Children with Autism Show Altered Autonomic Adaptation to Novel and Familiar Social Partners

Emily Neuhaus, Raphael A. Bernier, and Theodore P. Beauchaine

Social deficits are fundamental to autism spectrum disorder (ASD), and a growing body of research implicates altered functioning of the autonomic nervous system (ANS), including both sympathetic and parasympathetic branches. However, few studies have explored both branches concurrently in ASD, particularly within the context of social interaction. The current study investigates patterns of change in indices of sympathetic (pre-ejection period; PEP) and parasympathetic (respiratory sinus arrhythmia; RSA) cardiac influence as boys (ages 8–11 years) with ($N = 18$) and without ($N = 18$) ASD engage in dyadic social interaction with novel and familiar social partners. Groups showed similar patterns of autonomic change during interaction with the novel partner, but differed in heart rate, PEP, and RSA reactivity while interacting with a familiar partner. Boys without ASD evinced decreasing sympathetic and increasing parasympathetic influence, whereas boys with ASD increased in sympathetic influence. Boys without ASD also demonstrated more consistent ANS responses across partners than those with ASD, with parasympathetic responding differentiating familiar and novel interaction partners. Finally, PEP slopes with a familiar partner correlated with boys' social skills. Implications include the importance of considering autonomic state during clinical assessment and treatment, and the potential value of regulation strategies as a complement to intervention programs aiming to support social cognition and behavior. ***Autism Res*** *2015, 00: 000–000.* © 2015 International Society for Autism Research, Wiley Periodicals, Inc.

Keywords: autism spectrum disorder; autonomic; parasympathetic; sympathetic; social interaction; heart rate; respiratory sinus arrhythmia; cardiac pre-ejection period

Introduction

Social communication difficulties are a core feature of autism spectrum disorder (ASD). From very early in life, infants who later receive an ASD diagnosis demonstrate reduced social orienting, joint attention, imitation, and processing of others' faces and emotions [Dawson & Bernier, 2007; Mundy, Sigman, & Kasari, 1990]. Over the course of development, children and adults with ASD struggle to form age-appropriate peer relationships, understand others' perspectives, and interpret social cues [Bauminger-Zviely & Agam-Ben-Artzi, 2014; Happe & Frith, 2014; Orsmond, Shattuck, Cooper, Sterzing, & Anderson, 2013; Pierce, Glad, & Schreibman, 1997]. This altered trajectory of social cognition and behavior is often attributed to very early differences in neural and physiological systems, altered social interactions and experiences, and the interaction of these biological and experiential factors [Dawson, 2008].

Recently, autonomic nervous system (ANS) function has emerged as a putative biological marker of ASD, particularly with regard to social difficulties[e.g., Faja, Murias, Beauchaine, & Dawson, 2013; Ming, Julu, Brimacombe, Connor, & Daniels, 2005; Neuhaus, Bernier, & Beauchaine, 2014; Sheinkopf, Neal-Beevers, Levine, Miller-Loncar, & Lester, 2013; Vaughan Van Hecke et al., 2009; Zahn, Rumsey, & Van Kammen, 1987]. Within the ANS, both sympathetic (SNS) and parasympathetic (PNS) nervous system branches contribute to a variety of physiological functions, including those that support and promote social and communicative behavior [Porges, 2001, 2003]. Within the parasympathetic branch, which is mediated in part by the myelinated vagus, autonomic efferent fibers originate in the nucleus ambiguous and terminate on the sinoatrial node of the heart. In combination with other nerves, the vagus innervates a range of organs in the head and neck, and affects facial expressions, vocalizations, and cardiac activity, thereby influencing social and communicative behaviors. During opportunities for social interaction, increases in PNS influence facilitate approach and adaptive social behavior [Porges, 2001; Vaughan Van Hecke et al., 2009].

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In addition to parasympathetic influence, behavioral strategies during social engagement rely on a sympathetically mediated system as well. Originating in the thoracic and lumbar regions of the spinal cord, sympathetic fibers facilitate increases in heart rate, sweating, and alertness as needed. As a result, the SNS is often associated with "flight or fight" responding. Accordingly, increases in SNS influence during social encounters reflect a threat-oriented response, whereas sympathetic decreases better facilitate adaptive social engagement [Bal et al., 2010]. Although both PNS and SNS influences exert substantial control over the heart, effects of the PNS are nearly immediate following challenge, whereas SNS influences are delayed for 20–30 sec [Berntson et al., 1997]. Thus parasympathetic influence allows quicker, more sensitive, and more finely tuned social responses than would be possible from sympathetic input alone [Porges, 2001].

Thus far, sympathetic influences in ASD remain poorly characterized. Research using electrodermal responding as a marker of SNS activity indicates comparable baseline activity across samples with and without ASD [van Engeland, 1984; Zahn et al., 1987], but altered reactivity during social tasks, the nature of which is not fully understood. For instance, findings of reduced electrodermal activity during tasks of emotion judgment [Hubert, Wicker, Monfardini, & Deruelle, 2009] imply attenuated SNS influence. In contrast, findings of heightened reactivity and reduced habituation to human faces [Mathersul, McDonald, & Rushby, 2013] and direct eye-gaze [Kylliainen & Hietanen, 2006; Kylliainen et al., 2012] imply exaggerated SNS influence.

Sympathetic influences on cardiac activity can be indexed reliably by cardiac pre-ejection period (PEP), a systolic time interval spanning left ventricular depolarization and onset of ejection of blood into the aorta. Because SNS influences increase heart rate, greater sympathetic influence corresponds to shortened PEP. PEP is captured using both electrocardiography and impedance cardiography. Pharmacologic blockade studies indicate that task-related changes in PEP are heavily influenced by SNS effects [Cacioppo et al., 1994; Sherwood et al., 1990; Sherwood, Allen, Obrist, & Langer, 1986], with little to no influence of PNS mechanisms [Cacioppo et al., 1994]. The only study to date in which PEP was investigated among individuals with ASD found comparable patterns of PEP change in response to sensory tasks across groups [Schaaf, Benevides, Leiby, & Sendecki, 2013], but no literature exists as to PEP change during social interaction.

Parasympathetic functioning in ASD is somewhat better documented, and may be best captured through PNS contributions to heart rate variability [Porges, 2001, 2004]. These are reflected most purely by high frequency beat-to-beat variability, and quantified by respiratory sinus arrhythmia (RSA) [Berntson et al., 1997]. RSA captures variation in heart rate across the respiratory cycle, and is well validated as a marker of PNS-linked cardiac activity via cholinergic blockade studies [Berntson et al., 1997; Cacioppo et al., 1994]. Among typically developing samples, RSA trajectories during early childhood predict social responsiveness [Patriquin, Lorenzi, Scarpa, & Bell, 2014], and higher levels of tonic RSA (corresponding to greater degrees of parasympathetic influence) are associated with increased social competence, engagement with peers, adaptive and support-seeking coping strategies, sympathy for others, and spontaneous eye gazes [Eisenberg et al., 1995; Fabes, Eisenberg, & Eisenbud, 1993; Heilman, Bal, Bazhenova, & Porges, 2007; Henderson, Marshall, Fox, & Rubin, 2004].

Growing evidence indicates altered RSA among children with ASD. On average, individuals with ASD have lower baseline RSA than typical peers [Guy, Souders, Bradstreet, Delussey, & Herrington, 2014; Neuhaus, Bernier, & Beauchaine, 2014; Porges et al., 2013; Vaughan Van Hecke et al., 2009], as well as altered RSA reactivity to social stimuli [Vaughan Van Hecke et al., 2009]. Consistent with non-ASD samples, higher baseline RSA is associated with stronger social skills [Neuhaus et al., 2014; Vaughan Van Hecke et al., 2009], faster emotion recognition [Bal et al., 2010; Vaughan Van Hecke et al., 2009], better pragmatic language [Klusek, Martin, & Losh, 2013], and stronger communication skills [Watson, Baranek, Roberts, David, & Perryman, 2010].

In sum, alterations to both SNS and PNS function are observed among individuals with ASD during social interaction, with the degree of alteration corresponding to severity of social difficulties. However, these systems have rarely been studied in conjunction, despite their interdependent roles in determining cardiac output and regulating social behavior. Furthermore, the role of partner familiarity in affecting ANS responding has not been studied systematically despite its potential importance. For instance, brain activity to social input in ASD more closely approximates that of typical peers when social stimuli are familiar [Oberman, Ramachandran, & Pineda, 2008; Pierce, Haist, Sedaghat, & Courchesne, 2004]: one might anticipate a similar effect with regard to autonomic functioning. Whereas unfamiliar partners should elicit an autonomic state conducive to caution, with decreasing PNS and increasing SNS influence, familiar partners should elicit a state conducive to social engagement, with increasing PNS and decreasing SNS influence [Vaughan Van Hecke et al., 2009]. To date, the only study that has examined effects of familiarity on autonomic processes in ASD found a distinct RSA decrease to a video of an unfamiliar adult in ASD, whereas children with typical development maintained baseline RSA levels [Vaughan Van Hecke et al., 2009].

The authors suggested that ASD is characterized by a "chronically 'mobilized' state" (p. 1128) where unfamiliar people elicit autonomic reactions appropriate to threat responding rather than adaptive social engagement.

Our goal with the current paper was to characterize patterns of autonomic change among children with ASD during social interactions through three objectives. First, we aimed to disentangle SNS and PNS patterns with novel and familiar social partners. We anticipated that children with and without ASD would differ in PNS and SNS change during social interaction, and that differences would be most marked with an unfamiliar partner. Specifically, we anticipated that children without ASD would display increasing PNS and decreasing SNS during social interaction (conducive to social engagement), but that children with ASD would display this pattern only with a familiar social partner. Our second objective was to compare PNS and SNS responses across both social partners as an index of ANS response organization. We anticipated that those with ASD would show less consistency in their autonomic adaptation across social partners (in the form of lower correlations between reactivity across partners), indicating a less organized and systematic autonomic response. Finally, we sought to examine relations between autonomic and social functioning, anticipating that change in RSA and PEP would correlate with social skills such that better social skills and fewer social difficulties would correspond to PNS increases and SNS decreases during social interaction.

Method

Procedure

Data were collected as part of a larger research study at the University of Washington, and the UW Institutional Review Board approved all procedures and research activities. Parents and children gave informed consent and assent, respectively, prior to participating. Families visited the laboratory for a single visit. Following consent and assent procedures, children completed a standardized IQ assessment and then played a computerized game [described in Neuhaus, Bernier, and Beauchaine, 2015] while parents completed interviews and questionnaires. Finally, children participated in 5-min social interactions with each of two partners.

Participants

Thirty-six boys (18 with ASD, 18 with typical development) participated in the current study. Children in the ASD group (mean age = 119.8 months, SD = 13.2, range 97.8–141.1) met or exceeded the "autism" cut-off on the Autism Diagnosis Observation Schedule [ADOS; Lord, Rutter, DiLavore, & Risi, 2003] revised algorithm [Gotham, Risi, Pickles, & Lord, 2007]; met or exceeded CPEA [Lainhart et al., 2006] cut-offs for "autism spectrum" on the Autism Diagnostic Interview-Revised [ADI-R; Lord, Rutter, & Le Couteur, 1994]; and met DSM-IV criteria for autism, Asperger's or PDD-NOS. ADOS calibrated severity scores [Gotham, Pickles, & Lord, 2009] for the ASD group fell within the Moderate and High ranges (mean score = 7.8, SD = 1.55, range 6–10). All participants had communicative speech by parent report, with a mean full scale IQ in the average range (mean = 108.3, SD = 21.4).

Boys in the control group (mean age = 120.1 months, SD = 11.1, range 96.4–136.02) were free of head injury, seizure history, family history of ASD, and psychiatric diagnoses. They had a mean full scale IQ of 114.8 (SD = 13.5). Control participants were also screened for subthreshold symptoms of ASD with the Child Behavior Checklist [CBCL; Achenbach, 1991] and the lifetime version of the Social Communication Questionnaire [SCQ; Rutter, Bailey, & Lord, 2003], and were excluded if their *T*-score on the CBCL Thought Problems subscale (which contains items related to repetitive behaviors) exceeded 65 or their total score on the SCQ exceeded 9. Finally, although a number of participants (6 in the ASD group, 1 in the control group) regularly used psychiatric medications (primarily selective serotonin reuptake inhibitors or atypical antipsychotics), all participants were free of stimulant medications at the time of assessment to avoid effects on autonomic physiology [Swanson & Volkow, 2002]. The racial and ethnic composition of the sample as a whole was 66.7% Caucasian, 5.5% African American, 5.5% Asian/Pacific Islander, 2.8% Latino, and 19.4% who identified as more than one race. See Table 1 for participant characteristics.

Measures and Tasks

Diagnostic measures. ASD diagnoses were determined via the ADOS and ADI-R, standardized tools for the diagnosis of ASD. The ADOS is a play-based measure of social skills, communication, and restricted/repetitive behavior and interests. The ADI-R is a semistructured caregiver interview assessing these areas throughout development. Both measures provide scoring and diagnostic algorithms that identify children with ASD with high sensitivity and specificity [Gotham et al., 2007; Lord et al., 1997]. As noted, subthreshold symptoms of ASD in the control group were assessed with two parent-report questionnaires: the CBCL and the SCQ. The CBCL contains 113 items that assess social and emotional functioning, from which we extracted the Thought Problems subscale *T*-score to assess for potential repetitive behaviors. Internal consistency and test-retest reliability estimates for the CBCL are high and range from 0.66–0.92 and 0.63–0.97, respectively

[Achenbach & Rescorla, 2001]. The SCQ score was included as an index of social difficulties, and includes items to measure social communication (e.g., eye contact, pragmatic language). The lifetime version of the SCQ contains 40 items and is highly reliable with the ADI-R, with internal consistencies between 0.89 and 0.93 [Rutter et al., 2003].

Social behavior. Social skills were assessed via parent-report with the Social Skills Intervention System [SSIS; Gresham & Elliott, 2008] and the Vineland Adaptive Behavior Scale, 2nd Edition [Vineland-2; Sparrow, Cicchetti, & Balla, 2005]. The SSIS is a 55-item questionnaire that measures social skills and problem behaviors, from which we extracted the Social Skills standard score. In this age group, internal consistency estimates for the subscales of the SSIS range from 0.74 to 0.95 and test-retest reliability ranges from 0.70 to 0.92. The Vineland-2 is a semistructured parent interview of adaptive skills across several domains. Internal consistency values for domain scores of the survey interview form are high (range = 0.88–0.94), as are test-retest reliability values (range = 0.75–0.91). In particular, the Socialization domain assesses interpersonal, play/leisure, and coping skills in everyday life, and yields a standard score. In addition to these measures of social *skills*, social *difficulties* were assessed by extracting the *T*-score for the Social Problems subscale of the CBCL.

Autonomic measures. Participants were seated in a child-sized chair in a sound-attenuated room. Electrodes were applied in a spot configuration to allow for some physical movement with minimal signal disruption [Qu, Zhang, Webster, & Tompkins, 1986]. The impedance cardiographic (ICG) signal was obtained using a HIC2000 Impedance Cardiograph (Bio-Impedance Technologies, Chapel Hill, NC), at a sampling rate of 1 kHz. An external electrocardiographic (ECG) signal was obtained using a Grass Model 15LT Physiodata Amplifier System (West Warwick, RI), also sampled at 1 kHz. Both ICG and ECG data were collected and digitized using COP-WIN software, version 6.10 (Bio-Impedance Technologies, Chapel Hill, NC). Resulting data were processed and scored by the first author (E.N.) with consultation from the third author (T.B.) as necessary. All 36 participants tolerated the collection of autonomic data and were included in the analyses presented here.

SNS-linked cardiac activity (PEP) was derived from ICG and ECG signals. PEP was quantified by the QB interval: the time (ms) between the ECG Q-wave, which signifies the onset of ventricular depolarization, and the dZ/dt B-wave, which marks opening of the aortic valve [Lozano et al., 2007; Sherwood et al., 1990]. PEP data were ensemble-averaged [Kelsey & Guethlein, 1990] in 32 sec epochs by computer, with initial PEP values derived according to COP-WIN's algorithm. Placement of B- and Q-wave markers within each averaged waveform for each epoch were then inspected visually and corrected by hand as necessary [see Beauchaine, Katkin, Strassberg, & Snarr, 2001]. Epochs with obvious artifacts (e.g., due to movement or signal loss) were discarded. As a whole, the sample had valid PEP data for approximately 84% of epochs, and the number of valid epochs did not differ between ASD and control groups, $t(34) = -0.13$, $P = 0.90$.

PNS-linked cardiac activity (RSA) was quantified by spectral-analyzing the R-wave time series of the ECG using software developed by Richard Sloan and colleagues at Columbia University [see Beauchaine, 2001; Sloan et al., 1994]. Following data collection, interbeat intervals were inspected for possible artifacts (e.g., missed or spurious heartbeats), which were hand-corrected as appropriate by dividing (for missed beats) or summing (for spurious beats) adjacent interval values. Epochs in which the number of apparent artifacts exceeded an a priori cut-off were discarded. High frequency spectral densities (>0.15 Hz) were then computed using a Fast Fourier Transform in 32-sec epochs [Berntson et al., 1997]. As is standard, RSA values were natural log-transformed prior to analyses. The sample as a whole retained RSA data for approximately 85% of epochs, and the number of retained epochs did not differ between ASD and control groups, $t(34) = -0.33$, $P = 0.74$.

Social interaction task. Each child engaged in 5-min social interaction tasks with his parent (30 participants with mother, 6 with father) and with a female research assistant to assess social behavior with a familiar and novel partner, respectively. Half of the participants interacted first with their parent, and half interacted first with the research assistant. For each interaction, pairs were seated at a table to minimize movement and maximize quality of the physiological recording. All participants complied with requests to remain seated throughout the interaction. They were provided with a bin of toys and asked to play or talk with each other however they wished for approximately 5 min (10 epochs of 32 sec). Psychophysiological data were collected continuously throughout this task.

Results

Autonomic Patterns During Social Interaction with Novel and Familiar Partners

Our first hypothesis was that children with and without ASD would differ in PEP and RSA change over the

course of social interaction, particularly with an unfamiliar partner. To explore this, a series of multilevel models (MLMs) was constructed using Hierarchical Linear Modeling (HLM)–version 7.01 to model effects of diagnostic group on autonomic functioning. This approach was selected because it accounts for repeated measurements for each individual while also allowing for retention of participants despite occasional missing epochs. Separate MLMs were created for each variable (heart rate, PEP, RSA) with each interaction partner (novel, familiar), with repeated epochs entered at Level 1 (group-centered) and diagnostic group entered as a dummy-coded fixed effect at Level 2. Age in months was entered as a Level 2 covariate to control for developmental changes in heart rate, PEP, and RSA. In these models, differences in overall level of heart rate, PEP, or RSA were represented by the intercepts, while differences in change over the course of the interaction were represented by the slopes. Recall that greater SNS influence corresponds to decreasing PEP, whereas greater PNS influence corresponds to increasing RSA. See Figure 1.

Heart rate. With the novel partner, there were effects of age, $\beta = -4.38$, $t(33) = -2.58$, $P = 0.01$, and diagnostic group, $\beta = 7.43$, $t(33) = 2.07$, $P = 0.047$, on intercepts for heart rate. Children who were younger and those with ASD had higher heart rates than those who were older or did not have ASD. There were no effects of age or group on slopes of heart rate, all ts$(33) < 1.30$, all Ps$ > 0.22$; heart rate change during the interaction was unaffected by diagnosis and age.

With a familiar partner, in contrast, there was a significant effect of diagnostic group on heart rate slopes, $\beta = 0.48$, $t(33) = 2.16$, $P = 0.04$. Whereas the control group decreased heart rate during the interaction, the group with ASD increased heart rate.

Cardiac pre-ejection period. With a novel partner, there were no effects of participant age or diagnostic group on PEP intercepts, or on rate of change during the interaction, all ts$(33) < 1.48$, all Ps$ > 0.14$. These findings suggest that neither overall level of PEP nor change in PEP during social interaction with the novel partner were affected by participant age or ASD diagnosis.

In contrast, with a familiar partner, PEP slopes were characterized by an effect of diagnostic group, $\beta = -0.43$, $t(33) = -2.14$, $P = 0.04$, indicating that change in PEP differed according to ASD diagnosis. This effect was such that children in the control group demonstrated an increase in PEP (indicating a decrease in SNS influences) while interacting with their parent, whereas children with ASD displayed a sharp decrease (indicating an increase in SNS influence). The effect of age was not significant for PEP intercepts, $\beta = 2.88$, $t(33) = 1.50$, $P = 0.14$, or slopes, $\beta = 0.06$, $t(33) = 0.69$, $P = 0.50$.

Respiratory sinus arrhythmia. With the novel partner, there was a significant effect of diagnostic group on RSA intercepts, $\beta = -0.81$, $t(33) = -3.03$, $P = 0.005$. Children with ASD exhibited lower RSA overall relative to those without ASD. However, there was no effect of group on RSA slopes with the novel partner, $\beta = 0.00$, $t(33) = -0.23$, $P = 0.82$, suggesting that ASD diagnosis did not influence RSA change. Effects of age did not reach significance for RSA intercepts, $\beta = 0.24$, $t(33) = 1.85$, $P = 0.07$, or slopes, $\beta = -0.02$, $t(33) = -0.90$, $P = 0.38$.

With the familiar partner, there was an effect of diagnostic group on both RSA intercepts, $\beta = -0.65$, $t(33) = -2.14$, $P = 0.04$, and slopes, $\beta = -0.08$, $t(33) = -2.66$, $P = 0.01$. Children in the control group had higher RSA overall, and also increased in RSA over the course of the interaction, indicating an increase in PNS influence. In contrast, children with ASD had lower RSA overall, which was maintained at a consistent level during the task. There was no effect of age on either RSA intercepts, $\beta = 0.11$, $t(33) = 0.86$, $P = 0.39$, or slopes, $\beta = 0.00$, $t(33) = -0.20$, $P = 0.84$, with the familiar partner.

Together, the MLMs suggest that children with and without ASD differed in their overall level of heart rate and RSA (represented by intercepts) while engaging with a novel partner, but that patterns of change (slopes) were similar across the groups. This differs from the pattern observed with a familiar partner, in which the groups differed in rates of change on all three autonomic measures, heart rate, PEP, and RSA. Children without ASD displayed decreasing heart rate, increasing RSA, and slightly increasing PEP. Together, these changes indicate increasing parasympathetic and decreasing sympathetic influence. Children with ASD, in contrast, displayed level heart rate and RSA, with sharply decreasing PEP. This indicates an increase in sympathetic influence.

Consistency of Autonomic Response Across Partners

Our second hypothesis was that children with ASD would display reduced correspondence between their autonomic responses across multiple social partners, suggesting a less consistent or organized autonomic response. To test this, individual slopes in heart rate, PEP, and RSA were extracted from the MLMs and compared across novel versus familiar social partners. See Table 2. Within the typically developing group, PEP slopes were positively correlated across partners, $r(18) = 0.49$, $P = 0.04$. Boys without ASD showed similar

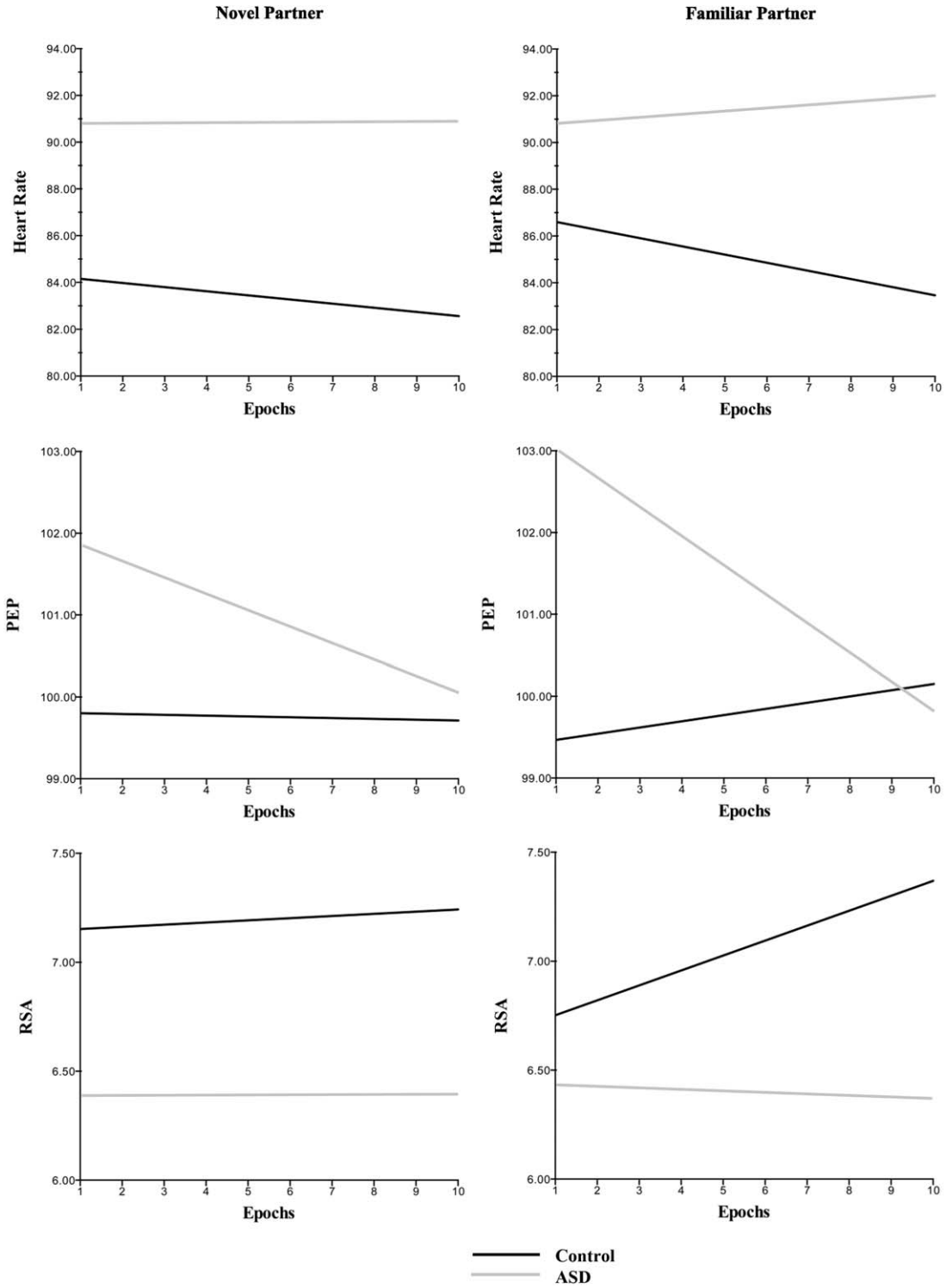

Figure 1. Autonomic change during social interaction by diagnostic group and social partner.

patterns of sympathetic change across novel and familiar partners. RSA slopes with novel and familiar partners were negatively correlated, $r(18) = -0.52$, $P = 0.03$, indicating that boys without ASD showed inverse patterns of RSA change to novel and familiar partners. Whereas sympathetic change was consistent across novel and familiar partners, parasympathetic change was sensitive to partner familiarity. See Figure 2.

Within the ASD group, in contrast, neither PEP nor RSA were correlated across interaction partners, PEP

Table 1. Means (SDs) of Behavioral and Autonomic Variables by Diagnostic Group

	Control	ASD	*F*	Effect size (η^2_p)
Age in months	120.1 (11.1)	119.8 (13.2)	0.01	0.00
Full scale IQ	114.8 (13.5)	108.3 (21.4)	1.17	0.03
SCQ total score	3.0 (2.3)	19.7 (5.0)	172.65***	0.84
SSIS social skills	101.3 (10.8)	79.8 (10.7)	36.13***	0.52
CBCL social problems	53.8 (4.5)	62.6 (7.6)	17.9***	0.35
Vineland-2 socialization	119.3 (6.9)	77.6 (17.7)	87.18***	0.72
Intercepts of MLMs				
Novel partner				
HR	83.4 (12.3)	90.9 (11.6)	3.54†	0.09
PEP	99.8 (10.6)	100.9 (11.3)	0.09	0.00
RSA	7.16 (1.0)	6.4 (0.8)	6.58*	0.16
Familiar partner				
HR	85.1 (11.9)	91.4 (10.1)	2.96†	0.08
PEP	99.8 (10.4)	101.4 (10.9)	0.19	0.01
RSA	7.1 (1.2)	6.4 (0.6)	4.28*	0.11
Slopes of MLMs				
Novel partner				
HR	−0.28 (0.9)	0.07 (0.9)	1.26	0.04
PEP	0.00 (0.6)	−0.3 (0.7)	1.19	0.03
RSA	0.01 (0.1)	−0.01 (0.1)	0.16	0.01
Familiar partner				
HR	−0.41 (0.8)	0.18 (0.8)	4.73*	0.12
PEP	0.1 (0.6)	−0.4 (0.7)	5.04*	0.13
RSA	0.08 (0.1)	−0.01 (0.1)	7.20*	0.18

Notes. SCQ, Social Communication Questionnaire; SSIS, Social Skills Improvement System; CBCL, Child Behavior Checklist; Vineland–2, Vineland Adaptive Behavior Scales, 2nd Edition; HR, heart rate; PEP, cardiac pre-ejection period; RSA, respiratory sinus arrhythmia.
†$P<.10$, *$P<.05$, ***$P<.001$.

Table 2. Correlations of Autonomic Slopes Across Novel and Familiar Social Partners by Diagnostic Group

	Full sample	Control	ASD	*z*
Heart rate slopes across partners	0.20	−0.18	0.46†	−1.86†
PEP slopes across partners	0.37*	0.49*	0.20	0.91
RSA slopes across partners	−0.17	−0.52*	0.18	−2.08*

Notes. PEP, cardiac pre-ejection period; RSA, respiratory sinus arrhythmia.
†$P<.10$, *$P<.05$.

$r(18) = 0.20$, $P = 0.42$; RSA $r(18) = 0.18$, $P = 0.49$. Boys with ASD did not display consistent or correlated changes in PEP or RSA across partners, and neither sympathetic nor parasympathetic responses distinguished novel from familiar partners. Furthermore, Fisher *r*-to-*z* transformations indicated that cross-partner RSA correlations were significantly stronger in the typically developing group than in the ASD group, $z = -2.07$, $P = 0.04$, suggesting a more consistent, organized parasympathetic response across social contexts.

Relations Between Autonomic Adaptation and Social Behavior

Our third goal was to examine associations between ANS responding and social behavior among our participants. Before exploring ANS-behavior associations, we first conducted reliability analyses for measures of social outcome within our sample. Cronbach's alpha ranged from 0.77 to 0.94 for measures of interest (SSIS Social Skills, Vineland-2 Socialization, and CBCL Social Problems), indicating good to excellent internal consistency in this sample. Next, to test relations between social measures and autonomic function, we examined correlations between MLM slopes and parent-reported social functioning, presented in Table 3. PEP slopes with a familiar partner were correlated positively with social skills, as measured by both the SSIS and the Vineland-2. Because positive PEP slopes indicate SNS withdrawal and negative PEP slopes indicate SNS increases, these correlations indicate that withdrawal of sympathetic influence was associated with better social skills, whereas increased SNS influence was associated with poorer social skills. In addition, a number of marginal correlations were such that better social skills and fewer social problems were associated with decreasing SNS and increasing PNS (increasing RSA) influence.

To better understand the relation between PEP slopes and social skills in our sample, we then examined these significant correlations within each diagnostic group separately. Within the control group, the correlation between PEP slopes with the familiar partner and Vineland-2 Socialization scores continued to reach significance and remained positively correlated, $r = 0.59$, $P = 0.01$, whereas the correlation between PEP slopes and SSIS Social Skills was no longer significant, $r = 0.29$, $P = 0.24$, likely due to the power reduction associated with the split sample. Within the ASD group, PEP slopes with the familiar partner were not correlated with either measure of social skill, rs < 0.14, Ps > 0.6. See Figure 3 for plots by diagnostic group.

Discussion

Our data represent one of the first efforts at concurrent investigation of SNS and PNS contributions to social functioning in children with ASD, and underscore notions of alterations to both of these systems as evidenced by higher heart rate, lower RSA, and different patterns of heart rate, PEP, and RSA change relative to controls. Contrary to our expectations that group differences would be most apparent with a novel social partner, the groups differed across all three indices of autonomic change while interacting with the familiar partner. Typically developing children demonstrated

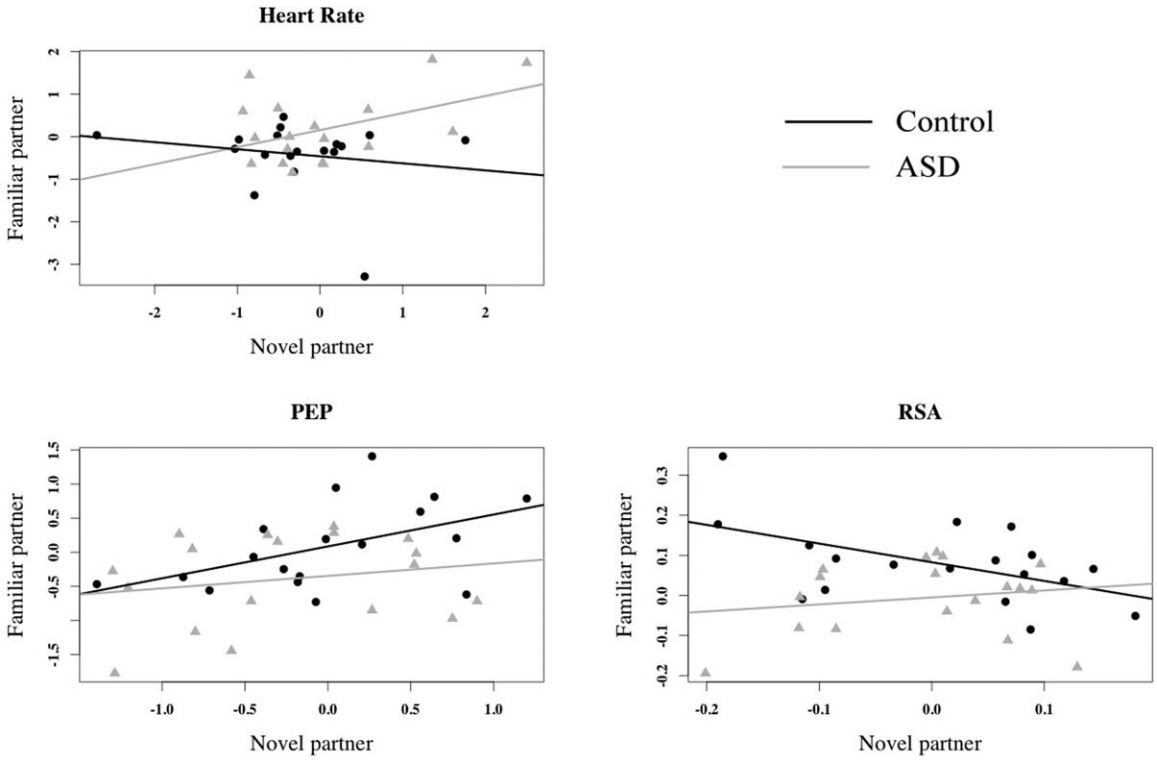

Figure 2. Correlations of autonomic slopes across social partners by diagnostic group.

Table 3. Correlations Between Autonomic Slopes and Social Behavior

	SSIS social skills	Vineland-2 socialization	CBCL Social problems
Heart rate slopes			
Novel partner	−0.08	−0.09	0.07
Familiar partner	−0.22	−0.26	0.28
PEP slopes			
Novel partner	0.30†	0.24	−0.12
Familiar partner	0.35*	0.33*	−0.33†
RSA slopes			
Novel partner	0.04	0.04	−0.10
Familiar partner	0.27	0.29†	−0.31†

Notes. SSIS, Social Skills Improvement System; Vineland–2, Vineland Adaptive Behavior Scales, 2nd Edition; CBCL, Child Behavior Checklist; PEP, cardiac pre-ejection period; RSA, respiratory sinus arrhythmia.
†$P<.10$, *$P<.05$.

decreasing heart rate, increasing PEP, and increasing RSA –indicating a reduction in sympathetic and an increase in parasympathetic influence, an autonomic state conducive to flexible social engagement [Porges, 2001, 2003; Vaughn Van Hecke et al., 2009]. Children with ASD, in contrast, demonstrated increasing heart rate, decreasing PEP, and level RSA, indicative of an increase in sympathetic influence. An SNS increase could result from increased verbal or physical activity over the course of the interaction, but such a pattern could also reflect a state conducive to cautious or threat-oriented responding [Vaughn Van Hecke et al., 2009] and thus be less conducive to sophisticated social interaction. Regardless, these findings suggest that social engagement elicits different SNS and PNS functioning from children with and without ASD, which likely then constrains the repertoire of social and communicative behaviors available to them in a given social setting.

Our results appear to contrast in part with findings from neuroimaging research, which have documented several instances in which familiarity facilitates social processing such that individuals with ASD more closely resemble typically developing peers when social stimuli are familiar [Oberman, Ramachandran, & Pineda, 2008; Pierce, et al., 2004]. In those studies, tasks have typically required passive viewing of social stimuli (e.g., human faces, videos of simple biological motion) that elicit relatively straightforward perceptual processing, assessed in relatively discrete neural regions/circuits. In those tasks, participants with ASD may have been able to process familiar stimuli more easily, with less demand on the compromised neural systems being assessed. In our study, in contrast, social stimuli (i.e., a live interaction partner) were far more complex and transactional, requiring participants to receive and interpret a variety of verbal and nonverbal behaviors from their partner, as well as produce appropriate behavioral responses. This constitutes a far greater

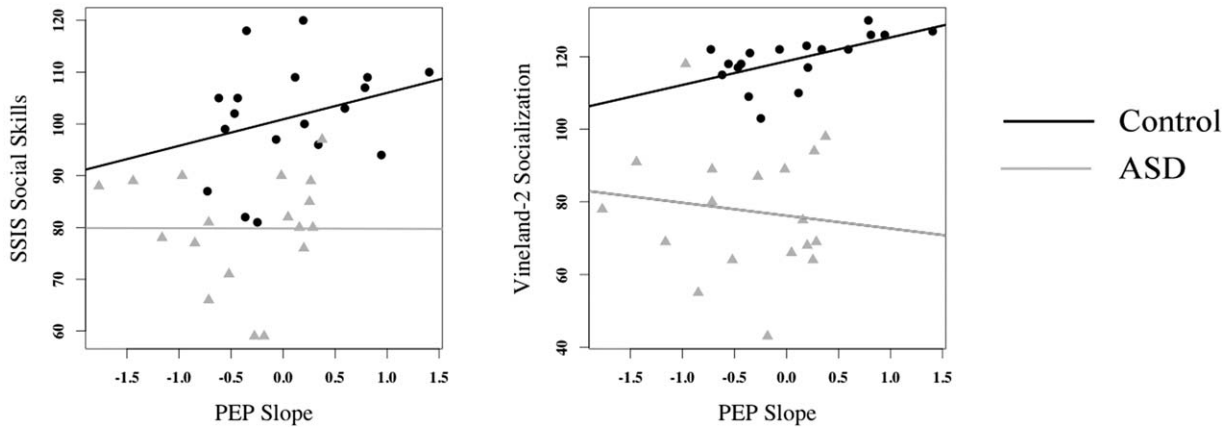

Figure 3. Within-group correlations between PEP slopes with familiar partner and social skills.

demand on participants, requiring integration of multiple neural and autonomic systems, and the familiarity of the social partner may not have been sufficient to overcome alterations to these systems.

More in accordance with our expectations, we found evidence of more consistent ANS responding to social engagement in the control group relative to the ASD group. Children without ASD demonstrated an organized physiological response to social engagement, with consistent SNS influences across interaction partners regardless of familiarity (evidenced by positively correlated PEP slopes across partners) and PNS influences that differentiated novel versus familiar partners (evidenced by negatively correlated RSA slopes across partners). The group with ASD, in contrast, did not show significantly correlated physiological responses across partners for either PEP or RSA, suggesting less coherent and organized ANS responding. To the extent that autonomic consistency translates into consistency in one's social and communication repertoire [Porges, 2001], this effect could limit the ability of individuals with ASD to reliably demonstrate a consistent set of social skills across instances, partners, or settings, with detrimental effects on relationships and day-to-day interactions.

With regard to ANS-behavior associations, autonomic slopes during interactions correlated with social skills across the sample as a whole, highlighting the importance of these systems for everyday social functioning. Better skills and fewer difficulties were associated with sympathetic withdrawal and parasympathetic increase when engaged in social interaction. Interestingly, significant correlations were observed largely in the context of the familiar social partner, each child's parent. One reason for this pattern may be the parent-report nature of our measures of social behavior. Parents' ratings would largely reflect social behaviors in their presence, and consequently could be more tightly coupled with the child's physiological functioning with the parent versus a different adult. Although plausible, we also observed several marginal correlations with the novel partner, and thus physiology-behavior links with a novel partner would likely become significant in a larger sample.

As described earlier, our participants with ASD were relatively high functioning—able to tolerate the data collection procedures and demonstrating a mean full scale IQ score well within the average range. Because of this relative homogeneity, our findings may be most applicable for high functioning children with ASD, and we cannot assume our findings would generalize to children with both ASD and intellectual disability. There is evidence to suggest links between ANS function and cognitive performance during standardized assessment in typical samples [e.g., Staton, El-Sheikh, & Buckhalt, 2009]. Indeed, post hoc correlations between IQ and ANS function in our data indicate an inverse relation between IQ and PEP intercepts with both partners (novel: $r = -0.42$, $P = 0.01$; familiar: $r = -0.34$, $P = 0.04$). Children with higher IQ tended to have lower PEP values overall. This suggests a potential role of overall developmental level for ANS function in the context of social interaction, and underscores both the need to replicate our efforts and the potential value of exploring moderators of ANS function among a more varied group of individuals with ASD.

A number of limitations temper our findings. First, our sample was entirely male, a strategy chosen to reduce etiological heterogeneity given evidence that genetic bases (and thus biological correlates) of ASD may differ by sex [Schellenberg et al., 2006]. Moving forward, sex differences in autonomic processes will be essential to explore, particularly given documented sex differences in both heart rate variability [D'Antono, Moskowitz, Miners, & Archambault, 2005; Snieder, van Doornen, Boomsma, & Thayer, 2007] and social skills [Crombie, 1988; Margalit & Eysenck, 1990] in the

general population. A second limitation relates to medication use in our sample. Due to the effects of stimulant medications on ANS functioning [Swanson & Volkow, 2002], we included only participants who were free of stimulants for at least 36 hr prior to assessment. However, the effects of other medications could not be evaluated, and this remains an important question for future investigation. In addition, our analyses did not control for effects of physical movement on autonomic activity during the social interaction, and we cannot be certain that participants were equivalent in this regard across diagnostic groups or interaction partners. Participants all remained seated in their chair throughout the interaction task and therefore we anticipate that motor movement was comparable across groups and partners, but such movement was not directly assessed.

Moving forward, it will be important to consider how ANS function during social engagement might be influenced by characteristics of the interaction partner. Although we suggest that findings of group differences with a parent but not with a research assistant are due to partner familiarity, it may be that other characteristics of the partner were confounded with familiarity. For example, the partner's biological sex, temperament, interpersonal style, or efforts to engage the child during the interaction could all have varied between parents and research assistants. If so, partners could have elicited differential social behavior and autonomic functioning from the child, regardless of familiarity. Related to this, the age of one's interaction partner could be an important factor, particularly considering reports that children with ASD may prefer interactions with adults over same-age peers [e.g., Henderson, 2001; Ozonoff, Dawson, & McPartland, 2002]. Across all of these characteristics, interacting with a partner who is socially skilled or preferred in some way could elicit increased PNS and reduced SNS influence, whereas a less skilled or preferred partner might elicit the opposite pattern. Clarifying these issues in future research will require incorporating thorough assessment of partner characteristics, as well as detailed behavioral coding of the interaction task.

These issues aside, evidence of altered autonomic adaptation during social engagement has implications for both assessment and intervention. A long history of clinical research with individuals with ASD has documented variability in behavioral repertoires across settings as well as difficulties with skill generalization [Krasny, Williams, Provencal, & Ozonoff, 2003; White, Keonig, & Scahill, 2007], and has consequently emphasized the importance of incorporating a variety of contexts (e.g., clinic, classroom, home) and social partners (e.g., clinicians, peers, teachers) into assessment and intervention settings. Data suggesting that different environments or social partners elicit different physiological states that then enhance or constrain the social skills available to a child in a given setting offer a potential mechanism for some of this observed variability.

Our data also speak to the potential value of incorporating strategies for physiological state regulation into treatment for social skill deficits and other psychological concerns (e.g., anxiety), as increasing an individual's ability to intentionally alter PNS and SNS influence through skills such as relaxation or deep breathing may permit greater flexibility to adapt to social demands. Such skills are part of some current treatment programs [e.g., Facing Your Fears; Reaven, Blakeley-Smith, Nichols, & Hepburn, 2011] and likely capitalize on the enhanced behavioral repertoires associated with increased parasympathetic and decreased sympathetic influence. Preliminary evidence suggests that multiple indices of both parasympathetic and sympathetic functioning may be alterable through behavioral treatment [Abukonna, Yu, Zhang, & Zhang, 2013; Porges et al., 2013; Suvorov, 2006], and increased emphasis on these skills (either through integration within existing treatments or as adjunctive modules) may further promote the effectiveness of behavioral treatments.

Finally, considering psychopathology more broadly, atypical ANS functioning characterizes a variety of clinical groups [Beauchaine, 2001], and relates to both emotion regulation and overall resilience across development. Interventions that explicitly address physiological well-being (e.g., one's ability to modulate regulation according to situational demands) could yield broader benefits beyond those initially targeted. For instance, regulation strategies taught in the service of improving social skills could also effect improvements in emotion regulation, frustration tolerance, aggressive behavior, or affective symptoms. In this way, comprehensive and integrative physiological and psychological treatment efforts could mitigate risk factors underlying a variety of diagnoses, thus dramatically increasing both the efficacy and efficiency of intervention programs.

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