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Converging Multi-modal Evidence for Implicit Threat-Related Bias in Pediatric Anxiety Disorders

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Abstract
This report examines the relationship between pediatric anxiety disorders and implicit bias evoked by threats. To do so, the report uses two tasks that assess implicit bias to negative-valence faces, the first by eye-gaze and the second by measuring body-movement parameters. The report contrasts task performance in 51 treatment-seeking, medication-free pediatric patients with anxiety disorders and 36 healthy peers. Among these youth, 53 completed an eye-gaze task, 74 completed a body-movement task, and 40 completed both tasks. On the eye-gaze task, patients displayed longer gaze duration on negative relative to non-negative valence faces than healthy peers, $F(1, 174) = 8.27$, $p = .005$. In contrast, on the body-movement task, patients displayed a greater tendency to behaviorally avoid negative-valence faces than healthy peers, $F(1, 72) = 4.68$, $p = .033$. Finally, implicit bias measures on the two tasks were correlated, $r(38) = .31$, $p = .049$. In sum, we found an association between pediatric anxiety disorders and implicit threat bias on two tasks, one measuring eye-gaze and the other measuring whole-body movements. Converging evidence for implicit threat bias encourages future research using multiple tasks in anxiety.

Keywords Anxiety · Threat · Bias · Attention · Avoidance

Introduction

Considerable research examines implicit threat biases in pediatric anxiety disorders (Eysenck et al. 2007; Mitte 2008; Mogg and Bradley 1998; Roefs et al. 2011). Attempts to extend this work face challenges that might be met by integrating multiple implicit threat bias tasks. The current report initiates such work by using two tasks in research on pediatric anxiety.

Threat bias studies relate to work on brain function, cognition, and emotion. The brain possesses insufficient resources to simultaneously represent all features of the environment, and cognitive functions prioritize features to compensate for this capacity limitation (Beck and Clark 1997). The term "threat bias" refers to the prioritization of threats over other stimuli, which occurs for many cognitive processes (Beck 1976; Beck and Clark 1997). For example, in mnemonic threat bias, children and adults more strongly remember threatening than non-threatening stimuli (Mitte 2008), whereas in attentional threat bias, children and adults allocate greater levels of attention to threatening than non-threatening stimuli (Bar-Haim et al. 2007; Lisk et al. 2019).

Many studies use methods that quantify implicit bias (Mitte 2008; Mogg and Bradley 1998; Roefs et al. 2011; Cisler et al. 2009). Implicit threat bias occurs when performance indices, such as reaction time, are influenced by threats that are unrelated to task instructions (Bantin et al.

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2016; Haas et al. 2017). For example, a task might require subjects to identify neutral objects, such as letters, but subjects might not be told about other, superfluous stimuli appearing near the letters. Some trials might include superfluous threat stimuli; others might include superfluous neutral stimuli. Implicit threat bias manifests as slower letter-identification on trials with superfluous threats than on trials with superfluous neutral stimuli.

Different theories emphasize distinct aspects of implicit threat bias. Some note how task setting affects bias (Mogg and Bradley 1998). For example, implicit threat bias might produce vigilance in safe settings but avoidance in dangerous settings (Bar-Haim et al. 2010). Theories also note how biases affect distinct processes, such as attention and memory (Mitte 2008; Mogg and Bradley 1998). Other theories emphasize bias in the neural circuits that broadly coordinate defensive behavior, physiology, and cognition. For these theories, one overarching construct, potentially indexed as a latent variable, shapes whole-organism responding (LeDoux 2019).

While studies examine different types of biases, excessive implicit attention bias to threat is one of the most consistent findings in cross-sectional research on adult anxiety disorders (Bar-Haim et al. 2007; Lazarov et al. 2016). The conclusion extends influential theories on biased information processing in anxiety (Beck 1976; Beck and Clark 1997). Moreover, when present in children, attention bias may impact development of other processes, including threat appraisal, as proposed by other theories (Field and Lester 2010). These theories shape current thinking. Thus, when inconsistent findings on attention bias arise, they often are attributed to task features that degrade reliability rather than inaccuracies in the theories (Price et al. 2015; Schmukle 2005).

Theories on the developmental role of attentional threat bias in anxiety extend data in youth and adults (Field and Lester 2010). Meta-analysis reveals biases of similar direction and magnitude in pediatric and adult anxiety disorders (Bar-Haim et al. 2007). Longitudinal studies extend this work (Fu and Perez-Edgar 2019). Prospective data show that children with high levels of attentional threat bias exhibit larger increases in anxiety symptoms than children with low levels of threat bias (White et al. 2017). Moreover, altering attention threat bias changes levels of anxiety, implicating the bias in the cause or maintenance of anxiety disorders (Bar-Haim 2010; MacLeod and Mathews 2012). Thus, techniques for reducing threat bias in at-risk or affected children might prevent or treat pediatric anxiety disorders, thereby clinically extending ideas on cognition in anxiety.

Inconsistent findings related to poor psychometrics create a need for improved task reliability (Price et al. 2015; Sipos et al. 2014). This could be accomplished by using multiple new, psychometrically-strong tasks to index a latent variable (Cardinale et al. 2019). However, estimating latent variables is laborious. Hence, this work can begin by merely demonstrating correlations between two new tasks. For anxiety disorders, such work might combine measures of attention and other implicit biases, given theory suggesting that neural circuitry mobilizes diverse outputs during coordinated threat responses (LeDoux and Daw 2018). For example, avoidance of threat could reflect such coordination. When encountering threats, attention bias might operate rapidly to prime and facilitate avoidance responses that occur seconds later. Detecting such reciprocal relationship between attention vigilance and behavioral avoidance in patients could extend an influential hypervigilance-avoidance model of anxiety (Mogg et al. 1997, 2004). From this perspective, coordination between early attention bias and later motor responding could generate stronger avoidance than would occur in the absence of attention bias.

Latent-variable estimation carries psychometric advantages. For example, it addresses reliability concerns, since latent variables are uncorrelated with errors in measurement for each indicator variable (Bollen 2002). Moreover, task performance reflects both constructs of interest and nuisance factors. Latent-variable approaches can isolate variance related to threat bias by using multiple tasks, each with distinct formats. This can dissociate bias-related influences shared across tasks from nuisance-related influences unique to each task.

The current study initiates a line of multi-task research that follows a path used with inhibitory control (Cardinale et al. 2019). The study utilizes two tasks, one with eye-tracking (Lazarov et al. 2016) and another indexing whole-body movements (Lebowitz and Francois 2018). Of note, the tasks differ in their effects, with the first task evoking attention bias toward threat and the second evoking behavioral avoidance of threat. Nevertheless, as in other implicit-bias paradigms, both tasks do not instruct subjects to detect, classify, or monitor emotion cues. Moreover, both tasks use evocative faces to engage threat-responsive circuitry (Ohman and Mineka 2001). This circuitry can coordinate gaze and other behaviors by implicitly biasing multiple pathways, including those that control eye movements and those that control whole-body movements (LeDoux and Daw 2018). Finally, neither task relies on button-press, reaction-time (RT) measures, since psychometric research suggests that such RT measures possess poor test–retest reliability (Sipos et al. 2014; Price et al. 2015). Of note, this is a significant departure from past research on implicit threat bias in youth, where most studies utilize button-press RT measures (e.g., Abend et al. 2018).

The first task used here measures gaze duration on faces featuring negative- vs. non-negative-valence expressions in face-set matrices (see Fig. 1A). Two relevant studies use the task with adults. One finds longer dwell time on disgust

Fig. 1 (A) Illustrative example of matrix stimuli from Study 1 (Neutral vs. Disgust contrast). Of note, actual task stimuli utilized the NimStim stimulus set (Tottenham et al. 2009); due to copyright restrictions, stimuli from a different set (see Lazarov, et al. 2016) are shown here for illustrative purposes only. (B) A participant engaging in the YIKES task from Study 2

vs. neutral faces in adults with vs. without social anxiety disorder (Lazarov et al. 2016); the other finds longer dwell time on sad vs. happy faces in adults with vs. without major depressive disorder (Lazarov et al. 2018). Matrix sets from both prior studies are used in the current report. In addition, because studies of pediatric anxiety often use angry faces, gaze to angry vs. happy faces also was contrasted. Happy rather than neutral faces were selected as a contrast to create matrices with stimuli easily distinguishable from angry faces. Prior work addresses psychometric concerns for other face-viewing, attention tasks (Price et al. 2015) and informs analyses in the current study. This prior work finds adequate reliability only for a measure of dwell-time bias used in analyses for the current study but not for other task parameters, such as initial saccade and other fixation features (Lazarov et al. 2016).

The second task, which also has adequate reliability (Lebowitz and Francois 2018), uses body movements to quantify bias as it manifests in movement relative to threat stimuli. This video-game task dynamically projects the participant's image adjacent to task-irrelevant neutral and threatening images (see Fig. 1B). Prior studies find that, compared to healthy youth, youth with anxiety disorders bias their movements away from threats (Lebowitz and Francois 2018; Lebowitz et al. 2015). Thus, each task uses a distinct behavioral context and outcome measure to index implicit threat-related bias. Correlations between two bias measures could initiate a search for other tasks that correlate with these two, eventually to estimate a latent implicit-bias construct.

Study 1 tests the hypothesis that patients with pediatric anxiety disorders, but not healthy comparisons, show gaze/dwell-time bias to negative-valence faces in face matrices. Study 2 tests the hypothesis that patients, but not comparisons, bias their movement away from task-irrelevant angry faces on a video-game, body-movement task. Finally, the report examines cross-task association, where between-task correlations are expected as a reflection of hypothesized task convergence. With the two tasks, the study aims to lay the groundwork for multi-task research on implicit bias in pediatric anxiety disorders.

General Method

Participants and Procedure

A total of 87 participants were studied, including 51 treatment-seeking youths with anxiety disorders (33 females, *M* age = 12.50 years, *SD* = 2.82, age range = 8.00–18.04) and 36 healthy youths (22 females, *M* age = 13.30 years, *SD* = 2.99, age range = 8.32–17.92). Participants could receive psychotherapy or medication for anxiety. Participants were recruited from the community for research at the National Institute of Mental Health (NIMH), using methods identical to previous research (Cardinale et al. 2019; Linke et al. 2019; Smith et al. 2019). Patients were recruited for a study on the treatment of pediatric anxiety (Linke et al. 2019); healthy youth were recruited to serve as comparisons. Participants completed a diagnostic assessment (see below) and at least one of two studies. Of 87 youths, 53 completed Study 1 (eye-tracking), 74 completed Study 2 (video-game), and 40 completed both studies (see Table 1). Patients completed the tasks prior to treatment. Written informed consent was obtained from parents of participants, and written assent was obtained from youth. Procedures were approved by the NIMH Institutional Review Board. Participants received monetary compensation for participation ($15 for each task).

Diagnosis

All participants were interviewed by trained clinicians using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (KSADS-PL; Kaufman et al. 1997). Clinicians were initially trained to achieve acceptable reliability with expert diagnosticians; diagnoses were confirmed by a senior psychiatrist (see supplementary materials for more details). Patients met criteria for generalized anxiety, social anxiety, and/or separation anxiety disorder as their primary source of distress (see Table 2 for diagnoses of patients). Of note, subjects were recruited specifically to be free of comorbidities for conditions besides anxiety disorders, as in past clinical trials (Walkup et al. 2001), but also exhibited the patterns of highly comorbid anxiety disorders as found in these trials. In the current study, 40 of the 51 patients suffered from more than one anxiety disorder. Healthy participants did not meet criteria for any psychiatric diagnosis. Additional exclusionary criteria for all subjects included IQ < 70 assessed using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler 1999), a diagnosis of autism spectrum disorder, posttraumatic stress disorder (PTSD), schizophrenia, the presence of either attention deficit hyperactivity disorder (ADHD) or irritability in oppositional defiant disorder (ODD) of sufficient severity to require treatment, obsessive compulsive disorder, major depressive disorder, use of any substance with psychoactive effects within three months of

Table 2 Diagnostic Information for Anxiety Patients in Study 1 and Study 2

Diagnosis	Study 1 (*N* = 29)	Study 2 (*N* = 45)
Generalized Anxiety Disorder [*N* (%)]	26 (90)	38 (84)
Social Anxiety Disorder [*N* (%)]	17 (59)	25 (56)
Separation Anxiety Disorder [*N* (%)]	7 (24)	20 (44)
Specific Phobia [*N* (%)]	12 (41)	19 (42)

Table 1 Demographics Information for Anxiety Patients and Healthy Participants in Study 1 and Study 2

	Anxiety Patients	Healthy Participants	Test Statistic	*P-Value*
Study 1 (Eye Tracking Task)				
N	29	24	-	-
Female [*N* (%)]	20 (69.97)	15 (62.50)	$\chi^2(1) = 0.04$	0.84
Age [*M* (*SD*)]	13.19 (2.85)	13.31 (2.99)	$t(51) = 0.14$	0.89
IQ [*M* (*SD*)]	110.86 (11.99)	110.88 (10.86)	$t(51) = 0.004$	> 0.99
SCARED [*M* (*SD*)]	31.77 (9.65)	5.86 (3.63)	$t(51) = 12.43$	< 0.001
Study 2 (Behavioral Avoidance Task)				
N	45	29	-	-
Female [*N* (%)]	28 (62)	17 (59)	$\chi^2(1) = 0.004$	0.95
Age [*M* (*SD*)]	12.37 (2.83)	13.40 (2.97)	$t(72) = 1.48$	0.14
IQ [*M* (*SD*)]	111.14 (11.36)	110.87 (11.98)	$t(70) = 0.10$	0.92
SCARED [*M* (*SD*)]	30.33 (10.52)	6.77 (6.87)	$t(70) = 9.79$	< 0.001
Both Tasks				
N	22	18	-	-
Female [*N* (%)]	14 (64)	11 (61)	$\chi^2 = 0.00$	> 0.99
Age [*M* (*SD*)]	13.06 (3.02)	13.26 (2.75)	$t(38) = 0.22$	0.83
IQ [*M* (*SD*)]	109.09 (12.88)	113.06 (11.04)	$t(37) = 1.01$	0.32
SCARED [*M* (*SD*)]	31.15 (8.56)	6.06 (3.54)	$t(38) = 11.62$	< 0.001

Note: IQ was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI). SCARED = The Screen for Child Anxiety Related Emotional Disorders; scores reflect averaged total scores for child- and parent-reports. Test-statistics and p-values reflect tests for group differences.

participation, neurological disorder, a history of trauma, or significant medical illness (Linke et al. 2019; Walkup et al. 2001).

Anxiety symptoms

In addition to the primary analyses, other analyses examined dimensional associations between anxiety symptom severity and task-related measures. Of note, other symptoms also were assessed, including symptoms of irritability and depression. However, associations were not examined with these other symptoms. This was because patients were excluded if they manifested clinically significant symptoms in these other domains. Examination of associations with these non-anxiety symptoms could generate findings that would fail to generalize to samples including patients seeking treatment for symptoms beyond anxiety disorders.

Anxiety symptom severity was assessed using the child- and parent-report versions of the Screen for Child Anxiety Related Emotional Disorders (SCARED), a frequently-used, standard, and psychometrically-robust instrument for assessing pediatric anxiety symptoms (Birmaher et al. 1999, 1997; Hale et al. 2011). The SCARED includes 41 items pertaining to anxiety-related symptoms or behaviors; each item is rated on a 3-point Likert-type scale (0 = not true, 2 = very true). As in past work (Guyer et al. 2008; Smith et al. 2019), the average of the child- and parent-reported SCARED total scores were used in analyses to reduce reporter discrepancies (Behrens et al. 2018; Abend et al. 2020a); additional analyses using child- and parent-reports separately are reported in supplemental material. Cronbach's alpha values for the child- and parent-reported versions in this sample ranged between 0.95—0.96.

Data Analysis

All statistical tests were 2-sided; effects were detected at a significance level of $\alpha < 0.05$. Effect sizes (ES) are reported as Cohen's *d* (t-tests) or b/SD (standard deviation of *b*; in regression analyses) values; an exception is the output from the *testInteractions* function (see below), which does not allow for generation of ES. Specific analytic plans for each study are described below.

Study 1: Attention Bias to Threat with Eye-tracking

Overview

This study used an established free-viewing eye-tracking task (Lazarov et al. 2016) to compare youth with anxiety disorders and healthy youth. The study tested the hypothesis that youth with anxiety disorders compared to healthy youth show longer dwell time on negative-valence face stimuli, as was previously reported in adults (Lazarov et al. 2016). Secondary analyses examined face-emotion-specific findings.

Method

Participants

A total of 57 youths were included. Data from 4 participants (3 patients, 1 healthy comparison) were excluded because of insufficient data due to aborting the task in the first run, leading to a final sample of 53 youth (29 patients and 24 healthy comparisons; see Table 1). Patients and healthy participants significantly differed in SCARED scores but not in age, sex, or IQ (see Table 1).

Eye-tracking Task

The eye-tracking task is a variant of a task shown to be a reliable measure of attention bias to socially-threatening faces in adults (Lazarov et al. 2016, 2018) and thus may be more advantageous than other tasks that show low reliability (Price et al. 2015). Stimuli were 4 × 4 matrices composed of photographs of 8 male and 8 female actors presenting a disgust, anger, sad, happy, or neutral expression. Facial stimuli were taken from the NimStim face stimulus set (Tottenham et al. 2009). Three sets of matrices, each showing one type of negative-valence expression and one type of non-negative expression, were constructed: 1) Neutral vs. Disgust (ND), 2) Happy vs. Angry (HA), and 3) Sad vs. Happy (SH); Fig. 1A depicts an illustrative example of an ND matrix. These contrasts model specificity in biased attentional deployment for various negative-valence stimuli (Hommer et al. 2014; Lazarov et al. 2016, 2018). Multiple emotions are needed as the current study represents the first use of the current task to compare healthy and patient youth. In such an initial application, firm hypotheses on emotion-specific findings are not possible, given that past work in anxiety disorders finds biases across a range of face emotions, including all the emotions included in the current study (e.g., Armstrong and Olatunji 2012; Brown et al. 2013; Knowles et al. 2019; Lazarov et al. 2016; Mogg and Bradley 1998; Shechner et al. 2013)). Different expressions from the same actors were used across blocks, to avoid potential block-actor confounds.

Each trial of the task began with a fixation cross displayed until a continuous fixation (1000 ms) ensured that participants' gaze was at the center of the subsequent matrix presentation. Then, a matrix was presented for 6000 ms, followed by an inter-trial interval of 2000 ms until the next fixation cross appeared. To maintain consistency with prior research (Lazarov et al. 2016), each of the three emotion contrasts was run as a separate block that included 30 matrices of that contrast type, for a total of 90 matrices. Order of contrast blocks and matrices within blocks was randomized across participants. Each run was preceded by a calibration procedure of the participants' gaze (see supplemental material). Participants were told that they would see a series of matrices of faces. They were also told to look freely at each matrix in any way they chose. Each subject was then shown an example. All participants completed the study in the same experimental room; identical lighting was used. The total task duration was approximately 45 min. Of the 53 participants included in analyses, 30 participants completed all three runs of the task, 11 participants completed two runs, and 12 participants completed one run. Thirty-seven participants completed the HA run, 40 participants completed the ND run, and 46 participants completed the SH run. See supplement for details. Linear mixed-effects models overcome missing data (Chen et al. 2013; Donders et al. 2006; Matta et al. 2017), allowing us to use all available data; see below.

Eye-tracking Measures and Analysis

Eye-tracking data were collected using an EyeLink 1000 Plus eye-tracking apparatus (SR-research, Ottawa, Ontario, Canada) that operated in remote mode using a forehead sticker. Participants were seated approximately 520 mm away from the desktop mounted eye tracking camera. Real-time binocular eye-tracking data were recorded continuously throughout the task using a 25 mm lens at 1000 Hz, with a 1920×1080-pixel display resolution. The dimensions of the screen were consistent for each participant at 475×270 mm.

Data were processed using Eyelink DataViewer software (SR-research, Ottawa, Ontario, Canada). Fixations were defined by at least 100 ms of stable fixation (Lazarov et al. 2016). For each of the matrices, we defined two Areas of Interest (AOIs), one including the eight negative-valence faces (disgust, angry, or sad expression) and one including the eight non-negative faces (neutral or happy expression). Prior work with this task as well as other tasks demonstrates that anxiety effects manifest on sustained attention patterns, as operationalized by total dwell time (sum of fixation durations per AOI, averaged across matrices), but not on more rapid processes relating to initial attention capture or disengagement (Lazarov et al. 2016; Lisk et al. 2019). Moreover, dwell time measures, but not initial attention orientation measures, show reliability (Lazarov et al. 2016). Accordingly, analyses focused on the dwell time index. The square root of the total dwell time was used to normalize the data, though similar results were obtained for total dwell time (see supplemental material).

Linear mixed effects models (*nlme* package in R; (Pinheiro et al. 2019) tested the Group × Contrast × Valence interaction effect on dwell time, with Group (Anxiety vs. Healthy) as a between-subjects factor, and Contrast (HA vs. SH vs. ND) and Valence (Negative vs. Non-negative) as within-subject factors; subject was used as a random effect. Follow-up analyses for significant interactions were tested using the *testInteractions* function (*phia* package; (De Rosario-Martinez 2015)). Outliers were excluded if they had a Cook's Distance above a threshold of (4/N–k–1), where N is the number of participants and k is the number of terms in the model (Cook 1977). Three outliers (2 healthy, 1 patient) were identified and removed from subsequent dwell-time analyses using this method, though results were similar with outliers included (see supplemental material). Correlational analyses complemented these analyses and examined dimensional associations between anxiety symptom severity (using SCARED scores) and dwell-time bias scores (average dwell time on negative faces minus average dwell time on non-negative faces; a larger score indicates more time spent looking at negative relative to non-negative faces). Secondary analyses tested links between anxiety symptoms and specific emotion contrasts.

Results

A significant Group × Valence interaction effect on dwell time emerged, F (1, 172) = 8.27, $b = 0.50$, $p = 0.005$, ES = 0.41. However, the three-way Group × Contrast × Valence interaction was non-significant. Thus, the association between diagnosis and valence manifested similarly across the three matrix types. Follow-up tests indicated that patients demonstrated greater dwell time on negative-valence faces relative to non-negative faces (across emotion contrasts; $b = 1.35$, $p = 0.004$), while healthy participants showed comparable dwell time across valence ($b = 0.65$, $p = 0.21$); see Table 3. Quantified in terms of bias (dwell time on negative faces minus non-negative faces), youth with anxiety demonstrated significantly greater bias relative to their healthy peers, t (31.25) = 2.14, $p = 0.041$, $d = 0.65$; see Fig. 2A. In addition, the dwell-time bias was significantly greater than 0 in the patient group (t-test vs.

Table 3 Mean Task Metrics for Study 1 and Study 2 by Group (Anxiety, Healthy)

	Anxiety Patients	Healthy Participants
Study 1 (Eye-Tracking Task)		
Dwell Time on Negative Stimuli (ms) [*M* (*SE*)]	47.13 (0.45)	46.94 (0.49)
Dwell Time on Non-Negative Stimuli (ms) [*M* (*SE*)]	45.77 (0.44)	47.58 (0.49)
Study 2 (Behavioral Avoidance Task)		
Turning Point from Negative Stimuli (Study 2) [*M* (*SE*)]	0.32 (0.005)	0.33 (0.005)
Turning Point from Non-Negative Stimuli (Study 2) [*M* (*SE*)]	0.69 (0.007)	0.67 (0.007)

Note: Dwell time is square-root-transformed.

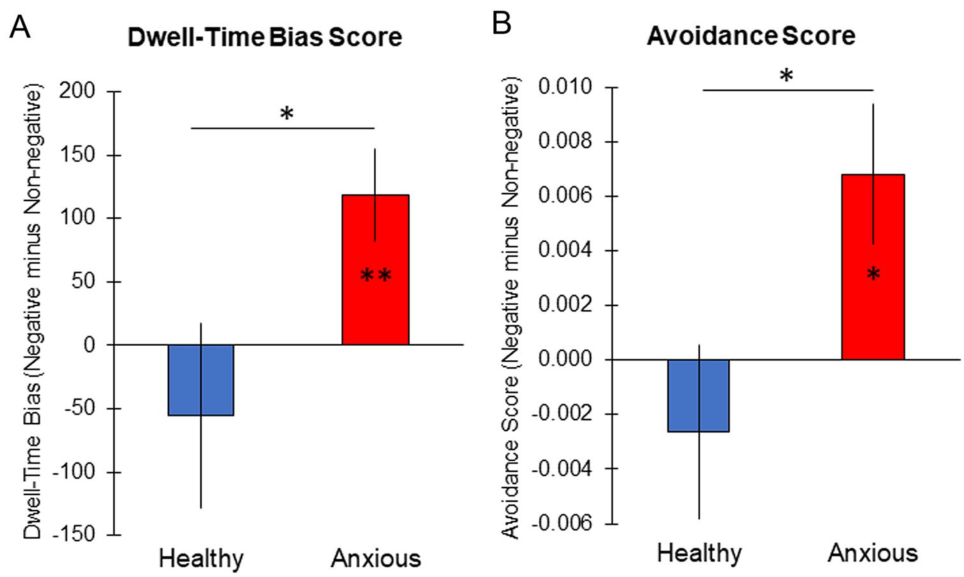

Fig. 2 (A) Study 1: Dwell-time bias scores (dwell time on negative-valence faces minus non-negative faces) by Group (healthy, patients). (B) Study 2: Behavioral avoidance scores (turning point from negative-valence faces relative to non-negative faces) by Group (healthy, patients). *Note*: Error bars denote one standard error of the mean. *, $p<0.05$; **, $p<0.01$

0: t (27) = 3.24, $p=0.003$, $d=0.61$); healthy youth did not show this bias (t (21) = 0.76, $p=0.45$, $d=0.16$). Dimensionally, a similar pattern was noted, with a positive correlation between dwell time bias score and overall anxiety symptom severity, r (48) = 0.29, $p=0.043$ (see Fig. S1A).

Conclusion

Eye-tracking indicates that pediatric anxiety patients show an attention bias toward negative-valence faces whereas healthy comparisons do not; further, the groups significantly differ in this bias. A dimensional analysis further demonstrated a correlation between bias and overall anxiety symptom severity.

Study 2: Behavioral Avoidance

Overview

This study used motion-tracking technology to compare youth with anxiety disorders and healthy youth in terms of behavioral avoidance of body movements away from task-irrelevant negative-valence faces. The study tested the hypothesis that patients relative to healthy youth show greater avoidance. Data from Study 2 also were combined with data from Study 1 to examine the correlation between the measures of negative-faces bias from the two studies.

Methods

Participants

A total of 74 youth (45 patients and 29 healthy controls; see Table 1) completed the behavioral avoidance task. Patients and healthy participants differed in SCARED scores but not in age, sex, or IQ (see Table 1).

Forty participants completed both attention and avoidance tasks, including 22 patients and 18 healthy controls (see Table 1). Of those, 28 completed the attention task first. Results remained the same for both tasks in Study 1 and Study 2 when controlling for task order (see supplemental material). The two tasks were completed between 0 and 458 days apart ($M=7.95$ days, $SD=94.66$); of the 40 participants, 37 completed both tasks within a six-month window. The wide variation in inter-task duration reflected the fact that participants completed multiple tasks while participating in multiple NIMH studies. Variability in task timing arose from limited availability for some families while completing these multiple tasks. For patients with delays of more than a month, diagnostic status was reconfirmed prior to testing. Analyses were repeated controlling for the number of days between tasks, yielding similar results (see supplemental material).

Behavioral Avoidance Task

Behavioral avoidance of aversive stimuli was measured using the YIKES (Yale Interactive Kinetic Environment Software) task. Previous work demonstrates the task is reliable over time and represents a valid measure of avoidance behavior in youth (Lebowitz and Francois 2018). In the task (see Fig. 1B), the participant's image was dynamically captured using a Kinect motion-tracking camera and continuously projected into the game environment on a large TV screen (76 cm x 137 cm). The game featured balls with set point value falling from the top of the screen (uniformly distributed horizontally across the screen). Participants were instructed to move sideways (left and right) to catch as many balls as possible. Following a brief practice run of the task, participants completed two 6-min runs of the game. One run was designed to examine avoidance of negative-valence social stimuli; a pair of face stimuli, one negative-valence (showing an angry expression) and one showing a non-negative (neutral) expression, were projected on opposing sides of the screen. Six pairs of negative and non-negative stimuli were presented in the game, for one minute each. As in Study 1, facial stimuli were taken from the NimStim face stimulus set (Tottenham et al. 2009). The side of the screen displaying the negative stimulus alternated for each pair. Another run involved an identical set-up with a pair of spider-related stimuli (a spider and a spider-like neutral object). This run was part of a different study testing cross-site reliability; these data are not analyzed here and will be reported elsewhere. Here, we focus on data from the faces game run to match the type of social stimuli used in Study 1. Order of game runs was randomized for each participant.

Avoidance Measures and Analysis

As in prior reports (Lebowitz and Francois 2018), analyses considered the average turning point away from the non-negative-valence faces and the negative-valence faces; i.e., the average location where participants turn away when pursuing balls appearing near non-negative vs. negative stimuli. Linear mixed effects models tested the Group × Valence interaction effect on turning point, with Group (Anxiety vs. Healthy) as a between-subjects factor, and Valence (Negative vs. Non-Negative) as within-subject factors; subject was used as a random effect. Follow-up analyses were conducted on a behavioral bias score indexing avoidance (average turning point away from the non-negative stimuli minus the additive inverse of the average turning point away from the negative stimuli; (Lebowitz and Francois 2018). These included comparing groups in terms of bias, and correlations to determine dimensional associations between avoidance scores and anxiety symptoms. No outliers were observed.

To examine associations between attentional bias and behavioral avoidance of negative-valence stimuli, we tested the correlation between dwell-time bias score (Study 1) and the behavioral avoidance scores (Study 2) across the sample.

Results

A significant Group × Valence interaction effect on turning point emerged, F (1, 72) = 4.68, $b = 0.01$, $p = 0.034$, ES = 0.25; mean turning-point measures are reported in Table 3. Follow-up tests using the behavioral avoidance index (average turning point away from the non-negative stimuli minus the additive inverse of the average turning point away from the negative stimuli) indicated that patients demonstrated significantly greater avoidance of negative-valence faces relative to their healthy peers, $t(72) = 2.32$, $p = 0.023$, $d = 0.55$. In addition, patients showed significant avoidance of the negative-valence faces (t-test vs. 0: t $(44) = 2.67$, $p = 0.010$, $d = 0.40$); healthy youth did not show avoidance (t $(28) = 0.82$, $p = 0.42$, $d = 0.15$); see Fig. 2B. Dimensionally, behavioral avoidance positively correlated with anxiety symptom severity across the sample, r $(70) = 0.34$, $p = 0.003$ (see Fig. S1B).

Finally, associations were examined between performance measures among subjects completing both the eye-tracking and avoidance tasks. A significant correlation emerged between attentional bias towards negative stimuli and behavioral avoidance of negative stimuli, r $(38) = 0.31$, $p = 0.049$. A similar magnitude of correlation was observed when controlling for the number of days in between tasks (see supplement).

Conclusion

The body-movement task indicates that pediatric anxiety patients show behavioral avoidance of negative-valence faces, whereas healthy comparisons do not. Dimensional analysis further show that avoidance correlates with anxiety symptom severity. Finally, across the sample, attention bias and behavioral avoidance scores correlated positively.

Discussion

This study tests the hypothesis that youth with pediatric anxiety disorders, but not healthy comparisons, show two forms of implicit bias: gaze/dwell-time bias to negative-valence faces in face matrices and biased movement away from task-irrelevant angry faces on a video game. The report also examines cross-task association, reflecting hypothesized task convergence. Three main findings emerge. First, patients, as compared to healthy youth, manifest longer gaze durations on negative- vs. non-negative-valence faces in the eye-tracking task. Second, patients, as compared to healthy youth, manifest greater behavioral avoidance of negative- vs. non-negative-valence faces on the body-movement task. Third, among 40 participants completing both tasks, bias in gaze time on negative-valence faces correlates with avoidance of such faces on the body-movement task, suggesting convergence as indicators of implicit threat bias.

Findings for the face-viewing task are relevant to past research. Considerable research uses eye-tracking to study attention bias in pediatric anxiety (Lisk et al. 2019). Nevertheless, no prior study utilizes the specific face-viewing task employed in the current study to compare healthy youth to children with anxiety disorders. Similar findings with this specific task arise in research on adult anxiety (Lazarov et al. 2016), where patients exhibit increased sustained attention towards threats than healthy peers. Of note, the current task utilizes three sets of matrices with different varieties of face emotions, including both disgust-neutral and sad-happy matrices, where findings in adults exist, as well as angry-happy sets, where no prior research exists. The choice to utilize angry faces reflects findings on other attention-bias tasks in pediatric anxiety disorders. Considerable prior research links anxiety disorders in children to excessive attention allocation to angry versus neutral faces (Roy et al. 2008; Abend et al. 2018).

In the current study, no interactions arise between anxiety measures and dwell patterns across the three face-emotion matrix types. Hence, statistical evidence suggests a generalized form of vigilance in anxiety for the more negative-valence face in patient-comparison differences across matrix types. Prior studies with the face-viewing task use two of the three matrices from the current study. In adults, one study utilizes disgust-neutral face matrices in social anxiety disorder (Lazarov et al. 2016), and another utilizes sad-happy matrices in major depressive disorder (MDD) (Lazarov et al. 2018). Thus, vigilance towards negative valence face-emotions occurs in both patient groups. However, research has not used sad-happy faces in adult anxiety or disgust-neutral faces in adult MDD. Moreover, no prior study has used the angry-happy matrix set, a critical limitation when comparing results in the current and prior studies.

Of note, the current face-viewing task differs from other face-viewing attention tasks. Across the three matrix sets, greater variety of valence combinations was used than in other attention-bias tasks (e.g., Abend et al. 2018; Harrewijn et al. 2020; Kujawa et al. 2011; Naim et al. 2015). Moreover, test–retest reliability is stronger for the current than other face-viewing, attention-bas tasks (Lazarov et al. 2016; Price et al. 2015; Schmukle 2005). Given these differences and the generalized negative-valence bias among patients in the current study, more research is needed across age groups and populations to evaluate valence specificity of attention bias. This includes studies using multiple matrix types in patients with MDD, anxiety, or no disorder. Longitudinal data suggest that anxiety disorders and MDD exhibit shared correlates (Beesdo et al. 2009; Pine et al. 1998). Overlapping patterns of generalized, negative-valence bias on face-viewing paradigms could reflect such shared correlates. Our use of multiple face-emotion matrices in one paradigm sets the stage for work in both children and adults on this issue.

Much like for the face-viewing task, findings for the body-movement task extend past work. More extensive data exist for a version of the task using spider images stimuli as opposed to faces. For spiders, prior research finds associations between participants' reported levels of specific spider fear and participants' levels of spider avoidance on the task (Lebowitz et al. 2015). For faces, only one prior study utilizes the version of the task employed in the current study (Lebowitz and Francois 2018); results in the current study are consistent with this prior study, such that avoidance of threatening faces correlates with anxiety symptoms. Of note, while treatment-oriented research previously adapted the vigilance task, this has not occurred for the body-movement tasks. Replication of face-avoidance across the current and prior body-movement studies might encourage attempts to adapt this task for treatment purposes (Loijen et al. 2020). Indeed, future treatments might utilize multiple cognitive tasks, adapted from both the eye-tracking and body-movement tasks. Such an approach might deploy suites of task-based interventions that work in a complementary fashion to influence an underlying latent construct and maximize symptom reductions.

Our observations in patients with anxiety disorders of threat-related attentional vigilance, coupled with behavioral avoidance, are predicted by existing theories. Hypervigilance-avoidance models suggest that hypervigilance towards threat precedes avoidance (Mogg et al. 1997, 2004). Thus, early attention bias to potential threat may facilitate later, strategic avoidance as manifested in behavior. While possibly acutely adaptive, such avoidance might ultimately reinforce anxiety symptoms (Arnaudova et al. 2017; Grupe and Nitschke 2013; Salters-Pedneault et al. 2004; Treanor and Barry 2017). Of note, previous work, focused narrowly on biases in attention, provides inconsistent support for the hypervigilance-avoidance model (Rosen et al. 2019). Other research suggests that attention bias to threat on a cognitive task predicts avoidance in the real world (Price et al. 2016). Extending this research, our findings may represent another such instance that links attention vigilance in one lab setting to whole-body avoidance in another. In the current study, this occurs in the same subjects across two tasks, one used to assess attention and another assess whole-body avoidance.

Beyond hypervigilance-avoidance models, findings in prior research might further explain co-occurring hypervigilance and avoidance in anxiety patients on two implicit bias tasks. Such research shows how unique task features can heighten tendencies for anxiety patients to show either avoidance or vigilance. Biased attention away from threat in anxiety patients arises in studies using tasks with clearly discernable threats, such as single faces presented on a blank screen (Heuer et al. 2007; Lisk et al. 2019; Michalska et al. 2017). In other tasks, avoidance in patients with anxiety is attributed to the use of extreme threats or aversive task settings (Bar-Haim et al. 2010; Mataix-Cols et al. 2017; Michalska et al. 2017; Mogg and Bradley 1998; Wald et al. 2013). Hence, tasks that evoke avoidance utilize more discernable or highly salient threats, as compared to tasks that evoke hypervigilance. In the current study, such factors could explain avoidance on the body-movement task, which presents threats in the form of isolated faces, as opposed to vigilance on the eye-movement task, which simultaneously presents multiple threat-faces embedded within a matrix also containing non-threat faces. Finally, attentional vigilance and behavioral avoidance could be viewed as defensive responses along a threat imminence continuum (Craske 1999; Fanselow et al. 1988). In this framework, identifying the presence of potential threat within an array of passive faces calls for vigilance, whereas watching one's image dynamically projected in close proximity to threat could elicit behavioral avoidance of the threat. Our findings indicate that both responses are enhanced in anxiety patients relative to healthy comparisons, consistent with prior research (Abend et al. 2020b).

Use of multiple implicit-bias tasks informs attempts to estimate latent constructs. Of note, the current report identifies only two behavioral outcomes that differentiate youth with anxiety from healthy youth; moreover, the cross-task association was modest. Thus, additional, robust indicators of implicit bias are needed to complement the ones identified here and to estimate a latent factor. Such additional indicators probably must come from tasks other than the two used in the current study. This is because prior research with the face-viewing and body-movement tasks used here previously examined various possible variables that could serve as indicators. Only two bias indicators, the two that are highlighted in the current report, exhibit strong reliability and consistent associations with anxiety (Lazarov et al. 2016, 2018; Lebowitz and Francois 2018; Lebowitz et al. 2015). This leads the current study to focus narrowly on these two indicators. In fact, across many other implicit-bias tasks, these two potential indicator variables remain among the few replicable task-based behavioral correlates of anxiety with acceptable psychometrics.

Given this dearth of behavioral indicators, research might consider physiological variables as indicators of a latent implicit-bias factor. Promising candidates exist, though selecting physiological measures departs from previous latent-variable approaches using only behavioral indicators (Cardinale et al. 2019). For example, change in skin-conductance indexing physiological response to implicit threats exhibits acceptable reliability and manifests consistent relationships with anxiety (Abend et al. 2020b; Shechner et al. 2015).

Arguments exist for treating physiology and behavior variables as indicators of one latent implicit-bias factor; these arguments also support combining eye-movement and whole-body movements. In these arguments, variables could be considered indicators of the same latent construct when they reflect the influences of shared circuitry, as demonstrated by imaging studies. For example, physiology and behavior responses to a threat might be considered indicators of one construct when imaging studies with implicit-bias tasks find threats to evoke correlated responses in physiology and behavior (Abend et al. 2020b; Harrewijn et al. 2020).

In the current study, other factors justify a view of eye-tracking and body-movement measures as indicators of one implicit threat-bias factor. On theoretical grounds, both measures index effects on dependent measures from the same class of threat stimulus, evocative faces that are presented in ways unrelated to task instructions or goals. On empirical grounds, correlations between measures further support the view of shared influences. As noted above, however, cross-measure correlation in the current study is marginally significant and somewhat low from an effect-size standpoint for two indicator variables of one latent factor.

The current study findings should be considered against its limitations. One major limitation affects the analysis of cross-task correlations, which provides only tentative support for combining behaviors across tasks. The relatively small sample size for this analysis and the large variation in the time between data collection should be addressed in future work. With delays between tasks, low cross-task correlation could reflect attenuation of inherently stronger task convergence from time-related instability. Future studies might include larger samples studied using the two tasks on the same day in an attempt to support statistical methods, such as structural equation modeling, which model relations among task measures. Moreover, as noted above, additional work is needed with other indicator variables before research can model an implicit bias latent factor. Along these lines, the reliability of the eye-tracking task in youth needs to be established as it has previously been established in adults.

Another important limitation concerns heterogeneity in research participants, both related to the broad age range and psychiatric symptoms. In general, inclusion criteria conform to those used in major treatment studies (Walkup et al. 2001). As such, the current findings do lay the groundwork for extensions in therapeutic research. However, increased relevance for anxiety disorder treatment comes at a cost: exclusion criteria limit extensions to other symptom domains, particularly irritability and MDD. Future studies might examine associations across these and other domains in samples that include patients seeking treatment for heterogeneous collections of diagnoses. Finally, the study design had limitations. The matrices contrasted specific emotion pairs, which are not commonly used in other studies of attention bias in pediatric anxiety disorders; considerable research utilizes angry-neutral face pairs as opposed to the angry-happy faces used in the current study (Abend et al. 2018; Roy et al. 2008). Moreover, disgust is a novel affect for research on attention in pediatric anxiety disorders. One also could argue that anxiety related to peer evaluation creates a need for studies using faces of children as opposed to adults, as used in the current study. Future research may wish to address these important limitations.

In conclusion, implicit threat bias represents one of the more commonly found correlates of pediatric anxiety disorders, findings that extend major theories on anxiety disorders (Beck 1976; Beck and Clark 1997). While prior research suggests that this bias informs studies of treatment and prevention, attention-bias tasks utilized in much of this prior research possess poor test–retest reliability. The current study generates data on pediatric anxiety disorders for implicit threat bias using two new tasks with adequate test–retest reliability. Data reveal stronger biases to threat-related stimuli in youth with anxiety disorders than in healthy youth, as well as a link between these two biases. These findings inform our understanding of the construct of implicit bias and its role in pediatric anxiety.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the NIMH institutional review board.

Informed Consent Written informed consent was obtained from parents of participants, and written assent was obtained from youth.

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