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Eye-tracking of attention to threat in child and adolescent anxiety: A meta-analytic study

Abstract

Objective: Attention biases for threat may reflect an early risk marker for anxiety disorders. Yet questions remain on the direction and time-course of anxiety-linked biased attention patterns in youth. A meta-analysis of eye-tracking studies of biased attention for threat was used to compare the presence of an initial vigilance towards threat and a subsequent avoidance in anxious and non-anxious youth. *Method:* Pubmed, Psycharticles, Medline, Psychinfo, and Embase were searched using anxiety, children and adolescent, and eye-tracking-related key terms. Study inclusion criteria were: studies including participants ≤18 years; reported anxiety using standardised measures; measured attention bias using eye-tracking with a free-viewing task; comparison of attention towards threatening and neutral stimuli; and available data to allow effect size computation for at least one relevant measure. A random effects model estimated between- and within-group effects of first fixations toward threat and overall dwell time on threat. *Results:* Thirteen eligible studies involving 798 participants showed that neither youth with or without anxiety showed significant bias in first fixation to threat versus neutral stimuli. However anxious youth showed significantly less overall dwell time on threat versus neutral stimuli than non-anxious controls (g=-0.26). *Conclusion:* Contrasting with adult eye-tracking data and child and adolescent data from reaction time indices of attention biases to threat, there was no vigilance bias towards threat in anxious youth. Instead anxious youth were more avoidant of threat across the time-course of stimulus viewing. Developmental differences in brain circuits contributing to attention deployment to emotional stimuli and their relationship with anxiety are discussed.

Keywords: child and adolescent anxiety, attention bias, threat processing, eye-tracking

Introduction

Anxiety disorders are a leading cause of morbidity globally[1]. As anxiety often starts in youth[2], identifying early risk markers that can be targeted through interventions is a clear public health priority. Biased attention processing of threat may maintain anxiety[3], and contribute to its' onset[4], making it a potential treatment target. Before the therapeutic potential of targeting attention biases can be realized, outstanding questions on the presence and direction of these biases in relation to youth anxiety need to be addressed, particularly as most studies measuring attention biases and youth anxiety rely on indirect reaction time indices. Here, we present the first meta-analysis of newer studies using eye-tracking measures of attention to assess bias for threat and their associations with youth anxiety.

Effective detection of danger is fundamental to survival. However, cognitive accounts of anxiety suggest that some individuals show exaggerated attentional processing of threat-related information, contributing to an interruption of daily functioning and manifesting as clinical anxiety[3]. Indirect support for these models has emerged in adults from tasks measuring Reaction Time (RT) under various experimental conditions. Most commonly used is the dot-probe task, a measure of biased visual spatial orienting towards (or away) from threat. Specifically, an attention bias towards threat (vigilance) is inferred by shorter RTs to detect a probe replacing a threatening stimulus than one replacing a non-threatening stimulus, while an attention bias away from threat (avoidance) is inferred by longer RTs to probe detection following a threatening versus non-threatening stimulus. Using these tasks under brief and long presentation times of the threatening and non-threatening stimuli, adult studies demonstrate anxiety-linked attention towards threat at early involuntary stages of threat processing, consistent with facilitated *threat-orienting* (*vigilance hypothesis*)[5-7]. To a lesser extent, *strategic avoidance of threat* at later stages of threat processing (*vigilance-avoidance hypothesis*) has also been reported[8]. Another common task, thought largely to tap the individuals' ability to disengage attention processing of distracting emotional information rather than orienting, is the emotional Stroop task. Here, RTs are compared to color-naming threatening versus non-threatening words. In adults, longer RTs to the former versus latter condition have been found; together with data from other variations of the dot-probe task[9,10] these are interpreted as being consistent with *attentional maintenance on threat* in anxiety. Thus, adult RT data suggest the contribution of varying components of attentional bias to anxiety[11].

A significant number of studies have applied RT-based tasks in children and adolescents with varying anxiety levels. Meta-analysing 38 studies Dudeney and colleagues[12] found that while both anxious and non-anxious youth displayed attention biases toward threat, anxious youth demonstrated a significantly greater bias than non-anxious youth. This between-group difference in bias increased with age across youth; was greater when using the emotional Stroop task than the dot-probe task; and only emerged in dot-probe studies using a 1250ms presentation time rather than shorter presentation times (≤500ms). Thus, while these data are clear in suggesting greater attentional maintenance on threat amongst anxious youth from the Stroop task, data from the dot-probe task are more mixed over whether there is also 'early' vigilance for threat as reported in adults[5,11,13,14].

One possibility why youth data vary from adult findings is methodological. A longer time to process stimuli before the button press to maximize accuracy may be needed in younger participants[12]. Such concerns underscore the distal relation between attentional processing and behavioral response. Indeed, RTs provide a relatively indirect measurement of attention[15]. The resultant RT score does not account for variation in attentional processing after stimulus presentation but before probe appearance, and factors such as preparation and execution of motor response that may vary between individuals particularly children can confound RT differences[15]. Furthermore, while RT tasks can potentially separate individual components underpinning attention bias (e.g. facilitated threat orienting from attentional maintenance), they require multiple tasks and conditions to achieve this, which can cause fatigue and response errors in children.

Alternative approaches such as taking eye gaze measures during the presentation of threatening and non-threatening stimuli[16] have been used to more directly and continuously measure attention[17]. By measuring fixations (time and location of attentional deployment between saccadic movements[18]) several components of attention bias can be assessed. Vigilance toward threat can be indexed by recording the location of the individual's *first fixation* after stimulus presentation in each trial. Comparison of first fixations to threat against first fixations to neutral provides a probability score to indicate the direction of initial orienting. Greater probability of first fixation toward threat indicates a threat vigilance bias. Alternatively, the latency of first fixations to each stimulus type can be compared: faster first fixations to threatening versus neutral stimuli could indicate a vigilance bias. To measure maintained attention on threat across stimulus presentation time, *dwell time* on each stimulus type is calculated, across the entire trial. Greater mean dwell time on threatening stimuli than on non-threatening stimuli indicates maintained attention toward threat, with the opposite suggesting overall threat avoidance. Attentional vigilance and avoidance patterns over time can also be derived through dwell time on threatening and non-threatening stimuli measured across *time-windows* (epochs).

Meta-analyses of eye-tracking data from adults[15] show that during free viewing and visual search tasks, anxious adults demonstrated greater initial vigilance for threat compared to non-anxious adults, consistent with RT studies[5]. Total dwell time on threat versus non-threat stimuli over the entire stimulus presentation time was not investigated in this meta-analysis. Developmental differences in brain circuits contributing to attention deployment in the presence of emotional stimuli[19] and more particularly, in how anxiety-linked attention biases change with maturation[12,20] means adult findings cannot be extrapolated to youth populations. Therefore, a growing number of eye-tracking studies of threat processing in youth have been conducted. Mixed findings across studies warrants pooling these data to evaluate combined effect sizes of anxiety-linked biases. Most studies have used free-viewing tasks as these reflect a more ecologically-valid assessment of attention deployment but also more importantly, may be suitable for children and adolescents as they are less dependent on task performance, which could introduce age-associated confounds. Most studies have investigated vigilance to threat, by measuring probability of first fixation towards threat, and maintained attention on threat, through total dwell time on threatening/non-threatening stimuli.

This meta-analysis aimed to address the following questions: First, do anxious children/adolescents and their non-anxious counterparts show an absolute bias (significantly different from zero) in probability of first fixation to threatening stimuli (as an index of initial threat-vigilance), and is there a between-group difference on this measure? Second, do anxious children/adolescents and their non-anxious counterparts show an absolute bias (significantly different from zero) in total dwell time on threatening versus neutral stimuli (as an index of maintained attention), and is there a between-group difference on this measure? As researchers have addressed these questions using different task parameters and recruiting specific sub-populations, which could affect findings, we investigated the effects of various procedural and population moderators: 1. *Primary attention task:* as these have varied between a free-viewing approach and dot-probe tasks which contain additional active components of probe selection resulting in anticipatory eye-movements during the free-viewing element, which may affect first fixation results[21]. 2. *Stimulus presentation time:* As brief presentation times are thought to capture involuntary attentional deployment and longer viewing times, more strategic processes[13], analyses of total dwell-time from studies using different viewing times may be prone to differential influences of involuntary and strategic processes, affecting the presence and direction of the bias. 3. *Age:* As attention biases vary with age[12] coinciding with developmental accounts that suggest that all children begin with an attention bias toward threat which "corrects" during healthy developmental trajectories[22], findings from studies using different age ranges (e.g. child/adolescent) may capture distinct attentional response to threat. 4. *Clinical diagnosis:* As some studies have found a threat-bias amongst clinically anxious youth only[23,24], symptom severity could modify the expression of the attention bias. 5. *Anxiety subtype:* As many studies investigating attention biases use samples containing individuals with mixed anxiety diagnoses or features, this may alter the intensity of the threat stimuli used in the tasks across participants.

Methods

Eligibility Criteria

We included studies that met the following criteria**: 1.** Due to practical considerations relating to translation, and as the majority of biomedical literature is published in English language journals[25], with no clear systematic bias of such language restriction in trials reported in conventional medicine[26], the study had to be available in English. 2. The study must be an original investigation. 3. The study must investigate human participants ≤18 years of age. 4. The study must use a standardized measure of anxiety (state or trait) for all participants; either clinical interview or a self/parent-report anxiety questionnaire. 5. The study must use eye-tracking to measure attention biases. 6. The study must use a free-viewing task, or task with a free-viewing element (such as dot-probe), during which gaze is tracked. As these tasks are less dependent on task performance, this minimizes age-associated confounds in studies of children and adolescents. 7. Appropriate data must be available to compute an effect size for at least one of the bias measures being investigated (probability of first fixation to threat; latency of first fixation to threat; total dwell time on threat versus neutral). This may be available as mean scores for 'anxious' and 'non-anxious' groups, a test statistic for group difference, or a correlation between the attention measure and anxiety severity. If data are unavailable in the paper, they must be made available by the author. 8. The design must allow for the comparison of attention towards threatening and neutral elements of the array. Studies pairing threatening stimuli with stimuli of any other valence were excluded (such as one that paired fear and angry faces with a mixture of happy and neutral faces[27]).

Information sources and search terms

In April 2018, Pubmed, Psycharticles, Medline, Psychinfo, and Embase databases were searched for eligible studies. We used anxiety-related key terms (anx*, anxiety disorder, GAD, depress*, fear, phobi*, dysphori*, and panic) that were crossed with key terms for eye-tracking measures (eye*, gaze*, fixation*, dwell time, and saccade) and key terms to identify child and adolescent participants (child*, adol*, pediatric, youth, juvenile, and teen*). Reference lists of identified studies were examined further for potentially eligible research, as were any identified relevant review papers. Titles and abstracts were screened for inclusion by the authors (SL, AV, JL) based on criteria 1-5. There was 100% agreement across authors. Studies that met this eligibility criterion were retained for full-text review to assess whether they met all criteria (SL, AV) again with 100% agreement. Where studies met all inclusion criteria, but further data was required, authors were contacted to request the necessary data.

Statistical analysis

Research questions and outcome measures: Meta-analyses were carried out to test two questions. First, the vigilance hypothesis was examined, that individuals with an anxiety disorder would detect threat more readily, and thus orient to it more often, than non-anxious controls. The vigilance hypothesis was investigated using studies that recorded the direction of initial gaze orienting; specifically, measures of probability of first fixation to threat versus neutral stimuli and latency of first fixation toward threatening stimuli were used. Studies that did not report first fixation probability or latency, but only reported total fixation time on threatening stimuli in the first 500+ms, were excluded from the analysis (k=2). Second, we tested the maintenance hypothesis, that anxiety is characterized by maintained attention on threat; thus, across the entire trial, individuals with anxiety will more often dwell upon threatening than neutral stimuli. This hypothesis was investigated using studies that recorded the mean duration of gaze (dwell-time) on threat versus neutral stimuli, when stimuli were displayed for longer than 1000ms.

Data coding: Studies were coded on the following variables: a) number of participants, b) participants' mean age, c) Gender split (% female), d) sample type (clinical/analogue), e) type of anxiety disorder, f) experimental task (free-viewing / dot-probe / other), g) type of threat stimulus (face / picture), h) threat emotion, i) number of stimuli presented, and j) stimulus presentation time. When the study included results from 'with/without stressor' groups separately, data from the 'without stressor' condition was used to retain consistency across the sample (k=2).

Analyses: With our measures of first fixation probability or latency, and overall dwell time, we performed within-group analyses for the anxious and non-anxious groups to evaluate presence of an 'absolute' bias toward threat in either group. We also estimated the between-group difference between anxious and non-anxious individuals on first fixation measures. Due to a lack of relevant data for within-group analysis of dwell time, only between-group analysis could be carried out for this attention bias measure.

Meta-analyses were conducted using comprehensive meta-analysis software (version 3.3.070). All effect sizes were calculated using Hedges' g. To interpret effects with this measure, Cohen's d guidelines were used[28]; small effect: .20, moderate effect: .50, large effect: .80. For the between-group analysis of both first fixation data and overall dwell time, effect size direction was calculated so that a positive effect size indicates the attentional bias toward threat is larger in anxious participants than in control participants. In studies that did not use high and low symptom groups, correlations between symptom severity and attention bias were used, with a positive effect size indicating a greater attention bias toward threat for more anxious individuals. In the within-group analyses, a positive effect size indicates that the attentional bias is greater for threat stimuli than neutral stimuli, with a negative effect size indicating the opposite. A random-effects model was chosen to compute combined effect sizes, as heterogeneity was expected across studies, and this method allows the results to be generalized to similar studies[29]. To assess heterogeneity of overall effect sizes, Cochran's Q[30] was used. Additionally, the I^2 statistic[31] was used, indicating the percentage of this variation across effect sizes.

Categorical variables were identified as potential moderators, consisting of procedural and population factors that differed across studies. Procedural variables included: Attention task (Dot-probe or Free-viewing); Stimulus presentation time (≤2000ms or >2000ms). Population variables included: Age group (Adolescent, mean age of 12 years and above or Child, mean age below 12 years); Sample Type (Clinical or Analogue); Anxiety Type (Social Anxiety Disorder / Social Phobia or Mixed, more than one anxiety disorder included). Moderator analyses were conducted in relation to outcomes on between-group measures of first fixation and dwell time. Due to the small number of studies eligible for within-group analysis moderator analysis was not carried out for the within-group results.

Risk of publication bias: Funnel plots were inspected for all analyses to assess publication bias. Rank correlation[32] and regression tests[33] were also carried out to evaluate evidence of publication bias, as well as Duval and Tweedie's trim and fill method[34]. Fail-safe numbers were computed to assess the magnitude of a potential file-draw problem. This provides an estimate of the number of studies, with an effect size of zero that would need to be added to the analysis to produce a cumulative effect that is statistically non-significant ($p>.05$). In addition, we used Orwin's fail-safe N[35] to calculate the number of studies with an effect size of zero that would need to be added to the analysis to produce a specified "trivial" Hedges' g value.

Results

Search Results

Figure 1 illustrates the literature search and study selection process. Initial searches identified 3871 studies. After removing duplicates, this was reduced to 1818 studies. After excluding by abstract, this number was reduced to 29 studies. Full-text screening resulted in exclusion of 16 more studies, resulting in 13 eligible studies.

Study Characteristics

Study characteristics are displayed in **Table 1**. The entire data set was scanned for outliers; these were identified as studies whose 95% confidence intervals did not overlap with the 95% confidence interval of the combined effect size. No studies yielded an effect size that was an outlier. Therefore, the total sample included data from 798 participants aged 3-18 years, from 13 studies. All studies were published in peer-reviewed journals. Although containing a free-viewing element, studies varied on the specific tasks used; 9 studies used a task that solely involved free-viewing of the presented stimuli, whereas 4 studies used a dot-probe task that required a user action after the period of free-viewing. Nine studies used a clinical sample of anxious participants, and 4 used an unselected sample. Five investigated attention bias in relation to social anxiety disorder (SAD) or social phobia (SP), 2 used broader overall anxiety scores, 1 for state anxiety, and the remaining 5 included patients with a mixture of anxiety diagnoses (including SAD, SP, generalized anxiety disorder (GAD), and separation anxiety (SEP). Ten studies used faces as the threatening stimuli: 5 of these using an angry emotion, 3 using fear, 1 using pain, and 1 specifying a general "threatening" face. Two studies used eyes as the threatening stimuli, one as part of the face, and the other, only the eyes. The final one study used pictures of social scenes, with faces within the scenes defined as the threatening stimuli. Effect sizes within each study, and confidence intervals can be seen in Figures 2 to 4.

Meta-analysis of anxiety and first fixation data

Within-group Analyses: The meta-analyses examining within-group differences in first fixation on threat versus neutral stimuli (**Figure 2**), show that the combined effect size was not significant in anxious participants (k=6; g=.315, p=.21, CI=−.17, .80), or in non-anxious controls (k=6; g=.27, p=.27, CI=−.21, .75). There was large heterogeneity in the effect sizes for anxious (Q(5)=46.32, p<.001, I^2=89.20%) and non-anxious (Q(5)=39.48, p<.001, I^2=87.33%) groups.

Between-group Analysis: The meta-analysis examining the between-group differences in first fixation on threat (**Figure 3**) found that anxious individuals did not significantly differ from non-anxious individuals in initial fixation towards threatening versus neutral stimuli (k=8; g=.04, p=.39, CI=−.18, .26). There was not significant heterogeneity in the effect sizes, Q(8)=8.56,p=.29, I^2=18.25%.

Meta-analysis of anxiety and overall dwell time

Between-group Analysis: The overall effect size for the meta-analysis examining the association between anxiety and dwell time (**Figure 4**) was significant (k=12; g=-.26, p=.004, CI=−.44, -.08), indicating anxious youth avoided threatening stimuli more than non-anxious youth across the stimulus viewing period. There was not significant heterogeneity in the effect sizes, Q(11)=15.48, p=.16, I^2=28.93%. Of note, because results from analogue samples can be difficult to interpret, as non-clinical individuals with high scores on self-reported anxiety measures do not always show similar patterns of attention as clinical patients, we re-ran analysis excluding analogue studies. Re-running the between-group analysis on dwell time data without analogue samples still showed the overall effect (k=8; g=-.24, p=.035, CI=−.45, -.02); heterogeneity: Q(11)=9.97, p=.19, I2=29.77%).

Sub-group moderator analyses

The non-significant χ^2 values in testing for heterogeneity in variance, and I^2 values that are not extremely high, suggests the studies in each sample were fairly homogenous. However, as the I^2 values were approaching 25%, and based upon a priori analysis plans, moderator analyses were conducted.

Sub-group moderator results for between-group comparisons of first fixation data: There were no significant moderation effects on first fixation data by population or procedural factors identified a priori (**Table 2**).

Sub-group moderator results for between-group comparisons of overall dwell time: For anxiety type, significantly greater (negative) between-group effect sizes (indicating more *avoidance* of threat for anxious compared to non-anxious individuals) was found for studies including participants with a mixture of anxiety types, than for studies using only social anxiety (*p*=.05) (**Table 2**).

Publication bias

Funnel plots were inspected (**Supplementary Figures 1 and 2**), and no evidence of asymmetry was observed. Egger's test[33] and rank correlation tests[32] were all non-significant (all *ps*>.49). Furthermore, using the Duval–Tweedie trim and fill procedure[34], no evidence of publication bias was found for any of the measures. For the dwell time meta-analysis, the fail-safe N[36] was 25, meaning there would need to be 25 studies with an effect size of zero added to the analysis to increase the p-value to above .05, i.e. produce a statistically non-significant cumulative effect. In addition to this, using Orwin's fail-safe N, in order to bring our criterion down to a Hedges g value of -.1, it would take 21 extra studies with an effect size of zero.

Discussion

This first meta-analysis of eye-tracking measures of attention bias in child and adolescent anxiety included data from 798 participants aged 3 to 18 years across 13 studies. A significantly greater tendency to direct first fixations on threatening over neutral stimuli did not characterize or differentiate anxious and non-anxious children or adolescents. Instead, anxious youth showed a greater tendency to avoid maintaining their gaze on threat compared to non-anxious youth, a difference that only emerged in studies where samples comprised mixed anxiety diagnoses.

At first glance, our findings that biased orienting toward threat did not differentiate anxious and non-anxious children and adolescents but that over the course of stimulus viewing, anxious youth avoided threatening over non-threatening stimuli more than non-anxious controls seems incompatible with the meta-analyses of RT data in children and adolescents[12]. However, it is possible that first fixation data may not be equivalent to attention capture/engagement in RT-based paradigms. There is therefore still work to do in mapping how RT-based indices relate to eye-tracking indices. Closer inspection of the moderator analysis in the meta-analyses also shows that anxiety group differences for attention bias a) only emerged when stimuli in dot-probe tasks were presented at 1250ms (rather than those >500ms) and b) were greater when considering emotional Stroop task results than dot-probe. These data could be interpreted to imply that any bias in attentional deployment for threat in youth is likely to occur beyond initial fixation, and driven by disturbances in voluntary top-down processes. Our findings extend these interpretations by suggesting that these later-stage biases result in an eventual strategic avoidance of threat. As our total dwell time score is unable to infer specific patterns of attention bias over time, it is less clear whether the direction of these biases indeed fluctuate across time in anxious versus non-anxious youth. In-Albon and colleagues found a pattern of vigilance-avoidance in anxious youth in two studies[37,38], although a third study[39] failed to report similar patterns. These conflicting data underscore a need for more studies utilizing time-windows with fixations and dwell-time across different epochs. There are alternative measures derived from eye-tracking that can be used to assess anxiety-linked differences across the entire viewing period of complex stimuli[40], such as assessing the visual scan-path, a sequence of fixations and saccades thought to reflect the manner in which information is attended to, reappraised and integrated.

Second, our meta-analytic findings appear inconsistent with adult RT[5] and eye-tracking data[15] which suggest that anxiety is characterized by facilitated detection and orienting of initial attention toward threat and greater maintained attention on threat in anxious individuals[41-45]. These differences may instead underscore the importance of developmental accounts of anxiety. Such accounts need to recognize greater variability in attention bias expression among young people compared to adults, manifesting between initial vigilance, rapid avoidance, sustained threat monitoring, and vigilance-avoidance patterns and may be attributable to the influences of multiple cognitive and learning processes unique to the developing individual[46]. However, that developmental factors may moderate attention bias expression across youth was not supported by our data. We found no within-group vigilance effect in anxious or non-anxious children and adolescents, and no moderating effect of age on between-group differences in vigilance within this age range. These data therefore seem to speak against developmental accounts that all children may begin with an attention bias toward threat which then "corrects" during healthy developmental trajectories [22]. However caution is needed before drawing firming conclusions. Whilst not reaching significance as a moderator, when categorizing the studies by age, there were differences in the strength of the association between dwell time on threat and anxiety across age groups: the child group showed a significant avoidance whereas the adolescent studies did not. This is surprising, as the literature proposes avoidance as a maladaptive emotion regulation strategy, largely driven by executive control processes which mature in youth[47,48]. Instead, putting our findings with those from adults suggests that while attentional avoidance of threat characterizes anxious children and difficulty disengaging from threat characterizes anxious adults, there are no clear attentional strategies in anxious adolescents, possibly as brain circuits underlying attentional deployment are still undergoing re-organization during adolescence. However, there was a relatively high heterogeneity of variance between effect sizes in the adolescent group, indicating other factors may be affecting the associations between anxiety and avoidance. Furthermore, as many studies used wide age ranges, we could not investigate the influence of age through a meta-regression. Instead we relied on sub-group analysis, which crudely used mean age of the sample to dichotomously categorize studies into children and adolescents. Further research assessing the association between anxiety-linked attention patterns across specific ages (or developmental stages) within youth would help elucidate the role of maturation and/or experience on the expression of these biases.

Finally, the only factor that significantly moderated maintained attention was ‘anxiety type’; only studies using participants with a mixture of anxiety types found a significant between-group difference in avoidance. It should be noted however that studies using mixed anxiety groups all included social anxiety patients within their samples; plus, given high level of homotypic comorbidity in anxiety disorders[49], several of the ‘only’ social anxiety studies may have included co-occurring anxiety disorders, making it difficult to disentangle biases in maintained attention per disorder. However, as a whole, the results imply that specific diagnostic sub-groups other than social anxiety disorder are driving this avoidance effect. Utilizing more specific disorder and symptom boundaries in future study designs may be more informative as attentional components increasingly show disorder and symptom specificity[50,51].

There are several limitations to our study. Compared to other meta-analyses of attention bias to threat[5,12,15], there were fewer studies in this meta-analysis, with a handful of published studies that were excluded due to inadequate and unavailable data to compute an effect size. Null results may have emerged from low power. A low number of studies also prevented some moderator analyses from being carried out; and others being considered such as a meta-regression of the ratio of females:males in the sample; and the presence of comorbidity with non-anxiety disorders in some samples (e.g. autistic spectrum disorders or depression). For one moderator, presentation time, the rationale for selecting a cut-off (2000ms) was somewhat arbitrary, driven by the distribution of the parameters used in individual studies, and the need to achieve a largely even split of studies into long and short durations (5 versus 7). Where moderation was examined, differential effects across levels of some variables may have reached significance with larger samples.

Second, while first fixation data via eye-tracking provides a more precise indication of where overt attention is first directed, it is unclear whether these measures in fact reflect a mixture of stimulus-driven and strategic processes. Previous research has found typical latency of exogenous first fixations to be around 175ms[52], whereas eye-tracking studies from anxious individuals generally show first fixation latency to be longer (250ms-400ms[16,53]). There are also suggestions first fixation measures of threat processing aren't as reliable as expected[41,54,55], and may be affected by participants favoring fixation to the top or left image regardless of its emotional valence. Relatedly, the free-viewing approach across long stimulus duration times (>1000ms) employed by many eye-tracking studies may impact upon identifying anxiety group differences in first fixations. As this task only measures spontaneous viewing behavior, and not attentional behavior related to task demands, it may be less powerful in tapping attentional engagement/disengagement as neither is necessary for task completion. Indeed group differences in attention bias are more readily identified when a task action is required, such as a visual search task[56-58]. Another way of potentially informing the attentional components contributing to anxiety is to simultaneously collect pupillary dilation data. Future studies could try and associate these measures and gain information on the online interplay between the temporal dynamics of gaze behavior and brain-mediated emotional responsiveness.

Finally, many studies may not always accurately identify biases in relation to threat due to differences in threat evaluations. For instance, all facial stimuli may be considered somewhat threatening in socially anxious individuals, and as such avoidance of all faces may occur[59]. Avoidance of all perceived social threat may mask any group differences in attention bias picked up with current measures, as only between-face differences are generally calculated. It could also be possible that no threat evaluation occurs because such threat stimuli lack personal relevance to young people, and that this also masks within or between-group anxiety differences in attention bias.

Notwithstanding these limitations there are some clinical implications of these findings. Based on relatively robust findings from anxious adults of an association with attention bias for threat[5], attention bias modification (ABM) tasks have been used as anxiety-reducing interventions in adults[60,61] and young people[62], mainly using the dot-probe task but also eye-tracking tasks[63,64]. These paradigms train attention away from threat mostly towards non-threatening stimuli. Results using ABM in anxious youth have been mixed, with meta-analyses finding that ABM did not lead to a significantly greater symptom reduction than a control condition[65]. The current meta-analysis results suggest that rather than modify an initial orienting bias for threat it may be valuable to modify strategic processes that reduce threat avoidance. Some studies have already suggested that ABM reduces anxiety by improving strategic attention control processes[66], and within this, some theorists suggest that visual search tasks may be more appropriate for modifying these voluntary aspects of attention[13]. Indeed, in youth, implementations of visual search tasks, where participants search for a benign target (smiling face) from amongst negative distractors (negative faces) has resulted in consistent symptom reduction[67,68] although it remains to be seen if this reduction can be explained by threat avoidance specifically, rather than exposure to threatening faces per se.

In summary, the current meta-analyses suggest that anxious and non-anxious youth do not differ in overt initial orienting to threat, as measured by eye movements; however, our results demonstrate a small effect of anxious youth avoiding threat. Future research with large sample sizes is required to investigate the avoidant pattern of strategic attention across time more discretely, and to delineate the factors contributing to the individual differences found in attention bias expression amongst anxious youth.

Table 1 Study Characteristics

Study	N	n (clinical)	n (control)	Age Range	Mean age (years)	% female	Sample type	Primary anxiety problem	Attention task	Threat stimulus	Threat emotion	Number of stimuli	Display Time (ms)
Capriola-Hall et al. (2018)[69]	41	41	N/A	Adolescents (12-16)	14.54	68%	Clinical	SAD	Free-viewing	Face	Angry	2	3000
Dodd et al. (2015)[70]	83	37	46	Children (3-4)	3.99	59%	Clinical	SAD, GAD, SEP, SP	Free-viewing	Face	Angry	2	1250
Haller et al. (2017)[71]	51	N/A	N/A	Adolescents (14-18)	16.73	100%	Analogue	SAD	Free-viewing	Scene	Social	Varying	5000
Heathcote et al. (2016)[72]	37	N/A	N/A	Adolescents (8-17)	12.1	64%	Analogue	State anxiety	Free-viewing	Face	Pain	2	3500
Kleberg et al. (2017)[73]	25	25	N/A	- Adolescents	15.2	84%	Clinical	SAD	Free-viewing	Eyes	Eyes	4	2000
Michalska et al. (2017)[74]	82	N/A	N/A	Children (9-13)	11.81	60 %	Analogue	Overall anxiety score	Free-viewing	Face	Eyes	1	7000-8000

Price et al. (2013)[75]	94	74	20	Children -	10.57	52%	Clinical	GAD, SEP, SP	Dot-probe	Face	Fear	2	2000
Price et al. (2016)[76]	67	67	N/A	Children (9-14)	11.1	53.7%	Clinical	GAD, SEP, SP	Dot-probe	Face	Fear	2	2000
Schmidtendorf et al. (2018)[77]	79	37	42	Children -	11.45	61%	Clinical	SAD	Free-viewing	Face	Angry	2	5000
Seefeldt et al. (2014)[78]	73	30	43	Children (8-12)	9.9	44%	Clinical	SP	Dot-probe	Face	Angry	2	3000
Shechner et al. (2013)[79]	33	18	15	Adolescents (8-17)	13.19	58%	Clinical	GAD, SAD, SP	Free-viewing	Face	Angry	2	10000
Shechner et al. (2017)[80]	45	19	26	Adolescents (8-17)	12.63	44%	Clinical	GAD, SAD, SP	Free-viewing	Face	Threat	3	5000
Tsypes et al. (2017)[81]	88	N/A	N/A	Children -	9.26	44%	Analogue	Overall anxiety score	Dot-probe	Face	Fear	2	1000

Note: GAD = generalized anxiety disorder; SAD = social anxiety disorder; SP = social phobia (spider); SEP = separation anxiety disorder.

Table 2. Moderator results for between-group comparisons of attentional vigilance and attentional maintenance

		Effect size		*Heterogeneity*	*Moderation*	
Moderators for between-group comparisons of attentional vigilance	**k**	**g**	**95% CI**	**I^2**	**Q**	**p**
Age group						
Adolescent	3.00	0.15	-0.62, 0.93	70.27	0.20	0.66
Child	5.00	-0.03	-0.25, 0.2	0.00		
Presentation Time						
<2001ms	4.00	-0.07	-0.33, 0.19	0.00	1.36	0.24
>2000ms	4.00	0.20	-0.18, 0.58	32.90		
Task						
Dot-probe	4.00	0.01	-0.26, 0.28	0.00	0.06	0.81
Free-viewing	4.00	0.08	-0.44, 0.6	63.17		
Anxiety Type						
Mixed	4.00	0.21	-0.11, 0.54	26.71	2.61	0.11
SAD/SP	4.00	-0.14	-0.43, 0.15	0.00		

		Effect size		*Heterogeneity*	*Moderation*	
Moderators for between-group comparisons of attentional maintenance	**k**	**g**	**95% CI**	**I^2**	**Q**	**p**
Age group						
Adolescent	5	-0.19	-0.61, 0.22	49.82	0.20	0.653
Child	7	-0.30*	-0.48, -0.11	14.22		
Presentation Time						
<2001ms	5	-0.35*	-0.60, -0.16	0	1.37	0.242
>2000ms	7	-0.16	-0.45, 0.13	50.47		

Task						
Dot-probe	4	-0.24	-0.57, 0.09	49.04	0.02	0.881
Free-viewing	8	-0.27*	-0.5, -0.05	26.70		
Sample Type						
Analogue	4	-0.30	-0.63, 0.04	41.35	0.07	0.791
Clinical	8	-0.24*	-0.46, -0.02	29.77		
Anxiety Type						
Mixed	6	-0.43*	-0.63, -0.24	0	3.83*	0.050
SAD/SP	5	-0.08	-0.37, 0.21	14.07		

SAD = Social Anxiety Disorder; SP = Social Phobia; Mixed = studies including patients with a range of anxiety diagnoses. The number of studies using an analogue group (k=0), was not enough to test moderation of “sample type”. Significant effects (p<.05) denoted by *.

List of Figures

Figure 1: Flowchart of screening processes for study inclusion. Criterion 4: Did not use standardised measure of anxiety; Criterion 6: Did not use appropriate attention task; Criterion 7: Necessary data was unavailable/unobtainable; Criterion 8: Did not allow for comparison of attention towards threatening and neutral stimuli.

Figure 2: Forest plot of within-group first fixation bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

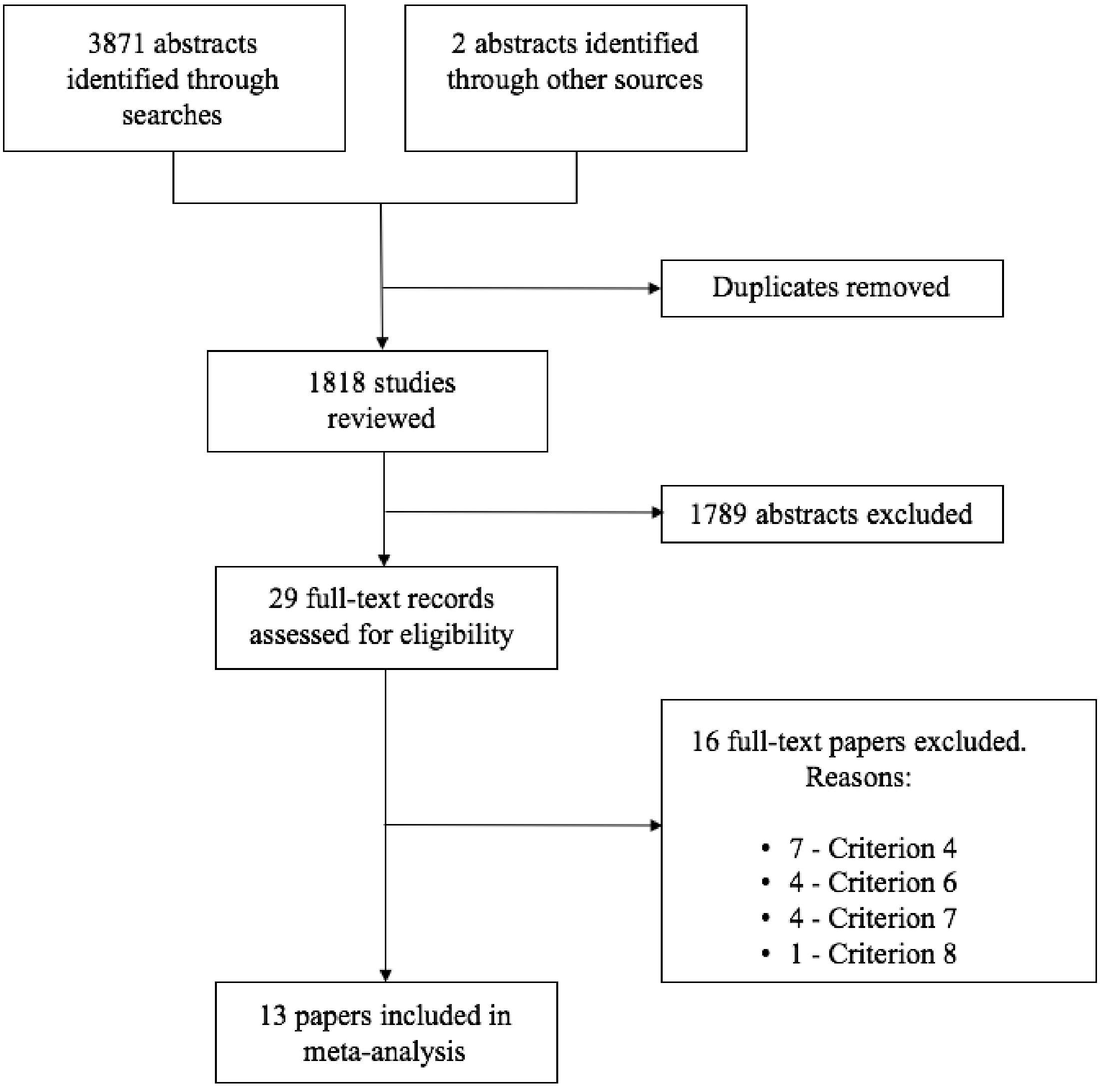
Figure 3: Forest plot of between-group first fixation bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

Figure 4. Forest plot of dwell time bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

Supplemental Figure 1: Funnel plot for between-group first fixation analysis

Supplemental Figure 2: Funnel plot for between-group dwell time analysis

Figure 1



3871 abstracts identified through searches
2 abstracts identified through other sources
Duplicates removed
1818 studies reviewed
1789 abstracts excluded
29 full-text records assessed for eligibility
16 full-text papers excluded. Reasons:
• 7 - Criterion 4
• 4 - Criterion 6
• 4 - Criterion 7
• 1 - Criterion 8
13 papers included in meta-analysis

Figure 2

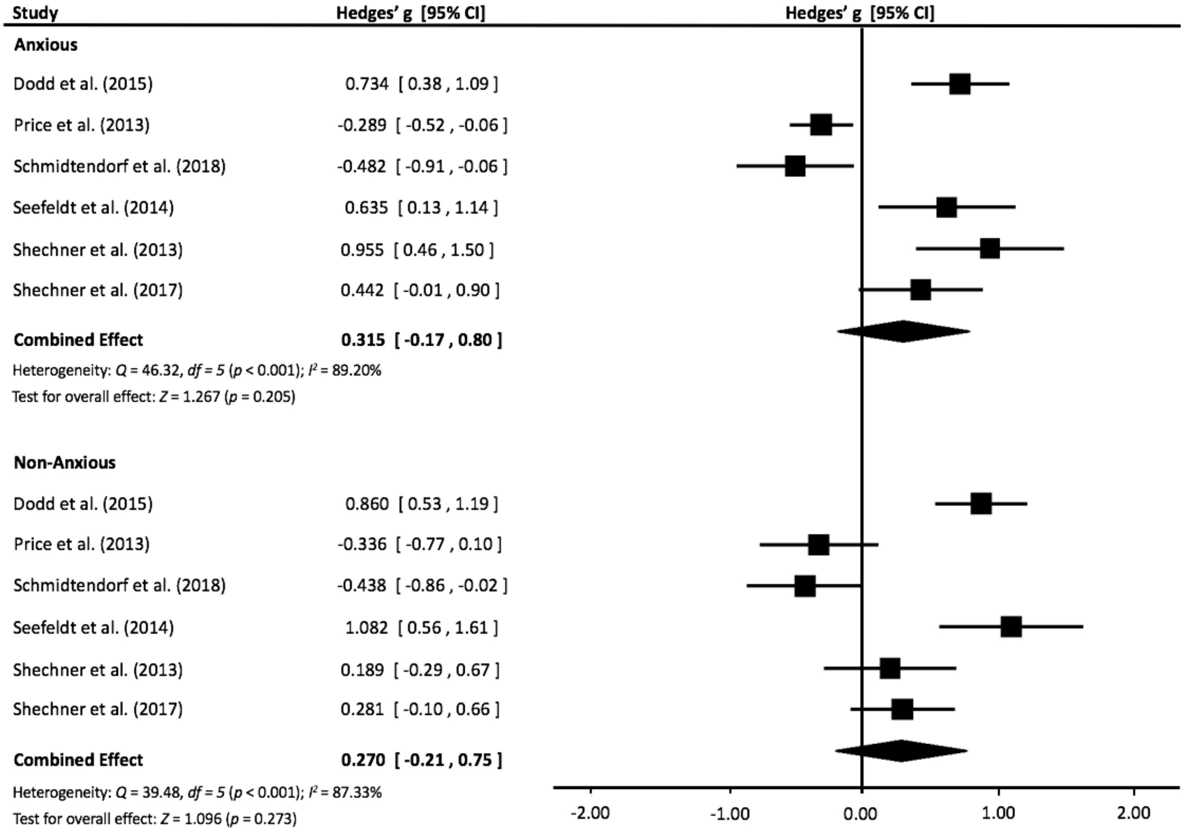

Study
Hedges' g [95% CI]
Hedges' g [95% CI]
Anxious
Dodd et al. (2015) 0.734 [0.38 , 1.09]
Price et al. (2013) -0.289 [-0.52 , -0.06]
Schmidtendorf et al. (2018) -0.482 [-0.91 , -0.06]
Seefeldt et al. (2014) 0.635 [0.13 , 1.14]
Shechner et al. (2013) 0.955 [0.46 , 1.50]
Shechner et al. (2017) 0.442 [-0.01 , 0.90]
Combined Effect 0.315 [-0.17 , 0.80]
Heterogeneity: Q = 46.32, df = 5 (p < 0.001); I^2 = 89.20%
Test for overall effect: Z = 1.267 (p = 0.205)
Non-Anxious
Dodd et al. (2015) 0.860 [0.53 , 1.19]
Price et al. (2013) -0.336 [-0.77 , 0.10]
Schmidtendorf et al. (2018) -0.438 [-0.86 , -0.02]
Seefeldt et al. (2014) 1.082 [0.56 , 1.61]
Shechner et al. (2013) 0.189 [-0.29 , 0.67]
Shechner et al. (2017) 0.281 [-0.10 , 0.66]
Combined Effect 0.270 [-0.21 , 0.75]
Heterogeneity: Q = 39.48, df = 5 (p < 0.001); I^2 = 87.33%
Test for overall effect: Z = 1.096 (p = 0.273)
-2.00
-1.00
0.00
1.00
2.00

Figure 3

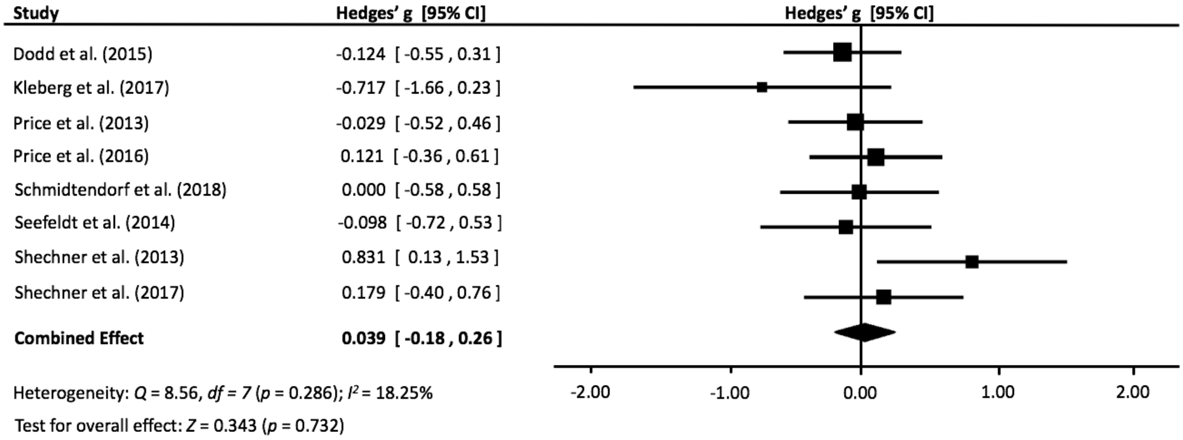
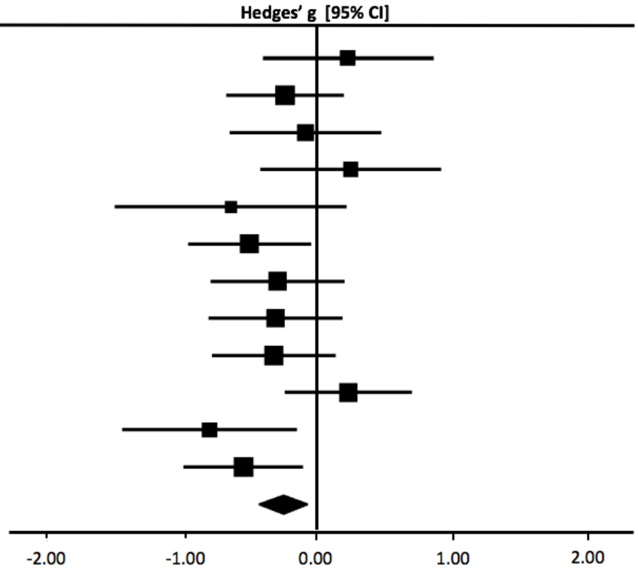

Study
Hedges' g [95% CI]
Hedges' g [95% CI]
Dodd et al. (2015)
-0.124 [-0.55 , 0.31]
Kleberg et al. (2017)
-0.717 [-1.66 , 0.23]
Price et al. (2013)
-0.029 [-0.52 , 0.46]
Price et al. (2016)
0.121 [-0.36 , 0.61]
Schmidtendorf et al. (2018)
0.000 [-0.58 , 0.58]
Seefeldt et al. (2014)
-0.098 [-0.72 , 0.53]
Shechner et al. (2013)
0.831 [0.13 , 1.53]
Shechner et al. (2017)
0.179 [-0.40 , 0.76]
Combined Effect
0.039 [-0.18 , 0.26]
-2.00
-1.00
0.00
1.00
2.00
Heterogeneity: Q = 8.56, df = 7 (p = 0.286); I² = 18.25%
Test for overall effect: Z = 0.343 (p = 0.732)

Figure 4

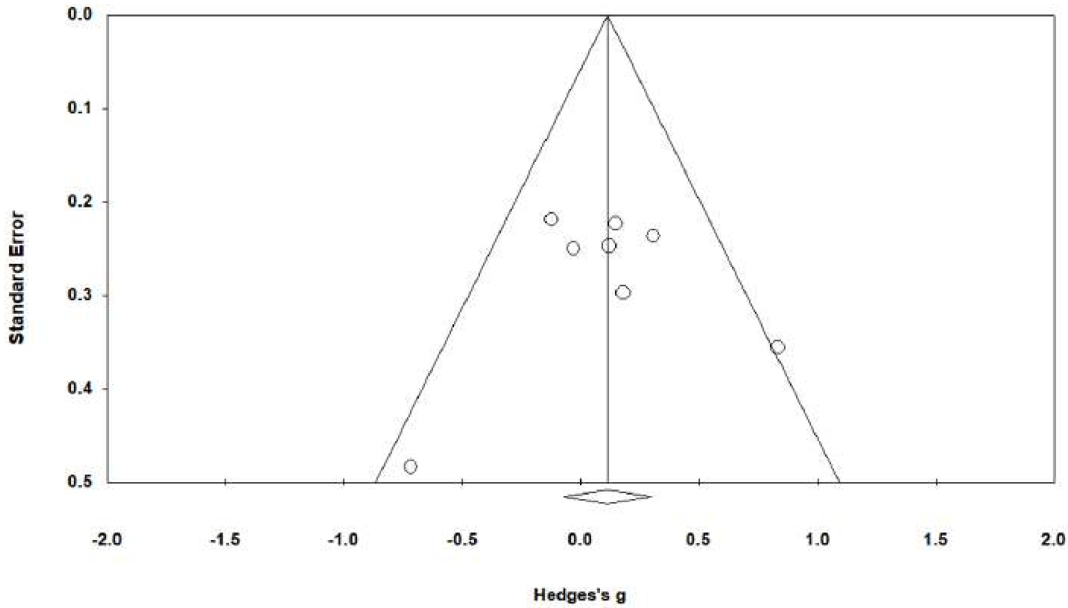
Study	Hedges' g [95% CI]
Capriola-Hall et al. (2018)	0.217 [-0.41 , 0.84]
Dodd et al. (2015)	-0.249 [-0.68 , 0.18]
Haller et al. (2016)	-0.099 [-0.66 , 0.46]
Heathcote et al. (2016)	-0.237 [-0.43 , 0.90]
Kleberg et al. (2017)	-0.651 [-1.50 , 0.20]
Michalska et al. (2017)	-0.512 [-0.96 , -0.06]
Price et al. (2013)	-0.304 [-0.80 , 0.19]
Price et al. (2016)	-0.320 [-0.81 , 0.17]
Schmidtendorf et al. (2018)	-0.331 [-0.78 , 0.12]
Seefeldt et al. (2014)	0.219 [-0.25 , 0.69]
Shechner et al. (2017)	-0.807 [-1.45 , -0.17]
Tsypes et al. (2017)	-0.556 [-0.99 , -0.12]
Combined Effect	**-0.263 [-0.44 , -0.08]**



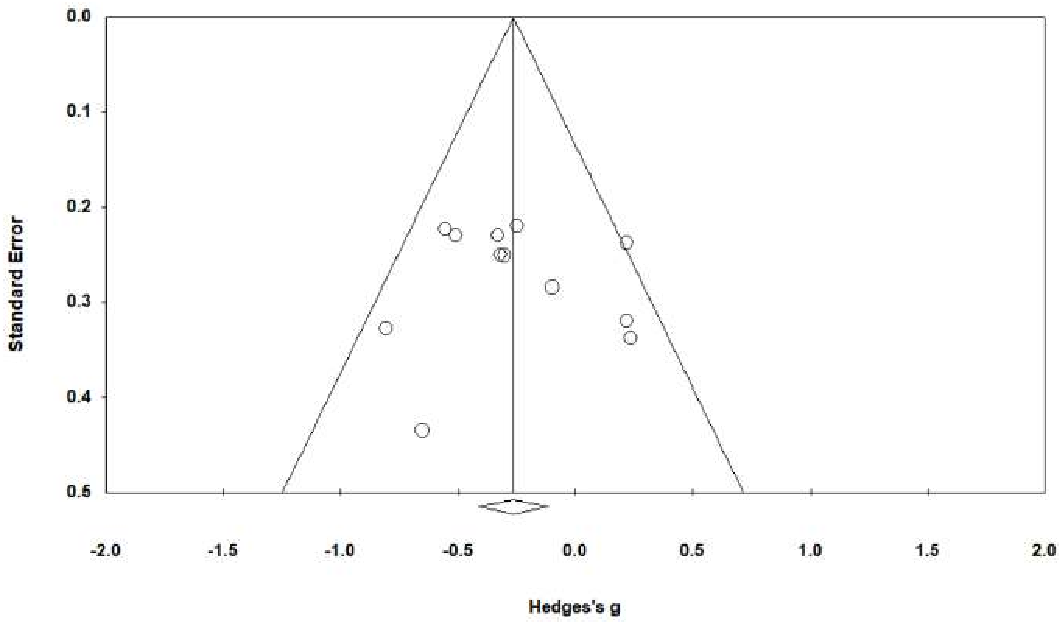
Heterogeneity: Q = 15.48, df = 11 (p = 0.162); I^2 = 28.93%

Test for overall effect: Z = -2.876 (p = 0.004)

Supplemental Figure 1



Supplemental Figure 2



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