Brief Empirical Report Word Count: 5,419
Tables/Figures: 1 Table/1 Figure
Abstract Word Count: 150
Supplementary Online Material (SOM-R): Methods; 3 Tables

Threat Appraisal and Pediatric Anxiety: Proof of Concept of a Latent Variable Approach

Rachel A. Bernstein,^{1*} Ashley R. Smith,² Elizabeth Kitt,³ Elise M. Cardinale,¹
Anita Harrewijn,⁴ Rany Abend,⁵ Kalina J. Michalska,⁶ Daniel S. Pine,¹ & Katharina Kircanski¹

- ¹ Emotion and Development Branch, National Institute of Mental Health
- ² Division of Translational Research, National Institute of Mental Health
 - ³ Department of Psychology, Yale University
- ⁴ School of Social and Behavioural Sciences, Erasmus University Rotterdam
 - ⁵ School of Psychology, Reichman University
 - ⁶ Department of Psychology, University of California-Riverside

*Corresponding author: Rachel A. Bernstein, B.A., Emotion and Development Branch, National Institute of Mental Health, 9000 Rockville Pike, Building 15K, Bethesda, MD 20892-2670, USA. E-mail: rachelbernstein97@gmail.com; Phone: 1 (614) 623-7159

Abstract

Elevated threat appraisal is a postulated neurodevelopmental mechanism of anxiety disorders. However, laboratory-assessed threat appraisals are task-specific and subject to measurement error. We utilized latent variable analysis to integrate youth's self-reported threat appraisals across different experimental tasks; we next examined associations with pediatric anxiety as well as behavioral and psychophysiological task indices. Ninety-two youth ages 8-17 years (M age=13.07, 65% female), including 51 with a primary anxiety disorder and 41 with no Axis I diagnosis, completed up to eight threat-exposure tasks. Anxiety symptoms were assessed using questionnaires and ecological momentary assessment. Appraisals both prior to and following threat exposures evidenced shared variance across tasks. Derived factor scores for threat appraisal were associated significantly with anxiety symptoms and variably with task indices; findings were comparable to task-specific measures and had several advantages. Results support an overarching construct of threat appraisal linked with pediatric anxiety, providing groundwork for more robust laboratory-based measurement.

Keywords: threat appraisal, anxiety disorders, children and adolescents, latent variable analysis, fear conditioning, ecological momentary assessment

Threat Appraisal and Pediatric Anxiety:

Proof of Concept of a Latent Variable Approach

Poorly replicated findings in psychological science are increasingly recognized (e.g., Open Science Collaboration, 2015; Tackett et al., 2019). Some have attributed such results to measurement error arising from laboratory paradigms with task-specific "noise" or poor reliability (e.g., Chapman et al., 2017; Lilienfeld & Strother, 2020). Illustrating one potential path forward, the current paper integrates multiple measures of self-reported threat appraisal collected across different laboratory tasks. This approach might estimate an overarching latent variable and diminish task-specific impurities. We further investigate how this latent variable compares to single-task variables, in capturing associations with anxiety symptoms as well as psychophysiological and behavioral task indices.

Robust, reliable assessment of threat appraisal supports research on anxiety-related mechanisms. Hallmarks of anxiety disorders involve threat responding disproportionate to the likelihood or intensity of possible harm (Barlow, 2004). Ample work has shown that individuals with higher, relative to lower, levels of anxiety exhibit heightened subjective, physiological, and neural responses to threat stimuli (reviewed in Chavanne & Robinson, 2021; LeDoux, 2015). Threat appraisal is a broad construct referring to stimulus classification in terms of potential for harm, and can be measured in multiple ways (Pine, 2007). This study focuses on the subjective or self-reported component of threat appraisal. Subjective threat appraisal reflects cognitive and affective processes, and is typically operationalized as verbal reports of one's internally-experienced fear and anxiety in response to threat stimuli (Britton et al., 2011). We focus on subjective report based on its clinical relevance (LeDoux & Pine, 2016) and because self-report measures tend to intercorrelate across tasks in pediatric anxiety research (e.g., Shechner et al., 2015), particularly ripe for a latent variable approach. Additionally, subjective threat appraisal can be measured both in anticipation of threat and when recovering from the experience

(reviewed in Kalisch & Gerlicher, 2014; Narvaez Linares et al., 2020). Heightened threat appraisals and responses are already evident in youth with clinical anxiety (reviewed in Strawn et al., 2020), possibly contributing to the etiology and maintenance of anxiety disorders into adulthood (reviewed in Pittig et al., 2018).

Over the past four years, our research group has used eight laboratory tasks to evoke threat responding in youth with and without clinically-significant anxiety (see task descriptions below). Each task uses unique techniques to do so. For example, the "Screaming Lady" task (Lau et al., 2008) involves viewing various facial stimuli, with the pairing of an aversive noise (scream) to one stimulus as an unconditioned threat. In contrast, the "Virtual Public Speaking" task (Westernberg et al., 2009) involves a speech performance while ostensibly being evaluated by peers. To date, we have examined these tasks largely in isolation. However, collectively they may capture common features of subjective threat appraisal in a way that robustly quantifies a construct related to anxiety. Thus, each task included one of two measures assessing subjective threat appraisal: the State Anxiety Subscale of the State-Trait Anxiety Inventory for Children (STAI-CH; Spielberger et al., 1970) or a Visual Analogue Scale (VAS; Abend et al., 2014). Importantly, the STAI-CH and VAS are two of the most commonly-administered measures before and after experimental threat (reviewed in Narvaez Linares et al., 2020).

Here, we first examine the coherence of youth's self-reported threat appraisals across tasks using confirmatory factor analysis. We hypothesized that threat appraisal ratings for all eight tasks would load significantly on a common latent variable. We next test relations of participants' factor scores for threat appraisal with (a) pediatric anxiety symptoms and (b) psychophysiological and behavioral response indices on four tasks. We expected factor scores to positively correlate with anxiety symptoms and task indices, more strongly and consistently than would single-task measures of threat appraisal. We report how we determined our sample size, all data exclusions, all manipulations, and all measures in the study.

Method

Participants

Demographic and clinical characteristics of the sample are presented in Table 1. Ninetytwo youth ages 8-17 years (M age=13.07, SD=2.71; 65.22% female) participated in the current study. Participants were recruited from the greater Washington, DC metropolitan area. Recruitment sources included fliers distributed in pediatrician offices, meetings and discussions with local schools and parent groups, and word of mouth in the greater community. Participants were recruited based on the presence or absence of a primary anxiety disorder (generalized, social, and/or separation anxiety disorder). Psychiatric diagnoses were assessed by trained, licensed clinicians using a semi-structured diagnostic interview (Kiddie Schedule for Affective Disorders and Schizophrenia- Present and Lifetime (KSADS-PL); Kaufman et al. 1997). Exclusion criteria for the current study included: meeting criteria for any DSM-5 diagnosis other than an anxiety disorder; magnetic resonance imagining (MRI) contraindications (e.g., braces, claustrophobia); IQ<70; or completing <2 (25%) of the 8 laboratory tasks described below. To maximize the number of participants in the analyses, all particiants who completed at least two tasks were included. All procedures were approved by the National Institute of Mental Health Institutional Review Board. Parents and pediatric participants provided written consent and assent, respectively, and participants received monetary compensation. Participants who met criteria for an anxiety disorder also received treatment following participation.

Of the 92 total participants meeting the above criteria, 51 (M age=13.24, SD=2.67; 70.59% female) met DSM-5 criteria for at least one current anxiety disorder. The remaining 41 (M age=12.86, SD=2.79; 58.54% female) did not have any Axis I diagnosis (healthy volunteers). The two groups (participants with an anxiety disorder and healthy volunteers) did not differ in age (t(90)=-0.67, p=0.508), IQ (t(90)=-.363, p=0.717), or distribution by gender (χ ²(1)=1.455, p=.228), race (χ ²(5)=6.05, p=.301), or ethnicity (χ ²(2)=3.99, p=.136).

Self-Reported Threat Appraisal Measures

Based on the reviewed literature (e.g., Britton et al., 2011; Narvaez Linares et al., 2020; Strawn et al., 2020) subjective threat appraisal was operationalized as self-reported ratings of anxiety during each task. Participants made threat appraisals before each task (acute threat appraisal) and after each task (post-threat appraisal). Three tasks employed the STAI-CH (Spielberger et al., 1970). The STAI-CH is a 20-item questionnaire that queries current behaviors and feelings of anxiety ("at this very moment") on 3-point Likert scales (e.g., 1=not upset, 3=very upset), and is considered a "gold standard" measure (Kain et al., 1997). Items were summed for a total score, ranging from 20-60. Across tasks, average internal consistency of the State Anxiety Subscale was strong (acute threat appraisal α=.92; post-threat appraisal α=.91). The other five tasks employed computerized versions of a Visual Analogue Scale (VAS; Abend et al., 2014). Specifically, participants answered, "How anxious do you feel right now?" on a sliding scale (left flank=I feel calm, right flank=I feel anxious). The VAS has high convergent validity and good discriminant validity (Abend et al., 2014). Generally, the VAS was used for certain tasks due to it being less time-consuming to complete than the STAI-CH. Our decision to utilize both the STAI-CH State Anxiety Subscale and VAS in the factor analyses was motivated by the fact that doing so would provide threat appraisal data for all eight tasks.

Supplementary Table 1 presents descriptive statistics for threat appraisals for each task. For the purposes of factor analysis, ratings were standardized using z-scores within task, within time point (e.g., acute-versus post-threat).

Laboratory Tasks

The eight laboratory tasks used in the current analyses are described briefly below (see referenced publications for full task details). Over the course of several months (M days=96.14, SD=71.74), participants completed as many tasks as were able to be scheduled, up to all eight tasks (number of tasks completed per participant: acute threat appraisal M=3.10, SD=1.25; post-threat appraisal M=3.10, SD=1.20). This provided a wide range of methodology (behavioral, psychophysiological, neuroimaging), task demands, and stimuli used.

Peer-Observed Flanker (Smith et al., 2020). This modified version of a classic Eriksen Flanker task (Eriksen & Eriksen, 1974) has participants complete half of the task alone, and half of the task while they believe they are being observed by a peer. This task was completed in the functional magnetic resonance imaging (fMRI) environment to examine neural correlates of making an error in the presence of a peer (i.e., social threat). Before and after the task, participants completed the STAI-CH.

Reversal Learning (Abend et al., 2021; Michalska et al., 2018). In this behavioral paradigm, participants learn associations between cues (shapes) and noxious thermal stimulation applied to the arm. This task is used to examine responses to cue-threat associations. Psychophysiological measures including skin conductance responses (SCRs) were collected throughout the task (see Supplementary Methods). Before and after the task, participants completed the VAS.

Safety Learning (Harrewijn et al., 2021). In this fMRI task, participants learn associations between different cues (shapes) and an aversive loud noise delivered through headphones. This task interrogates neural mechanisms of threat and safety learning. Participants completed the STAI-CH before and after the task.

Scary Movie. In this version of a naturalistic movie-watching fMRI methodology (Vanderwal et al., 2018), participants watch a six-minute animated movie clip intended to elicit threat anticipation. This task was designed to quantify dynamic neural responses to potential threat. Participants completed the VAS before and after watching the move clip.

Screaming Lady (Abend et al., 2020; Britton et al., 2013). In this threat learning paradigm, participants learn conditioned threat associations between a neutral facial stimulus and a fearful face coupled with an aversive loud scream heard through headphones.

Psychophysiological measures including SCRs were collected throughout the task (see Supplementary Methods). Participants completed the VAS before and after the task.

Trier Social Stress Test. In this adapted version of the Trier Social Stress Test (Kirschbaum et al., 1993), participants are asked to complete a five-minute speech in front of live confederates. Specifically, participants are asked to come up with an "exciting ending" to a story that was just shared with them. Following the speech, participants complete an unexpected five-minute oral arithmetic task. This paradigm investigates behavioral and physiological responses to social threat. Participants completed the VAS before and after the task.

Virtual Public Speaking. This task uses methods from Westenberg and colleagues (2009), and has participants introduce themselves for one minute in front of a virtual classroom of peers. Participants are then asked to look at the virtual audience members without speaking for one minute. This task is completed while wearing eye-tracking glasses to continuously monitor gaze fixation and potential avoidance of eye contact. A behavioral measure of avoidance was collected during the task (see Supplementary Methods). Participants completed the VAS before and after the task.

Yale Interactive Kinect Environment Software Behavioral Avoidance Task (YIKES; Lebowitz et al., 2015). Participants stand in front of an LCD screen and move side-to-side in order to catch different objects per task instructions. While participants are catching the falling objects, one threatening (angry face or spider, depending on task block) and one neutral image are presented on respective sides of the screen to assess physical avoidance of threat stimuli. A behavioral measure of avoidance was collected during the task (see Supplementary Methods). Participants completed the STAI-CH before and after the task.

Pediatric Anxiety Symptoms

Screen for Child Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997). Throughout participation in the study, participants and parents independently completed the SCARED questionnaire to assess severity of anxiety symptoms across the last 3 months. Items are endorsed on 3-point Likert scales (0=not true, 2=very true or often true) and summed

upon completion, with higher scores indicating greater anxiety. The SCARED has demonstrated strong test-retest reliability and discriminant validity (Birmaher et al., 1997), and showed strong internal consistency reliability in our sample (α =0.88).

Ecological Momentary Assessment (EMA; Smith et al., 2019). Additionally, naturalistically-occurring anxiety was measured via EMA methodology (Myin-Germeys et al., 2009; Russell & Gajos, 2020). We used a smartphone application in which youth were prompted three times per day (morning, afternoon, evening) over the course of one week (for details, see Smith et al., 2019). For the current analyses, we utilized responses to the following item rated on a 5-point Likert scale: "Since the last beep, I felt worried or scared" (1=None of the time; 5=The whole time; rated at afternoon and evening prompts only). This item was selected as best reflecting anxiety over the course of the day. Ratings were extracted and averaged for each participant across the one-week response period.

Data Analysis

Threat Appraisal Latent Variables. We ran confirmatory factor analyses (CFAs) to test whether threat appraisals across the tasks loaded on a common latent variable. Each factor loading indexed how strongly the observed variable for that task loaded on the latent variable. Separate CFAs were conducted for acute threat appraisal and post-threat appraisal. Each CFA included participant age, time in days between the first and last task completed, and total number of tasks completed as predictors of the factor of non-interest. All analyses were conducted in Mplus (Version 8.4). As the covariance coverage (proportion of participants in common) was <10% between some pairs of tasks, fit indices for the CFAs were not available.

Associations with Pediatric Anxiety. We extracted participants' factor scores from the CFAs and tested whether individual differences in threat appraisal were associated with pediatric anxiety. We used independent samples *t*-tests to examine group differences (anxiety disorder, healthy volunteer) in factor scores, and Pearson's correlations to test associations between factor scores and anxiety symptoms (SCARED, EMA).

Associations with Behavioral and Physiological Task Indices. We also tested whether individual differences in self-reported threat appraisal were associated with psychophysiological (SCR) and behavioral (avoidance) indices from the four tasks with available data. To further assess the utility of the latent variables, we compared associations of factor scores with anxiety symptoms and task indices to the associations of single-task measures of threat appraisal with anxiety symptoms and task indices. Fisher's *r*-to-*z* transformations were used for statistical comparisons of correlation strength. All tests were two-sided and used a significance threshold of 5%.

Results

Threat Appraisal Latent Variables. *Acute Threat Appraisal*. The CFA for acute threat appraisal indicated that ratings for six of the eight tasks loaded significantly on the common latent variable (all ps<.001) (**Figure 1A**). Threat appraisal ratings prior to the Scary Movie task (p=.199) and Safety Learning task (p=.432) did not significantly load on the latent variable. *Post-Threat Appraisal*. The CFA for post-threat appraisal indicated that ratings for seven of the eight tasks loaded significantly on the common latent variable (all ps<.001) (**Figure 1B**). Again, the Safety Learning task did not significantly load on the latent variable (p=.584).

Associations with Pediatric Anxiety. *Acute Threat Appraisal*. As expected, the anxiety disorder group had significantly higher acute threat appraisal factor scores than the healthy volunteer group (*t*(90)=5.63, *p*<.001). Similarly, there were significant positive associations between acute threat appraisal factor scores and anxiety severity (SCARED self-report: *r*=.54; SCARED parent-report: *r*=.42; EMA: *r*=.48; all *p*s<.001). When examining specific task subsamples, factor scores were comparable in their associations with symptoms of anxiety relative to the single-task threat appraisal measures (**Supplementary Table 2**). There were no significant differences in correlation strength when using factor scores vs. single-task measures. *Post Threat Appraisal*. Again, the anxiety disorder group had significantly higher post-threat appraisal factor scores than the healthy volunteer group (*t*(90)=6.14, *p*<.001). Similarly, there

were significant positive associations between post-threat appraisal factor scores and anxiety severity (SCARED self-report: *r*=.60; SCARED parent-report: *r*=.50; EMA: *r*=.46; all *p*s<.001). When examining specific task subsamples, factor scores were comparable in their associations with symptoms of anxiety relative to the single-task threat appraisal measures (**Supplementary Table 2**). There were no significant differences in correlation strength when using factor scores vs. single-task measures.

Associations with Psychophysiological and Behavioral Task Indices. Acute Threat Appraisal. There were significant positive associations between acute threat appraisal factor scores and SCRs on the Reversal Learning task (r=.33; p=.044), but not on the Screaming Lady task (r=-.02, p=.896). There were notable non-significant positive associations between acute threat appraisal factor scores and avoidance behaviors on the Virtual Public Speaking task (r=.42, p=.060), but not on the YIKES task (r=.19, p=.174). Depending on the task, factor scores were uniquely significant or comparable in their associations with task indices relative to the single-task threat appraisal measures (Supplementary Table 3). However, there were no significant differences in correlation strength when using factor scores vs. single-task measures. Post Threat Appraisal. There were significant positive associations between post-threat appraisal factor scores and SCRs on the Reversal Learning task (r=.35; p=.033) and notable non-significant associations on the Screaming Lady task (r=.31, p=.058) as well as between post-threat appraisal factor scores and avoidance behaviors on the Virtual Public Speaking task (r=.40, p=.072) and YIKES task (r=.24, p=.082). Depending on the task, factor scores were uniquely significant or comparable in their associations with task indices relative to the singletask threat appraisal measures (Supplementary Table 3). However, there were no significant differences in correlation strength when using factor scores vs. single-task measures.

Discussion

This proof-of-concept study used a latent variable approach to integrate experimental research on threat appraisal and anxiety. First, findings evidenced significant commonality

among acute threat appraisals in six of the eight tasks, and among post-threat appraisals in seven of the eight tasks. That is, subjective threat appraisals evoked by most tasks appeared to reflect a latent construct. Next, when utilizing factor scores, higher acute and post-threat appraisals related to pediatric anxiety disorder diagnoses and symptom severity measured using both lab questionnaires and EMA. Finally, factor scores were comparable in their associations with anxiety symptoms and behavioral and psychophysiological task indices, relative to task-specific measures, underscoring the potential added value of integrating measures across tasks. Potential implications of these findings are discussed below.

The results of the confirmatory factor analyses impact views on threat responding. The finding that threat appraisals across diverse tasks loaded onto a common factor indicates important shared variance across different contexts, such as social threat and physical threat, which may inform understanding of broad-based vulnerability to anxiety disorders in youth. In contrast, acute-threat ratings for two tasks (Safety Learning and Scary Movie) and post-threat ratings for one task (Safety Learning) did not significantly load on the respective common latent variables. That is, the measured variables from these two tasks did not share as much common variance with the measured variables from the other tasks. While not predicted, this finding suggests that in some contexts, participants might appraise their anxiety less similarly than with the other tasks. These two tasks shared several features with other tasks (e.g., fMRI environment, rating scale used) and had similar levels of ratings as the other tasks. It is possible that participants' acute threat appraisals prior to the Scary Movie task were differentially impacted by previous experiences watching these types of movies. Other tasks all exhibited strong factor loadings (standardized values>.50), despite differences in the nature of the threat stimuli and experimental methodology.

Recent perspectives have articulated establishing a latent construct, or shared variance among measures, as an important first step in testing for between-subjects differences on that construct (e.g., Cooper et al., 2017). Here, analyses demonstrated higher threat appraisal factor

scores in youth with vs. without anxiety disorders and as a function of higher vs. lower anxiety symptoms measured via lab questionnaires and naturalistically. Comparing associations based on the latent variables vs. single-task measures was also a necessary step in examining the utility of the latent variable approach. As noted in the results, factor scores were correlated as consistently with anxiety as were the single-task measures, regardless of the task subsample and despite the fact that factor scores were derived by combining data across subsamples.

A similar pattern was observed in relation to task performance. Factor scores were significantly associated with greater psychophysiological arousal on the Reversal Learning Task, and variably or marginally associated with psychophysiological arousal or avoidance behavior on the Screaming Lady, Virtual Public Speaking, and YIKES tasks. Relative to the single-task measures, these associations were uniquely significant or comparable. Importantly, a body of literature in adults demonstrates that the subjective, psychophysiological, and behavioral channels of threat responding do not consistently intercorrelate (reviewed in e.g., Kozak & Miller, 1982; LeDoux & Pine, 2016; Rachman & Hodgson, 1974). However, research on this topic is limited in youth (Clarkson et al., 2020; Kaurin et al., 2022). The low intercorrelations reported in the literature informed our decision to limit the latent variable observed measures to self-report, and to subsequently test the associations of factor scores with psychophysiological and behavioral task performance indices. The current findings add to the literature by suggesting that a latent variable approach may improve the ability to detect associations across response channels. Additionally, a reduction in the number of statistical tests conducted, and the ability to incorporate subsamples or allow missing data (e.g., if a participant was unable to complete a threat task), are advantages of a latent variable approach.

This evaluation helps build comprehensive, testable models of anxiety-related processes. For instance, researchers in executive functioning have taken similar approaches to evaluating paradigms and subsequently building data-driven models to understand individual differences (Friedman et al., 2011; Miyake & Friedman, 2012). Separately, important efforts

have been made in leveraging latent variable approaches for symptom reports to model the structure of psychopathology (e.g., HiTOP, Conway et al., 2019; tripartite model, Clark & Watson, 1991). The novelty of the current approach lies in the focus on self-reported threat appraisal in different threat contexts and its application in pediatric anxiety. Interrogating a latent construct of threat appraisal may improve the reliability and robustness of findings in studies of pediatric anxiety; in turn, this could aid the development of biobehavioral models of pediatric anxiety that incorporate other levels of analysis such as neural circuitry. It should be noted, however, that attempts at integration across domains or levels of analysis within factor analysis have produced mixed results and further work is needed (e.g., Eisenberg et al., 2019; Peng et al., 2021; Venables et al., 2018).

There are also important limitations to this approach that should be discussed. First, using multiple tasks may not always be feasible for researchers. Even in the current study, only about half of participants who completed at least one of the tasks completed a number (two) that met our threshold for use in the latent variable models. Second, the decision to include as many participants as possible (i.e., those who completed two or more of the eight tasks) decreased the number of participants in common between tasks, impacting the CFAs. We also combined two different measures of threat appraisal in the CFAs. However, the availability of large datasets and emphasis on collaborative, multisite studies with common measures may make this approach more viable. When possible, findings in smaller studies could also be examined in larger datasets with respect to replication. Third, there was a substantial time window between experimental tasks in this study. When working with emotionally evocative tasks, it can be challenging or unethical to complete multiple tasks in the same study session, as well as potentially problematic in terms of carryover effects. Nevertheless, we believe that the strengths of this approach outweigh such limitations.

Where do we go from here? First, we hope that these findings encourage the use of more than one threat appraisal task or measure whenever possible. Further, as some threat-

based paradigms appear to elicit appraisals more similarly to one another, this information could be used to inform task selection in future studies. In working toward increased replicability of findings, latent variable approaches complement continued efforts to improve the psychometric properties of laboratory-based measures.



Author Contributions

Conceptualization, Methodology: R.A. Bernstein, A.R. Smith, D.S. Pine, K. Kircanski. Formal Analysis: R.A. Bernstein, A.R. Smith, K. Kircanski. Investigation: R.A. Bernstein, A.R. Smith, E. Kitt, E.M. Cardinale, A. Harrewijn, R. Abend, K.J. Michalska. Data Curation: R.A. Bernstein, A.R. Smith. Writing: R.A. Bernstein, A.R. Smith under the supervision of D.S. Pine, K. Kircanski and reviewed/edited by E. Kitt, E.M. Cardinale, A. Harrewijn, R. Abend, K.J. Michalska. Project Administration, Funding Acquisition: D.S. Pine.

Conflicts of Interest

The authors declare that there were no conflicts of interest with respect to the authorship or the publication of this article.

Funding

This research was supported by the Intramural Research Program of the National Institute of Mental Health, National Institutes of Health, ZIAMH002781 (Pine), and was conducted under Clinical Study Protocol 01-M-0192 (ClinicalTrials.gov ID: NCT00018057).

References

- Abend, R., Bajaj, M.A., Harrewijn, A., Matsumoto, C., Michalska, K.J., Necka, E., ... & Pine, D. S. (2021). Threat-anticipatory psychophysiological response is enhanced in youth with anxiety disorders and correlates with prefrontal cortex neuroanatomy. *Journal of Psychiatry and Neuroscience*, *46*(2), E212-E221.
- Abend, R., Gold, A.L., Britton, J.C., Michalska, K.J., Shechner, T., Sachs, J.F., ... & Pine, D.S. (2020). Anticipatory threat responding: Associations with anxiety, development, and brain structure. *Biological Psychiatry*, *87*(10), 916-925.
- Abend, R., Dan, O., Maoz, K., Raz, S., & Bar-Haim, Y. (2014). Reliability, validity and sensitivity of a computerized visual analog scale measuring state anxiety. *Journal of Behavior Therapy and Experimental Psychiatry*, *45*(4), 447-453.
- Barlow, D.H. (2004). Anxiety and its disorders: The nature and treatment of anxiety and panic.

 New York, NY: *Guilford Press*.
- Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., & Neer, S.M. (1997).

 The Screen for Child Anxiety Related Emotional Disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36(4), 545-553.
- Britton, J.C., Grillon, C., Lissek, S., Norcross, M.A., Szuhany, K.L., Chen, G., ... & Pine, D.S. (2013). Response to learned threat: An fMRI study in adolescent and adult anxiety. *American Journal of Psychiatry*, *170*(10), 1195-1204.
- Britton, J.C., Lissek, S., Grillon, C., Norcross, M.A., & Pine, D.S. (2011). Development of anxiety: The role of threat appraisal and fear learning. *Depression and Anxiety*, *28*(1), 5-17.
- Chapman, A., Devue, C. & Grimshaw, G.M. (2019). Fleeting reliability in the dot-probe task. *Psychological Research* 83, 308–320.

Psychiatry, 178(2), 156-164.

Chavanne, A.V., & Robinson, O.J. (2021). The overlapping neurobiology of induced and pathological anxiety: A meta-analysis of functional neural activation. American Journal of

- Clark, L.A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. Journal of Abnormal Psychology, 100(3), 316.
- Clarkson, T., Kang, E., Capriola-Hall, N., Lerner, M.D., Jarcho, J., & Prinstein, M.J. (2020). Meta-analysis of the RDoC social processing domain across units of analysis in children and adolescents. Journal of Clinical Child & Adolescent Psychology, 49(3), 297-321.
- Conway, C.C., Forbes, M.K., Forbush, K.T., Fried, E.I., Hallquist, M.N., Kotov, R., ... & Eaton, N.R. (2019). A hierarchical taxonomy of psychopathology can transform mental health research. Perspectives on Psychological Science, 14(3), 419-436.
- Cooper, S.R., Gonthier, C., Barch, D.M., & Braver, T.S. (2017). The role of psychometrics in individual differences research in cognition: A case study of the AX-CPT. Frontiers in Psychology, 8, 1482.
- Eisenberg, I.W., Bissett, P.G., Enkavi, A.Z., Li, J., MacKinnon, D.P., Marsch, L.A., & Poldrack, R.A. (2019). Uncovering the structure of self-regulation through data-driven ontology discovery. Nature Communications, 10, 2319.
- Eriksen, B.A., & Eriksen, C.W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, 16(1), 143–149.
- Friedman, N.P., Miyake, A., Robinson, J.L., & Hewitt, J.K. (2011). Developmental trajectories in toddlers' self-restraint predict individual differences in executive functions 14 years later: A behavioral genetic analysis. *Developmental Psychology*, 47(5), 1410.
- Harrewijn, A., Kitt, E.R., Abend, R., Matsumoto, C., Odriozola, P., Winkler, A.M., ... & Gee, D.G. (2021). Comparing neural correlates of conditioned inhibition between children with and without anxiety disorders: A preliminary study. Behavioural Brain Research, 399, 112994.

- Kain, Z.N., Mayes, L.C., Cicchetti, D.V., Bagnall, A.L., Finley, J.D., & Hofstadter, M.B. (1997).
 The Yale Preoperative Anxiety Scale: How does it compare with a" gold standard"? *Anesthesia & Analgesia*, 85(4), 783-788.
- Kalisch, R., & Gerlicher, A.M. (2014). Making a mountain out of a molehill: On the role of the rostral dorsal anterior cingulate and dorsomedial prefrontal cortex in conscious threat appraisal, catastrophizing, and worrying. *Neuroscience and Biobehavioral Reviews*, 42, 1-8.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U.M.A., Flynn, C., Moreci, P., ... & Ryan, N. (1997).
 Schedule for Affective Disorders and Schizophrenia for School-age Children-present and
 Lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal of the American*Academy of Child and Adolescent Psychiatry, 36(7), 980-988.
- Kaurin, A., Sequeira, S. L., Ladouceur, C.D., McKone, K. M., Rosen, D., Jones, N., ... & Silk, J. S. (2022). Modeling sensitivity to social threat in adolescent girls: A psychoneurometric approach. *Journal of Psychopathology and Clinical Science*, *131*(6), 641.
- Kirschbaum, C., Pirke, K.M., & Hellhammer, D.H. (1993). The 'Trier Social Stress Test': A tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology*, *28*(1-2), 76-81.
- Kozak, M.J., & Miller, G.A. (1982). Hypothetical constructs versus intervening variables: A reappraisal of the three-systems model of anxiety assessment. *Behavioral Assessment*, *4*(3), 347–358.
- Lau, J.Y., Lissek, S., Nelson, E.E., Lee, Y., Roberson-Nay, R., Poeth, K., ... & Pine, D.S. (2008).

 Fear conditioning in adolescents with anxiety disorders: Results from a novel experimental paradigm. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(1), 94-102.

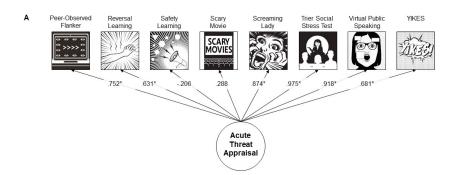
- Lebowitz, E.R., Shic, F., Campbell, D., MacLeod, J., & Silverman, W.K. (2015). Avoidance moderates the association between mothers' and children's fears: Findings from a novel motion-tracking behavioral assessment. *Depression and Anxiety*, *32*(2), 91-98.
- LeDoux, J.E. (2015). Anxious: Using the brain to understand and treat fear and anxiety. New York, NY: *Penguin Books*.
- LeDoux, J.E., & Pine, D.S. (2016). Using neuroscience to help understand fear and anxiety: A two-system framework. *American Journal of Psychiatry*, *173*(11), 1083-1093.
- Lilienfeld, S.O., & Strother, A.N. (2020). Psychological measurement and the replication crisis: Four sacred cows. *Canadian Psychology*, *61*(4), 281–288.
- Michalska, K.J., Shechner, T., Hong, M., Britton, J. C., Leibenluft, E., Pine, D.S., & Fox, N.A. (2016). A developmental analysis of threat/safety learning and extinction recall during middle childhood. *Journal of Experimental Child Psychology*, *146*, 95-105.
- Miyake, A., & Friedman, N.P. (2012). The nature and organization of individual differences in executive functions: Four general conclusions. *Current Directions in Psychological Science*, *21*(1), 8-14.
- Myin-Germeys, I., Oorschot, M., Collip, D., Lataster, J., Delespaul, P., & Van Os, J. (2009). Experience sampling research in psychopathology: Opening the black box of daily life. *Psychological Medicine*, *39*(9), 1533-1547.
- Narvaez Linares, N.F., Charron, V., Ouimet, A.J., Labelle, P.R., & Plamondon, H. (2020). A systematic review of the Trier Social Stress Test methodology: Issues in promoting study comparison and replicable research. *Neurobiology of Stress, 13,* 100235.
- Open Science Collaboration. (2015). Estimating the reproducibility of psychological science. *Science*, *349*(6251), aac4716.
- Peng, Y., Knotts, J.D., Taylor, C.T., Craske, M.G., Stein, M.B., Bookheimer, S., ... & Paulus, M. P. (2021). Failure to identify robust latent variables of positive or negative valence

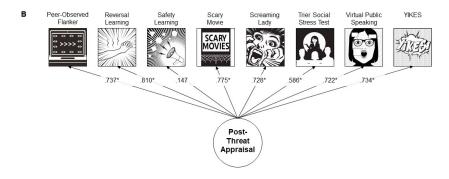
- processing across units of analysis. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 6(5), 518-526.
- Pine, D.S. (2007). Research review: A neuroscience framework for pediatric anxiety disorders. *Journal of Child Psychology and Psychiatry*, *48*, 631-648.
- Pittig, A., Treanor, M., LeBeau, R.T., & Craske, M.G. (2018). The role of associative fear and avoidance learning in anxiety disorders: Gaps and directions for future research. *Neuroscience and Biobehavioral Reviews*, *88*, 117-140.
- Rachman, S., & Hodgson, R. (1974). I. Synchrony and desynchrony in fear and avoidance. *Behaviour Research and Therapy*, *12*(4), 311-318.
- Russell, M.A., & Gajos, J.M. (2020). Annual research review: Ecological momentary assessment studies in child psychology and psychiatry. *Journal of Child Psychology and Psychiatry*, 61(3), 376-394.
- Shechner, T., Britton, J. C., Ronkin, E.G., Jarcho, J.M., Mash, J.A., Michalska, K.J., ... & Pine, D.S. (2015). Fear conditioning and extinction in anxious and nonanxious youth and adults: Examining a novel developmentally appropriate fear-conditioning task. *Depression and Anxiety*, *32*, 277-288.
- Spielberger, C.D. (1970). STAI manual for the Stait-Trait Anxiety Inventory. Palo Alto, CA:

 Consulting Psychologists Press.
- Smith, A.R., White, L.K., Leibenluft, E., McGlade, A.L., Heckelman, A.C., Haller, S.P., ... & Pine, D.S. (2020). The heterogeneity of anxious phenotypes: Neural responses to errors in treatment-seeking anxious and behaviorally inhibited youths. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(6), 759-769.
- Smith, A.R., Kircanski, K., Brotman, M.A., Do, Q.B., Subar, A.R., Silk, J.S., ... & Pine, D.S. (2019). Advancing clinical neuroscience through enhanced tools: Pediatric social anxiety as an example. *Depression and Anxiety*, 36(8), 701-711.

- Strawn, J.R., Lu, L., Peris, T.S., Levine, A., & Walkup, J.T. (2020). Research review: Pediatric anxiety disorders: What have we learnt in the last 10 years? *Journal of Child Psychology and Psychiatry*, *62*(2), 114-139.
- Tackett, J.L., Brandes, C.M., King, K.M., & Markon, K.E. (2019). Psychology's replication crisis and clinical psychological science. *Annual Review of Clinical Psychology*, *15*, 579-604.
- Vanderwal, T., Eilbott, J., & Castellanos, F.X. (2019). Movies in the magnet: Naturalistic paradigms in developmental functional neuroimaging. *Developmental Cognitive Neuroscience*, *36*, 100600.
- Venables, N.C., Foell, J., Yancey, J.R., Kane, M.J., Engle, R.W., & Patrick, C.J. (2018).

 Quantifying inhibitory control as externalizing proneness: A cross-domain model. *Clinical Psychological Science*, *6*(4), 561-580.
- Westenberg, P.M., Bokhorst, C.L., Miers, A.C., Sumter, S.R., Kallen, V.L., van Pelt, J., & Blöte, A.W. (2009). A prepared speech in front of a pre-recorded audience: Subjective, physiological, and neuroendocrine responses to the Leiden Public Speaking Task. *Biological Psychology*, *82*(2), 116-124.





 $\begin{array}{c} \text{Standardized loadings presented.} \\ *p{<}.001 \end{array}$

338x254mm (96 x 96 DPI)

Table 1

Participant Demographic and Clinical Characteristics

M (SD) or N (%)	Anxiety Disorder (<i>N</i> =51)	Healthy Volunteer (<i>N</i> =41)	Total (<i>N</i> =92)
Age	13.24 (2.67)	12.86 (2.79)	13.07 (2.71)
Race			
White	35 (68.63)	25 (60.98)	60 (65.22)
Black/African American	4 (7.84)	9 (21.95)	13 (14.13)
Asian/Asian American	1 (1.96)	2 (4.88)	3 (3.26)
American Indian/Alaskan Native	1 (1.96)	0 (0.00)	1 (1.09)
Multiple Races	6 (11.76)	2 (4.88)	8 (8.70)
Unknown	4 (7.84)	3 (7.32)	7 (7.61)
Ethnicity			
Latino or Hispanic	11 (21.57)	3 (7.32)	14 (15.22)
Not Latino or Hispanic	39 (76.47)	36 (87.80)	75 (81.52)
Unknown	1 (1.96)	2 (3.92)	3 (3.26)
Clinical Characteristics			
SCARED			
Self-Report	32.84 (13.35)	8.09 (8.11)	21.81 (16.73)
Parent-Report ^a	30.74 (12.27)	5.04 (7.20)	19.44 (16.45)
EMA Anxiety			
Self-Report	1.87 (0.61)	1.09 (0.13)	1.47 (0.58)
Anxiety Disorder Diagnoses ^b			
Generalized Anxiety Disorder	42 (82.35)	0 (0.00)	42 (45.65)
Social Anxiety Disorder	37 (71.15)	0 (0.00)	37 (40.22)
Separation Anxiety Disorder	8 (15.69)	0 (0.00)	8 (8.70)
Specific Phobia	10 (19.61)	0 (0.00)	10 (10.87)
Panic Disorder	3 (5.88)	0 (0.00)	3 (3.26)

Note. EMA=ecological momentary assessment; SCARED=Screen for Child Anxiety-Related Emotional Disorders; YIKES=Yale Interactive Kinect Environment Software Behavioral Avoidance Task. ^aData were missing for one participant.

^bParticipants could have more than one diagnosis; therefore, values do not sum to 100%.