An Experimental Approach to Examining Psychological Contributions to Multisite Musculoskeletal Pain


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Abstract: The present study examined the prospective value of pain catastrophizing, fear of pain, and depression in the prediction of multisite musculoskeletal pain following experimentally induced delayed-onset muscle soreness (DOMS). The study sample consisted of 119 (63 females, 56 males) healthy university students. Measures of pain catastrophizing, fear of pain, and depression were completed prior to the DOMS induction procedure. Analyses revealed that pain catastrophizing and fear of pain prospectively predicted the experience of multisite pain following DOMS induction. Analyses also revealed that women were more likely to experience multisite pain than men. There was no significant relation between depressive symptoms and the experience of multisite pain. The discussion addresses the mechanisms by which pain catastrophizing and fear of pain might contribute to the spreading of pain. Clinical implications of the findings are also addressed.

Perspective: The results of this experimental study suggest that pain catastrophizing and fear of pain might increase the risk of developing multisite pain following musculoskeletal injury.

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Key words: Multisite pain, fibromyalgia, catastrophizing, fear of pain, depression, sex differences.

Recent research indicates that musculoskeletal pain frequently occurs at more than 1 anatomic site.6,9,47 A survey of patients attending general practice clinics revealed that three quarters of chronic pain patients reported pain in more than 1 site.6 Multisite pain has been associated with poorer prognosis as indicated by heightened susceptibility to chronicity, increased health and mental health problems, and greater disability.11,32,33,38 In light of the high prevalence and increased costs associated with multisite pain, clinical researchers have called for more research on risk factors and determinants of multisite pain.33,38

Psychological factors such as pain catastrophizing, fear of pain, and depression have been discussed as possible risk factors for the development of multisite pain.4,9 Although it has been suggested that psychological variables might play a role in the onset or maintenance of multisite pain, the correlational nature of clinical studies precludes strong statements about causality. On the basis of research conducted to date, it cannot be ruled out that psychological variables such as pain catastrophizing, fear of pain, and depression might be consequences rather than antecedents of multisite pain.

The present study used an experimental approach to address the possible antecedent status of psychological variables in the experience of multisite pain. One advantage of using an experimental approach is that putative psychosocial risk factors can be assessed before pain induction, thereby permitting examination of the antecedent status of the variables. In addition, experimental methods permit specification and standardization of the pain stimulus, whereas the pain stimulus of many clinical pain conditions is unknown. To date, no experimental study has addressed the influence of psychological variables on the development of multisite pain.
In the present study, measures of pain catastrophizing, fear of pain, and depression were administered in healthy young adults while they were in a pain-free state. Musculoskeletal pain was then induced by means of a delayed-onset muscle soreness (DOMS) protocol.\textsuperscript{1,8} DOMS is characterized by soreness, swelling, stiffness, and strength loss in the 24- to 48-hour period following a strenuous bout of exercise.\textsuperscript{1,63} The muscle soreness that develops following strenuous exercise is the result of structural damage to the involved muscles, triggering a localized inflammatory response that produces pain on movement or tactile stimulation.\textsuperscript{65} DOMS has been associated with a number of pain-related changes, such as allodynia,\textsuperscript{13} referred pain,\textsuperscript{26} and temporal summation,\textsuperscript{49} similar to those observed in clinical pain conditions. Given the similarities in symptoms and pathophysiology, several investigators have used DOMS as an experimental analog for musculoskeletal injury.\textsuperscript{24,43,62}

The day following the DOMS protocol, participants returned to the laboratory and were asked to complete a body drawing to indicate the distribution of their pain symptoms. For the purposes of this study, multisite pain was operationalized as the number of body sites where participants reported experiencing pain. It was hypothesized that pain-related psychological variables would prospectively predict multisite pain following the DOMS protocol.

Demonstrating a prospective relation between psychological variables and multisite pain would have important clinical and theoretical implications. From a clinical perspective, knowing that certain psychological factors represent a heightened risk for multisite pain could permit early identification of high-risk individuals and might also provide the empirical foundation for the development of new avenues of intervention that might prevent the development or reduce the severity of multisite pain. From a theoretical perspective, findings linking psychological variables to the development of multisite pain would bring greater precision to conceptual models that address the mechanisms underlying the development of multisite pain.\textsuperscript{31,53}

### Measures

#### Contraindications to Physical Activity

The Physical Activity Readiness Questionnaire (PAR-Q) was used as a screening measure for potential contraindications to participation in the DOMS induction procedure. The PAR-Q screens for the presence of factors that are linked to increased health risk when engaging in strenuous activity (eg, shortness of breath, muscle or joint problems, fainting, circulatory problems). Participants endorsing any item on the PAR-Q were excluded.\textsuperscript{61}

#### Depression

The Patient Health Questionnaire-9 (PHQ-9) was used to assess the severity of depressive symptoms. On this scale, respondents indicate how often they have been troubled by each of 9 symptoms of depression during the last 2 weeks.\textsuperscript{52} A number of studies have supported the reliability and validity of the PHQ-9 as a measure of depressive symptom severity.\textsuperscript{27,36,41}

#### Pain Catastrophizing

The Pain Catastrophizing Scale (PCS) was used to measure catastrophic thinking related to pain. Participants indicated the frequency with which they experienced each of 13 different thoughts and feelings when in pain. Ratings were made on a 5-point scale with the endpoints 0 (not at all) and 4 (all the time). Research has supported the reliability and validity of the PCS.\textsuperscript{35,56}

#### Fear of Pain

The Fear of Pain Questionnaire-III–Short Form (FOP-III-SF) was used to assess pain-related fears. The FOP-III-SF is a 20-item self-report instrument describing different painful situations. Respondents are asked to rate how fearful they are of experiencing the pain associated with each situation described in the item content. Fear intensity ratings are made on a 5-point scale with the endpoints 1 (not at all) and 5 (extreme). Research has supported the reliability and validity of the FOP-III-SF.\textsuperscript{2}

#### Multisite Pain

A schematic body drawing modeled after Margolis and colleagues\textsuperscript{44} was used to assess the distribution of pain symptoms. Immediately after lifting a weighted canister (2.9 kg), participants shaded in the areas on the drawing that corresponded to where they felt pain. The schematic body drawing is subdivided into 45 different areas, covering the entire body. A score of 1 was assigned to any area that participants had shaded to indicate the experience of pain. A score of 0 was given if an area had been left blank. Four criteria were applied when determining if shading was present: 1) any mark within a body area was assigned a score of 1 regardless of the extent of shading, 2) marks to indicate intensity were disregarded, 3) circling of an area was counted as though the entire circled area had been shaded, and 4) any marks outside the schematic body drawing were disregarded. Consistent with Bortsov and colleagues,\textsuperscript{4,5} multisite pain was assessed as the number of sites on the body.
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Participants were asked to rate the intensity of their pain experience in response to lifting a 2.9-kg weighted canister. The soreness associated with DOMS is most intense when affected muscles are recruited for a physical task. Ratings were made on an 11-point numerical rating scale with the endpoints 0 (no pain) and 10 (excru-ciating pain).

DOMS Protocol

The procedure used to induce DOMS consisted of 4 different strength exercises (ie, chest press, lateral pull-downs, shoulder flexion, and shoulder abduction) involving repeated eccentric muscle actions. The DOMS protocol was modeled after a procedure described by Udermann and colleagues.63 The exercise protocol was performed using the K1 Strength Training System (Body Craft, Sunbury, OH). All exercises were performed in sets of 5 repetitions. To ensure appropriate resistance, participants completed each eccentric contraction in time to a 10-second countdown. Participants were asked to complete the first set of repetitions without any additional weight to become familiarized with the testing apparatus. The weight was increased in steps of 10 pounds until participants reached the point of volitional fatigue or completed 10 sets.64 Volitional fatigue was defined as the point at which the participant could no longer control the descent of the weight.28 For each participant, the relative intensity of the final set of repetitions was 80% of the estimated repetition max, which is defined as the amount of weight a person could only lift 1 time.54

Participants were asked to perform the eccentric contractions with maximal effort and were given verbal encouragement during the contraction. A 1-minute recovery period was provided between sets. Breaks of 2 minutes between exercises were implemented to avoid muscle fatigue. To ensure performance of resisted eccentric contractions only, the experimenter moved the load for the participants on the return from full flexion. The emphasis on the eccentric portion of the strength exercise is known to induce DOMS.7 During an eccentric contraction (lengthening contraction), the muscle elongates while under tension due to an opposing force, which causes microtrauma to the muscle fibers.

To induce DOMS in the pectoralis major and serratus anterior muscles, a chest press was used. This exercise involves lying face up on a horizontal bench, with buttocks on the bench and feet flat on the ground. Participants grasped the barbell with an overhand grip slightly wider than shoulder width and lowered the bar to the chest in a controlled movement. The lateral pull-down works the middle trapezius and latissimus dorsi muscles. Participants sat facing the machine, gripping the bar with a wide overhand grip. While puffing out the chest and pulling the elbows back, participants released the bar from their sternal notch until their arms were fully extended. To target the anterior deltoid muscles, participants performed a shoulder flexion. Participants stood with a straight back, legs slightly apart, holding a cable attachment in their dominant hand. Starting with the arm raised slightly above horizontal out to their side, participants lowered the cable attachment until it rested against their thighs. Lastly, to target the upper trapezius and middle deltoid muscles, participants performed a shoulder abduction. Participants were instructed to stand with their feet slightly apart, holding a cable attachment raised to eye level. The cable attachment was lowered until it rested against the front of participants’ thighs.

At the conclusion of the protocol, participants were asked to refrain from use of pain or anti-inflammatory medication prior to the next session unless experiencing significant discomfort.

Procedure

This research received ethical approval from the Research Ethics Board at McGill University. Participants were invited to the laboratory for 2 testing sessions 24 hours apart. On arrival, each participant signed a consent form as a condition of participation in the research. Participants were informed that the study was aimed at investigating psychological and physical factors associated with pain following repeated physical activity. Anthropometric measures were obtained and participants were asked to complete the PCS, FOP-III-SF, and PHQ-9. The height of the table on which the weighted canisters were placed was adjusted such that the handle of the canister was at standing elbow height.

To obtain baseline measures of pain, participants were asked to provide a verbal rating of their pain as they lifted a 2.9-kg weighted canister with their dominant arm fully extended for 5 seconds. Participants also completed the body drawing immediately after replacing the canister on the table in order to obtain a baseline measure of the distribution of pain symptoms. The DOMS protocol was then completed.

The second testing session occurred 24 hours (±3 hours) following the first testing session. During the second testing session, the height of the table was adjusted as in session 1, and participants were asked to lift a 2.9-kg weighted canister with their dominant arm fully extended for 5 seconds and provide a verbal rating of the intensity of their pain. Immediately after replacing the weighted canister on the table, participants again completed the body drawing. Finally, participants were debriefed.

Statistical Approach

Descriptive statistics were computed on sample characteristics and questionnaire scores. Correlational analyses were conducted to examine the bivariate relationships among the predictor and outcome variables. In addition,
Results

Sample Characteristics

Table 1 presents the means and standard deviations for participants’ demographics and pain-related psychosocial measures. There were no significant sex differences for age, t(117) = .17, nonsignificant. Compared to men, women obtained higher scores on measures of pain catastrophizing, t(117) = 2.1, P < .05, fear of pain, t(117) = 2.0, P < .05, and depression, t(117) = 3.3, P < .001. Scores on the PCS and the FOP-III-SF are comparable to those that have been reported in previous research using DOMS protocols in nonclinical samples.12,13

Pain Intensity and Multisite Pain

Pain intensity ratings and multisite pain scores are presented in Table 2. A 2-way (Sex × Session) analysis of variance on pain ratings revealed significant main effects for Sex, F(1, 117) = 15.74, P < .01, and Session, F(1, 117) = 173.97, P < .01, and a significant Sex × Session interaction, F(1, 117) = 11.55, P < .01. Tests of simple effects revealed that although DOMS was effective in increasing pain for both men and women, the magnitude of increase in pain was greater for women than for men. The majority of participants would be considered to be experiencing mild to moderate pain at Session 2. The pain intensity ratings provided by participants at Session 2 are comparable to pain intensity ratings reported in previous studies using pain-free nonclinical samples.2,55,57,58

Table 1. Sample Characteristics (N = 119)

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>WOMEN (n = 63)</th>
<th>MEN (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>22.2 (5.0)</td>
<td>22.4 (3.3)</td>
</tr>
<tr>
<td>PCS</td>
<td>18.0 (8.5)</td>
<td>15.0 (7.4)</td>
</tr>
<tr>
<td>FOP-III-SF</td>
<td>53.9 (13.0)</td>
<td>49.4 (12.0)</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>7.3 (3.7)</td>
<td>5.1 (3.1)</td>
</tr>
</tbody>
</table>

NOTE. Pain Intensity S1: pain intensity before DOMS induction; Pain Intensity S2: pain intensity after DOMS induction; Multisite Pain S1: number of pain sites before DOMS induction; Multisite Pain S2: number of pain sites after DOMS induction. Values in parentheses are standard deviations.

greater than the number of reported pain sites for Session 1.

Correlates of Pain Intensity and Multisite Pain

Table 3 shows the prospective partial correlations (controlling for pain intensity and multisite pain at Session 1) between psychological variables (ie, pain catastrophizing, fear of pain, depression) and pain intensity and multisite pain assessed at Session 2. Pain catastrophizing was correlated with pain intensity and multisite pain at Session 2. Fear of pain was significantly correlated with multisite pain but not pain intensity at Session 2. Depression was not significantly correlated with pain intensity or multisite pain at Session 2.

Figure 1 shows the distribution of pain sites in high and low catastrophizers (based on a median split of PCS scores). The values within the sections of the body drawing refer to the percentage of participants who indicated experiencing pain in that area of the body. The DOMS procedure was designed to elicit pain in the upper arms, shoulders, and chest. For both high and low catastrophizers, a greater percentage of participants reported pain on the right than on the left side. This was expected as participants rated their pain after lifting a weighted canister with their dominant arm. Significantly greater representation of high, compared to low, catastrophizers was observed for “core” muscles, including shoulders, chest, abdominals, and neck (high PCS = 83.3%, low PCS = 54.2%, χ² = 11.75, P < .01), and muscles of the “extremities,” including hands, upper arms, and lower arms (high PCS = 49.2%, low PCS = 8.45, P < .01).

Table 2. Pain Intensity and Multisite Pain Scores (N = 119)

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>WOMEN (n = 63)</th>
<th>MEN (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Intensity S1</td>
<td>.33 (.48)</td>
<td>.18 (.39)</td>
</tr>
<tr>
<td>Pain Intensity S2</td>
<td>2.90 (1.78)</td>
<td>1.70 (1.66)</td>
</tr>
<tr>
<td>Multisite Pain S1</td>
<td>.56 (.82)</td>
<td>.27 (1.62)</td>
</tr>
<tr>
<td>Multisite Pain S2</td>
<td>3.70 (3.19)</td>
<td>2.48 (2.49)</td>
</tr>
</tbody>
</table>

NOTE. For correlations with Pain Intensity S2, Pain Intensity S1 was controlled; for correlations with Multisite Pain S2, Multisite Pain S1 was controlled. *P < .05. **P < .01.
Figure 2 shows the distribution of pain symptoms in high-fear and low-fear (based on a median split of FOP-III-SF scores) participants. Similar to the PCS, for both high-fear and low-fear participants, a greater percentage of reported pain was observed on the right than on the left side. Analyses revealed that a greater percentage of high-fear compared to low-fear participants reporting pain for muscles of the “extremities” (high fear = 81.7%, low fear = 55.9%, $\chi^2 = 9.20$, $P < .01$), but not for “core” muscles (high fear = 70.0%, low fear = 54.2%, $\chi^2 = 3.14$, $P > .05$).

The Role of Pain-Related Psychological Variables in the Prediction of Multisite Pain

A hierarchical regression analysis was conducted to examine the shared and unique contributions of pain catastrophizing, fear of pain, and depression to the prediction of multisite pain after DOMS induction. In the analysis, Session 1 pain intensity and multisite pain were entered in the first step, age and sex were entered in the second step, and height and weight were entered in the third step of the analysis. In the fourth step of the analysis, pain catastrophizing and fear of pain were entered, yielding an 11% increase in explained variance in Session 2 multisite pain. Beta weights for the final regression equation indicated that sex ($\beta = -.24$, $P < .05$), pain catastrophizing ($\beta = .20$, $P < .05$), and fear of pain ($\beta = .23$, $P < .01$) contributed significant unique variance to the prediction of Session 2 multisite pain.

Discussion

Numerous investigators have recently raised questions about the possibility that the distribution of pain symptoms might represent a separate dimension of pain experience, distinct from pain quality or pain severity. It has been noted that within populations of pain sufferers,
the number of anatomic sites where pain is experienced varies widely.\textsuperscript{4,10} Research shows that multisite pain is actually more prevalent than single-site pain and is associated with higher levels of physical, mental, and occupational disability.\textsuperscript{6,32,33} As such, the identification of risk factors for the development of multisite pain has important implications, both clinical and theoretical.

The findings of the present study join a growing literature supporting the view that pain-related psychological variables such as pain catastrophizing and fear of pain increase the risk of experiencing adverse pain outcomes.\textsuperscript{40,51} In previous experimental research, measures of pain catastrophizing and fear of pain have been prospectively associated with measures of pain intensity, pain behavior, and disability.\textsuperscript{50,54,60} The results of the present study extend previous findings in showing that pain catastrophizing and fear of pain, measured in a pain-free state, prospectively predicted the number of reported pain sites 24 hours following a DOMS protocol. To our knowledge, this is the first study to show that psychological variables are prospectively associated with the experience of multisite pain.

Although the causes of multisite pain remain largely unknown, researchers have speculated about the peripheral and central mechanisms that could lead to the spreading of pain. Findings showing an association between the extent of impact, trauma, or physical loading and multisite pain suggest potential involvement of peripheral mechanisms such as tissue damage or inflammatory processes.\textsuperscript{4} It has also been suggested that stress-induced hyperalgesia consequent to physical trauma might explain the onset of multisite pain following motor vehicle collisions.\textsuperscript{4} It is possible that catastrophic thinking might augment stress reactions or shape proinflammatory responses to noxious stimulation, potentially contributing to the spreading of pain.\textsuperscript{5,10} Catastrophizing has also been associated with indices of central sensitization and with dysfunction of
It is possible that fear of pain might lead to muscle activation alterations that in turn lead to the spreading of pain. Protective movement alterations potentiated by fear might cause sustained activations of muscles, producing intramuscular ischemic reactions that might directly or indirectly increase peripheral pain afferrer activity.

In recent research, the “generalization” of fear of pain has been suggested as a mechanism by which fear might contribute to the spreading of pain. Generalization of fear of pain occurs when the expectation of a painful sensation is associated with a stimulus that resembles, but is not identical to, the original stimulus. Generalization of fear of pain is believed to be associated with increased and sustained vigilance to pain as a result of deficient safety learning. It is possible that fear of pain might lead to muscle activation alterations that in turn lead to the spreading of pain.

Increased vigilance to pain might cause ambiguous stimuli to be more readily interpreted as painful, leading to the experience of pain in multiple sites.

Previous research has suggested an association between symptoms of depression and multisite pain. The current study failed to reproduce this association. Failure to reproduce the association between depression and the number of pain sites might stem from the nature of the study sample. The present study used healthy university students in whom the majority obtained scores in the nondepressed range. Levels of depression in the current sample might have been too low to have an influence on the number of pain sites.

Analyses revealed that sex was a unique predictor of the number of pain sites. This finding is consistent with previous clinical research showing that a disproportionate number of women experience pain in multiple sites. Hormonal differences and the related effects of these hormones on neurotransmitter and endogenous opioid systems have been proposed as mechanisms to account for sex differences in pain experience. It is important to note, however, that with respect to the results of the present study, it is not possible to rule out the possibility that women experienced pain in more sites than men as a function of differences in physical mass and strength. Because of their smaller physical stature, the physical demands of the lifting task might have been disproportionately greater for women.

The emerging body of findings raises the possibility that pain catastrophizing and fear of pain might be risk factors for the development of pain in multiple sites. As such, the inclusion of measures of pain catastrophizing and fear of pain as screening measures for identifying individuals at risk for problematic outcomes following physical trauma, such as motor vehicle accidents, or the onset of musculoskeletal disorders might be warranted. Targeting these variables in the early stages of treatment might prevent individuals from developing pain in multiple sites and decrease the probability of transitioning from acute pain to more serious chronic pain syndromes. Currently, psychological interventions for individuals with pain in multiple sites are typically offered only once the condition has become chronic.

Caution must be used when interpreting the study findings. To maximize homogeneity of the study sample, a number of exclusion criteria were used. Consequently, the exclusion criteria that were employed in the current study limit the generalizability of findings. In addition, healthy undergraduates differ from individuals with clinical multisite pain conditions on a number of demographic (eg, age, education) and health status (eg, comorbidities) variables. These factors invite prudence in generalizing the present study to patients suffering from multisite pain. Furthermore, although exercise-induced DOMS is a useful technique to mimic musculoskeletal pain conditions, it lacks the affective and traumatic components of musculoskeletal injuries that might occur as a result of work injury or motor vehicle accidents. The results of the present study might not be generalizable to multisite pain conditions that arise in the absence of injury, such as chronic widespread pain or arthritis. Although the latter conditions include the presence of multiple pain sites, they are also associated with onset conditions, developmental processes, pathophysiology, and symptom profiles that differ from those generated by DOMS protocols.

It is also important to consider the present findings in the context of some inconsistencies in findings that have been reported in previous research. Not all studies have shown independent contributions of pain catastrophizing and fear of pain to adverse pain outcomes, and the magnitude of relations between pain catastrophizing, fear of pain, and pain outcomes has varied as well. There have also been inconsistencies with respect to the contextual factors influencing the predictive value of pain catastrophizing and fear of pain. Although some studies have shown that pain catastrophizing predicts pain outcomes when assessed in a pain-free state, others have shown that pain...
catastrophizing predicts pain outcomes only when participants have already experienced the pain stimulus. In light of these inconsistencies in findings, replication of the present findings is required before confidence can be placed in the conclusions drawn.

In spite of these limitations, the findings of the present study showed that pain-related psychological variables prospectively predicted the number of pain sites following experimentally induced musculoskeletal injury. It is possible that psychological factors such as pain catastrophizing and fear of pain might affect inflammatory processes, central sensitization, descending inhibition, muscle activation patterns, and associative learning processes in a manner that increases the probability of experiencing pain in multiple sites. Future research will need to examine more directly the role of various neurophysiological and psychological variables as processes linking pain catastrophizing and fear of pain to the development of multisite pain. If replicated under more clinically relevant conditions, the findings would argue for the inclusion of measures of pain catastrophizing and fear of pain in clinical practice to assess for risk of developing multisite pain and for the early implementation of psychological interventions that might reduce the risk of developing multisite pain.

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