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Association of Catastrophizing and Fatigue: A Systematic Review

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Individuals with chronic illness suffer from debilitating symptoms, such as pain, fatigue, and sleep impairment. Of these three symptoms, fatigue is reported to negatively impact quality of life, and in the worst instances, lead to disability [1]. Studies report that debilitating fatigue is experienced by nearly 50% of cancer patients, 80% of patients with rheumatic disease or fibromyalgia, and 90% of patients with multiple sclerosis [2–4]. Fatigue lasting longer than 6 months not only negatively impacts individuals physiologically [1], but economically [5]. In 1994, the United States (US) Centers for Disease Control and Prevention published the diagnostic criteria for chronic fatigue syndrome (CFS) [6]. The prevalence of CFS in the US is about 42 cases per 10,000 population, valuing as high as US \$7 billion of direct cost for medical care, annually [7]. The etiology of chronic fatigue remains elusive and its management continues to challenge practitioners and burden individuals.

Fatigue is defined as persisting and distressing physical, emotional, and cognitive exhaustion that is unrelated to the recent activity and interferes with the person's function [8]. Several psychological conditions such as depression, anxiety, stress, and catastrophizing have been associated with fatigue [9–12]. Among these psychological conditions, the relationship between catastrophizing and fatigue is the least explored. In this paper, articles that evaluated the association between catastrophizing and fatigue were systematically reviewed.

Catastrophizing is a psychological process characterized by maladaptive, negative evaluation and attention to specific symptoms [13–15]. When a person catastrophizes, it can contribute to increased intensity of the symptom experience and more emotional distress [16]. It has been used to evaluate stressful situations, where it is used as a primary and/or a secondary appraisal mechanism [17]. According to Lazarus and Folkman [18], primary appraisal mechanisms are affective projections of the impact of the stressful condition on the individual's well-being (e.g., "My condition will never get any better."), while secondary appraisals are cognitive processes that are ongoing in order to address the stressful situation (e.g., "There is no way I can go on any longer."). The multidimensional concept of catastrophizing is believed to be composed of three elements: rumination ("I can't stop thinking how exhausted I am."), magnification ("I worry that something worst will happen

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to me."), and helplessness ("Being exhausted all the time, is awful and overwhelming.") [19].

In pain studies, catastrophizing is known to significantly predict greater severity of pain behaviors, as well as increase the use of analgesics and health care services [14, 20–22]. Moreover, high catastrophizing is believed to influence the activities of neurotransmitters that act on brain structures that are involved with attention, emotion, and motor activity in response to pain [21]. Catastrophizing is very important to consider in measuring fatigue, because in the pain literature, if excessive negative attention is afforded to a symptom such as pain, individuals often avoid activities that can cause pain, therefore decreasing their physical functioning [23]. Decreased functional capacity in both cardiorespiratory and neuromuscular functioning due to lack of physical activity is an important contributor to persistent fatigue [24]. This review will examine the relationship between catastrophizing and fatigue, as well as, estimate the impact of catastrophizing on fatigue intensity.

Methods

An initial generic search in PubMed published at any date using the following key words as titles, "Fatigue AND Catastrophizing" yielded 39 articles. A basic search query based on the common terms from the 39 articles was developed. These common key words/phrases include: ("fatigue" [MeSH Terms] OR "fatigue" [All Fields]) AND ("catastrophization" [MeSH Terms] OR "catastrophization" [All Fields] OR "catastrophizing" [All Fields] OR "catastrophic" [All Fields]). This basic search query from PubMed yielded 130 articles (including the 39 articles found in the initial generic search). Search on other online databases using the key words, ("fatigue" [MeSH Terms] OR "fatigue" [All Fields]) AND ("catastrophization" [MeSH Terms] OR "catastrophization" [All Fields] OR "catastrophizing" [All Fields] OR "catastrophic" [All Fields]), yielded 52 articles using SCOPUS, 21 articles using PsycINFO, and 65 articles using EMBASE. Refinement of the search criteria was applied by excluding review, editorial, case studies, meta-analysis articles and those not written in English from the 268 articles initially found from all databases. The refined search yielded 22 articles. The abstracts of the 22 articles were visually reviewed to determine if they met the inclusion criterion of mentioning the role, influence, and/or association of catastrophizing with the level, duration and/or worsening in intensity of fatigue. We expanded the search to encompass broader key words to include, ("negative thinking" [MeSH Terms] OR "negative thoughts" [MeSH Terms] OR "negative affect" [MeSH Terms] OR "catastrophe" [MeSH Terms] OR "catastrophizer" [MeSH Terms] OR "catastrophize" [MeSH Terms] AND "tiredness" [MeSH Terms] OR "loss of energy" [MeSH Terms] in PubMed, SCOPUS, PsycINFO and EMBASE. The expanded search yielded 3,361 articles. We refined the expanded search by selecting articles that were healthrelated articles and excluded review, editorial, case studies, meta-analysis articles, and those not written in English. This expanded search yielded 274 articles. Further refinement was conducted to limit the search to articles that were specific to psychological behavior and/or distress. This further selection yielded 49 articles. The abstracts of these 49 articles were individually reviewed to select articles that specifically investigated the association of the concept of catastrophizing (e.g., negative thinking, negative affect) and fatigue (e.g., tiredness, loss of energy). The initial and expanded searches with the individual inspection of the 71 abstracts (initial search = 22 abstracts + expanded search = 49 abstracts) yielded 14 publications (13 articles and 1 dissertation) to be included in this review.

To estimate the magnitude of the association between catastrophizing and fatigue, effect sizes were calculated from the statistical data provided by each reviewed article. These effects sizes were expressed as correlation coefficient *r* because most of the reviewed articles reported associations between two continuous variables, catastrophizing and fatigue,

and *r* values have been reported to provide the most versatile effect size in investigating associations of binary data [25] The magnitude of the relationships between variables using correlation coefficient can vary from small effect size of r = 0.10, moderate effect of r = 0.24, to a large effect size of r = 0.37 [25].

Results

Fourteen publications were included in this review. The earliest article was published in 1995 [26] and 71% (n = 10) were published from 2004 to the present. Approximately 50% (n = 7) were written by one research team using a similar patient population (women with early stage breast cancer) [11, 12, 27–31]. Clinical populations investigated in the articles were early stage breast cancer (50%, n = 7 articles), chronic fatigue syndrome (21.3%, n = 3), multiple sclerosis (14.3%, n = 2), fibromyalgia (7.1%, n = 1) and healthy volunteers (7.1%, n=1). A significant relationship between catastrophizing and fatigue (p < 0.05) was found in all studies except one [32]. Table 1 summarizes the associations between catastrophizing and fatigue in the reviewed articles.

Cancer

Seven studies explored the association of catastrophizing and fatigue in women with early stage breast cancer [11, 12, 27–31]. Five longitudinal and two cross-sectional studies were conducted by the same research group. Three of the five longitudinal studies measured the association between catastrophizing and fatigue before and immediately after completion of cancer treatment [27, 28, 31], while the remaining two longitudinal studies measured the association between these variables from completion of cancer treatment up to 42 months post treatment [12, 30]. The results of these longitudinal studies are discussed in detail below.

All studies defined catastrophizing as a cognitive process that involved negative outcome expectations (e.g., thinking that fatigue will get worse, fatigue will cause something to get seriously wrong). Catastrophizing in these studies was measured using the Fatigue Catastrophizing Scale (FCS), a modified version of a catastrophizing scale from the Cognitive Coping Strategies Inventory, which is a 10-item instrument using a 5-point rating scale (1= never true) to (5 = all the time true) with proven high internal consistency reliability (coefficient alpha = 0.85 - 0.92) [27, 28, 31, 32]. These studies showed that high catastrophizing was a significant predictor of fatigue severity (r^2 change = 0.14, p < 0.001) [29], (t = 7.42, p < 0.01)[31] and intensity (t = 7.48, p < 0.0001)[32], as well as a significant predictor of the prevalence of off treatment cancer-related fatigue (Odds ratio = 1.19, p < 0.001) [27].

One study found that fatigue catastrophizing was not significantly different among four groups of breast cancer patients (former radiotherapy group, current radiotherapy group, current chemotherapy group, and current bone marrow transplantation [BMT] group), however, younger subjects reported higher fatigue catastrophizing than older subjects [11]. When subjects were grouped into high and low catastrophizing using their FCS scores (cutoff score = 16), high catastrophizing subjects reported almost three times higher fatigue than low catastrophizing subjects [11]. Another study showed a significant association of high catastrophizing not only with fatigue severity but also with disruptiveness in daily function. A longitudinal study showed that the level of catastrophizing at pretreatment significantly predicted fatigue severity and its disruptiveness of daily function at post treatment in subjects receiving radiotherapy, but not in those receiving chemotherapy [31]. These differences may be related to the variability in demographic/clinical variables, side effects, or severity of fatigue experienced by patients during chemotherapy versus those

experienced by patients during radiotherapy [33]. Further investigation is necessary to understand this finding.

Three studies investigated the association of catastrophizing and fatigue post cancer treatment. One study showed that women with high fatigue were more likely to be single, have low income, have high Blatt Menopausal Index (BMI), high catastrophizing, and low physical activity [30]. Only BMI (r^2 change = 0.36, p < 0.001) and catastrophizing (r^2 change = 0.14, p < 0.001) significantly predicted post breast cancer treatment fatigue [30]. A second study investigated the incidence of cancer-related fatigue (CRF) at 6 and 42 months post treatment [12]. Characteristics associated with CRF, such as age, body mass index, disease stage, obesity (defined as body mass index 30 kg/m^2), postmenopausal, catastrophizing, history of major depression, and type cancer treatments (RT only, CT only, or CT+RT) were compared between CRF cases and non-CRF cases. The result showed that fatigue catastrophizing scores were significantly higher in the CRF cases than in the non-CRF cases at 42 months post treatment (p < 0.01) [12]. Catastrophizing was not significantly different at 6 months post-treatment between the two groups, which may be related to the differences in the distribution of subjects between the groups (CRF, n = 26; non-CRF, n =256). Another study examined the influence of catastrophizing on the memory of the fatigue experience by examining the magnitude of response shift in fatigue rating overtime, pre and immediate post cancer treatment [28]. This study demonstrated that high catastrophizing was significantly associated with small response shifts in fatigue ratings [28], which suggested that recall and momentary self-report of fatigue scores of these patients were closely identical. Four of the seven cancer articles in this section showed moderate to large associations of catastrophizing on fatigue severity [11, 27, 29, 30].

Chronic Fatigue

Two longitudinal and one cross-sectional studies examined catastrophizing in individuals with chronic fatigue syndrome (CFS) [26, 34, 35]. One of the two longitudinal studies was a natural history study [35], and the other was an interventional study [36]. The natural history study investigated the association between catastrophizing and fatigue weekly for three weeks [35], while the interventional study measured the association of these variables pre and post (2 and 6 months) mindfulness-based cognitive therapy (MBCT) [36]. The results of these studies are discussed in detail below.

Catastrophizing was defined in these three studies as a belief that fatigue can cause negative outcomes such as dying [26, 34, 35]. One study measured catastrophizing by coding (catastrophizing versus noncatastrophizing) the patients' responses to the question, "what would be the consequences of pushing yourself beyond your present physical state?" [26]. The reliability of coding patients' responses was confirmed by three raters, which showed agreement ratings of 84% and 88%. Another study used the 6-item catastrophizing subscale from the Cognitive and Behavior Responses to Symptoms Questionnaire (CBRSO) [35], while the third study used the 10-item catastrophizing subscale of the Fatigue-Related Cognition scale, which demonstrated acceptable internal consistency reliability ($\alpha = 0.79$) [34]. Individuals with CFS grouped as high catastrophizers reported significantly greater fatigue severity than the non-catastrophizers [26]. Although the high catastrophizers and non-catastrophizers experienced the same number of CFS-related symptoms, the high catastrophizers reported significantly greater disruption of fatigue with their activities of daily living than the non-catastrophizers [26]. High levels of catastrophizing and depression in CFS were associated with low discrepancies between recall and momentary fatigue rating (r=0.43, p<0.01) [34], which suggests that high catastrophizing patients recalled fatigue more accurately than the low catastrophizing patients. One study investigated the effect of MBCT on fatigue by specifically targeting catastrophizing [36]. Both fatigue and catastrophic thinking of CFS patients decreased immediately, at two and six months after

MBCT [36]. This result indicated that catastrophizing may serve as a behavioral marker that can be a target for fatigue reduction intervention like MBCT. Two of the three articles reviewed in this section showed small to moderate associations of catastrophizing on fatigue severity [26, 35] and one showed a large association of catastrophizing on momentary fatigue and fatigue recall discrepancy [34].

Multiple sclerosis

Two cross-sectional studies explored the association between fatigue and catastrophizing in patients with multiple sclerosis (MS) [37, 32]. Both studies defined catastrophizing as fearful interpretations of the meaning of symptoms that are characterized by exaggerated negative thinking, magnification of symptoms, and helplessness (e.g., fatigue is a sign of something bad or a sign that the body is being damaged) [36, 37]. One study used the Dutch version of the 16-item fatigue catastrophizing scale (FCS), which is a modified pain catastrophizing scale with three additional MS-specific items to measure catastrophizing [37]. This modified fatigue catastrophizing scale showed high internal consistency reliability ($\alpha = 0.91$) in this study [36]. Using structural equation modeling, this study showed that catastrophizing was a key factor in mediating the relationship between fatigue and fatigue-related fear and avoidance behaviors, based on the cognitive behavioral model [37]. The other study investigated the influence of catastrophizing on fatigue, specifically in patients with active, relapsing-remitting MS [37].

This study used the 4-item catastrophizing scale from the cognitive and behavioral response to symptoms. The cognitive and behavioral response to symptoms has seven subscales: somatic attribution, symptom-focusing, catastrophizing, damaging, embarrassment, all-or nothing, and avoidance/resting, in which all of these subscales showed acceptable internal consistency reliability with Cronbach's alphas ranging from 0.72 to 0.88 [37]. The result of this study showed that the catastrophizing subscale scores are related to levels of physical fatigue (r = 0.30, p < 0.001) and mental fatigue (r = 0.20, p < 0.05). However, when the predictive value was evaluated on all cognitive and behavioral variables, catastrophizing was not found to be a significant predictor for both physical and mental fatigue [37].

Other Medical Conditions

The association of catastrophizing and fatigue was also examined in individuals with fibromyalgia (FM). A longitudinal study compared the differences of evening fatigue levels between FM patients who were high and low catastrophizers [38]. Catastrophizing was defined as a coping strategy for pain, and was measured by the catastrophizing subscale of the coping strategies questionnaire, which showed acceptable internal consistency reliability (coefficients = 0.78), in this study [38]. Thirty FM women were categorized into high catastrophizing (catastrophizing score above 75 percentile, n = 16) and low catastrophizing (catastrophizing score below 25 percentile, n = 14) groups. Daily evening fatigue scores were collected for 56 days (8 weeks) and compared between the two groups, which showed that FM women in the high catastrophizing group reported significantly higher evening fatigue level than those in the low catastrophizing group (t = 3.2, p < 0.01) [38]. A hierarchical linear regression model showed that FM women in the high catastrophizing group were more likely to report higher morning pain intensity and were associated with higher increases in fatigue levels by the end of the day ($\beta = 0.55, p < 0.01$) than the low catastrophizing group [38].

Another cross-sectional study showed a significant association between catastrophizing and fatigue in a healthy community sample using the 16-item FCS (r = 0.64, p < 0.01) [39]. Hierarchical linear regression modeling further revealed strong association of catastrophizing ($\beta = 0.39$) and emotional distress ($\beta = 0.45$) with fatigue severity [38]. Both

Discussion

This is the first study to systematically review the literature on the association of catastrophizing and fatigue. Significant associations between catastrophizing and fatigue were reported in the reviewed articles, and most of these articles suggest that catastrophizing influences the fatigue experience. However, a number of inconsistencies were found that may influence the interpretations of the findings.

Most of the reviewed articles showed strong, significant associations between high catastrophizing and high fatigue severity [11, 12, 27, 29–31, 36–39]. Twelve of the 14 reviewed studies showed moderate to high association (r > 0.37) of catastrophizing on fatigue severity [11, 12, 27, 29–32, 35–39], suggesting that catastrophizing is an important variable to consider when measuring fatigue severity. Patients with high catastrophizing reported higher fatigue severity than patients with low catastrophizing [30]. High catastrophizing individuals reported more fatigue-related disruption in their functional performance compared to low catastrophizers [26, 31]. Patients with high catastrophizing also recalled fatigue more accurately than patients with low catastrophizing [28, 34]. Catastrophizing was shown to be a good predictor of fatigue in healthy volunteers [39], in cancer patients during [11, 29] and post cancer treatment [12, 27], and may even serve as a possible behavioral marker for fatigue intervention [33]. Catastrophizing seems to mediate the relationship between pain and fatigue, where high catastrophizers were more likely to report higher pain intensity, which in turn was associated with higher increases in fatigue levels [38]. Even with the positive significant association observed between high catastrophizing and high fatigue, the 14 reviewed studies only enrolled individuals from five medical conditions (cancer, chronic fatigue syndrome, fibromyalgia, multiple sclerosis, healthy individuals). Moreover, only 8 of the 14 studies used a longitudinal design.

Catastrophizing was also defined differently among the reviewed articles. Nine studies viewed catastrophizing as a coping strategy, describing it as a negative exaggeration of the person's evaluation of the fatigue experience [11, 12, 27-31, 38, 39], while five studies defined catastrophizing as a negative thought and belief related to physical limitation [26, 34–37]. While belief can be considered as a cognition that influences the appraisal process, a coping strategy is a process that occurs after the event is evaluated and the individual has used catastrophizing as a tool to deal with the stressful event [18]. Based on the stress and coping theory, beliefs serve as a "perceptual lens" to determine the meaning of stressful events, which can be influenced by past history, experience, and culture [18]. As a negative belief, catastrophizing can lead to negative responses (e.g., avoiding physical activity, depression, motivational deficit) to fatigue. As a coping strategy, fatigued individuals use catastrophizing to exaggerate the display of symptom expression to maximize assistance or empathy from others [16]. Conceptually defining catastrophizing is important in any investigative exploration, because it can help clarify the research questions and its relationships with other variables of the study. The definition of catastrophizing remains an issue of intense discussion in the pain literature.

In the pain literature, the role of negative personality traits, such as neuroticism in the relationship of catastrophizing and pain has been extensively investigated [40, 41, 42]. These studies suggested that high neuroticism individuals were more likely to catastrophize and more likely to report more intense pain and more negative mood [41, 42]. One study further established the high correlation between neuroticism and catastrophizing [43]. None of the reviewed articles investigated the role of personal trait variables on the association

between catastrophizing and fatigue. This is an important issue to address in future studies to determine the extent of the influence of negative personality traits on the relationship between catastrophizing and fatigue. Six different instruments were used to measure fatigue catastrophizing in these 14 reviewed articles. The Fatigue Catastrophizing scale (FCS) was used to measure catastrophizing in eight of the reviewed articles [11, 27–31]. Items in this instrument were modified from the Cognitive Coping Strategies Inventory (CCSI) and validated in patients with postoperative fatigue [44]. The second instrument used was a fatigue catastrophizing scale that was adapted from the Pain Catastrophizing Scale (PCS). This scale was used in two studies, one using healthy volunteers [39], and the other added three items related to fatigue specific in multiple sclerosis [36]. Although the items in the PCS and FCS are similar, no study investigated the similarities and differences between the two scales. Four other fatigue catastrophizing instruments were used in the reviewed articles, in which one coded subjects' responses to the question, 'what would be the consequences of pushing yourself beyond your present physical state?' [26]. The question asked by this semi-qualitative instrument was not specifically aimed to measure fatigue, but the individual's perception of his/her physical capacity to perform activities of daily living. Another instrument used by the reviewed articles was the catastrophizing subscale of the Fatigue-related Cognitions Scale [34]. Similar to pain catastrophizing measurement, this subscale reflects three dimensions of catastrophizing: magnification (exaggerating the worse possible), rumination (unnecessary focus on symptom), and helplessness (perceived inability to deal with the situation). This instrument was developed and validated in patients with chronic fatigue syndrome [45]. Another instrument used by the reviewed articles was a catastrophizing subscale from the Cognitive and Behaviour Responses to Symptoms questionnaire (CBRSQ) [35, 37]. This instrument focused on measuring catastrophic thoughts. Another instrument is the coping strategies questionnaire, which is widely used to measure catastrophizing as a coping method [39]. All the reviewed articles selected the questionnaires based on the definition of catastrophizing they want to measure. Catastrophizing subscale from the CBRSQ and catastrophizing subscale from the Fatiguerelated Cognition Scale appear to appropriately measure catastrophizing as a belief because their items attempt to describe catastrophizing as a negative perception of events related to their fatigue symptoms. On the other hand, the coping strategies questionnaire, together with the fatigue catastrophizing scales that were modified from two different instruments: Cognitive Coping Strategies Inventory and Pain Catastrophizing Scale were designed to measure catastrophizing as a coping strategy to deal with fatigue.

Catastrophizing was found to be a good predictor of fatigue severity and its disruptiveness on functional performance in most of the reviewed articles [26, 27, 29, 31, 36, 39]. However, two studies found treatment-related differences in the association of catastrophizing and fatigue, where baseline level of catastrophizing was predictive of post treatment fatigue only in women who received radiotherapy but not in those who received chemotherapy [27, 31]. This observation may be related to the differences in fatigue severity between women receiving chemotherapy and women receiving radiotherapy, which corroborates a previous finding that women who received chemotherapy report greater fatigue than those who received radiotherapy [31]. The authors explained that other variables (e.g., age, type of surgery, disease stage) were considered as covariates in the analysis; however, other psychological factors such as anxiety and depression were not controlled.

The consistency of individual ratings of catastrophizing at different time points is clinically important. Two studies showed that high catastrophizing was associated with a low discrepancy between recall and momentary fatigue rating [28, 34]. Moreover, one study found a moderate association of catastrophizing on the relationship between morning pain rating and evening fatigue. This information suggests that catastrophizing may serve as an

Catastrophizing may not only serve as an important behavioral marker for fatigue, it may provide information on the peripheral and central mechanisms of fatigue. While peripheral fatigue is the inability to sustain work or force caused by a physical limitation, central fatigue is the failure to initiate or sustain task or physical activities due to insufficiency of self-motivation [46]. The unnecessary increase of attention to the symptom in catastrophizers may influence the person's motivation to perform activities of daily living, making catastrophizing as an ideal behavioral marker for central fatigue.

Future Research Direction

Catastrophizing is one of the psychological factors that influences the fatigue experience [11, 29, 31, 34, 36–39]. This review consistently found significant associations between high catastrophizing and high fatigue. However, only five clinical populations were represented in the studies reviewed. Investigating the relationship of catastrophizing and fatigue on other populations is important to pursue to confirm the findings of this review. Furthermore, catastrophizing is highly associated with depression [22, 47, 48] and negative personality traits [42, 43], in the pain literature. It is important to understand the relationship of catastrophizing with other behavioral markers of fatigue such as depression, and determine the role of negative personality traits on the association of catastrophizing and fatigue.

The mechanisms that can explain how catastrophizing influences fatigue remain unclear. It is important to clarify the definition of catastrophizing and the role it plays in the fatigue experience. Phenotypic and genotypic characterizations of high catastrophizers must be considered to understand possible mechanisms. Exploring the best measures of catastrophizing to use and its relationship with other behavioral markers is an important step to initiate.

Conclusion

This review found that catastrophizing is significantly associated with fatigue and could serve as a good predictor of fatigue severity. This observation was made on limited number and types of patients, thus further investigation is warranted to establish this relationship. Catastrophizing may be an important behavioral marker for fatigue severity and may serve as an interventional target for the clinical management of fatigue.

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Authors	Population	Catastrophizing measure	Fatigue Measure	Design	Association	Variables for Effect Size	Correlation Coefficient r (95%	Comments	
			D	D			Confidential Interval)		
					Cancer				
Broeckel et al., 1998	BC completed adjuvant CT ($n = 61$), Non-cancer	FCS modified from CCSI	POMS-F FSI MFSI	Cross-sectional	$r = 0.55 \ (p < 0.001)$	Catastrophizing on fatigue severity among chemotherapy patients	$\begin{array}{c} 0.55\ (0.04\ -\ 0.70)\ 0.70) \end{array}$	Catastrophizing is correlated with the fatigue severity	
	(6C = II)				$\beta = 0.40$ r2 change = 0.14 ($p < 0.001$)	Catastrophizing on fatigue severity (all patients)	0.64 (0.46 – 0.77)	Catastrophizing is a significant predictor and accounts for 14 % of the variability in fatigue severity.	
Jacobsen et al., 1999	BC receiving BMT or CT or RT $(n = 146)$	FCS modified from the CCSI	POMS-F, FSI, MFSI	Cross-sectional	POM-F: $r = 0.36 - 0.49 \ (p < 0.001)$	Catastrophizing on subscales of POMS-F	0.36 (0.02 – 0.49) to 0.49 (0.36 – 0.60)		
					FSI: $r = 0.50 - 0.66$ ($p < 0.001$)	Catastrophizing on subscales of FSI	$\begin{array}{c} 0.50 \ (0.37 - \\ 0.61) \ \text{to} \ 0.66 \\ (0.56 - 0.74) \end{array}$		
					MFSI: $r = -0.47 - 0.72$ ($p < 0.001$)	Catastrophizing on subscale of MFSI	$\begin{array}{c} 0.47 \ (0.33 - \\ 0.59) \ \text{to} \ 2.08 \\ (0.63 - 0.79) \end{array}$	High catastrophizing is associated with high fatigue severity with all subscales in all fatigue measurements	
				-	$t = 7.48 \ (p < 0.001)$	High/low catastrophizing and fatigue (POMS-F)	$\begin{array}{c} 0.53 \ (0.40 - 0.64) \\ 0.64) \end{array}$	High catastrophizers are 3 times higher in fatigue intensity than low catastrophizers	
Andrykowski et al., 2005	Early stage BC undergoing RT or CT or both (n = 288)	FCS modified from the CCSI	FSI, POMS-F	Longitudinal: pre and post treatment Pre	$t(279) = 7.52 \ (p < 0.001)$ no CRF $(n = 213)$, CRF $(n = 75)$	Catastrophizing and prevalence of fatigue in BC patients	0.41 (0.31 – 0.50)	At baseline, patients with a higher prevalence of CRF reported higher catastrophizing than non-CRF patients	
					$t(264) = 5.06 \ (p < 0.001)$ no CRF $(n = 258)$, CRF $(n = 30)$	Catastrophizing and incidence of fatigue in BC patients	0.29 (0.18 – 0.39)	At baseline, patients with a higher incidence of CRF reported higher catastrophizing than non-CRF patients	1
					CRF Prevalence, (OR = 1.19) (<i>p</i> < 0.001)	Catastrophizing on prevalence of CRF, based on the case definition criteria	0.05 (0.04 – 0.06)	Catastrophizing at baseline was a significant predictor for prevalence of CRF. One point increase in fatigue catastrophizing score is associated with 19% increase in likelihood of being classified as having prevalent CRF.	1
					Incidence (OR =1.14) (p < 0.001)	Catastrophizing on incidence of CRF, based on the case definition criteria	0.04 (0.03 – 0.05)	Catastrophizing at baseline was a significant predictor of the incidence of CRF. One point increase of catastrophizing score was associated with a 14% increase in the likelihood of CRF development.	l

Table 1

Associations between catastrophizing and fatione

Jomments	he CT or RT group (n= 73): Low catastrophizing is ssociated with large fatigue rating response shift in most	atigue rating.	he CT +RT group (n=39): Low catastrophizing is	ssociated with large latigue rating response suit in oou nost fatigue and average fatigue rating.	months post treatment: CRF cases have higher level of atigue catastrophizing, but not statistically significant	2 months post treatment: CRF cases have significantly igher level of fatigue catastrophizing.	Inivariate regression analysis shows subjects with high atastrophizing are associated with membership in the high-atigue classification	Aultivariate logistic regression shows that catastrophizing is significant predictor of the membership of the high fatigue lass
Correlation Coefficient r (95% Confidential Interval)	0.24 (0.01 – 0.44)	0.16 (-0.07 - 0.38)	0.43 (0.13 – 0.66)	0.40 (0.10 – 0.64)	0.10 (-0.02 - 0.21)	0.26 (0.11 – 0.36)	0.33 (0.21 – 0.44)	0.64 (0.64 – 0.65)
Variables for Effect Size	Catastrophizing on the response shift in most fatigue rating	Catastrophizing on the response shift in average fatigue rating	Catastrophizing on the response shift in most fatigue rating	Catastrophizing on the response shift in average fatigue rating	Catatrophizing on cases of CRF 6-months post treatment, based on the case definition criteria	Catatrophizing on cases of CRF 42-months post treatment, based on the case definition criteria	Catastrophizing on high- fatigue classification (univariate regression)	Catastrophizing on high- fatigue classification (multivariate regression)
Association	Most fatigue rating: (<i>n</i> = 73) $\beta = -0.17 (p 0.05) r^2$ = 0.06	A verage fatigue rating: (n = 73) $\beta = -0.14, n^2 = 0.03$	Most fatigue rating: (<i>n</i> = 39) $\beta = -0.29 (p \ 0.01) r^2$ = 0.18	A verage fatigue rating: ($n = 39$) $\beta = -0.26$ ($p = 0.05$) r^2 = 0.162	6 months post- treatment: compare catastrophizing mean between CRF case (mean [SD] = 16.5 [4.1], $n = 26$) and CRF moncases (mean [SD] = 14.8 [5.1] $n = 256$) (p = 0.91)	42 months post- treatment: compare catastrophizing means between CRF cases (mean [SD] = 18.0 [6.6], $n = 29$) and CRF moncases (mean [SD] = 14.4 [4.6], $n = 193$) ($p = 0.000$)	OR = 39.69 ($p < 0.001$) Low fatigue ($n = 85$): Low fatigue ($n = 85$): catastrophizing mean (SD) = 1.09 (0.17) High fatigue ($n = 176$): catastrophizing mean (SD) = 1.36 (0.45)	OR = 20.76 (<i>p</i> < 0.001)
Design	Longitudinal: pre and post treatment	-			Longitudinal: 6 month and 42 months post treatment		Longitudinal: end of treatment, and 2, 4 and 6 months after treatment	
Fatigue Measure					FSI, POMS-F		FSI	
Catastrophizing measure	FCS modified from the CCSI				FCS modified from the CCSI		FCS modified from the CCSI	
Population	Early stage BC receiving adjuvant CT and/ or RT CT or RT	$(c_1 = \pi)$ dno1g	CT+RT group (<i>n</i> = 39)		Stages $0-2$ BC ($n = 304$) compare the CRF and CRF noncases 6 month post treatment: CRF cases ($n = 26$) CRF noncases ($n = 256$)	42 month post treatment: CRF case (n-29) CRF noncases ($n =$ 193)	Early stage BC (post cancer treatments) ($n = 261$)	
Authors	Andrykowski et al., 2009				Andrykowski et al., 2010		Donovan et al., 2007	

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	ing associated with high fatigue tT group	ing associated with high fatigue `and RT group	h high catastrophizing reported those low in catastrophizing		lity Index score, the lower the hows that the catastrophizers group tdex.		Control versus Treatment	
Comments	High fatigue catastrophizi severity in both CT and R	High fatigue catastrophizi disruptiveness in both CT	Patients receiving RT wit more severe fatigue than		The higher the Rand Vita fatigue level. The result sl has lower Rand vitality in	Immediate post treatment: MBCT had	lower fatigue, lower catastrophizing than control group,	2 months post treatment: significant difference between intervention and control groups on levels of fatigue and catastrophizing
Correlation Coefficient <i>r</i> (95% Confidential Interval)	$0.36\ (0.15\ 0.52)$	0.29 (0.08 – 0.46)	0.28 (0.07 – 0.48)		0.18 (0.07 – 0.29)	0.34 (0.01 – 0.60)	0.38 (0.06 – 0.63)	0.29 (-0.04 - 0.56)
Variables for Effect Size	Catastrophizing on fatigue	Treatment and catastrophizing on fatigue severity	Treatment and catastrophizing on fatigue disruptiveness		Catastrophizing on vitality (fatigue) measured by Rand vitality index	MBCT on fatigue level, immediate post treatment	MBCT on catastrophizing level, immediate post treatment	MBCT on fatigue level at 2 months post treatment
Association	$H(1,75) = 7.42 \ (p = 0.01)$	$R(1,75) = 6.93 \ (p < 0.05)$	R(1,76) = 13.21, p < 0.001	c Fatigue Syndrome	Catastrophizers ($n = 87$): vitality mean (SD) = 8.37 (3.65) Non-catastrophizers (n = 195): vitality mean (SD) = 9.55 (n) F (1, 275) = 9.45 (p < 0.002)	MBCT ($n = 15$) fatigue mean (SD) = 21.3 (6.2) 21.3 (6.2) fatigue mean (SD) = 25.2 (n .7) F(1,31) = 6.8 (fatigue) ($p = 0.014$)	MBCT ($n = 16$) catastrophizing mean (SD) = 3.6 (3.1) Control ($n = 19$) catastrophizing mean (SD) = 7.4 (5.6) R1,32 = 9.7 (catastrophizing) ($p = 0.004$)	MBCT (n = 15) fatigue mean (SD) = 21.3 (6.2) = 21.3 (6.2) fatigue mean (SD) = fatigue mean (SD) = 25.0 (6.1) F(1.31) = 5.0 (fatigue) (p = 0.033)
Design	Longitudinal: pre and post treatment			Chroni	Cross-sectional	Longitudinal: A pilot randomized, controlled trial Time points, pre, post, 2 month follow and 6 month follow up		
Fatigue Measure	FSI				 The Rand Vitality Index fatigue item in the Mental Health Index - 5 	Chalder Fatigue Scale		
Catastrophizing measure	FCS modified from the CCSI				Response to the question, "what would be the consequences of pushing yourself beyond your present physical state?"	Catastrophizing subscale from CBRSQ		
Population	Stage 0,1 or 2 BC	C1 (n = 39) RT $(n = 37)$			223 women 59 men	CFS with excessive fatigue after cognitive behavioral therapy Mindfulness - based cognitive therapy (MBCT)	Control (waiting list) = 19	
Authors	Jacobsen et al., 2004				Petrie et al., 1995	Rimes & Wingrove, 2011		

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Comments		Comparing baseline and 6 months post treatment levels:	MBCT group had One group pre-post significantly lower fatigue and catastrophizing	High catastrophizing is significantly associated with momentary fatigue.	High catastrophizing is associated with low discrepancies between recall and momentary fatigue ratings.		Catastrophizing subscale is significantly correlated with	physical and mental fatigue	After controlling for neurological and remission status, catastrophizing did not predict physical fatigue	After controlling for neurological and remission status, catastrophizing did not predict mental fatigue
Correlation Coefficient r (95% Confidential Interval)	0.26 (-0.06 - 0.54)	0.52 (0.19 – 0.74)	0.35 (0.01 – 0.61)	0.51 (0.29 – 0.69)	0.43 (0.18 - 0.63)		0.30 (0.15 – 0.44)	0.20 (0.04 – 0.35)	0.52 (0.39 – 0.63)	0.57 (0.45 - 0.67) (0.67)
Variables for Effect Size	MBCT on catastrophizing level at 2 months post treatment	MBCT on fatigue level between baseline and 6 months post treatment	MBCT on catastrophizing between baseline and post treatment	Catastrophizing on momentary fatigue	Catastrophizing on fatigue recall discrepancy		Catastrophizing on physical fatigue	Catastrophizing on mental fatigue	Catastrophizing on physical fatigue	Catastrophizing on mental fatigue
Association	MBCT $(n = 16)$ catastrophizing mean (SD) = 4.0 (3.1) Control $(n = 19)$ catastrophizing mean(SD) = 6.7 (6.1) F(1,32) = 2.2 (catastrophizing) $(p = 0.152)$	Baseline $(n = 15)$: fatigue mean $(SD) = 25.4 (5.1)$ 6 month $(n = 15)$: fatigue mean $(SD) = 173$; fatigue mean $(SD) = 173 (gaugue mean (Fd) = 0.010)t(14) = 3.0$ (fatigue) $(p = 0.010)$	Baseline $(n = 16)$: catastrophizing mean (SD) = 5.3 (4.0) 6 month (n = 16): fatigue mean (SD) = 2.9 (2.3) t(15) = 2.9 (catastrophizing) ($p =$ 0.012)	r = 0.51 (momentary fatigue) ($p < 0.01$)	r = -0.43 (fatigue recall discrepancy) (p < 0.01)	ultiple Sclerosis	Partial correlation $r = 0.30 \ (p < 0.001)$	Partial correlation $r = 0.20 \ (p < 0.05)$	F = 4.37 (p < 0.001), r^2 = 0.27	F = 6.76 ($p < 0.001$), r^2 = 0.33
Design				Longitudinal: week 1, 2 and 3		Mı	Cross-sectional			
Fatigue Measure				Electronic diary (momentary fatigue); Recall rating of	laugue anu negauve aneci		Chalder fatigue questionnaire			
Catastrophizing measure				Catastrophizing subscale of the Fatigue-related Cognition	ocare		Catastrophizing subscale of the cognitive and behavioral	response to symptoms		
Population				n = 53			Active relapsing- remitting	(n = 149)		
Authors				Sohl & Friedberg,	0007		Skerrett & Moss-Morris,	0007		

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Image: black						$F = 1.51 \ (p > 0.05), r^2 = 0.31$	Catastrophizing on physical fatigue	0.31 (0.16 – 0.45)	After controlling for depression, anxiety, neurological and remission status, catastrophizing did not predict physical fatigue
Bet et. 3010 i= 320 Control version for the processerption for the processerptice processerption for th						F = 4.63 ($p < 0.001$), r^2 = 0.41	Catastrophizing on mental fatigue	0.64 (0.27 – 0.53)	After controlling for depression, anxiety, neurological and remission status, catastrophizing did not predict mental fatigue
Image: control in the product of flag in the product product of flag in the product prod	Bol et al., 2010	<i>n</i> = 262	FCS (Dutch version) modified from the Pain Catastrophizing	AFQ (Dutch version) TSK-F (Dutch version)	Cross-sectional	<i>r</i> = 0.56 (fatigue) (<i>p</i> < 0.001)	Catastrophizing on fatigue	0.56 (0.47 – 0.64)	High catastrophizing is significantly associated with fatigue and fatigue-related fear and avoidance.
Image: bit is a standImage: bit is a sta			scale with 3 additional items specific to Multiple sclerosis			r = 0.64 (fatigue- related fear and avoidance) ($p < 0.001$)	Catastrophizing on fatigue- related fear and avoidance	0.64 (0.56 – 0.71)	
Arron, 1999 $n = 30$ Catastrophizing subscale of the induce scale (0 = no)Evening fingues (SD): 3.2 ($\rho < 0.01$)Ethompolizing on evening 0.73)0.50 (0.17 - fingues significantly higher than patients in the low catastrophizing group catastrophizing drop percentile) groupDestingues (SD): fingues (SD): mand low catastrophizing con evening and low catastrophizing (SD)0.50 (0.17 - fingues (SD): fingues (SD): mand low catastrophizing group ($\sigma = 10, 0 = 74, 0.00$)Catastrophizing on evening ($\sigma = 10, 0 = 74, 0.00$)Output fingues (SD): fingues (SD): mand low catastrophizing group ($\sigma = 10, 0 = 74, 0.00$)Catastrophizing on evening ($\sigma = 10, 0 = 74, 0.00$)Output fingues (SD): ($\sigma = 10, 0 = 74, 0.00$)Catastrophizing on evening ($\sigma = 10, 0 = 74, 0.00$)Output fingues catastrophizing group ($\sigma = 10, 0 = 74, 0.00$)Catastrophizing on the onothing group ($\sigma = 10, 0 = 74, 0.00$)Catastrophizing on the onothing group ($\sigma = 10, 0 = 74, 0.00$)Patients on the onothing group ($\sigma = 10, 0 = 74, 0.00$)Patients on the onothing group ($\sigma = 10, 0 = 74, 0.00$)Auron, 1999 $n = 189$ The fingue cognities catastrophizing scalePOMS-FCatastrophizing on the onothing group ($\sigma = 0.01$), $i^2 = 0.16$ DotCatastrophizing on the onothing group ($\sigma = 0.01$), $i^2 = 0.16$ DotCatastrophizing on the onothing group ($\sigma = 0.01$), $i^2 = 0.16$ Auron Lingue ScalePOMS-FCatastrophizing on the onothing group ($\sigma = 0.01$), $i^2 = 0.16$ DotCatastrophizing on the onothing group ($\sigma = 0.01$), $i^2 = 0.16$ DotDotCatastrophizing on the papositive relationship between normi						Structural Equation model = χ^2 (<i>df</i>) 25.93 (5), ($p < 0.001$)	Fatigue on catastrophizing using the structural equation modeling	$\begin{array}{c} 0.31\ (0.20\ -\ 0.41)\ 0.41) \end{array}$	Catastrophizing is a significant predictor of fatigue-related fear and avoidance. Fatigue is a significant predictor of catastrophizing using the structural equation modeling.
Arron, 1999 $n = 30$ Catastrophizing subscate of fargue to 10 = fargue sub to estomation (Using the strendto to scalific the potentian (Using the constrophizing group ($n = 14$) = 5.0 $3.50 < 0.01$, the mean fargue (SD): as it could possibly be potentian (Using the strendto to scalific the potentian (Using the catastrophizing group ($n = 14$) = 5.0 $3.50 < 0.01$, the potentian (Using the group ($n = 14$) = 5.0 $3.50 < 0.01$, the potentian (Using the group ($n = 14$) = 5.0 $1.50 < 0.01$, the potentian (Using the group ($n = 14$) = 5.0 					ł	ibromyalgia			
$ \left\{ \begin{array}{l lllllllllllllllllllllllllllllllllll$	Aaron, 1999	n = 30	Catastrophizing subscale of the Coping Strategies Questionnaire (Using the percentile to classified the patient into high catastrophizing (75 percentile) and low catastrophizing (25	Visual analogue scale (0 = no fatigue to 10 = fatigue as bad as it could possiblybe)	Longitudinal: 56 days (8 weeks)	Evening fatigue: $t = 3.2$ ($p < 0.01$) Mean fatigue (SD): low catastrophizing group ($n = 14$) = 5.0 (2.1), high catastrophizing group ($n = 16$) = 7.4 (2.0)	Catastrophizing on evening fatigue	0.50 (0.17 – 0.73)	Patients who have high catastrophizing rated their evening fatigue significantly higher than patients in the low catastrophizing group
Healthy VolunteersKangas & $n = 189$ The fatigue cognitive scalePOMS-FCross-sectional $r = 0.64, p < 0.01$ Catastrophizing on fatigueIfigh catastrophizing is associated with high fatigueMongomery, 2011modified from the pain catastrophizing scalePOMS-FCross-sectional $r = 0.64, p < 0.01$ Satestrophizing on fatigue $0.64(0.55 - 16)$ High catastrophizing is associated with high fatigue2011modified from the pain catastrophizing scale $0.01, r^2 = 0.41$ $0.01, r^2 = 0.41$ $0.72)$ Hierarchical linear regression model showed that $0.01, r^2 = 0.41$ Model $reverity$ (linear regression $0.72)$ Hierarchical linear regression model showed that $0.01, r^2 = 0.41$ $0.72)$ Catastrophizing is associated with fatigue severity						Model: $F_5,24$) = 9.36 ($p < 0.01$), $r^2 = 0.16$	Catastrophizing on the relationship between moming pain and evening fatigue	0.40 (0.05 – 0.66)	Hierarchical linear regression model showed that after controlling for demographic/historical factors and disability compensation, catastrophizing was a significant predictor of a positive relationship between morning pain and evening fatigue
Kangas & Montgomery, 2011 $n = 189$ The faigue cognitive scale modified from the pain catastrophizing scalePOMS-FCross-sectional $r = 0.64, p < 0.01$ $r = 0.64, 0.55 - 0.40$ High catastrophizing is associated with high faigue severityMontgomery, 2011modified from the pain catastrophizing scale $0.64, 0.55 - 0.72$ High catastrophizing is associated with high faigue severity2011 $0.01, r^2 = 0.41$ $0.64, 0.55 - 0.40$ Hierarchical linear regression model showed that $0.01, r^2 = 0.41$ $0.64, 0.55 - 0.40$ Hierarchical linear regression model showed that model scalared with faigue severity					Hea	Ithy Volunteers			
$ \begin{array}{c} \text{Model: } F = 123.93 \ p < \\ 0.01 \ r^2 = 0.41 \\ \text{model} \end{array} \\ \begin{array}{c} \text{Model: } F = 123.93 \ p < \\ \text{Catastrophizing on fatigue} \\ \text{o.61 \ r^2 = 0.41 \\ \text{model} \end{array} \\ \begin{array}{c} \text{Model: } F = 123.93 \ p < \\ \text{Catastrophizing on fatigue} \\ \text{O.64 \ (0.55 \ - \\ \text{catastrophizing is associated with fatigue severity} \\ \text{model showed that} \\ \begin{array}{c} \text{model: } P = 123.93 \ p < \\ \text{Catastrophizing on fatigue} \\ \text{O.61 \ r^2 = 0.41 \\ \text{model} \end{array} \\ \begin{array}{c} \text{Model showed that} \\ \text{model showed that} \\ \begin{array}{c} \text{model showed that} \\ \text{model showed that} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \text{Model showed that} \\ \text{model showed that} \\ \begin{array}{c} \text{Model showed that} \\ \text{model showed that} \\ \end{array} \\ \begin{array}{c} \text{Model showed that} \\ \text{model showed that} \\ \end{array} \\ \end{array} \\ \end{array}$	Kangas & Montgomery,	<i>n</i> = 189	The fatigue cognitive scale modified from the pain	POMS-F	Cross-sectional	r = 0.64, p < 0.01	Catastrophizing on fatigue severity	0.64 (0.55 – 0.72)	High catastrophizing is associated with high fatigue severity
	1107		catastrophizing scare			Model: F = 123.93 p < 0.01 r^2 = 0.41	Catastrophizing on fatigue severity (linear regression model)	0.64 (0.55 – 0.72)	Hierarchical linear regression model showed that catastrophizing is associated with fatigue severity. This model explain 41% of the variance

BC= breast cancer, CT = chemotherapy, RT = radiation therapy, FCS = fatigue catastrophizing scale, CCSI = Cognitive Coping Strategies Inventory, POMS-F = fatigue scale from profile of mood states, FSI = fatigue symptom inventory, MFSI = multidimensional fatigue symptom inventory, BC= breast cancer, GT = chemotherapy, RT = radiation therapy, FCS = fatigue catastrophizing scale, CCSI = Cognitive Coping Strategies Inventory, POMS-F = fatigue symptom inventory, MFSI = multidimensional fatigue symptom inventory, BMT = bone marrow transplantation, OR= odds ratio, FSI-TT = fatigue symptom inventory. Thentest, CRF= cancer related fatigue, CFS = chronic fatigue syndromes, CBRSQ = Cognitive and Behaviour Responses to Symptoms questionnaire, AFQ = abbreviated fatigue questionnaire, TSK-F = fatigue version of the Tempa Scale for Kenesiophobia

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