis was also unable to adequately distinguish patients with PCD from patients with CGV. For example, with k = 4, 88% of the patients with PCD were misclassified as CGV, and 18% of the patients with CGV were misclassified as PCD.

**TABLE 1.** Demographic Information for the Physiologic PCD and Cervicogenic/Vestibular Diagnostic Groups*<sup>+</sup>

<table>
<thead>
<tr>
<th></th>
<th>Physiologic (n = 36)</th>
<th>Cervicogenic/Vestibular (n = 92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)—mean (SD)</td>
<td>28.0 (13.9)</td>
<td>26.4 (13.0)</td>
</tr>
<tr>
<td>Male gender—count (%)</td>
<td>20 (56)</td>
<td>49 (53)</td>
</tr>
<tr>
<td>Athlete—count (%)</td>
<td>19 (53)</td>
<td>39 (42)</td>
</tr>
<tr>
<td>Weight (kg)—mean (SD)</td>
<td>74.6 (12.5)</td>
<td>70.1 (16.4)</td>
</tr>
<tr>
<td>Months injury to BCTT—mean (SD)</td>
<td>8.4 (18.7)</td>
<td>10.2 (19.1)</td>
</tr>
</tbody>
</table>

*All group differences were nonsignificant.

**TABLE 2.** Symptom Mean, SDs, and Univariate Hypothesis and Equivalence Test Results

<table>
<thead>
<tr>
<th>Symptom</th>
<th>PCS (n = 36)</th>
<th>CVG (n = 92)</th>
<th>Welch T Test P</th>
<th>Two One-Sided Test P</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3.1 (1.4)</td>
<td>2.4 (1.7)</td>
<td>0.0119</td>
<td>0.9407</td>
<td>Significant difference</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.1 (1.4)</td>
<td>0.9 (1.3)</td>
<td>0.3982</td>
<td>0.441</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0.1 (0.7)</td>
<td>0.1 (0.2)</td>
<td>0.5314</td>
<td>0.3572</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Balance problems</td>
<td>1.7 (1.6)</td>
<td>1.6 (1.6)</td>
<td>0.597</td>
<td>0.3205</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.8 (1.6)</td>
<td>1.7 (1.6)</td>
<td>0.6924</td>
<td>0.2744</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2.9 (1.7)</td>
<td>2.3 (1.8)</td>
<td>0.0772</td>
<td>0.7849</td>
<td>Suggestive difference</td>
</tr>
<tr>
<td>Trouble falling asleep</td>
<td>2.7 (2.2)</td>
<td>2.0 (2.0)</td>
<td>0.1502</td>
<td>0.6757</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Sleeping more than usual</td>
<td>0.8 (1.4)</td>
<td>1.5 (1.8)</td>
<td>0.0422</td>
<td>0.8548</td>
<td>Significant difference</td>
</tr>
<tr>
<td>Sleeping less than usual</td>
<td>1.7 (2.2)</td>
<td>1.3 (1.9)</td>
<td>0.3536</td>
<td>0.4743</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>2.3 (1.6)</td>
<td>1.9 (1.7)</td>
<td>0.1971</td>
<td>0.6187</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Sensitivity to light</td>
<td>2.0 (1.7)</td>
<td>2.1 (1.7)</td>
<td>0.7326</td>
<td>0.2568</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Sensitivity to noise</td>
<td>2.1 (2.0)</td>
<td>2.9 (1.8)</td>
<td>0.6115</td>
<td>0.3132</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Irritability</td>
<td>2.1 (1.9)</td>
<td>1.2 (1.6)</td>
<td>0.6602</td>
<td>0.2893</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Sadness</td>
<td>1.7 (2.0)</td>
<td>1.2 (1.6)</td>
<td>0.147</td>
<td>0.6806</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Nervousness</td>
<td>1.7 (1.9)</td>
<td>1.3 (1.6)</td>
<td>0.2567</td>
<td>0.558</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Feeling more emotional</td>
<td>2.1 (2.0)</td>
<td>1.4 (1.8)</td>
<td>0.1003</td>
<td>0.7474</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Numbness and tingling</td>
<td>0.8 (1.4)</td>
<td>0.8 (1.4)</td>
<td>0.837</td>
<td>0.2152</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Feeling slowed down</td>
<td>2.8 (1.8)</td>
<td>2.2 (2.0)</td>
<td>0.1264</td>
<td>0.7069</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Feeling mentally foggy</td>
<td>2.8 (1.9)</td>
<td>2.4 (2.1)</td>
<td>0.3589</td>
<td>0.4697</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>3.0 (1.8)</td>
<td>2.8 (1.9)</td>
<td>0.6617</td>
<td>0.2885</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Difficulty remembering</td>
<td>2.5 (2.0)</td>
<td>2.3 (2.0)</td>
<td>0.6213</td>
<td>0.3081</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Visual problems</td>
<td>1.2 (1.6)</td>
<td>1.4 (1.7)</td>
<td>0.5242</td>
<td>0.3601</td>
<td>Indeterminate</td>
</tr>
</tbody>
</table>

CVG, cervicogenic/vestibular PCD.
The plots from the MDS analysis of the subjects (not shown) confirmed the previous analyses. Differences between response distributions of the PCD and CGV groups were small compared with the overall variability of the data. Multidimensional scaling projections into 2-dimensional space did not provide differential clustering of patients with PCD and those with CGV.

The results of the principle components analysis were similar to those from the MDS analysis. Figure illustrates that subjects do not cluster into 2 distinct groups. Plots of the rotation coefficients (not shown) for symptoms for the first 2 principal components indicated that symptom 3 (nausea) and symptom 8 (sleep more than usual) might contribute to a larger portion of the observed variability in the data for the first 2 principle components than other symptoms. Sleep-related symptoms 7, 8, and 9 seem to make the largest relative contributions to the second principal component.

**DISCUSSION**

The results of our study suggest that symptoms reported on the PCS do not accurately distinguish between patients with physiologic concussion versus those with cervicogenic/vestibular symptoms after head injury. Our univariate analysis yielded mostly indeterminate results, in that none of the tests for statistical difference nor the tests for statistical equivalence between the 2 diagnostic groups were significant at a family-wise controlled error rate of 0.05. Although it is possible that some differences with respect to certain symptoms could emerge as discriminatory in a larger sample, our multivariate analyses strongly suggest that the classifiers built upon such symptom responses are likely to have problems with accuracy. We took several optimistic looks at the data using multivariate methods and were unable to detect evidence that the variability associated with the differences in symptom responses between diagnostic groups was large when compared with the overall variability in the data. Our classifiers failed to provide evidence of sufficient accuracy, even when we overfit the models and ascertained their effectiveness to predict the same data upon which they were built (ie, providing an overly optimistic estimator of predictive accuracy). Thus, we rejected our hypothesis that the symptom reports of those with physiologic concussion would distinguish symptoms from those with cervical/vestibular injury. Although, intuitively, cognitive symptoms would seem likely to distinguish between injury to the brain and injury to the neck, our results were indeterminate. A previous study found that neuropsychological test results did not discriminate between whiplash patients and those with moderate to severe traumatic brain injury.20

The symptoms of concussion reported after head injury have traditionally been ascribed to brain injury, but there is actually little evidence to attribute the symptoms of concussion to a process exclusively involving the brain. Symptoms of concussion and whiplash-associated disorders such as headache, neck pain, disturbance of concentration or memory, dizziness, irritability, sleep disturbance, and fatigue have been described in both patients with concussion21 and whiplash.22 Thus, nonspecific symptoms such as headache, dizziness, or fatigue can be used to support the diagnosis of concussion but should not definitively establish a diagnosis of concussion based on their appearance alone. The Veterans Affairs and the American Department of Defense state that the symptoms associated with concussion/mild traumatic brain injury occur frequently in day-to-day life among healthy individuals and are highly subjective in nature.23

Neck injuries, including contusion or sprain, have an incidence of 2.6% to 7.5% in contact sports and can occur simultaneously with head injury in the athlete.24,25 Symptoms of neck injury have been shown to closely mimic those of head injury in athletes.26 Hynes et al,27 for example, found a strong association between whiplash-induced neck injuries and the symptoms of concussion in hockey players. Cervical injuries alone, or in combination with head injury, can cause persistent dizziness and balance difficulties, result in continuing headaches, and increase the risk of PCD.28–31 Isolated chronic neck injuries can result in headaches, dizziness, unsteadiness, visual disturbances, and poor postural control.9,32 It is possible that the symptom overlap between whiplash and concussive injuries is related to rotational forces imparted to the head and neck during head injury, with effects on nerve tracts in the brain as well as on the proprioceptive fibers in the cervical soft tissues.26,33 Other possible sources of cervical symptoms include the cervical zygapophyseal joints, which may cause headache and dizziness in patients with whiplash.34

A careful physical examination of the cervical spine and a neurologic examination focusing on the vestibular system and oculomotor responses can help identify sources other than brain concussion that produce similar symptoms.35 Abnormal findings on examination of the cervical region may indicate that a neck injury is the source or a contributor to symptoms yet there is no standardized evaluation of the neck for patients who have sustained a concussion. Impairments in...
position sense have been observed in patients with whiplash-type injuries and in individuals with chronic head and neck pain of nontraumatic origin (eg, cervical spondylosis). Armstrong et al provide an excellent review of the pathophysiology of cervical proprioception and its role in neck injury and continued disequilibrium. Accurate and early detection of concomitant neck injury and/or vestibular/ocular abnormalities in concussed patients could allow for the appropriate prescription of cervical spine and vestibular therapy, which has the potential to reduce symptoms and speed recovery. Furthermore, the management of neck injury includes encouraging patients to engage in their regular daily activities, even in the presence of symptoms. The recognition of whiplash injury and other treatable conditions as part of the concussion syndrome would move treatment guidelines away from strict rest-based protocols and the disability that they have the potential to perpetuate.

Limitations of this study include that it is retrospective and the sample size may be too small for the types of analysis included. Formal neuropsychological testing of cognition was not performed and may have improved the discriminant potential of cognitive variables. Instead, we were limited to 4 cognitive symptoms on the self-report scale. Furthermore, despite the fact that the Zurich Guidelines state that exercise intolerance indicates lack of recovery from concussion, exercise intolerance has not been proven definitively to differentiate concussion from other disorders. Prospective studies of patients with head injury should attempt to define unique patient cohorts based on physiological and physical examination findings to better classify patients for therapeutic and research purposes.

In conclusion, the results of this study show that symptom reports from patients with delayed recovery after head injury, including cognitive symptoms, do not discriminate between those with a physiologic PCD and those with a cervical/vestibular injury. The nonspecificity of symptoms after head injury means that clinicians should perform a careful physical examination of the cervical spine and of the vestibular/ocular systems and may also wish to use specific testing of exercise tolerance to better determine the etiology of postconcussion symptoms so that proper therapy can be directed to the causative condition(s).

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REFERENCES


