Depression, Pain Intensity, and Interference in Acute Spinal Cord Injury

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Background: The high prevalence of pain and depression in persons with spinal cord injury (SCI) is well known. However the link between pain intensity, interference, and depression, particularly in the acute period of injury, has not received sufficient attention in the literature. **Objective**: To investigate the relationship of depression, pain intensity, and pain interference in individuals undergoing acute inpatient rehabilitation for traumatic SCI. **Methods:** Participants completed a survey that included measures of depression (PHQ-9), pain intensity ("right now"), and pain interference (Brief Pain Inventory: general activity, mood, mobility, relations with others, sleep, and enjoyment of life). Demographic and injury characteristics and information about current use of antidepressants and pre-injury binge drinking also were collected. Hierarchical multiple regression was used to test depression models in 3 steps: (1) age, gender, days since injury, injury level, antidepressant use, and pre-injury binge drinking (controlling variables); (2) pain intensity; and (3) pain interference (each tested separately). **Results:** With one exception, pain interference was the only statistically significant independent variable in each of the final models. Although pain intensity accounted for only 0.2% to 1.2% of the depression variance, pain interference accounted for 13% to 26% of the variance in depression. **Conclusion:** Our results suggest that pain intensity alone is insufficient for understanding the relationship of pain and depression in acute SCI. Instead, the ways in which pain interferes with daily life appear to have a much greater bearing on depression than pain intensity alone in the acute setting. **Key words:** *depression, pain, spinal cord injuries*

The high incidence and prevalence of pain following spinal cord injury (SCI) is well established[1-6] and associated with numerous poor health outcomes and low quality of life (QOL).[1,7,8] Although much of the literature on pain in SCI focuses on pain intensity, there is emerging interest in the role of pain interference or the extent to which pain interferes with daily activities of life.[7,9] With prevalence as high as 77% in SCI, pain interference impacts life activities such as exercise, sleep, work, and household chores.[2,7,10-13] Pain interference also has been associated with disease management self-efficacy in SCI.[14] There is a significant relationship between pain intensity and interference in persons with SCI.[7] Like pain, the high prevalence of depression after SCI is well-established.[15-17] Depression and pain often co-occur,[18,19] and their overlap ranges from 30% to 60%.[19] Pain is also associated with greater duration of depressed mood.[20] Pain and depression share common biological pathways and neurotransmitter mechanisms,[19] and pain has been shown to attenuate the response to depression treatment.[21,22]

Despite the interest in pain and depression after SCI and implications for the treatment of depression, their co-occurrence has received far less attention in the literature.[23] Greater pain has been associated with higher levels of depression in persons with SCI,[16,24] although this is not a consistent finding.[25] Similarly, depression in persons with SCI who also have pain appears to be worse than for persons with non-SCI pain, suggesting that the link between pain and depression may be more intense in the context of SCI.[26] In one of the few studies of pain intensity and depression in an acute SCI rehabilitation setting, Cairns et al[27] found a co-occurrence of pain and depression in

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22% to 35% of patients. This work also suggested an evolution of the relationship between pain and depression over the course of the inpatient stay, such that they become associated by discharge. Craig et al[28] found that pain levels at discharge from acute rehabilitation predicted depression at 2-year follow-up. Pain interference also has been associated with emotional functioning and QOL in persons with SCI[1,7,29,30] and appears to mediate the relationship between ambulation and depression.[31]

Studies of pain and depression in person with SCI are often limited methodologically to examine the independent contributions of pain intensity and interference to depression in an acute setting. For example, they include only pain intensity[16,23,25,28,30]; classify subjects by either pain plus depression[23] or pain versus no pain[8,28,30]; use pain intensity and interference as predictor and outcome, respectively[1]; collapse pain interference domains into a single score[1]; or use only univariate tests (eg, correlations).[7,8,25,30] In addition, the vast majority focus on the chronic period of injury. To fill a gap in knowledge, we examined the independent contributions of pain intensity and pain interference to depression, while accounting for injury and demographic characteristics, antidepressant treatment, and pre-injury binge drinking in a sample of persons with acute SCI. We hypothesized that when accounting for *both* pain intensity and interference in the model, interference would have an independent and significant relationship with depression, above and beyond pain intensity.

Method

Participants

Participants were recruited between February 2008 and December 2010 from the inpatient rehabilitation units at the University of Washington Medical Center, Seattle; Harborview Medical Center, Seattle; The Institute for Rehabilitation and Research, Houston; and the University of Michigan, Ann Arbor. Patients were invited to participate if they met inclusion criteria for the SCI Model Systems, that is, had sustained a traumatic SCI, were 18 years or older, and were admitted for inpatient rehabilitation. Those who did not speak English or had severe motor speech, cognitive, or psychotic disorders precluding reliable assessment were not eligible to participate. Study procedures were approved by the institutional review boards at each center.

Data collection procedures

This current study is part of a larger study that examined the natural history of depression after new, traumatic SCI. After completing the informed consent process, participants completed a baseline interview prior to discharge from inpatient rehabilitation. Subsequent interviews took place if participants met criteria for major depression at baseline. Only data collected at the baseline interview were used in this current analysis.

Measures

Outcome variable

The Patient Health Questionnaire-9 (PHQ-9)[32] queries respondents about 9 symptoms of depression over the previous 2 weeks. Items duplicate the criteria for diagnosing depression as adopted by the DSM-IV.[33] The items are self-rated according to what, if any, depressive symptoms have been present over the past 2 weeks and how persistent the endorsed symptoms have been, ranging from *not at all* (0) to *nearly every day* (3). Symptoms include depressed mood, loss of appetite, sleep disturbance, psychomotor slowing, feelings of worthlessness, and suicidal ideation. The symptom severity score is the sum of item responses, ranging from 0 to 27. The PHQ-9 has excellent criterion-related validity for major depression in acute, traumatic SCI.[34] Internal consistency in this sample was excellent ($\alpha = 0.81$).

Predictors and covariates

Pain variables were drawn from the Brief Pain Inventory–Short Form (BPI-SF),[35] an 11-item instrument designed for assessment of the intensity of pain as a sensory experience and the degree to which pain interferes with function. The BPI is

recommended for measuring pain in persons with SCI.[36] *Pain interference* was assessed in 6 domains: general activity, mood, mobility, relations with others, sleep, and enjoyment of life. The domain of "normal work" was not included in this study as it was not applicable at baseline. *Pain intensity* is measured for "right now": average pain in last 24 hours, worst pain in last 24 hours, and least pain in last 24 hours. In this analysis, we used only pain intensity "right now" given the major criticism of recall bias in studies of pain.[37,38] Pain interference is rated on numeric rating scales ranging from 0 (*does not interfere*) to 10 (*completely interferes*); pain intensity is rated on a scale of 0 (*no pain*) to 10 (*pain as bad as it could be*).

Covariates were the current use of antidepressants (yes or no) and pre-injury binge drinking; the latter was assessed by the frequency with which the participant consumed 6 or more drinks per occasion in the 3 months prior to injury, ranging from 0 (*never*) to 4 (*daily or almost daily*). The time frame of prior to injury versus currently was selected because participants were inpatients at the time of the baseline interview. Demographic characteristics were gender and age at injury. Injury characteristics were days post injury and level of injury (tetraplegia vs paraplegia).

Statistical analysis

We used hierarchical multiple regression to examine the unique contribution to depression of each type of pain interference and pain intensity. For each regression analysis (6 in total; 1 for each pain interference type), data were first examined for adherence to assumptions of collinearity, outliers, normality, linearity, homoscedasticity, and independence of residuals. In the first step, we entered age, gender, days since injury, injury level, antidepressant use, and pre-injury binge drinking. In the second step, we entered pain intensity. In the third step, we entered pain interference. Semi-partial correlations of pain intensity and interference were also calculated to determine the proportion of variance that each contributed to the total depression variance. IBM SPSS 20.0 (IBM, Corp., Armonk, NY) was used to conduct all analyses.

Table 1. Demographic and injury characteristics (N = 203)

Characteristics	Mean (*SD*) [range] or *n* (%)
Mean age at injury, years	40.97 (16.14) [17 to 88]
Mean days post injury	53.42 (40.72), [3 to 279]
Male gender	160 (78.8)
Race	173 (85.2)
Caucasian	15 (7.4)
African American	8 (3.9)
Native American	4 (2.0)
Asian	3 (1.5)
Other	
Level of injury	130 (64.0)
Cervical	73 (36.0)
Thoracic and below	
Etiology of injury	
Falls	71 (35.0)
Vehicular crash	68 (33.5)
Recreation	31 (15.3)
Violence	18 (8.9)
Surgical complications	12 (5.9)
Pedestrian	3 (1.5)

Results

Demographic and injury characteristics of the sample

A total of 509 patients were eligible for the study across all sites; 359 patients were approached and 211 (59%) were enrolled. Of those, 203 completed the baseline interview and provided complete data for this analysis. Characteristics of the sample are given in **Table 1**. Consistent with gender distributions in the SCI population, the sample was predominantly male. Most were injured in either falls or vehicular accidents. The majority of the sample had cervical injuries and was Caucasian.

Descriptives

The average (*SD*) PHQ-9 score in the sample was 6.94 (5.5), which was in the mild range,[32] and ranged from 0 to 27. Fifty-seven (28%) participants had a PHQ-9 score ≥10 indicating moderate to severe depressive symptomatology. Average (*SD*) pain intensity was 3.20 (2.5) and ranged from 0 to 10. The mean (*SD*) pain interference score for

each type was 3.33 (3.22) for general activity, 3.22 (3.12) for mood, 3.68 (3.43) for mobility, 1.87 (2.80) for relations with others, 3.71 (3.20) for sleep, and 3.21 (3.30) for enjoyment of life. Slightly less than half of the sample was currently taking an antidepressant (47.3%) at the time of baseline assessment. The majority had no 3-month pre-injury binge drinking history (70.9%).

Model testing

Preliminary analyses were conducted to ensure no violation of normality, linearity, multicollinearity, and homoscedasticity. Because pain intensity and interference were presumed to have at least a moderate relationship, the bivariate correlation of pain intensity and each type of pain interference was examined to check for multicollinearity. Pearson r ranged from 0.382 to 0.536; because the value did not exceed 0.70, both factors were retained. The same 2 outliers were identified for each of the 6 regression models; we elected not to delete these cases as a few outliers can be expected with large samples. Step 1 (controlling variables) was nonsignificant; the addition of pain intensity in step 2 produced a significant change in R^2. For each pain interference model, step 3 also produced significant changes in R^2. In the final model (step 3), pain intensity became non-significant and explained only 0.2% to 1.2% of the depression variance (not shown in **Table 2**) for all 6 models. With one exception, pain interference was the only statistically significant independent variable in the models and, as hypothesized, accounted for the majority of the variance in depression. In the model that included pain interference with relations with others, injury level was also statistically significant ($P = .036$). In steps 1 and 2, only antidepressant use was statistically significant ($P = .024$ and $P = .038$, respectively), but it was no longer significant in step 3 ($P = .133$). Change statistics for each model, including the partial correlation coefficient for pain interference, are summarized in **Table 2**.

Discussion

Our results suggest that, for persons with acute SCI, pain intensity alone is not sufficient for understanding the relationship of pain and depression. In each analysis, the effect of pain interference completely displaced the effect of pain intensity on depression, highlighting its importance in the pain experience in acute SCI. The association of pain intensity and depression, before accounting for pain interference, in this study was consistent with the SCI literature[16,24,27] as was the relationship of pain interference and depression.[1,7,29,30] When taken together, the relationship of pain intensity and interference and depression in the acute setting provides an additional perspective that can provide insight into treatment approaches.

In this study, the presence of depression may amplify the impact of pain on life activities, thereby driving the strong relationship of pain interference and depression. For example, there is considerable evidence that there is an amplification of symptoms in persons with anxiety and depression who also have chronic medical conditions.[39] Our results suggest that for individuals in this sample, how pain interferes with life activities has considerably more influence on depression than simply the degree to which pain is present. To further highlight this, Stroud et al[40] found that a partner's negative responses to pain behaviors in the partner with SCI increased the link between pain interference and depression.

The few longitudinal studies of pain and depression in SCI make it difficult to establish a causal link between pain and depression, although there is some evidence to suggest that pain is a likely risk factor for the development of depression in SCI.[16,28] This is supported by broader literature across populations indicating that pain likely precedes depression.[41] Although we were unable to test causality in this study, our results suggest that pain interference and not just pain intensity should be accounted for in longitudinal studies of pain and depression.

Pain is now considered the "5th vital sign"; numeric pain intensity rating scales are used widely when assessing pain intensity and are also recommended for use in patients with SCI.[36] However, others have argued that relying solely on pain intensity rating change (ie, 50% change) is insufficient for evaluating the effectiveness of pain management strategies because pain is a multidimensional experience.[42,43] Our results

Table 2. Pain interference hierarchical regression models

Steps	R^2	Standard error of the estimate	R^2 change	Change statistics				Model *F*, significance	Semi-partial correlation for interference
				F change	df1	df2	Significance, *F* change		
Interference with general activity									
Step 1	0.05	5.46	0.05	1.66	6	193	.13		
Step 2	0.13	5.23	0.08	18.02	1	192	≤.001		
Step 3	0.26	4.85	0.13	32.16	1	191	≤.001	8.21, ≤.001	**0.35**
Interference with mood									
Step 1	0.05	5.46	0.05	1.66	6	193	.13		
Step 2	0.13	5.23	0.08	18.02	1	192	≤.001		
Step 3	0.35	4.54	0.22	63.94	1	191	≤.001	12.78, ≤.001	**0.47**
Interference with mobility									
Step 1	0.05	5.46	0.05	1.66	6	193	.13		
Step 2	0.13	5.23	0.08	18.02	1	192	≤.001		
Step 3	0.25	4.89	0.12	29.31	1	191	≤.001	7.80, ≤.001	**0.34**
Interference with relations with others									
Step 1	0.05	5.46	0.05	1.65	6	192	.13		
Step 2	0.13	5.23	0.08	17.93	1	191	≤.001		
Step 3	0.32	4.63	0.19	54.40	1	190	≤.001	11.40, ≤.001	**0.44**
Interference with sleep									
Step 1	0.05	5.46	0.05	1.66	6	193	.13		
Step 2	0.13	5.23	0.08	18.02	1	192	≤.001		
Step 3	0.28	4.79	0.15	38.28	1	191	≤.001	9.10, ≤.001	**0.38**
Interference with enjoyment of life									
Step 1	0.05	5.46	0.05	1.65	6	192	.13		
Step 2	0.13	5.23	0.08	17.93	1	191	≤.001		
Step 3	0.36	4.50	0.23	68.30	1	190	≤.001	13.40, ≤.001	0.48

Note: Semi-partial correlations squared are the amount of depression variance accounted for by pain interference (only given in step 3). Step 1 = age, gender, days post-injury, injury level, use of antidepressants, pre-injury alcohol use; Step 2 = pain intensity; Step 3 = pain interference.

support this argument. Despite the growing recognition of the multidimensional experience of pain, a 2008 consensus meeting on interpreting the clinical importance of treatment outcomes in clinical trials of chronic pain treatments included pain intensity and mood but not pain interference as important outcomes.[44]

As the understanding of the pain–depression relationship has grown in recent decades, there is greater appreciation for the need to treat pain and depression simultaneously.[19] For example, Cardenas et al[45] recently reported on the efficacy of pregabalin to significantly reduce neuropathic pain in chronic SCI as well as depression symptoms; pregabalin did not appear to have an effect on anxiety. The acute phase of SCI is also an important period in which pain management is crucial. Acute pain, if poorly controlled, has the potential to develop into chronic pain.[46] Kennedy et al[47] found that pain at 6 weeks post traumatic SCI was a strong predictor of pain 1 year post injury. High pain levels at the start of depression treatment also can result in poorer response to treatment[19] and lower rates of remission.[48] As such, effective pain management in acute SCI has implications for the development of chronic pain and depression. Our results also emphasize the importance of addressing pain and depression

in the acute setting not as separate entities, but as linked by the impact of pain on important life domains. These results suggest that treating pain intensity alone, typically the primary focus of medical intervention, may not be sufficient to reduce depression and/or reduce future risk. Instead, comprehensive treatment approaches that target pain intensity, pain interference, and depression, in combination and with multidisciplinary collaboration, may be the most effective in the short and long term. This is supported by recent findings from clinical trials that collaborative approaches to treat depression and pain are superior to usual care.[21,49,50]

Although this study fills some gaps in the understanding of pain and depression in SCI, results should be considered in light of several limitations. This was a cross-sectional study, which limits our ability to make causal inferences. We did not differentiate between those who did and did not agree to be interviewed, so there may be systematic differences between the 2 groups. The measurement of pain interference in the confines of acute rehabilitation limits the variability of experience of the ways in which pain interferes in major life domains. The impact of pain interference, when also accounting for pain intensity, may vary in important ways when the assessment occurs in the chronic phase of injury. The average pain intensity in this sample was relatively low; a sample of persons with high pain levels may produce different findings. Finally, our sample size precluded the examination of whether there is an indirect effect of pain intensity through pain interference; future studies with larger samples should use techniques such as path analysis to test the mediating effects of pain intensity on the relationship of pain interference and depression.

Conclusions

The findings of this study suggest that pain interference and not just pain intensity alone has a strong relationship with depression during the acute phase of SCI rehabilitation. As such, an exclusive reliance on pain intensity creates an incomplete picture. Our findings have important implications for treatment approaches that address both pain and depression in acute settings. Longitudinal studies are needed to further understand the link between pain intensity, interference, and depression in SCI over time and to examine the efficacy and effectiveness of collaborative approaches to treatment.

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