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Sympathetic-Parasympathetic Interaction and Externalizing Problems in Children with Autism Spectrum Disorder

Rachel M. Fenning,

California State University, Fullerton, California

Stephen A. Erath,

Auburn University, Auburn, Alabama

Jason K. Baker,

California State University, Fullerton, California

Daniel S. Messinger,

University of Miami, Coral Gables, Florida

Jacquelyn Moffitt,

California State University, Fullerton, California

Brian R. Baucom,

University of Utah, Utah, Salt Lake City, Utah

Alexander K. Kaeppler

Auburn University, Auburn, Alabama

Abstract

Children with autism spectrum disorder (ASD) exhibit significant difficulties with emotion regulation and reactivity, which may be linked to underlying psychophysiology. The present study examined associations between autonomic nervous system activity and individual differences in externalizing behavior problems in children with ASD. A multisystem approach was adopted to consider the interplay between markers of sympathetic (electrodermal reactivity—EDA-R) and parasympathetic reactivity (respiratory sinus arrhythmia reactivity—RSA-R) in relation to behavioral challenges. Fifty-two children with ASD ages 6–10 years contributed complete psychophysiological data. Measures of EDA-R and RSA-R (RSA withdrawal) were obtained in response to a laboratory challenge task and parents reported on child externalizing behavior problems using a standardized questionnaire and a structured clinical interview. An equifinality model was supported, with two distinct psychophysiological pathways linked to heightened externalizing behavior problems. Greater RSA-R was associated with more externalizing problems in the context of higher levels of EDA-R, and lower EDA-R was associated with increased externalizing problems at lower levels of RSA-R. Findings underscore the importance of considering the role of psychophysiology in the unfolding of comorbid externalizing problems in children with ASD. Potential implications for tailoring coregulatory supports are discussed.

Lay Summary

Children with autism spectrum disorder (ASD) exhibit elevated rates of challenging behavior. This study identified specific psychophysiological profiles (low sympathetic-low parasympathetic reactivity, and high sympathetic-high parasympathetic reactivity) that may place these children at greater risk for behavior problems. Findings have implications for better understanding behavioral challenges in children with ASD, and for tailoring supports to address underlying psychophysiology.

Keywords

autism spectrum disorder; autonomic nervous system; respiratory sinus arrhythmia; electrodermal activity; externalizing behavior problems; psychophysiology; emotion regulation

Introduction

Children with autism spectrum disorder (ASD) exhibit significant difficulties with emotion regulation and reactivity, which are thought to underlie the heightened prevalence of comorbid behavior problems in this population [Fenning, Baker, & Moffitt, 2018; Mazefsky & White, 2014; Weiss, 2014]. Efforts to understand the biological underpinnings of dysregulation have often used psychophysiological measures, including indicators of autonomic nervous system activation [Beauchaine, 2015a; Beauchaine, Gatzke-Kopp, & Mead, 2007; Benevides & Lane, 2015]. The autonomic nervous system is comprised of two branches, the sympathetic (SNS) and the parasympathetic nervous systems (PNS), which have distinct, but synergistic functions. The SNS is responsible for mobilizing resources to respond to challenges or threats [Beauchaine, 2001; Sheppes, Catran, & Meiran, 2009], whereas the PNS is involved in slowing heart rate and reducing arousal through increased output along the vagus nerve [Beauchaine, 2015a; Benevides & Lane, 2015]. To date, research on children with ASD has predominantly focused on the SNS or the PNS in isolation, with only a few studies measuring both systems concurrently [e.g., Bujnakova et al., 2016; Cohen, Masyn, Mastergeorge, & Hessel, 2015; Levine et al., 2012; Neuhaus, Bernier, & Beauchaine, 2016; Schaaf, Benevides, Leiby, & Sendekci, 2015]. Extending this work by considering interactions between the SNS and PNS increases the specificity with which psychophysiological responses can be characterized, and enhances comprehensive conceptualization of the role of autonomic activity in the manifestation of behavioral pathology [Buss, Jaffee, Wadsworth, & Kliever, 2018; El-Sheikh et al., 2009].

Recent work has centered on understanding individual differences among children with ASD through examination of psychophysiological reactivity [Baker et al., 2018; Fenning et al., 2017; Lydon et al., 2016; Neuhaus, Bernier, & Beauchaine, 2014; Neuhaus et al., 2016; White et al., 2014]. Electrodermal activity (EDA) is an SNS response and index of the behavioral inhibition system, which promotes inhibition and risk assessment in situations that involve potential negative consequences [Beauchaine, 2001; McNaughton & Corr, 2004]. Higher EDA reactivity is generally considered to index more intense emotional reactivity, whereas low EDA reactivity (EDA-R) has been associated with increased risk for externalizing problems through reduced sensitivity to environmental contingencies

[Beauchaine et al., 2007; Cappadocia, Desrocher, Pepler, & Schroeder, 2009]. Among children with ASD, greater EDA reactivity has been linked with more social impairment and higher levels of core ASD symptoms [Fenning et al., 2017; Joseph, Ehrman, McNally, & Keehn, 2008; Kaartinen et al., 2012; Neuhaus, Bernier, & Beauchaine, 2015; Stagg, Davis, & Heaton, 2013], although not universally [Faja, Murias, Beauchaine, & Dawson, 2013; Louwerse et al., 2013; McCormick et al., 2014]. Conversely, EDA under-arousal has been associated with increased externalizing behavior problems in children with ASD, particularly when measured during compliance contexts or when accompanied by less-optimal coregulatory support [Baker, Fenning, Erath, et al., 2018].

PNS activity is frequently indexed through high-frequency heart-rate variability related to respiration, or respiratory sinus arrhythmia (RSA). Baseline RSA is a robust biomarker of emotion regulation [Beauchaine, 2015b], but the nature and implications of RSA-reactivity (RSA-R; i.e., withdrawal of PNS influence to increase arousal) may depend upon study population [Beauchaine, 2015a; Graziano & Derefinko, 2013; Obradovic, Bush, & Boyce, 2011]. In community samples, RSA-R (i.e., reduction in RSA) to challenge may index an adaptive response [Graziano & Derefinko, 2013], but excessive reactivity may also signify loss of regulatory control, especially for children presenting with clinical concerns [Beauchaine, 2015a, 2015b; Beauchaine et al., 2007; Cole, Zahn-Waxler, Fox, Usher, & Welsh, 1996]. Despite evidence that children with ASD exhibit notable challenges with emotion regulation [Fenning et al., 2018; Mazefsky & White, 2014; Weiss, 2014], relatively few investigations have examined RSA-R in this population [Lydon et al., 2016; Neuhaus et al., 2016; Vaughn Van Hecke et al., 2009], and even less so in relation to behavioral functioning.

Although studies that separately examine SNS and PNS activation have informed understanding of psychophysiology in children with ASD, consideration of multisystem interactions is critical to advancing knowledge regarding behavioral phenotypes and the development of behavior problems [Bauer, Quas, & Boyce, 2002; Buss et al., 2018]. Several theoretical models describe the concurrent, but opposing functions of the SNS and PNS. For example, polyvagal theory [Porges, 1995, 1997] posits a hierarchical system that involves initial PNS withdrawal (i.e., RSA-R) in response to challenge, followed either by reengagement of the PNS or activation of the SNS, depending on the nature of the stressor and the individual's stress response pattern. From this perspective, excessive PNS withdrawal in response to challenge increases reliance on SNS fight-flight responding, which heightens risk for poor stress response regulation and emotional lability.

Beauchaine [2001] proposed an integration of polyvagal theory with Gray's motivational theory [Gray, 1987] to further articulate how the behavioral activation and inhibition systems associated with SNS functioning interact with the PNS to predispose individuals to different forms of psychopathology. Beauchaine and colleagues [Beauchaine, 2001; Beauchaine et al., 2007] have proposed that SNS under-responsivity coupled with strong PNS withdrawal may result in externalizing behavior problems, whereas SNS over-responsivity combined with excessive PNS withdrawal may lead to internalizing problems. Studies of children with Attention-Deficit/Hyperactivity Disorder and children with behavioral disorders provide support for the broad tenets of this model [Beauchaine, 2001; Beauchaine et al., 2007].

The multisystem, interactive physiological processes that underlie risk for externalizing problems likely share important commonalities across diagnostic groups [Bauer et al., 2002; Buss et al., 2018], but distinct pathways may emerge for children with ASD given the unique developmental differences that characterize this disorder. In community samples of children without ASD, evidence suggests that the combination of higher EDA-R and higher RSA-R (withdrawal) may serve a protective function [El-Sheikh et al., 2009]. However, this psychophysiological profile may also confer risk [Abaied et al., 2018], especially in clinical samples for whom such a pattern has been posited to index excessive reactivity coupled with a significant loss of regulatory control [Beauchaine et al., 2007; Scarpa & Raine, 1997].

In the context of *lower* EDA-R, some studies of children without ASD suggest that higher RSA-R further increases vulnerability to externalizing problems [Beauchaine et al., 2007; El-Sheikh et al., 2009]. Conversely, blunted RSA-R may also be problematic in the context of low SNS activation [Beauchaine et al., 2007; Boyce et al., 2001; Murray-Close, Holterman, Breslend, & Sullivan, 2017], as RSA-R in response to challenge can be adaptive in promoting increased cognitive and emotional engagement to meet environmental demands [Graziano & Derefinko, 2013; Porges, 1997]. Given that ASD, as a disorder, is largely typified by difficulties with social engagement, it is possible that lower levels of RSA-R may compound risk associated with lower EDA-R, reflecting extreme disengagement with the task or related social contingencies.

Of the few studies that have examined SNS and PNS processes concurrently in children with ASD [e.g., Bujnakova et al., 2016; Cohen et al., 2015; Levine et al., 2012; Neuhaus et al., 2016; Schaaf et al., 2015], most have focused largely on diagnostic group differences, and none have examined interactions between these systems. To our knowledge, the extent to which interactions between the SNS and PNS predict meaningful individual differences in behavioral outcomes is hitherto untested in children with ASD.

The current study examined interactions between SNS and PNS reactivity in the prediction of externalizing behavior problems in an ethnically and developmentally diverse sample of children with ASD ages 6–10 years. The focal age range represents an important period for parental influence on emotion regulation in children with ASD [Baker, Fenning, & Moffitt, 2019; Fenning et al., 2018] and without ASD [Morris, Silk, Steinberg, Myers, & Robinson, 2007], and a period that overlaps with previous examinations of physiology and externalizing behaviors in children with ASD [e.g., Baker, Fenning, Erath, et al., 2018; Neuhaus et al., 2014; Vaughn Van Hecke et al., 2009].

Given that a degree of autonomic activation is necessary to promote appropriate engagement and cognitive effort, but excessive reactivity may reflect problematic emotion lability [Beauchaine, 2001; Graziano & Derefinko, 2013; Porges, 1995, 1997], it was anticipated that reciprocal autonomic reactivity would be associated with poorer behavioral functioning in children with ASD. Specifically, it was expected that high autonomic responsivity, reflected by the combination of higher EDA-R and higher RSA-R (RSA reduction in response to challenge), and low autonomic responsivity, as indexed by lower EDA-R and lower RSA-R, would be associated with increased externalizing problems in this population. Our hypotheses are aligned with the developmental principle of equifinality, wherein

multiple pathways eventuate in similar child outcomes. Identifying different psychophysiological patterns that underlie challenging behavior in this population has the potential to enhance understanding of individual needs and to inform possible avenues for tailoring supports.

Method

Participants

An initial sample of 77 children with ASD ages 6–10 years and their primary caregivers participated in a laboratory visit that included child assessment, psychophysiological data collection, structured parent–child tasks (not utilized in the current study), parent interview, and parent completion of questionnaires. Children with an existing ASD diagnosis provided by a physician or psychologist were recruited from the community and from local service providers via flyers. Exclusionary criteria for the child included the presence of a genetic disorder of known etiology and motor impairment that would prevent task engagement.

Nine children refused all electrodes, an additional two children refused the RSA electrodes but wore those measuring EDA, and the EDA electrodes fell off one child early in the tasks. Additionally, some EDA ($n = 9$) and RSA ($n = 4$) data were determined to be artifactual (e.g., noise or loss of signal due to pulling on electrode wires); these data were excluded. Missing data analyses involving demographic and outcome variables indicated that only estimated intelligence quotient (IQ) distinguished groups, $t = -2.52$, $P = 0.019$, with a lower mean IQ for children with missing data ($M = 69.60$, $SD = 22.79$; range 47–115) as compared to those with usable data ($M = 82.73$, $SD = 20.65$; range 47–121). Of the children with an estimated IQ within the range suggestive of intellectual disability (ID; $IQ < 76$), 50% accepted the electrodes and provided usable data, as compared to 81% of children with higher measured IQ. Among the children scoring within the ID range, individual differences in IQ were not further related to missing data, $t = -0.64$, $P = 0.525$, nor were any other demographic or outcome variables.

The remaining sample of 52 children (77% male) was diverse with regard to intellectual ability and ASD symptom levels (Table 1), with estimated IQ ranging from 47 to 121, and 35% of children scoring within the ID range. The majority of the families identified their children as Hispanic (48%), 31% as Caucasian, non-Hispanic, 4% as Asian American, 6% as African American, 4% as “other,” and 8% as “multiethnic/racial.” The median annual family income was between US \$50,000 and 70,000. The majority of primary caregivers were married (69%) and 4% of the primary caregivers were fathers. Fifteen (29%) of the children were reported to take medication, most commonly for attention problems/hyperactivity, asthma, allergies, or seizures. Anticholinergic medications and SSRIs may be related to psychophysiological measurement [Beauchaine et al., 2019; Green, Nuechterlein, & Satz, 1989]; only one child was reported to take the former, and no children were taking SSRIs at the time of the present study.

Procedures

All procedures were approved by the local institutional review board. Parents consented for themselves and for their children, and assent was obtained from children, prior to data collection.

EDA and RSA data collection—The child was seated at a table that faced a small television on a stand. A wall was to the child's left and a temporary partition was placed to the child's right, behind which the parent was eventually seated. The electrodes were placed on the child by a female research assistant with the help of the parent.

Electrodes were placed on the lower ribs and on the right clavicle for RSA, and on the lower palm of the nondominant hand for EDA. A short adjustment period occurred during which the data acquisition systems were checked for appropriate signal and then a 3-min baseline procedure was performed. This baseline involved viewing a series of slides on the television that included images of trees, water, mountains, and other nature scenes [Erath, Bub, & Tu, 2016]. Parents were asked beforehand if they perceived their children to have any particular interests in, or fears of, these types of stimuli; none were reported. A video camera mounted high above the television recorded the child for later data assurance and allowed the parent to view the child from behind the partition. The child then engaged in a 3-min challenging task. As in previous studies utilizing this task to elicit physiological arousal [e.g., El-Sheikh, 2005], the child was provided with a pencil and instructions to trace an image of a star using a structure that permitted only an indirect, mirrorimage view of the child's hand and paper. The reversed directionality of the image makes this a difficult task to perform. Despite the large range of cognitive functioning present in our sample, every child was judged to have understood the request for basic tracing.

Parent interview and forms—Parents reported on their children's externalizing behavior problems using a child behavior checklist, and were also interviewed individually about their children's symptoms of oppositional defiant disorder (ODD) using a module from a structured diagnostic interview.

Measures

Diagnostic confirmation and ASD symptom level—All children presented with an established diagnosis of ASD by a community physician or psychologist. Children were evaluated in the laboratory using the Autism Diagnostic Observation Schedule-2 [ADOS-2; Lord et al., 2012] completed by research-reliable assessors. The ADOS-2 is a semistructured assessment that facilitates observation and recording of child behaviors related to language, social communication, play, repetitive behaviors, and restricted interests. Children were administered Module 3 (71%), Module 2 (21%), and Module 1 (8%). The ADOS-2 comparison score was used to characterize the sample and to provide a robust measure of ASD symptom severity for use in analyses. The comparison score allows for examination of symptom levels across different modules, with 1 indicative of minimal to no evidence of ASD-related symptoms, and 10 reflecting a high level of symptoms.

Four children did not meet the ADOS-2 criterion for an ASD classification, but were retained in the sample following completion of an in-depth, multimethod clinical best estimate by a licensed clinical psychologist with research reliability in the ADOS-2 and significant expertise in ASD assessment. All four children met clinical criteria on the Social Responsiveness Scale-2 [Constantino & Gruber, 2012], a widely used parent report measure of ASD symptoms, and on the Social Communication Questionnaire, Lifetime Version [Rutter, Bailey, & Lord, 2003], a screening instrument based on the Autism Diagnostic Interview-Revised [Rutter, LeCouteur, & Lord, 2003].

Child IQ—An estimate of child IQ was obtained using the Stanford-Binet 5 Abbreviated Battery IQ (ABIQ) [Roid, 2003], which has been used previously for children with ASD [Matthews et al., 2015; Roid, 2003]. The ABIQ is comprised of two subscales with high g loadings: a Matrix Reasoning task that assesses nonverbal fluid reasoning and a Vocabulary task that evaluates expressive word knowledge.

Psychophysiological indices—EDA and RSA were measured with a MindWare data acquisition system (MindWare Technologies, Inc., Gahanna, OH) in a room set at 74° Fahrenheit, following guidelines provided by the developers. Children were seated throughout the physiological assessment.

Electrodermal reactivity—Skin conductance (units = microsiemens or μS) was measured with two disposable Ag-AgCl electrodes placed on the palm of the nondominant hand. Data were sampled at 500 Hz, and skin conductance scores were computed with MindWare EDA analysis software (version 3.0.22). Building upon methods used by Munro, Dawson, Schell, and Sakai [1987], we considered complementary indices of EDA-R by examining change in both mean level of EDA [skin conductance level reactivity; SCL-R; Erath, El-Sheikh, Hinnant, & Cummings, 2011] and in the occurrence of nonspecific skin conductance responses [NSCR-R; Dawson, Schell, & Fillion, 2000] from baseline to challenge. The threshold for NSCR was greater than 0.05 μS in amplitude. SCL-R and NSCR-R were calculated as the residual of the regression of SCL and NSCRs during the star-tracing period on the score for the relevant variable during the baseline period [Burt & Obradovi, 2013]. Higher SCL-R and NSCR-R scores reflect increases in SCL and NSCRs, respectively, from the baseline to the star-tracing period. SCL-R and NSCR-R were significantly correlated at $r = 0.41$, $P < 0.01$, and were combined to create the composite of EDA-R.

Respiratory sinus arrhythmia reactivity—Electrocardiography data were collected through disposable Ag-AgCl electrodes placed on participants' right clavicle and lower left and right ribs. Data were sampled at 500 Hz. RSA scores were quantified using spectral analysis [Berntson et al., 1997] with MindWare HRV analysis software (version 3.0.22) as the natural log of the variance in heart period within age-adjusted respiratory frequency bands (e.g., 0.27–0.50 Hz for 9-year-old children, 0.25–0.50 Hz for 10-year-old children; see Shader et al., 2018 for ranges). RSA is expressed in units of $\ln(\text{ms}^2)$. Possible artifacts were flagged by an algorithm that detects improbable interbeat intervals [Minimal Artifact Difference/Maximum Expected Difference artifact detection algorithm; Berntson, Quigley, Jang, & Boysen, 1990], allowing for visual inspection and editing when necessary.

Relatively few artifacts were detected and were corrected manually [Berntson et al., 1997]. RSA-R was calculated as the residual of the regression of RSA during the star-tracing period on RSA during the baseline period [Burt & Obradović, 2013]. Residualized change scores were multiplied by -1 so that higher RSA-R scores indicated greater reductions in RSA (i.e., greater RSA withdrawal) from the baseline to the star-tracing period.

Externalizing behavior problems—Externalizing problems were partially indexed by parent report using the standardized Externalizing Problems *T*-score from the ageappropriate version of the Child Behavior Checklist [Achenbach, 2009], a widely used measure with demonstrated validity in children with ASD [e.g., Pandolfi, Magyar, & Dill, 2012]. Parents were also interviewed using the ODD subscale of the Diagnostic Interview Schedule for Children [DISC; Costello, Edelbrock, & Costello, 1985; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000], a computer-assisted structured diagnostic interview based upon criteria from the Diagnostic and Statistical Manual [American Psychiatric Association, 2013]. The DISC has been used in previous studies to assess comorbid behavior disorders in children with neurodevelopmental disabilities [Baker, Neece, Fenning, Crnic, & Blacher, 2010]. The current study considered the total number of ODD symptoms endorsed. Only the ODD module was administered due to meta-analytic findings suggesting low rates of conduct disorder among children with ASD [e.g., 4% as opposed to 30% to 37% with comorbid ODD; Kaat & Lecavalier, 2013; Simonoff et al., 2008]. The CBCL externalizing *T*-score and the DISC ODD symptom count were highly correlated ($r = 0.70$), and were combined to create an externalizing behavior problems composite.

Data Analysis Plan

Bivariate correlations were considered, followed by a linear regression that included EDA-R, RSA-R, and the EDA-R $\times$ RSA-R interaction as predictors of externalizing problems. Follow-up analyses involved estimation of the relevant simple slopes of the association between each predictor and externalizing problems at the mean of the other predictor, as well as 1 *SD* below and 1 *SD* above the mean [Roisman et al., 2012].

Results

Children demonstrated a significant increase in SCL as a group when moving from baseline ($M = 9.18$, $SD = 4.52$) to the challenge task ($M = 10.34$, $SD = 4.92$), $t = -4.03$, $P = 0.000$, $d = 0.57$, but no increase was observed for NSCRs (baseline: $M = 29.34$, $SD = 23.34$; challenge: $M = 27.10$, $SD = 13.18$; $t = 0.68$, $P = 0.498$; $d = 0.10$). RSA decreased from baseline ($M = 6.01$, $SD = 1.17$) to challenge ($M = 5.67$, $SD = 1.22$), $t = 3.03$, $P = 0.004$, $d = 0.42$, indicating a pattern of withdrawal for children as a group. The current sample mean for externalizing problems on the CBCL was at the threshold for “borderline” clinical problems (see Table 1), with over a quarter of the children (27%) falling within the clinical range. Similarly, and consistent with previous reports [Kaat & Lecavalier, 2013; Simonoff et al., 2008], 33% of the sample met criteria for ODD on the DISC ($M = 2.52$, $SD = 2.70$).

As reported in Table 1, EDA-R was inversely related to externalizing problems, and RSA-R was positively related, although associations did not meet statistical significance. Neither child medication status nor any other demographic variable was significantly related to the

outcome variable, and none were controlled in the regression. A significant main effect of EDA-R in the prediction of externalizing problems was observed in the regression (Table 2). However, emergence of the hypothesized significant interaction qualified this finding. EDA-R and RSA-R interacted in the prediction of externalizing problems.

Follow-up analyses of the interaction with RSA-R moderating the association between EDA-R and externalizing problems indicated that the simple slope of EDA-R was significant at low (-1 SD) RSA-R, $t = -3.05$, $P = 0.004$, and medium RSA-R, $t = -2.08$, $P = 0.042$, but not at high RSA-R ($+1$ SD), $t = 0.46$, $P = 0.649$. Regions of significance analyses indicated that lower EDA-R predicted more externalizing problems at RSA-R values lower than 0.03 (Fig. 1).

Parallel analyses examining EDA-R as a moderator of the association between RSA-R and externalizing problems indicated that the simple slope of RSA-R was significant at high ($+1$ SD) EDA-R, $t = 2.24$, $P = 0.029$, but not at medium EDA-R, $t = -0.01$, $P = 0.995$, or low (-1 SD) EDA-R, $t = -1.62$, $P = 0.113$. Regions of significance analysis indicated that higher RSA-R predicted more externalizing problems when accompanied by EDA-R values greater than 0.69 (Fig. 2).

Overall, follow-up analyses of the interaction suggested that children were most at risk for externalizing problems when concurrent reactivity of sympathetic and parasympathetic systems was observed (low–low or high–high). Because child IQ was associated with EDA-R at the level of a trend, ancillary post-hoc analyses were conducted substituting child IQ for EDA-R in interaction analyses. The interaction term for IQ and RSA-R was not statistically significant, $\beta = 0.21$, $t = 1.50$, $P = 0.14$, and when added to the regression, the original interaction term for EDA-R and RSA-R remained significant, $\beta = 0.47$, $t = 3.30$, $P = 0.002$. Child IQ did not appear to be contributing to, or accounting for, the findings.

Discussion

The current study tested whether interactions between sympathetic and parasympathetic nervous system reactivity were associated with externalizing behavior problems in children with ASD. Higher RSA-R was associated with more externalizing problems at higher levels of EDA-R, and lower EDA-R was associated with more externalizing problems at lower levels of RSA-R. Understanding how different psychophysiological processes manifest in similar behavioral challenges for children with ASD provides insight into the marked heterogeneity of externalizing problems in this population, and informs avenues for delivering effective coregulatory support.

PNS or vagal withdrawal, as indexed by RSA-R, allows for increased SNS influence to meet contextual demands [Graziano & Derefinko, 2013; Porges, 1997]. Although this process can be adaptive in some cases, higher RSA-R can also reflect a loss of regulatory control, particularly for clinical populations at risk for dysregulation [Beauchaine, 2012; Beauchaine, 2015a, 2015b; Cole et al., 1996]. Consistent with this perspective, we found that higher RSA-R was associated with externalizing problems for children with ASD at higher levels of EDA-R, but not at lower levels of EDA-R. These results suggest that a preponderance of

SNS activation may underlie the loss of regulatory control commonly described as behavioral “meltdowns” in children with ASD [Mazefsky, Pelphrey, & Dahl, 2012]. The present findings seem to contrast somewhat with theories developed for children without ASD, wherein high EDA-R and higher RSA-R are thought to impart risk for *internalizing* problems [Beauchaine, 2001; Beauchaine et al., 2007]; however, for children with ASD, it is possible that intense anxiety in response to challenge or frustration may more readily manifest in co-occurring externalizing behaviors.

Lower EDA-R has been identified as a risk factor for externalizing problems, with this association thought to be mediated by a reduced physiological sensitivity to threat or socialization efforts [Beauchaine et al., 2007]. A direct link between lower EDA-R in compliance contexts and externalizing behavior problems has been replicated in children with ASD, but this effect may be open to moderation when EDA-R is measured under conditions with less emphasis on compliance [Baker, Fenning, Erath, et al., 2018]. Results of the present study suggested an association between lower EDA-R during a challenge task and externalizing problems at lower and moderate levels of RSA-R. These results are consistent with considerable evidence that low autonomic arousal is a risk factor for externalizing problems [Murray, Close, 2013]. However, lower EDA-R was not associated with more problems when accompanied by higher RSA-R, suggesting a potential protective process wherein a “freeing” of the SNS may have allowed for appropriate psychophysiological mobilization and task engagement [Graziano & Derefinko, 2013; Murray-Close et al., 2017; Porges, 2007].

Theory and research involving children without ASD have tended to link the profile of low SNS reactivity and high RSA-R to antisocial behavior and risk for conduct disorder [Beauchaine et al., 2007; Beauchaine, 2012]. Despite the high rates of clinically elevated externalizing problems observed in children with ASD, the type of antisocial behaviors associated with conduct disorder are relatively rare [Kaat & Lecavalier, 2013; Simonoff et al., 2008], suggesting that this particular pathway to externalizing problems may be less prevalent for children with ASD. Enhanced understanding of psychophysiological mechanisms may also inform ongoing debate regarding the extent to which clinically concerning externalizing behavior problems in children with ASD reflect the presence of conventional comorbid disorders or potential variants that should be considered differently [Gadow, DeVincent, & Drabick, 2008].

Although our sample was relatively large in comparison with other investigations of psychophysiological functioning in children with ASD, it was somewhat modest for testing interactions, and analyses should be replicated with a larger sample. Given the very large sample sizes required to confidently test three-way interactions, it was not possible for us to consider the interplay between multisystem physiological processes and parenting factors in the current study. However, recent evidence suggests that certain SNS–PNS profiles may sensitize children to parenting effects [Abaied et al., 2018], and it is possible that different types of parental reactions might be more or less beneficial depending upon children’s underlying psychophysiology. For instance, parenting that promotes increased task engagement while providing effective behavioral contingencies may be particularly important for reducing comorbid behavior problems in children with ASD exhibiting low

SNS arousal tendencies [Baker, Fenning, Erath, et al., 2018]. In contrast, reducing parental criticism and harsh discipline may be especially helpful for children with ASD with high SNS or PNS reactivity [Baker, Fenning, Howland, & Huynh, 2018; Baker et al., 2019]. Further exploration of the association between coregulatory parenting behaviors, children's psychophysiology, and behavioral outcomes is needed, and may serve to enhance development of tailored supports. Use of psychopharmacological interventions that target relevant processes may also prove differentially efficacious depending upon children's psychophysiological and behavioral profiles [Connor, Glatt, Lopez, Jackson, & Melloni Jr, 2002; Porges et al., 1981].

Consistent with many studies of psychophysiology in children with [Neuhaus et al., 2014; Vaughn Van Hecke et al., 2009] and without ASD [e.g., Liew et al., 2011], we did not control for children's hydration status or body mass. Body mass, primarily at extreme levels, may be related to RSA baseline [not RSA-R; El-Sheikh, 2005; Fraley, Birchem, Senkottaiyan, & Alpert, 2005], but many studies have not found such associations [Calkins, Graziano, & Keane, 2007; Gentzler, Rottenberg, Kovacs, George, & Morey, 2012; Scarpa, Haden, & Tanaka, 2010]. A direct measure of respiration would also afford greater precision in RSA measurement [Grossman & Taylor, 2007], although assessing high-frequency heart rate variability within age-adjusted respiratory frequency bands is generally accepted as a valid approach [Shader et al., 2018]. In addition, we did not assess children's motor skills, which could have contributed to variation in responses to the challenge task. Nonetheless, children with significant motor impairments were not included in the study, and it is unlikely that motor skills were associated with variables in a manner would confound interaction findings.

The present investigation focused on concurrent EDA and RSA-R as a way to index patterns of psychophysiological activation in response to challenge. Extending this work by examining interactions between baseline levels and indices of reactivity would provide additional insight into the dynamics of SNS and PNS arousal. It may also prove helpful to consider the directionality of activation as articulated by the doctrine of autonomic space [Berntson, Cacioppo, & Quigley, 1991], in which joint SNS and PNS influences on the same target organ (e.g., the heart) can be conceptualized as reciprocal or nonreciprocal. Additional conceptualizations of RSA and the nervous system exist [Grossman & Taylor, 2007; Thayer & Lane, 2009], which may offer further insight into psychophysiological processes for children with ASD [see also Benevides & Lane, 2015]. The potential influence of measurement context upon indices of psychophysiology is important to consider as well [Gatzke-Kopp & Ram, 2018]. We examined children's regulatory response to an external request for completion of a frustrating task. Other contexts may evoke different patterns of responding. For example, understanding SNS and PNS interaction in relation to social demands [e.g., Levine et al., 2012; Neuhaus et al., 2016; Vaughn Van Hecke et al., 2009] may be especially relevant given the social communication deficits intrinsic to the diagnosis of ASD.

Externalizing behavior problems were the focal outcome in this study. Future work would benefit from examining the interplay between the SNS and the PNS in relation to other symptoms and domains of functioning, such as anxiety [White et al., 2014]. The present

study examined psychophysiological correlates of externalizing behavior problems at a single point in time. Although certain psychophysiological profiles may place children at risk for behavior problems, it is also the case that the existence of problem behaviors, and the environmental response to those behaviors, may affect children's psychophysiology. Carefully controlled longitudinal investigations that include measurement of intrinsic and extrinsic influences on children's psychophysiology and behavioral presentation are needed.

Our sample was diverse with regard to ethnicity and developmental functioning. We were successful in obtaining valid psychophysiological data on the majority of our participants, including many children with measured IQ in the ID range for whom individual differences in IQ did not further differentiate data retention or quality. Previous studies on psychophysiology in children with ASD have predominantly excluded children scoring within the ID range. However, psychophysiological measures may be especially valuable in providing insight into covert processes for children with more pronounced limitations in their ability to express internal experiences. Our data in combination with that of others [e.g., Cohen et al., 2015] reveals the feasibility of gathering psychophysiological measures from children presenting with a wide range of developmental functioning and symptom severity, and accordingly underscores the relevance and importance of extending this work to the broader population of children with ASD. Ultimately, this investigation provides support for utilizing multiple psychophysiological measures and applying a multisystem framework to inform understanding of the role of autonomic nervous system functioning in the manifestation of individual differences in behavior problems in diverse children with ASD.

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Figure 1. Respiratory sinus arrhythmia reactivity (RSA-R) as a moderator of the association between electrodermal activity reactivity (EDA-R) and externalizing problems.

Figure 2. Electrodermal activity reactivity (EDA-R) as a moderator of the association between respiratory sinus arrhythmia reactivity (RSA-R) and externalizing problems.

Table 1. Descriptive Statistics and Correlations Among Variables of Interest ($n = 52$)

	1	2	3	4	5	6	7	8	9	<i>M (SD)</i>
1. Age in years	–									7.87 (1.43)
2. IQ	–0.20	–								82.29 (20.68)
3. ASD symptom level	–0.13	–0.18	–							7.36 (2.02)
4. EDA: NSCR reactivity	–0.05	–0.19	0.05	–						0.00 ^a (12.75)
5. EDA: SCL reactivity	–0.15	–0.20	0.16	0.41 ^{**}	–					0.00 ^a (2.07)
6. EDA reactivity (EDA-R)	–0.12	–0.23 ⁺	0.13	0.84 ^{***}	0.84 ^{***}	–				0.00 ^b (0.84)
7. RSA reactivity (RSA-R)	–0.01	–0.01	0.07	0.20	–0.02	0.11	–			0.00 ^a (0.78)
8. Externalizing CBCL	–0.16	0.17	–0.07	–0.22	–0.04	–0.16	0.10			59.77 (8.35)
9. ODD symptom level	–0.19	0.17	–0.14	–0.13	–0.22	–0.21	0.08	0.70 ^{***}		2.52 (2.70)
10. Externalizing problems	–0.19	0.18	–0.11	–0.19	–0.14	–0.20	0.10	0.92 ^{***}	0.92 ^{***}	0.00 ^b (0.92)

^aThese scores represent the unstandardized residuals from a regression.^bThese scores represent composites derived from standardized scores.

Abbreviations: ASD, autism spectrum disorder; EDA, electrodermal activity; NSCR, nonspecific skin conductance responses; SCL, skin conductance level; RSA, respiratory sinus arrhythmia; CBCL, child behavior checklist; ODD, oppositional defiant disorder.

^{**} $P < 0.01$ ^{***} $P < 0.001$ ⁺ $P < 0.10$.

Table 2.

Multiple Linear Regression Predicting Externalizing Problems

	Externalizing problems					<i>R</i> ²
	<i>B</i>	<i>SE</i>	β	<i>t</i>	<i>P</i>	
Model						0.17
EDA reactivity (EDA-R)	−0.31	0.148	−0.28 *	−2.09	0.042	
RSA reactivity (RSA-R)	−0.00	0.165	−0.00	−0.01	0.993	
EDA-R × RSA-R	0.51	0.191	0.38 *	2.65	0.011	

Note. Confidence interval for the significant interaction is 0.12–0.89.

Abbreviations: EDA, electrodermal activity; RSA, respiratory sinus arrhythmia.

* $P < 0.05$.