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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.

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

Highlight points: Pain catastrophizing, and fear of pain prospectively predict the experience of multisite pain following DOMS-induction.

Women are more likely to experience multisite pain than men.

Depressive symptoms have no influence on the experience of multisite pain.

Fear of pain may underlie the experience of multisite pain through generalization.

Recent research indicates that musculoskeletal pain frequently occurs at more than one anatomical 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 one 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 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 prior to 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 [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 [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 which produces pain upon movement or tactile stimulation [65]. DOMS has been associated with a number of pain-related changes, such as allodynia [13], referred pain [26] and temporal summation [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 [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 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 [31, 53].

Methods

Participants

The study sample consisted of 119 healthy undergraduate students (63 females, 56 males). Participants were recruited through advertisements placed in the classifieds section of the McGill University website. The mean age of the sample was 22.3 years, with a range of 18 – 52 years. A standardized telephone interview was used to screen participants for the exclusion criteria. Individuals were not considered for participation if (1) they had a medical condition that could be aggravated by participation in the study, (2) suffered from a chronic pain condition, (3) were currently experiencing joint or muscle problems, or (4) had engaged in resistance training of upper body or trunk muscles more than once per week in the 6 months prior to participation.

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 (e.g. shortness of breath, muscle or joint problems, fainting, circulatory problems). Participants endorsing any item on the PAR-Q were excluded [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 nine symptoms of depression during the last two weeks [52]. A number of studies have supported the reliability and validity of the PHQ-9 as a measure of depressive symptom severity [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 five-point scale with the endpoints '0' (not at all) and '4' (all the time). Research has supported the reliability and validity of the PCS [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 [2].

Multisite Pain. A schematic body drawing modeled after Margolis and colleagues [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, (4) any marks outside the schematic body drawing were disregarded. Consistent with Bortsov and colleagues [4], multisite pain was assessed as the number of sites on the body drawing where participants reported experiencing pain. Multisite pain was assessed prior to the DOMS protocol to control for pre-existing pain, and again when participants returned for the second testing session 24 hours after the DOMS protocol.

Pain Intensity. 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 [13]. Ratings were made on an 11-point numerical rating scale (NRS) with the endpoints '0' (no pain) and '10' (excruciating pain).

DOMS protocol. The procedure used to induce DOMS consisted of four different strength exercises (i.e. 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, USA). All exercises were performed in sets of five 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 ten pounds until participants reached the point of volitional fatigue or completed ten 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 one time [54].

Participants were asked to perform the eccentric contractions with maximal effort and were given verbal encouragement during the contraction. A one-minute recovery period was provided between each set. Breaks of two 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 faceup 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 pulldown works the middle trapezius and latisimus 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 two testing sessions 24 hours apart. Upon 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. T-tests for independent samples were used to examine sex differences on demographic and dependent measures. Hierarchical linear regression analyses were conducted to assess the value of pain catastrophizing, fear of pain, and depression in predicting the experience of multisite pain following DOMS-induction. Initial scores on pain intensity, multisite

pain, as well as sex and age were used as covariates. Diagnostic tests of tolerance and variance inflation revealed all of the measures fell within acceptable ranges of collinearity (Variance Inflation Factors < 2).

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, ns. Compared to men, women obtained higher scores on measures of pain catastrophizing, t (117) = 2.1, $p < 0.05$, fear of pain, t (1, 117) = 2.0, $p < .05$, and depression, t (117) = 3.3, $p < 0.001$. Scores on the PCS and the FOP-III-SF are comparable to those that have been reported in previous studies using pain-free non-clinical samples [2, 55, 57, 58].

Pain Intensity and Multisite Pain

Pain intensity ratings and multisite pain scores are presented in Table 2. A two-way (Sex X Session) ANOVA on pain ratings revealed significant main effects for Sex, F (1, 117) = 15.74, $p < 0.01$, and Session, F (1, 117) = 173.97, $p < 0.01$, and a significant Sex X Session interaction, F (1, 117) = 11.55, $p < 0.01$. Tests of simple effects revealed that while 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 research using DOMS protocols in non-clinical samples [12 13].

Frequency distribution revealed a wide range of multisite pain scores (range 0 – 16). A two-way (Sex X Session) ANOVA on multisite pain scores revealed significant main effects for Sex, F (1, 117) = 7.85, $p < 0.05$ and Session, F (1, 117) = 103.82, $p < 0.01$. The Sex X Session interaction was not significant, F (1, 117) = 3.48, *ns*. Women reported pain in more sites than men, and the number of reported pain sites for Session 2 was significantly 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 (i.e., 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 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%, $X^2 = 11.75$, $p < .01$), and muscles of the ‘extremities’, including hands, upper arms, and lower arms (high PCS = 75.0%, low PCS = 49.2%, $X^2 = 8.45$, $p < .01$).

Figure 2 shows the distribution of pain symptoms in high and low fear (based on a median split of FOP-SF scores) participants. Similar to the PCS, for both fear and low fear participants a greater percentage of reported pain was observed on the right than left side. Analyses revealed a greater percentage of high, compared to low, fear participants reporting pain for muscles of the ‘extremities’ (high fear = 81.7%, low fear = 55.9%, $X^2 = 9.20$, $p < .01$), but not for ‘core’ muscles (high fear = 70.0%, low fear = 54.2%, $X^2 = 3.14$, $p > .05$).

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. Depression was not included in the analysis since the partial correlation between the PHQ-9 and multisite pain was not significant.

As shown in Table 4, Session 1 pain intensity and multisite pain failed to contribute significantly to the prediction of Session 2 multisite pain. Age and sex

were entered in the second step of the analysis and made a marginally significant contribution to the prediction of Session 2 multisite pain. Participant height and weight were entered in the third step of the analysis but did not contribute significantly to the prediction of Session 2 multisite pain. In the final step of the analysis pain catastrophizing, and fear of pain were entered in the analysis, yielding a 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 [9, 10, 33]. It has been noted that within populations of pain sufferers, the number of anatomic sites where pain is experienced varies widely [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 [6 32, 33]. As such, the identification of risk factors for the development of multisite pain has both important clinical and theoretical implications.

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 [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 [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 correlated, pain catastrophizing and fear of pain likely represent distinct constructs with different etiologies and different mechanisms of action [59, 66]. Research shows that measures of pain catastrophizing and fear of pain load on separate factors, and are differentially associated with pain and disability; catastrophizing frequently emerges as the better predictor of pain intensity, and fear of pain frequently emerges as the better predictor of disability [39 50, 67]. The results of the present study, showing that pain catastrophizing and fear of pain made independent contributions to the prediction of multisite pain, further support the notion that these variables impact on pain outcomes through different mechanisms.

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 extent of impact, trauma or physical loading and multisite pain suggest potential involvement of peripheral mechanisms such as tissue damage or inflammatory processes [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 [4]. It is possible that catastrophic thinking might augment stress reactions or shape pro-inflammatory

responses to noxious stimulation, potentially contributing to the spreading of pain [5, 18]. Catastrophizing has also been associated with indices of central sensitization, and dysfunction of descending noxious inhibitory control, both of which have also been discussed as processes underlying the pathogenesis of multisite pain [19, 29, 37].

It is possible that fear of pain might lead to muscle activation alterations that in turn lead to the spreading of pain [22, 42, 48]. Protective movement alterations potentiated by fear might cause sustained activations of muscles, producing intra-muscular ischemic reactions that might directly or indirectly increase peripheral pain afferent activity [30].

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 [15, 45, 46]. 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 [15]. Generalization of fear of pain is believed to be associated with increased and sustained vigilance for pain, as a result of deficient safety learning [14, 40]. 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 [16, 32, 69]. 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 where the majority of participants obtained scores in the

non-depressed 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 [21, 25]. 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 [21]. 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. Due to 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 [4], 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 (e.g., age, education) and health status variables (e.g., co-morbidities). These factors invite prudence in generalizing the present study to patients suffering from multisite pain. Furthermore, while 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. While 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 [20, 68].

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 [3, 23, 24, 34, 50]. There have also been inconsistencies with respect to the contextual factors influencing the predictive value of pain catastrophizing, fear of pain. While some studies have shown that pain catastrophizing predicts pain outcomes when assessed in a pain-free state,

others have shown pain catastrophizing predicts pain outcomes only when participants have already experienced the pain stimulus [17, 50]. In light of such 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 impact on inflammatory processes, central sensitization, descending inhibition, muscle activation patterns as well as 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.

Table 1. *Sample Characteristics*

Variables	Women (n = 63)	Men (n = 56)
Age	22.2 (5.0)	22.4 (3.3)
PCS	18.0 (8.5)	15.0 (7.4)
FOP-III-SF	53.9 (13.0)	49.4 (12.0)
PHQ-9	7.3 (3.7)	5.1 (3.1)

Note: N = 119: PCS: Pain Catastrophizing Scale; FOP-III-SF: Fear of Pain Questionnaire III Short Form; PHQ-9: Patient Health Questionnaire – 9.

Table 2. *Pain Intensity and Multisite Pain Scores*

Variables	Women (n = 63)	Men (n = 56)
Pain Intensity (S1)	0.33 (0.48)	0.18 (0.39)
Pain Intensity (S2)	2.90 (1.78)	1.70 (1.66)
Multisite Pain (S1)	0.56 (0.82)	0.27 (0.62)
Multisite Pain (S2)	3.70 (3.19)	2.48 (2.49)

Note: N = 119: 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.

Table 3. *Partial Correlations Between Session 1 Psychological Variables and Session 2 Pain Intensity and Multisite Pain Scores*

	Pain Intensity S2	**Multisite Pain S2**
PCS	.24*	.32**
FOP-III-SF	.16	.32**
PHQ-9	-.05	. 01

Note: N = 119. PCS = Pain Catastrophizing Scale; FOP-III-SF = Fear of Pain Questionnaire – III – Short Form; PHQ-9 = Patient Health Questionnaire – 9; For correlations with Pain Intensity S2, Pain Intensity S1 was controlled; for correlations with Multisite Pain S2, Multisite Pain S1 was controlled. * $p < .05$, ** $p < .01$.

Table 4. *Regression Analysis Predicting Multisite Pain After DOMS-induction*

Variables	β	R^2 change	F-change	*p* value
Step 1		0.04	2.20 (2, 116)	.11
Pain Intensity S1	-0.19			
Multisite pain S1	0.22			
Step 2		0.05	2.87 (2, 114)	.06
Age	-0.04			
Sex	-0.24*			
Step 3		0.04	2.19 (2, 112)	.11
Height	0.12			
Weight	0.09			
Step 4		0.11	7.99 (2, 110)	.001
PCS	0.20*			
FOP-III-SF	0.23**			

Note: N = 119. Pain Intensity S1: Pain Intensity before DOMS-induction; Multisite Pain S1: Number of pain sites before DOMS-induction; PCS = Pain Catastrophizing Scale; FOP-III-SF = Fear of Pain Questionnaire – III – Short Form. Values in parentheses are degrees of freedom. Beta weights are from the final regression equation.
* $p < .05$; ** $p < .01$

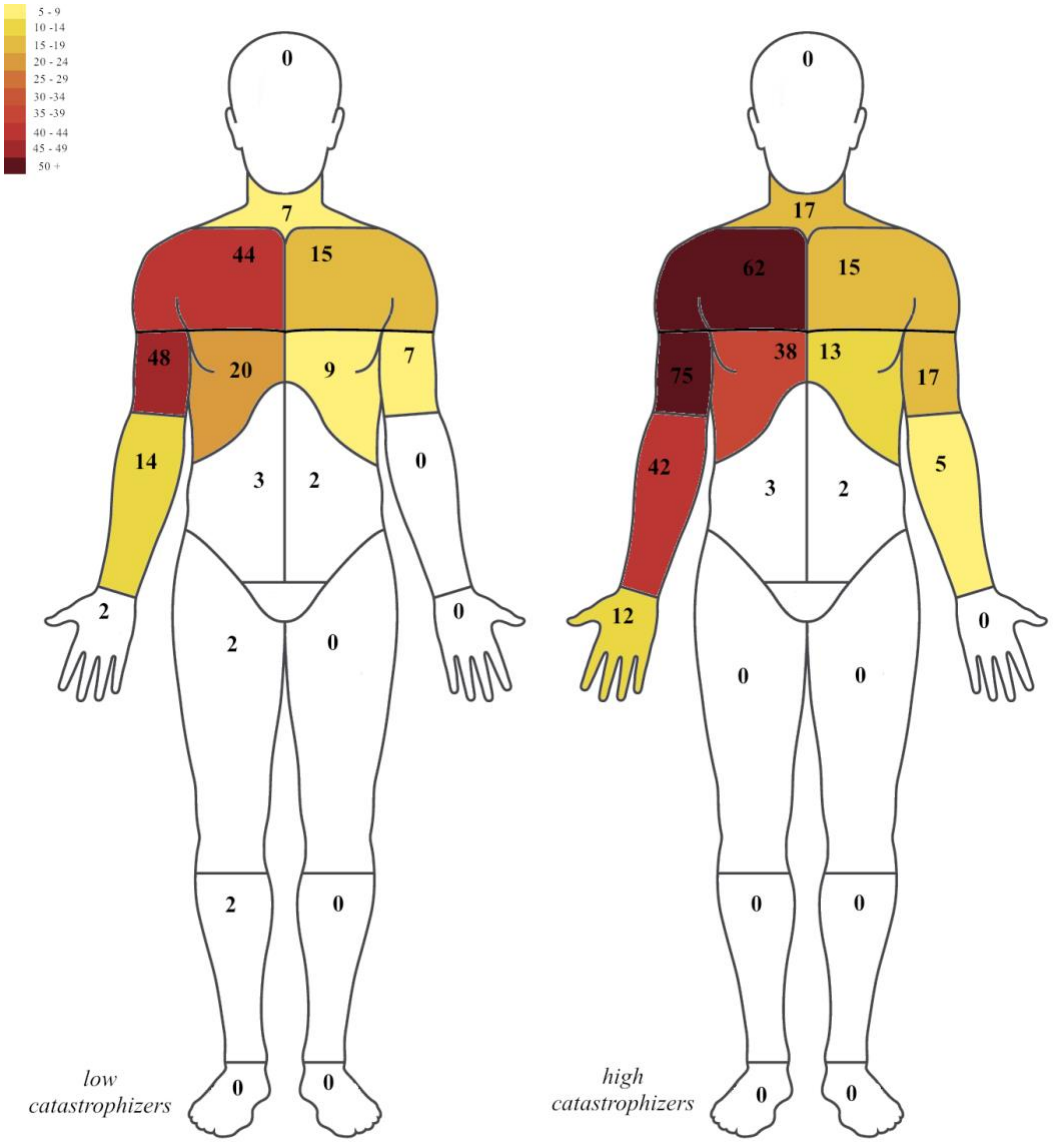

Figure 1*: Percentage of High and Low Catastrophizers Reporting Pain After DOMS-induction.*

Note: Percentages are summed for the front and back of the body drawing.

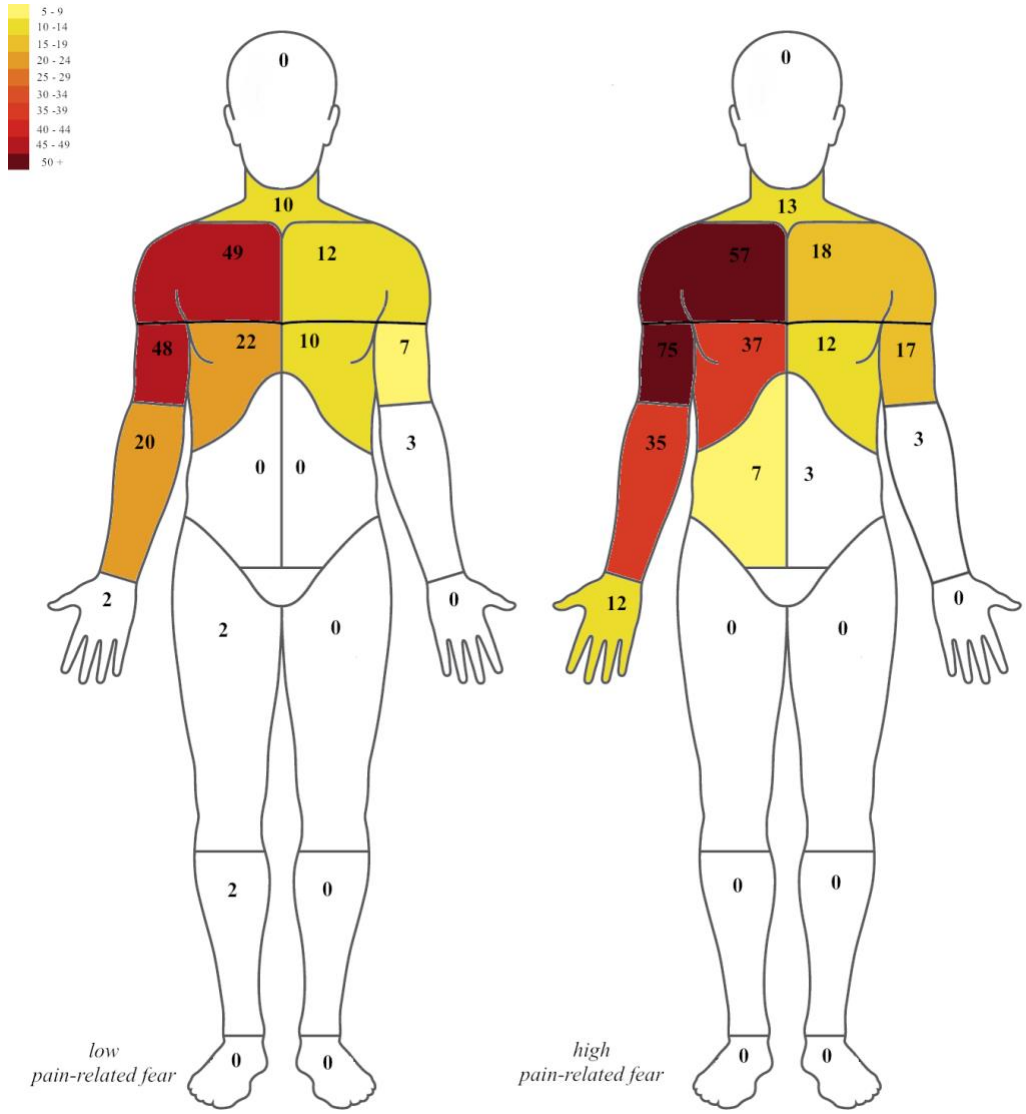

Figure 2*: Percentage of Participants Reporting Pain After DOMS-induction According to Body Region with a median split for low and high fear of pain, values combined for front and back.*

Note: Percentages are summed for the front and back of the body drawing.

Disclosures

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1. Armstrong RB. Mechanisms of exercise-induced delayed onset muscular soreness: A brief review. *Med Sci Sports Excercise.* 16:529 - 538, 1984

2. Asmundson GJ, Bovell CV, Carleton RN, McWilliams LA. The Fear of Pain Questionnaire-Short Form (FPQ-SF): factorial validity and psychometric properties. *Pain.* 134:51-58, 2008

3. Beneciuk JM, Bishop MD, George SZ. Pain catastrophizing predicts pain intensity during a neurodynamic test for the median nerve in healthy participants. *Manual therapy.* 15:370-375, 2010

4. Bortsov AV, Platts-Mills TF, Peak DA, Jones JS, Swor RA, Domeier RM, Lee DC, Rathlev NK, Hendry PL, Fillingim RB, McLean SA. Pain distribution and predictors of widespread pain in the immediate aftermath of motor vehicle collision. *Eur J Pain.* 2013

5. Campbell CM, Edwards RR. Mind-body interactions in pain: the neurophysiology of anxious and catastrophic pain-related thoughts. *Translational research : the journal of laboratory and clinical medicine.* 153:97-101, 2009

6. Carnes D, Parsons S, Ashby D, Breen A, Foster NE, Pincus T, Vogel S, Underwood M. Chronic musculoskeletal pain rarely presents in a single body site: results from a UK population study. *Rheumatology.* 46:1168-1170, 2007

7. Clarkson PM, Nosaka K, Braun B. Muscle function after exercise-induced muscle damage and rapid adaptation. *Med Sci Sports Exerc.* 24:512-520, 1992

8. Clarkson PM, Tremblay I. Exercise-induced muscle damage, repair, and adaptation in humans. *J Appl Physiol.* 65:1-6, 1988

9. Coggon D, Ntani G, Palmer KT, Felli VE, Harari R, Barrero LH, Felknor SA, Gimeno D, Cattrell A, Serra C, Bonzini M, Solidaki E, Merisalu E, Habib RR, Sadeghian F, Masood Kadir M, Warnakulasuriya SS, Matsudaira K, Nyantumbu B, Sim MR, Harcombe H, Cox K, Marziale MH, Sarquis LM, Harari F, Freire R, Harari N, Monroy MV, Quintana LA, Rojas M, Salazar Vega EJ, Harris EC, Vargas-Prada S, Martinez JM, Delclos G, Benavides FG, Carugno M, Ferrario MM, Pesatori AC, Chatzi L, Bitsios P, Kogevinas M, Oha K, Sirk T, Sadeghian A, Peiris-John RJ, Sathiakumar N, Wickremasinghe AR, Yoshimura N, Kelsall HL, Hoe VC, Urquhart DM, Derrett S, McBride D, Herbison P, Gray A. Disabling musculoskeletal pain in working populations: is it the job, the person, or the culture? *Pain.* 154:856-863, 2013

10. Coggon D, Ntani G, Palmer KT, Felli VE, Harari R, Barrero LH, Felknor SA, Gimeno D, Cattrell A, Vargas-Prada S, Bonzini M, Solidaki E, Merisalu E, Habib RR, Sadeghian F, Masood Kadir M, Warnakulasuriya SS, Matsudaira K, Nyantumbu B, Sim MR, Harcombe H, Cox K, Marziale MH, Sarquis LM, Harari F, Freire R, Harari N, Monroy MV, Quintana LA, Rojas M, Salazar Vega EJ, Harris EC, Serra C, Martinez JM, Delclos G, Benavides FG, Carugno M, Ferrario MM, Pesatori AC, Chatzi L, Bitsios P, Kogevinas M, Oha K, Sirk T, Sadeghian A, Peiris-John RJ, Sathiakumar N, Wickremasinghe AR,

Yoshimura N, Kelsall HL, Hoe VC, Urquhart DM, Derrett S, McBride D, Herbison P, Gray A. Patterns of multisite pain and associations with risk factors. *Pain.* 154:1769-1777, 2013

11. Croft P, Dunn KM, Von Korff M. Chronic pain syndromes: you can't have one without another. *Pain.* 131:237-238, 2007

12. Dannecker EA, Liu Y, Rector RS, Thomas TR, Fillingim RB, Robinson ME. Sex differences in exercise-induced muscle pain and muscle damage. *J Pain.* 13:1242-1249, 2012

13. Dannecker EA, Sluka KA. Pressure and activity-related allodynia in delayed-onset muscle pain. *Clin J Pain.* 27:42-47, 2011

14. Dehghani M, Sharpe L, Nicholas MK. Modification of attentional biases in chronic pain patients: a preliminary study. *European journal of pain.* 8:585-594, 2004

15. Dunsmoor JE, Prince SE, Murty VP, Kragel PA, LaBar KS. Neurobehavioral mechanisms of human fear generalization. *NeuroImage.* 55:1878-1888, 2011

16. Dworkin SF, Vonkorff M, Leresche L. Multiple Pains and Psychiatric Disturbance - an Epidemiologic Investigation. *Archives of general psychiatry.* 47:239-244, 1990

17. Edwards RR, Campbell CM, Fillingim RB. Catastrophizing and experimental pain sensitivity: only in vivo reports of catastrophic cognitions correlate with pain responses. *The journal of pain : official journal of the American Pain Society.* 6:338-339, 2005

18. Edwards RR, Kronfli T, Haythornthwaite JA, Smith MT, McGuire L, Page GG. Association of catastrophizing with interleukin-6 responses to acute pain. *Pain.* 140:135-144, 2008

19. Edwards RR, Smith MT, Stonerock G, Haythornthwaite JA. Pain-related catastrophizing in healthy women is associated with greater temporal summation of and reduced habituation to thermal pain. *The Clinical journal of pain.* 22:730-737, 2006

20. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. *Radiol Clin North Am.* 42:1-9, v, 2004

21. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL, 3rd. Sex, gender, and pain: a review of recent clinical and experimental findings. *The journal of pain : official journal of the American Pain Society.* 10:447-485, 2009

22. Geisser ME, Haig AJ, Wallbom AS, Wiggert EA. Pain-related fear, lumbar flexion, and dynamic EMG among persons with chronic musculoskeletal low back pain. *The Clinical journal of pain.* 20:61-69, 2004

23. George SZ, Dannecker EA, Robinson ME. Fear of pain, not pain catastrophizing, predicts acute pain intensity, but neither factor predicts tolerance or blood pressure reactivity: an experimental investigation in pain-free individuals. *European journal of pain.* 10:457-465, 2006

24. George SZ, Dover GC, Fillingim RB. Fear of pain influences outcomes after exercise-induced delayed onset muscle soreness at the shoulder. *The Clinical journal of pain.* 23:76-84, 2007

25. Gerdle B, Bjork J, Coster L, Henriksson K, Henriksson C, Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. *BMC musculoskeletal disorders.* 9:102, 2008

26. Gibson W, Arendt-Nielsen L, Graven-Nielsen T. Delayed-onset muscle soreness at tendon-bone junction and muscle tissue is associated with facilitated referred pain. *Exp Brain Res.* 174:351 - 360, 2006

27. Gilbody S, Richards D, Brealey S, Hewitt C. Screening for depression in medical settings with the Patient Health Questionnaire (PHQ): a diagnostic meta-analysis. *Journal of general internal medicine.* 22:1596-1602, 2007

28. Glasgow PD, Ferris R, Bleakley CM. Cold water immersion in the management of delayed-onset muscle soreness: Is dose important? A randomised controlled trial. *Physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine.* 2014

29. Goodin BR, McGuire L, Allshouse M, Stapleton L, Haythornthwaite JA, Burns N, Mayes LA, Edwards RR. Associations between catastrophizing and endogenous pain-inhibitory processes: sex differences. *The journal of pain : official journal of the American Pain Society.* 10:180-190, 2009

30. Graven-Nielsen T. Fundamentals of muscle pain, referred pain, and deep tissue hyperalgesia. *Scandinavian journal of rheumatology. Supplement.* 122:1-43, 2006

31. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. *Nature reviews. Rheumatology.* 6:599-606, 2010

32. Gureje O, Von Korff M, Kola L, Demyttenaere K, He Y, Posada-Villa J, Lepine JP, Angermeyer MC, Levinson D, de Girolamo G, Iwata N, Karam A, Guimaraes Borges GL, de Graaf R, Browne MO, Stein DJ, Haro JM, Bromet EJ, Kessler RC, Alonso J. The relation between multiple pains and mental disorders: results from the World Mental Health Surveys. *Pain.* 135:82-91, 2008

33. Haukka E, Kaila-Kangas L, Ojajarvi A, Miranda H, Karppinen J, Viikari-Juntura E, Heliovaara M, Leino-Arjas P. Pain in multiple sites and sickness absence trajectories: a prospective study among Finns. *Pain.* 154:306-312, 2013

34. Hirsh AT, George SZ, Bialosky JE, Robinson ME. Fear of pain, pain catastrophizing, and acute pain perception: relative prediction and timing of assessment. *The journal of pain : official journal of the American Pain Society.* 9:806-812, 2008

35. Hsieh AY, Tripp DA, Ji LJ, Sullivan MJL. Comparisons of catastrophizing, pain attitudes, and cold-pressor pain experience between Chinese and European Canadian young adults. *The journal of pain : official journal of the American Pain Society.* 11:1187-1194, 2010

36. Huang FY, Chung H, Kroenke K, Delucchi KL, Spitzer RL. Using the Patient Health Questionnaire-9 to measure depression among racially and ethnically diverse primary care patients. *Journal of general internal medicine.* 21:547-552, 2006

37. Julien N, Goffaux P, Arsenault P, Marchand S. Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition. *Pain.* 114:295-302, 2005

38. Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D. Does the number of musculoskeletal pain sites predict work disability? A 14-year prospective study. *European journal of pain.* 13:426-430, 2009

39. Lee JE, Watson D, Frey-Law LA. Psychological factors predict local and referred experimental muscle pain: a cluster analysis in healthy adults. *European journal of pain.* 17:903-915, 2013

40. Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. *Journal of behavioral medicine.* 30:77-94, 2007

41. Li C, Friedman B, Conwell Y, Fiscella K. Validity of the Patient Health Questionnaire 2 (PHQ-2) in identifying major depression in older people. *Journal of the American Geriatrics Society.* 55:596-602, 2007

42. Lund JP, Donga R, Widmer CG, Stohler CS. The pain-adaptation model: a discussion of the relationship between chronic musculoskeletal pain and motor activity. *Canadian journal of physiology and pharmacology.* 69:683 - 694, 1991

43. Mankovsky-Arnold T, Wideman T, Lariviere C, Sullivan MJL. TENS attenuates repetition-induced summation of activity-related pain following experimentally induced muscle soreness. *J Pain.* 14:1416 - 1424, 2013

44. Margolis RB, Tait RC, Krause SJ. A Rating System for Use with Patient Pain Drawings. *Pain.* 24:57-65, 1986

45. Meulders A, Vansteenwegen D, Vlaeyen JW. The acquisition of fear of movement-related pain and associative learning: a novel pain-relevant human fear conditioning paradigm. *Pain.* 152:2460-2469, 2011

46. Meulders A, Vlaeyen JW. The acquisition and generalization of cued and contextual pain-related fear: an experimental study using a voluntary movement paradigm. *Pain.* 154:272-282, 2013

47. Natvig B, Ihlebaek C, Grotle M, Brage S, Bruusgaard D. Neck pain is often a part of widespread pain and is associated with reduced functioning. *Spine.* 35:E1285-1289, 2010

48. Nederhand MJ, Hermens HJ, Ijzerman MJ, Groothuis KG, Turk DC. The effect of fear of movement on muscle activation in posttraumatic neck pain disability. *The Clinical journal of pain.* 22:519-525, 2006

49. Nie H, Arendt-Nielsen L, Madeleine P, Graven-Nielsen T. Enhanced temporal summation of pressure pain in the trapezius muscle after delayed onset muscle soreness. *Experimental brain research.*

Experimentelle Hirnforschung. Experimentation cerebrale. 170:182 - 190, 2006

50. Parr JJ, Borsa PA, Fillingim RB, Tillman MD, Manini TM, Gregory CM, George SZ. Pain-related fear and catastrophizing predict pain intensity and disability independently using an induced muscle injury model. *The journal of pain : official journal of the American Pain Society.* 13:370-378, 2012

51. Quartana PJ, Campbell CM, Edwards RR. Pain catastrophizing: a critical review. *Expert review of neurotherapeutics.* 9:745-758, 2009

52. Spitzer RL, Williams JBW, Kroenke K, al. e: *Patient Health Questionnaire - 9.*, Pfizer Inc.: Prime MD Today., 1999.

53. Staud R. Peripheral pain mechanisms in chronic widespread pain. *Best practice & research. Clinical rheumatology.* 25:155-164, 2011

54. Sullivan MJ, Rodgers WM, Wilson PM, Bell GJ, Murray TC, Fraser SN. An experimental investigation of the relation between catastrophizing and activity intolerance. *Pain.* 100:47-53, 2002

55. Sullivan MJL, Adams H, Sullivan ME. Communicative dimensions of pain catastrophizing: social cueing effects on pain behaviour and coping. *Pain.* 107:220-226, 2004

56. Sullivan MJL, Bishop S, Pivik J. The Pain Catastrophizing Scale: Development and validation. *Psychological assessment.* 7:524-532, 1995

57. Sullivan MJL, Martel MO, Tripp D, Savard A, Crombez G. The relation between catastrophizing and the communication of pain experience. *Pain.* 122:282-288, 2006

58. Sullivan MJL, Rouse D, Bishop SR, Johnston S. Thought suppression, catastrophizing and pain. *Cog Ther Res.* 21:555 - 568, 1997

59. Sullivan MJL, Thorn B, Haythornthwaite JA, Keefe F, Martin M, Bradley LA, Lefebvre JC. Theoretical perspectives on the relation between catastrophizing and pain. *The Clinical journal of pain.* 17:52-64, 2001

60. Sullivan MJL, Tripp D, Santor D. Gender differences in pain and pain behavior: The role of catastrophizing. *Cog Ther Res.* 24:121 - 134, 2000

61. Thomas S, Reading J, Shephard RJ. Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Canadian journal of sport sciences = Journal canadien des sciences du sport.* 17:338-345, 1992

62. Trost Z, France CR, Sullivan MJL, Thomas JS. Pain-related fear predicts reduced spinal motion following experimental back injury. *Pain.* 153:1015-1021, 2012

63. Udermann BE, Mayer JM, Graves JE, Ploutz-Synder LL. Development of an exercise protocol to elicit delayed-onset muscle soreness in the lumbar muscles. *Int Sports J.* 6:128 -135, 2002

64. Udermann BE, Reineke DM, Mayer JM, Murray SR, Battista RA, Uhrich MJ. Developing Delayed Onset Muscle Soreness in the Lumbar Extensor Muscles. *Med Sci Sport Exer.* 38:S387-S387, 2006

65. Vecchiet L, Vecchiet J, Bellomo R, Giamberardino MA. Muscle pain from physical exercise. *J Musculoskeletal Pain.* 7:43 - 53, 1999

66. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain.* 85:317-332, 2000

67. Wideman TH, Sullivan MJL. Differential predictors of the long-term levels of pain intensity, work disability, healthcare use, and medication use in a sample of workers' compensation claimants. *Pain.* 152:376-383, 2011

68. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbroun AS, Masi AT, Mccain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American-College-of-Rheumatology 1990 Criteria for the Classification of Fibromyalgia - Report of the Multicenter Criteria Committee. *Arthritis and rheumatism.* 33:160-172, 1990

69. Yap AUJ, Chua EK, Dworkin SF, Tan HH, Tan KBC. Multiple pains and psychosocial functioning/psychologic distress in TMD patients. *Int J Prosthodont.* 15:461-466, 2002