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The Co-Occurrence of Pain and Depression in Adults With Multiple Sclerosis

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Abstract

Purpose/Objective—To define the rates of pain, depression, and their co-occurrence in persons with multiple sclerosis (MS).

Research Method/Design—Participants were 161 persons with MS who previously participated in research and indicated a willingness to be contacted for future studies. Data were collected via postal survey and included the Patient Health Questionnaire—9 for depressive symptoms and a numerical rating scale (0–10) for pain. Descriptive statistics, chi-square analyses, and odds ratios were calculated to describe the prevalence, difference, and likelihood of depression, pain, and their comorbidity.

Results—Some level of pain was experienced by 73% of the sample, with 40% of the entire sample reporting moderate or worse pain severity. Clinically significant levels of depressive symptoms were reported by 22% of the sample, and 8% reported sufficient symptoms to meet major depressive episode diagnostic criteria. Of persons meeting depression criteria, 86–100% reported experiencing *any* pain; 67–77% of persons meeting depression criteria reported experiencing pain of at least moderate severity. Of persons experiencing *any* pain, 11–34% met depression criteria; 15–37% of persons experiencing pain of at least moderate severity met depression criteria.

Conclusions/Implications—Pain and depression co-occur frequently in persons with MS. However, it is more common for individuals with depression to report pain than for individuals with pain to endorse symptoms of depression. Future studies should explore the implications of this co-occurrence, such as whether these individuals experience greater levels of disability, higher medical costs, or fewer benefits from treatment than persons with either condition alone.

Keywords

pain; depression; multiple sclerosis

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Introduction

Pain and depression are both common in persons with multiple sclerosis (MS). Chronic pain is experienced by about 50% of those with MS at any point in time (O'Connor, Schwid, Herrmann, Markman, & Dworkin, 2008), and approximately 25% of those with pain describe it as severe (Ehde et al., 2003). The point prevalence of major depressive disorder is 15–25%, and as many as 50% of individuals with MS experience clinically significant levels of depressive symptoms at any one time (Chwastiak et al., 2002; Mohr, Hart, Julian, & Tasch, 2007; Patten & Metz, 1997; Sadovnick et al., 1996).

The literature on MS also often references high rates of comorbid pain and depression (Ehde, Kratz, Robinson, & Jensen, 2012), but to our knowledge, only one study has explicitly reported prevalence data of this comorbidity (Ehde et al., 2003). However, in that study, “depression” was measured in terms of severity of symptoms and not the presence of an actual diagnosis of a major depressive episode or disorder. Furthermore, the criterion for pain in this study was simply the presence of any pain, without any indication of severity. Outside of the aforementioned study, there has not yet been an explicit description of the prevalence of this comorbidity in the literature; rather, previous research presents findings that only hint at comorbidity. O'Connor et al. (2008) stated that pain is more common in persons with MS who also have depression, but they did not provide research that supports this conclusion. Rather, prior research on pain and depression in people with MS has focused more on the association of symptom severity. For example, a number of studies have reported that pain and depression severity are associated with one another (see Arnett, Barwick, & Beeney, 2008, for review). These findings are important to research and clinical care, but they provide little information regarding the prevalence of pain, depression, and, especially, their comorbidity.

Lastly, there is a question of how to define pain and depression for purposes of examining their comorbidity. For example, *pain* could be defined in terms of presence or absence, severity, or pain type (e.g., neuropathic vs. nociceptive). Similarly, *depression* can be considered in terms of severity of symptoms, meeting a clinical cutoff, or meeting diagnostic criteria for a depressive disorder. The definition one uses to identify someone as having pain or depression is important because the number of individuals included in a prevalence estimate will vary depending on how stringent or inclusive a chosen criterion is.

A clear understanding concerning the co-occurrence of pain and depression is important in the assessment and treatment of individuals with MS. Although research from non-MS populations with pain suggests that depression and pain often co-occur and mutually impact each other through their reciprocal impact on each other across the biopsychosocial spectrum (from shared neurotransmitter pathways to shared effects on cognitions and behaviors to shared impact on the individual's environment; see Bair, Robinson, Katon, & Kroenke, 2003, for comprehensive review), it is not clear whether the same phenomena are present for persons with MS. If pain and depression occur independently in persons with MS, suggesting little mutual impact or interaction, then clinicians would know that it is important to assess and treat each independently. On the other hand, if the frequency and severity of pain and depression are closely linked in persons with MS, then clinicians would

know that it would be important to thoroughly assess for one when the other is present. Moreover, such a finding would indicate that research examining the bidirectional impact of pain and depression in persons with MS is needed to understand how best to treat these conditions when present.

Given these considerations, we sought to provide more detailed prevalence data on pain, depression, and their comorbidity as reported by a community sample of persons with MS. We hypothesized that depression and pain would co-occur more often than they occur individually, and that the rates of comorbidity would vary as a function of the criterion being used to define the presence of each condition. A secondary purpose was to exemplify how prevalence estimates can vary based on the definitions of the conditions being examined, in this case, depression and pain. To address this issue, we used a numerical rating scale (NRS) to assess pain and the Patient Health Questionnaire—9 (PHQ-9) to assess depression. Each has established criteria that vary in selectivity, as the NRS can be used to indicate the presence or absence of either pain or pain of a specific level (Alschuler, Jensen, & Ehde, 2012b; Jensen & Karoly, 2011), and the PHQ-9 can be used to indicate a clinically meaningful level of depressive symptoms or sufficient symptoms to meet diagnostic criteria for a depressive episode (Kroenke, Spitzer, & Williams, 2001).

Method

Procedure

Participants were part of a larger survey study of pain, depression, and quality of life in individuals with MS (nonoverlapping data have previously been presented in Kratz, Molton, Jensen, Ehde, & Nielson, 2011, and Alschuler, Jensen, & Ehde, 2012a). Participants had either previously participated in research through the University of Washington's Multiple Sclerosis Rehabilitation Research and Training Center and expressed interest in being contacted for future studies or self-referred to study staff to participate. Inclusion criteria were 18 years of age or older and a diagnosis of MS by a medical professional. A total of 381 surveys were mailed and 161 were returned.

Participants completing the survey were paid \$25 for their time. All study procedures were approved by the University of Washington Human Subjects Review Committee, and informed consent was obtained from each participant.

Measures

Pain: 0–10 NRS (Jensen, Turner, Romano, & Fisher, 1999)—The NRS has been shown to be a valid and reliable measure of pain intensity (Jensen et al., 1999). In the present study, the NRS was interpreted two ways. First, any score >0 was considered an indication of the presence of pain. Second, consistent with research on persons with MS, scores of 3 are indicative of at least moderate pain severity (Alschuler et al., 2012b).

Depression: PHQ-9 (Kroenke et al., 2001)—The PHQ-9 can be scored as a continuous score from 0 to 27. In the present study, the PHQ-9 was interpreted through two methods. First, using the PHQ-9 score as a continuous variable for depressive symptom severity, we interpreted a cutoff of at least 10 as the cutoff for clinical levels of depressive

symptoms (Kroenke et al., 2001). Second, the PHQ-9 maps directly onto the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) diagnostic criteria for major depressive episode (MDE). Participants who indicated that five or more symptoms were present more than half the days were considered to have a probable MDE diagnosis. The PHQ-9 is a commonly used measure in the study of persons with MS, having been used recently to assess prevalence of depression (Sjonnese et al., 2012) and the association of depression with factors such as physical activity (Jensen, Molton, Gertz, Bombardier, & Rosenberg, 2012), fatigue (Amtmann, Bamer, Noonan, et al., 2012), and self-efficacy (Amtmann, Bamer, Cook, et al., 2012). Although there is overlap in symptoms between MS and depression, validation of the PHQ-9 in persons with MS suggests that the measure does not need to be altered to measure depression in persons with MS (Sjonnese et al., 2012).

Demographic and MS disease characteristics—Participants provided extensive demographic and disease-related information as part of their participation in this project. This included indicating that their MS had been diagnosed by a medical professional, selecting the most representative disease course from detailed descriptions and pictorial representations of common MS disease courses, and providing a date of diagnosis. This information is described in detail in a prior report of other data from this project by Kratz et al. (2011).

Data Analysis

Descriptive statistics were computed to identify the rates of pain alone, depression alone, comorbid pain and depression, and neither pain nor depression. Four parallel analyses were conducted to account for all of the combinations of the two definitions of pain (any pain or pain ≥ 3) and the two definitions of depression (PHQ-9 ≥ 10 or participant indicated sufficient criteria for MDE). A chi-square analysis was conducted for each categorization scheme to assess for statistically significant associations. This analysis also allowed for the calculation of odds ratios, which in this case were calculated to determine the odds that (a) a participant with depression would have pain relative to participants without depression and (b) a participant with pain would have depression relative to participants without pain.

Results

Demographics

Participants were 161 persons with multiple sclerosis. The majority of participants were Caucasian (97%) women (83%). Mean time since MS diagnosis was 183.50 months, and pain symptoms were experienced for a mean of 137.68 months. A majority of the sample was unemployed because of their disability (45%) or pain (6%), and 53% were currently receiving disability payments.

Pain, Depression, and Their Comorbidity

The proportion of all persons with MS in our sample with pain, depression, both, or neither varied depending on the method of categorizing depression and pain (see Table 1). Overall, 73% of the sample was experiencing some level of pain, with 40% of the entire sample reporting moderate or worse pain severity. Almost one fourth of the sample (22%) reported

clinically significant levels of depressive symptoms, and 8% reported sufficient symptoms to meet MDE diagnostic criteria.

Across analyses, pain was shown to be highly prevalent among persons reporting depressed mood. Between 86% and 100% of persons meeting depression criteria reported experiencing any pain, and between 67% and 77% of persons meeting depression criteria reported experiencing pain of at least moderate severity. Depression was also shown to be highly prevalent among persons reporting pain, although not at the same levels as found for the presence of pain in persons with depression. Of persons experiencing any pain, 11–34% met depression criteria. Of persons experiencing pain of at least moderate severity, 15–37% met depression criteria. As displayed in Table 1, chi-square analyses revealed statistically significant differences ($p < .05$) in the presence of pain based on depression group membership for all criterion levels except for the least stringent (i.e., PHQ–9 = 10 and any pain). A participant meeting depression criteria was 1.196–2.070 times more likely to also meet pain criteria relative to a nondepressed participant. Participants meeting pain criteria were 2.050–4.923 times more likely to also meet depression criteria relative to a participant without pain.

Discussion

Given the prevalence rates of depression and pain and their association with each other in terms of severity, there is a widespread belief that depression and pain frequently co-occur in persons with MS. However, to our knowledge, no prior study has specifically reported on the prevalence of this comorbidity. Given the popular assumption about this comorbidity, we hypothesized that more participants would have comorbid pain and depression than either pain or depression alone. Inconsistent with our hypothesis, however, we found that the participants were more likely to report pain alone than to have either (a) depression alone or (b) endorse both pain and depression; pain was very common in our sample and depression was less so.

It is important, however, to understand the nuances of these findings. First, we found that the *prevalence of the comorbidity* is modest, present in only 6–19% of participants. Thus, it is not the case that most persons with MS have comorbid pain and depression, which is consistent with the broader literature on persons with neurologic conditions that suggests that 27% of persons have comorbid pain and depression (using the less stringent criteria of daily pain and PHQ–9 = 10; Williams, Jones, Shen, Robinson, & Kroenke, 2004). On the other hand, we also found that when depression or pain is present, it is likely that the individual also has the other problem. For example, we found that participants with pain of at least moderate severity were almost 5 times more likely to meet criteria for MDE than participants without pain. Thus, our findings are consistent with the research findings that individuals with MS and pain also have depression and the parallel finding on individuals with MS and depression that suggests these individuals also have pain (Arnett et al., 2008; Ehde et al., 2003, 2012; O'Connor et al., 2008). In short, although the prevalence of the comorbidity may not be particularly high, pain and depression do often co-occur.

A secondary purpose of this study was to demonstrate how prevalence estimates vary based on the criterion used to classify participants as having pain and depression. The results support our hypothesis that rates of comorbidity vary as a function of classification cutoffs. Under our least stringent criteria for both pain and depression, we could conclude that pain and depression co-occur in almost one of five individuals. On the other hand, using the most stringent criteria suggested that the rate was only one of 20. Researchers in future studies are encouraged to carefully consider the criteria they use to define pain and depression, and to use transparency in describing the results so that the terms *pain*, *depression*, and *co-occurring pain and depression* are clearly defined.

Two potential limitations of the present study were the use of self-report measures and the study sample. Regarding self-report measures, the use of the PHQ-9 to estimate meeting criteria for MDE is not sufficient for formal diagnosis without subsequent follow-up from a provider. The present study also had a modest sample size, leaving relatively few participants in some of the lower frequency categories, such as “depression only.” In terms of study sample, the participants were recruited from a community sample who chose to participate in the study. It is possible that sample selection bias might account for the lower rates of depression in the sample relative to commonly cited prevalence statistics (Chwastiak et al., 2002; Mohr et al., 2007; Patten & Metz, 1997; Sadovnick et al., 1996) as such recruitment may be biased against depressed persons who would be less likely to participate. On the other hand, in a recent validation study of the PHQ-9 in persons with MS (Sjonnese et al., 2012), results revealed prevalence of depression to be 9.8% using the MDE scoring criteria and 21.4% using the cutoff criteria, which are comparable to our findings of 8.1% and 22.4%, respectively. In addition, the participants self-reported that they were diagnosed with MS by a medical professional and provided additional detailed information regarding their MS, but we recognize that it is a possibility that one or more participants did not truly meet diagnostic criteria.

Despite the study’s limitations, the findings have important implications for clinical care of persons with MS, as well as for research on pain and depression in individuals with MS and other rehabilitation populations. For example, the finding that when depression was present, pain was also highly likely to be present suggests that when clinicians identify depression in patients with MS, they should be careful to provide a thorough evaluation (and of course treatment) of pain. Also, other studies using non-MS samples have found that co-occurring depression and pain are associated with greater levels of disability and greater medical costs relative to either condition alone (Bair et al., 2003; Kroenke et al., 2011). Given that a substantial subset of participants in this study reported this co-occurrence, the findings indicate that research studying the synergistic effects of these conditions on disability and health care costs in persons with MS is warranted. Moreover, it is possible that the presence of one condition (depression or pain) may reduce the effectiveness of treatment for the other (Bair et al., 2003; Kroenke et al., 2011); in that vein, a prior study reported that individuals with MS, depression, and pain use more pain treatments than their nondepressed counterparts (Alschuler et al., 2012a). Finally, other studies have highlighted the reciprocal relationship between depression and pain in other medical populations and suggest the need for research and treatment that address both to maximize outcomes (Bair et al., 2003;

Kroenke et al., 2011). Our findings suggest that more research is needed in persons with MS to understand the reciprocal nature of these two common conditions.

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Impact and Implications

- This study is the first to explicitly describe the prevalence of pain, depression, and their comorbidity in a sample of adults with multiple sclerosis.
- By using multiple criteria for describing pain and depression, this study exemplifies how prevalence estimates can vary significantly by criterion measure.
- These results support the conclusion that pain and depression tend to occur together, and suggest that clinicians who identify one problem should carefully assess for the other, given that depression is prevalent among persons with pain and pain is highly prevalent among persons with depression.

Table 1

Rates of Depression, Pain, and Their Comorbidity for Adults With Multiple Sclerosis ($N = 161$)

Variable	PHQ-9 10 and any pain	PHQ-9 MDE criteria and any pain	PHQ-9 10 and pain 3	PHQ-9 MDE criteria and pain 3
Pain only, % (n)	55.9 (90)	67.1 (108)	25.5 (41)	34.2 (55)
Depression only, % (n)	3.1 (5)	0.0 (0)	7.5 (12)	1.9 (3)
Pain and depression, % (n)	19.3 (31)	8.1 (13)	14.9 (24)	6.2 (10)
Neither pain nor depression, % (n)	21.7 (35)	24.8 (40)	52.2 (84)	57.8 (93)
Odds ratios ^a				
Odds that depressed participant will have pain relative to nondepressed participant	1.196	1.370	2.033	2.070
Odds that participant with pain will be depressed relative to participant without pain	2.050	<i>b</i>	2.954	4.923
χ^2	2.981, <i>ns</i>	4.675, $p < .05$	13.317, $p < .001$	7.848, $p < .01$

Note. PHQ-9 = Patient Health Questionnaire—9; MDE = major depressive episode.

^a Odds ratios were calculated to show the odds that a participant with depression has pain relative to a nondepressed participant, as well as the odds that a participant with pain has depression relative to a participant without pain.

^b All participants who met PHQ-9 MDE criteria reported some pain, so an odds ratio for this could not be computed.