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Alexithymia in individuals with chronic pain and its relation to pain intensity, physical interference, depression, and anxiety: a systematic review and meta-analysis

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Abstract

Numerous studies have examined how alexithymia (difficulty identifying and describing one's emotions and a preference for externally oriented thinking) relates to chronic pain and associated disability. We conducted a systematic review and meta-analysis to summarize individual studies that either assessed alexithymia in individuals with chronic pain vs controls or related alexithymia to pain intensity, physical interference, depression, and anxiety. We searched MEDLINE, Embase, and PsyclNFO from inception through June 2017; 77 studies met the criteria (valid assessment of alexithymia in adults or children with any chronic pain condition) and were included in analyses (n = 8019 individuals with chronic pain). Primary analyses indicated that chronic pain samples had significantly higher mean alexithymia scores compared with nonclinical (d = 0.81) and clinical nonpain (d = 0.55) controls. In chronic pain samples, alexithymia was significantly positively associated with pain intensity (d = 0.20), physical interference (d = 0.17), depression (d = 0.46), and anxiety (d = 0.43). Secondary meta-analyses of 14 studies that conducted partial correlations that controlled for negative affect-related measures revealed that alexithymia was no longer significantly related to pain intensity or interference. Meta-analysis findings demonstrated that alexithymia is elevated in individuals with chronic pain and related to greater pain intensity and physical interference, although the latter relationships may be accounted for by negative affect. Critical future work is needed that examines alexithymia assessed using non-self-report measures, develops a person-centered perspective on this construct, and identifies how alexithymia is relevant to the assessment and treatment of individuals with chronic pain.

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Conflict of interest statement

The authors have no conflict of interest to declare.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/A734.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painjournalonline.com).

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Keywords

Chronic pain; Alexithymia; Pain intensity; Physical interference

1. Introduction

Chronic pain is common, occurring in approximately 11% to 31% of adults[50,87] and children.[46,55] Chronic pain affects physical, social, and emotional functioning[13,93] and can be severely disabling.[46,87] Chronic pain is also associated with heightened symptoms of depression and anxiety.[2,89,102] Given the high costs and societal burden of chronic pain,[30,37] identifying biopsychosocial treatment targets to improve functioning in this population is critical.

Individual differences in emotional awareness may relate to the experience of chronic pain, and various constructs within this domain have been studied and debated. One specific concept, labeled with the term alexithymia, has received considerable theoretical and empirical attention over the past several decades.[118] Alexithymia refers to the inability to label and describe one's emotions and a preference for externally oriented thinking (EOT).[110] Alexithymia has been assessed primarily with self-report measures, the most common of which is the Toronto Alexithymia Scale-20 (TAS-20[6]). Alexithymia has been found to be elevated in adults and youth with chronic pain compared with healthy samples[22,31] and may be associated with greater pain intensity and disability.[3,72] In addition, alexithymia is associated with greater depressive and anxiety symptoms in various populations[63,64] including individuals with chronic pain.[23] This may be because alexithymia relates to reduced ability to successfully regulate, or reduce, negative emotion.[115] Although a number of factors—such as self-efficacy, stressor intensity, contextual cues, and cultural norms—influence an individual's choice of emotion regulation strategy, increased awareness of one's emotional states is thought to be key to taking active steps towards adaptive emotion regulation.[39,54] In his extended process theory of emotion regulation, Gross[39] explains that emotion identification enables an individual to take adaptive steps to regulate their emotions and is thus an essential first step in the emotion regulation process. Lieberman et al.[65,66] show that the simple act of applying a verbal label to one's emotional state results in reductions in negative affect both subjectively and neurologically, further demonstrating the emotion-regulating properties of emotional awareness.

Although most research examining the relationship between alexithymia and chronic pain has relied on cross-sectional methods, some prospective studies show that alexithymia may constitute a risk factor for pain outcomes.[10,100] Recent research highlights the malleability of alexithymia with psychological interventions,[11,14,79] which increases the relevance of alexithymia to chronic pain clinical practice. For example, in a recent single-arm trial, adults with chronic musculoskeletal pain undergoing group intervention targeting emotional awareness and expression demonstrated improvements in alexithymia, which were associated with reductions in psychological distress and improvements in pain intensity and interference.[12] A better understanding of the relationship between alexithymia and chronic pain has potential to clarify aspects of emotion awareness that relate to chronic pain and lead

to more specific psychological prevention or intervention programs to improve emotional functioning in individuals with chronic pain.

A great deal of research has examined alexithymia in individuals with chronic pain; however, no systematic reviews or meta-analyses of this literature have been conducted to summarize individual studies and provide estimates of the magnitude of the relationships between alexithymia and relevant pain variables. We conducted a systematic review of alexithymia in people with chronic pain and its relation to pain intensity, physical interference, anxiety, and depression. Specifically, we had 3 primary aims: (1) to determine levels of alexithymia in adults and youth with chronic pain; (2) to estimate the magnitude of the difference in alexithymia levels between samples with chronic pain and various comparison samples; and (3) to estimate the associations between alexithymia and pain intensity, physical function, and symptoms of depression and anxiety in people with chronic pain. There is ongoing debate in this field as to whether observed associations between measures of alexithymia, pain intensity, and functional impairment are confounded by depression or psychological distress.[43,75] Thus, a secondary aim was to identify and summarize studies that covaried measures of negative affect when testing the relationship between alexithymia and pain intensity and interference. In conducting the present systematic review and meta-analysis, we hope to make the available evidence more accessible, to facilitate a critical examination of the application of this construct, and to generate broad conclusions that help pave the path for next steps in the area of emotions and pain.

2. Methods

The systematic review and meta-analysis protocol for the current study was registered on September 25, 2017, and can be found through PROSPERO (ID: CRD42017077551).

2.1. Search methods

We conducted systematic searches in MEDLINE, PsyclNFO, and EMBASE from the inception of each database through June 2017. We included general search terms of “pain,” “alexithymia,” and related search terms to capture all studies conducted in this area. See Appendix for the specific search criteria. Two authors (R.A. and E.F.) independently sorted through abstracts to determine possible relevance (available as supplemental digital content at http://links.lww.com/PAIN/A734). The 2 resulting abstract lists were then reviewed together, and inconsistencies were resolved. Where disagreements emerged, a third author (T.P.) was consulted until 100% agreement was achieved. Next, articles identified as possibly relevant were reviewed in full to determine their eligibility against inclusion/exclusion criteria. Once a final set of studies was generated from our search, we reviewed their reference lists to ensure that other relevant articles had not been overlooked. Studies identified in this manner were then reviewed and assessed for eligibility. In addition, as described below, we contacted authors of articles that were missing key data or analyses to request those data.

2.2. Inclusion criteria

Inclusion criteria for individual studies were the following: (1) included youth (age <18 years) or adults (age ≥18 years) with chronic pain conditions including, but not limited to, headache, abdominal pain, musculoskeletal pain, and autoimmune disease-related pain; (2) assessed alexithymia using an established, psychometrically sound measure; and (3) published in English in a peer-reviewed journal.

2.3. Exclusion criteria

We excluded studies that (1) included chronic pain participants with primary psychiatric diagnoses (eg, substance abuse); (2) combined individuals with acute and chronic pain without reporting data separately for these groups; (3) screened and recruited based on "high" or "low" alexithymia; and (4) had less than 20 participants.

2.4. Data extraction

Data were extracted by R.A. and R.V. We extracted only the baseline data from longitudinal studies. When data from the same study were published in different articles, we extracted data from the earliest published article that met our inclusion criteria, unless a subsequently published article reported a larger sample size. Some studies provided data on distinct pain samples (eg, people with fibromyalgia vs headache). Some studies also provided data on nonclinical comparison samples and/or nonpain clinical samples (eg, diabetes). These data were extracted separately.

2.4.1. Study characteristics—We extracted study characteristics including sample size, chronic pain characteristics (condition, location, and duration), and demographic information (age, sex, and country of study) from included studies. When studies included a comparison sample, we extracted the sample size and type of comparison.

2.4.2. Alexithymia—Measures of alexithymia typically yield a continuous alexithymia score and a clinical cutoff score. The most commonly used measure, the Toronto Alexithymia Scale-20 (TAS-20[6]), which was adapted from the original 26-item TAS,[5] yields a continuous score ranging from 20 to 100, with higher scores indicating greater alexithymia and a clinical cutoff score of ≥61 indicating elevated alexithymia.[106] The TAS-20 has 3 subscales: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and EOT. The Alexithymia Questionnaire for Children (AQC)[103] is parallel to the TAS-20 but is linguistically adapted for children. We extracted mean alexithymia total and subscale scores and percentage of people above clinical cutoff scores in both chronic pain and comparison samples. We also recorded information on how alexithymia was assessed (ie, assessment tool and scoring parameters).

2.4.3. Correlation analysis—We extracted correlation coefficients describing the relationship between alexithymia and pain intensity, physical interference, anxiety, and depression. Some studies have examined partial correlations between alexithymia and pain intensity and physical interference while controlling for an index of depression or psychological distress. In the present review, we identified studies that conducted such partial correlations and extracted the resulting correlation coefficients for use in a secondary

meta-analysis of partial correlations. A number of studies reported correlations selectively based on significance. Where we were unable to achieve representative analyses, we applied a rule established a priori to exclude selectively reported findings to avoid biasing results towards statistically significant findings.

2.4.4. Study quality—For the purpose of better characterizing studies included in the meta-analysis, we extracted information related to study quality. We adapted the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies,[88] excluding items that were irrelevant or inconsistent with our study inclusion/exclusion criteria. Of the remaining items, some were adapted or reworded to more directly align with our criteria. Given the numerous international studies in this field, we evaluated whether authors included an alexithymia measure that had been validated in their country's language. We assigned studies 1 point per each criterion met, which were summed for a total quality score of 0 to 8 (0 indicating lowest quality and 8 highest quality).

2.4.5. Missing data—Of studies that met our inclusion criteria, many were missing some or all data points relevant to our meta-analyses. In many cases, it was clear from the authors' Methods section that relevant variables had been measured. Specifically, we requested (1) mean values and SDs of alexithymia total and subscale scores;(2) correlations between alexithymia and key variables (pain intensity, physical interference, depression, and anxiety); and (3) partial correlations of alexithymia with pain intensity and physical interference, controlling for negative affect (eg, explicit measures of negative, depression, or anxiety). We provided 1 follow-up email for those authors who did not initially respond.

2.5. Data analysis

For aim 1, we summarized alexithymia (total and subscales) scores and percentage of people exceeding clinical cutoff scores separately for adults and youth with chronic pain. All pooled mean values were calculated using the formula indicated in Higgins and Green[42] (p. 177).

For aim 2, we meta-analyzed the effect sizes of group differences in alexithymia scores between chronic pain and comparison groups with random effects models using Review Manager 5.1. We calculated standardized mean differences and 95% confidence intervals (CIs). Some studies compared 2 chronic pain samples with a single nonclinical comparison sample. In such cases, we extracted each of these comparisons separately and halved the n of the nonclinical sample to prevent inflating the weight of the individual study. For total alexithymia scores, we included in our analyses any alexithymia measure and scoring convention. However, for alexithymia subscale analyses, we examined only the TAS-20, given that this was the most commonly used measure, and other measures have different factor structures.

For aim 3, we meta-analyzed correlations of alexithymia with pain intensity, physical interference, depression, and anxiety using random effects models. Finally, for our secondary analysis, we meta-analyzed partial correlations that examined the relationship between alexithymia and pain intensity and physical interference when controlling for measures of negative affect using random effects models. Meta-analyses of correlation coefficients were conducted in STATA using the DerSimonian-Laird random effects method.

We examined the effect size and 95% CIs. When there were more than 8 studies in a meta-analysis, trim and fill analyses were used to detect publication bias using Duval and Tweedie's[25] method and Rosenthal's fail-safe N (1979). Trim and fill analyses evaluate the overall effect and variance of each study included in a meta-analysis, identifies possible missing studies that may have resulted from publication bias (eg, selective publication of statistically significant results), and imputes values for these missing studies.[25] We subsequently reran meta-analyses to ensure that significant findings were not the result of publication bias.

For all meta-analyses, we considered between-study heterogeneity (I^2) and interpreted findings using Cochrane standards as a guide (Higgins and Green[42]). Specifically, we adopted the following cutoffs for describing heterogeneity: (0%−29% low heterogeneity; 30%−49% moderate heterogeneity; 50%−74% substantial heterogeneity; and 75%−100% considerable heterogeneity). To explore whether variability in study quality influenced study findings, we conducted correlations between effect size estimates and quality ratings for analyses of group differences in alexithymia, and for analyses of correlations of alexithymia with pain intensity, physical interference, depression, and anxiety.

3. Results

3.1. Study selection

Our systematic search resulted in 1240 abstracts. After screening these abstracts, we identified 157 full texts to review for eligibility. Through review, we excluded 80 studies (Fig. 1). This resulted in 77 full studies for analysis. Among these 77 studies, 10 reported data from distinct chronic pain samples (eg, a study reported data from 2 distinct samples of individuals with an autoimmune disease and headache). We preserved data from these distinct samples and therefore included a total of 87 chronic pain samples in our review. We use the terminology "study" to identify overarching studies, or articles, and the terminology "sample" to identify a distinct group of individuals with chronic pain.

3.2. Missing data

We contacted 71 authors to request additional data and analyses. Additional data were obtained for 22 studies. Authors of an additional 17 studies responded but could not complete the request because they lacked access to the original data (n = 12) or their schedules were too busy (n = 5).

3.3. Study characteristics

From the 77 studies, there were data from 82 adult and 5 youth chronic pain samples (Table 1). Of note, 1 additional study examined a mixed sample of adolescents and young adults (aged 16–20 years) with inflammatory bowel disease or irritable bowel syndrome.[44] Developmentally, alexithymia scores in individuals within this age range are more similar to adults,[95] and therefore, we categorized this study as an adult sample.

From 82 adult samples (across 77 studies), data were available on alexithymia mean scores or clinical cutoff scores from 74 (90%), comparison of alexithymia scores of a chronic pain

sample to a comparison sample from 34 (41%), zero-order correlations between alexithymia and pain intensity, physical interference, depression and/or anxiety from 40 (49%), and partial correlations from 14 (17%). From 5 youth samples (across 5 studies), we obtained alexithymia mean scores or clinical cutoff scores from 4; correlations between alexithymia and key variables of interest from 2; and group differences between a chronic pain and comparison sample from 1. There were not enough extractable data in studies of youth to conduct meta-analyses. All included studies used some variation of the Toronto Alexithymia Scale, including the TAS-26 (k = 14), TAS-20 (k = 72), and AQC (k = 1). In this case, the AQC was scored using the same scale as the TAS-20 (ie, 20–100). Other psychometrically sound self-report measures (eg, Bermond-Vorst Alexithymia Questionnaire[128]) or clinician-administered measures (eg, Toronto Structured Interview for Alexithymia[7]) of alexithymia were not used in this body of literature.

3.3.1. Pooled mean values and prevalence of alexithymia in individuals with chronic pain—

Among the 82 samples of adults with chronic pain, TAS-20 total scores were available for 61, and TAS-26 total scores were available for 9. The pooled mean values of TAS-26 total and TAS- 20 total and subscale scores are presented in Table 2. In addition to total scores, the percentage of individuals with a total alexithymia score beyond the clinical cutoff score for TAS-20 was available for 39 samples (n = 4092). Of these, 28% of adults with chronic pain exceeded this threshold. The percentage of individuals with a total alexithymia score beyond the clinical cutoff scores for TAS-20 was available for 5 samples(n = 460); of these, 36% of adults exceeded this threshold.

Two studies including youth-reported mean alexithymia using a standard scoring convention: Gatta et al. (2011) measured alexithymia using the AQC in a sample of 32 youth with tension-type headache and reported a mean total score of 58.13 (SD = 10.64). Cerutti et al. (2016) assessed alexithymia with the TAS-20 in 53 youth with migraines and reported a mean total score of 56.3 (SD = 12.14); 31% of the youth exceeded clinical cutoffs for alexithymia. These data should be interpreted with caution, however, as the validity of applying adult-derived clinical cutoff scores to characterize alexithymia in youth has been questioned.[95]

3.3.2. Group differences in alexithymia in pain vs comparison groups—

We examined group differences in alexithymia total scores in adults with chronic pain (n = 1706) compared with nonclinical comparison samples (n = 1370; k = 27). We also examined 4 studies that compared alexithymia total scores in adults with chronic pain (n = 170) compared with nonpain clinical comparison samples (n = 207). One study in the latter analysis was an outlier, reporting an unexpectedly large effect size difference in alexithymia, and was excluded from analyses.[101] A significant and large group difference in total alexithymia between adults with chronic pain and nonclinical comparison samples remained (d = 0.81, 95% CI 0.62–1.00), although with substantial heterogeneity (I^2 = 83%). Among studies that compared alexithymia total scores in adults with chronic pain with nonpain clinical comparison samples (k = 4), there was a statistically significant medium-sized effect (d = 0.55, 95% CI 0.34–0.77) with no observed heterogeneity (I^2 = 0%). A forest plot depicting group differences in alexithymia total scores is presented in Figure 2.

We also examined group differences in alexithymia subscale scores (Table 3). Adults with chronic pain had greater DIF scores compared with nonclinical samples, and this was statistically significant with a large effect size. Adults with chronic pain had greater DDF compared with nonclinical samples with a medium effect size. Findings were similar for group differences between adults with chronic pain and nonpain clinical comparison samples. There was no statistically significant group difference in EOT between adults with chronic pain and nonclinical samples. There were too few studies to examine group differences in EOT between adults with chronic and nonpain clinical samples and group differences in alexithymia total and subscale scores in youth.

3.3.3. Relationships of alexithymia with pain intensity, physical interference, depression, and anxiety within pain samples—As shown in Table 4, we found significant, small-magnitude, positive correlations between alexithymia and pain intensity and pain interference and significant, medium-size magnitude, positive relationships between alexithymia and depression and anxiety. Across all analyses, DIF was the most strongly associated alexithymia subscale with these measures, followed by DDF. Small relationships were observed between EOT and all variables except pain interference. Trim and fill analyses identified missing studies in just 1 analysis (relationship between EOT and depression). When missing studies were subsequently filled, the pattern of significance remained the same.

Only 2 studies examined these correlations in youth; thus, meta-analyses for youth could not be conducted. One study showed a significant positive relationship between alexithymia and anxiety and a nonsignificant relationship between alexithymia and depression[108] in a small sample (n = 21) of youth with mixed headache and abdominal pain. The other study showed significant correlations between alexithymia and anxiety and depression in a sample of youth with migraine.[17]

3.3.4. Meta-analysis of partial correlations controlling for psychological distress—Partial correlations between alexithymia and pain measures (intensity and interference) were published in only 3 studies, and we obtained unpublished data from authors of 11 additional studies (thus, k = 14). We meta-analyzed partial correlations between alexithymia (total and subscale scores), pain intensity, and pain interference while controlling for negative affect. As shown in Table 5, there were no significant partial correlations of alexithymia total or subscale scores with pain intensity and pain interference.

3.4. Quality assessment

Overall quality ratings are depicted in Figure 3, offering a relative assessment of the overall quality of included studies. For studies of adults, quality ratings ranged from 2 to 8 (mean = 5.13, SD = 1.21; median = 5). For youth studies, quality ranged from 3 through 6 (mean = 4.60, median = 5). Study quality was not significantly correlated with effect size for group differences in alexithymia ($r = 0.13$, $P = 0.429$) or correlations of alexithymia with pain intensity ($r = -0.21$, $P = 0.282$), physical interference ($r = 0.20$, $P = 0.403$), depression ($r = 0.29$, $P = 0.138$), or anxiety ($r = 0.10$, $P = 0.650$).

4. Discussion

This is the first systematic review and meta-analysis of alexithymia in individuals with chronic pain. We identified a large number of articles (k = 77), reflecting substantial interest in the assessment of alexithymia, primarily in adults, with a range of pain conditions. Overall, our findings demonstrated that alexithymia was higher in individuals with chronic pain compared with both nonclinical samples (large effect) and clinical samples without pain (medium effect). The latter finding suggests that the elevated alexithymia is not solely a bias associated with health care seeking or having a chronic illness. We found that 26% of adults with chronic pain met the threshold of a clinical cutoff score for alexithymia—an estimate that is higher than the 13% reported in the general population.[106] In addition to elevated alexithymia in people with chronic pain, our meta-analyses indicated that among adults with chronic pain, alexithymia was associated with greater pain intensity and physical interference, with correlations that were small in magnitude. Alexithymia was also positively associated with depression and anxiety, with correlations that were medium in magnitude.

Among adults with chronic pain, greater alexithymia was associated with greater pain intensity and physical interference, with small-magnitude effect sizes. These findings are consistent with laboratory-based studies demonstrating altered pain processing in relation to heightened alexithymia in healthy adults.[45,52,90] As expected, alexithymia was associated with greater depression and anxiety with large effect sizes. Emotional awareness is important for effective emotion regulation,[38,54] and alexithymia is associated with reliance on ineffective approaches to emotion regulation including suppression and avoidance.[94,115] The experience of chronic pain confers additional stress in many life domains (eg, social, emotional, physical)[119]; in the face of these stressors, alexithymia may be associated with greater difficulty regulating emotions, contributing to poor mental health outcomes.[69]

Specific subscales of alexithymia measures showed differential effects; in particular, effects were larger for DIF and DDF, but lower or nonsignificant for EOT. Contributing to this pattern may be the weak psychometric properties of the EOT subscale of the TAS-20,[58] particularly in non-Western cultures.[20] It is also possible that chronic pain is more tightly linked to the constructs of difficulty identifying and describing feelings. With the inability to identify or describe one's emotions, it is possible that awareness of or attention to interoceptive cues is associated with misinterpreting emotional cues as harmful or as signs of illness.[70,117] Our review highlights the important need for future research on the conceptualization and assessment of emotional awareness as it applies to chronic pain.

We meta-analyzed partial correlations from 14 studies that examined relationships of alexithymia to pain intensity and pain interference while controlling for psychological distress. These analyses revealed that alexithymia was no longer uniquely related to pain variables. There are several possible interpretations of these results. First, some scholars have questioned the validity of self-reported alexithymia, especially given its convergence with measures of negative affect,[62,67] which could spuriously inflate alexithymia's correlations with self-reported measures of pain and other symptoms. Relatedly, individuals with depressive symptoms are more likely to evaluate themselves and their abilities negatively on a self-report survey.[62,67] Another intriguing possibility is that distress or

negative affect may mediate the links between alexithymia and pain. Unfortunately, cross-sectional analyses such as those in the current review cannot differentiate these 2 possibilities. We also note that potential confounding by negative affect is by no means limited to studies of alexithymia; such bias complicates the assessment and interpretation of many or most self-reported psychological constructs that are related to pain.[114,129] It should also be noted that only 3 of the 14 sets of partial correlations that we meta-analyzed had been peer reviewed and published; the other 11 were provided to us directly by the authors on our request. Given these considerations, we suggest caution in making conclusions about the role of negative affect in the relationship between alexithymia and pain based on the current findings. Of note, the fact that partial correlation analyses were available but rarely published raises the issue of a publication bias in scientific literature towards positive findings.[104] Moving forward, we recommend that investigators examine and report the role of negative affect in the relationship between alexithymia or other psychological constructs and chronic pain and to test alternative models (eg, moderation and mediation) to better parse these relationships.

Results from the present systematic review and meta-analysis reveal many significant gaps in this large body of literature. For example, only 5 studies examined alexithymia in youth with chronic pain, and it is unclear whether this construct can be adequately measured in youth. These studies typically applied adult-derived alexithymia cutoff scores, not considered valid in youth populations.[136] Data were insufficient to examine group differences and correlations in youth with chronic pain. Future studies are needed to clarify the role of emotional awareness in youth with pain, using age-appropriate assessment (cf. [136]), to determine how it relates to pain intensity, physical interference, depression, and anxiety. Adolescence is a critical window for the development of emotional insight and emotion regulation (Somerville, 2016). Clarifying the role of emotional awareness in youth with pain may have developmental implications and unique treatment considerations.

Another gap in the broad alexithymia and chronic pain literature is the preponderance of cross-sectional study designs. Very few studies in this field have examined temporal patterns or longitudinal relationships between alexithymia and chronic pain. Alexithymia may be a risk factor for subsequent pain where reduced ability to label and describe emotions leads to misperceptions of the physiological correlates of emotion as signs of illness.[61,71,116] On the other hand, chronic pain may contribute to affective deficits observed in alexithymia. Constructivist theories of emotion argue that the subjective experience of emotion results in part from awareness of bodily cues.[9] A recent systematic review concluded that individuals with chronic pain have reduced accuracy in detecting interoceptive cues compared with comparison samples.[21] The presence of pain, a potentially threatening biological cue, may distract from awareness of relevant interoceptive cues, particularly those subtle cues involved in daily experiences and interactions with others. This is an empirical question for future research.

Addressing these gaps in the literature has potential implications for clinical intervention. It is possible that individuals with both chronic pain and elevated alexithymia may benefit from interventions that directly target processes related to emotional awareness, such as emotional awareness and expression training.[73] On the other hand, more general

psychological interventions may function to reduce depression and anxiety and in turn result in reduced alexithymia. Future research is needed to investigate ontological distinctions between alexithymia and negative affect, and if and how they relate temporally.

Current findings should be considered in light of additional limitations. There is substantial debate about the alexithymia construct more broadly. Alexithymia generally, and the TAS-20 specifically, has been criticized for relying on Western norms, which value individual emotional experience and verbal expression of emotion.[56] Diverging from this norm may indicate psychopathology in Western culture, but not necessarily in others. Nonetheless, a strength of the current meta-analysis is representation from many different geographic regions and cultures, and the TAS-20 has been validated in a number of Eastern cultures.[85,135] Future studies should examine whether ethnicity or culture moderates the relationship between alexithymia and chronic pain. Another limitation of the TAS-20, particularly the DIF subscale, is that it contains items pertaining to physiological sensations (eg, “I have physical sensations that even doctors don’t understand;” “I am often puzzled by sensations in my body.”). Such items likely reflect the experience of chronic pain, artificially inflating correlations between the TAS-20 and pain-related measures. A number of interview or observer-based measures of alexithymia have been developed, although, unfortunately, we did not identify studies that made use of these assessment tools in the current meta-analysis.

Meta-analyses in the current study were generally characterized by substantial heterogeneity and thus should be interpreted with caution. There may be relevant demographic or clinical differences that contribute to such heterogeneity. For example, the relationship of alexithymia to pain severity and interference may vary by sex or ethnicity[20,91] and be a function of pain characteristics, such as duration of pain or specific pain condition. Examining demographic and clinical moderators was beyond the scope of the present metaanalysis and represent potential future avenues of research.

We examined study quality using general criteria and assigned a relative quality value to each included study. The overall mean and median quality scores of included studies were relatively high; however, a large subset of studies was characterized by low study quality. Future studies with rigorous methodology and reporting are needed to increase confidence in this body of work. Relative areas of weakness include failing to provide sample size justification and to report participation rates. In addition, very few studies tested the unique validity of alexithymia measures by controlling for various potential confounds: future studies should consider accounting for demographic (eg, education and age) and clinical factors (eg, psychological distress) that relate differentially to alexithymia scores.

In conclusion, this systematic review helps summarize a substantial literature examining alexithymia in chronic pain, finding that alexithymia is elevated in youth and adults with chronic pain conditions. In adults, alexithymia is associated with greater pain intensity, physical interference, depression, and anxiety. Alex-ithymia may be relevant to the presence and severity of chronic pain and associated mental health symptoms. Future empirical research is needed to better illuminate these relationships and clarify the potentially confounding role of negative affect. In particular, using prospective designs and non-self-

repot alexithymia assessment tools would add greater clarity to this construct and inform development of targeted interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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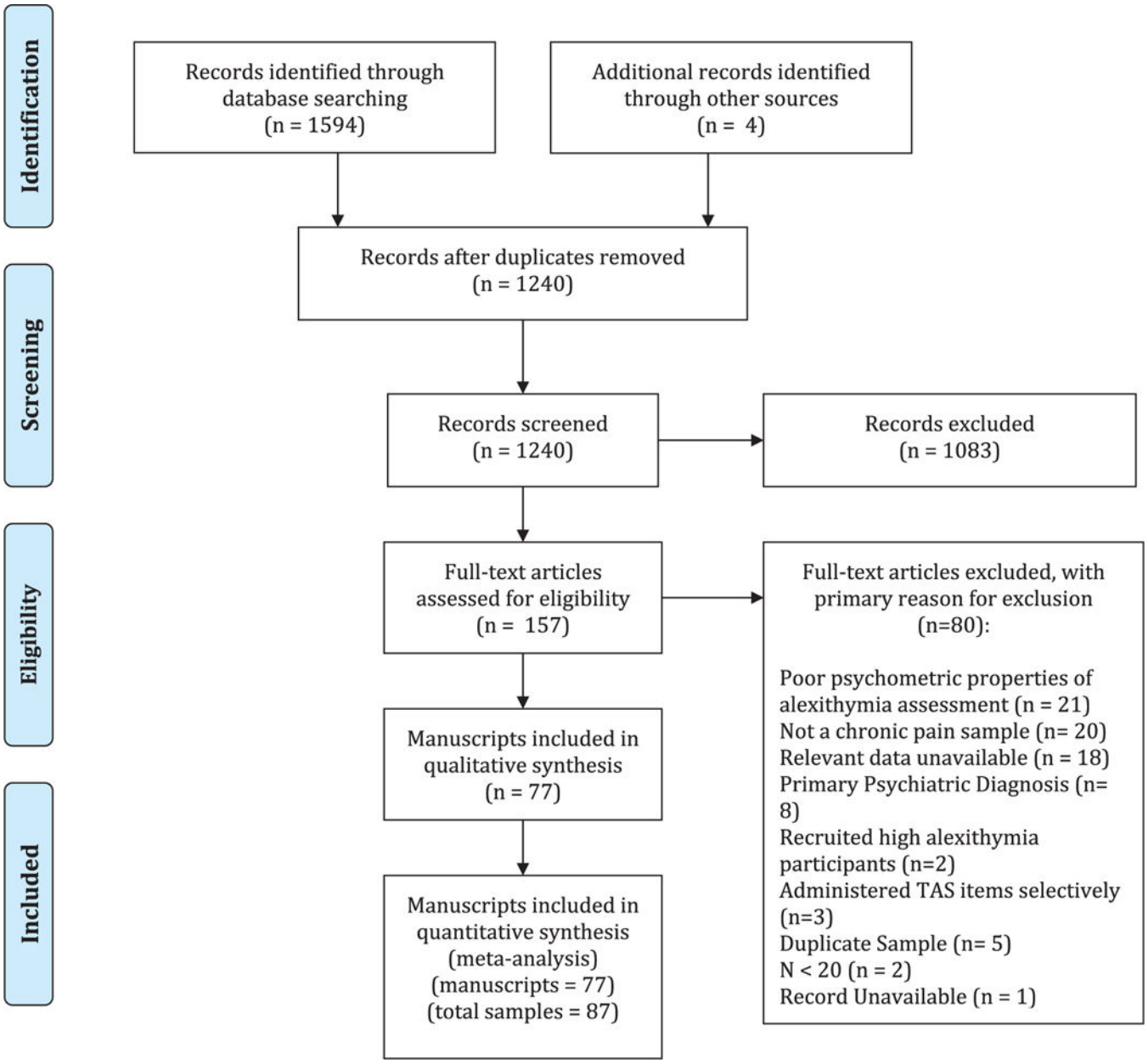

Figure 1.
PRISMA flowchart diagramming studies Included In meta-analyses.

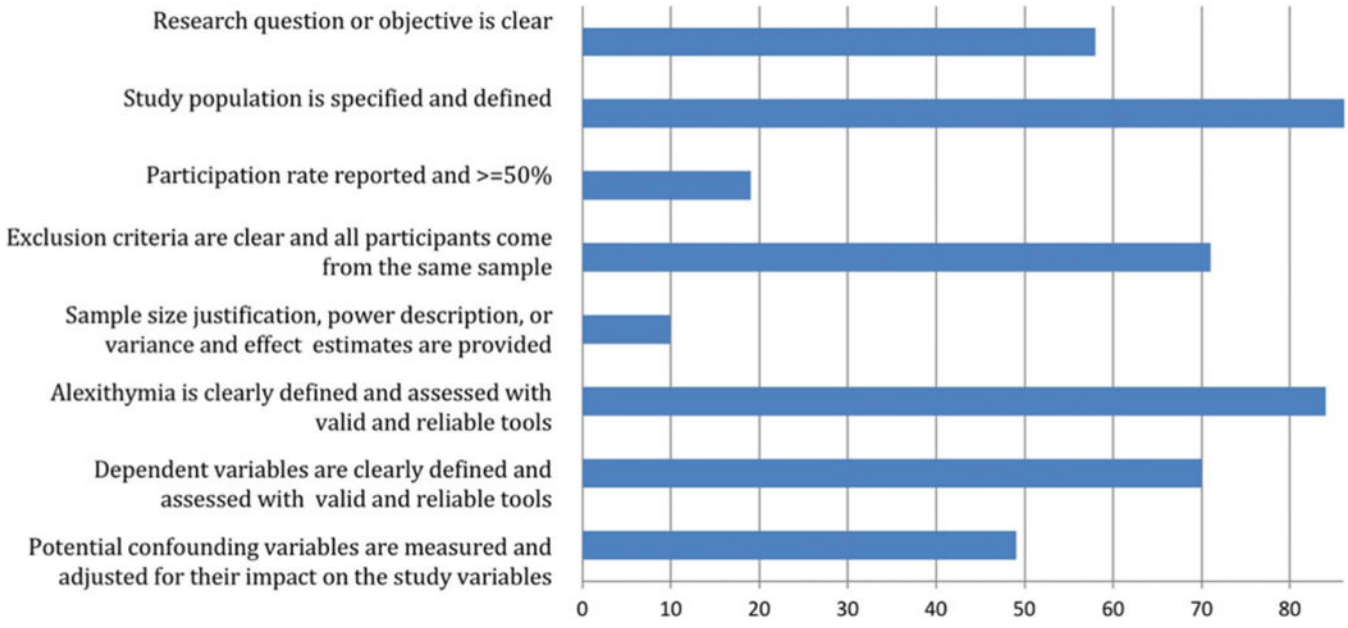

Figure 2.
Summary of quality ratings across all samples (87) included in the manuscript.

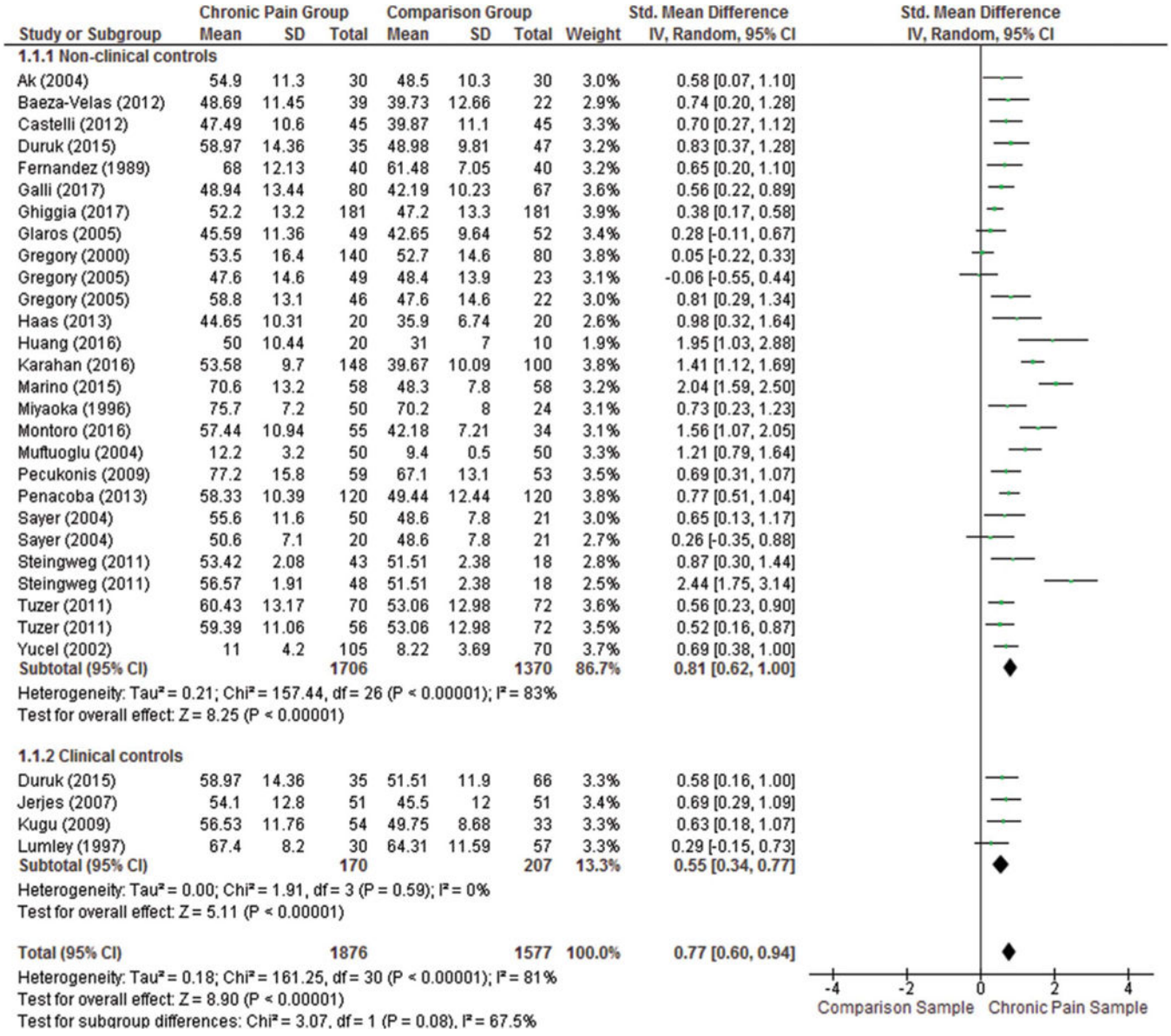

Figure 3.

Forest plot depicting group differences in the alexithymia score between adults with chronic pain and nonclinical and clinical comparison samples.

Table 1

Summary of studies included in meta-analysis.

Study author and year	Pain condition	Study design	Country of study	Pain group (N)	Age (mean and SD)	Sex (% female)	Alexithymia measure	Quality assessment (0–8)
Adult studies								
Ak (2004)[1]	Mixed chronic pain	G, M	Turkey	30	40.6 (11.4)	83%	TAS-20	5
Atagun (2012)[3]	Fibromyalgia	C, M	Turkey	57	40.9 (6.9)	100%	TAS-20	5
Baeza-Velasco(2012)[4,*]	Mixed chronic pain	C, G, M	France	39	52.2 (8.9)	100%	TAS-20	3
Balaban (2012)[8]	Headache	M	Turkey	31	20.9 (1.7)	81%	TAS-20	5
Burger (2012)[12,*]	MSK	C, M	United States	72	49.3 (15.6)	79%	TAS-20	8
Castelli (2012)[16]	TMD	C, M	Italy	45	38.9 (11.6)	100%	TAS-20	4
Castelli (2012)[15]	Fibromyalgia	G, M	Italy	55	52.8 (10.5)	100%	TAS-20	4
Cerutti (2016)[17,*,†]	Headache	M	Italy	53	41.8 (3.9)	53%	TAS-20	4
Chang (2017)[18,†]	Chronic pain	G, M	Taiwan	121	54.0 (15.6)	9%	TAS-20	6
Chang (2017)[18,†]	Fibromyalgia	G, M	Taiwan	58	57.5 (15.8)	71%	TAS-20	6
Cologno (2005)[19]	Headache	M	Italy	35	38.0 (9.3)	80%	TAS-20	3
Di Tella (2017)[23,*]	Fibromyalgia	C, M	Italy	159	52.5 (10.2)	100%	TAS-20	6
Duruk (2015)[24,*]	Fibromyalgia	C, G, M	Turkey	35	41 (9.7)	100%	TAS-20	6
Esin (2017)[26]	Headache	M	Russia	137	40.8 (6.3)	61%	TAS-26	3
Evren (2006)[27]	Fibromyalgia	C, M	Turkey	51	37.2 (9.3)	100%	TAS-20	6
Fernandez (1989)[28]	Autoimmune	G, M	India	40	36.1 (11.3)	65%	TAS-26	3
Galli (2017)[29,*]	Headache	G, M	Italy	80	44.7 (8.6)	74%	TAS-20	5
Ghiggia (2017)[33,*]	Fibromyalgia	C, G, M	Italy	181	51.7 (10.2)	100%	TAS-20	5
Glaros (2005)[34]	TMD	C, G, M	United States	49	39.9 (12)	NR	TAS-20	5
Gregory (2000)[35]	Chronic pain	G, M	United States	140	44.7 (11.2)	75%	TAS-20	5
Gregory (2005)[36,†]	Chronic pain	G, M	United States	46	NR	NR	TAS-20	6
Gregory (2005)[36,†]	MSK	G, M	United States	49	NR	NR	TAS-20	7
Gulec (2008)[40,*]	Fibromyalgia	C, M	Turkey	75	43.6 (10.6)	100%	TAS-20	7

Study author and year	Pain condition	Study design	Country of study	Pain group (N)	Age (mean and SD)	Sex (% female)	Alexithymia measure	Quality assessment (0–8)
Haas (2013)[41]	TMD	G	Germany	20	40.6 (14.7)	90%	TAS-26	7
Hosoi (2010)[43]	Autoimmune	C	United States	129	52 (12.4)	56%	TAS-20	6
Huang (2016)[44]	Mixed chronic pain	G, M	United States	20	17 (NR)	55%	TAS-20	5
Huber (2009)[45, *]	Fibromyalgia	C, M	Italy	68	43.4 (11.1)	100%	TAS-20	5
Jasinski (2016)[47]	MSK	M	United States	95	46.9 (9.7)	52%	TAS-20	4
Jerjes (2007)[48]	Headache	G, M	United Kingdom	51	40 (13)	67%	TAS-20	5
Jerlang (1997)[49]	BMS	M	Denmark	20	67 (NR)	100%	TAS-26	4
Johannsen (2017)[51, *]	Cancer	C, M	Denmark	129	56.8 (9.1)	100%	TAS-20	4
Karahan (2016)[53]	Autoimmune	G, M	Turkey	148	52.6 (12.0)	78%	TAS-20	5
Kojima (2014)[57, *]	Autoimmune	C, M	Japan	213	60 (12)	82%	TAS-20	7
Kosturek (1998)[59]	MSK	M	United States	50	43.6 (10.9)	46%	TAS-20	6
Kugu (2009)[60]	Fibromyalgia	G, M	Turkey	54	48.1 (8.1)	100%	TAS-20	4
Lumley (1997)[68]	Chronic pain	C, G	United States	30	40.4 (NR)	70%	TAS-26	5
Lumley (20 02)[74, *]	Myofascial	C, M	United States	80	48.7 (11.8)	75%	TAS-20	6
Lumley (2005)[72, †]	Autoimmune	C, M	United States	155	55 (NR)	88%	TAS-20	5
Lumley (2005)[72, †]	Headache	C, M	United States	160	31.8 (NR)	84%	TAS-20	5
Makino (2013)[75]	Mixed chronic pain	C, M	Japan	128	52.3 (16.3)	74%	TAS-20	7
Margalit (2014)[76, †]	CRPS	C, M	Israel	30	38.3 (14.3)	40%	TAS-20	5
Margalit (2014)[76, †]	MSK	C, M	Israel	30	38.2 (12.5)	40%	TAS-20	5
Marino (2015)[77]	BMS	C, G, M	Italy	58	65.6 (10.5)	79%	TAS-20	4
Martinez (2015)[78, *]	Fibromyalgia	C	Spain	100	48.4 (7.5)	100%	TAS-20	4
Melin (2010)[79, *]	Chronic pain	C, M	Sweden	59	46 (NR)	88%	TAS-20	4
Melis (2014)[80, *]	Pelvic pain	C, M	Italy	41	31.5 (6.4)	100%	TAS-20	5
Millard (1992)[81]	Mixed chronic pain	C, M	United States	194	42.8 (11.2)	64%	TAS-26	5
Mingarelli (2013)[82]	TMD	C, M	Italy	132	39.2 (13.6)	85%	TAS-20	7
Miyaoka (1996)[83]	BMS	G	Japan	50	55.8 (8.7)	100%	TAS-26	2
Montoro (2016)[84, *]	Fibromyalgia	C, G, M	Spain	55	51.9 (8.8)	100%	TAS-20	6

Study author and year	Pain condition	Study design	Country of study	Pain group (N)	Age (mean and SD)	Sex (% female)	Alexithymia measure	Quality assessment (0–8)
Muftuoglu (2004)[86]	Headache	G	Turkey	50	32.1 (NR)	64%	TAS-26	4
Ozturk (2015)[92]	Mastalgia	M	Turkey	88	29.6 (8.2)	100%	TAS-20	6
Pecukonis (2009)[96]	MSK	G	United States	59	33.3 (11.9)	100%	TAS-26	6
Periacoba (2013)[97]	Fibromyalgia	G	Spain	120	50.9 (9.8)	100%	TAS-20	5
Pepe (2014)[98,*]	MSK	C, M	Italy	40	44.8 (9.7)	30%	TAS-20	6
Porcelli (2014)[99,*]	IBS	C, M	Italy	177	34.5 (11.7)	71%	TAS-20	5
Portincasa (2003)[101]	IBS	G, M	Italy	100	48 (2)	27%	TAS-20	4
Saariaho (2016)[105]	Chronic pain	C, M	Finland	83	49.5 (7.19)	41%	TAS-20	5
Sayar (20 04)[107,†]	Fibromyalgia	C , M	Turkey	50	40.5 (8.8)	100%	TAS-20	4
Sayar (2004)[107,†]	Autoimmune	C , M	Turkey	20	45.6 (14.9)	100%	TAS-20	4
Shibata (2014)[109,*]	Chronic pain	C, M	Japan	439	61.1 (11)	65%	TAS-20	6
Sinikallio (2006)[111]	MSK	M	Finland	100	61.6 (11.2)	58%	TAS-20	4
Slavin-Spenny (2003)[112]	Headache	M	United States	147	22.1 (6)	88%	TAS-20	7
Steinweg (2011)[113,†]	Autoimmune	G, M	United States	43	59.8 (13.7)	9%	TAS-20	7
Steinweg (2011)[113,†]	Fibromyalgia	G, M	United States	48	54.1 (13.4)	92%	TAS-20	7
Tuzer (2011)[120,†]	Fibromyalgia	G, M	Turkey	70	39.0 (7.9)	100%	TAS-20	6
Tuzer (2011)[120,†]	MSK	G, M	Turkey	56	44.2 (9.3)	100%	TAS-20	6
Vadacca (2014)[121,*,†]	Autoimmune	C, M	Italy	25	46 (11)	100%	TAS-20	5
Vadacca (2014)[121,*,†]	Autoimmune	C, M	Italy	24	64 (10)	100%	TAS-20	5
Valkamo (2001)[122]	Chest pain	M	Finland	200	58.1 (9.4)	34%	TAS-20	4
van Middendorp (2008)[123]	Fibromyalgia	C, G, M	Netherlands	403	46.5 (12.3)	100%	TAS-20	6
Veehof (2011)[124]	Fibromyalgia	M	Netherlands	141	43.1 (10.9)	92%	TAS-20	5
Vieira (2013)[125,*]	Headache	C, M	Brazil	39	43.6 (10.7)	100%	TAS-26	6
Villani (2005)[126]	Headache	M	Italy	42	35.7 (10.6)	83%	TAS-20	3
Villani (2010)[127]	Headache	M	Italy	465	34.7 (10.9)	82%	TAS-20	3
White (2011)[130]	Chest pain	M	United States/ Israel	229	50 (10.3)	56%	TAS-20	6

Study author and year	Pain condition	Study design	Country of study	Pain group (N)	Age (mean and SD)	Sex (% female)	Alexithymia measure	Quality assessment (0–8)
Wise (1994)[131,†]	Headache	M	United States	61	37.8 (13.6)	NR	TAS-26	5
Wise (1994)[131,†]	Headache	M	United States	39	37.8 (13.6)	NR	TAS-26	5
Yalug (2010)[132]	Headache	C, M	Turkey	300	37.4 (13.8)	83%	TAS-20	7
Yucel (2002)[133]	Headache	G	Turkey	105	33 (10)	78%	TAS-26	6
Zeng (2016)[134]	Chronic pain	C	China	147	34.9 (11.3)	100%	TAS-20	4
Zincir (2014)[137]	Chest pain	G, M	Turkey	51	33 (7.3)	73%	TAS-20	6
Youth studies:								
Cerutti (2016)[17,*,†]	Headache	C, M	Italy	53	13.4 (2.4)	57%	TAS-20	4
Gatta (2011)[31]	Headache	M, G	Italy	32	11.2 (2)	81%	AQC	6
Gatta (2015)[32,†]	Headache	M	Italy	42	13.1 (2.4)	57%	TAS-20	5
Gatta (2015)[32,†]	Headache	M	Italy	47	12.4 (2.3)	77%	TAS-20	5
Sayin (2007)[108]	Mixed chronic pain	C	Turkey	21	14.4 (2.6)	33%	TAS-26	3

The study design column refers to included analyses relevant for the present meta-analysis: C, correlational; G, group difference; M, mean or prevalence.

*Additional data provided by the author on personal request.

†Represents data from 1 of 2 samples reported in the same article.

AQC, Alexithymia Questionnaire for Children; BMS, burning mouth syndrome; CPRS, complex regional pain syndrome; IBS, irritable bowel syndrome; MSK, musculoskeletal pain; NR, not reported; TMD, temporomandibular disorder.

Table 2

Pooled alexithymia total and subscale scores for the overall adult sample.

	Range	k	N	Mean	SD
TAS-20					
Total score	20–100	60	5964	52.08	12.97
Difficulty identifying feelings	7–35	46	4654	17.79	6.75
Difficulty describing feelings	5–25	46	4654	13.73	5.05
Externally oriented thinking	8–40	45	4216	20.06	4.83
TAS-26					
Total score	26–156	9	630	66.99	17.66

Range indicates minimum to maximum score.

Table 3

Meta-analysis of differences in alexithymia total and subscale scores between adult samples with chronic pain and comparison samples.

Alexithymia subscale	Studies (k)	Chronic pain (n)	Comparison (n)	Overall effect and heterogeneity		
				Effect size	95% CI	I^2, %
All comparisons						
Total	31	1876	1577	0.77	0.60 to 0.94	81
DIF	21	1506	995	0.86	0.63 to 1.10	85
DDF	21	1506	995	0.46	0.32 to 0.61	62
EOT	18	1068	692	0.18	−0.07 to 0.44	83
Nonclinical comparison						
Total	27	1706	1370	0.81	0.62 to 1.00	83
DIF	18	1401	845	0.92	0.66 to 1.19	86
DDF	18	1401	845	0.46	0.29 to 0.62	67
EOT	16	963	608	0.13	−0.15 to 0.40	85
Medical comparison						
Total	4	170	207	0.55	0.34 to 0.77	0
DIF	3	140	150	0.51	0.27 to 0.75	0
DDF	3	140	150	0.57	0.33 to 0.81	0

Insufficient datato meta-analyze differences in EOT in chronic pain vs medical comparison.

CI, confidence interval; DIF, difficulty identifying feelings; DDF, difficulty describing feelings; EOT, externally oriented thinking.

Table 4

Summary of meta-analyses of correlations between alexithymia total and subscale scores with variables of interest.

Variable	Alexithymia subscale	Overall effect and heterogeneity					
		Studies (k)	Participants (n)	Effect size	95% CI	I^2	Trim and fill (Y or N)
Pain intensity							
	Total	27	2749	**0.20**	**13 to 0.28**	70.94	N
	Difficulty identifying feelings	24	2718	**0.18**	**0.14 to 0.23**	30.94	N
	Difficulty describing feelings	23	2591	**0.19**	**0.12 to 0.25**	57.47	N
	Externally oriented thinking	22	2188	**0.08**	**0.01 to 0.14**	51.67	N
Physical interference							
	Total	19	2049	**0.17**	**0.10 to 0.24**	57.22	N
	Difficulty identifying feelings	18	1880	**0.21**	**0.12 to 0.30**	70.44	N
	Difficulty describing feelings	17	1752	**0.16**	**0.10 to 0.23**	46.49	N
	Externally oriented thinking	17	1752	0.03	−0.05 to 0.11	60.32	N
Depression							
	Total	20	2678	**0.46**	**0.41** to **0.51**	48.27	N
	Difficulty identifying feelings	21	2260	**0.42**	**0.34** to **0.49**	74.81	N
	Difficulty describing feelings	20	2132	**0.38**	**0.31** to **0.46**	69.36	N
	Externally oriented thinking	20	2132	**0.20**	**0.12** to **0.28**	70.43	Y
Anxiety							
	Total	22	2431	**0.43**	**0.36** to **0.49**	62.54	N
	Difficulty identifying feelings	19	2114	**0.46**	**0.40** to **0.52**	60.71	N
	Difficulty describing feelings	17	1933	**0.38**	**0.31** to **0.46**	45.10	N
	Externally oriented thinking	18	1986	**0.12**	**0.04** to **0.20**	68.01	N

Small effect size = 0.2; moderate effect size = 0.5; large effect size = 0.8. Significant effects are bolded. I^2:0% to 29% low heterogeneity; 30% to 49% moderate heterogeneity; 50% to 74% substantial heterogeneity; 75% to 100% considerable heterogeneity.

CI, confidence interval.

Table 5

Summary of meta-analyses of partial correlations between alexithymia total and subscale scores with variables of interest, while controlling for a measure of negative affect.

Variable	Alexithymia subscale	Overall effect and heterogeneity					
		Studies (k)	Participants (n)	Effect size	95% CI	I^2	Trim and fill (Y or N)
Pain intensity							
	Total	14	1621	0.09	−0.04 to 0.21	83.28	N
	Difficulty identifying feelings	13	1582	0.06	−0.03 to 0.15	65.23	N
	Difficulty describing feelings	11	1323	0.07	−0.40 to 0.36	82.27	N
	Externally oriented thinking	12	1522	0.06	−0.04 to 0.16	71.70	N
Physical interference							
	Total	10	1101	0.06	−0.06 to 0.16	63.25	N
	Difficulty identifying feelings	11	1176	0.03	−0.05 to 0.11	36.42	N
	Difficulty describing feelings	11	1176	0.04	−0.06 to 0.13	51.36	N
	Externally oriented thinking	11	1176	−0.01	−0.13 to 0.10	69.65	N

Small effect size = 0.2; moderate effect size = 0.5; large effect size = 0.8. I^2: 0% to 29% low heterogeneity; 30% to 49% moderate heterogeneity; 50% to 74% substantial heterogeneity; 75% to 100% considerable heterogeneity.

CI, confidence interval.