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REVIEW

Is interpretation bias for threat content specific to youth anxiety symptoms/diagnoses? A systematic review and meta-analysis

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Abstract

Anxiety is the most common mental health problem in youth. Numerous studies have identified that youth anxiety is associated with interpretation bias or the attribution of threatening meaning to ambiguity. Interpretation bias has been proposed as a mechanism underlying the development and maintenance of pediatric anxiety. Theoretically, interpretation bias should be content-specific to individual youth anxiety symptom domains. However, extant studies have reported conflicting findings of whether interpretation bias is indeed content specific to youth anxiety symptoms or diagnoses. The present meta-analysis aimed to synthesize the literature and answer the question: is the relationship between interpretation bias and anxiety content specific? Search of PubMed and PsycINFO databases from January 1, 1960 through May 28, 2019 yielded 9967 citations, of which 19 studies with 20 comparisons and 2976 participants met eligibility criteria. Meta-analysis with random effects models was conducted to examine an overall effect (Pearson *r*) between anxiety domain and content-specific interpretation bias in single sample studies, and an overall effect size difference (Cohen's *d*) in studies comparing anxious to non-anxious youth. Results support a content specific correlation between interpretation bias and anxiety symptom domain in single sample studies ($r=0.18$, $p=0.03$). However, it is currently undetermined whether this relationship holds in studies that compare the relationship between content-specific interpretation bias and anxiety in anxious versus non-anxious youth. A variety of methodologic considerations across studies are discussed, with implications for further investigation of interpretation bias and youth anxiety.

Keywords Child · Adolescent · Interpretation bias · Cognitive bias · Anxiety · Meta-analysis

Introduction

Anxiety is the most common mental health problem across development, with onset during the pediatric period [1, 2]. The presence of anxiety disorder in childhood and/or adolescence is associated with significant impairments in home, school, and social domains [3]. Additionally, without treatment anxiety confers significant risk for future mental health problems, including worse anxiety, depression, suicidality, and substance abuse/dependence [3–5]. However, even current gold-standard treatments (cognitive behavioral therapy; selective serotonin reuptake inhibitors) are ineffective for a substantial proportion of youth [6], and approximately 50% of children and adolescents who initially experience treatment benefits will go on to experience symptom and disorder recurrence by adulthood [7]. Experts have called for the identification of mechanisms that underlie anxiety, and directly targeting those processes in treatment, which may improve the ways in which we both understand and are able to address youth anxiety [8, 9].

One such possible anxiety mechanism is interpretation bias or the appraisal of threatening meaning from environmental ambiguity [10–12]. For example, a noise at night outside one's window may be perceived as the wind (neutral interpretation) or a robber (threatening interpretation). Numerous studies have determined that anxious youth [13, 14] and adults [15] exhibit a threat interpretation bias when presented with ambiguous information, as compared to their non-anxious counterparts. Within anxious samples, this bias is strongly associated with anxiety severity [16], as well as other anxiety-related constructs such as physiological reactivity during stress [17].

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Threat-focused interpretation bias has also been shown as a more stable and reliable marker of pediatric anxiety disorder than other forms of cognitive bias (e.g., attention bias for threat; [16]). Moreover, self-reported interpretation bias in anxious youth can be modified with CBT [18], and novel cognitive bias modification interventions for interpretation bias (CBM-I) provide preliminary support for directly targeting and reducing interpretation bias with subsequent reductions in anxiety [19, 20]. Together, these data suggest that interpretation bias may have significant potential as a malleable target that might be modified to treat youth anxiety.

However, questions remain about interpretation bias, answers to which would have a significant bearing on how this construct is assessed with experimental and self-report methods, as well as modified in CBM-I. Specifically: is threat-focused interpretation bias content specific to youth anxiety symptoms? Asked differently, do anxious youth exhibit threat-focused interpretation bias irrespective of whether ambiguous stimuli are congruent with their anxiety symptoms, or is content specificity, or congruency between ambiguous stimuli and symptoms, necessary to demonstrate a strong and stable link between bias and anxiety? Answers to this question would have several important research/experimental and clinical implications. For example, a content-specific relationship would argue that interpretation bias assessment tools and CBM-I intervention stimuli would need to match the content of youth anxiety symptoms. In contrast, if the relationship between bias and symptoms is not content-specific, and youth exhibit interpretation biases for many types of ambiguous stimuli (even those that are not directly relevant to their symptoms), this would argue that addressing all interpretation biases, rather than using a targeted, personalized approach, may serve as both treatments for current symptoms and prevention of future anxiety symptoms.

Some initial evidence does support content specificity of interpretation bias to anxiety symptoms. First, anxiety is extremely heterogeneous. Youth with the same diagnoses (e.g., generalized anxiety) can report widely variable fears (e.g., academic failure versus health concerns), and even different specific fear beliefs within the same disorder subtype and content domain (e.g., fears about the future might be expressed as never getting into college versus teachers and other authority figures perceiving that one is not smart versus not being able to live as an independent adult). It is therefore not surprising that fear belief and subsequent cognitive bias, profiles support the notion that interpretation bias may be content specific to individuals' symptoms [21]. Yet extant studies that have examined content specificity of interpretation bias to youth anxiety have evidenced mixed results, without a definitive answer regarding whether bias is strongest for matched anxiety domain.

One prior meta-analysis has tested the relationship between youth anxiety and negative interpretation bias broadly and included a smaller subset of studies in a moderation analysis to test content specificity [22]. This meta-analysis found a moderate positive effect size ($d=0.62$), suggesting a relationship between negative interpretation bias and anxiety in youth. In a subsample of studies, they also found that when interpretation bias was content specific to the anxiety subtype, the association between bias and anxiety was stronger. However, this work has some methodological constraints that limit inferences about the relationship between content specificity of threat-focused interpretation bias to anxiety in youth, particularly related to the broad inclusion criteria. First, and perhaps most importantly, the meta-analysis included studies that assessed both threat and negative biases broadly, although there is evidence that broadly negative, non-threat stimuli are linked to depression, and not anxiety, in youth [23]. Second, studies were included in which parents reported on youth bias, which could be a reflection of parental anxiety and not necessarily reflect youth perceptions of ambiguity. Interpretation bias by its operational definition would best be reported by the individual for whom the bias is being assessed. Third, the meta-analysis included a wide variety of bias measures, some of which do not reflect bias as the interpretation of threat (or even negative information) from ambiguity and rather might reflect other stages of information processing. Finally, it excluded studies that were only comprised of a clinically anxious or elevated anxiety symptom group. Arguably, determining whether interpretation bias is content specific to anxiety or not is most relevant to clinical groups for purposes of translation to intervention for youth anxiety. Despite these limitations, the Stuijfzand meta-analysis [22] provides support for the relationship between anxiety and interpretation bias broadly, and preliminary support for the content specificity hypothesis.

To extend and specify the work previously conducted by Stuijfzand and colleagues, and to synthesize the small but growing empirical literature, the present meta-analysis was conducted. We aimed to answer the question: is the relationship between threat interpretation bias and youth anxiety content specific to the youth anxiety symptom domain? Answering this question with a focus on threat interpretation bias (which of the various cognitive biases has the strongest link to youth anxiety) may have significant implications for how we understand interpretation bias and its relationship to anxiety, as well as how bias is assessed and targeted in clinically anxious youth.

Methods

Operational definitions and eligibility criteria

Included studies were those that examined the content specificity of threat interpretation bias as related to youth anxiety. Interpretation bias measures were defined as those which provided objectively ambiguous and hypothetical information to which participants interpreted or attributed either threatening or neutral meaning, designed to elicit biased or neutral responses [24]. Content specificity was defined as an assessment of bias that was relevant to and congruent with an anxiety symptom subtype. For example, examination of interpretation bias for social threat would be content specific to social anxiety symptoms.

A priori inclusion criteria included: (1) paper published in peer-reviewed English journal, (2) empirical investigation (e.g., not a review), (3) included youth under the age of 18, (4) included a measure of interpretation bias where youth attributed threatening or non-threatening meaning (or responses were coded to identify threatening or non-threatening meaning) to ambiguous information, (5) included a measure of anxiety, (6) examined content specificity to one or more sets of anxiety symptom subtypes (e.g., separation, social, generalized, spider), and (7) provided sufficient data to examine the relationship between content-specific interpretation bias and anxiety symptom subtype (including either Means and standard deviation, effect sizes, correlation or group comparison statistic and significance values, and/or covariance to calculate correlations).[1]

Systematic literature review and data extraction

A flow diagram of study selection is provided in Fig. 1. Identification of key articles occurred in two ways. We searched PsycINFO and PubMed databases for peer-reviewed data sources (January 1, 1960 through May 28, 2019) that included the following stem keywords: *interpretation*, interpretation bias, cognitive bias, appraisal*, judgement*, attribution*, content specificity, specific*, child*, adolesc*, pediatric*, youth*, anxi*, phobia**. The search was limited by publication in English peer-reviewed journals. Title, abstracts and, if eligible, full articles, were reviewed independently by the first author and either the second author or another research assistant. The first and last authors resolved questions or discrepancies. Given the few studies produced by the search that met criteria for inclusion (particularly inclusion of an interpretation bias measure that included and provided data for ambiguous stimuli), there was 100% agreement on study inclusion/exclusion. The first author also reviewed reference lists, as well as previously published review articles to identify studies that may have been missed in the database search.

In total, 19 studies were included in the meta-analysis (see Tables 1 and 2). One study [34] included two sets of comparisons: a diagnosed group compare to a control group, and an elevated anxiety symptoms group compared to a control group. Separate effects were calculated comparing the diagnosed versus control group, and elevated anxiety symptoms versus control group, and for this reason, the study is listed twice in Table 2, separating demographic information for each diagnosed and elevated symptoms groups. To meet core exclusion criteria for this meta-analysis, studies at minimum had to examine interpretation bias stimuli that were congruent to the anxiety symptom domain in the same participants. For example, some studies compared GAD interpretation bias stimuli to GAD symptoms, representing content specificity, in a single group of youth or compared between two groups of youth. In addition, some studies also examined incongruent interpretation bias and anxiety symptom domain (e.g., comparing GAD-relevant interpretation bias stimuli with social anxiety symptoms in a single group of youth, or comparing across two groups). Importantly, the inclusion of interpretation bias stimuli that was incongruent to the anxiety symptom domain was not necessary to meet study inclusion criteria. However, as some studies examined both congruent and incongruent interpretation bias stimuli and anxiety symptoms, we examined both relationships.

Data were extracted from the information published in the 19 articles. Data were extracted and coded for: total number of participants, youth age, gender, racial/ethnic composition, target population (for single sample studies: unselected, elevated symptoms/subclinical, or diagnosed; for group comparison studies: diagnosed or elevated symptom anxious group), interpretation measure used (i.e., sentences, pictures) and type of interpretation task. Assessments of interpretation bias varied in the included studies. In regard to type of bias task, as shown in Table 1, 10 out of 12 single sample studies used a bias task (i.e., reading a vignette with unlimited time, subjective ambiguous situations questionnaire) that would be considered to tap "controlled cognition"—computerized or other non-paper–pencil task with stimuli presented and youth responds without time limit [e.g., 43, 45, 49]. The tasks and questionnaires tapping "controlled cognition" are also susceptible to social desirability—the tendency for individuals to present a more favorable or desirable image of themselves on questionnaires [58]. In contrast, two of those 12 studies used a forced-choice reaction time task—during which participants had to respond quickly (200–36,500 ms),

[1] Seven studies met inclusion criteria 1 through 4 described above, but did not provide sufficient data to calculate effect sizes and were therefore excluded: [25–31]

Two studies met inclusion criteria 1 through 4 described above but examined bias in other disorder group samples and were therefore excluded: [32, 33]

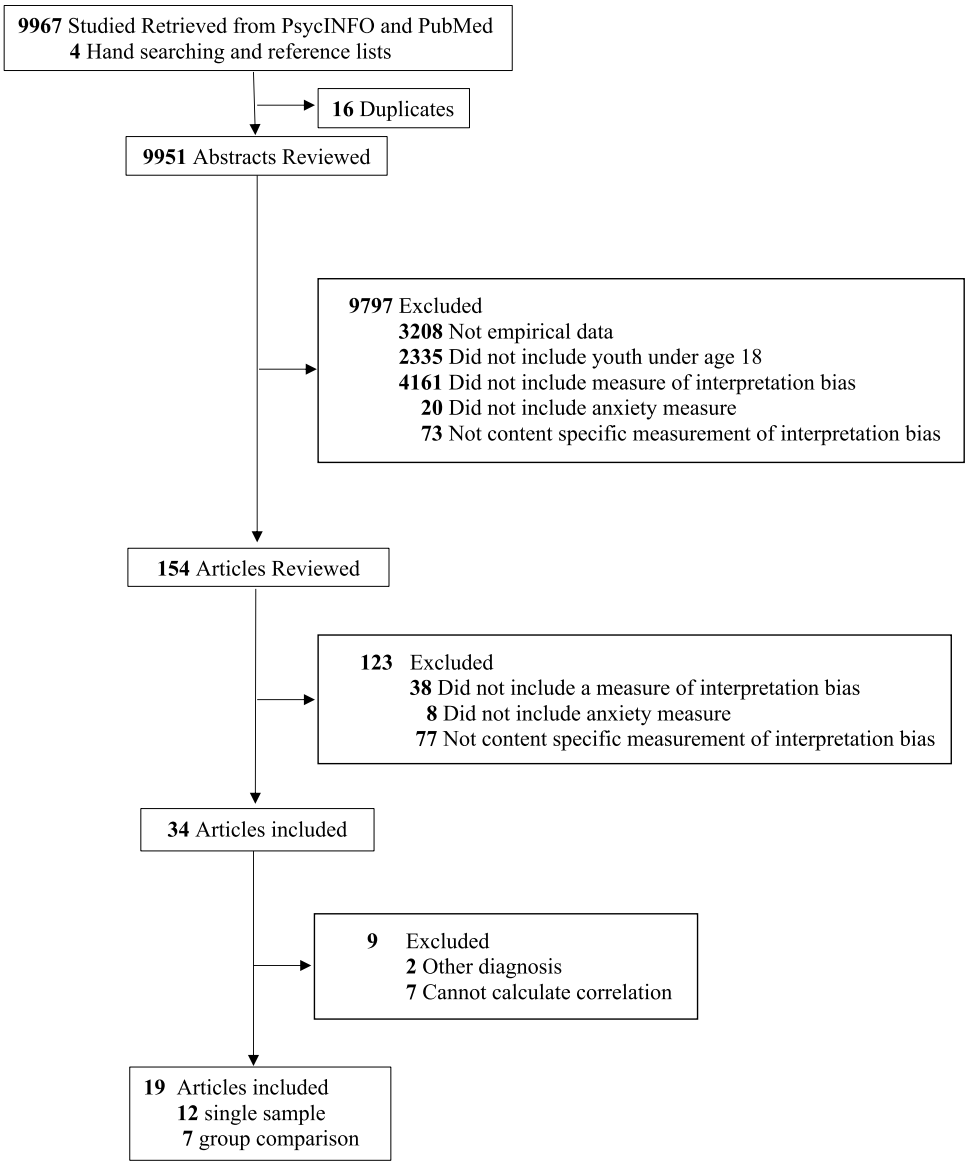

Fig. 1 Consort diagram of study selection

which would be presumed to tap "uncontrolled cognition" because participants would not have time to fully process stimuli before a response was required. Type of interpretation task was coded into three categories: subjective questionnaire (SQ; i.e., ambiguous situations questionnaire), uncontrolled bias task (UT; i.e., forced-choice reaction time task during which participants had to respond quickly), and controlled bias task (CT; e.g., unlimited time to read a vignette or view a picture).

Studies were identified as containing single sample correlational data or group comparison data based on study methods. The single sample correlational studies used a single sample of participants, and the group comparison studies compared a diagnosed or elevated symptom group to a control group. For single sample studies, correlations (Pearson's *r*) were extracted for the association between interpretation bias and anxiety symptoms for each available content specific (e.g., social bias and social anxiety symptoms) and incongruent (e.g., social bias and generalized anxiety symptoms) domain. For group comparison studies, data were extracted for means and standard deviations of content specific and incongruent interpretation bias in both affected (anxious diagnosed or symptomatic) and control groups. In studies with more than one content-specific or incongruent bias/anxiety relationship, data for all outcomes were entered within the study, with a summary effect across those outcomes entered for the study for each content specific and incongruent relationships. Raw data for anxiety and bias outcomes were extracted by the first and second author, with 100% agreement.

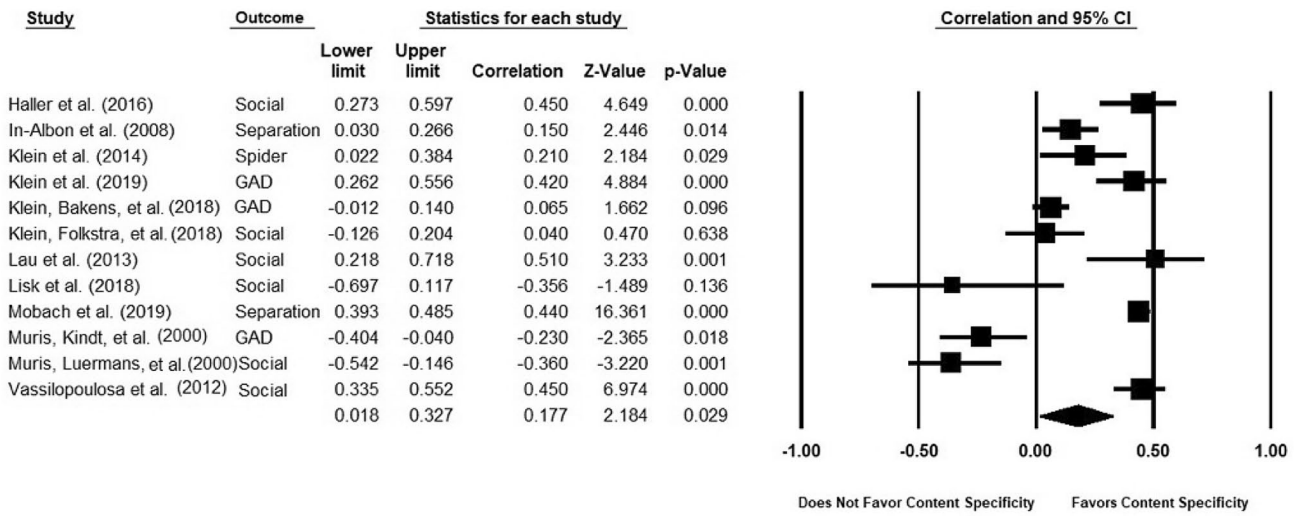

Fig. 2 Correlations for content specific bias

Statistical approach and outcomes by aim

Our first aim was to test whether interpretation bias is content-specific, or stronger for bias stimuli that are matched to the anxiety symptom domain. To achieve this aim, we conducted two sets of analyses. First, we conducted two overall effect size calculations for single sample correlational studies, with an overall effect for interpretation bias that was content specific to anxiety symptom domain, and a separate overall effect for interpretation bias that was incongruent with anxiety symptoms. Second, we conducted an overall effect size calculation for group comparison studies examining bias that was content specific to the anxiety domain. There was only one study [35] that examined an incongruent bias-anxiety relationship, which was determined to be insufficient to examine within a meta-analytic framework. Thus, three total overall effect sizes were calculated: single sample/congruent (12 studies), single sample/incongruent (6 studies), group comparison/congruent (7 studies), as well as the single effect for the single group comparison/incongruent study.

The second aim was to examine whether the relationship between interpretation bias and anxiety was moderated by content specificity of bias. Therefore, we decided a priori that if the overall effect for content specificity of interpretation bias was statistically significant, a post-hoc exploratory moderation analysis would be conducted for that set of studies with bias congruency vs. incongruency as the moderator. As only a single group comparison study included data that would allow examination of incongruent bias, a moderation analysis for bias type was not possible for group comparison studies.

Data were analyzed with Comprehensive Meta-Analysis Version 3 software [36]. Whenever possible, raw data (means and standard deviations, Pearson's r) were used to calculate effect sizes. When data reported used significance tests or other effect size measures, data were transformed to r values for single sample studies and d values for group comparisons. For the first aim, effect sizes (ES) for single sample studies were indexed and are presented in Figs. 2 and 3 using Pearson's r (correlation coefficient) for single sample correlational studies.[2] Effect sizes for group comparisons were indexed and presented in Fig. 4 using Cohen's d (standardized mean difference). Positive ES reflect a greater relationship between the type of interpretation bias (content-specific or congruent, incongruent) and anxiety. Based on Cohen's guidelines for ES interpretation [38, 39], for single sample studies that included correlations, we interpret a small ES as an $r = 0.1$, medium ES as an $r = 0.3$, and large ES as an $r = 0.5$ [38, 59, 60]. For group comparison studies that included means and standard deviations, we interpreted a small ES as $d = 0.20$, medium ES as $d = 0.50$, and large ES as $d = 0.80$ [38, 59, 60].

However, we also required that the p value of the effect should be significant (i.e., ≤ 0.05) in order to interpret the magnitude of the effect. For the second aim, models analogous to analysis of variance were estimated comparing mean effect sizes for interpretation bias grouped by classification on the potential moderator of content specificity (content

[2] Comprehensive Meta-Analysis software converts the correlation coefficient to the Fisher's z scale, with analyses performed using transformed values, with the results converted back to correlations to presentations [37]

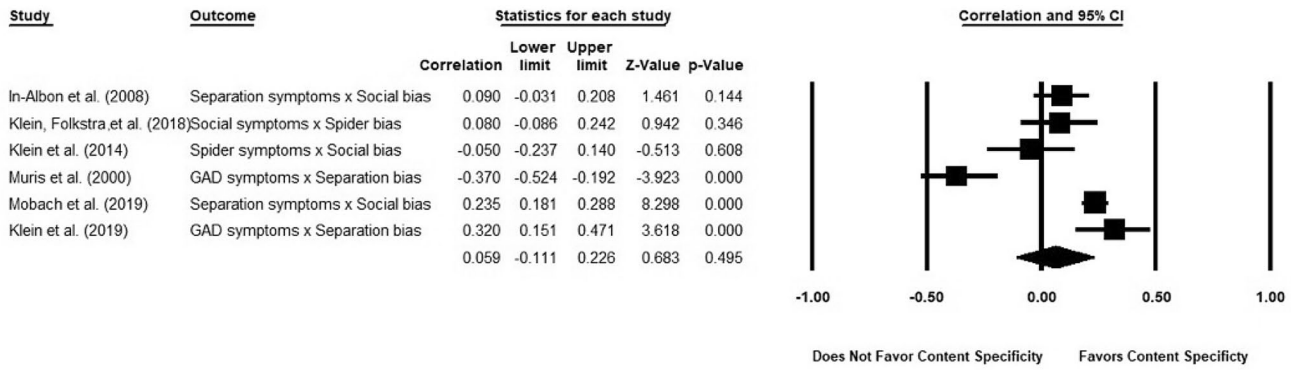

Fig. 3 Correlations for incongruent content bias

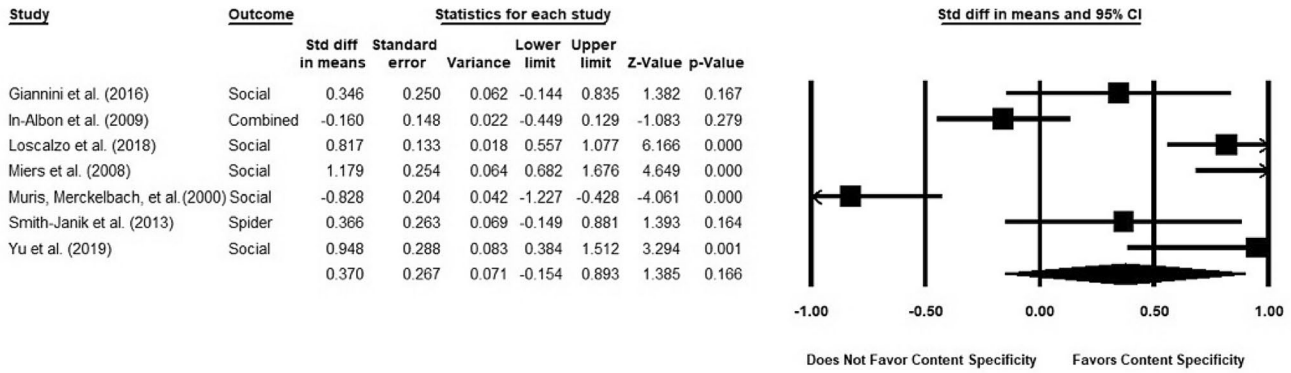

Fig. 4 Group comparison for content specific bias

specific/congruent versus incongruent) effects. Importantly, and as discussed in the Limitations section, we did not calculate power a priori and as such, results should be interpreted with caution and consideration of this limitation. Additionally, it is important to consider the results of this study within the context of a small number of included studies. It should also be noted that prior research has concluded that meta-analyses can be used to synthesize and identify trends from as few as two studies [64].

Given the heterogeneity between studies in regard to both sample selection, how interpretation bias was assessed, and interpretation bias type, a random-effects model was selected in order to be more conservative, rather than a fixed-effects parameter. Heterogeneity across studies was examined with the forest plot and Q and I^2 statistics. Finally, publication bias was examined with a visual inspection of the funnel plot for asymmetry and Egger's test. The likelihood of unpublished studies was accounted for using the Duval and Tweedie's Trim-and-Fill method, which tests the influence of possible adjustments to the estimated effect due to publication bias [40]. Sensitivity analysis was examined using the Rosenthal fail-safe N test. The fail-safe number is computed as the number of studies with average sample size and non-significant outcomes that are needed in order for the effect size of the meta-analysis to reach a non-significance level [41].

Results

Included studies and study characteristics

Of the 9967 citations identified, 19 studies examined content specificity for one or more threat interpretation bias domains in the context of youth anxiety and were included in the final analysis (Tables 1 and 2; [14, 34, 35, 42–57]. Of these 19 studies, 12 examined correlations between content specificity (or incongruency) of interpretation bias to anxiety domain in a single sample, and 7 examined content specificity of interpretation bias between a diagnosed or elevated anxiety symptom group to a non-anxious or low anxiety symptom group. As mentioned above, as one study [34] included two sets of comparisons, a total of 20 ES calculations were conducted based on 2976 participants. Within-study sample sizes ranged from 25 to 603. Across studies,

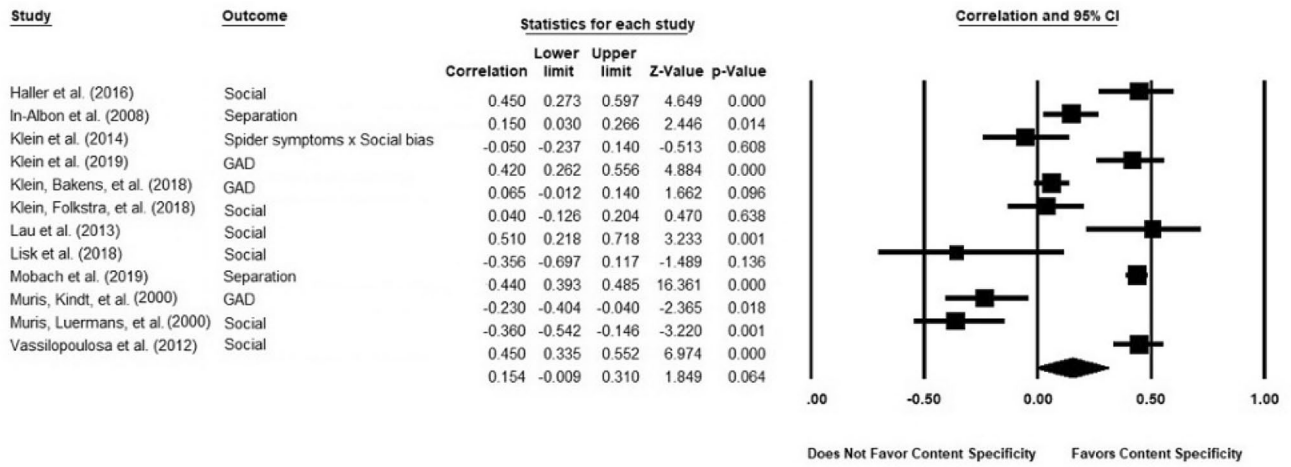

Fig. 5 Correlation by content specificity moderation

youth age included both children and adolescents, ranging from 5 to 18 years old.

Notably, interpretation bias measures varied widely. The current study classified tasks into three categories: subjective questionnaires (SQ; 6 studies), uncontrolled bias tasks (UT; i.e., stimuli presented and/or youth had to respond in a time-limited manner; 3 studies), and controlled bias tasks (CT; i.e., computerized or other non-paper–pencil task with stimuli presented and youth responds without time limit; 10 studies). Additionally, the total number of items or stimuli varied widely across interpretation bias measures, ranging from a single stimulus [54] to 56 [46]. As discussed in the limitations section of the discussion below, prior research has questioned the psychometric properties of tasks consisting of only a few items [20, 62].

Overall effect size calculations

The overall summary effect examining content specific bias in single sample studies resulted in a small and statistically significant effect ($r = 0.18$; 95% CI 0.02–0.33; $p = 0.03$). The forest plot and Q and I^2 statistics indicated significant heterogeneity ($Q = 171.514$, $p < 0.001$, $I^2 = 93.59\%$), with the effect size for individual studies ranging from a r of − 0.36 [53] to 0.51 [49]. See Fig. 2 for a summary of individual study effects.

The overall summary effect examining incongruent bias in single sample studies did not result in a significant effect ($r = 0.06$; 95% CI − 0.11–0.23; $p = 0.50$). See Fig. 3 for a summary of individual study effects.

The overall summary effect examining content specific bias in group comparison studies resulted in a small, statistically insignificant effect ($d = 0.37$; 95% CI − 0.15–0.89; $p = 0.17$). See Fig. 4 for a summary of individual study effects.

Only one group comparison study provided data to calculate incongruent content bias and anxiety symptoms [35]; this study did not indicate a significant relationship between anxiety and incongruent content interpretation bias ($d = -0.05$; 95% CI − 0.34–0.24; $p = 0.06$).

Results suggest that there may be evidence of content specificity of threat-focused interpretation bias by anxiety symptom domain across single sample studies of youth, but that evidence of content specificity across group comparison studies of youth with diagnosed/elevated symptom compared to typically-developing/low symptom youth is not significant. As findings in this important domain of research continue to accumulate, future meta-analytic work may help to clarify whether these results hold.

Content specificity of interpretation bias with anxiety: moderation

Because the overall summary effect for content specific bias in single sample studies was statistically significant, we examined whether bias type (congruent versus incongruent) moderated the relationship between interpretation bias and anxiety. This moderation analysis revealed a small effect that trended toward but did not quite reach, significance ($r = 0.19$ 95% CI − 0.01–0.31; $p = 0.06$). See Fig. 5 or a summary of individual study effects which reflect the moderation analysis; each effect is interpreted as estimated models analogous to analysis of variance (i.e., the correlation reflects the difference between effects for congruent versus incongruent effects within that study. Results reveal that bias type (congruent or incongruent) did not significantly moderate the relationship between interpretation bias and anxiety. As mentioned above, since we did not calculate power a priori, there are various conclusions that can be inferred. One such conclusion from these results suggests that the relationship

between interpretation bias and anxiety is the same regardless of bias type. Meta-analysis replication with more studies (as they are published) may increase confidence or identify alternative findings.

Publication bias

Publication bias, or effects associated with a greater likelihood of publication with significant outcomes, was examined for content specific bias in single sample studies. Visual inspection of the funnel plot and Egger's test suggested that publication bias was not significant ($t = 1.33$, $p = 0.21$). The Duval and Tweedie trim-and-fill method suggested that no studies were likely missing that would increase the effect. The Rosenthal fail-safe *N* suggested that 322 studies with null findings would reduce the overall-effect *p* value to become non-significant. We did not examine publication bias for the other effects calculated above because the summary effects were not statistically significant. Results demonstrate that publication bias is not significant, providing evidence that the published literature is systematically representative of the population of completed studies [61]. Thus, it is unlikely that conclusions are drawn from this meta-analysis conflict with results from completed studies.

Discussion

In attempts to improve our understanding and treatment of pediatric anxiety, researchers have turned to the assessment and intervention of underlying cognitive mechanisms [8, 9]. One such mechanism—interpretation bias, or the threatening appraisal of ambiguity—has been consistently and strongly linked to youth anxiety. Interpretation bias has also demonstrated preliminary efficacy as a malleable treatment target, with downstream effects on anxiety symptoms, using experimental therapeutic intervention (i.e., cognitive bias modification; [19, 20]). However, interpretation bias is also typically measured and manipulated (in CBM-I) using a standardized set of questionnaire items or stimuli across multiple anxiety disorders/symptoms. This may be inconsistent with theoretical models, which propose that this bias might be most strongly associated with anxiety when the introduced ambiguity is content-specific to individual youth anxiety-related symptoms (i.e., fears and worries). To this end, the current systematic review and meta-analysis sought to answer the question: is threat interpretation bias content specific to anxiety subtype in youth?

Results of this investigation suggest that, across single sample studies of youth, there is evidence for a small and statistically significant effect for content specificity of threat-focused interpretation bias by anxiety symptom domain ($r = 0.18$, $p = 0.03$). In contrast, across the single sample studies, there was no evidence that higher levels of anxiety or anxiety diagnoses were associated with interpretation bias for incongruent symptom domains. These findings occur in the context of extant literature in which all but one of the included studies were unselected youth or those with elevated symptoms; only one single sample study included clinically anxious youth. These findings support the notion that to accurately measure interpretation bias in typically-developing youth or those with elevated symptoms, the bias should be relevant to youth anxiety symptom domains. Thus, it is uncertain at this time whether these results might be generalized to youth with anxiety disorders.

In group comparisons that examined youth with anxiety disorders or elevated anxiety symptoms against youth who were non-anxious or those with low anxiety symptoms, the non-significant *p* value revealed a lack of group differences. As indicated above, replication of this meta-analysis with a greater number of studies (as work is conducted and results published) may increase confidence or identify alternative findings. The overall effect was small but not statistically significant ($d = 0.37$; 95% CI − 0.15–0.89; $p = 0.17$). When interpreting this result, two critical methodologic factors emerged from these studies that may have influenced this non-significant finding. First, as illustrated in Fig. 4, there was much heterogeneity in effects between studies, and the study that evidenced the strongest effects against content specificity [54] was also the study with the largest sample size, and therefore had the largest weight when calculating the overall pooled effect size across studies. Second, the number of trials or items in the interpretation bias tasks, particularly within the group comparison studies, was quite small: total number of items or stimuli ranged from 1 to 8 (with the study with the largest sample size [54] and one other study [55] only including 1 item). Thus, many effects in the group comparison analysis were dependent on youth responses to one or a very few numbers of stimuli, raising questions about the psychometric validity of extant tasks for assessing content specificity of bias to anxiety symptom domain. This review of the extant literature provides compelling evidence for a need to consider whether and how use of the extant threat-focused interpretation bias measures might be divided into item/stimuli subtypes for purposes of assessing content specificity. Answering these questions would have significant research, experimental, and clinical implications, particularly related to how interpretation bias is assessed with experimental and self-report methods, as well as how modifications may be made to current cognitive bias modification for interpretations (CBM-I) stimuli.

Limitations

This review and meta-analysis are not without limitations. The various interpretation tasks used and how they

operationally defined interpretation bias may reflect different stages of interpretation (e.g., uncontrolled versus controlled). We attempted to minimize heterogeneity with a stringent definition of interpretation bias (e.g., calculation of possible risk or other related constructs were not included). Relatedly, interpretation bias may operate differently in anxious and non-anxious youth. We were not able to parse apart examination of content specificity of bias to anxiety between clinically anxious youth, those with elevated symptoms, and youth without any history of anxiety due to the number of studies and various recruitment strategies/inclusion criteria employed. As interpretation bias continues to be studied in the context of youth anxiety, future work to understand the relationship between bias and anxiety in youth across a variety of anxiety symptom and diagnostic levels, and compared to non-anxious youth, may help to clarify whether there are differences in groups of youth for whom content specificity of bias to symptoms is relevant. As mentioned above, we did not conduct a priori power analyses in this meta-analysis. Power analyses can be important as they aid in determining if there is a reasonable probability of detecting significant effect sizes. It should be noted that while this is a limitation of the current meta-analysis, it is also a limitation of the field, as it is rare that meta-analytic studies utilize a priori power analyses. Relatedly, we were deliberate in our a priori analytic decisions given significant heterogeneity in measures, methods, and samples; effects were analyzed using a random-effects rather than a fixed-effects model. This more conservative approach accounts for the fact that individual study results included may be affected by random sampling errors and covariates—both measured and unmeasured."

Finally, some may consider our work a "mini-meta-analysis" [63] given the relatively few number of studies that met the criteria for each analysis. Simultaneously, as mentioned above, there are compelling data and recommendations that meta-analyses can be used to identify trends from as few as two studies if there is theoretical and empirical rationale to do so [64]. Some researchers conducting meta-analyses will contact authors for information that was not previously published in an attempt to include more data. Indeed, this was our prior approach with meta-analytic work previously conducted by our group to answer different questions. With this project and with our future meta-analytic work, however, we deliberately chose not to contact authors. From a practical perspective, in another Meta-Analysis recently conducted by our research group, only 2 of 6 authors who we contacted responded, despite three attempts to contact each author. Difficulties in obtaining data from authors have been identified previously as a significant challenge in meta-analysis, and the reason for examining publication bias [65] which we do in the current manuscript. Including studies from a subset of those contacted because others did not respond may still result in publication bias. Finally, and importantly, this limitation reflects a larger issue in the field regarding raw data being excluded from published papers. It has been recommended that researchers publish raw data so that others can benchmark and calculate effect sizes [66–70]. Thus, our decision to exclude studies that did not include raw data for the current project and our work moving forward is consistent with expert recommendations to the field.

The number of studies that met all inclusion and no exclusion criteria reflects a small yet growing literature, and we hope that this work further encourages clinical and experimental psychologists to continue pursuing the relationship between interpretation bias and youth anxiety. Given these limitations, we still view this work as valuable and important, particularly given the fact that extant studies examining content specificity have yielded mixed results.

Recommendations and future directions

The findings of this systematic review and meta-analysis have implications with clear recommendations for ourselves and our colleagues as we continue to work toward clarifying the relationship between interpretation bias and anxiety. First, careful attention to how interpretation bias is measured, including assessment modality, method, and the number of stimuli may result in bias assessment that is more suited to examine content specificity. Equally important, 7 studies were excluded from this meta-analysis that appeared to have methods from which content specific bias and symptom data might be extracted, but for which no data were presented in their papers. Including raw data (covariance for the association between bias and anxiety symptoms in single sample studies; means and standard deviations for group comparison studies) or providing effect sizes whenever possible will allow those conducting research in this area to benchmark findings against one another, particularly in comparing the same or similar measures. Next, work is currently being conducted to assess the time course and components of interpretation bias more broadly—from brief reaction time measures to self-reports. Some data suggest that uncontrolled interpretation bias (i.e., for which stimuli are presented quickly and/or response required quickly) may be more strongly associated with anxiety [16], as controlled processing measures such as self-reports may draw upon higher level cognitive processes beyond the interpretation stage of information processing. While this meta-analysis only found three studies that assessed bias in a way that draw upon uncontrolled rather than controlled cognition, as more researchers pursue performance-based measures of bias, the relationship between content specificity of bias to anxiety symptoms may be clarified. Additionally, if the current results for single sample effects, which found content specificity of bias to symptoms, are replicated with a larger number of group comparison studies in youth, content-specific

stimuli might be used to modify interpretation bias with cognitive bias modification interventions. Furthermore, as noted in the limitations section, the primary goal of this work was to examine whether interpretation bias is content specific, or stronger for interpretation stimuli matched to anxiety symptom domain. The examination of gender, race/ethnicity, age, type of bias task, anxiety subtype, and presence/absence of anxiety diagnosis are all important variables that may affect the relationship between interpretation bias and anxiety and would require a larger accumulation of research studies to pursue. Future research should investigate interpretation bias in diverse samples, both clinically and demographically, to see if effects are specific to certain groups or are generalizable across all youth.

Finally, this work has the potential for clinical translation. Prior work, particularly in adult samples, has begun to support the use of cognitive bias modification for interpretation bias (CBM-I). CBM-I is a computerized intervention that attempts to reduce anxiety symptoms by directly targeting and reducing interpretation bias; in this experimental intervention, participants are provided with real-time corrective feedback when they select threat-relevant interpretations of ambiguity, with the expectation that they will learn to automatically make more neutral (rather than threat) interpretations over time. To date, CBM-I studies in both youth and adults have demonstrated preliminary efficacy, but primarily use a standardized set of stimuli across all participants irrespective of participant anxiety symptoms [19, 20, 49]. The present findings, should they be replicated as the interpretation bias literature continues to grow, may support the use of personalized, rather than standardized, CBM-I stimuli. Additionally, as this meta-analysis found a relationship between content-specific interpretation bias stimuli and youth anxiety symptoms in unselected youth, future work is needed to determine the extent to which interpretation bias might be an adaptive versus problematic feature of youth cognition that confers risk for anxiety disorder.

In conclusion, given the above-described limitations and relatively small extant literature, at this time we are unable to definitively answer whether interpretation bias is content specific to youth anxiety symptoms. The data presented herein adds more rigorous support to the prior meta-analytic work [22] and child anxiety theories about information processing [10–12] that threat interpretation bias may indeed be content specific to individual youths' anxiety symptoms. As with all scientific literature, more work in this area will clarify the present ambiguity, leading to a better understanding of interpretation bias as an anxiety mechanism and treatment target.

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Compliance with ethical standards

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