Externalizing and Internalizing Problems in Relation to Autonomic Function: A Population-Based Study in Preadolescents

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ABSTRACT

Objective: To investigate whether externalizing and internalizing problems are related to lower and higher heart rate (HR), respectively, and to explore the relationship of these problems with respiratory sinus arrhythmia (RSA) and baroreflex sensitivity (BRS). Moreover, to study whether problems present at both preschool and preadolescent age show stronger associations with autonomic function than those that were not. **Method:** In a population cohort of 10- to 13-year-old children (N = 931; 11.6 ± 0.5 years; 47% boys), autonomic measurements in supine and standing position were performed at school. RSA and BRS were determined by spectral analysis. Current externalizing and internalizing problems were assessed by the Child Behavior Checklist and problems at age 4 to 5 retrospectively by the Preschool Behavior Questionnaire. **Results:** At supine rest, current externalizing problems were associated with lower HR and higher RSA, but not with BRS and current internalizing problems with higher HR and lower RSA, but not with BRS. These results were specifically found in children with problems that were retrospectively reported to have been also present at preschool age. Standing-induced changes in autonomic parameters were unrelated to the behavioral dimensions. **Conclusions:** Externalizing and internalizing problems are associated with divergent autonomic patterns, suggesting autonomic underarousal and overarousal, respectively. Problems starting early in life may specifically account for this. This should be confirmed in prospective studies. *J. Am. Acad. Child Adolesc. Psychiatry*, 2007;46(3):378–386. **Key Words:** autonomic nervous system, baroreflex sensitivity, psychopathology, respiratory sinus arrhythmia.

An extensive literature suggests an association between both externalizing and internalizing psychopathology and autonomic nervous system function in adults as well as in children (Beauchaine, 2001; Lorber, 2004; Ortiz and Raine, 2004). One of the best-replicated biological correlates of child psychopathology is a lower resting heart rate (HR) in children with externalizing problems (Lorber, 2004; Ortiz and Raine, 2004). This

association has often been explained by theories of autonomic underarousal or fearlessness leading to sensation-seeking and disruptive behaviors (Ortiz and Raine, 2004; Raine, 1993).

The relationship of resting HR with internalizing problems in children is less clear. Kagan et al. (1994) argued that increased autonomic activity (overarousal) may be characteristic of children who are prone to extreme fearfulness and withdrawal from unfamiliar situations, which is a risk factor for developing anxiety symptoms (Kagan and Snidman, 1999). Indeed, the few available and often small-sized studies mostly reported increased resting HR in children with internalizing problems (Kagan et al., 1987, 1988; Monk et al., 2001; Scarpa et al., 1997), although not universally so (Dorn et al., 2003; Pine et al., 1998).

HR reflects the balance between activity of the two main branches of the autonomic nervous system, the sympathetic and parasympathetic (vagal) divisions. Sympathetic activation aims to mobilize bodily resources to cope with threats or challenges. Parasympathetic influences promote restoration of health following threats or challenges and are primarily associated with calm states. In resting states, HR is largely mediated by vagal tone, which functions to slow down HR (Jose, 1966). Thus, in general, there is an inverse relationship between HR and vagal activity (Beauchaine, 2001; Berntson et al., 1993).

Respiratory sinus arrhythmia (RSA), a measure of the magnitude of rhythmic fluctuations in HR caused by respiration, is the preferred indicator of vagal activity (Beauchaine, 2001; Berntson et al., 1993). Thus, high RSA is a marker of increased vagal tone. Baroreflex sensitivity (BRS), in contrast, is an integrated measure of both sympathetic and vagal activity. The baroreflex is a short-term blood pressure (BP) control mechanism; BRS reflects changes in beat-to-beat HR resulting from variations in BP. A reduced BRS is a well-known indicator of autonomic dysfunction.

The relationship between vagal function and both externalizing and internalizing problems is still understudied and unclear (Lorber, 2004; Scarpa and Raine, 2004). Given the inverse relationship between HR and vagal activity and the association between lower HR and externalizing psychopathology, higher vagal activity would be expected in children with externalizing problems (Scarpa and Raine, 2004), whereas in those with internalizing problems, lower vagal activity would

be expected as an explanation for their higher HR. Some studies found indeed a link between externalizing problems and increased vagal activity in children and adults (Cole et al., 1996; Scarpa and Ollendick, 2003; Van Voorhees and Scarpa, 2002) and between internalizing problems and decreased vagal activity in children (Beauchaine, 2001; Kagan et al., 1987; Monk et al., 2001; Pine et al., 1998; Rubin et al., 1997). However, most studies suggested lower vagal activity in children with externalizing problems, possibly indicating autonomic dysfunction (Beauchaine et al., 2001; Mezzacappa et al., 1997; Pine et al., 1996, 1998).

Furthermore, studies investigating BRS in relation to externalizing and internalizing problems are lacking in children. In adults, a reduced BRS has been associated with depression and anxiety (Broadley et al., 2005; Virtanen et al., 2003). However, we know of only one study regarding the relationship between BRS and psychopathology in children, in which reduced BRS was linked to externalizing behavior (impulsiveness) in boys, but not in girls (Allen et al., 2000).

Thus, despite a number of intriguing findings in favor of an association between behavior profiles and autonomic function, this field of research is still characterized by inconsistent and sometimes conflicting results. These inconsistencies may be explained by the use of mostly moderately sized study samples and specific study populations (e.g., males only, high-risk populations), thereby limiting generalizability of results.

Autonomic reactions induced by orthostatic challenge have also been reported to be related to behavioral and emotional problems (Mezzacappa et al., 1997; Yeragani et al., 1991). Compared to psychological stressors, orthostatic stress may have the advantage of reducing confounding influences in terms of anticipatory anxiety (Stein et al., 1992) and of being independent from the participant's motivation, attention, and intellectual abilities. Therefore, we hypothesized that this basic reflexive physical stressor could be a viable alternative to commonly used psychological stressors (e.g., public speaking, cognitive tests), the use of which is limited in large study samples for practical reasons.

The primary goal of the present study was to examine the relationship between different autonomic indices (HR, RSA, BRS) and both externalizing (i.e., aggression, delinquency) and internalizing (i.e., anxiety, depression, somatic complaints) problems by using a

large preadolescent community sample as part of an ongoing cohort study. As a secondary goal, we explored the validity of using autonomic nervous system reactions to orthostatic challenge (i.e., standing) as a marker of psychopathology.

Our epidemiological design enabled us to determine the relevance of autonomic parameters in the general population, given the high statistical power associated with large samples and the possibility to study gender differences (Bauer et al., 2002; Fox et al., 2005). We were specifically interested in whether we could find a lower HR in children with externalizing problems and a higher HR in children with internalizing problems. Also, we examined whether both types of problem dimensions would be associated with altered RSA and BRS, which had been understudied so far.

Finally, we preliminarily investigated the possible relevance of problems that started early in life (based on retrospective report) in relation to autonomic function. It may be argued that children with problems that begin early in life form an etiologically distinct group with specific biological features (Kagan and Snidman, 1999). We expected that children with early-starting problems would show stronger associations with autonomic indices than children without a history of early problems.

METHOD

Participants

This study included 931 10- to 13-year-old Dutch children (47% boys; 11.6 ± 0.5 years, 93% white) who took part in the baseline assessment of the longitudinal cohort "Tracking Adolescents' Individual Lives Survey" (TRAILS; N = 2,230). Using biennial assessments, TRAILS investigates the development of mental health from preadolescence into adulthood (until age 24), both at the level of psychopathology and the levels of underlying vulnerability and environmental risk.

Participants were recruited through written invitations to parents and children of the required age range from five municipalities in the northern Netherlands, including both urban and rural areas. Children from schools for special education within our catchment area were part of the study; however, children with mental retardation were excluded. A more detailed description of the sample selection procedures and sample characteristics of TRAILS has been provided by de Winter et al. (2005).

A subgroup of 1,868 (84%) from the 2,230 children participated in the autonomic measurements; not all children have been included, mainly because autonomic measurements started a few months after the TRAILS data collection had begun. This also explains why the present subsample is slightly older (11.6 ± 0.5 years) than the general TRAILS sample (11.1 ± 0.6 years; t = 38.6,

p < .001). The 1,868 autonomic measurements were checked according to quality criteria, resulting in 1,472 reliable supine and 1,129 reliable standing measurements that met our quality standards (described in detail by Dietrich et al., 2006). We included only children of whom reliable autonomic values in both the supine and standing positions (n = 1,027) as well as behavioral scores (931 of these 1027) were available to avoid bias because of differences in group sizes. Behavioral scores were missing when, for unknown reasons, parents did not return the survey. The present subsample (n = 931) does not differ from the general TRAILS sample (n = 2,230) regarding gender, body mass index (BMI), pubertal stage, and externalizing and internalizing problems.

The mean BMI in the present sample was 18.9 ± 3.1 kg/m^2; 31.0% of the participants were in Tanner stage 1 (preadolescence), 55.2% in stage 2 (early adolescence), 13.5% in stage 3 (middle adolescence), and 0.3% in stage 4 (late adolescence (Tanner, 1962). A more detailed description of the study population that participated in the autonomic measurements has been reported elsewhere (Dietrich et al., 2006).

Written informed consent was obtained from the children's parents. All of the children voluntarily participated in the measurements, although no formal assent procedure has been followed for children. The study was approved by the National Dutch Medical Ethics Committee.

Measures and Procedure

Externalizing and Internalizing Problems. Children's current externalizing and internalizing problems were based on their parents' responses to the Child Behavior Checklist (CBCL/6–18; Achenbach and Rescorla, 2001). The CBCL allows for the determination of an externalizing (Aggression and Delinquency subscales) and internalizing (Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints subscales) dimension. We used only parent-based ratings for two reasons. First, we judged that the subjects' preadolescent age would make them a less reliable source of information than their parents. Second, we aimed to compare subgroups of children with and without early problems, for which we had to rely on retrospective parent reports.

Children's externalizing and internalizing behavior at age 4 to 5 was assessed retrospectively by their parents, who compared their child's behavior to that of other children (which we thought would more readily facilitate detection of behavioral deviations) on a 5-point Likert scale using the TRAILS Preschool Behavior Questionnaire (TPBQ). The TBPQ is nonvalidated, but was used given the lack of validated instruments that retrospectively assess children's preschool behavior. The TPBQ externalizing subscale has four items (Cronbach's α = .70) assessing whether the child was ill-tempered, disobedient, bossy, or bullying. The internalizing subscale has seven items (Cronbach's α = .80) on obsessive-compulsive behaviors, sadness, general anxiety, school anxiety, being bullied by other children, shyness, and being avoided by other children. Mean scores were computed for each CBCL and TPBQ problem dimension.

Autonomic Parameters. Autonomic measurements were performed individually in a quiet room at school, generally in the morning (8.30 AM–12:00 PM) and occasionally in the early afternoon (1:00–3:00 PM). Spontaneous fluctuations in continuous beat-to-beat systolic finger BP were measured noninvasively by the Portapres device. HR was registered by a three-lead electrocardiogram. Recordings did not start after a few minutes of supine rest and only after signals had reached a stabilized steady state after

circulatory readjustments of body fluid changes. Then, BP and HR signals were registered for 4 minutes in the supine position during spontaneous breathing, followed by 2 minutes in the standing position, again after signals had stabilized.

Calculation of RSA and BRS was performed by power spectral analysis using the transfer function technique as previously described (Dietrich et al., 2006; Robbe et al., 1987). The CARSPAN software program allows for discrete Fourier transformation of nonequidistant systolic BP and interbeat-interval (IBI) series. IBI refers to the time between two heartbeats. The analyzed time series were corrected for artifacts and checked for stationarity. RSA was defined as the high-frequency power (ms^2) in the 0.15- to 0.40-Hz respiratory band. BRS was defined as the mean modulus between systolic BP and IBI in the 0.07- to 0.14-Hz frequency band (ms/mmHg) with a coherence of >0.3. We have previously shown that coherence levels of 0.3 and 0.5 yield highly similar BRS values (Dietrich et al., 2006). A more detailed description of the autonomic data assessment, analysis, and variables was reported in our previous study (Dietrich et al., 2006).

Statistical Analysis

To approximate a normal distribution, RSA and BRS values were transformed to their natural logarithm, and the TPBQ and CBCL scores to z scores. Relationships between the autonomic variables were investigated by Pearson's correlation coefficients. We performed two subsequent sets of analyses: (1) to study current externalizing and internalizing problems in relation to autonomic function, we used continuous CBCL scores, thus, without regarding preschool scores (TPBQ), and (2) to investigate the role of early-starting problems, we compared three groups of children with either externalizing or internalizing problems, which were or were not present at preschool or preadolescent age. The groups were based on the median split of TPBQ and CBCL scores and described as (1) early starters (TPBQ >P50 and CBCL >P50), (2) current-only (TPBQ <P50 and CBCL >P50), and (3) controls (TPBQ <P50 and CBCL <P50). A fourth group with preschool but not current problems (TPBQ >P50 and CBCL <P50) was not included in the analyses because we primarily aimed to investigate whether possible relationships between current CBCL problems and autonomic function could be specifically found in children with problems that were already present at preschool age rather than to study the role of early problems per se.

We used analyses of variance (ANOVAs) for the two sets of analyses as described above. To analyze autonomic measures in the supine resting position, we conducted separate univariate ANOVAs with each autonomic measure (HR, RSA, BRS) as the dependent variable, and gender, age, CBCL or TPBQ externalizing and internalizing problems, and gender-behavior interactions as independent variables. By including both externalizing and internalizing problems, we adjusted for the influence of the other, given the correlations between both dimensions in our sample (TPBQ: Pearson's r = 0.28; CBCL: Pearson's r = 0.48). In case of a significant gender-behavior interaction, we repeated the analyses stratified for gender. Bonferroni post hoc corrections for multiple comparisons were applied.

To analyze standing-induced autonomic reactivity scores (i.e., difference between supine and standing), we performed separate repeated-measures ANOVAs for each autonomic measure in both the supine and standing positions (HR, RSA, BRS) as the dependent variables (thus, difference scores between autonomic variables in supine and standing position were calculated in repeated-measures

ANOVAs). In accordance with the law of initial values (Benjamin, 1963), we adjusted for baseline (supine) autonomic levels by including them as covariates. We applied the same procedure regarding the independent variables as described above.

Exploratory analyses (correlational and multivariate) in this study sample did not reveal associations between autonomic variables and potential confounders, including BMI, pubertal stage, physical activity level, alcohol and tobacco consumption, socioeconomic status, and physical health problems (i.e., diabetes mellitus, anemia, eczema, acne, and sinusitis), with the exception of allergies and asthma or bronchitis (see also Dietrich et al., 2006). Moreover, the results of this study remained unchanged after adjusting for these potential confounders in multivariate analyses. Hence, these factors were not considered further in this study.

As a measure of strength of associations, we reported partial η^2, which is comparable to r^2, expressing the percentage of explained variance when multiplied by 100. In terms of Cohen's criteria, effect sizes expressed as the percentage of explained variance may be considered as small (1.0%–5.8%, Cohen's d = 0.20), medium (5.9%–13.8%, Cohen's d = 0.50), or large (≥13.9%, Cohen's d = 0.80; Cohen, 1988). Tests were two-tailed using a p value of .05.

RESULTS

Behavioral Characteristics

Table 1 shows gender-specific means and SDs of the externalizing and internalizing CBCL and TPBQ dimensions.

Autonomic Variables and Gender Effects

Table 2 describes autonomic variables measured in the supine and standing positions. HR was significantly higher in the standing than in the supine position, whereas RSA and BRS were lower in the standing position. Girls had higher supine and standing HR, but lower supine RSA and lower supine and standing BRS

TABLE 1
Externalizing and Internalizing Problems in Boys and Girls

	Boys (n = 438) Mean (SD)	Girls (n = 493) Mean (SD)	Boys vs. Girls[a] t	p
CBCL[b]				
Externalizing	9.3 (7.2)	7.0 (5.9)	5.8	<.001
Internalizing	7.7 (5.7)	7.9 (6.1)	0.2	.883
TPBQ[c]				
Externalizing	2.7 (0.6)	2.5 (0.6)	3.9	<.001
Internalizing	2.7 (0.6)	2.6 (0.6)	1.5	.136

Note: CBCL = Child Behavior Checklist; TPBQ = TRAILS Preschool Behavior Questionnaire.
[a] Student t tests.
[b] Sum scores.
[c] Mean scores.

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TABLE 2
Autonomic Variables Measured in Supine and Standing Positions

	Supine, Mean (SD)	Standing, Mean (SD)
All children (N = 931)		
HR (bpm)	77.7 (11.1)	94.3 (13.5)
RSA ln (ms^2)	7.3 (1.3)	6.0 (1.3)
BRS ln (ms/mmHg)	2.6 (0.6)	2.0 (0.6)
Boys (n = 438)		
HR (bpm)	75.8 (10.5)	92.8 (13.4)
RSA ln (ms^2)	7.5 (1.3)	6.0 (1.3)
BRS ln (ms/mmHg)	2.6 (0.6)	2.1 (0.6)
Girls (n = 493)		
HR (bpm)	79.4 (11.3)	95.7 (13.4)
RSA ln (ms^2)	7.2 (1.3)	5.9 (1.2)
BRS ln (ms/mmHg)	2.5 (0.6)	2.0 (0.5)

Note: Posture and gender effects by Student t tests. Supine versus standing: all significant at $p < .001$. Boys versus girls: supine: all significant at $p < .001$, standing: HR $p < .001$, RSA nonsignificant, BRS $p < .010$. HR = heart rate; bpm = beats per minute; RSA = respiratory sinus arrhythmia (0.15–0.40 Hz); BRS = baroreflex sensitivity (0.07–0.14 Hz).

than boys. There were no gender differences regarding autonomic reactivity scores.

In both the supine and standing positions, HR was inversely related to both RSA ($r = -0.63$, $p < .001$ and $r = -0.69$, $p < .001$, respectively) and BRS ($r = -0.52$, $p < .001$ and $r = -0.66$, $p < .001$, respectively). In addition, RSA was positively correlated with BRS in both the supine ($r = 0.65$, $p < .001$) and standing positions ($r = 0.70$, $p < .001$). Furthermore, children with higher supine HR displayed lower HR reactivity ($r = -0.13$, $p < .001$), whereas children with higher supine RSA and supine

BRS showed increased RSA reactivity (i.e., greater suppression of RSA, $r = 0.48$, $p < .001$) and BRS reactivity ($r = 0.56$, $p < .001$), respectively.

Externalizing and Internalizing Problems

Externalizing Problems: Supine. Externalizing problems were negatively associated with HR ($F_{1,926} = 6.5$, $p = .011$, $\eta^2 = .007$) and positively with RSA ($F_{1,926} = 3.9$, $p = 0.048$, $\eta^2 = .004$), but unrelated to BRS ($F_{1,926} = 0.1$, $p = .777$, $\eta^2 = .001$).

Externalizing Problems: Reactivity. Externalizing problems were not associated with HR reactivity ($F_{1,925} = 0.7$, $p = .414$, $\eta^2 = .001$), RSA reactivity ($F_{1,925} = 1.1$, $p = .285$, $\eta^2 = .001$), nor BRS reactivity ($F_{1,925} = 0.5$, $p = .498$, $\eta^2 = .001$).

Internalizing Problems: Supine. Internalizing problems were positively related to HR ($F_{1,926} = 9.1$, $p = .010$, $\eta^2 = .010$) and negatively to RSA ($F_{1,926} = 11.9$, $p < .001$, $\eta^2 = .013$). There was no relationship with BRS ($F_{1,926} = 0.4$, $p = .545$, $\eta^2 = .001$).

Internalizing Problems: Reactivity. Internalizing problems were not associated with HR reactivity ($F_{1,925} = 0.4$, $p = .530$, $\eta^2 = .001$), RSA reactivity ($F_{1,925} = 1.2$, $p = .279$, $\eta^2 = .001$), nor BRS reactivity ($F_{1,925} = 0.1$, $p = .815$, $\eta^2 = .001$).

Early Presence of Externalizing and Internalizing Problems

Tables 3 and 4 describe the results of group comparisons (early starters versus current-only versus controls) for externalizing and internalizing problems, respectively.

TABLE 3
Externalizing Problems With and Without Presence at Preschool Age in Relation to Autonomic Supine Scores

	Early Starters (n = 292), Mean (95% CI)	Current-Only (n = 179), Mean (95% CI)	Controls (n = 261), Mean (95% CI)	F	p	η^2	Group Differences[a] ($p < .05$)
HR (bpm)	76.3 (75.1–77.6)	78.0 (76.4–79.6)	79.0 (77.6–80.4)	3.8	.022	.011	ES < CL
RSA ln (ms^2)	7.6 (7.4–7.7)	7.1 (7.0–7.3)	7.2 (7.1–7.4)	6.7[b]	.001	.019	ES > CU, ES > CL
BRS ln (ms/mmHg)	2.6 (2.6–2.7)	2.5 (2.4–2.6)	2.5 (2.5–2.6)	3.4[b]	.034	.009	ES > CU, ES > CL

Note: Means represent estimated marginal means adjusted for covariates. Main effects of the behavioral dimension are described in the table. df = 2,722. HR = heart rate; bpm = beats per minute; RSA = respiratory sinus arrhythmia; BRS = baroreflex sensitivity; ES = early starters (both preschool and current problems); CU = current-only; CL = controls.

[a] Pairwise comparisons of group means followed by Bonferroni type I error adjustment.

[b] In addition to the main effect, there was a significant gender-behavior interaction (RSA: $F_{2,722} = 3.3$, $p = .037$, $\eta^2 = .009$; BRS: $F_{2,722} = 3.0$, $p = .048$, $\eta^2 = .008$). Subsequent gender stratification revealed significant effects for girls only (RSA: $F_{2,373} = 9.7$, $p = .001$, $\eta^2 = .049$, ES > CU, ES > CL; BRS: $F_{2,373} = 5.6$, $p = .004$, $\eta^2 = .029$, ES > CU, ES > CL). RSA in girls: early starters (n = 124, mean 7.6, 95% CI 7.4–7.8), current-only (n = 89, mean 6.9, 95% CI 6.9–7.1), controls (n = 166, mean 7.1, 95% CI 6.9–7.3). BRS in girls: early starters (n = 124, mean 2.6, 95% CI 2.5–2.7), current-only (n = 89, mean 2.3, 95% CI 2.2–2.4), controls (n = 166, mean 2.4, 95% CI 2.3–2.5).

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TABLE 4
Internalizing Problems With and Without Presence at Preschool Age in Relation to Autonomic Supine Scores

	Early Starters (n = 260), Mean (95% CI)	Current-only (n = 211), Mean (95% CI)	Controls (n = 249), Mean (95% CI)	F	p	η^2	Group Differences[a] (p < .05)
HR (bpm)	79.4 (78.0–80.7)	76.7 (75.3–78.3)	76.3 (75.0–77.8)	5.5	.004	.015	ES > CU, ES > CL
RSA ln (ms^2)	7.1 (7.0–7.3)	7.3 (7.2–7.5)	7.5 (7.3–7.7)	5.0	.007	.014	ES < CL
BRS ln (ms/mmHg)	2.6 (2.5–2.6)	2.6 (2.5–2.6)	2.5 (2.5–2.6)	0.6	.946	.001	NS

Note: df = 2,711. NS = nonsignificant; HR = heart rate; bpm = beats per minute; RSA = respiratory sinus arrhythmia; BRS = baroreflex sensitivity.
[a] Description of the table and index as in Table 3.

Externalizing Problems: Supine. Children with early-starting externalizing problems had lower HR than controls. In addition to the main effect, we found a gender–behavior interaction for both RSA and BRS. Subsequent gender-stratified analyses revealed significant effects for girls only. In girls with externalizing problems, RSA of early starters was higher than that of the current-only group and of controls. Likewise, in girls, BRS of early starters was higher than of the current-only group and of controls.

Externalizing Problems: Reactivity. There were no significant group differences between children with early-starting externalizing problems, those with current-only problems, and those with no externalizing problems (controls) regarding all autonomic difference scores; in other words, HR reactivity (early starters: mean 17.1, 95% CI 16.0–18.2; current-only: mean 16.5, 95% CI 15.1–17.9; controls: mean 16.2, 95% CI 15.0–17.4; $F_{2,722}$ = 0.8, p = .453, η^2 = .002), RSA reactivity (early starters: mean −1.5, 95% CI −1.6 to −1.4; current-only: mean −1.3, 95% CI −1.5 to −1.2; controls: mean −1.3, 95% CI −1.4 to −1.2; $F_{2,722}$ = 2.6, p = .075, η^2 = .007), and BRS reactivity (early starters: mean −0.6, 95% CI −0.6 to −0.5; current-only: mean −0.5, 95% CI −0.6 to −0.4; controls: mean −0.5, 95% CI −0.5 to −0.4; $F_{2,722}$ = 3.5, p = .032, η^2 = .009, nonsignificant after Bonferroni adjustment).

Internalizing Problems: Supine. Children with early-starting internalizing problems demonstrated higher HR than children with current-only problems and controls. In addition, early starters showed lower RSA compared with controls. There were no group differences regarding BRS.

Internalizing Problems: Reactivity. No significant group effects were present for all three autonomic difference scores; in other words, HR reactivity (early starters: mean 16.7, 95% CI 15.6–17.8; current-only:

mean 17.3, 95% CI 16.0–18.5; controls: mean 16.2, 95% CI 15.0–17.4; $F_{2,710}$ = 0.7, p = .518, η^2 = .002), RSA reactivity (early starters: mean −1.4, 95% CI −1.5 to −1.3; current-only: mean −1.4, 95% CI −1.5 to −1.2; controls: mean −1.4, 95% CI −1.5 to −1.2; $F_{2,710}$ = 1.0, p = .529, η^2 = .002), and BRS reactivity (early starters: mean −0.6, 95% CI −0.6 to −0.4; current-only: mean −0.5, 95% CI −0.6 to −0.4; controls: mean −0.5, 95% CI −0.5 to −0.4; $F_{2,710}$ = 1.7, p = .826, η^2 = .001).

DISCUSSION

Current externalizing and internalizing problems in preadolescents were related to divergent autonomic patterns: externalizing problems were associated with decreased HR and increased vagal tone, and internalizing problems with increased HR and decreased vagal tone. Moreover, these associations between both problem dimensions and autonomic function were specifically found in children with behavioral and emotional problems retrospectively reported to have been already present early in the child's development.

Our finding of increased vagal activity associated with externalizing problems is in line with a few other studies that also used nonclinical, non–high-risk samples (Scarpa and Ollendick, 2003; Slobodskaya et al., 1999), but contrasts with findings of decreased vagal activity associated with externalizing problems in selected groups (Mezzacappa et al., 1997; Pine et al., 1998). This highlights the difference between behavioral problems in the general population and high-risk samples. In addition, in girls with early-starting externalizing problems, we found an increased resting BRS compared with a reduced BRS in impulsive boys in the study of Allen et al. (2000). Resting BRS represents largely (although not exclusively) vagal

activity, as reflected by the high correlation between resting RSA and BRS in our sample. The present findings of an increased RSA and BRS in combination with a lower HR also fits well with previous research in unselected population-based samples, in which RSA was inversely correlated with HR ($r = -0.60$ to -0.80), apparently helping to slow down HR (Berntson et al., 1993). Thus, it appears that a lower HR and increased RSA or BRS in relation to externalizing problems may be primarily encountered in unselected community samples, which may be characterized by a relatively lower degree of behavioral problems compared with selected samples.

Several other explanations for the contrasting findings regarding vagal tone in association with externalizing problems are possible. First, gender differences may play a role. We found increased vagal activity in association with externalizing behavior primarily in girls, whereas most studies that reported decreased vagal activity was restricted to boys (Mezzacappa et al., 1997; Pine et al., 1998). This is of particular interest, given the known lower prevalence of externalizing behavior in girls in comparison with boys and the generally lower vagal tone in girls. Second, previous studies mostly did not control externalizing behavior for internalizing problems. Failing to do so may affect the relationship between vagal function and externalizing problems (Pine et al., 1996) because comorbidity between externalizing and internalizing problems is common (Bauer et al., 2002), and internalizing problems have been associated with reduced vagal activity (Monk et al., 2001). Finally, vagal activity may be differentially related to specific types of externalizing behavior (Scarpa and Raine, 1997). In one study, lower HR and increased RSA were specifically related to proactive but not reactive aggression (Van Voorhees and Scarpa, 2002). Proactive aggression tends to be unemotional and goal directed, whereas reactive aggression is emotional, impulsive, and defensive (Scarpa and Raine, 1997). In line with this, higher vagal tone has been found to be associated with increased self-regulation and decreased negative emotional arousal when confronted with moderate-to-high–level stressors (Fabes and Eisenberg, 1997), whereas lower vagal tone plays a role in emotional lability and negative affect (Porges et al., 1994). Thus, our results of reduced HR and increased vagal tone in relation to externalizing problems could be explained by the presence of a kind

of externalizing behavior characterized by a high degree of emotion regulation and low levels of negative emotionality, which has been associated with increased vagal activity (Scarpa and Raine, 1997). Clearly, more research is needed to more fully understand the relationship between vagal function and externalizing psychopathology, preferably testing specific hypotheses regarding type and severity of externalizing symptoms.

In accordance with the concept of autonomic overarousal, we found internalizing problems to be associated with increased resting HR (Kagan et al., 1988, 1994). Also, in keeping with the results reported in the literature (Monk et al., 2001), internalizing problems were related to lower vagal tone, as indexed by RSA. This is consistent with the view that reduced vagal function reflects deficient emotion regulation (Porges et al., 1994). Decreased vagal activity has been tentatively linked to dysfunction of limbic brain structures, in particular the amygdala (Kagan et al., 1988). Future studies could prospectively investigate whether children with internalizing problems combined with an autonomic profile characterized by a higher HR and lower RSA would be at increased risk of future anxiety disorders or depression.

Internalizing problems were unrelated to BRS in this sample. This is somewhat surprising, when regarding the present high correlation between RSA and BRS and the inverse relationship between RSA and internalizing problems. Compared with RSA, which is an index of vagal activity, BRS reflects both sympathetic and vagal activity. Thus, differences in sympathetic function in relation to internalizing problems may have played a role in explaining the present result. More research is needed to elucidate the relationship between BRS and internalizing problems, given the lack of studies in children and the inconclusive findings in adults (Broadley et al., 2005; Virtanen et al., 2003; Volkers et al., 2004). Future studies may consider comparing different types of internalizing problems in relation to baroreflex function.

Finally, we tested the hypothesis that psychological functioning is related to basic autonomic reactions to orthostatic challenge, as had been suggested previously (Mezzacappa et al., 1997; Yeragani et al., 1991). However, we found no relationship between children's behavior profiles and autonomic reactivity scores. In contrast to most studies, we adjusted reactivity scores for baseline autonomic levels to rule out the influence of initial baseline (supine) levels on the magnitude of

difference scores (Beauchaine, 2001; Benjamin, 1963). The failure to control for initial values complicates a proper interpretation of the results of many previous studies (Beauchaine, 2001). The present negative findings with regard to orthostatic challenge indicate that externalizing and internalizing problems are not linked with reflexive physiological processes at the brainstem level, given that orthostatic stress predominantly engages brainstem systems (Berntson and Cacioppo, 2004). In contrast, psychological stressors may induce activation of higher central brain structures, such as the limbic system or frontal cortex involved in behavior and emotion regulation (Kagan et al., 1988). Based on the present findings, we cannot recommend orthostatic challenge as an autonomic stress test in future psychophysiological research.

Limitations

Participants' age was restricted to preadolescence, which may limit generalization of findings to other age groups. Another weakness may have been the use of single informants (parent reports) rather than multiple informants (parent and child reports) to assess externalizing and internalizing problems. However, because of the exploratory nature of this study and that parents and children have been shown to rarely agree on the presence of diagnostic conditions, regardless of diagnostic type (Jensen et al., 1999), we thought it best to use only one source of information to assess psychopathology and judged parents to be the most reliable source. However, in relying on parent reports, we may have underestimated children's internalizing problems because parents may not be fully aware of their child's anxiety or depressive symptoms, especially when children approach adolescence. Future studies may certainly use multiple informants to increase diagnostic reliability.

Another limitation of this study was that children's preschool problems were determined in retrospect by a nonvalidated instrument. Bias by current state may be involved (i.e., parents of children with more severe current problems may have been more likely to report early problems, whether or not they were present). Thus, early problems may have been overrated. Hence, the results regarding the role of early problems in relation to autonomic function should be regarded as preliminary and awaiting confirmation in prospective studies. Furthermore, the current results do not allow

inferences about causality. In theory, behavioral and emotional problems may either result from or influence autonomic function or underlying factors may independently determine behavior as well as autonomic function.

Finally, data were not collected in standardized laboratory conditions, but at schools. This may have contributed to the large interindividual differences in autonomic measures that may partly explain the small effect sizes. However, these small effect sizes should also be seen in the light of the use of a large population cohort, with rather nonspecific and relatively mild levels of behavioral and emotional problems. Larger effect sizes may be expected in clinical groups with more severe levels of psychopathology.

Clinical Implications

In conclusion, the present large preadolescent population study confirms earlier smaller scale investigations that had pointed to an association between autonomic underarousal and externalizing problems as well as between autonomic overarousal and internalizing problems. Moreover, it provides new, if preliminary, evidence that problems starting early in children's development may specifically account for these associations. The latter possibility should certainly be the focus of future, preferably prospective, research.

The present findings may help clinicians to better understand children's externalizing and internalizing problems: autonomic underarousal may facilitate risk-taking and disruptive behavior, whereas autonomic overarousal may play a role in behavioral withdrawal.

REFERENCES

Achenbach TM, Rescorla LA (2001), *Manual for the ASEBA School-Age Forms & Profiles.* Burlington: University of Vermont, Research Center for Children, Youth & Families

Allen MT, Matthews KA, Kenyon KL (2000), The relationships of resting baroreflex sensitivity, heart rate variability and measures of impulse control in children and adolescents. *Int J Psychophysiol* 37:185–194

Bauer AM, Quas JA, Boyce WT (2002), Associations between physiological reactivity and children's behavior: advantages of a multisystem approach. *J Dev Behav Pediatr* 23:102–113

Beauchaine T (2001), Vagal tone, development, and Gray's motivational theory: toward an integrated model of autonomic nervous system functioning in psychopathology. *Dev Psychopathol* 13:183–214

Beauchaine TP, Katkin ES, Strassberg Z, Snarr J (2001), Disinhibitory psychopathology in male adolescents: discriminating conduct disorder

from attention-deficit/hyperactivity disorder through concurrent assessment of multiple autonomic states. *J Abnorm Psychol* 110:610–624

Benjamin LS (1963), Statistical treatment of the law of initial values in autonomic research: a review and recommendation. *Psychosom Med* 25:556–566

Berntson GG, Cacioppo JT, Quigley KS (1993), Respiratory sinus arrhythmia: autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology* 30:183–196

Berntson GG, Cacioppo JT (2004), Heart rate variability: stress and psychiatric conditions. In: *Dynamic Electrocardiography*, Malik M, Camm AJ, eds. New York: Futura, pp 57–64

Broadley AJ, Frenneaux MP, Moskvina V, Jones CJ, Korszun A (2005), Baroreflex sensitivity is reduced in depression. *Psychosom Med* 67:648–651

Cohen J (1988), *Statistical Power Analysis For the Behavioral Sciences*, 2nd edition. Hillsdale, NJ: Lawrence Erlbaum Associates

Cole PM, Zahn-Waxler C, Fox NA, Usher BA, Welsh JD (1996), Individual differences in emotion regulation and behavior problems in preschool children. *J Abnorm Psychol* 105:518–529

De Winter AF, Oldehinkel AJ, Veenstra R, Brunnekreef JA, Verhulst FC, Ormel J (2005), Evaluation of nonresponse bias in mental health determinants and outcomes in a large sample of preadolescents. *Eur J Epidemiol* 20:173–181

Dietrich A, Riese H, van Roon AM et al. (2006), Spontaneous baroreflex sensitivity in (pre)adolescents. *J Hypertens* 24:345–352

Dorn LD, Campo JC, Thato S et al. (2003), Psychological comorbidity and stress reactivity in children and adolescents with recurrent abdominal pain and anxiety disorders. *J Am Acad Child Adolesc Psychiatry* 42:66–75

Fabes RA, Eisenberg N (1997), Regulatory control and adults' stress-related responses to daily life events. *J Pers Soc Psychol* 73:1107–1117

Fox NA, Henderson HA, Marshall PJ, Nichols KE, Ghera MM (2005), Behavioral inhibition: linking biology and behavior within a developmental framework. *Annu Rev Psychol* 56:235–262

Jensen PS, Rubio-Stipec M, Canino G et al. (1999), Parent and child contributions to diagnosis of mental disorder: are both informants always necessary? *J Am Acad Child Adolesc Psychiatry* 38:1569–1579

Jose AD (1966), Effect of combined sympathetic and parasympathetic blockade on heart rate and function in man. *Am J Cardiol* 18:476–478

Kagan J, Reznick JS, Snidman N (1987), The physiology and psychology of behavioral inhibition in children. *Child Dev* 58:1459–1473

Kagan J, Reznick JS, Snidman N (1988), Biological bases of childhood shyness. *Science* 240:167–171

Kagan J, Snidman N (1999), Early childhood predictors of adult anxiety disorders. *Biol Psychiatry* 46:1536–1541

Kagan J, Snidman N, Arcus D, Reznick JS (1994), *Galen's Prophecy: Temperament in Human Nature*. New York: Basic Books

Lorber MF (2004), Psychophysiology of aggression, psychopathy, and conduct problems: a meta-analysis. *Psychol Bull* 130:531–552

Mezzacappa E, Tremblay RE, Kindlon D et al.(1997), Anxiety, antisocial behavior, and heart rate regulation in adolescent males. *J Child Psychol Psychiatry* 38:457–469

Monk C, Kovelenko P, Ellman LM et al. (2001), Enhanced stress reactivity in paediatric anxiety disorders: implications for future cardiovascular health. *Int J Neuropsychopharmacol* 4:199–206

Ortiz J, Raine A (2004), Heart rate level and antisocial behavior in children and adolescents: a meta-analysis. *J Am Acad Child Adolesc Psychiatry* 43:154–162

Pine DS, Wasserman G, Coplan J et al. (1996), Serotonergic and cardiac correlates of aggression in children. *Ann N Y Acad Sci* 794:391–393

Pine DS, Wasserman GA, Miller L et al. (1998), Heart period variability and psychopathology in urban boys at risk for delinquency. *Psychophysiology* 35:521–529

Porges SW, Doussard-Roosevelt JA, Maiti AK (1994), Vagal tone and the physiological regulation of emotion. *Monogr Soc Res Child Dev* 59:167–186

Raine A (1993), *The Psychopathology of Crime: Criminal Behavior As a Clinical Disorder*. San Diego: Academic Press

Robbe HW, Mulder LJ, Ruddel H, Langewitz WA, Veldman JB, Mulder G (1987), Assessment of baroreceptor reflex sensitivity by means of spectral analysis. *Hypertension* 10:538–543

Rubin KH, Hastings PD, Stewart SL, Henderson HA, Chen X (1997), The consistency and concomitants of inhibition: some of the children, all of the time. *Child Dev* 68:467–483

Scarpa A, Ollendick TH (2003), Community violence exposure in a young adult sample: III. Psychophysiology and victimization interact to affect risk for aggression. *J Community Psychol* 31:321–338

Scarpa A, Raine A (1997), Psychophysiology of anger and violent behavior. *Psychiatr Clin North Am* 20:375–394

Scarpa A, Raine A (2004), The psychophysiology of child misconduct. *Pediatr Ann* 33:296–304

Scarpa A, Raine A, Venables PH, Mednick SA (1997), Heart rate and skin conductance in behaviorally inhibited Mauritian children. *J Abnorm Psychol* 106:182–190

Slobodskaya HR, Roifman MD, Krivoschekov SG (1999), Psychological health, physical development and autonomic nervous system (ANS) activity in Siberian adolescents. *Int J Circumpolar Health* 58:176–187

Stein MB, Tancer ME, Uhde TW (1992), Heart rate and plasma norepinephrine responsivity to orthostatic challenge in anxiety disorders. Comparison of patients with panic disorder and social phobia and normal control subjects. *Arch Gen Psychiatry* 49:311–317

Tanner JM (1962), *Growth at Adolescence: With a General Consideration of the Effects of Heredity and Environmental Factors Upon Growth and Maturation From Birth to Maturity*. Oxford, UK: Blackwell Scientific

Van Voorhees E, Scarpa A (2002), Psychophysiological variables in childhood proactive and reactive aggression. *Psychophysiology* 39:82

Virtanen R, Jula A, Salminen JK et al. (2003), Anxiety and hostility are associated with reduced baroreflex sensitivity and increased beat-to-beat blood pressure variability. *Psychosom Med* 65:751–756

Volkers AC, Tulen JH, van den Broek WW, Bruyn JA, Passchier J, Pepplinkhuizen L (2004), Effects of imipramine, fluvoxamine and depressive mood on autonomic cardiac functioning in major depressive disorder. *Pharmacopsychiatry* 37:18–25

Yeragani VK, Pohl R, Balon R et al. (1991), Heart rate variability in patients with major depression. *Psychiatry Res* 37:35–46