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Prevalence and Impact of Pain in Multiple Sclerosis: Physical and Psychologic Contributors

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Abstract

Objective—To characterize the prevalence and impact of pain in veterans with multiple sclerosis (MS) and to assess their association with demographic, biologic, and psychologic variables.

Design—Cross-sectional cohort study linking computerized medical record information to mailed survey data.

Setting—Veterans Health Administration (VHA).

Participants—Sixty-four percent (2994/4685) of veterans with MS who received services in VHA and also returned survey questionnaires.

Interventions—Not applicable.

Main Outcome Measures—Items assessing pain intensity, pain interference, and physical and mental health functioning.

Results—Ninety-two percent of participants reported bodily pain within the prior 4 weeks, with 69% of the total sample indicating pain of moderate or higher intensity. Eighty-five percent indicated that pain caused functional interference during the past 4 weeks, with 71% of the total sample reporting pain-related interference that was moderate or greater. No significant sex or race differences emerged for the pain indices. A significant but modest relationship between increasing age and pain interference emerged ($r=.05$, $P<.01$); however, age was not significantly related to pain intensity. Multivariate regression analyses identified pain intensity ($\beta=.73$), physical health functioning ($\beta=-.07$), and mental health functioning ($\beta=-.13$) variables as significant, unique contributors to the prediction of pain interference. The interaction of pain intensity and physical functioning was also significant but of minimal effect size ($\beta=-.03$).

Conclusions—Pain is highly prevalent and causes substantial interference in the lives of veterans with MS. The functional impact of pain in veterans with MS is influenced by pain intensity, physical health, and emotional functioning. Clinical practice should take each of these domains into consideration and reflect a biopsychosocial conceptualization.

Keywords

Mental health; Multiple sclerosis; Pain; Rehabilitation

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Pain is a serious problem for many persons with MS, affecting between 44% and 80% at any one time.¹ Pain in MS is often chronic, severe, and widespread.^{2,3} Although less extensively studied, it frequently causes interference in a variety of functional domains, including sleep, recreation, and occupational activities.^{2,4-6} Several biological and psychosocial factors have been identified that play a role in the experience and impact of pain in the broader pain literature.⁷ Less is known about the contributors to and impact of the pain experience, particularly pain-related interference, in persons with MS.

Two recent studies by Osborne et al^{8,9} have begun to address this gap in the literature. Taken together, they indicated biological variables such as poorer general health and greater disease severity and psychosocial variables such as greater depressive symptoms and poorer coping were significantly associated with greater levels of pain interference. Although biological variables are generally recognized as important in MS, these data are consistent with the non-MS pain literature in highlighting that psychologic distress (eg, depression, anxiety) is prevalent and an important consideration in this context. The contribution of these studies notwithstanding, the understanding of the prevalence and impact of pain in persons with MS remains insufficient. Limitations, such as small sample size, nonnational cohort, and participant homogeneity, place particular constraints on the conclusions that may be drawn from the extant literature.

In the context of these gaps in the literature, the purpose of this study was to address the following questions in a large sample of veterans with MS enrolled in the national VA health care system: (1) What is the prevalence of pain reported by veterans with MS? (2) What is the reported impact of pain in persons with MS in terms of pain-related interference? (In other words, to what extent does bodily pain serve as a functional impediment in the completion of life activities for veterans with MS?) and (3) In the context of a biopsychosocial model, how are demographic variables (particularly sex), physical functioning, and mental health functioning related to pain in veterans with MS?

Methods

Participants

Participants were identified by using the VA MS National Data Repository, a database containing information on all veterans receiving MS-related health care services within the Veterans Health Administration (N=32,009 for period 1998–2006). Veterans were included in a final target population if they met 1 or more of the following 4 criteria: (1) hospitalization for MS (coded with *International Statistical Classification of Diseases, 9th Revision* diagnostic code 340 for MS), (2) received disease-modifying agent (interferon beta-1a, interferon beta-1b, glatiramer acetate) used only to treat MS, (3) VA service connected for MS (diagnosis confirmed through medical review for purposes of VA service reimbursement), or (4) 1 outpatient encounter for which the primary diagnostic code was 340 during each year in which they received some VA medical service. The use of a search algorithm to identify a target population within the VA MS National Data Repository has been previously validated and shown to be effective in screening out individuals who do not have MS.¹⁰ A total of 17,470 veterans were included in the target population.

Information on individuals in the target population was linked to data from the VA Office of Quality and Performance LHS,¹¹ which was conducted in 1999 to establish the health status and behavior patterns of a nationally representative sample of VA health care system enrollees. The LHS was returned by 877,775 of 1.4 million enrollees who were mailed surveys (63.1% response). Among persons with MS, the LHS was returned by 2994 out of 4685 enrollees who were mailed surveys (63.9% response). All study procedures were approved by the local human subjects review committee.

Measures

Demographic information—Race (white vs nonwhite), education (high school or less vs more than high school), marital status (married vs other), and living alone (yes vs no) were obtained from the LHS. Sex and age at the time of the survey were obtained from the VA MS National Data Repository.

Physical health—Physical health was measured by using the 10-item PFS of the VR-36, which is adapted from the SF-36.^{12,13} Participants rated to what extent health limits physical activities such as “walking one block” and “bathing or dressing yourself” ranging from 1 (yes, limited a lot) to 3 (no, not limited at all). Responses were summed and transformed to a standardized score (range, 0–100); higher scores reflected better physical functioning. The SF-36 is widely used and validated for persons with MS.^{14–16} Internal consistency in the current sample was excellent ($\alpha=.95$).

Mental health—Mental health was measured by using the 5-item MHS of the VR-36.^{12,13} Participants responded to questions about mental health such as “have you felt downhearted and blue” and “have you been a nervous person” in the past 4 weeks with values ranging from 1 (all of the time) to 6 (none of the time). Responses were summed and in some instances reverse scored and then transformed to a standardized score (range, 0–100). Higher scores reflected better mental health. Internal consistency in the current sample was good ($\alpha=.86$).

Pain—Pain was measured by using the pain intensity and interference items from the Bodily Pain Scale of the VR-36.^{12,13} Participants were asked about pain intensity by rating how much bodily pain they experienced during the past 4 weeks ranging from 1 (none) to 6 (very severe). Additional characteristics (eg, location, quality) and etiology of participants' pain were not assessed by the VR-36. They also rated how much pain interfered with normal work, including both work outside the home and housework, on a scale ranging from 1 (not at all) to 6 (extremely).

Data Analysis

We examined the dataset to determine the extent to which the final sample was representative of the larger population of veterans with MS by using available age and sex variables in the repository. Selection bias (whether a person was or was not sent a survey) based on age and sex and response bias (whether a person did or did not return a survey) based on age and sex were examined.

Descriptive statistics characterized the prevalence and intensity of pain and pain-related interference. Physical and mental health functioning was similarly assessed. Sex, race, and age differences were investigated with the *t* test (sex, race) and correlation (age) analyses. Pearson correlation coefficients characterized the strength of association between pain and functioning (physical and mental health) indices. Finally, multiple regression analyses were conducted to explore the relative associations of physical and mental health indices to pain-related interference; these analyses are consistent with a biopsychosocial conceptualization of pain, which holds that the impact of pain is multidetermined and influenced by factors in addition to pain intensity.

Results

Comparability of the Study Sample

Selection bias—Persons who were and were not mailed the LHS were compared on sex and age. No sex differences emerged, but persons who were mailed surveys were

significantly older than those who were not (mean $\pm$ SD, 54.19 $\pm$ 12.60 vs 52.78 $\pm$ 13.05, respectively, $F_{1,16944}=40.06$, $P<.001$), although this difference was small.

Response bias—Persons who returned the LHS were compared with those who did not regarding sex and age. There were no sex differences, but persons who returned surveys were older than those who did not (mean $\pm$ SD, 55.30 $\pm$ 12.22 vs 52.18 $\pm$ 13.03, respectively, $F_{1,4633}=66.23$, $P<.001$).

Sample Characteristics

The final sample was primarily male (87%), with an average age of 55.30 $\pm$ 12.22 years. The majority was white (87%) and married (62%). Nineteen percent were living alone, and 61% had achieved some level of education after high school.

Prevalence of Pain

Table 1 contains results of descriptive analyses for pain-related variables. Among all respondents with MS, 92% reported bodily pain within 4 weeks preceding survey completion. Sixty-nine percent of respondents reported pain of moderate or higher intensity. The average pain intensity score for the entire sample was 3.84 $\pm$ 1.34 on the 1 to 6 scale. Eighty-five percent of veterans with MS indicated that pain interfered with normal work during the past 4 weeks, with 71% of the entire sample reporting that pain-related interference was moderate or greater. The average pain interference score was 3.22 $\pm$ 1.32 on the 1 to 6 scale.

No significant sex or race differences emerged for either of the pain indices ($P>.05$). Increasing age was significantly and positively associated with pain interference ($r=.05$, $P<.01$); however, the magnitude of this association was small and likely of limited clinical importance. Age was not significantly associated with pain intensity.

Physical Health

Physical health was assessed with the PFS of the VR-36. Results indicated an average score of 23.09 $\pm$ 28.30 on the PFS (see table 1). A significant sex difference emerged with females scoring higher on the PFS than males ($t_{447.86}=6.78$, $P<.001$, $d=.40$). Thus, females self-reported to be in better physical health than their male counterparts.

In terms of race differences, nonwhite veterans had higher PFS scores than white veterans ($t_{328.34}=-2.73$, $P<.01$, $d=.19$). Although small, this difference indicates that nonwhite veterans were in better physical health than white veterans as measured by this index score. A significant correlation emerged between age and PFS ($r=-.24$, $P<.001$). Increasing age was associated with worse self-reported physical health, although the magnitude of this relationship was modest.

Mental Health

Mental health was assessed with the MHS of the VR-36. Analysis of the MHS yielded an average score of 61.09 $\pm$ 22.77 (see table 1). Similar to the PFS, females had significantly higher scores than males on the MHS ($t_{2579}=2.32$, $P<.05$, $d=.13$), indicating better self-reported mental health among these female veterans with MS. The magnitude of this difference was small compared with that for physical health.

There was no significant difference between white and nonwhite participants on the MHS. Age was significantly but modestly related to the MHS ($r=.07$, $P<.01$), such that advancing age was associated with better self-reported mental health.

Correlates of Pain

Correlation analyses were conducted to determine the strength of relationships between pain, physical health, and mental health. Table 1 contains results of these analyses. Not surprisingly, pain intensity and interference scores were highly related ($r=.79$, $P<.001$). Pain intensity and interference were also significantly associated with the PFS ($r=-.23$ and $-.25$, respectively, $P<.001$). These relationships were small to moderate and in the expected direction, such that increased pain intensity and interference were related to worse physical health. In the domain of mental health, significant associations emerged between the MHS and both pain intensity ($r=-.38$, $P<.001$) and interference ($r=-.42$, $P<.001$). As expected, increased pain intensity and interference were associated with poorer mental health. There was a noted difference in the relationships between PFS and pain and those of MHS and pain. Compared with the PFS, the MHS was more strongly related (coefficients were approximately 60% greater) to both pain intensity and interference.

Prediction of Pain Interference

A hierarchical multiple regression analysis was conducted to determine the relative associations of physical and mental health indices to pain-related interference. Given the significant bivariate relationship between age and pain interference, age was entered first in the model. Pain intensity was entered in step 2, and the PFS and MHS scales were entered simultaneously in step 3. The interactions of PFS and pain intensity and MHS and pain intensity were entered simultaneously in step 4. With the exception of age, independent variables were centered because of the inclusion of interaction terms in the model. Table 2 contains results of this analysis. After controlling for age, pain intensity accounted for 63% ($P<.001$) of the variance in pain interference in the second step of the model. PFS and MHS were a statistically significant addition to the model in step 3 and accounted for an additional 2% ($P<.001$) of the variance in pain interference. The 2 interaction terms accounted for a statistically significant ($P<.05$) but very small amount of variance in step 4; however, only the interaction of PFS and pain intensity was a significant contributor in this step. The evaluation of the regression coefficients for the final model indicated age ($\beta=.03$), bodily pain ($\beta=.73$), PFS ($\beta=-.07$), MHS ($\beta=-.13$), and pain intensity $\times$ PFS ($\beta=-.03$) were significant components and, thus, made independent contributions to the prediction of pain interference. Examination of these coefficients indicated that older age, greater pain, and worse physical and mental health predicted higher levels of pain interference. The pain intensity $\times$ PFS interaction was of such small magnitude as to be practically inconsequential; nevertheless, it did indicate a stronger relationship between pain intensity and interference for those with worse physical health.

Discussion

The current study was conducted to characterize the prevalence and impact of pain in veterans with MS and contribute additional data to an emerging literature on the relevant biopsychosocial factors in this context. In this large VA sample, pain was a nearly universal phenomenon and of moderate to severe intensity. The impact of pain on the lives of these persons was considerable. Both physical and mental health functioning were identified as uniquely important elements in the experience and impact of pain.

That pain was a common experience among veterans with MS is not surprising, given the literature indicating prevalence rates between 45% and 80%.¹ However, the ubiquity and severity of the experience was somewhat surprising; 92% of this sample reported the presence of pain within the previous 4 weeks, and 69% (of the entire sample) indicated pain of moderate or greater intensity. These prevalence and intensity data are greater than those typically reported in the literature.¹ These results are even more striking when considered in

the context of the assessment method. Rather than conduct a pain survey per se, we used a general measure that assessed a number of health-related domains. This potentially reduced the impact of pain-related response bias that may artificially inflate prevalence rates derived from pain-specific instruments.

Although MS is an important diagnostic group for the VA system,^{17,18} very little research has been conducted on pain in this population. A review of the literature did not reveal any epidemiologic studies on the prevalence and severity of pain among veterans with MS. One study⁸ examined pain-related interference in functioning among veterans with MS; however, the prevalence of pain in that sample was not reported. The present study, then, addresses a conspicuous gap in the literature and highlights the importance of pain in this cohort.

This study also characterized the impact of pain among veterans with MS. Not only was pain reported to cause functional interference in the majority (85%), but also nearly three quarters reported pain-related interference of moderate or greater severity. The literature on pain-related interference in persons with MS remains remarkably sparse. The most relevant comparison study to our data found a moderate level of pain interference overall in a sample of veterans with MS, with approximately one quarter reporting pain interfered with their functioning “quite a bit” or “to an extreme degree” across the assessment domains.⁸ That study used a different assessment instrument than the one used in the current study, thus limiting any strong, direct comparisons between the 2. Nevertheless, taken together, these 2 studies indicate pain as a source of significant functional interference in the lives of veterans with MS.

In the broader pain literature, significant advances in the understanding and treatment of chronic pain occurred when pain stopped being viewed exclusively from a biomedical perspective and when biopsychosocial models of chronic pain were developed.¹⁹ Biopsychosocial models acknowledge that pain usually has an underlying biological basis but that psychosocial factors (eg, emotional functioning, social context) may also have a significant impact on the experience of pain and its effects on physical, psychologic, and social functioning. A biopsychosocial conceptualization of pain in MS has received recent empirical support.^{8,9} Consistent with this conceptualization, we examined the relationships between pain, pain interference, demographic variables, and indices of physical and mental health.

Pain intensity was the largest predictor of pain interference in the regression model, accounting for 63% of the variance, which is consistent with previous reports.^{8,9} These data highlight the close relationship between pain intensity and interference that one would expect. Although the statistical overlap is substantial, which may also be caused, in part, by the pain measurement issues noted later, it would be ill advised to assume these constructs are indistinct. As an analog, height and weight are often highly related statistically but maintain their clinically relevant conceptual distinctiveness. The uniqueness of pain intensity and interference is particularly important given the increased popularity of acceptance-based mental health interventions focused on pain interference rather than pain intensity. That physical and mental health indices accounted for additional, unique variance, above and beyond pain intensity, speaks to the importance of these factors in the functional impact of MS-related pain. Mental health functioning played a larger role in the prediction of pain interference, such that worse scores on this measure were related to increased pain interference. The extant literature on pain interference and mental health is relatively thin. In 2 recent smaller studies, Osborne et al^{8,9} found variables related to mental health status including catastrophizing, pain coping, and a composite measure of psychologic functioning to be important considerations in this context. The relationships between mental health and both pain intensity and pain interference are likely to be of particular importance to veteran

populations given their overwhelming male demographic. Hirsh et al²⁰ found a stronger pain-mood relationship in males with chronic pain compared with similar females. Additionally, negative mood has been found to mediate the pain-disability relationship in males with mixed chronic pain conditions.²¹ Taken together, these studies indicate that mental health functioning is a key component of the pain experience in persons with MS and should be a primary focus of clinical management.

Large differences in reported pain among demographic groups did not emerge from our data. No significant sex or race differences were found for any of the pain variables examined; age was significantly associated with pain interference but not pain intensity. Although considerable data in the broader, non-MS pain literature indicate females are more likely than males to report pain (see review by Unruh²²), the current findings are consistent with the available evidence regarding sex and pain in MS.^{4,5,23-26} We were unable to locate relevant literature to guide interpretation of the lack of race difference. In the larger pain literature, persons of racial/ethnic minority groups, in particular, blacks and Hispanics, show increased sensitivity to experimental and clinical pain.^{27,28} Conflicting data exist on the relationship between race and disability in MS, with a recent report that blacks experience greater MS-related disability than whites.²⁹ More work is needed on possible racial and ethnic differences in the experience of MS-related pain. In regards to age and pain, the current results reflect the inconsistency of the extant literature; a positive association between age and pain is sometimes found,⁵ whereas no relation has been reported by others.²³ At this point, there does not appear to be a preponderance of evidence in 1 direction or the other to warrant any strong conclusions about age and pain in MS. Additional work is needed to better characterize the relationship between age and both the presence and impact of pain in persons with MS.

The current study has multiple strengths and makes an important contribution to the literature. The focus on both pain intensity and pain interference reflects a promising shift in the literature away from solely characterizing the presence of pain and instead including the functional impact of that pain. Additionally, the current sample consisted of a large number of persons with MS who were unique for both their status as veterans and primarily male sex. Veterans and males have historically been underrepresented in the MS literature. We also used a well-validated and standardized measure of physical and mental health and followed a rigorous methodologic process.

Study Limitations

Several study limitations should also be considered. First, we did not use a multidimensional measure of pain such as the McGill Pain Questionnaire³⁰ or Multidimensional Pain Inventory.³¹ Although the instrument used herein is an established measure and showed good psychometric properties for this study, the reliability and validity of the present findings should be considered in light of this measurement issue. A second measurement-related limitation is that the assessment of physical and psychologic functioning was conducted only by means of self-report instruments. Third, although this study and analytic approach was informed by the biopsychosocial model, we adopted a broad-based assessment of mental health functioning and did not include a full complement of psychosocial variables, such as specific mood states (eg, depression, anxiety), coping, and social support. Fourth, data from this study were cross-sectional and did not allow us to examine changes in the experience of pain or pain interference over time. This issue is particularly important because MS is a progressive neurologic disease that presents different physical challenges throughout its course. Persons who are ambulatory, predominantly wheelchair users, or bed bound may experience pain that is both qualitatively and quantitatively different. Furthermore, the cross-sectional nature of these data precludes any examination of how the biopsychosocial components of the experience of pain provide more or less of a contribution

to the impact of pain over time. Methodologically, our singular assessment point also does not allow us to draw cause-effect conclusions. Fifth, current data were unable to determine the etiology of pain or differentiate pain associated with an acute exacerbation versus pain that was more chronic or stable. Sixth, because of the large sample size and consequent power of this study, both significance tests and effect size estimates should be used in determining whether results are clinically meaningful. Finally, these findings may not generalize to persons with MS who are not veterans and/or do not receive care through the VA system.

Conclusions

The current study found a very high rate of pain and pain-related interference among veterans with MS. The functional impact of pain in these participants is not exclusively related to pain intensity; mental and physical health status may also be an important consideration. Additional research is needed to elucidate the temporal aspects of these relationships and inform interdisciplinary clinical interventions that address these important issues.

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List of Abbreviations

LHS	Large Health Survey
MHS	Mental Health Scale

MS	multiple sclerosis
PFS	Physical Functioning Scale
SF-36	Medical Outcomes Study 36-Item Short-Form Health Survey
VA	Veterans Affairs
VR-36	Veteran RAND 36-Item Health Survey

Table 1
Descriptive and Correlational Data for Pain, Physical, and Emotional Health Indices

Measure	Mean $\pm$ SD					Correlation With*	
	Total	Female	Male	White	Nonwhite	Pain Intensity	Pain Interference
Pain intensity	3.84 $\pm$ 1.34	3.77 $\pm$ 1.34	3.84 $\pm$ 1.34	3.88 $\pm$ 1.32	3.78 $\pm$ 1.47	NA	NA
Pain interference	3.22 $\pm$ 1.32	3.10 $\pm$ 1.31	3.23 $\pm$ 1.32	3.25 $\pm$ 1.32	3.28 $\pm$ 1.36	.79	NA
PFS	23.09 $\pm$ 28.30	32.18 $\pm$ 30.06	20.65 $\pm$ 27.12	20.59 $\pm$ 26.81	26.05 $\pm$ 31.39	-.23	-.25
MHS	61.09 $\pm$ 22.77	63.80 $\pm$ 22.72	60.80 $\pm$ 22.53	60.50 $\pm$ 22.61	59.30 $\pm$ 22.62	-.38	-.42

NOTE. n=2708–2809 (because of missing data). All correlations significant at $P<.001$.

Abbreviations: NA, not applicable; Pain intensity, pain intensity item from VR-36; Pain interference, pain interference item from VR-36.

* Correlations are for the total sample.

Table 2
Results of Hierarchical Regression Analyses Predicting Pain Interference

Variable	ΔR^2	ΔF	$P(\Delta F)$	β
Step 1	.00	6.98	.01	
Age				.05*
Step 2	.63	4140.27	<.001	
Age				.03*
Pain intensity				.79 [†]
Step 3	.02	64.80	<.001	
Age				.03*
Pain intensity				.73 [†]
PFS				-.06 [†]
MHS				-.13 [†]
Step 4	.00	3.13	.04	
Age				.03*
Pain intensity				.73 [†]
PFS				-.07 [†]
MHS				-.13 [†]
Pain × PFS				-.03*
Pain × MHS				.00

NOTE. n=2450 (because of missing data).

Abbreviations: β , standardized beta coefficient for that step; pain intensity, pain intensity item from VR-36; pain interference, pain interference item from VR-36.

* $P < .05$.

[†] $P < .001$.