Emotion Regulation and Heterogeneity in Attention-Deficit/Hyperactivity Disorder

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Objective: How best to capture heterogeneity in attention-deficit/hyperactivity disorder (ADHD) using biomarkers has been elusive. This study evaluated whether emotion reactivity and regulation provide a means to achieve this. **Method:** Participants were classified into three groups: children with ADHD plus low prosocial behavior (hypothesized to be high in callous/unemotional traits; n = 21); children with ADHD with age-appropriate prosocial behavior (n = 54); and typically developing children (n = 75). Children completed a task with four conditions: negative induction, negative suppression, positive induction, and positive suppression of affect. The task required children to view an emotion-laden film clip, while either facially mimicking (induction) or masking (suppression) the emotion of the main character. Parasympathetic and sympathetic nervous system activity were assessed via respiratory sinus arrhythmia (RSA) and cardiac pre-ejection period (PEP), respectively. Symptoms of anxiety, conduct, and oppositional defiant disorders were treated as covariates. **Results:** The ADHD-typical-prosocial group displayed atypically elevated parasympathetic reactivity (emotion dysregulation) during positive induction, along with increased sympathetic activity (elevated arousal) across conditions. In contrast, the ADHD-low-prosocial group displayed reduced parasympathetic reactivity and reduced sympathetic activity (low emotional arousal) across baseline and task conditions. Thus, both ADHD groups had altered patterns of autonomic functioning, but in two distinct forms. **Conclusion:** Although ADHD is heterogeneous clinically, results suggest that ADHD is also heterogeneous with regard to physiological indices of emotion and regulation. Future studies of emotion, regulation, and ADHD should take this into account. Further study of physiological responding in ADHD may yield clinically and etiologically distinct domains or groups. J. Am. Acad. Child Adolesc. Psychiatry; 2013; 52(2):163-171. **Key Words:** attention-deficit/hyperactivity disorder, autonomic nervous system, callous/unemotional traits, emotionality, emotion regulation

Attention-deficit/hyperactivity disorder (ADHD) is a clinically heterogeneous condition; however, its presumed biological heterogeneity remains in need of elucidation.[1–3] Emotion reactivity and dysregulation may provide a promising way to achieve this.[4–8] The present study evaluated the heterogeneity in ADHD using physiological indicators of emotion reactivity and regulation.

One suggestion for how to conceptually organize the interpretation of emotion and regulation data was put forward by Beauchaine.[9] This formulation suggests that respiratory sinus arrhythmia (RSA) can be understood as an index of parasympathetic-based regulation, and cardiac pre-ejection period (PEP) as an index of sympathetic arousal. The idea that RSA reactivity is an index of parasympathetic regulation, albeit heuristic, has been proposed by several theories[9–13] and has received empirical support.[14–17] The idea that PEP is an index of sympathetic arousal, although less extensively suggested in the literature, has support with regard to its sympathetic and β-adrenergic origins[18,19] and sensitivity to reward.[20] We have adopted this perspective because of its heuristic value in the current study.

These measures of autonomic reactivity in child psychopathology have been examined before. Indeed, an association of externalizing behavior with reduced sympathetic activity and altered parasympathetic response during emotion-based tasks and reward is rather well established.[22–27] However, it cannot be assumed that these same results will hold for ADHD. One study concluded

Supplemental material cited in this article is available online.

that ADHD was also associated with reduced sympathetic activity during baseline.[21] In a separate study of preschoolers, autonomic responses to reward tasks were characterized by lengthened PEP, as well as parasympathetic withdrawal (dysregulation) in children with both ADHD and oppositional defiant disorder (ODD), suggesting that emotion dysregulation may be associated with both ADHD and ODD in young children.[26] Furthermore, altered parasympathetic nervous system reactivity has also been observed during both the induction and suppression of negative and positive affect in ADHD, with larger effects in the positive domain.[29] Thus, it is possible that physiological indices may help to clarify the heterogeneity in ADHD and reconfirm previous findings of elevated reactivity in response to emotional challenge.

In addition to the emerging role that emotion dysregulation has been hypothesized to play in ADHD, a particular ambiguity in ADHD concerns whether ADHD is characterized by over- or underarousal.[8,9,26–29] One group of children who reliably show underarousal is children with callous/unemotional traits (CU).[30–35] These children are deficit in prosocial emotions and behaviors, including low empathy, lack of a sense of guilt or remorse, shallow or blunted affect, and physiological underarousal.[30–35] In this study, we examine children with ADHD who differed on their prosocial behavioral phenotype (an empirically valid, and perhaps less stigmatizing proxy for CU traits) and validate this physiologically in an effort to clarify differences in arousal and emotion regulation.

In previous studies, CU traits have been studied primarily in the context of conduct disorder and antisocial behavior,[30–35] but, to a lesser degree, in children with ADHD. Experts have called for more careful consideration of CU in relation to ADHD.[36–38] Indeed, CU traits are associated with ADHD even after controlling for comorbid conduct disorder.[36–40] Thus, CU traits (and low prosocial behavior) are clinically important and perhaps theoretically informative for understanding heterogeneity of emotional arousal and regulation in ADHD.

It was hypothesized that variation in prosocial behavior will index biologically distinctions in ADHD on the basis of emotional arousal and regulation. To test this hypothesis, we assessed prosocial behavior and physiological indicators of emotional arousal and regulation in children with ADHD, excluding children with comorbid conduct disorder. We tested a double dissociation that may resolve prior contradictory conclusions about arousal and may also clarify the nature of emotion regulation variation in ADHD. Specifically, children with ADHD with age-typical prosocial behavior (here termed "ADHD") were predicted to have a pattern of parasympathetic reactivity that is characteristic of ADHD per se, which is to say, elevated parasympathetic activity from baseline across the affective and regulatory demands of an emotional task. If so, this would support prior findings of atypical regulation in response to emotional challenge among children with ADHD.[21,26,27] In contrast, we hypothesized that children with ADHD and low prosocial behaviors (here termed "ADHD-low-prosocial") would show a pattern more similar to that of past research on antisocial youths with CU traits—namely, reduced parasympathetic reactivity across task conditions along with reduced sympathetic activity (lower arousal).[30,31]

METHOD

Participants

Overview. Participants were 150 children 7 to 11 years of age (mean age = 7.60 years, SD = 0.56 years); 75 met *DSM-IV*[41] criteria for ADHD combined type, and 75 were typically developing comparison youth (Table 1). Of the ADHD group, we assigned 21 to the ADHD-low-prosocial group (criteria outlined below). None of the control group had atypical prosocial behavior scores. By design, none of the children in met *DSM-IV* criteria for conduct disorder.

Families were recruited from the community through advertisements and mailings. The local Institutional Review Board approved the study. All procedures conformed to the Ethical Principles of Psychologists and Code of Conduct.[42] Parents provided written informed consent, and children provided written assent.

Recruitment and Identification. Sample recruitment, assessment, and diagnostic assignment followed procedures identical to those described in more detail elsewhere.[27] In brief, volunteers passed through a multi-gate screening process to establish eligibility and group assignment. After completing a clinical structured diagnostic interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic Version [KSAD-S-E]), parent and teacher standardized ratings, and an IQ screen, a clinical diagnostic team comprising a board-certified psychiatrist and licensed clinical psychologist independently reviewed all case information to arrive at diagnoses using *DSM-IV* criteria.

TABLE 1 Descriptive and Diagnostic Statistics for Attention-Deficit/Hyperactivity Disorder (ADHD) and Control Groups

Variable	Control (n = 75)	ADHD: ADHD Only (n = 54)	ADHD: ADHD + Low Prosocial (n = 21)
Demographic			
Age, mo, mean (SD)	97.41 (6.91)	97.30 (7.08)	97.63 (8.83)
Gender, % male	49.3[a]	52.6[a]	70.4[b]
Race/ethnicity, % white	88.0	86.2	89.5
Family income, $K, mean (SD)	100.35 (46.23)	84.81 (41.43)	98.06 (51.48)
% Two-parent homes	86.7	79.6	75.7
Stimulant med, % on med	0.00[a]	29.6[b]	26.3[b]
WISC-IV FSIQ, mean (SD)	109.11 (5.19)	107.14 (6.84)	104.85 (5.91)
SDQ Subscales–Parent, mean (SD)			
Emotional symptoms	1.34 (1.57)	1.86 (2.04)	2.11 (1.60)
Conduct problems	0.76 (1.28)[a]	2.26 (1.60)[b]	2.89 (1.91)[b]
Hyperactivity	2.32 (2.40)[a]	7.72 (2.07)[b]	7.67 (2.93)[b]
Peer problems	0.81 (1.26)[a]	2.18 (2.11)[b]	2.28 (1.45)[b]
Prosocial behavior	8.97 (1.43)[a]	8.24 (1.90)[a]	4.67 (1.46)[b]
Total difficulties	5.23 (5.04)[a]	14.02(5.22)[b]	14.94 (4.68)[b]
Impact/impairment score	0.23 (0.82)[a]	2.65 (1.98)[b]	3.12 (2.04)[b]
SDQ Subscales–Teacher, mean (SD)			
Emotional symptoms	1.23 (1.54)	1.44 (1.87)	1.56 (1.95)
Conduct problems	0.33 (1.11)[a]	1.83 (1.91)[b]	2.22 (2.77)[b]
Hyperactivity	1.51 (1.93)[a]	7.15 (2.38)[b]	6.50 (3.17)[b]
Peer problems	0.77 (1.06)[a]	1.91 (1.94)[b]	2.20 (2.21)[b]
Prosocial behavior	8.19 (1.83)[a]	7.37 (2.47)[a]	4.29 (1.88)[b]
Total difficulties	3.43 (3.95)[a]	12.23 (5.15)[b]	14.79 (7.13)[b]
Impact/impairment score	0.14 (0.65)[a]	1.83 (1.45)[b]	1.89 (1.88)[b]
Comorbid Disorders, %, K-SADS[c]			
Mood disorder (lifetime)	2.7	3.7	3.7
Anxiety disorder	21.3[a]	23.9[a]	4.7[b]
CD	0.0	0.0	0.0
ODD	8.1[a]	24.7[b]	23.8[b]
Tic disorder	0.0	3.7	0.0
Sleep disorder	5.4	7.1	4.7
CD symptoms, mean (SD), K-SADS	0.02 (0.13)[a]	0.09 (0.25)[ab]	0.18 (0.42)[b]
ODD symptoms, mean (SD), K-SADS	0.44 (1.15)[a]	1.29 (1.86)[b]	1.42 (1.1.84)[b]
Total anxiety Sx, mean (SD), K-SADS	1.31 (1.59)	2.31 (4.19)	1.19 (2.45)

Note: CD = conduct disorder; FSIQ = Full-Scale Intelligence Quotient (estimated); K-SADS = Kiddie Schedule of Affective Disorders and Schizophrenia; med. = medication; ODD = oppositional defiant disorder; Sx = symptoms; WISC-IV = Wechsler Intelligence Scales for Children.

[a, b]Differing superscripts indicate pairwise comparisons that were significant after a modified Bonferroni correction for multiple group comparisons ($\alpha = 0.025$) for continuous variables, including: age, family income, estimated full-scale IQ, Strengths and Difficulties Questionnaire (SDQ) parent and teacher sub-scales, and comorbid symptoms; and χ^2 comparisons for categorical variables, including gender, race, parent marital status, child stimulant medication status, and presence of comorbid disorders.

[c]None (0%) of the sample had autism, eating disorders, learning disorders, post-traumatic stress disorder, psychosis, or substance use disorders.

Agreement rates were acceptable ($\kappa > 0.70$ for all disorders with base rate of greater than 5%, including ADHD). Cases were excluded if agreement was not readily achieved.

Exclusion Criteria. Exclusion criteria for included the use of long-acting psychoactive medications (except stimulants), neurological impairments, seizures, traumatic brain injury, major medical conditions, mental retardation, pervasive developmental disorders, conduct disorder, current mood disorder, lifetime psychosis, or current learning disability. Other disorders were free to vary.

Identification of Social–Emotional Groups. A parent and a teacher of eligible youth completed the 25-item Strengths and Difficulties Questionnaire (SDQ), a well-validated, well-normed survey of child problems and impairment.[43] The Prosocial Behavior scale (inverted) served as a measure of social–emotional maladjustment; it has been previously shown to be a reliable index of CU traits and to load on the same factor in factor analyses of CU measures.[44,45] We specifically chose the SDQ because we wished to evaluate clinical severity in identifying our subgroups, as it has extensive published norms.[43] To confirm the convergent validity of the measure of prosocial behavior in our sample, a subsample of parents (n = 90; 52 ADHD, 38 control) completed the Inventory of Callous/Unemotional Traits (ICU).[46] Total score on the ICU was correlated negatively with the parent SDQ Prosocial Behavior domain at r = 0.742, $p < .001$ (reliability-corrected r = 0.853, $p < .001$). We therefore used the SDQ to identify our clinically low-prosocial group.

To be classified as ADHD-low-prosocial behavior, both the parent and teacher had to endorse a lack of prosocial behaviors in the 90th percentile. This was intended to select children who likely had clinically significant problems in this area. Clinical and demographic features of the groups are provided in Table 1.

Medication Washout. All children who were prescribed stimulant medications were required to complete a washout period of at least five half-lives. All children were stimulant medication free at the time of testing. Twenty-three ADHD children (31% of the ADHD group) were prescribed stimulants. Stimulant prescription status (present or absent) was treated as a covariate to remove the effect of the medication washout (e.g., rebound effects), with no effect on results. Results are presented without covarying medication status.

Emotion Induction and Suppression Procedure. The emotion task and physiological recording procedures were identical to those reported by Musser *et al.*,[27] where they are described in detail. In brief, each child underwent an emotion induction and suppression procedure using both negative and positive emotion-laden film clips.

Four experimental conditions were presented in the same order for all children. In the induction condition, children were to facially mimic the emotion of the main character. In the suppression condition, children were to mask (suppress) the emotion. Each child had the same sequence as follows: negative induction, negative suppression, positive induction, and positive suppression of emotion.

To confirm that "positive" and "negative" film clips had the intended valence, all children completed the Self-Assessment Manikin (SAM) valence and arousal scales[47] for each clip; all groups equally strongly rated the four conditions as differing in valence and arousal (Table S1, available online).

Baseline Conditions. A resting baseline of 2 minutes was presented before the task. A neutral baseline of 2 minutes was presented between the negative and positive task conditions. The neutral baseline consisted of observing a set of 10 neutral pictures from the International Affective Picture System (IAPS).[48] Children again completed the SAM ratings (of the IAPS neutral pictures), and groups did not differ in their SAM ratings of the neutral pictures, all $F < 1.0$; all $p > .10$. All three groups rated them as more neutral than the positive and negative conditions (Table S1, available online).

Physiological Recording

Overview. Disposable silver or silver chloride electrodes were placed in an electrocardiography (ECG) and impedance cardiography (ICG) configuration. The ECG electrodes were placed at the right collar bone and the 10th-left rib with a ground electrode placed at the 10th-right rib. For ICG, two voltage electrodes were placed below the suprasternal notch and xiphoid process, and two current electrodes were placed on the back 3 to 4 cm outside the voltage electrodes. ECG and ICG recordings were made throughout each of the baselines and task epochs. The R-R series was sampled at 1,000 Hz. Interbeat interval and respiration rate data were derived using the ECG and ICG data.

Cardiac Pre-ejection Period. The cardiac pre-ejection period (PEP) was derived from ECG and ICG, in 60-second epochs, using MindWare Impedance Cardiography V. 2.6.[49] PEP was indexed as the time interval in milliseconds from the onset of the Q-wave to the B-point of the dZ/dt wave.[50] Artifacts were examined and removed using the completed by two raters ($\kappa > 0.85$ for each epoch). There were no between-group differences in the rate of artifacts (all $p > .50$).

Respiratory sinus arrhythmia. Respiratory sinus arrhythmia (RSA) was indexed by extracting the high frequency component (>0.15 Hz) of the R-R series. R-R waves were examined for artifacts and outliers using MindWare Heart Rate Variability software V. 2.6.[51] Artifacts were removed using the software by two raters (all $\kappa > 0.91$). Again, there were no group differences in the rate of artifacts (all $p > .50$). RSA was derived using spectral analysis, in 60-second epochs. Spectral analysis was performed on the R-R time series from the ECG. The time series was detrended and submitted to a Fourier transformation. The high-frequency band (ln [ms^2]) was set over the respiratory frequency band of 0.24 to 1.040 Hz. Respiratory rates and amplitudes were derived from the impedance cardiograph signal (Z0).

Analytic Decisions and Plan

Main Hypothesis Tests of Group Comparisons. Group comparisons were conducted using mixed-model, repeated-measures analysis of covariance (ANCOVA). Thus, simple effects for RSA and PEP were tested only when justified by the results of higher-order effects, and no further corrections were implemented.

Group Versus Dimensional Analysis. Analyses were also completed with ADHD group status and continuous prosocial behavior scores as independent variables (as prosocial behavior or CU may be continuous traits, and group cutoffs were a heuristic). The overall results of the analyses did not differ when prosocial behavior was treated as a continuous variable. Although creating groups rather than using continuous scores may reduce power, we chose to present the findings using group assignments because the overall outcomes did not differ, and because the group assignments enable visualization across different subgroups within ADHD. (The results for a dimensional approach are available to interested readers upon request to the first author. Further validity checks are provided in Supplement 1, available online.)

RESULTS

Preliminary Analyses

Descriptive and Diagnostic Overview of Sample. Descriptive statistics and comparisons are reported in Table 1. Groups did not differ with respect to age, race/ethnicity, family income, parent marital status, or IQ, nor did inclusion of any of these variables as covariates affect the results reported. Results are therefore reported without these variables treated as covariates. Groups differed in gender ratio. Gender was unrelated to physiological parameters. However, to remove ambiguity, gender was covaried in all results.

Clinical characteristics are provided in Table 1. Although the ADHD groups had more ODD than the control group, the two ADHD groups did not differ on incidence of ODD. The ADHD-low-prosocial behavior group had significantly fewer anxiety disorders than either the control or ADHD-only group, consistent with past findings that anxiety and CU traits are inversely related.[52,53] The inclusion of comorbid disorders as covariates did not affect any of the main study results, nor did covarying of total ODD symptoms, total conduct disorder (CD) symptoms, or total anxiety symptoms (K-SADS-E). For clarity, we present results with CD, ODD, and anxiety symptoms covaried (as well as gender). Results from models without covariates are available upon request and did not differ from results presented here.

Primary Analyses: Effects of Emotion Induction and Suppression on PEP and RSA

RSA and PEP data for all task conditions and baselines are listed in Table 2.

Effects on Sympathetic Arousal (PEP). A 2×2×3 repeated-measures ANCOVA examined the effects of task condition on raw scores for PEP with covariates as noted. The interaction of valence (negative versus positive) by condition (induction versus suppression) by group (control versus ADHD versus ADHD-low-prosocial) was nonsignificant ($F < 1.0$, $p > .4$). However, there was a group main effect ($F_{1,149} = 3.16$, $p < .05$, $\eta^2 = 0.05$). Specifically, the grand mean of PEP for the control group (97.85, SD = 7.42) was longer than for the ADHD group (95.22, SD = 7.91), but shorter than for the ADHD-low-prosocial behavior group (99.10, SD = 5.71), consistent with the hypothesis that low prosocial behavior would be associated with lower sympathetic arousal. These data are presented in Table 2 and Figure 1.

Effects on Parasympathetic-Based Emotional Regulation (RSA). The mixed-model, 2×2×3, repeated-measures ANCOVA (with gender, CD, ODD, and anxiety symptoms treated as covariates) revealed a significant three-way interaction of valence (negative versus positive) by condition (induction versus suppression) by group (control versus ADHD versus ADHD-low-prosocial) ($F_{1,149} = 3.748$, $p < .01$, $\eta^2 = 0.04$). Simple effects revealed that the ADHD-low-prosocial group showed a smaller increase than the ADHD and control group during negative induction ($t[91] = 2.97$, $p < .05$ and $t[74] = 2.41$, $p < .05$, respectively; Figure 2) and negative suppression ($t[91] = 3.07$, $p < .05$ and $t[74] = 2.08$, $p < 0.05$, respectively; Figure 2). Thus, the children in the ADHD-low-prosocial group did not increase their parasympathetic regulation, whereas both the ADHD and typically developing children did.

Furthermore, in the positive induction condition, the ADHD group's RSA increased from baseline (suggesting regulatory demand was activated), while the control and ADHD-low-prosocial behavior group's RSA decreased from baseline (suggesting no regulatory demand), suggesting that children with ADHD (but not low-prosocial) had a more challenging time regulating positive emotions ($t[129] = 1.96$, $p < .05$ and $t[74] = 2.25$, $p < .05$, respectively; Figure 2). A similar picture emerged during the positive suppression condition: RSA increased from baseline for the control and ADHD group, and this differed

TABLE 2 Respiratory Sinus Arrhythmia (RSA; ms^2) and Pre-Ejection Period (PEP; ms) in Task Epochs for Attention-Deficit/Hyperactivity Disorder (ADHD) and Control Groups

Variable	Control (n = 75)	ADHD: ADHD Only (n = 54)	ADHD: ADHD+CU (n = 21)
Baseline Physiology Data			
Rest baseline			
RSA	7.07 (0.86)	7.22 (0.93)	7.23 (0.83)
PEP	98.64 (8.07)	96.02 (8.27)	99.55 (6.91)
Picture baseline 1			
RSA	6.66 (0.86)	6.93 (0.93)	6.99 (0.83)
PEP	97.38 (5.58)	93.04 (6.24)	101.10 (5.14)
Task Physiology Raw Scores			
Negative induction			
RSA	6.98 (0.80)	7.21 (0.67)	7.28 (0.67)
PEP	97.59 (7.49)	94.40 (8.02)	101.17 (5.73)
Negative suppression			
RSA	7.12 (0.75)	7.25 (0.75)	7.00 (0.66)
PEP	97.45 (7.59)	95.09 (7.71)	99.31 (5.44)
Positive induction			
RSA	6.61 (0.79)	7.09 (0.83)	6.98 (0.71)
PEP	98.18 (7.33)	94.21 (7.55)	98.04 (5.35)
Positive suppression			
RSA	6.90 (0.79)	7.23 (0.82)	7.04 (0.74)
PEP	98.18 (7.45)	95.51 (8.27)	98.34 (6.32)
Task Physiology Change Scores			
Negative induction			
RSA	0.33 (0.48)	0.25 (0.28)	0.06 (0.33)
PEP	0.61 (4.82)	0.98 (4.22)	1.58 (4.96)
Negative suppression			
RSA	0.43 (0.52)	0.32 (0.58)	0.06 (0.48)
PEP	0.59 (4.59)	1.58 (4.62)	0.62 (4.34)
Positive induction			
RSA	−0.05 (1.12)	0.15 (0.33)	−0.05 (0.35)
PEP	0.88 (3.75)	1.51 (3.74)	−0.71 (4.55)
Positive suppression			
RSA	0.25 (0.58)	0.26 (0.58)	−0.06 (0.54)
PEP	1.16 (4.09)	1.68 (4.49)	−0.11 (3.86)

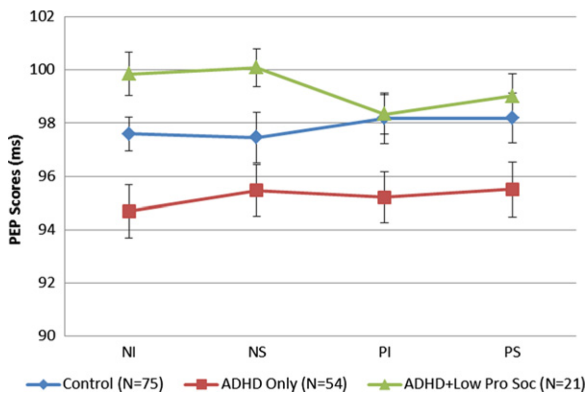
Note: Repeated-measures analysis of variance was used to examine group differences in RSA and PEP reactivity scores across the emotion induction and suppression conditions. CU = callous/unemotional traits.

from that in the ADHD-low-prosocial behavior group, which did not change from baseline (t[129] = 2.29, $p < .05$ and t[74] = 2.27, $p < .05$, respectively; Figure 2). All other simple effects comparisons were nonsignificant (all t values < 1.0).

DISCUSSION

Grouping children with ADHD on the basis of a clinical indicator of atypical levels of prosocial behavior revealed distinct patterns of autonomic reactivity during emotion regulation demands, suggesting that the autonomic response validates this aspect of behavioral heterogeneity in ADHD. The cut-point of 90th percentile received physiological validation: however, other cut-points were not examined. Performance at different cut-points is a future direction. However, results did not depend on this cut-point, as the same results were observed using dimensional analyses. These results also were not explained by associated conduct problems, conduct disorder, other comorbid symptoms or disorders, sex, age, prescription medication status, or conceivable methodological artifacts (i.e., order effects). Thus, the most parsimonious conclusion is that variation

FIGURE 1 Mean cardiac pre-ejection period (PEP) raw scores for each task epoch: negative induction (NI), negative suppression (NS), positive induction (PI), and positive suppression (PS) for control, attention-deficit/hyperactivity disorder (ADHD), and ADHD-low-prosocial behavior groups. Note: Standard error estimates were obtained via analysis of variance.



in emotional processing distinguishes among children with ADHD and is a promising way forward for capturing heterogeneity in ADHD.

Children with ADHD and clinically significant low prosocial behavior displayed blunted parasympathetic and sympathetic activity both at baseline and across task conditions, consistent with tonic reduction of autonomic arousal, even though these children did not have conduct disorder and the effects held after covarying conduct symptoms. This reduced autonomic activity is consistent with past research on low-prosocial children with antisocial behavior. In contrast, children with ADHD and age-typical prosocial behavior displayed elevated sympathetic activity (i.e., high arousal).

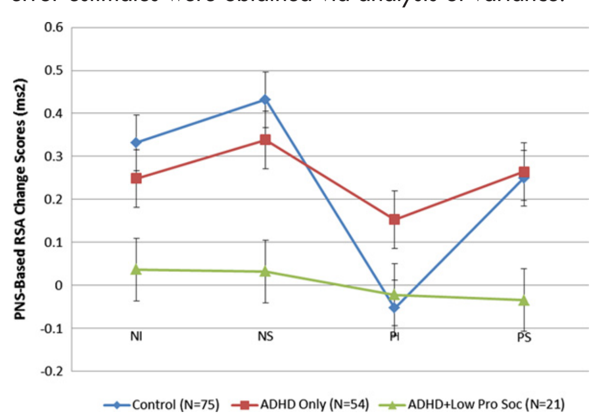
These children also had the strongest activation of their parasympathetic system (largest parasympathetic increase from baseline of all the groups), during the positive emotion induction condition, suggesting that the experience of positive emotions introduces additional regulatory demand for these children. In fact, that this occurred most during the positive condition, may support theories of approach (or reward processing) alteration in ADHD.[29,54,55]

Several alternative interpretations of these data were ruled out, in addition to ruling out effects of comorbid disorders and symptoms. As described above, sympathetic nervous system activity differed across the groups during baseline conditions, and these differences held regardless of task condition. This is consistent with the view that sympathetic nervous system activity/arousal is reduced tonically in individuals with CU traits.[56,57] In contrast, differences in parasympathetic nervous system activity held even after controlling for baseline effects, suggesting that these differences were not due to pre-existing parasympathetic differences in homeostatic functioning but rather to regulatory differences. Furthermore, children's self-reported emotion valence and arousal levels during the emotionally neutral task suggested no pre-existing differences in emotion or task engagement among the groups.

These results are broadly consistent with past research findings in children with conduct disorder and co-occurring CU traits, in which CU traits have been shown to moderate emotional responding.[53] However, this study breaks new ground in isolating the effects of prosocial behavior (i.e, CU traits) in ADHD. This design was intended to facilitate parsing the unique heterogeneity of ADHD by examining a specific subgroup of children with ADHD and altered social–emotional functioning. These findings build upon other studies that report differences in sympathetic functioning among children with ADHD and comorbid conduct problems when compared to typically developing youth, but which found attenuated sympathetic activity in response to reward-based tasks.[26,27,58]

Results should be interpreted in light of key limitations. First, the sample size, albeit larger

FIGURE 2 Mean respiratory sinus arrhythmia (RSA) change scores from baseline to each of the task epochs: negative induction (NI), negative suppression (NS), positive induction (PI), and positive suppression (PS) for control, attention-deficit/hyperactivity disorder (ADHD), and ADHD-low-prosocial behavior groups. Note: Standard error estimates were obtained via analysis of variance.



than most physiological studies of ADHD, was not designed to have the power to test diagnosis-by-sex interactions or other subgroups of ADHD, including those with comorbid disorders. It will be interesting to examine children with comorbid CD and ADHD or comorbid anxiety and ADHD, for example. Furthermore, as this sample was recruited from the community, the clinical severity of both prosocial behavior deficits and ADHD may be less than a sample recruited from clinics or forensic samples, although the prosocial behavior levels used to designate a distinct group were quite low for the general population in that very few children would be rated above the 90th percentile in this domain by both parents and teachers. To evaluate the clinical meaningfulness of this finding, it will be of interest whether the patterns observed are stable over time or are predictive of course, impairment, response to treatment, the development of comorbid disorders, and other clinical outcomes. From a clinical and public health perspective, caution should be used in diagnosing children low in prosocial behaviors who do not have conduct disorder, until more research is done to determine their level of clinical impairment.[37]

In conclusion, this study revealed that when children with ADHD are divided according to social–emotional functioning (in this case, indexed by the prosocial scale of the SDQ), distinct patterns of autonomic responding within the ADHD population may be revealed. This clarifies that emotion reactivity and regulation alterations are features of ADHD differentially across children with the syndrome, and this variation can be validated and characterized physiologically. Two groups of children with ADHD had altered autonomic functioning compared with typically developing youth, but the two ADHD groups differed from typically developing children in quite different and easily distinguished ways. ADHD was associated with disruptions in emotional processing during positive emotions (as indexed by overactive parasympathetic activity), but this effect was masked in a subgroup who also had low levels of prosocial behavior. In turn, the latter group displayed a pattern of blunted autonomic functioning in both branches. Future studies of ADHD and emotional regulation must take into account this dramatic heterogeneity. &

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SUPPLEMENT 1

Validity Check of Task Manipulations

Emotional Valence. Beginning with valence ratings, scores for the full sample differed according to both the valence condition ($F_{1,149} = 434.81, p < .001, \eta^2 = 0.75$) and the regulation condition ($F_{1,149} = 8.01, p < .005, \eta^2 = 0.06$). The interaction of valence and regulation conditions was significant, consistent with the interpretation that the experience of each emotion valence (negative and positive) was greater in the suppression than the expression of an emotion, particularly for negative emotions ($F_{1,149} = 21.95, p < .001, \eta^2 = 0.13$). Analysis of the simple effects confirmed that the four conditions differed as indicated by our labeling of the conditions: higher (more positive) ratings for positive than negative emotion (all $p < .001$). In addition, higher (more positive) ratings for induction than suppression were also observed (all $p < .001$) (see Table S1, available online). Also reassuringly, the attention-deficit/hyperactivity disorder (ADHD), ADHD-low-prosocial, and control groups were similar with respect to Self-Assessment Manikin (SAM) valence rating scores, as none of the interactions involving group status were significant (all $F < 1.0$, all $p > .10$), suggesting that interpretation of changes in autonomic reactivity were not confounded by differences in self-reported valence appraisal of the task conditions. Furthermore, groups did not differ with respect to valence during any of the task conditions (all $F < 1.0$, all $p > .10$) (see Table S1, available online).

Emotional Arousal. The arousal rating scores showed a similar picture (see Table S1, available online). There was a significant main effect for arousal scores between positive and negative segments ($F_{1,149} = 107.31, p < .001, \eta^2 = 0.43$). In addition, the interaction of valence and regulation conditions was significant, $F_{1,149} = 8.35, p < .005, \eta^2 = 0.06$). However, the suppression versus induction difference was not significant ($F_{1,149} = 1.52, p = .22, \eta^2 = 0.01$), and none of the interactions involving group status were meaningful (all $F < 1.0$) (see Table S1, available online) for the task condition descriptive data according to group. Specifically, groups did not differ with respect to arousal level during any of the task conditions (all $F < 1.0$, all $p > .10$) (Table 2). Thus, on the whole, these data suggest that the task manipulations were effective and valid across all groups.

Validity Check Based on Task Habituation and Order Effects. Task habituation and order effects were evaluated by comparing physiological measures across the resting and neutral baseline conditions. Repeated-measures analysis of variance (ANOVA) indicated that respiratory sinus arrhythmia (RSA), interbeat interval, and pre-ejection period (PEP) differed across the baselines (all $F > 8.76, p < .01$), suggesting systematic changes in physiology when comparing rest to the demands imposed

TABLE S1 Self-Assessment Manikin (SAM) Scores Across Task Conditions, by Group.

		ADHD	
Variable	**Control (n = 75)**	**ADHD Only (n = 54)**	**ADHD-Low-Prosocial (n = 21)**
SAM Valence/Pleasure			
Baseline 1	3.39 (0.67)	3.54 (0.79)	3.45 (0.81)
Negative induction	2.44 (1.17)	2.48 (1.31)	2.58 (1.08)
Negative suppression	1.73 (0.88)	1.74 (1.07)	1.91 (1.05)
Baseline 2	3.38 (0.71)	3.45 (1.22)	3.46 (0.81)
Positive induction	4.47 (0.81)	4.44 (1.13)	4.68 (0.67)
Positive suppression	4.64 (0.77)	4.67 (0.89)	4.79 (0.42)
SAM Intensity/Arousal			
Baseline 1	2.04 (0.72)	2.31 (0.80)	2.15 (0.76)
Negative induction	3.51 (1.25)	3.61(1.45)	3.37 (0.89)
Negative suppression	3.20 (1.14)	3.09 (1.46)	3.19 (1.11)
Baseline 2	1.93 (0.91)	2.23 (0.81)	1.85 (0.72)
Positive induction	2.11 (1.24)	2.20 (1.48)	2.11 (1.29)
Positive suppression	2.32 (1.36)	2.48 (1.63)	2.16 (1.26)

Note: For this table, no significant group differences were observed. Each row represents next time point in design. Time increasing down table for the repeated-measures design. ADHD = attention-deficit/hyperactivity disorder.

by attending to and orienting to a neutral task, as expected. Second, a polynomial repeated-measures ANOVA for the full sample revealed that the linear effect of time on RSA across all task conditions was significant ($F_{1,149} = 9.82$, $p = .002$, $\eta^2 = 0.06$), as was the quadratic effect ($F_{1,149} = 8.24$, $p = .00$, $\eta^2 = 0.05$) and the cubic effect ($F_{1,149} = 32.92$, $p < .001$, $\eta^2 = 0.18$). This is consistent with participants responding to the task manipulations and inconsistent with a habituation effect. Simple examination of the means (Figures 1 and 2) confirms that neither PEP nor RSA simply decreased across task conditions. The Appendix lists the exact means for specialists wishing to make detailed comparisons.

A different pattern was observed for PEP: here, no significant effect was seen for the linear, quadratic, or cubic effect (all $F < 1.0$, all $p > .05$). This suggests there was no change in PEP across task conditions and that group main effects of PEP would be the more appropriate focus of results. Interbeat interval and respiration rate displayed a similar consistency across conditions all linear, quadratic, and cubic effects (all $F < 2.3$, all $p > .05$).

In addition, group comparisons revealed that during the neutral and resting baselines there were no significant differences in RSA, heart rate, or respiration rate (all $F < 1.0$, all $p > .10$) (see Table S1, available online). However, groups did differ with respect to PEP during the neutral baseline only, during which the ADHD and control groups showed higher arousal than the ADHD + callous/unemotional traits (CU) group ($F_{2,148} = 3.7$, $p < .05$ (Figure 1). We conclude that habituation and order effects were trivial relative to task manipulation effects, which further supports the results of our primary analyses and hypothesis testing.

Validity Check Based on Overall Physiological Responding. In addition, our hypothesis was that there would be specific responses in sympathetic and parasympathetic systems. However, an alternative explanation for the PEP and RSA results might be that they are caused by global fluctuations in the participants' overall physiology, such as interbeat interval or respiration rate, rather than isolated actions of sympathetic or parasympathetic systems. If so, the results should emerge similarly if we simply look at interbeat interval or respiration rate.

To test this possibility, the main effects and interactions for interbeat interval and respiration rate were examined using the same $2 \times 2 \times 3$ repeated-measures ANOVA. The main effects of task valence (positive/ negative affect) and regulation (suppression/induction) for interbeat interval were significant ($F_{1,149} = 5.392$, $p < .05$, $\eta^2 = 0.04$) and $F_{1,149} = 21.555$, $p < .001$, $\eta^2 = 0.13$), respectively, with interbeat interval changing in the task-appropriate direction. However, none of the interactions by group were significant (all $F < 2.10$ and $p > .10$). In addition, there were no significant effects with respect to respiration rates (all $F < 3.10$, $p > .10$). Thus, the groups did not differ on general, multi-determined, physiological parameters, suggesting that it was appropriate to interpret the PEP and RSA effects as specific indexes of sympathetic and parasympathetic activity, respectively, as intended.