

# PSYCHOLOGY, PSYCHIATRY, IMAGING & BRAIN NEUROSCIENCE SECTION

## Original Research Article

# Evaluation of How Depression and Anxiety Mediate the Relationship Between Pain Catastrophizing and Prescription Opioid Misuse in a Chronic Pain Population

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### Abstract

**Objective.** We investigated the extent to which anxiety and depression mediate the relationship between pain catastrophizing and the risk of prescription opioid misuse in chronic pain patients.

**Methods.** 215 patients with chronic occupational musculoskeletal disorders completed self-report measures upon admission to a functional restoration program. A bootstrap multivariate regression analysis was conducted to assess how depression and anxiety mediated the relationship between pain catastrophizing and prescription opioid misuse.

**Results.** Catastrophizing, anxiety, and depression predicted higher risk for prescription opioid misuse. Furthermore, anxiety and depression acted as mediators while controlling for the effects of gender and age. Finally, it was found that the effects of catastrophizing on risk for prescription opioid misuse were completely eliminated by those of depression.

**Conclusion.** Due to the partially independent relationship of anxiety and catastrophizing, it is recommended that treatments for chronic pain patients

employ techniques addressing both behaviors. The relationship between depression and catastrophizing requires more research since it was observed that their effects were confounded.

**Key Words.** Chronic Pain; Anxiety; Depression; Catastrophizing; Opioids

### Introduction

Opioids are commonly used to treat both acute and chronic pain [1]. Recently, the use of opioids to treat chronic pain has gained popularity [1], partly due to narrative reports indicating that long-term use of opioids can assist some patients in improving their quality of life and regaining function [2]. Conversely, the prolonged use of opioids to treat chronic pain has caused problems with prescription opioid misuse and addiction to this type of pain medication [3–5]. This has led to prescription opioids being the second most commonly abused substance after marijuana [6].

Studies have found that young age, a history of substance abuse [7,8], higher levels of pain [9], and increased pain sensitivity [10] act as predictors in the development of prescription opioid misuse and addiction. Research has also shown that psychological constructs, such as cognitive styles and negative affect, play a crucial role in the development of opioid misuse and abuse. In fact, researchers have theorized that negative thought processes can lead to fear and avoidant behaviors; which subsequently can decrease an individual's emotional response to pain and increase their risk of misusing and abusing opioids [11]. Catastrophizing is a type of maladaptive cognitive style, and consists of an individual's tendency to exaggerate the threat of a painful experience. Research has indicated that individuals who catastrophize their pain often have a reduced level of self-confidence in their ability to endure the pain [12].

It has long been observed that, among chronic pain patients, those who score higher on catastrophizing scales tend to be at a much higher risk for prescription opioid misuse [9,10,13]. These patients are unable to generate effective thoughts about how to deal with constant pain and often report helplessness and increased levels of pain severity [14], pain sensitivity [15], and negative affect [10].

Therefore, because of this demonstrated distress in individuals with chronic pain, it is important to identify the specific type of psychological constructs that are significantly involved in prescription opioid misuse. Anxiety and depression are two comorbid psychological conditions commonly diagnosed in patients with chronic pain [16]. Furthermore, anxiety [8,17,18] and depression [17,19] have been consistently linked to an increased risk for prescription opioid misuse throughout the literature.

Researchers have theorized that anxiety may be one of the ways through which catastrophizing brings an increased risk for prescription opioid misuse. This may be due to the feelings associated with anxiety causing individuals, who are taking opioids to relieve chronic pain, to change their personal beliefs about their increased need for this type of medication to relieve their pain. Such behaviors have been observed in patients with higher pain sensitivity whose pain-related distress has been shown to be related to increased opioid misuse [10]. As a result, the misuse and abuse of prescription opioids observed in patients scoring high on anxiety [8] could be a coping mechanism to relieve related symptoms of distress [20].

Research has also shown that depression can increase an individual's risk of misusing their opioid medication. In a study of 1,334 participants regarding the usage of their opioid medication, the results indicated that participants, without prior history of substance abuse, were more likely to misuse their opioid medication to relieve stress or assist with sleep, and were more likely to take more of their medication than was prescribed by their physician [19]. Research has shown that opioids have mood altering properties which could increase the risk of misuse in individuals who are experiencing depression symptoms such as insomnia or feelings of hopelessness to alleviate their distress. Furthermore, depression may also cause individuals to experience their pain as more severe and as a result, lead to the misuse of their opioid medication [19].

As mentioned, studies have shown that there are several possible ways through which catastrophizing may lead to increased prescription opioid misuse, such as higher levels of clinical pain, heightened pain sensitivity, alterations in the processing of sensations by the central nervous system, and higher levels of negative affect [13]. However, based on the presented research, there is a lack of literature regarding the effect of depression and anxiety on the relationship between catastrophizing and the increased risk of opioid misuse.

One study has focused on this gap in the literature. Martel et al. (2013) found a partial mediating effect of anxiety between catastrophizing and the increased risk of prescription opioid misuse. However, the effect of depression on the relationship between catastrophizing and prescription opioid misuse was insignificant. Researchers in this study emphasized the need for more research in this area [13].

Therefore, the current study hoped to expand on previous research and on the Martel et al. (2013) study by examining the association of anxiety and depression symptoms on the relationship between pain catastrophizing and risk for prescription opioid misuse, both separately and simultaneously [13]. It was hypothesized that there would be a mediating effect of anxiety and depression between catastrophizing and the risk for prescription opioid misuse for chronic pain patients.

## **Methods**

### *Participants*

Data from 282 chronic pain patients, prescribed opioid medications who were admitted to a functional restoration program between 2009 and 2013, were utilized for this study. Participants were admitted to the program through worker compensation claims that had been approved by their appropriate governing jurisdictions. Exclusion of participant data was based only on inconsistencies in the process of data collection for the variables of interest, which reduced the final sample to 215 patients.

### *Procedures*

Participants completed a 4-week functional restoration treatment protocol, concordant with their workers' compensation claim, and consented to complete questionnaires regarding several physiological and psychological measures that are relevant to their treatment. Participants' data included in this study indicated that the patients were prescribed opioid medication by a clinician upon admission and during their time at the program. However, the type of opioid medication or the prescribed amount was not recorded in the database. The questionnaires were administered upon admission, which served as the baseline measure. The functional restoration program consisted of an interdisciplinary approach which involved the following: medical evaluation and management, physical therapy, occupational therapy, mindfulness therapy, group therapy, Pilates, yoga, and nutrition consultations. Only the data collected at the time of the patients' admission into the program were utilized for this study.

### *Measures*

#### **Demographic Information**

Patients admitted into the program were asked for the following information: sex, age, ethnicity, area of injury

(which included: lumbar, thoracic, cervical, upper extremity, and lower extremity, and total body).

### Psychosocial Assessments

The *Beck Anxiety Inventory* (BAI) [21] is a 21-item scale used to assess the severity of anxiety in individuals. The items in the scale are symptoms of anxiety which participants have to rate based on their perceptions of how much they are affected over the past week through the use of a 4-point scale which ranges from 0 (Not at all) to 3 (Severely-I could barely stand it). The BAI has been found to be reliable and valid in measuring symptoms related to anxiety severity [21,22]

The *Beck Depression Inventory II* (BDI-II) [23] is a 21-item self-report measure used to assess the presence and severity of depressive symptoms in individuals. The items in the scale are rated using a 4-point scale rated from 0 to 3 which reflect severity in a range that goes between neutral and maximum amount. The BDI-II has consistently shown good reliability and validity in measuring symptoms of depression [24].

The *Coping Skill Questionnaire* (CSQ) [25] is a self-report measure consisting of seven subscales which measure cognitive and behavioral strategies used by people who cope with pain. The items in this questionnaire use a 7-point scale to rate how much each coping strategy is used. For the purposes of this study, only the catastrophizing subscale (CSQ-CAT) was used as it specifically measures pain catastrophizing and also because it has been observed to have a good internal consistency [26].

The *Current Opioid Misuse Measure* (COMM) [27] is an instrument aimed at identifying indicators of current medication misuse among patients with chronic pain taking opioids. It consists of 17 items that ask patients about how they are using their medication through the use of questions that describe usage over the past 30 days which can be rated from 0 (Never) to 4 (Very often). This scale has shown good validity and reliability when compared with other self-report measures of prescription opioid misuse [28]

Finally, pain intensity was measured through the use of four items that ask for reports about average, least, and worst pain in the past 24 h, as well as pain right now, through the use of a Likert-scale which ranges from 0 to 10. For the purposes of this study, the measure of "average pain" was used for comparing reports of pain between males and females.

### Statistical Methods

All analyses were conducted using SPSS version 22. Data were screened for outliers and missing data, and tested for normality of continuous variables. For univariate analyses, independent samples *t*-tests were used to

measure differences by gender among the main variables: pain catastrophizing (CSQ-CAT), risk of prescription opioid misuse (COMM), anxiety (BAI), depression (BDI-II), and average pain. Pearson correlations were used to assess the relationship between main variables. To test the mediating effects of anxiety and depression, **a bootstrapping hierarchical** mediation regression analysis, using 5,000 bootstrap resamples, was conducted according to the methods described by Preacher and Hayes (2008) [29]. Additional hierarchical regression analyses were conducted to test the individual mediating effects of depression and anxiety between catastrophizing and risk of **prescription** opioid misuse. Due to previous research which regarded age and gender as important variables in the study of risk of prescription opioid misuse, [21,30–32] these variables were included in the analyses as possible covariates. The alpha level was set at 0.05.

### Results

Descriptive analyses revealed that the sample was comprised of 61.4% males and 38.6% females and the median age was 46.2. Furthermore, the ethnicity of participants included: whites (48.4%), Hispanic/Latino (38.6%), and African Americans (13%). In addition, the area of injury was also recorded and is shown in Table 1. The results of the independent samples *t*-tests, as observed in Table 2, show that gender was not significantly associated with any of the main variables except for **BDI-II**, for which females showed higher levels of depression severity ( $P=0.04$ ).

Bivariate correlations among variables revealed that COMM, CSQ-CAT, BAI, **BDI-II**, and the average pain of participants significantly correlated with each other ( $P<0.05$ ). The Pearson coefficients for the correlations can be seen in Table 3. It can be noted that all the

**Table 1** Descriptive data for study measures

	Full Sample (n=215)
Age	$M=46.22$ (SD = 10.03)
Gender	
Male	61.4% (n=132)
Female	38.6% (n=83)
Ethnicity	
White	48.4% (n=104)
Hispanic/Latino	38.6% (n=83)
African American/Black	13% (n=28)
Area of injury	
Lumbar	44.7% (n=96)
Thoracic/cervical	6.5% (n=14)
Upper extremity	13.5% (n=29)
Lower extremity	14.9% (n=32)
Multiple areas	20.5% (n=44)

**Table 2** *t*-tests for gender

	Male M (SD)	Female M (SD)	<i>P</i>
Pain Catastrophizing (CSQ-CAT)	13.45 (8.80)	14.66 (8.83)	0.326
Risk of Opioid Misuse (COMM)	10.82 (8.98)	10.65 (8.42)	0.887
Anxiety (BAI)	16.33 (12.33)	18.82 (13.5)	0.167
Depression (BDI-II)	18.7 (11.63)	22.21 (13.05)	0.041
Average Pain	5.51 (1.65)	5.69 (1.82)	0.474

*t*-tests revealed no differences between males and females except for BDI-II.

**Table 3** Correlations among measures

	1	2	3	4	5	6
1. Age	–	–0.02	–0.07	0.07	–0.001	0.11
2. COMM		–	0.45***	0.54***	0.61***	0.16*
3. CSQ-CAT			–	0.543***	0.62***	0.31***
4. BAI				–	0.63***	0.34***
5. BDI-II					–	0.19**
6. Average Pain						–

COMM, Current Opioid Misuse Measure; CSQ-CAT, Coping Skills Questionnaire-Catastrophizing subscale; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory.

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

correlations among COMM, CSQ-CAT, BAI, **BDI-II**, and average pain were positive.

In addition, a series of regressions were conducted to test the possible mediating effects of BAI and **BDI-II** in the relationship between CSQ-CAT and COMM. The results of the regressions suggest that catastrophizing significantly predicted both anxiety,  $B = 0.80$ ,  $t(213) = 9.51$ ,  $P < 0.001$ , and depression  $B = 0.86$ ,  $t(213) = 11.42$ ,  $P < 0.001$ . Furthermore, anxiety and depression significantly independently predicted risk for prescription opioid misuse,  $B = 0.17$ ,  $t(213) = 3.55$ ,  $P < 0.001$ , and  $B = 0.31$ ,  $t(213) = 5.74$ ,  $P < 0.001$ , respectively. The effect of catastrophizing on the risk for prescription opioid was also significant,  $B = 0.45$ ,  $t(213) = 7.41$ ,  $P < 0.001$ .

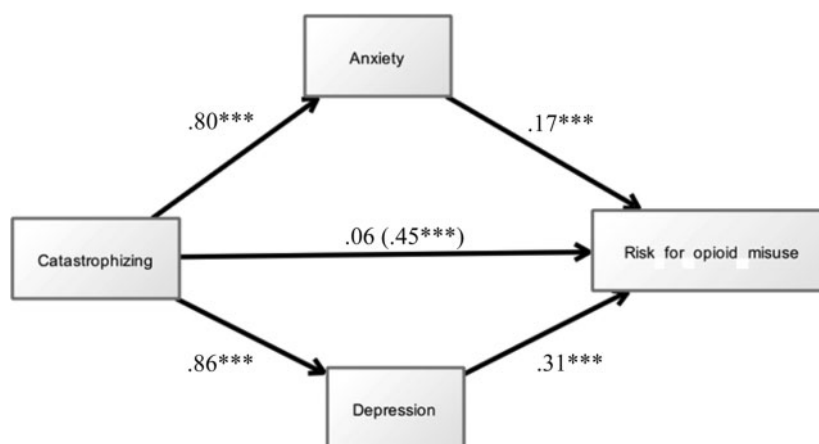
However, when anxiety and depression were included together with catastrophizing to predict risk for prescription opioid misuse, the effect of catastrophizing became nonsignificant,  $B = 0.06$ ,  $t(213) = 0.80$ ,  $P = 0.43$ . As the regression analyses suggested that anxiety and depression might play a mediating role between catastrophizing and the risk for prescription opioid misuse, the bootstrap mediation analysis indicated that both the mediating effects of anxiety and depression were significant. The indirect effect of catastrophizing on the risk for prescription opioid misuse through anxiety is 0.14, with a 95% CI [0.05, 0.24], and the indirect effect of catastrophizing on the risk for

prescription opioid misuse through depression is 0.26, with a 95% CI [0.17, 0.40]. Figure 1 shows the indirect effect of catastrophizing on the risk for prescription opioid misuse through the mediating effect of anxiety and depression.

Next, two hierarchical regressions were conducted to assess in more detail whether catastrophizing contributed any significant unique variance to risk for prescription opioid misuse while controlling for anxiety and depression separately. In the first hierarchical regression, age, gender, and anxiety are controlled for and it was found that BAI explained 29.5% of the variance in COMM after controlling for age and gender,  $F_{\text{change}}(1, 211) = 88.475$ ,  $P < 0.001$ . CSQ-CAT was then included in a third model and it was observed that it explained 3.5% of the variance in COMM, after controlling for age, gender, and BAI,  $F_{\text{change}}(1, 210) = 10.981$ ,  $P < 0.01$ . As it can be seen in Table 4, the contribution of CSQ-CAT in predicting COMM remained significant after controlling for BAI, although it went down from 21% to 3.5%. Finally, in a second regression, depression was added to the model and it was found that **BDI-II** explained 37.8% of the variance in COMM after controlling for age and gender,  $F_{\text{change}}(1, 211) = 128.13$ ,  $P < 0.001$ . CSQ-CAT was then included in a third model and it was observed that it explained 0.9% of the variance in COMM, after controlling for age, gender, and BAI,  $F_{\text{change}}(1, 210) = 3.07$ ,  $P < 0.01$ . As it can be seen in Table 5, the association between **CSQ-CAT and COMM** became insignificant after controlling for **BDI-II**.

## Discussion

The relationship between catastrophizing and pain has been repeatedly demonstrated to be significant throughout the literature [14,15]. Previous literature has also shown that anxiety and depression can have negative effects on pain and an increased risk of misusing opioids [6,33,34]. However, as mentioned, there is a lack of research regarding the mediating effects of depression and anxiety in the relationship between pain and prescription opioid misuse. The results obtained in this study suggest that both anxiety and depression can act as mediators in this relationship.



**Figure 1** Indirect effect of catastrophizing on the risk for opioid misuse through anxiety and depression. Note: \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$

**Table 4** Hierarchical multiple regression analyses examining the influence of catastrophizing on risk for prescription opioid misuse while controlling for anxiety

	B	SE B	B	R <sup>2</sup>	R <sup>2</sup> Change	F change	df
Step 1				0.00	0.00	0.042	(2, 212)
Age	0.015	0.061	0.018				
Gender	.221	1.24	0.012				
Step 2				0.296	0.295	88.475***	(1, 211)
BAI	0.373	0.040	0.547				
Step 3				0.331	0.035	10.981**	(1, 210)
CSQ-CAT	0.223	0.067	0.225				

COMM, Current Opioid Misuse Measure; CSQ-CAT, Coping Skills Questionnaire-Catastrophizing subscale; BAI, Beck Anxiety Inventory.

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

**Table 5** Hierarchical multiple regression analyses examining the influence of catastrophizing on risk for prescription opioid misuse while controlling for depression

	B	SE B	B	R <sup>2</sup>	R <sup>2</sup> Change	F change	df
Step 1				0.00	0.00	0.042	(2, 212)
Age	0.015	0.061	0.018				
Gender	0.221	1.24	0.012				
Step 2				0.378	0.378	128.13***	(1, 211)
BDI-II	0.442	0.039	0.621				
Step 3				0.387	0.009	3.07	(1, 210)
CSQ-CAT	0.120	0.069	0.121				

COMM, Current Opioid Misuse Measure; CSQ-CAT, Coping Skills Questionnaire-Catastrophizing subscale; BDI-II, Beck Depression Inventory.

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

The results from this study demonstrate that the CSQ-CAT can be very useful in allowing researchers to study relationships between catastrophizing and risk for prescription opioid misuse, as measured with the COMM,

with significant results. Furthermore, these results should be reassessed on different samples which may vary in core characteristics such as age, ethnicity, type of injury, and length of injury to test whether they remain



consistent. Previous research has shown that factors such as low self-efficacy [35], poor pain coping skills [36], impulsivity and sensation seeking [37,38], and social environment [39] are responsible for increasing the risk of substance use. Therefore, it would be beneficial to address how they may interact with catastrophizing on individuals with different types of chronic pain and their risk for prescription opioid misuse.

Our analysis indicated that, consistent with previous studies [8,17,18], individuals who scored high in anxiety have an increased risk to misuse prescribed opioid medications. This study also found that anxiety can act as a partial mediator in the relationship between pain catastrophizing and the risk for prescription opioid misuse. Additionally, it was observed that the effect of anxiety through catastrophizing can increase the risk for opioid misuse independently from the symptoms of depression. Studies have shown that one of the reasons why chronic pain patients may overuse opioids is to gain control over their situation by trying to lessen negative psychological states [17,20,40]. Therefore, it would not be a surprise that chronic pain patients suffering from high levels of anxiety might overuse prescription opioids to attempt to deal with the enduring distress.

Furthermore, hierarchical regression analysis showed that catastrophizing is partially independent from anxiety in its relationship to risk for opioid misuse. This finding is consistent with Martel et al. [21] and would suggest that when considering possible strategies to treat chronic pain patients at risk for prescription opioid misuse, it is important to implement those which address symptoms of both catastrophizing and anxiety.

It was also observed that chronic pain patients who scored high on depression were more likely to present a higher risk for **prescription** opioid misuse. This finding is consistent with previous research which has shown this type of relationship within patient populations suffering from arthritis, fibromyalgia, low back pain, migraine headaches, neck or joint pain, and neuropathy [6]. However, the results from this study also showed that although catastrophizing was associated with increased risk for prescription opioid misuse, the effect of catastrophizing on the increased risk for opioid misuse was completely eliminated once depression was simultaneously assessed.

Research has established that catastrophizing acts as a cognitive distortion that mediates the relationship between pain and depression [41]. However, the effect that depression has in chronic pain patients is not entirely clear as previous studies have reported that depression can cause or be a consequence of increased pain [42,43]. This proposition is important because a catastrophizing coping style (rumination, magnification, helplessness) could be confused with the cognitions of a depressed person.

In addition, the results obtained in this study can also be explained by problems in the multidimensionality of

the instruments used. Indeed, it has been observed that when compared to the Pain Catastrophizing Scale (PCS), which is a well-utilized method of self-assessment for catastrophizing, CSQ-CAT has been related mostly to the helplessness dimension of PCS which is linked to pessimistic cognitions and depression [44]. These findings would suggest that if this study were to be repeated with a different method of assessing catastrophizing, such as the PCS, or a different method of assessing depression, perhaps the results could have been different.

Some researchers argue that the use of catastrophizing as a coping strategy can actually have positive outcomes when individuals are dealing with acute pain as increased empathic support from others tends to be beneficial [45]. For example, Keefe et al., reported that cancer patients who scored high in catastrophizing received more caregiver support when compared to those who scored low in catastrophizing [46]. Furthermore, Giardino et al. observed that patients who perceived more kindness from a spouse exhibited more catastrophizing and pain reports [39]. In another study, researchers filmed patients experiencing chronic pain performing physical activities. Results from this study illustrated that high catastrophizers displayed more pain behaviors even when controlling for pain severity which allows them to elicit helplessness [36].

Although catastrophizing can be beneficial in some cases, during prolonged chronic pain conditions, catastrophizing will usually bring about interpersonal conflict, rejection from others [46], and as observed in this study, depression, and anxiety. Therefore, it could be beneficial to study additional factors that may limit the degree to which chronic pain patients engage in catastrophizing behaviors. In addition, due to the relationship that catastrophizing, anxiety, and depression can have in increasing the risk for prescription opioid misuse in chronic pain patients, it is important that future studies further assess any possible associations with substance abuse of other drugs. Some examples of the most common substances abused by chronic pain patients include alcohol, marijuana, nicotine, sedatives, stimulants, heroin, cocaine, and hallucinogens [6].

This study is not without limitations. The cross-sectional nature of its design does not allow us to make any long-term conclusions with regards to our participants. In addition, we were not able to verify the duration of the opioid treatment, specific dose or type of opioids, nor the presence of any other type of medication prescribed which might have altered the results observed here. Furthermore, it should be acknowledged that this study employed self-report measures for assessing all of the variables of interest. Future studies could address these issues by employing more objective measures such as urine drug screens and/or physician assessments. Although researchers from the present study felt that the sample was representative of the population of

people diagnosed with chronic pain under worker's compensation and the sample size was adequate enough for the amount of variables used in our regression analyses, replication of this study, specifically paying special attention to area of injuries, is warranted.

Although some research has been done in recent years to decipher the nature of pain catastrophizing, anxiety, depression, and their relationship to medication misuse among chronic pain patients, more research is necessary. The implications of this study are important as they can lead future research to focus toward the development of treatments that individually address catastrophizing and anxiety in chronic pain patients with risk for prescription opioid misuse, and to study in-depth the relationship between depression and catastrophizing.

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