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Examining the Relations Between Children's Vagal Flexibility Across Social Stressor Tasks and Parent- and Clinician-Rated Anxiety Using Baseline Data from an Early Intervention for Inhibited Preschoolers

Nicholas J. Wagner[1], **Nila Shakiba**[1], **Hong N.T. Bui**[2], **Kathy Sem**[1], **Danielle R. Novick**[2], **Christina M. Danko**[2], **Lea R. Dougherty**[2], **Andrea Chronis-Tuscano**[2], **Kenneth H. Rubin**[3]

[1]Boston University, Department of Psychological and Brain Sciences

[2]University of Maryland, Department of Psychology

[3]University of Maryland, Human Development and Quantitative Methodology

Abstract

Early behavioral inhibition (BI) is a known risk factor for later anxiety disorder. Variability in children's parasympathetic nervous system (PNS) functioning may provide insight into the substantial heterogeneity in anxiety outcomes for children high in BI. However, gaps persist due to an over-reliance on static measures of functioning, which limits our ability to leverage PNS functioning to identify risk for anxiety. We address these gaps using baseline data from an early intervention study of inhibited preschoolers by characterizing vagal flexibility (VF), an index of non-linear change in PNS functioning, across social stressor tasks and by examining the associations between VF and anxiety. One hundred and fifty-one parents and their 3.5- to 5-year-old children were selected on the basis of BI to participate in an early intervention program (ClinicalTrials.gov registration: NCT02308826). A structural equation modeling framework was used to model children's VF across tasks designed to mimic exposure to novel social interactions and to test the predictive links between VF and anxiety. Children who showed less VF, characterized by less suppression and flatter recovery, were rated by both parents and clinicians as more anxious. Moreover, a multiple group model showed that children meeting diagnostic criteria for social anxiety disorder demonstrated significantly less VF across social stressor tasks. Among inhibited youth, reduced VF is a risk factor for anxiety and may reflect an individual's reduced capacity to actively cope with external demands. Study results contribute to our understanding of the regulatory processes underlying risk for anxiety in early childhood.

Keywords

Anxiety; Psychophysiology; Biomarkers; Developmental Psychopathology

Corresponding author: Nicholas J. Wagner, njwagner@bu.edu, Room 119, 64 Cummington Mall, Boston, MA 02215.

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Introduction

Behavioral inhibition (BI), a temperamental predisposition to experience negative affect and behaviorally withdraw in the face of novelty (Fox et al., 2021; Kagan et al., 1989), is an early antecedent to social reticence (Rubin et al., 2009) and is the best-known risk factor for the later diagnosis of anxiety, particularly social anxiety (Buss et al., 2013; Chronis-Tuscano et al., 2009). Moreover, early and elevated BI, which can be reliably identified in infancy (Fox et al., 2005), may indicate risk for an early-starting, chronic, and severe course of anxiety (Ramsawh et al., 2011). However, prominent theoretical models (e.g., Rubin & Chronis-Tuscano, 2021) and substantial empirical evidence (see Fox et al., 2005 for review) converge to support the notion that there are multiple influences, including those which are physiologically mediated (Beauchaine 2015; Wagner & Waller, 2020), on the associations between BI and anxiety outcomes.

Research that clarifies the relationship between variability in physiological functioning and anxiety among youth high in BI advances our understanding of the mechanisms underlying risk for anxiety and may provide insight into potential moderators and mediators of treatment response (Chronis-Tuscano et al., 2018). Although researchers have examined links between children’s physiological functioning and risk for anxiety, important gaps persist, in part, due to an over-reliance on static measures of baseline physiological functioning and reactivity which lack temporal sensitivity to fluctuations in regulation that unfold over time in response to stimuli (Burt & Obradović, 2013). The current study addresses this gap by examining the associations between anxiety and non-linear changes in children’s parasympathetic nervous system (PNS) functioning across a series of novel exposure tasks, some of which were designed to mimic children’s social interactions.

One factor that may indicate vulnerability towards anxiety is reduced flexibility of the PNS (Friedman & Thayer 1998), which hinders an individual’s ability to adequately regulate and respond to a constantly changing environment. The myelinated vagus nerve is the main mechanism of parasympathetic innervation of the heart, through which the PNS provides ongoing and dynamic influence to maintain homeostasis and support the allocation of attentional and regulatory resources to engage with the environment (Cacioppo et al., 2007). The vagus nerve exerts an inhibitory and chronotropic (i.e., frequency) cardiac influence which results in reduced heart rate and increased heart rate variability, commonly referred to as vagal tone (Porges, 1992). Respiratory sinus arrhythmia (RSA), or the variability in heart rate associated with a respiration cycle, is a specific measure of PNS functioning (Cacioppo et al., 2007).

Children’s resting RSA and patterns of reactivity (e.g., reduction or suppression of RSA in response to stimuli) and recovery (e.g., return to tonic or basal levels of functioning following stimuli) represent key neurophysiological substrates of individual differences in regulatory behaviors. They provide insight into the capacity for flexible physiological self-regulation that underlies effective emotion regulation, social communication, and attentional orienting (Porges 2007; Wagner et al., 2021). Research has also established RSA as a valid transdiagnostic biomarker of emotion dysregulation and psychopathology (Beauchaine

2012, 2015; Wagner & Waller, 2020), including anxiety (Friedman & Thayer, 1998; Ugarte, Liu et al., 2021; Wagner et al., 2015).

A growing body of literature demonstrates meaningful links between children's RSA, inhibition or fearfulness, and anxiety. For example, Viana and colleagues (2017) find the highest anxiety disorder symptoms among children (M = 9.61 years) with high levels of BI and low resting RSA. The authors also report higher anxiety symptoms among youth with high levels of BI and lower RSA during a social challenge, possibly indicating reduced RSA suppression or a smaller reduction in RSA (Viana et al., 2017). In addition, Brooker and colleagues (2013) report that infants showing less RSA suppression during a stranger approach task are likelier to show behavioral fear to strangers than those infants showing more RSA suppression or a greater reduction in RSA (Brooker et al., 2013). A longitudinal study of children aged 24 to 48 months finds that children demonstrating fear and inhibition to both social (e.g., stranger approach) and nonsocial (e.g., robot exposure) stimuli may fail to suppress RSA in response to novelty or threat (Buss et al., 2018). Finally, a study of older children (M = 10.07 years) finds that high anxiety and low RSA suppression are associated with difficulties regulating fear responses (Viana et al., 2021). However, contradictions also exist in the literature, with some studies reporting varying associations between internalizing constructs and measures of resting RSA (Smith et al., 2019; Wagner et al., 2015) and RSA reactivity (Beauchaine et al., 2019). Inconsistencies in the literature likely stem from many things, including sample characteristics, contexts of measurement, and reliance on measures of resting physiology or static measures of change (i.e., difference scores).

Although researchers have established links between internalizing problems and lower resting RSA (i.e., higher heart rate) and aberrant patterns of reactivity (Paniccia et al., 2017; Smith et al., 2019; Wagner et al., 2015), approaches to characterizing non-linear patterns of RSA change likely have utility when it comes to characterizing the dynamic functioning of the PNS as it occurs over time (Burt & Obradović, 2013). These approaches may also support research aiming to elucidate the links between children's physiological functioning and anxiety across ecologically valid contexts. As such, an increasing number of studies have used methods to characterize non-linear patterns of change in RSA that unfold over the course of stimulation (Ugarte, Miller et al., 2021; West et al., 2020), a metric of PNS reactivity and recovery often referred to as vagal flexibility (VF; Miller et al., 2013). Employing modeling approaches to assess VF is consistent with the basic premises of biopsychosocial and systems theories that have been successfully applied to research on the biological underpinnings of psychopathology: that adaptive responsiveness to changing environments is achieved through a flexible relation between an individual's regulatory systems and their context (Bertalanffy, 1972; Friedman, 2007). Indeed, patterns of RSA suppression followed by recovery, or greater VF, in children have been linked with better self-control (Miller et al., 2013), empathy and prosociality (Miller et al., 2016), and better emotion regulation (Cui et al., 2015, 2019).

Although limited, there is a body of existing research employing dynamic measures of RSA, including VF, to better understand the regulation of inhibited or fearful youth. For example, a review of studies examining the links between heart rate variability, a measure of cardiac autonomic nervous system functioning, and anxiety in young people reports that clinical cross-sectional studies overwhelmingly find links between anxiety and reduced variability across a variety of non-linear measures (Paniccia et al., 2017), including one study reporting that individuals in a ‘high anxious’ group (75 percentile of symptomatology) demonstrated less complexity in their heart rate as compared to the ‘low anxious’ group (Bornas et al., 2015). In addition, Brooker and Buss (2010) found that non-linear (i.e., quadratic) measures of toddlers’ RSA change across a fear-eliciting paradigm provided unique insight into behavioral displays of shyness over and above static change scores. Specifically, their findings suggest that high-fear children demonstrated RSA suppression later in the fear episode than did low-fear children, possibly indicating a link between fearfulness and reduced VF.

Despite these promising advances, important gaps persist in our understanding of the links between VF and risk for anxiety in early childhood. For the most part, approaches to modeling non-linear change in RSA have not been extended to contexts characterized by multiple iterations of reactivity and recovery, but have instead characterized quadratic change across two tasks. Moreover, researchers have yet to examine links between VF and anxiety among inhibited children, which limits our ability to test whether VF can be leveraged to identify risk for anxiety among inhibited youth. Addressing these gaps is particularly important given findings linking restricted autonomic flexibility (i.e., reduced RSA reactivity and slower recovery) and social phobia in a sample of children aged 8 to 12 years (Schmitz et al., 2011) and a study demonstrating that RSA reactivity predicts treatment response in the context of cognitive behavioral therapy for social anxiety disorder among adults (Mathewson et al., 2013). The current study addresses these gaps using baseline data from an early intervention study of inhibited preschoolers by 1) characterizing VF across a series of tasks designed to mimic exposure to novelty; 2) testing whether and how patterns of VF predict parent- and clinician- ratings of anxiety; and 3) formally testing whether patterns of VF vary as a function of meeting criteria for clinically-significant impairment in social anxiety. We hypothesize that a non-linear pattern of RSA suppression and recovery will best characterize children’s VF, that reduced VF (i.e., less suppression and flatter recovery across tasks) will be associated with higher anxiety ratings, and that children meeting criteria for clinically-significant impairment in social anxiety will demonstrate lower VF than those children not meeting these criteria.

Method

Participants

The current study uses baseline data from an intervention study for preschool children with elevated BI (ClinicalTrials.gov registration: NCT02308826.). Participants were recruited from preschools, pre-kindergarten programs, childcare centers, pediatrician offices, and community organizations in the Washington D.C. metropolitan area. Families participated in the study in cohorts and the study comprised twelve total cohorts. For inclusion, children were required to: (1) be between 45–64 months (M = 52.9 months, SD = 5.7 months) and attending a structured educational program; (2) score within the top 15% on the Behavioral Inhibition Questionnaire (BIQ; Bishop, Spence, & McDonald, 2003) based on conceptual models of risk associated with heightened BI in this range (Henderson et al., 2004; Kagan et al., 2007); (3) not be diagnosed with autism spectrum disorder (ASD), or exceed the clinical cutoff (15 ≤) on the Social Communication Questionnaire (SCQ; Eaves et al., 2006), a parent-report screen for social/communication deficits characteristic of ASD; (4) not be receiving anxiety treatment; (5) not have selective mutism; and (6) have custodial parent(s) who consent(s) to participate. Based on parents' reports of children's demographic information, children's sex was reported as 51% female, and children's race was categorized as European American (50.5%), Asian American (14%), African American (12.5%), or Other (23%). Parents reported that 9% of the sample identified as Hispanic or Latinx. Participants reported annual incomes in buckets ranging from $0 – $24,599 to $150,000+ ($M$ = $100,000 – $124,999). Parents' education included 3 years of college or less (10.5%), 4 years of college (24%), a master's degree or equivalent (42%), and a doctoral degree or equivalent (23.5%). Additional information regarding sample descriptives, including information about parents' educational attainment and children's sex and race, can be found in Table 1.

Ethical Considerations

Interested parents completed a telephone screen assessing basic inclusion criteria. Those who met inclusion criteria provided written informed consent and were invited to a laboratory assessment, during which diagnostic interviews, parent reports, and social stressor tasks were completed. Study protocols were approved by the University of Maryland Institutional Review Board.

Procedures

In total, 151 families met criteria and were randomized to one of two treatment conditions (for more information see Chronis-Tuscano et al., 2021). The current analyses involve baseline (i.e., pre-treatment) data only which were collected when participating families completed a laboratory visit before the start of treatment. Children were seated at a small desk before a computer screen to complete exposure to novelty tasks. The child completed these tasks near the beginning of the baseline laboratory visit, and the child's parent was seated behind the child during the socially challenging conditions such that the child could not see the parent during the tasks.

The tasks were comprised of three *calm-Video* conditions, interspersed with validated socially challenging conditions (Buss et al., 2013; Fox et al., 2001; Rubin et al., 2009). The *Calm-Video* conditions, which were each 3 minutes in length, consisted of a Sesame Street music lullaby and were included to establish tonic levels of physiological functioning *prior to* each of the socially challenging conditions and to provide opportunities for recovery *following* each of the socially challenging conditions. The *Clown* condition began immediately following *Calm-Video 1* and was designed to mimic the challenge of being asked to speak to an unfamiliar, novel individual. In this condition, a research assistant dressed as a clown entered the assessment room through a door that was immediately adjacent to the computer screen located in front of the child, waited 10 seconds while staring at the child with neutral affect, and then engaged in a structured conversation for approximately 60 seconds. The *Clown* condition is a well-validated paradigm commonly used in studies examining BI and social fear (Buss et al., 2017; Fox et al., 2001; Kagan et al., 1989). *Calm-Video 2* was shown immediately following the *Clown* condition. Following *Calm-Video 2*, the experimenter explained to the child that they wanted to introduce several children with whom the child might meet in the future (i.e., *Kids* condition). The *Kids* condition was designed to mimic the common experience of learning about unfamiliar, same- aged peers. This condition involved viewing images of 6 smiling children's faces at 10-second intervals. Smiling images for the fictitious children were taken from the *Child Affective Facial Expression* set (LoBue & Thrasher, 2014). For the first 5 seconds, only the image of a fictitious child appeared on the screen. For the next 5 seconds, the image of the child was accompanied by clip art indicating an object or a place the fictitious child enjoys. The experimenter offered the fictitious child's name and a description of the fictitious child's interests during the task. In total, participating children were shown six fictitious children which were counterbalanced on race and biological sex.

Next, the experimenter requested the focal child to introduce themselves to "the kids who you just learned about so that they can learn something about you." The experimenter directed the child's attention to a camera mounted on a nearby wall. This *Introduction* condition was designed to mimic aspects of the Trier Social Stress Test (Kirschbaum et al., 1993). The Trier Social Stress Test is a well-established task known to elicit changes in autonomic signaling, particularly along the hypothalamic-pituitary-adrenal axis, which is a sympathetic signaling circuit (Kudielka et al., 2010). Notably, the camera that the child was asked to speak into was mounted next to a mirror to reinforce self-conscious emotional states. If the child remained silent (which was common), the experimenter offered standardized prompts such as, "You can tell them how old you are" or "You can describe something you like to do." Children were given 90 seconds to complete the task. Finally, *Calm-Video 3* was presented following the completion of the *Introduction* task.

Measures

Respiratory Sinus Arrhythmia (RSA).—Measures of RSA were derived from data collected using the Biopac MP150 data acquisition system at a sampling rate of 2000Hz. During the assessment, participating children wore wireless Bio-Nomadix PPG-ED transmitters ("BIOPAC Systems, Inc." 2005). The receiver device was attached to the MP150 acquisition device in a control room adjacent to the assessment room. Concurrent with the collection of heart rate, two separate video streams were recorded in the room. The first captured video of the child from a wall-mounted camera feed, and the second captured the presentation screen where videos and other visual cues were presented during the assessment. These two video streams were used by research assistants to identify the time boundaries for the four different conditions that occurred during each assessment: *Calm-Video* (repeated three times), *Clown*, *Kids*, and *Introduction*.

Measures of RSA were derived from inter-beat interval (IBI) data, following the "Porges–Bohrer method" (Porges & Bohrer, 1990) which conforms to the assumptions of parametric analysis, is not moderated by respiration, is robust to non-stationarity, and is the most sensitive to vagal blockade (Lewis et al., 2012). First, a peak identification algorithm was used to derive IBI data ("BIOPAC Systems, Inc." 2005). Then, IBI data were visually inspected and edited for movement artifact (Porges, 1985; Brain-Body Center for

Psychophysiology and Bioengineering) by trained and reliable research assistants. No more than 5% of the included data required editing, and approximately 6% of average missingness across tasks was due to movement artifact. Finally, RSA (i.e., the high-frequency component of heart rate variability), defined as variance within the frequency band associated with spontaneous breathing, was calculated for each task across 15-second epochs consistent with procedures developed by Porges and Byrne (1992).

Parent-Rated Anxiety.—The *Child Behavior Checklist/1.5–5* (CBCL, Achenbach, 1991) is a well-established instrument for assessing emotional and behavioral problems in children. The 99-item parent-report requires parents to rate a series of statements about their child’s behavior. The anxiety subscale was used to assess parent-rated anxiety (e.g., *clings to adults or too dependent, gets too upset when separated from parents, too fearful or anxious)*. The CBCL is a well-established measure and demonstrated good reliability in the current sample (α =.89).

Child Diagnostic Assessment.—The *Anxiety Disorders Interview Schedule for Children for DSM 5—Parent Version* (ADIS-V-P; Silverman & Albano, 1996) is a semi-structured parent interview for clinical anxiety and associated disorders in youth based on the DSM-5. The ADIS- V-P was administered to parents at baseline. Level of impairment was measured using the Clinician Severity Rating (CSR), ranging from 0–8 (≥4 indicating clinically-significant impairment). Total anxiety severity was calculated as the sum of separation, specific, social, and generalized anxiety modules CSRs (Ginsburg et al., 2015). The ADIS-IV-P has demonstrated good reliability in preschoolers (e.g., Kennedy et al., 2009). The intraclass correlation (ICC) for the sum of all anxiety module CSRs ranged from .78 to .87.

Covariates.—Parents reported on children’s biological *sex* and *race*, *age* at the time of the baseline laboratory visit, and their own *educational attainment*. Children’s biological sex was included to account for documented differences in anxiety diagnoses (Asher, Asnaani, & Aderka, 2017) and children’s race was included to account for potential differences in the development of the autonomic nervous system (Wagner et al., 2021). Age was included to account for the range of eligible ages of participating children, and parents’ educational attainment was a general proxy for variation in family resources. All statistical models included these variables and children’s cohort membership as covariates.

Analysis Plan—Study aims were investigated using a multi-method analytic approach. First, latent growth curve modeling was performed using Mplus v8 (Muthén & Muthen, 2017) to examine intra- and interindividual RSA change (i.e., VF) across the social stressor tasks. Latent factors were estimated for tonic RSA during *Calm-Video 1* (intercept) and change in RSA over the course of the social stressor tasks (slope) using mean RSA values from each task as indicators. Unconditional growth curves were tested and compared to determine which model best characterized the change in RSA across social stressor tasks. Specifically, linear, quadratic, and latent basis models were estimated and formally compared using several fit indices including χ^2, the Comparative Fit Index (CFI; Bentler, 1990), and the root mean square error of approximation (RMSEA; Browne & Cudeck, 1993). Higher CFI values and lower RMSEA values indicate superior fit (Hu and Bentler 1998). Bootstrapped Likelihood Ratio Test (LRT; Mendell & Rubin, 2001) were conducted to formally compare nested models.

Second, the best fitting latent growth curve model was extended to examine the extent to which model-implied tonic RSA (intercept) and RSA change across social stressor tasks predicted parent- and clinician-rated anxiety. Specifically, parent- and clinician-rated anxiety were included as endogenous outcomes which were separately regressed on the latent intercept, latent slope, and study covariates. Third, latent growth curves were estimated in a multiple group framework to test whether intra- and interindividual RSA change across the social stressor tasks differed as a function of meeting diagnostic criteria for clinically-significant impairment in social anxiety. The MODEL TEST command in Mplus (Muthen & Muthen, 1998–2017) was used to conduct a joint test of equality of the model intercepts and slopes across groups using the Wald test with k-1 degrees of freedom. This final step offered a formal comparison of tonic RSA during *Calm-Video 1* and RSA change across groups. Full-information maximum likelihood (Enders, 2001) was implemented in all models allowing the use of all available data.

Results

Descriptive Statistics

Means, standard deviations, and zero-order bivariate correlations are presented in Table 1. Cohort membership was positively related to RSA during the *Introduction* condition and negatively related to clinician-rated anxiety. Children's sex (male = 1; female = 2) was negatively associated with RSA during the *Clown* condition. All RSA measurements during each condition were positively associated.

Characterizing Intra- and Interindividual RSA Change

Fit statistics comparing unconditional linear, quadratic, and latent basis models (Table 2) favored the latent basis model which demonstrated adequate fit, X^2 (12) = 41.59; CFI = 0.96; RMSEA = 0.13. Modification indices suggested a residual covariance between the indicators for RSA during the *Introduction* and *Calm-Video 3* conditions which improved fit, X^2 (11) = 23.71; CFI = 0.98; RMSEA = 0.09. The latent basis model was parameterized such that the intercept represented initial RSA during the *Calm-Video* 1 condition. Based on the lower mean RSA during the *Clown* condition as compared to *Calm-Video* 1 and the assumption that children would demonstrate RSA withdrawal in response to the clown, the slope factor loadings for the first two tasks were set to 0 and −1, respectively. The slope factor loadings for the remaining conditions were freely estimated to model a potential non-linear pattern of RSA change. The latent basis model was retained for all subsequent analyses.

The intercept, $M = 6.31$, $p < 0.001$, represented the model-implied average RSA level during *Calm-Video* 1. The slope, $M = 0.19$, $p < 0.001$, in conjunction coefficients (0, −1, 0.10, 0.35, −0.95, −0.13) indicated a non-linear change in RSA across social stressor tasks (see Figure 1). On average, children initially suppressed RSA during the introduction of the *Clown*, recovered to starting RSA levels during *Calm-Video 2*, slightly augmented RSA during the presentation of the same-aged peers (*Kids)*, suppressed RSA when introducing themselves (*Introduction)*, and recovered to near starting RSA levels during the final recovery video (*Calm- Video 3)*. Higher model-implied starting RSA values during the first video were associated with more dynamic change across tasks, $\psi = 0.08$, $p < 0.001$.

Testing Links between RSA Change and Anxiety

A series of models were estimated to test the predictive associations between this dynamic pattern of RSA change and parent- and clinician-rated anxiety by separately regressing these outcomes on the latent intercept and slope of RSA along with study covariates (Table 3). Model-implied RSA during *Calm-Video 1* (intercept) did not predict parent- or clinician-rated anxiety, $\beta = 0.15$, $p = 0.16$ and $\beta = 0.19$, $p = 0.07$, respectively. However, the latent slope of RSA, negatively predicted both parent-rated, $\beta = -0.28$, $p = 0.03$, and clinician-rated, $\beta = -0.27$, $p = 0.03$, anxiety. These findings suggest that children who showed less dynamic change in RSA across social stressor tasks, characterized by less suppression and flatter recovery, were rated by both parents and clinicians as more anxious.

Finally, a multiple group model was estimated to formally test differences in children's dynamic RSA change across social stressor tasks as a function of meeting diagnostic criteria for clinically-significant impairment in social anxiety. Model-implied estimates of dynamic RSA change by group are presented in Figure 2. Consistent with the findings from the prediction models, children meeting diagnostic criteria for clinically-significant impairment in social anxiety demonstrated overall less dynamic RSA change across tasks. Specifically, children meeting criteria for social anxiety disorder demonstrated less suppression during the *Clown*, $\lambda = -0.09$ vs. -0.33, blunted recovery during *Calm-Video 2*, $\lambda = 0.02$ vs. 0.09, less augmentation during the *Kids* task, $\lambda = 0.01$ vs. 0.03, less suppression during the *Introduction*, $\lambda = -0.13$ vs. - 0.45, and less recovery during *Calm-Video 3*, $\lambda = -0.05$ vs. -0.21. Moreover, a formal test of equality suggested that model-implied starting RSA during *Calm-Video 1* (intercept) did not meaningfully differ across groups, *Wald's* $X^2(1) = 0.87$, $p = 0.35$, but that children meeting diagnostic criteria for social anxiety disorder demonstrated significantly less dynamic RSA change across tasks, *Mslope* = 0.03 vs. 0.27, *Wald's* $X^2(1) = 7.07$, $p = 0.0078$.

Discussion

Early BI is one of the best-known risk factors for childhood anxiety disorders (Chronis-Tuscano et al. 2009), which represent the most prevalent class of psychopathology among youth (Merikangas et al. 2010) and are associated with significant functional impairments (Chronis- Tuscano et al., 2018; Granic, 2014; Towe-Goodman et al., 2014). There is substantial heterogeneity in the links between BI and anxiety outcomes, and research implicates children's VF as one potential mechanism underlying these associations (Friedman & Thayer, 1998; Ugarte, Liu, et al., 2021; Viana et al., 2021). The current study contributes to this literature by using baseline data from a sample of inhibited preschoolers to model children's VF across a series of tasks designed to mimic exposure to novel stimuli and social interactions and by testing the links between patterns of VF and multiple ratings of anxiety. Results indicated that children who showed less VF, characterized by less suppression and flatter recovery across tasks, were rated by both parents and clinicians as more anxious. Moreover, a multiple-group model showed that children meeting diagnostic criteria for social anxiety disorder demonstrated significantly less VF across social stressor tasks. Taken together, study results contribute to our understanding of the regulatory processes underlying risk for anxiety in early childhood.

Low resting RSA is broadly indicative of deficiencies in self- and emotion regulatory capacities, including the decreased capacity to maintain regulatory control over affective arousal (Beauchaine, 2001; Hinnant & El-Sheikh, 2009), and has demonstrated consistent links with various psychopathology across the lifespan, including anxiety (Beauchaine, 2015; Paniccia et al., 2017; Wagner et al., 2015). Despite this body of literature, the current study did not find evidence for links between RSA during *Calm-Video 1* (i.e., model-implied RSA before the presentation of stressors) and anxiety when considered alongside the relative influence of children's VF. These results should not be taken to undermine the utility of measures of resting RSA in developmental psychopathology research, rather they highlight the potential for modeling patterns of dynamic PNS regulation to provide detailed insight into how physiology underlies the experience and regulation of emotion *across ecologically valid contexts*. The current findings suggest that, among inhibited youth, reduced VF (i.e., attenuated patterns of reactivity and recovery) is a risk factor for anxiety and may reflect an individual's reduced regulatory capacity to actively cope with external demands.

The current findings are consistent with literature conceptualizing VF as a transdiagnostic factor underlying emotion regulation and reduced VF as conferring risk for a range of psychopathological outcomes. Indeed, Miller and colleagues (2013) report that children ages 4 – 6 who demonstrated greater VF, characterized by more initial RSA suppression and a subsequent return to baseline in response to anger-inducing stimuli, also displayed better emotion regulation (Miller et al., 2013). Another study from the same sample demonstrates links between reduced VF and children's externalizing problems (Ugarte, Miller, et al., 2021). This research advances the notion that context-appropriate variability in autonomic functioning reflects adaptive regulatory coherence and viability (Friedman, 2007), and that reduced VF may provide insight into transdiagnostic, dimensional risk for psychopathology.

Research also suggests that there may be particular utility in clarifying the links between children's VF and risk for *social* anxiety. In addition to sharing peripheral connections to neural structures that support ongoing assessments of safety and threat (Cacioppo et al., 2007; Wagner & Waller, 2020), the PNS has neuroanatomical links with the cranial nerves that regulate and facilitate social engagement and communication via facial expression and vocalization (Porges, 2009). The PNS also promotes effective social communication by inhibiting sympathetic arousal, promoting homeostatic functioning, and supporting flexibility in attention and behavior, all of which are necessary for effective functioning in a dynamic social world (Carter & Porges, 2013; Mendes, 2019; Yaroslavsky et al., 2014). Indeed, individual differences in PNS flexibility (e.g., withdrawal and recovery) are related to the accurate detection of social and emotional cues, as well as adaptive responses to dynamic social feedback across contexts (Hastings et al., 2008; Muhtadie et al., 2015). Recent evidence also demonstrates links between context-specific VF and observations of preschoolers' socially competent behaviors in the classroom (Darling et al., 2022). Determining whether children's VF can be leveraged to differentiate risk for social anxiety specifically will require additional research, including work that assesses children's VF across both social and nonsocial contexts and explores whether their associations with anxiety vary by subtype. That said, research does support the assertion that VF provides insight into the integration and functioning of multiple systems (e.g., cognitive, affective, neurophysiological) underlying children's social functioning. As noted, whether measures of children's autonomic regulation, including VF, can enhance diagnostic specificity remains an open question, particularly in light of the well-documented heterogenous nature of psychological disorders and the promise of dimensional approaches to classification and measurement (e.g., Beauchaine & Hinshaw, 2020; Kotov et al., 2017; Waldman et al., 2022). However, the current findings do support the possibility that measures of VF may hold clinical value, particularly in their ability to provide insight into mechanisms and processes underlying etiological risk for psychopathology, including risk for anxiety.

Measures of VF may also hold value both as a direct treatment target and as a supplement to treatment outcome measures. One prospective longitudinal study (n = 956) reported that reduced autonomic flexibility at ages 10–12 years predicted anxiety levels two years later (Greaves-Lord et al., 2010), and Schmitz and colleagues (2011) demonstrated links between restricted autonomic flexibility (i.e., reduced RSA reactivity and slower recovery) and social phobia in a sample of children aged 8 to 12 years (Schmitz et al., 2011). Mathewson and colleagues (2013) reported that change in RSA levels over time was a stronger predictor of anxiety reduction than was baseline RSA in the context of cognitive behavioral therapy intervention for social anxiety disorder among adults (Mathewson et al., 2013). Finally, there is evidence that parenting interventions contribute to children's improved autonomic regulation (Hastings et al., 2019), and research provides preliminary support for the efficacy of Autonomic Nervous System Biofeedback Modality treatments for child attention problems (Eisenberg et al., 2004). However, much more research is needed to clarify the potential utility of measures of VF in the context of treatment and intervention, including work that carefully considers the complex intersection between the developmental course of the PNS and the onset of psychological disorder.

Strengths of the current study include the use of a modeling strategy that allows for the estimation of non-linear patterns of vagal functioning across a series of tasks designed to mimic exposure to novelty. Pre-treatment data also allows for examining the links between children's VF and risk for anxiety among behaviorally inhibited preschoolers, a group of children at an increased risk for anxiety outcomes. However, using a highly-BI sample in the current study also limits the extent to which these findings generalize to broader populations. Future studies should test whether the current findings generalize to larger, community-based samples. In addition, the current study used exposure to a clown as one of the socially stressful tasks. Although clown exposures have been used in BI research for decades (e.g., Kagan et al., 1989; Kagan & Snidman, 1999), this paradigm lacks ecological validity compared to other tasks, such as exposure to an unfamiliar adult (i.e., stranger approach). Moreover, the task designed to mimic social introductions used images of same-aged peers rather than actual interactions with peers. It is also possible that more variability in RSA change across tasks would have been observed the use of more ecologically valid tasks. Future studies can advance this line of research by examining links between anxiety and children's VF while interacting with unfamiliar adults or children in ecologically valid contexts (e.g., classrooms). Despite these limitations, the current study suggests that, among inhibited youth, less VF may be a risk factor for anxiety, possibly reflecting an individual's reduced capacity to regulate effectively in novel contexts.

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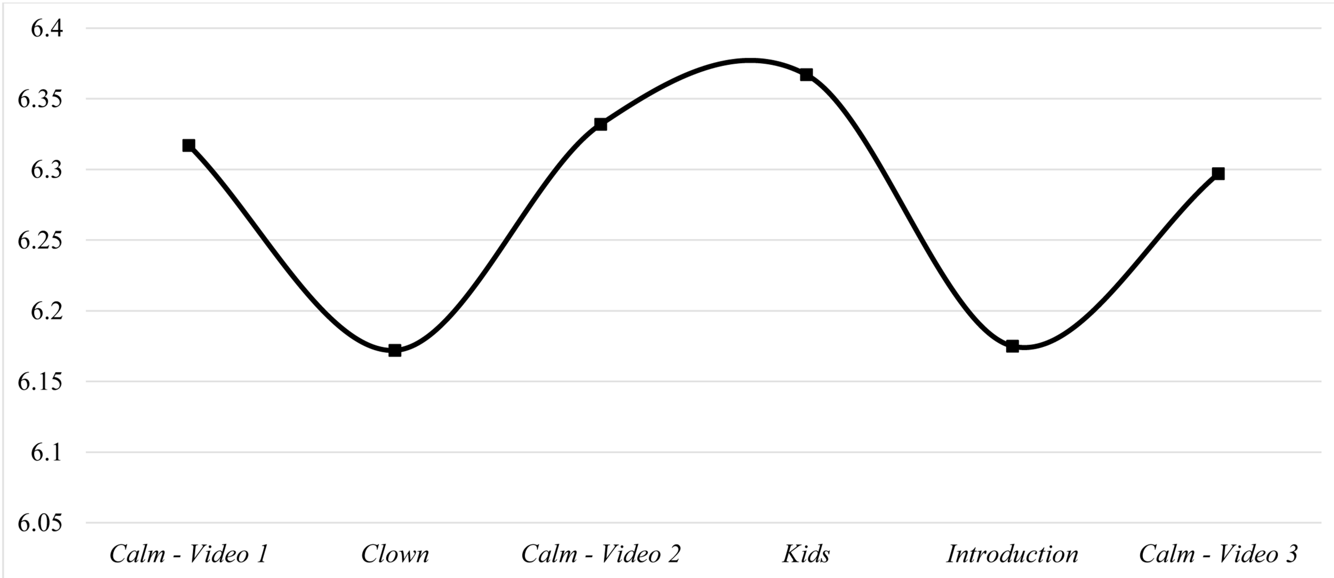

Figure 1.
Model-implied RSA levels across social stressor tasks.

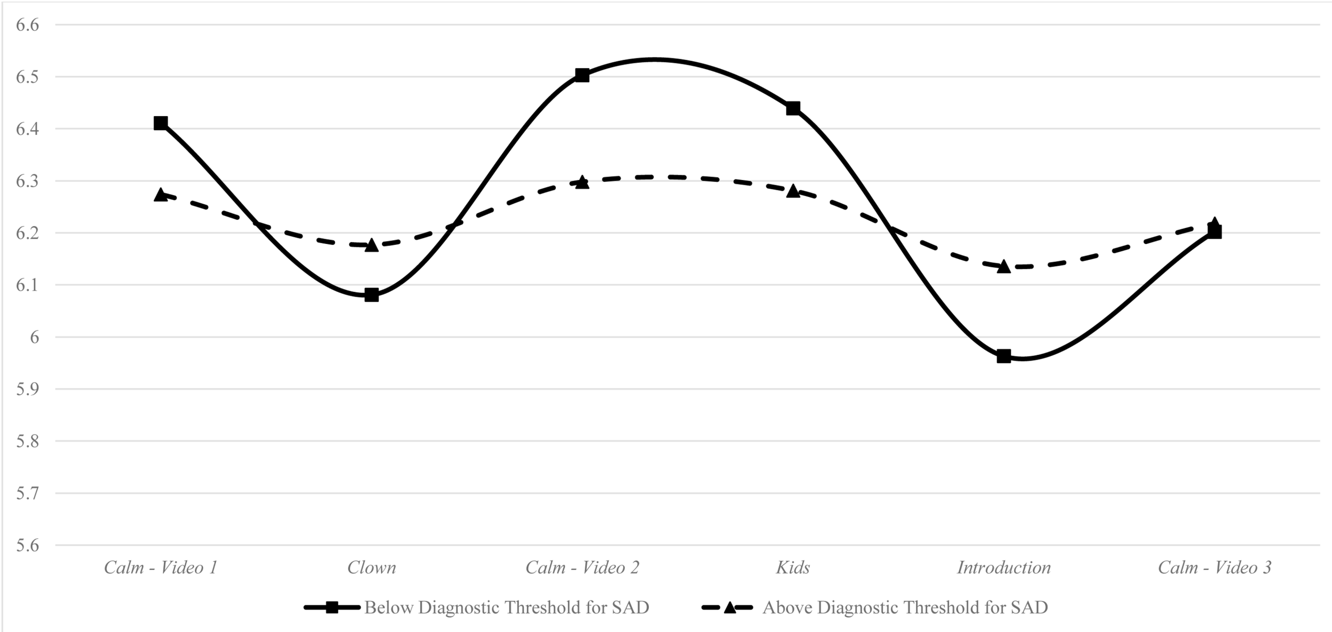

Figure 2.

Model-implied RSA levels across social stressor tasks as a function of meeting diagnostic criteria for clinically-significant impairment in social anxiety. Group intercepts did not significantly vary, Wald's $X^2(1) = 0.87$, $p = 0.35$, but group slopes did significantly vary, Wald's $X^2(1) = 7.07$, $p = 0.0078$.

Table 1

Zero-order bivariate correlations and descriptive statistics

	1	2	3	4	5	6	7	8	9	10	11	12	14
1. Cohort	-												
2. Child Sex (2=female)	−0.02	-											
3. Child Age in Months	0.04	−0.12	-										
4. Child Race (2=white)	−0.12	−0.07	−0.07	-									
5. Parent Education	0.03	0.03	−0.05	−0.07	-								
6. RSA Calm-Video 1	0.02	−0.02	−0.06	0.04	0.04	-							
7. RSA Clown	0.04	−.19*	−0.04	0.13	0.06	.72**	-						
8. RSA Calm-Video 2	0.09	−0.05	0.08	0.09	0.01	.86**	.73**	-					
9. RSA Kids	0.11	−0.13	0.06	0.06	0.04	.79**	.73**	.88**	-				
10. RSA Introduction	.23**	−0.03	−0.05	0.11	0.05	.65**	.64**	.71**	.76**	-			
11. RSA Calm-Video 3	0.10	−0.02	−0.04	0.16	0.02	.78**	.68**	.81**	.84**	.81**	-		
12. Parent-Rated Anxiety	−0.09	−0.02	0.05	0.08	−0.13	0.05	0.04	0.07	0.11	0.16	.22*	-	
13. Clinician-Rated Anxiety	−.38**	−0.15	0.01	0.05	−0.01	0.06	0.12	0.02	0.02	0.16	0.13	.35**	-
Number	151	151	151	151	147	129	117	131	127	126	126	144	148
Mean	-	1.5	52.9	1.5	7.7	6.34	6.11	6.33	6.38	6.13	6.31	1.32	4.84
Standard Deviation	-	-	5.7	-	1.16	0.80	0.87	0.83	0.87	0.81	0.80	0.19	2.34

Note: Parent education ranged from 1 = less than high school to 9 = doctoral degree or equivalent.

Table 2

Fit statistics for unconditional and unmodified growth models fit to the RSA data during social stressor tasks

	Linear	Quadratic	Latent Basis
x^2 (*df*)	71.74 (16)	55.88 (13)	41.59 (12)
LRT	-	Δx^2 = 15.86 (3), *p =0.001*	Δx^2 = 14.29 (1), *p = 0.0002*
CFI	0.926	0.943	0.961
RMSEA	0.159	0.155	0.134

Note: *df* = degrees of freedom; CFI = comparative fit index; RMSEA = root mean square error of approximation; Likelihood Ratio Test

Table 3

Parameter estimates for tests of the predictive relations between children's dynamic RSA change and anxiety outcomes

Parameter	Clinician-Rated Anxiety B (β)	Parent-Rated Anxiety B (β)
Cohort	−0.43 (−0.46)**	−0.02 (−0.19)*
Child Sex	−0.51 (−0.08)	−0.02 (−0.04)
Child Age	−0.01 (0.01)	0.01 (0.05)
Child Race	−0.38 (−0.06)	0.02 (0.04)
Parent Education	−0.05 (−0.02)	−0.04 (−0.13)
RSA Intercept	0.81 (0.19)^	0.06 (0.15)
RSA Slope	−4.94 (−0.27)*	−0.47 (−0.28)*

Note:

** = $p > .01$

* = $p > .05$

^ = $p < 0.1$