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Systematic Review

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Associations between anger and chronic primary pain: a systematic review and meta-analysis

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Abstract

Objectives: Anger is a negative emotion characterized by antagonism toward someone or something, is rooted in an appraisal or attribution of wrongdoing, and is accompanied by an action tendency to undo the wrongdoing. Anger is prevalent in individuals with chronic pain, especially those with chronic primary pain. The associations between anger and pain-related outcomes (e.g., pain intensity, disability) have been examined in previous studies. However, to our knowledge, no systematic review or meta-analysis has summarized the findings of anger-pain associations through a focus on chronic primary pain. Hence, we sought to summarize the findings on the associations of anger-related variables with pain and disability in individuals with chronic primary pain.

Methods: All studies reporting at least one association between anger-related variables and the two pain-related outcomes in individuals with chronic primary pain were

eligible. We searched electronic databases using keywords relevant to anger and chronic primary pain. Multiple reviewers independently screened for study eligibility, data extraction, and methodological quality assessment.

Results: Thirty-eight studies were included in this systematic review, of which 20 provided data for meta-analyses (2,682 participants with chronic primary pain). Of the included studies, 68.4% had a medium methodological quality. Evidence showed mixed results in the qualitative synthesis. Most anger-related variables had significant positive pooled correlations with small to moderate effect sizes for pain and disability.

Conclusions: Through a comprehensive search, we identified several key anger-related variables associated with pain-related outcomes. In particular, associations with perceived injustice were substantial.

Keywords: anger; chronic primary pain; meta-analysis; perceived injustice; systematic review.

Introduction

Anger has long been a topic of interest in the context of pain research [1–4]. Anger is a negative emotion characterized by antagonism toward someone or something, is rooted in an appraisal or attribution of wrongdoing, and is accompanied by an action tendency to undo the wrongdoing [5–7]. A study reported that 70% of individuals with chronic pain experience anger [8]. The International Association for the Study of Pain (IASP) has put forth a new classification of chronic pain, which includes the category of chronic primary pain (CPP) [9, 10]. CPP is defined as “pain in one or more anatomical regions that persists or recurs for longer than three months and is associated with *significant emotional distress* or functional disability and that cannot be better accounted for by another chronic pain condition” [10, 11]. Moreover, the IASP task force places anger as a significant emotional distress in CPP [11]. These studies and recent developments support the notion that anger is and will continue to be an important target to support well-being in individuals with chronic pain.

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Anger has a variety of related constructs. Several factors have been examined in the anger-pain association, such as state and trait anger, and anger management style [12–14]. State anger refers to the psychological state of experiencing subjective anger with the arousal of the autonomic nervous system, and trait anger refers to individual differences in the frequency of state anger over time [14, 15]. Anger management style is the degree to which individuals with pain express, suppress, or regulate their expression of anger [2, 14]. Each of these styles is called anger-out, anger-in, and anger-control, respectively. Perceived injustice, which is an appraisal cognition comprising elements of severity and irreparability of loss, blame, and unfairness [16, 17], is suggested as one of the cognitive appraisal components of anger [3]. A systematic review found a significant association between perceived injustice and pain-related outcomes in individuals with musculoskeletal pain resulting mainly from injuries [18].

Various patterns of associations between anger and pain have been investigated, such as when anger can predispose, exacerbate, be a consequence of, or maintain pain [5, 19–22]. In addition, mediation and moderation effects of anger on pain have been examined [23–26]. Given the diverse research findings, it would be helpful for researchers and healthcare providers to have access to a summary of research findings regarding the associations between anger and pain, especially CPP. To the best of our knowledge, no systematic reviews and meta-analyses have summarized the findings on these associations.

Hence, we sought to summarize the findings on the associations of anger-related variables with pain and disability in individuals with CPP. We included all types of study designs. By indicating the link between anger and pain, the significance of targeting anger in CPP treatment can become clearer. In the present meta-analysis, we hypothesized anger-related variables to have statistically significant pooled correlations with pain or disability in at least a small magnitude of effect size ($r \geq 0.10$) [27].

Methods

Inclusion and exclusion criteria

The criteria for the inclusion of researches in the present study were as follows: (1) study participants being individuals with CPP lasting at least three months, (2) measurement of the anger-related variable using a self-reported questionnaire, (3) measurement of pain or disability using a self-reported questionnaire, (4) reporting of at least one association between the anger-related variable and pain or disability, (5) research paper published in peer-reviewed journals or

books, and (6) research paper published in English or Japanese. We included several diseases and pain types under CPP based on the International Classification of Disorders-11 [28, 29] criteria. The pain types included were irritable bowel syndrome, fibromyalgia, chronic low back pain, chronic migraine, chronic tension-type headache, complex regional pain syndrome, and burning mouth syndrome, among others. For studies involving participants with all types of chronic pain, we included studies in which we could confirm that 50% or more of the participants had conditions corresponding to CPP. We summarized an analogous construct of disability, such as pain interference, impairment, and low function, as a variable labeled “disability.”

The following researches were excluded from this study: (1) studies on pain conditions other than CPP, such as acute pain lasting less than three months, experimental pain, cancer pain, and post-traumatic/postoperative pain; (2) non-primary studies such as review articles and commentaries; and (3) studies published in the abstract books of conference proceedings and dissertations.

Search strategy

We searched the following databases on June 8, 2018: PubMed, CINAHL, PsycINFO, Cochrane, and ICHUSHI. ICHUSHI is a bibliographic database of the Japan Medical Abstracts Society. ICHUSHI contains bibliographic citations and abstracts from more than 2,500 biomedical journals and other serial publications published in Japan. Our search covered the time period from the date of inception of each database to the search date. The search terms consisted of the target population (several types of chronic pain corresponding to CPP) and exposure measurement (anger-related variables) (see Appendix S1). We performed a hand-search with the reference lists of the relevant reviews discussing the association between anger-related variables and pain [1–5, 12, 13, 17, 23, 30–34], and with the table of contents of some journals in the field of pain and psychosomatic medicine.

Screening and data extraction

First, two authors (TA and KY) independently screened the titles and abstracts of the studies that were shortlisted from the search to check their eligibility. Disagreements between the two authors were discussed, and the disagreements remained, another author (HF or KE) was invited to the discussion to reach a consensus. The two authors then screened the full texts of the studies that were retained after the title/abstract screening. The same process as stated earlier in this paragraph was employed to resolve disagreements. Finally, we included studies that passed the full text screening for data synthesis.

The following data were extracted from the included studies: authors; year of publication; study design; pain types; age; sample size; proportion of sex at birth; domains and measures for assessing anger-related variables, pain, and disability; statistical analysis; and a summary of key findings. TA independently extracted data from all included studies. Moreover, two authors (HF and MS) independently extracted data from each half of the included studies. Disagreements in data extraction were discussed to reach a consensus between TA and each author in charge. For the meta-analysis, TA extracted the correlation coefficients and sample sizes.

Methodological quality assessment

We developed a tool to assess the methodological quality of the included studies based on previous systematic reviews exploring the associations between psychological factors and chronic disease [35–40]. The following 12 items were included in our quality assessment tool: study rationale, study design, demographic variables, recruitment source, response rate, sample size, assessment, statistical analyses, confounding variables, presentation of the results, conclusions, and limitations (see Table S2 for details). Each item was rated as positive (1), negative (0), or unclear (?); hence, the

highest possible score was 12 points. Total positive scores for all items of each study were calculated, and the study was accordingly ranked as being of low (≤ 5 points), medium (6–9 points), or high methodological quality (≥ 10 points). TA independently completed the quality assessment of all the included studies. In addition, HF and MS independently assessed the methodological qualities of each half of the included studies. Disagreements regarding the quality assessment were discussed to reach a consensus between TA and each author in charge. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the study selection process in detail (Figure 1).

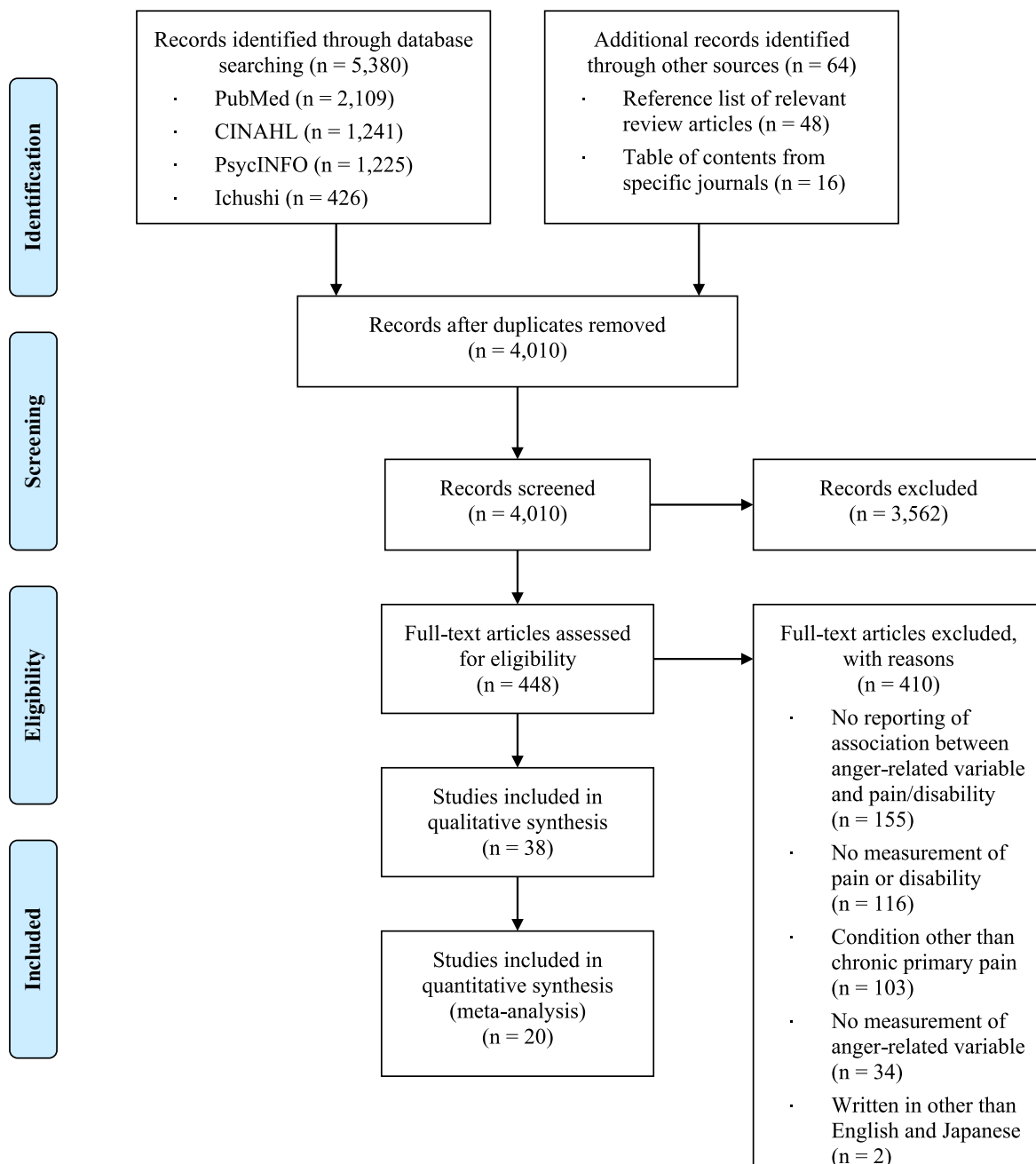


Figure 1: PRISMA 2009 flow diagram.

Data synthesis

In the qualitative synthesis, we summarized the extracted information for each anger-related variable. The primary focus was on the associations of anger-related variables with pain and disability.

We conducted a meta-analysis with R version 3.6.0 [41], especially the package “meta” version 4.9.7 [42]. In case there were at least two studies reporting sample sizes and correlation coefficients (Pearson’s r or Spearman’s ρ) for the associations between anger-related variables and pain and disability, we computed pooled correlations to indicate the effect sizes of the bivariate associations. If eligible studies for the meta-analysis reported several types of pain, such as sensory and affective pain, we focused on pain scales representing overall pain experience (e.g., the Visual Analogue Scale [VAS] [43], Numerical Rating Scale [NRS] [44], and Present Pain Index of the McGill Pain Questionnaire [MPQ] [45]). Since we were interested in associations of anger-related variables with pain and disability in natural situations, we excluded those studies from the meta-analysis that reported correlations based on changes in scores of anger-related variables, pain, and disability under experimental manipulations. When there were several studies utilizing the same dataset with overlapping study variables, we adopted the study published the earliest. However, in case a study extended the earlier dataset using larger sample size, we adopted such a study over the study published earlier. A random-effects model was used to pool the extracted data (correlation coefficients and sample sizes). Based on Cohen’s criterion [27], we interpreted effect sizes of $r=0.10$, 0.30 , and 0.50 as small, moderate, and large, respectively. Cochran’s Q test, I^2 statistic, and 95% prediction interval (PI) were computed to evaluate heterogeneity. I^2 values of 0–40%, 30–60%, 50–90%, and 75–100% were regarded as indicating not important (i.e., low), moderate, substantial, and considerable heterogeneity, respectively [46]. The PI represents the variation in effect sizes over different settings on the same scale as the utilized effect size measure [47]. In this case, when the PI contained zero, it indicated that the association between anger-related variables and pain-related outcomes in future settings would be null or in the opposite direction. The package “meta” required more than two studies to output the PI. Additionally, we inspected funnel plots to assess publication bias.

Results

Characteristics of included studies

Thirty-eight studies including 4,123 participants with CPP and 663 controls (92 individuals with other chronic pain types, 218 spouses, and 353 healthy controls) met the established criteria. Twenty studies provided data for meta-analyses (2,682 participants with CPP). Table S3 provides a summary of the contents of each included study. In terms of the study design, 30 studies were observational (78.9%), six were experiments (15.8%), and two were interventional (5.3%). Cross-sectional design was the most prevalent (25 studies, 65.8% of the included studies). Pain types included chronic low back pain (42.1% of the 38

studies), fibromyalgia (13.2%), headaches (e.g., migraine, tension-type headache, and other types of chronic headache; 13.2%), chronic musculoskeletal pain (7.9%), mixed chronic pain (15.8%), and others (7.9%). The mean ages of the participants with CPP ranged from 17.1 years [48] to 55.9 years [49, 50]. The proportion of women in the included studies ranged from 11.0% [51] to 100.0% [52–55]. The most commonly used anger-related measures were from the family of the State-Trait Anger Expression Inventory [56, 57] (STAXI; 18 studies, 47.4%). Several studies also used the Injustice Experience Questionnaire [16] (IEQ; seven studies, 18.4%). The pain measures included the MPQ and its short form [58] (11 studies, 28.9%), VAS (10 studies, 26.3%), and NRS (nine studies, 23.7%). Disability was assessed using a variety of scales, including disease-specific scales (e.g., the Fibromyalgia Impact Questionnaire [59, 60] and Roland Morris-Disability Questionnaire [61]) and non-disease-specific scales (e.g., the West Haven–Yale Multidimensional Pain Inventory [62] and Pain Disability Index [63]).

Methodological quality of included studies

The total quality scores for the included studies had a mean of 8.26 (SD=1.77) and range of 3–11. Most studies were of medium quality (26 studies: 68.4%), 10 studies were of high quality, and only two studies were of low quality. Major limitations included no *a priori* sample size justification (34 studies, 89.5%), unclear reporting of response rates (21 studies, 55.3%), insufficient reporting of statistics for the main analysis (20 studies, 52.6%), unclear reporting of the study design (19 studies, 50.0%), and unclear reporting of the control of confounders (18 studies, 47.4%). The correlation between the year of publication and the total quality score was substantial ($r=0.59$, 95% CI: 0.33–0.76, $p<0.001$). A summary of the methodological quality of the included studies is indicated in Table S4.

Qualitative synthesis

Sixteen anger-related variables were identified from the 38 studies for the qualitative synthesis. We summarized the contents of the studies on the following seven anger-related variables: anger, state anger, trait anger, anger-in, anger-out, anger-control, and perceived injustice: these variables were selected as they had been assessed in more than two studies. Information about the remaining nine anger-related variables was also summarized.

Anger

We summarized five studies that examined non-specific, general anger. Cross-sectional studies reported that more anger was associated with more pain [50, 51] and more disability even after controlling for confounding variables including demographics, depression, social desirability, and anger-regulation style [51]. Experiments involving the manipulation of participants' emotional states showed a positive association between change in anger and change in pain. Burns reported that anger increase due to recalling a recent anger-inducing event accounted for pain increase even after controlling for the effects of changes in anxiety and sadness [64]. In addition, anger change due to an anger-inducing task was positively associated with pain change due to a pain behavior task; however, after controlling for emotion suppression (suppression or non-suppression), anger change did not account for the variance of change in pain [26]. One of the studies reported a non-significant association between anger and pain [65]. Kerns et al. reported a positive association between anger and pain that turned non-significant after controlling for the aforementioned confounding variables [51].

State anger

Ten studies reported an association between state anger and pain-related outcomes. Cross-sectional data revealed more state anger to be associated with more pain [22, 66–68] and more disability [22, 68, 69]. The positive association between state anger and affective pain was observed even after controlling for ambivalence over emotional expression to pain [70]. A study involving daily diary entries from the participants showed that more state anger during the day was associated with more pain at the end of the day [55]. Another study suggested that state anger mediates the association between the perception of injustice and pain [68]. Statistically non-significant results were also reported. Two studies indicated that state anger was not associated with pain [71, 72]. In another study, the reduction of state anger on taking topiramate, a type of anticonvulsant used for pain treatment, did not correlate with pain reduction in individuals with chronic low back pain [73].

Trait anger

Nine studies reported associations between trait anger and pain-related outcomes. Cross-sectional data suggested more trait anger as being associated with more pain [54, 71, 74] and more disability [75]. However, a substantial

number of studies reported non-significant associations of trait anger with pain [66, 68, 75, 76] and disability [54, 68, 76]. In addition to state anger, reduction of trait anger on taking topiramate did not correlate with pain reduction [73]. One study reported a negative association between trait anger and disability in a regression model; however, it was assumed to be a product of multicollinearity between trait anger and depression in the model [72].

Anger-in

Twelve studies reported an association between anger-in and pain-related outcomes. Cross-sectional data suggested that more anger-in was associated with more pain [51, 68, 74, 77] and more disability [22, 51, 68]. Even after controlling for demographics, pain history, social desirability, and depression, more anger-in was associated with more pain [51]. A study involving daily diary entries from the participants found that trait anger-in, a relatively stable property, was positively associated with pain at the end of the day, but state anger-in during the day was not [55]. Furthermore, a study utilizing an ecological momentary assessment (EMA) revealed that more behavioral anger inhibition (i.e., state anger-in) at one time predicted more pain interference 3 h later after adjusting for state anger at the same prior time [22]. Another study suggested that trait anger-in moderates the association between chronic pain intensity and subsequent behavioral anger expression [78]. This means that more pain at one time predicts more state anger-out later in individuals with low trait anger-in. Several studies reported non-significant associations between anger-in and pain [22, 52, 54, 66] and disability [54]. Behavioral anger inhibition did not predict pain a few hours later [22]. A non-significant association between the reduction of anger-in on taking topiramate and pain reduction was also found [73]. An experiment revealed that trait anger-in did not moderate the association between emotion regulation strategy (suppression or no-suppression) and pain intensity change from baseline to pain behavior tasks but did moderate the associations between emotion regulation strategy and pain behaviors [25].

Anger-out

Twelve studies reported an association between anger-out and pain-related outcomes. Cross-sectional data showed that more anger-out was associated with more pain [22, 51, 54, 74, 77] and more disability [22, 51]. A clinical trial showed that the greater the reduction in anger-out on taking topiramate, the greater the reduction in pain and

disability [73]. Longitudinal studies found significant associations between anger-out and pain-related outcomes. An EMA study showed that greater behavioral anger expression (i.e., state anger-out) predicted a subsequent increase in pain intensity during the hours immediately following that anger expression [78]. Another EMA study revealed that greater behavioral anger expression at one time was associated with more pain intensity and more pain interference 3 h later when controlling for state anger at the same prior time [22]. Several studies suggested that trait anger-out moderates the bidirectional association between state anger-out and pain. For instance, one study reported actual anger expression (i.e., state anger-out) to be associated with diminished pain compared with no anger expression in individuals with high trait anger-out; however, it did not impact pain in individuals with low trait anger-out [55]. Additionally, the former EMA study suggested that trait anger-out moderated the influence of pain on subsequent behavioral anger expression (i.e., state anger-out) [78]. In this study, more pain predicted more behavioral anger expression a few hours later in individuals with low trait anger-out. Some studies also reported non-significant associations between anger-out and pain [66, 68, 72] and disability [54, 68]. In addition to trait anger-in, trait anger-out did not moderate the association between emotion regulation strategy and pain intensity change from baseline to pain behavior tasks but did moderate the associations between emotion regulation strategy and pain behaviors [25].

Anger-control

Three studies reported an association between anger-control and pain-related outcomes. A cross-sectional study showed a weak positive correlation between anger-control and pain [51]. However, another study reported a non-significant association of anger-control with pain and disability [54]. Additionally, an increase in anger-control on taking topiramate did not correlate with pain reduction [73].

Perceived injustice

Seven studies reported an association between perceived injustice and pain-related outcomes. Cross-sectional data revealed a positive association between perceived injustice and pain [53, 68, 79–82] and disability [68, 79–81]. Even after controlling for pain, acceptance, and pain catastrophizing, perceived injustice explained a unique variance of disability [80]. Scott et al. revealed the moderating role of perceived injustice, with the association between pain and depression

being stronger among people reporting greater perceived injustice, and weaker among people who were less likely to perceive injustice [83]. This moderating effect remained after controlling for pain catastrophizing. Studies also suggested that several factors, including acceptance, depression, pain interference, and state anger, mediate the association between perceived injustice and pain-related outcomes such as pain, disability, and life satisfaction [68, 79, 81]. Two studies reported a non-significant association between perceived injustice and pain [53, 83]. After controlling for partner's age, women's own and their partner's perceived injustice were not associated with women's pain resulting from provoked vestibulodynia [53]. In addition, acceptance and attention bias to pain did not mediate the association between perceived injustice and pain [79, 82].

Other anger-related variables

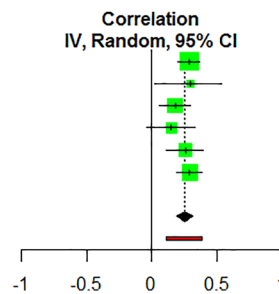
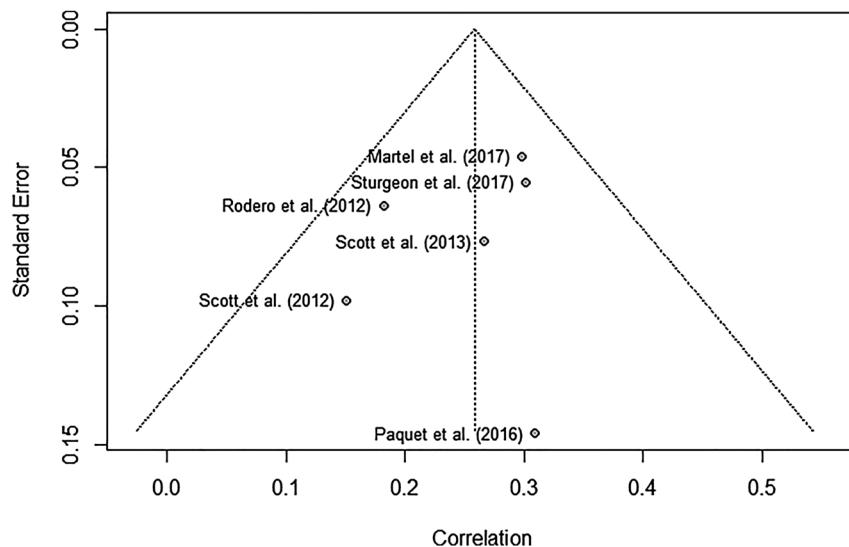
Under this category, we briefly summarized the studies that examined other anger-related variables. First, with regard to the variable of aggressiveness, a study employing a single-arm pre-post comparison showed that aggressiveness in the pre-treatment phase did not predict changes in pain and disability due to multidisciplinary treatment [84]. Second, regarding conflict, a cross-sectional study indicated that more conflict among family members was associated with greater disability, but not pain [85]. However, after controlling for income, this conflict-disability association was no longer significant. Third, a cross-sectional study investigating goal frustration (i.e., the difficulty one encounters when trying to achieve a goal) suggested that none of the domains of goal frustration—including personal values, social acceptance, self-acceptance, school, and health—were associated with pain among adolescents and young adults experiencing chronic musculoskeletal pain [48]. Forth, considering hostility, no substantial associations were reported between hostility and pain [86, 87]. Fifth, a few cross-sectional studies examined the association between life satisfaction/marital satisfaction and pain-related outcomes. Higher life satisfaction was associated with lower pain intensity and less pain interference [81]. More spouse-reported marital satisfaction was associated with less spouse-rated disability; however, patient-reported marital satisfaction was not associated with patient-reported disability [85]. Additionally, marital dissatisfaction in women, but not men, with chronic low back pain was associated with disability [88]. Sixth, with regard to other-blame, a cross-sectional study suggested more other-blame to be associated with greater impairment in individuals with fibromyalgia [49]. Finally, considering self-aggression and self-blame, both of which imply negative consequences for an individual, two cross-

Table 1: Pooled correlation coefficients between pain-related outcomes and anger-related variables.

Outcome	Anger-related variable	k	n	Correlation					Heterogeneity					
				Point estimate	95% CI: lower limit	95% CI: upper limit	Z	p-Value	Q	df	p-Value	I ²	95% PI: lower limit	95% PI: upper limit
Pain	Anger	2	275	0.35	0.23	0.46	5.40	<0.001	0.83	1	0.364	0.0%	—	—
	State anger	3	339	0.44	0.32	0.55	6.55	<0.001	2.79	2	0.248	28.3%	-0.70	0.95
	Trait anger	6	520	0.18	0.07	0.29	3.19	0.001	5.32	5	0.379	5.9%	-0.09	0.43
	Anger-in	7	647	0.22	0.10	0.33	3.65	<0.001	11.26	6	0.081	46.7%	-0.12	0.52
	Anger-out	6	602	0.20	0.09	0.30	3.47	0.001	6.93	5	0.226	27.8%	-0.10	0.46
	Anger-control	2	192	0.11	-0.07	0.30	1.20	0.232	1.24	1	0.266	19.3%	—	—
	Perceived injustice	6	1,385	0.25	0.19	0.31	7.77	<0.001	4.12	5	0.533	0.0%	0.11	0.39
Disability	State anger	2	278	0.40	0.21	0.55	4.03	<0.001	2.96	1	0.085	66.2%	—	—
	Trait anger	4	375	0.20	0.05	0.35	2.64	0.008	7.22	3	0.065	58.5%	-0.34	0.64
	Anger-in	4	470	0.24	0.14	0.33	4.77	<0.001	1.76	3	0.624	0.0%	-0.02	0.46
	Anger-out	4	470	0.15	0.06	0.25	3.06	0.002	1.96	3	0.581	0.0%	-0.12	0.40
	Anger-control	2	192	-0.07	-0.21	0.08	-0.95	0.343	0.24	1	0.626	0.0%	—	—
	Perceived injustice	4	1,228	0.55	0.49	0.61	15.19	<0.001	5.55	3	0.136	46.0%	0.31	0.73
	Self-aggression/self-blame	3	425	0.28	-0.17	0.64	1.22	0.221	25.85	2	<0.001	92.3%	-1.00	1.00

Random effect model was used. k, number of studies.

Study	Total	Weight	Correlation IV, Random, 95% CI
Martel et al. (2017)	475	28.7%	0.29 [0.21; 0.37]
Paquet et al. (2016)	50	4.8%	0.30 [0.02; 0.53]
Rodero et al. (2012)	250	19.1%	0.18 [0.06; 0.30]
Scott et al. (2012)	107	9.7%	0.15 [-0.04; 0.33]
Scott et al. (2013)	173	14.5%	0.26 [0.12; 0.39]
Sturgeon et al. (2017)	330	23.1%	0.29 [0.19; 0.39]
Total (95% CI)	1385	100.0%	0.25 [0.19; 0.31]
Prediction Interval			[0.11; 0.39]
Heterogeneity: Tau ² = 0.0017; Chi ² = 4.12, df = 5 (P = 0.53); I ² = 0%			

**Figure 2:** Forest plot for perceived injustice with pain.**Figure 3:** Funnel plot for perceived injustice with pain.

sectional studies supported positive associations between self-aggression/self-blame and disability [49, 89]. However, another cross-sectional study reported a non-significant association between self-blame and pain or disability [90].

Meta-analysis

For the meta-analysis, eight anger-related variables from 20 studies (seven variables for pain and disability) were identified. Self-aggression and self-blame were treated as one variable because of their similarities. Table 1 presents the results of this meta-analysis. Figures 2 and 3 are a forest plot and a funnel plot for perceived injustice with pain, respectively. Forest plots and funnel plots for other anger-related variables are provided in Figures S5–S30.

Pain

Two to seven studies reported correlation coefficients between anger-related variables and pain, with their sample sizes ranging from 192 to 1,385. Six anger-related variables showed significant positive pooled correlations with small to moderate effect sizes ($r_s=0.18$ – 0.44 , $p_s \leq 0.001$), but anger-control did not reach statistical significance ($r=0.11$, $p=0.232$). Six anger-related variables showed I^2 values representing low heterogeneities ($I^2=0$ – 28.3%). Only the I^2 value of anger-in presented moderate heterogeneity ($I^2=46.7\%$). Only the PI of perceived injustice did not contain zero. The PI for state anger showed a relatively wide range. A substantial risk of publication bias was not found through visual inspection of the funnel plots.

Disability

Two to four studies reported correlation coefficients between anger-related variables and disability, with their sample sizes ranging from 192 to 1,228. Five anger-related variables showed significant positive pooled correlations with small to large effect sizes ($r_s=0.15$ – 0.55 , $p_s \leq 0.001$ – 0.008), but anger-control and self-aggression/self-blame did not reach statistical significance ($r_s=-0.07$ and 0.28 , $p_s=0.343$ and 0.221 , respectively). It was shown that the I^2 value for each anger management style was low ($I^2=0\%$), perceived injustice was moderate ($I^2=46\%$), state and trait anger were substantial ($I^2=66.2$ and 58.5% , respectively), and self-aggression/self-blame was considerable ($I^2=92.3\%$). Only the PI of perceived injustice did not contain zero. The PIs for trait anger and self-aggression/self-blame showed a relatively wide and a very wide range, respectively. Risk of publication bias was

observed for self-aggression/self-blame, but not for the other anger-related variables.

Discussion

The objective of the present study was to summarize the findings on the associations between anger-related variables and pain and disability in individuals with CPP. Among the 38 studies, 65.8% used a cross-sectional design and 68.4% were of medium methodological quality. The included studies tested the various roles of anger-related variables, including as mediators and moderators. Our hypothesis on the meta-analysis was largely supported. The anger-related variables, except for anger-control and self-aggression/self-blame, had significant positive pooled correlations with small to moderate effect sizes. Cumulative evidence supported the notion that anger-related variables are substantially related to the outcomes of CPP.

The summary of the findings did not provide a definite conclusion on the association between non-specific anger and pain-related outcomes. Although many studies reported bidirectional and causal positive associations between anger and pain, these associations became null in several studies when controlling for confounders [26, 51]. Hence, our positive pooled correlation with a moderate effect size might be reflecting the effects of other factors. Such conclusions for the association between non-specific anger and disability could not be made because only one study tested this association [51].

Studies generally supported the bidirectional positive association between state anger and pain. A positive pooled correlation with moderate effect size and the low I^2 value reinforced this association. A study indicated significant mediation by state anger [68]. It might be promising to explore anger fluctuation as a background mechanism of worsening pain. Regarding disability, a positive association with state anger was observed in the qualitative synthesis; however, the meta-analysis showed substantial heterogeneity. Therefore, it would be better to not conclude on this matter.

There was support for trait anger having a small association with pain, but not with disability. In the qualitative synthesis, studies showed mixed results for the bidirectional association between trait anger and pain and disability; significant positive pooled correlations were observed, but the effect sizes were small. Substantial heterogeneity for disability lessened the credibility of the results. Considering that trait anger is stable anger-proneness [14, 15], it might be a moderator of pain. Further research is required because none of the included studies tested moderation by trait anger.

Our meta-analyses indicated that situational anger may have a closer association with pain compared to dispositional anger. Considering that pain is highly variable [91–93], a stronger correlation with state anger may reflect accurately the synchronization of pain with anger that fluctuates moment to moment depending on the situation. However, in performing meta-analysis, a small number of studies may cause a risk of overestimation of the true effect [94, 95]. The fewer studies and wide range of PI in state anger may imply the overestimation of its association with pain. Thus, this result should be interpreted with caution.

Studies did not support an association between anger-in and pain. In the qualitative synthesis, only half of the studies supported this association. A pooled correlation was significantly positive with a small effect size but moderate heterogeneity. A narrative review [13] pointed out a limited link between trait anger-in as measured by the STAXI family of scales and pain, suggesting that the anger-in subscale reflects general negative affect rather than state, actual inhibition of anger expression that relates closely to subsequent pain increase. Since most studies used the anger-in subscale of the STAXI family of scales, our meta-analysis might indicate an association between general negative affect and pain; further research targeting state anger-in needs to be conducted to validate this association. Additionally, we hypothesized that individuals may view suppressing anger as a socially acceptable anger management strategy. This might blur the link between anger-in and pain. Two studies [25, 78] testing moderation by anger-in treated pain as a predictor on behavioral anger expression or as an outcome of emotion suppression, showing mixed results. The effect of anger-in as a moderator depending on how the pain is treated can catalyze further research. A positive bidirectional association between anger-in and disability was generally supported by the results of the qualitative synthesis and meta-analysis. Additionally, anger-in was predictive of disability a few hours later, but was not associated with pain [22]. Therefore, it is possible that anger-in has a stronger link with disability than with pain.

Our meta-analysis supported weak positive bidirectional associations between anger-out and pain-related outcomes despite the mixed results observed in the cross-sectional studies. A clinical trial of an analgesic and longitudinal studies supported covariation and the effects of anger-out on pain and disability [22, 73, 78]. However, some studies argued for an interaction between trait anger-out and state behavioral anger expression on pain [12, 23, 96, 97]. In one study, when the participants with high trait anger-out and chronic pain got angry and engaged in

behavioral anger expression, their pain reduced temporarily [55]. The opioid triggering hypothesis [12, 23, 77] explains this interaction. Under this hypothesis, the endogenous opioid system is considered the key for inherent pain and emotion regulation [98–100]. Behavioral anger expression triggers the endogenous opioid analgesia system in individuals with high trait anger-out. The use of behavioral anger expression is maintained by negative reinforcement and results in the stabilizing of trait anger-out over time. Our social context refuses to accept the possibility of behavioral anger expression being adaptive, causing suffering in individuals with high trait anger-out.

Associations between anger-control and the two pain-related outcomes were not supported. Even the limited evidence did not suggest a substantial effect of anger-control on individuals with CPP.

Perceived injustice had significant associations with pain and disability, as determined by the results of the included studies, most of which had a cross-sectional design. Similarly, our meta-analysis showed significant positive associations with a small effect size for pain and a large effect size for disability. This reinforces the notion that a cognitive appraisal component of anger plays a significant role in the exacerbation of pain-related problems. The present results and previous studies, including a systematic review of studies involving participants with slightly different kinds of pain, suggest that perceived injustice might have a stronger correlation with disability than with pain [16, 18]. However, the reason for this is unclear. The aforementioned systematic review found moderate to strong associations of perceived injustice with negative emotions [18]. Perceived injustice might have a closer link with subsequent responses such as negative emotion and disability caused by pain considering that individuals who perceive injustice sustain with fruitless behaviors to recover from pain [33, 101]. A few studies tested moderation by perceived injustice and investigated mediators of the association between perceived injustice and pain-related outcomes [68, 79, 81, 83]. Further attempts to explore the complex effects of perceived injustice on pain-related outcomes are required because this topic has only recently gained attention and evidence on it is inadequate.

It is difficult to conclude the association between other identified anger-related variables and pain/disability in individuals with CPP because of the limited number of studies per variable. Statistical significance was observed for life and marital satisfaction/marital dissatisfaction, other-blame, and self-aggression/self-blame. However, our meta-analysis did not support a significant association between self-aggression/self-blame and

disability. Considering that anger is oriented toward someone or something [6], further exploration of anger-related variables in terms of the source of anger, such as failure to achieve personal life goals and one's marital partner might be useful in finding more promising interventions for CPP.

It is important to consider treatments that target anger-related variables in individuals with CPP. A systematic review of meta-analyses showed that cognitive-behavioral treatments (CBTs) including relaxation and thought management were consistently effective with at least moderate effect sizes for anger among both non-clinical and psychiatric populations [102]. For individuals with chronic pain, anger management and coping strategies for regulating intense emotions have been incorporated as a part of CBT-oriented programs [103–105]. It remains to be tested whether incorporating anger management enhances the efficacy of CBT for individuals with CPP. Another promising intervention is emotion awareness and expression therapy (EAET) [106], which is an integrated approach to help individuals become aware and adaptively express their emotions stemming from external adversity, internal conflict, and trauma. Randomized controlled trials have demonstrated the efficacy of EAET in individuals with CPP [107, 108].

The present study had several limitations. First, we included only those studies that reported recruiting individuals with pain lasting at least three months. Therefore, we might have excluded studies that simply did not report the detailed pain duration of participants with CPP and might have provided important findings on anger-pain associations. Second, despite a comprehensive literature search, the number of included studies for each anger-related variable was relatively small. Inclusion of a limited number of studies, especially in meta-analyses, carries the risk of introducing biased results. Third, we would like to raise the issue of heterogeneities, which reflects the clinical and methodological diversity among the studies [46]. As high heterogeneity, along with the issue of a small number of studies, impairs the reliability of results, we need to interpret the present results with caution. Fourth, measurement tools of included studies might influence the results. For example, anger, by definition, has the property to increase behaviors to correct a wrongdoing. Most of the scales assessing disability usually ask the respondent to rate the degree of activity limitation. The tools for measuring disability, possibly, missed precisely capturing the action-provoking tendency due to anger as disability. Fifth, we limited the literature search to English and Japanese, and studies that met the eligibility criteria but were published in other languages were excluded.

In conclusion, the present study successfully provided a summary of the findings on the associations between anger-related variables and pain-related outcomes in individuals with CPP. We identified several key anger-related variables through a comprehensive search. In particular, perceived injustice was substantially associated with pain-related outcomes.

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