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An Initial Investigation of Baseline Respiratory Sinus Arrhythmia as a Moderator of Treatment Outcome for Young Children Born Premature With Externalizing Behavior Problems

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The aim of the current study was to examine the moderating effect of baseline respiratory sinus arrhythmia (RSA) on Parent-Child Interaction Therapy (PCIT), a behavioral parent-training intervention, for young children born premature. In this pilot randomized controlled trial, 28 young children (mean age of 37.79 months), who were born <37 weeks gestation and presented with elevated externalizing behavior problems, were randomly assigned to an immediate treatment or waitlist control group. RSA, which provides an approximate marker of individual differences in cardiac vagal tone, was measured during a baseline period. Past research has generally shown that higher levels of baseline RSA correlate with various positive psychological states (e.g., empathy, sustained attention), whereas lower levels of baseline RSA correlate with less optimal psychological states (e.g., higher externalizing behavior problems). Results indicated that baseline RSA significantly interacted with treatment condition in predicting changes in child disruptive behavior. Specifically, low levels of baseline RSA were associated with greater improvements in child disruptive behavior following PCIT. While acknowledging the caveats of measuring and interpreting RSA and the need to include a sympathetic-linked cardiac measure in future research, these findings provide preliminary evidence that children with lower capacity for emotion regulation receive even greater treatment gains. Future research should also examine the moderating effect of RSA in larger samples and explore the potential mediating role of RSA on behavioral parenting interventions.

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Externalizing behavior problems occur frequently in early childhood (Carter, Briggs-Gowan, & Davis,

2004) and are associated with high impairment and poor outcome without treatment (Campbell, Shaw, & Gilliom, 2000). Preterm birth, which has increased considerably in the last decade (Berman & Butler, 2006), is a common risk factor for these behavior problems (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Bhutta, Cleves, Casey, Cradock, & Anand, 2002). Prematurity has been associated with difficulties in emotional regulation in infants ages 6 to 22 months (Lowe, Woodward, & Papile, 2005; Maclean, Erickson, & Lowe, 2009), which influences the course of child externalizing behavior problems (Eisenberg et al., 2001; Gilliom, Shaw, Beck, Schonberg, & Lukon, 2002) and can affect a child's response to treatment. Therefore, the purpose of this study was to assess the potential or capacity for emotion regulation[1] in children born premature as a moderator of treatment outcome.

Recent research has examined physiological correlates of emotion and/or its regulation in young children, including cortisol (Blair et al., 2008), skin conductance (El-Sheikh, 2007), and electroencephalography (EEG) asymmetry (Fox & Calkins, 2003). For example, respiratory sinus arrhythmia (RSA), which measures the variability in heart rate (HR) that occurs at the frequency of respiration (Berntson et al., 1997), has emerged as an approximate marker of both child and adult differences in cardiac vagal tone (Beauchaine, 2001; Grossman & Taylor, 2007; Porges, 2001). During a baseline period, high levels of RSA are thought to represent an inhibitory influence of the brainstem on the heart (via the vagus or 10th cranial nerve), allowing the individual to appropriately respond and regulate to the environment (Porges).

Consistent with polyvagal theory, research has suggested that baseline RSA is a correlate of child emotion regulation difficulties (Porges, 2007) and can be one useful measure of the child's potential for emotion regulation or vulnerability to stress (Beauchaine, 2001; Calkins, 2007). However, criticisms of polyvagal theory suggest RSA does not always accurately reflect tonic vagal efferent discharge originating in the nucleus ambiguous and can, in fact, be affected by sympathetic tone (Berntson, Cacioppo, & Quigley, 1993; Grossman & Taylor, 2007). For example, pharmacological blockage studies have shown that beta-adrenergic effects increase the magnitude of RSA (Cacioppo et al., 1994; Taylor, Myers, Halliwill, Seidel, & Eckberg, 2001). Research has also shown the influence respiration and physical activity both have on RSA variance (Grossman & Taylor, 2007). In addition to the associated measurement issues, we recognize that a single physiological indicator does not necessarily have a one-to-one correspondence with behavioral events (Cacioppo & Tassinary, 1990). Given these limitations, the present study conceptualizes RSA as a *broad marker* of individual differences in cardiac vagal tone, which can partially contribute to children's potential for emotion regulation.

Research examining the relationship between baseline RSA and externalizing behavior problems in young children has yielded varying results depending on the child's age. School-aged children with clinically elevated externalizing behavior problems had lower baseline RSA than matched controls (Pine, et al., 1998), but this negative relationship has not been demonstrated among preschool-age children (Beauchaine, Gatzke-Kopp, & Mead, 2007; Crowell, et al., 2006). Hinnant and El-Sheikh (2009) found that low baseline RSA among 6-year-old children predicted higher externalizing behavior problems at 8 years of age. However, this finding was only present for children with low RSA suppression during a stressor condition, which has also been shown to be associated with externalizing behavior problems in young children (Calkins, Blandon, Williford, & Keane, 2007). While low baseline RSA also correlates with less optimal psychological states in toddlers, such as externalizing behavior problems (Calkins & Dedmon, 2000), higher levels of baseline RSA correlate with positive child psychological states, including sustained attention in school-age children (Suess, Porges, & Plude, 1994) and sociability in 5- to 6-year-old children (Doussard-Roosevelt, Montgomery, & Porges, 2003).

Measuring baseline RSA in children born premature is particularly relevant because prenatal and perinatal risk factors are thought to affect core brain systems (e.g., brainstem, limbic system) that relate to regulatory functions, including stress and emotion (Geva & Feldman, 2008). Given the rapid brain development during the last quarter of gestation, children born premature are hypothesized to be at greater risk for a disruption in the flow of these systems, especially given that the brainstem precedes the development of higher-order cortical functions important for effortful levels of emotion regulation (Geva & Feldman). However, there has been limited research focusing on the relationship between RSA and externalizing behavior problems during early childhood among children born premature. In one

[1] The term *regulation* has been defined by researchers in several different ways and can include emotional, physiological, attentional, and behavioral processes (Feldman, 2009). In this paper, the focus is on a broad physiological marker for emotion regulation, but we recognize that this is a highly complex system in which all these processes are interrelated.

study, lower baseline RSA of 20 very low-birth-weight (i.e., < 1,500 grams) preterm neonates was associated with more behavior problems at 3 years of age (Doussard-Roosevelt, McClenny, & Porges, 2001). A more recent longitudinal study employed structural equation modeling to demonstrate that low baseline RSA of 125 preterm neonates predicts a higher prevalence of behavior problems 5 years later both directly and indirectly via emotional and attentional processes during the first 2 years of life (Feldman, 2009). Based on these studies, lower baseline RSA during the neonatal period appears to be related to higher levels of behavior problems in children born premature.

The previously described research findings suggesting RSA is a physiological correlate of externalizing behavior problems has implications for translational research on evidence-based treatments for young children. Assessment of biological factors such as RSA may predict treatment response and provide information about how to enhance current evidence-based practices. For example, parents' positive limit setting has been shown to be positively associated with preschoolers' self-regulation (Lecuyer-Maus & Houck, 2002). Children with decreased capacity for emotion regulation may respond better to positive changes in parental discipline. However, only two studies have examined physiological measures as potential moderators of treatment response for children with externalizing behavior problems, and findings have varied.

A study of 23 school-age children (7 to 12 years) with disruptive behavior disorders indicated that children with lower baseline HR were less likely than children with higher baseline HR to respond to a 2-week summer treatment program (Stadler, et al., 2008). While this study is consistent with some previous developmental psychology research showing an association between low HR and greater levels of antisocial behavior (Raine, Venables, & Mednick, 1997), it did not assess for parasympathetic influences on HR variability (i.e., RSA). In fact, a recent study has shown that when examined together, RSA, but not HR, distinguishes young children with and without externalizing behavior problems (Calkins, Graziano, & Keane, 2007). Therefore, it is particularly important to simultaneously measure HR and RSA in order to better approximate the parasympathetic influences on HR variability.

To our knowledge, there has only been one study examining the moderating effect of RSA (while controlling for HR) on psychosocial treatment outcome for children. Beauchaine, Gartner, and Hagen (2000) found that RSA, measured during an inpatient intake procedure, interacted with diagnostic status in predicting inpatient treatment response among 56 adolescent males with conduct disorder. Specifically, low baseline RSA before treatment was associated with increased aggression for patients with comorbid depression but decreased aggression for patients without depression. This study suggests low RSA is associated with an improved treatment response for children and adolescents with disruptive behaviors. A comorbid diagnosis of depression, however, reverses this relationship, which may be due to the effect of emotionality on RSA. Taken together, the limited research on the effect of physiology on treatment yields conflicting findings and highlights the need for further research in this area.

The present study is the first to examine the moderating effect of RSA on psychosocial treatment response among young children with externalizing behavior problems. In addition, no study has examined the relationship between any physiology measure and treatment response among an at-risk sample of children born premature. Based on the findings described above, we predict that baseline RSA before treatment will be associated with treatment response. There have been a number of studies demonstrating children with higher levels of behavior problems and ecological risk display an increased benefit from parent-training interventions (Drugli, Larsson, Fossum, & Mørch, 2010; Hemphill & Littlefield, 2006; Lundahl, Risser, & Lovejoy, 2006). Given the association between low baseline RSA and higher levels of behavior problems among children born premature (Doussard-Roosevelt et al., 2001; Feldman, 2009), we expected low baseline RSA would be associated with an enhanced treatment response as measured by the frequency of parent-reported child disruptive behaviors.

Method

PARTICIPANTS

Participants were 28 mothers and their young child between the ages of 20 and 60 months who was born <37 weeks gestation. Eighty-two percent had either very low (<1,500 grams) or extremely low (<1,000 grams) birth weight, with only 1 child weighing >2,500 grams (3,000 grams), highlighting the high-risk nature of the sample. Children were referred between August 2007 and December 2008 by the director (B.R.V.) of a neonatal follow-up clinic (79%), health professionals at other pediatric sites (9%), staff at state-funded early-intervention programs (6%), or self-referred by their mother after seeing a study brochure (6%). Children were mostly boys (71%), with a mean age of 37.79 months ($SD = 13.29$). Racial composition was 82% White, 10% Biracial, 4% African

American, and 4% Asian, and 21% of children were Hispanic. Families had a mean Hollingshead (1975) score of 43.39 ($SD = 13.21$), which falls in the middle range of socioeconomic status.

For study inclusion, the child had to have been born <37 weeks gestation and mothers had to rate their child above the clinically significant range on the Externalizing Problems scale of the Child Behavior Checklist for 1½ to 5 Year Olds (Achenbach & Rescorla, 2000) and be able to speak and understand English. Exclusion criteria for children included major sensory impairments (e.g., deafness, blindness), significant motor impairments (e.g., cerebral palsy significantly affecting mobility), and oxygen dependence for chronic lung disease. None of the 53 children attending the initial screening assessment were excluded based on these criteria. Children with symptoms of autism spectrum disorder were excluded at the screening evaluation ($n = 2$). Mothers had to obtain a score of at least 75 on the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999), a cognitive screening measure, but no mother was excluded based on this criterion. Seven children did not meet entry criteria at the screening evaluation due to scores below the borderline clinically significant range on the measure of externalizing behavior problems. The remaining 11 families were not interested in continued participation despite their child meeting screening criteria.

SCREENING MEASURES

Child Behavior Checklist for 1½ to 5 Year Olds (CBCL; Achenbach & Rescorla, 2000)

The CBCL is a 99-item parent-rating scale designed to measure the frequency of children's behavior and emotional problems. The CBCL has demonstrated very good 8-day test-retest reliability ($r = .68$ to $.92$, mean $r = .84$), interrater reliability (mean mother-father $r = .61$, mean parent–child care provider $r = .65$), and success in discriminating between referred and nonreferred children (Achenbach & Rescorla). Raw scores on the Externalizing Problems scale (Cronbach's $\alpha = .81$ in the current sample) are converted to T-scores, with a mean of 50 and a standard deviation of 10. A T-score greater than 60 (i.e., borderline clinically significant range) on the Externalizing Problems scale was required for study inclusion.

Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, Barton, & Green, 2001)

The M-CHAT is a 23-item parent-rating scale of yes/no responses designed to identify children at risk for autism, and it is considered appropriate for children ages 18 to 48 months (Snow & Lecavalier, 2008). Children are identified as at-risk on the M-CHAT with 3 or more failed responses. The standardization sample of 1,293 children yielded high internal consistency (.85), as well as moderate sensitivity (.85–.87) and high specificity (.93–.99; Robins et al., 2001), and Cronbach's α in the current sample was .56. Parent report in conjunction with clinical judgment was used for identification of autism in children older than 48 months.

Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999)

The WASI is a short and reliable measure of intelligence, and the two-subtest version yields a Full Scale Intelligence Quotient (FSIQ-2) with a mean score of 100 and a standard deviation of 15. The WASI FSIQ-2 correlated .87 with the FSIQ of the Wechsler Adult Intelligence Scale–Third Edition (Wechsler, 1997) and has high test-retest reliability, ranging from .83 to .90 (Wechsler, 1999), as well as good concurrent validity with other tests of intelligence (Hays, Reas, & Shaw, 2002). The WASI FSIQ-2 was used to exclude mothers with cognitive impairment.

MEASURES OF CHILD BEHAVIOR AND PHYSIOLOGICAL FUNCTIONING

Eyberg Child Behavior Inventory (ECBI; Eyberg & Pincus, 1999)

The ECBI is a 36-item parent-rating scale of child disruptive behavior in children. The Intensity scale measures the frequency with which disruptive behavior occurs on a scale from 1 (*never*) to 7 (*always*) with the range of possible values between 36 and 252. The ECBI Intensity scale yields an internal consistency coefficient of .95 (Eyberg & Pincus); interrater (mother-father) reliability coefficient of .69 (Eisenstadt, McElreath, Eyberg, & McNeil, 1994); and test-retest reliability coefficient of .80 across 12 weeks and .75 across 10 months (Funderburk, Eyberg, Rich, & Behar, 2003). The ECBI has also shown sensitivity to treatment change (Taylor, Schmidt, Pepler, & Hodgins, 1998; Tynan, Schuman, & Lampert, 1999; Webster-Stratton & Hammond, 1997). Although no minimal difference score has been identified, most treatment researchers use the clinical cutoff of 132 (T-score of 60) as an index of clinical improvement. The ECBI Intensity scale (Cronbach's $\alpha = .90$ in the current sample) was used as the outcome measure of child disruptive behavior.

RSA

RSA was computed from Electrocardiogram (ECG) signals that were recorded by telemetry and digitized at a 1 millisecond sampling rate using the BIOPAC MP100 Data Acquisition System (BIOPAC Systems Inc., Goleta, CA). ECG was acquired by placing three electrodes on the child's chest and abdomen. The electrodes were connected to a wireless transmitter, stored in a small backpack worn by the child, and sent to a PC in an adjacent observation room. RSA values were calculated based on automated and manual approaches (Berntson et al., 1997). To control for movement-related artifact, including activity level of the child, a series of automated algorithms detected R–R intervals outside of expected values and corrected them by linear interpolation. Additionally, children's physical activity level was coded using the Laboratory Temperament Assessment Battery (LAB-TAB; Goldsmith & Rothbart, 1993), in which children could receive a value from 0 (*not active; still most of time, even when unfocused on activity*) to 4 (*very active; constantly moving, can't be distracted into being still*). Forty percent of the tapes were recoded for reliability and yielded an interrater reliability of 91%. A majority (89%) of the children displayed minimal activity (scores of 0 or 1) while seated on a chair during the baseline period. Given such minimal activity, it was not surprising that children's scores on this measure were not significantly related to HR or RSA ($p > .05$). Therefore, we did not include physical activity in subsequent analyses involving the physiological measures.

RSA values were calculated based on a set of stringent criteria. Baseline RSA was collected during a 10-min baseline period and represents an average score of the first continuous 2 min with no more than 15% artifact rates on average. The computations for the RSA index utilized the time-series analysis and calculations developed by Porges (1986), which is the natural log of the variance of the R–R interval measurements in milliseconds squared. The computational algorithm used a .24–1.04 Hz filter, corresponding with the frequency band of spontaneous respiration in young children. Although lower frequency bands may be used, research with young children has consistently examined this band and identified associations with child functioning (Huffman et al., 1998). This measurement of RSA attempts to estimate vagal influences on cardiac chronotropy, although a number of limitations of this approach need to be considered (see Berntson et al., 1997).

STUDY DESIGN AND PROCEDURE

This study, approved by the Hospital Institutional Review Board, is a secondary analysis of a pilot randomized, controlled trial to determine the efficacy of Parent-Child Interaction Therapy (PCIT) compared to a waitlist control (WL) comparison group that has been published elsewhere (Bagner, Sheinkopf, Vohr, & Lester, 2010). Two computer-generated random numbers lists, one for boys and one for girls, were maintained by a statistician uninvolved in recruitment, intervention delivery, and data collection. After a family met eligibility and provided written informed consent with an assessor during the screening assessment, the statistician assigned the family to the immediate treatment (IT) group if the number was even and the WL group if the number was odd. All families participated in a baseline assessment (Time 1) and were informed of their group status at that time.

At the Time 1 assessment, mothers were asked to complete the ECBI, and the child was provided some toys to play with to get familiar with the new, clinic environment for 20 min. Following the 20-min acclimation period, each mother and child were then observed during a 10-min baseline period seated while watching a pleasant video (e.g., cartoon of Dora the Explorer) to measure resting RSA. An undergraduate research assistant who was masked to intervention status coded the start and end time of the videos in order to determine the start and end time of the baseline period. These times were then used to derive RSA values during the same time period as described above. Four months after the Time 1 assessment, all families were seen for the Time 2 assessment, in which the mother completed the ECBI again. Families participated in a Time 3 follow-up assessment 4 months after the Time 2 assessment, which was a follow-up assessment for IT families and the posttreatment assessment for WL families. All assessments were conducted in the clinic.

Of the 14 IT families receiving PCIT, 11 (79%) completed treatment (average of 13 sessions) and the Time 2 assessment, which was also scheduled 4 months after the Time 1 assessment. A follow-up assessment was completed 4 months after the Time 2 assessment. This follow-up assessment (Time 3) was completed by 10 of the 11 IT families that had completed treatment and the Time 2 assessment. All 14 WL families completed the Time 2 assessment after the 4-month waitlist period. Of the 14 WL families receiving PCIT after the Time 2 assessment, 10 completed treatment and the Time 3 assessment. Due to only the IT group participating in a true follow-up assessment (Time 3 was the posttreatment assessment for WL families), we were unable to examine the long-term effect of RSA on treatment outcome.

INTERVENTION DESCRIPTION

PCIT is a manualized parent-training intervention with extensive research demonstrating its efficacy and long-term maintenance in treating young children with disruptive behavior disorders (Eyberg, Nelson, & Boggs, 2008) and showing promise with other at-risk populations, such as children with abuse history (Chaffin et al., 2004), chronic illness (Bagner, Fernandez, & Eyberg, 2004), and mental retardation (Bagner & Eyberg, 2007). Treatment progresses through two distinct phases: the Child-Directed Interaction (CDI) and the Parent-Directed Interaction (PDI). During CDI, the parents learn to follow their child's lead in play and use differential attention. During PDI, the parents learn to use effective commands and time-out for noncompliance. The therapist coaches each parent in-vivo through a one-way mirror (using a wireless headset) in their use of the skills with their child. Sessions were conducted once a week for approximately 1 hour in length. All therapy sessions were videotaped, and 50% were randomly selected and coded for integrity by a research assistant uninvolved in coding behavioral observations. Accuracy, defined as the percent with which the therapist adhered to key elements of each session detailed in the treatment manual, was 94% (range = 89% – 99%).

DATA ANALYSIS

The moderating effect of baseline RSA on the effect of PCIT on child disruptive behavior was examined using multiple regression analysis with product terms (Jaccard, Guilamo-Ramos, Johansson, & Bouris, 2006). The independent variable was treatment group and was dummy coded (0 = WL group and 1 = IT or PCIT group). The dependent variable was the posttreatment ECBI Intensity score, and the moderator variable was the index of baseline RSA (described above). The Time 1 or baseline ECBI Intensity score was entered as a covariate in the regression equation, so the analysis reflects the effect of PCIT on covariate adjusted change in ECBI Intensity scores as moderated by RSA. Given previously described findings that RSA varies as a function of age, and that age is also associated with Time 1 ECBI intensity scores ($r = .39$, $p = .039$) and Time 1 RSA ($r = .46$, $p = .013$) in the current sample, age (in months) was included as a covariate.

As recommended by Grossman and Taylor (2007), to better estimate the ability of RSA to index cardiac vagal tone, it is important to jointly include HR and RSA in analyses. As expected, HR and RSA were negatively correlated in the two sets of analyses described below ($r = -.57$ and $-.48$). Therefore, HR was also included as a covariate. The moderating effect of RSA was represented with a product term between the dummy variable for treatment group and RSA. Results from this randomized trial demonstrating preliminary efficacy of PCIT for disruptive behavior among children born premature with very large effect sizes between IT and WL groups (Cohen's d range from 0.9 to 2.3) have been reported elsewhere (Bagner et al., 2010). In this study, we focused on *how* this treatment effect changed depending on baseline levels of RSA at pretreatment, and all analyses were planned on an a priori basis. Based on the negative association between baseline RSA and behavior problems among children born premature (Doussard-Roosevelt et al., 2001; Feldman, 2009), the evidence that children with more problems show increased benefit from parent-training interventions (Drugli et al., 2010; Hemphill & Littlefield, 2006; Lundahl Risser, & Lovejoy, 2006), and the finding that low RSA was associated with an improved treatment response for children and adolescents with disruptive behavior disorders (Beauchaine et al., 2000), we predicted that low baseline RSA would be associated with larger decreases in the frequency of parent-reported child disruptive behaviors following PCIT.

In addition to examining the moderating effect of baseline RSA on mean differences in ECBI Intensity scores between the IT and WL groups, we also examined evidence for moderation for both the IT and WL groups after the WL group had "crossed over" and completed treatment. At this point, all individuals were considered treatment completers in one group, so a product term was not calculated for this analysis. We hypothesized that baseline RSA would also predict child response to treatment, defined as the ECBI Intensity score as measured just after completion of PCIT, holding constant the baseline ECBI Intensity score. In this secondary analysis, the pretreatment scores for the WL families were represented by their Time 2 scores, and the posttreatment scores were their Time 3 scores, whereas the pre and posttreatment scores for IT families were represented by their Time 1 and Time 2 scores. Age and HR were again included as covariates. In all regression analyses, the covariates and RSA were mean centered.

Outlier Analyses and Evaluation of Nonnormality

Prior to analysis, the data were evaluated for multivariate outliers for all continuous measures included in the analyses by examining leverage indices for each individual. We defined an outlier as a leverage score 4 times greater than the mean leverage value. No outliers were evident using this criterion in any of the analyses. Standardized df betas were also examined for each individual and each predictor (as well as the intercept) in the linear equations. An outlier was defined as any case with an absolute standardized df beta larger than 1.0. No outliers were observed using this criterion in any of the analyses.

Examination of univariate indices of skewness and kurtosis revealed no skewness above an absolute value of 1.08 and no kurtosis value above an absolute value of 1.14 in any of the analyses. The analyses described below were repeated using robust estimation with bootstrapping as implemented in AMOS 17.0, and all conclusions were the same.

MISSING DATA

In the primary analysis (i.e., IT versus WL groups), 3 IT families dropped out of treatment and did not have Time 2 ECBI Intensity scores; all WL families completed the Time 2 assessment. In addition, baseline RSA was not collected for one child in the IT group due to technological problems. Time 2 ECBI Intensity scores for the 3 families that dropped out of treatment and the baseline RSA score for the one child were imputed using the expectation maximization (EM) method as implemented in SPSS. There were no statistically significant differences between the families with missing data and the families with complete data on the Time 1 ECBI Intensity score, $t(26) = 0.43$, $p = .668$.

In the secondary analysis (i.e., combined dataset), an additional 4 WL families dropped out of treatment and 1 WL child did not have a score for baseline RSA due to technological problems. Scores were again imputed using the EM approach for these 5 WL families, and there were no significant differences between the families with missing data and the families with complete data on the Time 1 ECBI Intensity score, $t(26) = 0.59$, $p = .558$.

Results

PRELIMINARY ANALYSES

Demographic Characteristics and Checks for Successful Random Assignment

IT and WL families were compared on all demographic variables, and there were no statistically significant demographic differences between groups (Table 1). Additionally, there were no significant group differences in baseline HR, RSA, and ECBI Intensity scores in either dataset (see Table 2). These results suggest successful random assignment of participants to group. Therefore, no additional demographic variables (e.g., birth weight, gestational age) were included as covariates in the moderation analyses as random assignment renders these variables uncorrelated with the treatment. As illustrated in Table 2, mothers in the IT group reported significantly lower ECBI Intensity scores at posttreatment than mothers in the WL group in both datasets. Mean baseline RSA levels for children in both groups was comparable to baseline RSA levels reported in another study of young children with externalizing behavior problems (Calkins & Dedmon, 2000).

MODERATION ANALYSIS IN IT VERSUS WL GROUPS

In the primary multiple regression analysis (see Table 3), we first evaluated the unstandardized regression coefficient for the product term (RSA * treatment group), which represents the hypothesized interaction contrast. This term was significant ($p < .05$), suggesting that baseline RSA moderates the effect of PCIT on child disruptive behavior. Specifically, the product term coefficient suggests

Table 1
Demographic Characteristics of Groups

Characteristic	*M* (*SD*) or percent		*t*(26)	$X^2(1)$	*p*
	IT (*n*=14)	WL (*n*=14)			
Child Age (months)	39.71 (14.17)	36.50 (12.96)	-0.63	–	.537
Birth Weight (grams)	1157.00 (651.48)	1246.07 (563.23)	0.39	–	.702
Gestational Age (weeks)	27.71 (3.99)	28.93 (2.34)	0.98	–	.335
APGAR 1 min [a]	3.70 (2.71)	5.50 (2.47)	1.63	–	.119
APGAR 5 min [a]	5.60 (2.84)	7.08 (1.73)	1.51	–	.147
Perinatal Morbidity (%) [b]	85.7	92.9	–	0.37	.541
Child Sex (% male)	71.4	71.4	–	0.00	1.00
Child Ethnicity (% minority)	35.7	21.4	–	0.70	.403
Hollingshead	40.04 (12.86)	46.75 (13.15)	1.37	–	.184

Note: IT = Immediate Treatment; WL = Waitlist Control.

[a] APGAR scores, only available from 22 of the 28 children, are a simple method to assess the health of newborns (e.g., breathing, heart rate, skin color) measured both 1 and 5 min after birth. Scores ≥ 8 are considered normal, whereas lower scores suggest the newborn needs help adjusting to the new environment and may be indicative of longer-term difficulties.

[b] Perinatal morbidity, dummy coded as a dichotomous variable (1 = yes, 0 = no), was based on maternal report of any of the following: newborn difficulties during the neonatal period (i.e., after birth), including respiratory distress; jaundice; problems with breathing, sucking, swallowing, or feeding; intraventricular bleeding; and other neonatal complications. All but one child (IT group) were admitted to the Neonatal Intensive Care Unit, which is common among preemies.

Table 2
Descriptive Statistics for Physiological and Behavior Measures

	IT		WL		t	p
IT Versus WL Groups	M (SD)	n	M (SD)	n		
Time 1 HR	109.70 (17.49)	13	112.93 (13.65)	14	0.54	.596
Time 1 RSA	6.02 (2.05)	13	5.07 (1.34)	14	-1.43	.164
Time 1 ECBI Intensity Score	147.93 (39.70)	14	146.29 (28.08)	14	-0.13	.900
Time 2 ECBI Intensity Score	71.73 (15.34)	11	147.79 (33.14)	14	7.01	< .001
Combined Group						
Pretreatment HR	109.70 (17.49)	13	104.82 (11.23)	13	-0.85	.278
Pretreatment RSA	6.02 (2.05)	13	6.08 (0.98)	13	0.10	.919
Pretreatment ECBI Intensity Score	147.93 (39.70)	14	147.79 (33.14)	14	-0.01	.992
Posttreatment ECBI Intensity Score	71.73 (15.34)	11	104.00 (39.43)	10	2.51	.021

Note: IT = Immediate Treatment; WL = Waitlist Control; HR = heart rate; RSA = respiratory sinus arrhythmia; ECBI = Eyberg Child Behavior Inventory

that for every 1 unit that baseline RSA increases at baseline, the mean difference between the IT and WL groups on the Time 2 ECBI score (holding constant baseline ECBI scores) was predicted to change, on average, by 12.91 units. Additionally, this interaction term yielded a small to medium effect size ($r^2 = .05$) after controlling for all the other variables. Of note, the interaction between HR and treatment group was not a statistically significant predictor of Time 2 ECBI scores regardless of the presence of RSA as a covariate.

The unstandardized regression coefficient for the treatment variable reflects a simple main effect for treatment. This coefficient was also statistically significant ($p < .05$), indicating the children in the IT group had significantly lower Time 2 ECBI scores than children in the WL group, holding all other variables (including RSA) constant at their mean value. The coefficient value of –72.65 suggests that when RSA is at its mean value, the children in the IT group were predicted to have Time 2 ECBI Intensity scores, on average, 72.65 points lower than children in the WL group. This difference between the IT and WL groups is predicted to increase by 12.91 units with every 1 unit increase in baseline RSA (e.g., for children with a RSA score 1 unit higher than the mean, the IT group is predicted to have Time 2 ECBI scores 59.74 units lower than the WL group) and decrease by 12.91 units with every 1 unit decrease in baseline RSA (e.g., for children with a RSA score 1 unit lower than the mean, the IT group is predicted to have Time 2 ECBI scores 85.56 units lower than the WL group). Figure 1 illustrates the interaction between treatment group and baseline RSA in predicting posttreatment ECBI Intensity scores.

Table 3
Multiple Regression of the Moderation of Respiratory Sinus Arrhythmia on Child Behavior

	Time 2 ECBI Intensity Score B (SE)
IT Versus WL Groups[a]	
Time 1 ECBI Intensity Score	0.39 (0.16)*
Child Age	0.45 (0.52)
Treatment Group	-72.65 (9.37)*
HR	0.28 (0.45)
Time 1 Baseline RSA	-2.48 (5.54)
Time 1 Baseline RSA * Treatment Group	12.91 (6.16)*
Combined Group[b]	
Time 1 ECBI Intensity Score	0.35 (0.13)*
Child Age	-0.72 (0.41)
HR	0.35 (0.37)
Treatment Group	-20.01 (8.47)*
Time 1 Baseline RSA	13.72 (3.10)*

Note. ECBI = Eyberg Child Behavior Inventory; RSA = respiratory sinus arrhythmia.
[a]The multiple correlation for this analysis was .88, $F(6, 21) = 12.41$, $p < .05$.
[b]The multiple correlation for this analysis was .77, $F(5, 22) = 6.30$, $p < .05$.
$*p < .05$.

MODERATION ANALYSIS IN COMBINED GROUP

In the secondary multiple regression analysis for the combined group, we examined the unstandardized regression coefficient predicting the covariate-adjusted posttreatment ECBI Intensity score from baseline RSA and the covariates described earlier. As illustrated in Table 3, this coefficient was statistically significant ($p < .05$), which is consistent with the analyses in the preceding section. The coefficient of 13.72 indicates that for every 1 unit that RSA scores increased at baseline, covariate-adjusted predicted change in ECBI Intensity scores of 13.72 units was observed, on average. Additionally, RSA yielded a large effect size ($r^2 = .36$) after controlling for all the other variables. These findings are consistent with the results from the IT versus WL group dataset, and indicate that higher RSA scores before treatment are

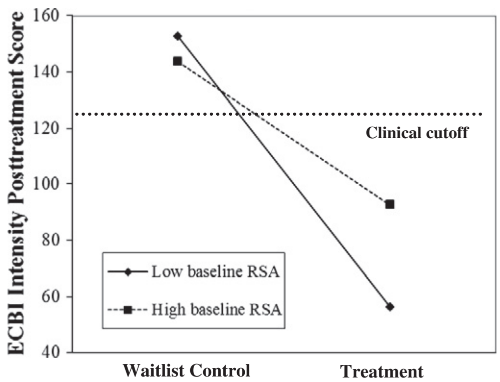

FIGURE 1 Interaction between treatment group and baseline RSA in predicting posttreatment ECBI Intensity scores. Note. Interaction controls for pretreatment ECBI Intensity scores, child age, and child HR.

associated with higher ECBI Intensity scores after treatment for all children.

Discussion

The current study examined the moderating role of baseline RSA on changes in child disruptive behavior following PCIT, a behavioral parent-training intervention, for young children born premature with clinically elevated levels of externalizing behavior problems. The results of this study suggest that children with lower levels of baseline RSA before treatment demonstrate more improvements in child disruptive behavior than children with higher levels of baseline RSA before treatment. Lower levels of baseline RSA were associated with more improvements in child behavior both when examining the effect of treatment between groups (IT vs. WL) and when collapsing across groups in the carry-over design. Observing effects in both forms of analysis increases our confidence in the existence of a moderating effect of baseline RSA on treatment outcome. The findings of the current study were somewhat consistent with the limited research in this area, suggesting that RSA, a broad marker of the child's potential for emotion regulation, before psychosocial treatment is associated with treatment response.

Although the findings supported our initial hypothesis and the limited research in this area, the fact that children with lower baseline RSA demonstrated an enhanced treatment response may seem somewhat counterintuitive. Why would young children with more vulnerability to stress respond better to a psychosocial intervention? One possible explanation is that children with a decreased ability to regulate their emotions are more impaired by their behavioral symptoms and, therefore, have more room to improve in their behavior. Unfortunately, impairment was not measured in the current study but should be examined in future research to test this hypothesis. PCIT also aims to increase positive parent-child interactions, which may improve the child's vulnerability to stress and, in turn, lead to lower frequency of disruptive behavior problems. However, the mediational role of emotion regulation was not examined in the current study but should be explored in future research as well.

Another possible reason for the current findings is that the mothers of children with lower RSA at baseline were more motivated to improve in treatment due to their child's low capacity to regulate their emotions. These mothers may have practiced the learned parenting skills more frequently and applied the discipline strategies more consistently. In addition, changes in child disruptive behavior may have been perceived as more dramatic among mothers of children with lower baseline RSA. It is important to note, however, that PCIT was effective for most of the treated sample of children, which is described in more detail in the main outcome study (Bagner et al., 2010). Therefore, most children benefited from PCIT, but there were differential effects based on the child's initial level of baseline RSA.

This study was the first to explore the moderating effect of physiology on psychosocial treatment among young children born premature, a population at risk for behavior problems and difficulties with emotion regulation. In addition to the innovative nature of the study, there were several methodological strengths. First, the use of a randomized, controlled trial to examine the differential effect of treatment increases internal validity and reduces the possibility of confounding variables. Second, we utilized best statistical practices recommendations for the moderation analyses (Jaccard & Turrisi, 2003) by examining the interactive effects of RSA and treatment. Third, we controlled for child age and HR, which have both been shown to influence RSA in young children. Hence, the variability in HR related to treatment response appears to be at least partially reflecting vagal activity over and above the effect of HR alone. Lastly, our study was careful in accounting for other influences on RSA variance such as children's physical activity during the baseline period, which was found not to influence the current findings.

Despite the preliminary nature of the study, the findings, if supported in future research, have important clinical implications. PCIT led to more improvements for children with low RSA at baseline, suggesting psychosocial parenting interventions may be a particularly good fit for children with more vulnerability to stress. For example, children with comorbid internalizing behavior problems, such as anxiety disorders, may demonstrate an increased benefit from a parenting intervention like PCIT. There has been some evidence suggesting the applicability of PCIT for children with separation anxiety disorder (Chase & Eyberg, 2008; Pincus, Santucci, Ehrenreich, & Eyberg, 2008), but these studies did not specifically examine the effect of treatment on emotion regulation. Additionally, research has supported the relationship between RSA and attention regulation (Marcovitch et al., 2010), which places children at higher risk for later disruptive behavior problems (Hill, Degnan, Calkins, & Keane, 2006). Therefore, an important area of future research is to examine the moderating effect of RSA with other dimensions of child psychopathology, such as anxiety disorders and ADHD.

Children born premature are at risk for poor emotion regulation, and these difficulties have been shown to impact early mother-infant interactions (Feldman, 2006). Taken together with the findings from the current study, it may be helpful to begin targeting mother-infant interactions earlier in life in order to improve these impaired physiological systems and possibly prevent the future occurrence of externalizing behavior problems. Assessment of emotional processes are important in understanding the development and maintenance of child psychopathology (Zeman, Klimes-Dougan, Cassano, & Adrian, 2007), and this knowledge can help inform future efforts at developing effective preventive interventions for at-risk infant populations.

There were several limitations to the current study that need to be addressed. First, the caveats of measuring RSA discussed throughout the manuscript indicate that it is "an approximate marker of individual differences in vagal tone" (Grossman and Taylor, 2007), and the small effect sizes in relation to child behavior in previous research further indicates that it at best represents a broad marker of potential for emotion regulation and/or vulnerability to stress (Calkins, Graziano, et al., 2007; El-Sheikh, 2005; Graziano, Keane, & Calkins, 2007). However, the only study to date examining the effect of RSA on treatment response (Beauchaine et al., 2000) yielded a large effect size ($d = .75$). Therefore, despite our small sample, our large effect size when combining all children who received treatment, while taking into account the caveats of interpreting RSA (i.e., controlling for physical activity and heart rate), increases confidence that our findings were not due to chance.

Nevertheless, it is important to rule out other factors that might have affected our findings. For example, a larger sample may have yielded greater variability in baseline perinatal characteristics (e.g., APGAR scores), which could be important to consider in future research examining the effect of RSA on psychosocial treatment. In addition, the current results may be limited to predominantly middle-class samples, rather than children from lower SES backgrounds, who typically experience more proximal risk factors, such as maternal depression and the home environment (Pachter, Auinger, Palmer, & Weitzman, 2006). Given the concerns associated with the small sample size and issues with generalizability, the current results should be replicated in a larger, more diverse sample.

A second limitation to the study findings is attrition. The treatment dropout rate of the IT group for the main outcome study was relatively low (3 of 14 or 21%) in comparison to other psychosocial treatments (40% to 60%; Wierzbicki & Pekarik, 1993). However, the retention rate was lower (68%) after collapsing groups because the secondary, carry-over design included the 7 families that dropped out of treatment from both the IT and WL groups and the 2 children with missing RSA data due to technological problems. Subsequent analyses revealed no significant baseline differences between completers and dropouts on any of the measures used in the present study. However, it is possible that families that dropped out of treatment prematurely differed on other constructs not measured in the current study (e.g., parental psychopathology), which may have impacted study findings. Unfortunately, families that dropped out of treatment did not respond to our attempts to contact them, so we were unable to determine specific reasons for dropout. A related limitation of this study is the absence of follow-up data, which does not allow us to evaluate the moderating effect of RSA on child behavior past treatment completion. It is important to examine the long-term effect of baseline RSA on child treatment outcome in future research.

Third, there was no control group of children that were born full term. Therefore, it would be important to examine whether the effect of RSA on treatment is the same for children born full-term or whether this effect is specific to children born premature. Fourth, child behavior problems were based on maternal report, which is subject to rater bias. It would also be important to examine whether the moderating effect of baseline RSA was similar when measuring more objective measures of child disruptive behavior, such as behavioral observations. In addition, we did not have other objective behavioral indicators of emotion regulation to increase confidence that baseline RSA is linked to the child's potential for emotion regulation. Baseline RSA in the current study was not significantly correlated with maternal report on the ECBI or the emotionally reactive subscale on the CBCL, which may have been due to the limited variability of the scores (64% of children scored above the clinical cutoff on both measures). Additionally, the emotionally reactive subscale on the CBCL contains some items that appear to be more related to anxiety (e.g., nervous movements or twitching; shows panic for no good reason) than emotion regulation. Therefore, future research examining RSA among children with elevated externalizing behavior problems should incorporate other parent-report measures (e.g., Emotion Regulation Checklist, Children's Behavior Questionnaire) and behavioral observations (e.g., frustration tasks) that were designed specifically to measure emotion regulation.

Finally, while we conceptualized baseline RSA as a broad marker of potential for emotion regulation and/or overall vulnerability to stress, we recognize that RSA does not equate to cardiac vagal tone and represents one of several physiological markers of young children's capacity to regulate emotion. A review by Grossman and Taylor (2007) highlights several important caveats regarding vagal tone interpretation, including the influence of respiration and physical activity on the magnitude of RSA. For example, anxious children may breathe more quickly and shallowly, which would contribute to a lower baseline RSA level. Although we accounted for children's physical activity, we did not account for individual differences in respiration. Therefore, the current findings should be interpreted in light of this limitation, and future research should include measures of respiration when examining the effect of baseline RSA on the outcome of parent-training interventions.

The interpretation of RSA differences between individuals is also obscured by residual vagal activity while the magnitude of RSA can be affected by beta-adrenergic tone, suggesting RSA is not a pure measure of cardiac vagal control (Grossman & Taylor, 2007). Although it may be difficult to measure beta-adrenergic responses in young children via pharmacological blockage studies, it is feasible to examine sympathetic-linked cardiac activity (i.e., preejection period [PEP]). Simultaneously examining RSA and PEP can help differentiate whether heart rate variability stems from the sympathetic and/or parasympathetic branches of the autonomic nervous system (ANS). For example, Crowell et al. (2006) found that heart rate variability among children with ADHD and ODD were mediated entirely by RSA and not by PEP. Given that the current study did not have a sympathetic cardiac-linked measure, it is possible that RSA would not have predicted treatment response if PEP was included in the analyses. Therefore, we cannot be certain which branch of the ANS was contributing to children's heart rate variability and subsequently whether the mechanism predicting treatment response represented the child's capacity for emotion regulation or general arousal levels.

Despite the limitations, the current study addressed a novel and relatively unexplored research question by examining the influence of RSA on child behavioral response to a behavioral treatment. In addition, the sample included children born premature who are at risk for impaired emotion regulation. The finding that children with lower RSA at baseline display enhanced response to treatment has implications to improve treatment and develop effective preventive intervention programs. Future research should examine the moderating role of other physiological measures of emotion regulation on treatment response in children born premature and other at-risk child populations. In addition, exploring the mediating role of RSA in child psychosocial treatment will help provide a more comprehensive understanding of the mechanisms of behavioral parent-training interventions for young children with behavioral problems.

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