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Temperamental activation and inhibition associated with autonomic function in preadolescents. The TRAILS study

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ABSTRACT

We investigated the temperamental traits high-intensity pleasure (temperamental activation) and shyness (temperamental inhibition) in relation to autonomic function as measured by heart rate (HR), respiratory sinus arrhythmia (RSA), and baroreflex sensitivity (BRS) in 938 10–13-year-old preadolescents from a population cohort. Temperament was evaluated by parent reports on the Revised Early Adolescent Temperament Questionnaire. Autonomic measurements were obtained in supine and standing position. High-intensity pleasure was negatively associated with supine HR and positively with supine RSA and BRS in both genders. Shyness was positively related to supine BRS in girls only. Orthostatic-based autonomic reactivity (difference) scores adjusted for supine values were unrelated to temperamental measures. It appeared that higher scores on temperamental activation and inhibition are associated with higher cardiac vagal activity (RSA) and/or flexible regulation of autonomic balance (BRS), implicating healthy physiological functioning. Moreover, results suggest a physiological basis promoting the tendency towards engagement in high-intensity activities.

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1. Introduction

Temperament refers to individual differences in overt behavior, emotion, and motivational styles. Two core dimensions of temperament may be distinguished: activation, referring to an approaching and disinhibited behavioral style, and inhibition, comprising avoidant behaviors and withdrawal responses from unfamiliar situations guided by feelings of anxiety (Elliot and Thrash, 2002; Kagan et al., 1994).

Differences in temperament are thought to have an underlying neurobiological basis (Strelau, 1994). Considerable support has indeed been found for an association between temperament and autonomic nervous system functioning, although not universally so. Research in this field has traditionally focused on heart rate (HR), which is influenced by both sympathetic and parasympathetic (vagal) activity. Low HR is thought to reflect a low level of

sympathetic arousal. The stimulation-seeking theory states that this is physiologically unpleasant and may lead to engagement in exciting, sensation-seeking (approaching) behaviors that increase the low arousal level to an optimal or normal level (Eysenck, 1997). In contrast, pioneering work by Kagan and colleagues has suggested that high HR may be characteristic of individuals who are prone to extreme fearfulness and withdrawal from unfamiliar situations (Kagan et al., 1987, 1988, 1994). Indeed, the notion of an autonomic pattern reflecting autonomic overarousal in inhibition has longstanding support in the literature (Friedman, 2007).

In the past years, indices of cardiac vagal activity [such as heart rate variability (HRV) and respiratory sinus arrhythmia (RSA)] have become increasingly important as psychophysiological markers of emotion regulation and a wide range of other psychological variables (Beauchaine, 2001; Beauchaine et al., 2007; Berntson et al., 1997; Movius and Allen, 2005). The influential polyvagal theory provides a framework for the role of the parasympathetic system in children's emotion regulation and behavioral adjustment (Beauchaine et al., 2007; Porges, 1995, 2007; Porges et al., 1996). Increased cardiac vagal activity is thought to be associated with increased openness to new experiences, active engagement with and temperamental responsivity to the environment, and to

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promote effective and flexible functioning to meet changing environmental demands (Beauchaine, 2001; Porges et al., 1994, 1996; Porges, 1995).

Baroreflex sensitivity (BRS), a measure of the quality of short-term blood pressure (BP) control that reflects the relationship between BP variability and HRV, has also been shown to be a useful indicator of autonomic function (Thayer and Brosschot, 2005; van Roon et al., 2004). BRS indicates the autonomic balance (i.e., reciprocal, dynamic relationship) between sympathetic and parasympathetic activity. Especially during rest, a high BRS points to a shift towards the latter, and is as such closely related to RSA. The autonomic flexibility–neurovisceral integration model, founded in polyvagal theory, suggests that high BRS reflects autonomic flexibility (i.e., the flexible regulation of autonomic balance), thus facilitating adaptability and health (Thayer and Brosschot, 2005; Thayer and Lane, 2000). In contrast, lower levels of vagal activity and reduced autonomic flexibility are assumed in relation to inhibition (Friedman, 2007).

To summarize, based on theoretical perspectives, temperamental activation is expected to be related to low HR and both high RSA (indicating high cardiac vagal activity) and high BRS (indicating flexible regulation of autonomic balance). Temperamental inhibition, in contrast, may be linked to high HR and both low RSA (indicating low cardiac vagal activity) and low BRS (indicating inflexible regulation of autonomic balance).

Despite some intriguing findings in favor of these theoretical assumptions, this field of research has been characterized by inconsistent results. While an association between temperamental activation and low HR has indeed been shown in a few pediatric and adult studies (Puttonen et al., 2008; Raine, 1996; Raine et al., 1997; Zuckerman, 1990), other reports (in adults) have suggested no association between both measures (Heponiemi et al., 2004; Keltikangas-Jarvinen et al., 1999; Knyazev et al., 2002). Increased resting RSA levels in infants, children, and adults with a high tendency to approach have indeed been suggested in some studies (Beauchaine, 2001; Puttonen et al., 2008; Richards and Cameron, 1989), but not all (Blair, 2003). Regarding BRS, we previously found a positive association with externalizing problems in girls (Dietrich et al., 2007), whereas the only other child study reported a lower BRS in impulsive boys (Allen et al., 2000).

With respect to inhibition, a number of studies have found increased HR at different ages (Garcia Coll et al., 1984; Kagan et al., 1987, 1988; Mezzacappa et al., 1997; Puttonen et al., 2008; Scarpa et al., 1997). There have, however, also been some negative studies in this respect, in children as well as in adults (Calkins and Fox, 1992; Heponiemi et al., 2004; Knyazev et al., 2002; Marshall and Stevenson-Hinde, 1998; Schmidt et al., 1999). A similar picture emerges for cardiac vagal activity. Whereas early studies have suggested lower vagal activity in inhibited young children (Garcia Coll et al., 1984; Reznick et al., 1986) and recently also in a population sample of adults (Puttonen et al., 2008), many other studies failed to find such a relationship (Brenner, 2005; Heponiemi et al., 2004; Hofmann et al., 2005; Knyazev et al., 2002; Marshall and Stevenson-Hinde, 1998; Movius and Allen, 2005; Ravaja, 2004; Schmidt et al., 1999). In our earlier study (Dietrich et al., 2007), we did not find an association between BRS and internalizing problems in preadolescents either.

The ambiguous findings regarding the relationship between autonomic function and temperamental activation and inhibition, and the paucity of studies in this area, especially regarding temperamental activation and BRS, highlight the need of further investigation of this subject (Fox et al., 2005; Marshall and Stevenson-Hinde, 2001). One explanation for the inconsistent findings may have been the use of small samples. Studying a large population sample offers the opportunity to reliably investigate

these relationships, detect possible gender-specificity, and generalize findings to the general population.

In the present study, we investigated the possible relationship of high-intensity pleasure (as a specific example of temperamental activation) and shyness (as a specific example of temperamental inhibition) with resting HR, RSA, and BRS in a large population cohort of preadolescents. Typically, relations between temperament and autonomic function have focused on the early years of life (see Beauchaine, 2001). However, Rothbart and Derryberry (1981) used a more developmental framework of temperament in that it is shaped over time by an interplay between heredity, maturation, and experiences. This stresses the necessity of investigating temperament dimensions that are not limited to the first years of life.

We were specifically interested in high-intensity pleasure and shyness, as these traits have been shown to steer the conditional probability of externalizing and internalizing problems, thus functioning as direction markers (Oldehinkel et al., 2004). Additionally, we investigated autonomic reactions to orthostatic stress (standing), which have previously been related to psychological functioning (Kagan et al., 1994; Mezzacappa et al., 1997; Yeragani et al., 1991). We expected opposite autonomic patterns to be associated with high-intensity pleasure (i.e., low HR and both high RSA and BRS) versus shyness (i.e., high HR and both low RSA and BRS).

2. Methods

2.1. Participants

This study was performed in 938 10–13-year-old Dutch preadolescents (442 boys, mean 11.6 years, SD 0.5, 93% Caucasian) who all participate in the ongoing longitudinal community study “TRacking Adolescents’ Individual Lives Survey” (TRAILS; De Winter et al., 2005). The key objective of TRAILS is to chart and explain the development of mental health from preadolescence into adulthood, both at the level of psychopathology and the levels of underlying vulnerability and environmental risk. Sample selection procedures and methods of TRAILS have been described earlier (De Winter et al., 2005). In the present TRAILS subsample, we included all preadolescents for whom parent reported temperament scores and reliable BRS values in both the supine and standing position were available. There was no selective attrition in this subsample regarding temperament scores and general demographics.

The mean body mass index in the current sample was 18.9 ± 3.1 kg/m². About 12.5% of the participants (almost) never engage in physical activities, 24.5% once a week, 34.8% 2–3 times a week, and 14% 4–7 times a week. Drinking alcohol on a regular basis was reported by 0.6% of the participants, sometimes or a little bit by 5.7%, and (almost) never by 93.7%. Smoking tobacco regularly was reported by 0.2%, sometimes or a little bit by 2%, and (almost) never by 97.8%. The proportion of boys and girls in the prepubertal and pubertal phase was similar in both genders (Tanner stage 1: 32% and 29.8%, and stages 2–5: 68% and 70.2%, respectively; Tanner stage according to parental judgement). A more detailed description of the study population that participated in the cardiovascular measurements has been described in our previous studies (Dietrich et al., 2006, 2007). Written informed consent was obtained from the preadolescents’ parents, but participant’s assent was not asked for, given their relatively young age. The study was approved by the National Dutch Medical Ethics Committee, in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2.2. Measurements

2.2.1. Temperament

Temperament was assessed by parents’ responses on the short form of the Early Adolescent Temperament Questionnaire Revised (EATQ-R; Hartman, 2000; Putnam et al., 2001). We included only those subscales of the EATQ-R that fitted to the two basic temperamental dimensions of activation and inhibition (Elliot and Thrash, 2002), and which steered the conditional probability of externalizing and internalizing problems, respectively (Oldehinkel et al., 2004). Those subscales were high-intensity pleasure (i.e., parents indicated how much pleasure their child would derive from activities involving high-intensity or novelty, such as deep sea diving and mountain climbing; six items, Cronbach’s alpha 0.77) and shyness (i.e., behavioral inhibition to novelty and challenge, especially social; four items, Cronbach’s alpha 0.84), measured on a 5-point scale. The factor structure and internal consistency of the EATQ-R scales have been verified empirically in the TRAILS cohort, overall being similar to the original instrument (Oldehinkel et al., 2004; Putnam et al., 2001). We used the parent report, because of its better

Table 1
Temperament in boys and girls.

	Boys (<i>n</i> = 442), mean (SD)	Girls (<i>n</i> = 496), mean (SD)	Boys versus girls
High-intensity pleasure	3.4 (0.9)	3.2 (0.9)	$t = -3.4, p < .001$
Shyness	2.4 (0.9)	2.6 (0.9)	$t = 2.3, p < .05$

Note: gender differences by Student's *t*-tests.

psychometric outcomes compared to the child report (with Cronbach's alpha's near 0.60; Oldehinkel et al., 2004).

Regarding the relationship between temperament and psychopathology in the present sample (see also Oldehinkel et al., 2004), high-intensity pleasure was negatively correlated with internalizing problems (as assessed by the Child Behavior Checklist; CBCL depression and anxiety scale; $r = -.18, p < .001$) and positively with externalizing problems (CBCL delinquency and aggression scale; $r = .08, p < .05$). Shyness was positively correlated with internalizing problems ($r = .27, p < .001$) and uncorrelated with externalizing problems ($r = -.03, p = .354$). Table 1 shows gender-specific means and standard deviations of the temperament scales.

2.2.2. Cardiovascular variables

Cardiovascular measurements took place individually in a quiet room at school. First, participants lied down on a table (if unavailable, on a cushion on the floor) and were encouraged to relax and not to move or speak. While in supine position, the procedure was explained to them and a three-lead electrocardiograph was attached to register HR. A Portapres device was used to non-invasively measure spontaneous fluctuations in continuous beat-to-beat systolic finger BP (SBP). Data acquisition did not commence until HR and BP were considerably stable (i.e., as visually observed through the levelling out of the signals after initial fluctuations), usually within 5 min. BP and HR signals were registered for 4 min in the supine position during spontaneous breathing. Then, participants were requested to stand up and, again, after signal stabilization measurements proceeded for 2 min. The sample rate was 100 Hz. To obtain interbeat-intervals (IBI) with sufficient resolution for HRV determination, a special interpolation algorithm was used, increasing the time resolution for R-peak detection by a factor of 2.5.

After initial visual inspection and exclusion of unusable signals (e.g., flat recordings), calculation of RSA and BRS was performed by spectral analysis using the transfer function technique as described previously (Dietrich et al., 2006). The CARSPAN software program allows for discrete Fourier transformation of non-equidistant SBP and IBI-series. Stationarity of the time series was checked and artifacts were corrected using CARSPAN, i.e., poor quality signal intervals of up to 5 s of IBI and 10 s of SBP signals were interpolated (with a maximum of 10% of the total SBP signal length). Otherwise, data were excluded. There was no gender-specific attrition of autonomic data. RSA was defined as the high-frequency power (ms^2) in the 0.15–0.40 Hz respiratory band. RSA is associated with the rhythmic fluctuations in HR caused by respiration and is an index of vagal activity (Berntson et al., 1997). BRS was defined as the mean modulus between SBP and IBI-series in the 0.07–0.14 Hz frequency band (ms/mmHg) with coherence of more than 0.3. We have previously shown that use of coherence levels of 0.3 and 0.5 yield highly similar BRS values (Dietrich et al., 2006). A more detailed description of cardiovascular data assessment, analysis, attrition, and internal reliability is given by Dietrich et al. (2006).

2.3. Statistical analysis

RSA and BRS values were transformed to a normal distribution by taking their natural logarithm before analyzing them statistically. Pearson's correlation coefficients were calculated to determine correlations between the cardiovascular and temperament measures, respectively.

To examine the effects of temperament on autonomic function, univariate and repeated measures analyses of variance [ANOVA's, using the General Linear Model (GLM), hierarchical method, SPSS 15.00] were performed for each cardiovascular variable (HR, RSA, BRS) separately, using supine and both supine and standing cardiovascular measures respectively as continuous dependent variables. Within the repeated measures design, within-subjects difference scores (i.e., supine minus standing, or autonomic reactivity scores) were calculated, being the dependent variable. GLM was chosen given the repeated measures design and high power associated with it. In the first model, to adjust for possible confounding, firstly, gender was entered as a control variable, and secondly age, given the association of gender with both temperament (Oldehinkel et al., 2004) and cardiovascular measures (Dietrich et al., 2006), and of age with the latter. Then, both continuous temperament scales, which were modestly inversely correlated ($r = -.29, p < .05$), were entered.

In the second model, two-way interactions between gender and temperament (both gender $\times$ high-intensity pleasure and gender $\times$ shyness) were added to the first main effects model, considering possible gender-specificity of associations (Beauchaine, 2001). When analyzing autonomic reactivity scores, we adjusted for baseline (supine) cardiovascular levels by including the supine variable as an

Fig. 1. High-intensity pleasure versus supine heart rate (HR). To visualize the continuous temperament scores, three groups of boys and girls with low (<1 SD below mean), moderate (values >1 SD below and <1 SD above mean), and high (>1 SD above mean) temperament scores were composed. Given gender differences in sample characteristics of temperament and cardiovascular measures, bars are shown separately for boys and girls (analyses were conducted in the entire group). The mean scores are adjusted for covariates. Error bars represent SE.

Fig. 2. High-intensity pleasure versus supine respiratory sinus arrhythmia (RSA). Descriptions as in Fig. 1.

independent covariate, in accordance with the law of initial values (Benjamin, 1963). To further analyze significant gender-interactions, we repeated analyses stratified for gender.

Preliminary analyses in the present study sample had not revealed associations between cardiovascular variables (HR, RSA, BRS) and body mass index, pubertal stage, physical activity level, alcohol and tobacco consumption, and socio-economic status (see also Dietrich et al., 2006). Hence, these factors were not further considered here. Only for the purpose of presentation of the continuous temperament scores, three groups separately for boys and girls were composed, with low, moderate, and high temperament scores (see Figs. 1–4). 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 (1988), effect sizes expressed as the percentage of explained variance may be considered as small ($<5.8\%$, $d = 0.20$), medium (5.9 – 13.8% , $d = 0.50$), or large ($>13.9\%$, $d = 0.80$). The significance level p was set at 0.05.

3. Results

3.1. Cardiovascular variables and gender effects

Table 2 presents gender-specific means and standard deviations of HR, RSA, and BRS measured in the supine and standing position. HR was significantly higher in the standing than in the

Fig. 3. High-intensity pleasure versus supine baroreflex sensitivity (BRS). Descriptions as in Fig. 1.

Fig. 4. Shyness versus supine baroreflex sensitivity (BRS). Represent results from gender-stratified analyses separately for boys and girls. Further descriptions as in Fig. 1.

supine position ($F_{1,933} = 3006.4$, $p < .001$, $\eta^2 = .763$), whereas RSA ($F_{1,933} = 1265.7$, $p < .001$, $\eta^2 = .576$) and BRS ($F_{1,933} = 739.5$, $p < .001$, $\eta^2 = .442$) were significantly lower. Girls had higher supine HR values ($F_{1,933} = 19.3$, $p < .001$, $\eta^2 = .020$), but lower

Table 2
Gender-specific means and standard deviations of the cardiovascular variables.

	Supine position, mean (SD)	Standing position, mean (SD)
Boys ($n = 442$)		
HR (bpm)	75.9 (10.5)	92.9 (13.5)
RSA ln(ms ²)	7.5 (1.3)	6.0 (1.3)
BRS (ms/mmHg)	16.4 (9.4)	9.5 (5.3)
BRS ln(ms/mmHg)	2.6 (0.6)	2.1 (0.6)
Girls ($n = 496$)		
HR (bpm)	79.3 (11.3)	95.6 (13.4)
RSA ln(ms ²)	7.2 (1.3)	5.9 (1.2)
BRS (ms/mmHg)	14.1 (8.7)	8.4 (4.4)
BRS ln(ms/mmHg)	2.5 (0.6)	2.0 (0.5)

Note: HR: heart rate; RSA: respiratory sinus arrhythmia (power in the 0.15–0.40 Hz high-frequency band); BRS: baroreflex sensitivity (modulus in the 0.07–0.14 Hz low-frequency band); ln: natural logarithm. Supine versus standing based on t -tests: all significant at $p < .001$; boys versus girls: supine all significant at $p < .001$; standing: HR and BRS significant at $p < .01$.

supine RSA ($F_{1,933} = 10.0$, $p = .002$, $\eta^2 = .011$) and supine BRS values ($F_{1,933} = 17.2$, $p < .001$, $\eta^2 = .018$) than boys. There was no gender effect regarding HR, RSA, and BRS reactivity (i.e., difference scores between supine and standing).

RSA was positively correlated with BRS in both the supine ($r = .65$, $p < .001$) and standing position ($r = .71$, $p < .001$). HR was inversely related to RSA and BRS, also in both the supine (RSA: $r = -.63$, $p < .001$; BRS: $r = -.52$, $p < .001$) and standing position (RSA: $r = -.70$, $p < .001$; BRS: $r = -.67$, $p < .001$). Furthermore, subjects with higher supine HR displayed lower HR reactivity ($r = -.13$, $p < .001$), whereas those with higher supine RSA and supine BRS showed increased RSA reactivity (i.e., greater suppression of RSA, $r = .48$, $p < .001$) and BRS reactivity ($r = .56$, $p < .001$), respectively.

3.2. Temperament and autonomic function

3.2.1. High-intensity pleasure

3.2.1.1. Supine. Main effects were found in the whole study group, i.e., in both boys and girls, in whom high-intensity pleasure was negatively associated with HR ($F_{1,933} = 14.1$, $p < .001$, $\eta^2 = .015$; Fig. 1), and positively with RSA ($F_{1,933} = 6.9$, $p = .009$, $\eta^2 = .007$; Fig. 2) and BRS ($F_{1,933} = 4.0$, $p = .046$, $\eta^2 = .004$; Fig. 3), adjusted for the covariates gender (HR: $F_{1,933} = 23.2$, $p < .001$, $\eta^2 = .024$; RSA: $F_{1,933} = 11.3$, $p < .001$, $\eta^2 = .012$; BRS: $F_{1,933} = 18.3$, $p < .001$, $\eta^2 = .019$) and age (HR: $F_{1,933} = 2.7$, $p = .099$, $\eta^2 = .003$; RSA: $F_{1,933} = 21.1$, $p < .001$, $\eta^2 = .022$; BRS: $F_{1,933} = 0.2$, $p = .633$, $\eta^2 = .001$). In the second model, including gender-temperament interactions, no significant gender-specific effects were detected regarding HR ($F_{1,931} = 0.1$, $p = .925$, $\eta^2 = .001$), RSA ($F_{1,931} = 0.1$, $p = .984$, $\eta^2 = .001$), and BRS ($F_{1,931} = 0.4$, $p = .511$, $\eta^2 = .001$).

3.2.1.2. Reactivity. There was no relationship between high-intensity pleasure and orthostatic stress induced HR reactivity ($F_{1,932} = 1.0$, $p = .317$, $\eta^2 = .001$; $F_{1,930} = 0.4$, $p = .504$, $\eta^2 = .001$), RSA reactivity ($F_{1,932} = 1.4$, $p = .244$, $\eta^2 = .001$; $F_{1,930} = 0.5$, $p = .476$, $\eta^2 = .001$), and BRS reactivity ($F_{1,932} = 0.1$, $p = .723$, $\eta^2 = .001$; $F_{1,930} = 0.2$, $p = .670$, $\eta^2 = .001$), neither regarding the first model including only main effects, nor regarding the second with respect to the gender-interactions, respectively.

3.2.2. Shyness

3.2.2.1. Supine. There was no main effect of shyness on HR ($F_{1,933} = 0.1$, $p = .857$, $\eta^2 = .001$) and RSA ($F_{1,933} = 0.8$, $p = .370$, $\eta^2 = .001$), and no gender-temperament interaction regarding HR ($F_{1,931} = 0.3$, $p = .556$, $\eta^2 = .001$) and RSA ($F_{1,931} = 0.1$, $p = .724$, $\eta^2 = .001$). However, in addition to a main effect ($F_{1,933} = 5.0$, $p = .025$, $\eta^2 = .005$), there was a significant gender-interaction between shyness and BRS ($F_{1,931} = 4.6$, $p = .032$, $\eta^2 = .005$), both adjusted for gender and age (see above). Subsequent gender-stratification showed a significant positive relationship between shyness and BRS in girls ($F_{1,492} = 9.6$, $p = .002$, $\eta^2 = .019$), but not in boys ($F_{1,438} = 0.1$, $p = .956$, $\eta^2 = .001$) (Fig. 4).

3.2.2.2. Reactivity. Again, in both sets of analyses, with respect to the main effects and gender-temperament interactions, respectively, shyness was not related to HR reactivity ($F_{1,932} = 0.8$, $p = .379$, $\eta^2 = .001$; $F_{1,930} = 0.8$, $p = .381$, $\eta^2 = .001$), RSA reactivity ($F_{1,932} = 2.4$, $p = .122$, $\eta^2 = .003$; $F_{1,930} = 0.1$, $p = .804$, $\eta^2 = .001$), and BRS reactivity ($F_{1,932} = 0.2$, $p = .627$, $\eta^2 = .001$; $F_{1,930} = 0.7$, $p = .396$, $\eta^2 = .001$).

4. Discussion

The temperamental traits of high-intensity pleasure (indicating activation) and shyness (indicating inhibition) appeared not to be

related to opposite autonomic patterns. In line with expectations, high-intensity pleasure was associated with a lower HR and higher RSA (indicating higher cardiac vagal activity) and higher BRS (indicating flexible regulation of autonomic balance). However, unexpectedly, shyness was also associated with a higher BRS in girls. Higher scores on both temperament dimensions thus appeared to be linked to increased autonomic flexibility.

Basal autonomic reactions to orthostatic challenge (adjusted for supine levels) were not related to the two temperamental traits. Apparently, in contrast to psychological stressors, the present physiological stimulus did not evoke autonomic responses in higher brain structures (e.g., amygdala), proposed in emotion and behavior regulation (Kagan et al., 1988; Schwartz et al., 2003). Rather, orthostatic challenge has been shown to engage predominantly brain stem systems and to trigger a basal, reflexive autonomic reaction (Berntson and Cacioppo, 2004). Still, individual differences in stress reactivity may become manifest not only at the frontal-limbic and hypothalamic level, but also at the peripheral level (including orthostasis; Lavallo, 2005). However, peripheral functions typically involve structural alterations on the long-term, unlikely to be observed as an expression of temperamental traits in preadolescents. Psychological stress reactivity tasks are therefore recommended for future studies at this young age.

Our finding of a lower supine resting HR in relation to high-intensity pleasure in both genders appeared to largely result from increased cardiac vagal activity, given the high correlation between HR and RSA in the present sample. It may also partially be explained by decreased sympathetic activity, which was, however, not measured. The present result provides support to the sparse pediatric literature pointing to autonomic underarousal in association with a stimulation-seeking trait (Puttonen et al., 2008; Raine, 1996; Zuckerman, 1990). It thus appears that HR is not only decreased in relation to externalizing psychopathology (Ortiz and Raine, 2004), but also decreased in relation to a stimulation-seeking temperament, which is thought to underlie externalizing behavior problems (Raine et al., 1998). Autonomic underarousal may trigger engagement in sensation-evoking activities in order to counterbalance the low arousal levels, explaining pleasure-seeking, risk-taking behaviors (Raine, 2002).

The temperamental trait of high-intensity pleasure appeared to be positively associated not only with RSA, but also with BRS, in both genders. Supine RSA and BRS were highly correlated, pointing to a high level of vagal activity expressed by BRS. The present findings are in support of Porges' polyvagal theory and other related models (autonomic flexibility–neurovisceral integration model), emphasizing that increased dynamic and flexible autonomic regulation reflects healthy (physiological and psychological) processes (Beauchaine, 2001; Beauchaine et al., 2007; Friedman, 2007; Porges, 2007; Thayer and Brosschot, 2005; Thayer and Lane, 2000). The findings are also in line with earlier reports linking increased vagal activity to a greater capacity for active engagement with the environment, increased openness, and behavioral responsivity (Beauchaine, 2001; Movius and Allen, 2005). The seemingly contradictory interpretation of our findings within the framework of both arousal and polyvagal theory, i.e., linking high-intensity pleasure both to the risk of externalizing psychopathology and healthy functioning, may be reconciled by taking on a developmental perspective. It may be assumed that behavior considered as 'healthy' at one point in development, may (in conjunction with other risk factors) eventually contribute to the emergence of pathology during a later (more sensitive, high-risk) period. For instance, (late) adolescence and early adulthood are known to witness an exponential rise of psychopathology.

Unexpectedly, neither HR nor RSA was related to shyness in the present large preadolescent population cohort. Developmental

changes in the maturation of the autonomic system and differentiation of temperament characteristics may play a role. Indeed, most studies that have reported increased HR and decreased RSA in relation to inhibition were conducted in infants and young children (Garcia Coll et al., 1984; Kagan et al., 1987; Reznick et al., 1986; Scarpa et al., 1997), whereas studies that did not find a relationship concerned mostly older children and adults (Brenner, 2005; Heponiemi et al., 2004; Hofmann et al., 2005; Marshall and Stevenson-Hinde, 1998; Knyazev et al., 2002; Schmidt et al., 1999). Those findings stress that HR and RSA may be related to measures of temperamental inhibition primarily in infants and young children (Marshall and Stevenson-Hinde, 2001).

To our knowledge, we are the first to indicate an association between BRS and a measure of inhibition in a pediatric sample. Interestingly, BRS was positively rather than negatively associated with shyness in girls, whereas RSA was unrelated to it. We suspect that, despite the high inter-correlation between both autonomic measures, BRS (indicating reflexive autonomic regulation) more sensitively reflects the balance between parasympathetic and sympathetic autonomic activity than does RSA (indicating tonic cardiac vagal activity).

An explanation for the positive as opposed to negative association between BRS and shyness in girls is not readily available. Based on the existing adult literature linking BRS with various inhibition measures (e.g., pathological or trait anxiety; Virtanen et al., 2003; Watkins et al., 2002) and the notion that shyness generally represents a more cumbersome temperamental trait (implying stress sensitivity), a negative relationship would have been expected between BRS and shyness. Adult samples may differ from pediatric populations in that important confounders, such as lifestyle factors (e.g., low exercise level, drug use), cardiovascular disease, and emotional illness, known to be related to decreased vagal activity (Thayer and Brosschot, 2005) may have contributed to such a negative relationship. However, studies with infants and young children have also found lowered vagal function in association with inhibition measures (Garcia Coll et al., 1984; Reznick et al., 1986). We know of one pediatric study that has reported higher vagal activity associated with inhibition in young children (Blair, 2003), and another study showing a marginally significant positive association between both variables in adult men (Movius and Allen, 2005). Apparently, measures of temperamental inhibition, such as shyness, are not necessarily related to cardiovascular autonomic abnormalities or dysfunction, but may also reflect physiologically adaptive functioning. In this context, it may be noted that shyness (social fear) is a basic human emotion, and may as such be assumed to represent an evolutionary adaptive coping strategy (Vingerhoets et al., 2008). Furthermore, interestingly, in keeping with polyvagal theory, a recent study has found that women with higher vagal activity experienced and expressed more negative emotion (Butler et al., 2006), a predisposition of shy individuals (Eisenberg et al., 1998). Finally, our results suggest that gender-specific maturational processes are involved, considering the typical increase of shyness (and self-awareness) in preadolescence, and shyness representing a characteristic female gender role.

4.1. Limitations and future directions

The introduced error through variability in experimental settings is a limitation of this study. This as well as the focus on resting autonomic measurements may partly explain the present small effect sizes. The somewhat static and limited autonomic measurements, including the lack of sympathetic measures are weaknesses. Yet, the study of BRS as an index of autonomic flexibility may be considered as strength. It should further be noted

that the assessment of temperament was based on subjective parent reports, reflecting parents' perception of reality. A possible disadvantage of our approach to measure specific, narrowly defined temperament constructs is the reduced generalizability to other, often broadly defined concepts of temperamental activation and inhibition. Nevertheless, this provides the opportunity to gain insight into specific aspects of temperament, and minimize confounding influences of temperamental tendencies within the broader definitions.

Future studies are needed to further support our findings on the relationship between autonomic function and temperament, particularly shyness (inhibition). Preferably, a developmental framework should be used, to detect possible maturation effects. Preadolescence might be a relatively 'silent developmental period', without evident autonomic dysregulation associated with temperamental traits. Furthermore, future research may investigate the potential role of autonomic indices as protective or risk factors in the relationship between temperamental traits and the development of psychopathology.

4.2. Conclusions

This study provides new evidence for a direct, albeit weak, association between autonomic function and high-intensity pleasure (indicating temperamental activation) and shyness (indicating temperamental inhibition), thus supporting the idea that temperament is related to adaptive autonomic regulation. The finding of increased cardiac vagal activity (RSA) and flexible regulation of autonomic balance (BRS) in relation to high-intensity pleasure fits with the theoretical notion that variability in the dynamic and flexible relationship among system elements represents healthy (psychological and physiological) functioning (Beauchaine, 2001; Thayer and Brosschot, 2005). The higher BRS associated with girls' shyness possibly suggests that, at least in preadolescent girls, shyness may be a physiologically adaptive trait.

Moreover, the present autonomic profile found in relation to high-intensity pleasure may promote the tendency towards engagement in high-intensity activities and thus provide an explanation for sensation-seeking behaviors. It must be noted, however, that causal chains cannot be inferred from this cross-sectional study. To conclude, this study indicates that individual differences in autonomic function play some role in individual differences in overt behavior, emotion, and motivation.

Conflict of interest

There are no conflicts of interest to declare.

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References

- Allen, M.T., Matthews, K.A., Kenyon, K.L., 2000. The relationships of resting baroreflex sensitivity, heart rate variability and measures of impulse control in children and adolescents. *International Journal of Psychophysiology* 37, 185–194.
- Beauchaine, T., 2001. Vagal tone, development, and Gray's motivational theory: toward an integrated model of autonomic nervous system functioning in psychopathology. *Developmental Psychopathology* 13, 183–214.
- Beauchaine, T.P., Gatzke-Kopp, L., Mead, H.K., 2007. Polyvagal theory and developmental psychopathology: emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology* 74 (2), 174–184.
- Benjamin, L.S., 1963. Statistical treatment of the law of initial values in autonomic research: a review and recommendation. *Psychosomatic Medicine* 25, 556–566.
- Berntson, G.G., Cacioppo, J.T., 2004. Heart rate variability: stress and psychiatric conditions. In: Malik, M., Camm, A.J. (Eds.), *Dynamic Electrocardiography*. Futura, New York, NY, pp. 57–64.
- Berntson, G.G., Bigger Jr., J.T., Eckberg, D.L., Grossman, P., Kaufmann, P.G., Malik, M., Nagaraja, H.N., Porges, S.W., Saul, J.P., Stone, P.H., van der Molen, M.W., 1997. Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology* 34, 623–648.
- Blair, C., 2003. Behavioral inhibition and behavioral activation in young children: relations with self-regulation and adaptation to preschool in children attending Head Start. *Developmental Psychobiology* 42, 301–311.
- Brenner, S.L., 2005. A comparison of psychophysiological and self-report measures of BAS and BIS activation. *Psychophysiology* 42, 108–115.
- Butler, E.A., Wilhelm, F.H., Gross, J.J., 2006. Respiratory sinus arrhythmia, emotion, and emotion regulation during social interaction. *Psychophysiology* 43, 612–622.
- Calkins, S.D., Fox, N.A., 1992. The relations among infant temperament, security of attachment, and behavioral inhibition at 24 months. *Child Development* 63, 1456–1472.
- De Winter, A.F., Oldehinkel, A.J., Veenstra, R., Brunnekreef, J.A., Verhulst, F.C., Ormel, J., 2005. Evaluation of nonresponse bias in mental health determinants and outcomes in a large sample of preadolescents. *European Journal of Epidemiology* 20, 173–181.
- Dietrich, A., Riese, H., van Roon, A.M., van Engelen, K., Ormel, J., Neeleman, J., Rosmalen, J.G.M., 2006. Spontaneous baroreflex sensitivity in (pre)adolescents. *Journal of Hypertension* 24, 345–352.
- Dietrich, A., Riese, H., Sondeijker, F.E.P.L., Greaves-Lord, K., van Roon, A.M., Ormel, J., Neeleman, J., Rosmalen, J.G.M., 2007. Externalizing and internalizing problems in relation to autonomic function: a population-based study in preadolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* 46 (3), 378–386.
- Eisenberg, N., Shepard, S.A., Fabes, R.A., Murphy, B.C., Guthrie, I.K., 1998. Shyness and children's emotionality, regulation, and coping: contemporaneous, longitudinal, and across-context relations. *Child Development* 69, 767–790.
- Elliot, A.J., Thrash, T.M., 2002. Approach-avoidance motivation in personality: approach and avoidance temperaments and goals. *Journal of Personality and Social Psychology* 82, 804–818.
- Eysenck, H.J., 1997. Personality and the biosocial model of antisocial and criminal behavior. In: Raine, A., Brennan, P., Farrington, D.P., Mednick, S.A. (Eds.), *Bio-social bases of violence*. Plenum Press, New York, NY, pp. 21–38.
- Fox, N.A., Henderson, H.A., Marshall, P.J., Nichols, K.E., Ghera, M.M., 2005. Behavioral Inhibition: linking biology and behavior within a developmental framework. *Annual Review of Psychology* 56, 235–262.
- Friedman, B.H., 2007. An autonomic flexibility-neurovisceral integration model of anxiety and cardiac vagal tone. *Biological Psychology* 74, 185–199.
- Garcia Coll, C., Kagan, J., Reznick, J.S., 1984. Behavioral inhibition in young children. *Child Development* 55, 1005–1019.
- Hartman, C.A., 2000. Dutch translation of the Early Adolescent Temperament Questionnaire. Internal report, Department of Psychiatry, University Medical Center Groningen, The Netherlands.
- Heponiemi, T., Keltikangas-Jarvinen, L., Kettunen, J., Puttonen, S., Ravaja, N., 2004. BIS-BAS sensitivity and cardiac autonomic stress profiles. *Psychophysiology* 41, 37–45.
- Hofmann, S.G., Moscovitch, D.A., Kim, H.J., 2005. Autonomic correlates of social anxiety and embarrassment in shy and non-shy individuals. *International Journal of Psychophysiology* 61 (2), 134–142.
- Kagan, J., Reznick, J.S., Snidman, N., 1987. The physiology and psychology of behavioral inhibition in children. *Child Development* 58, 1459–1473.
- Kagan, J., Reznick, J.S., Snidman, N., 1988. Biological bases of childhood shyness. *Science* 240, 167–171.

- Kagan, J., Snidman, N., Arcus, D., Reznick, J.S., 1994. *Galen's Prophecy: Temperament in Human Nature*. Basic Books, New York, NY.
- Keltikangas-Jarvinen, L., Kettunen, J., Ravaja, N., Naatanen, P., 1999. Inhibited and disinhibited temperament and autonomic stress reactivity. *International Journal of Psychophysiology* 33, 185–196.
- Knyazev, G.G., Slobodskaya, H.R., Wilson, G.V., 2002. Psychophysiological correlates of behavioural inhibition and activation. *Personality and Individual Differences* 33, 647–660.
- Lovallo, W.R., 2005. *Stress and Health: Biological and Psychological Interactions*, second ed. Sage, Oklahoma City, pp. 197–219.
- Marshall, P.J., Stevenson-Hinde, J., 1998. Behavioral inhibition, heart period, and respiratory sinus arrhythmia in young children. *Developmental Psychobiology* 33, 283–292.
- Marshall, P.J., Stevenson-Hinde, J., 2001. Behavioral inhibition: physiological correlates. In: Crozier, W.R., Alden, L.E. (Eds.), *Handbook of social anxiety: concepts, research and interventions relating to the self and shyness*. John Wiley, Chichester, pp. 53–76.
- Mezzacappa, E., Tremblay, R.E., Kindlon, D., Saul, J.P., Arseneault, L., Seguin, J., Pihl, R.O., Earls, F., 1997. Anxiety, antisocial behavior, and heart rate regulation in adolescent males. *Journal of Child Psychology and Psychiatry* 38, 457–469.
- Movius, H.L., Allen, J.J., 2005. Cardiac vagal tone, defensiveness, and motivational style. *Biological Psychology* 68, 147–162.
- Oldenhinkel, A.J., Hartman, C.A., De Winter, A.F., Veenstra, R., Ormel, J., 2004. Temperament profiles associated with internalizing and externalizing problems in preadolescence. *Development and Psychopathology* 16, 421–440.
- Ortiz, J., Raine, A., 2004. Heart rate level and antisocial behavior in children and adolescents: a meta-analysis. *Journal American Academy Child Adolescent Psychiatry* 43, 154–162.
- Porges, S.W., 1995. Orienting in a defensive world: mammalian modifications of our evolutionary heritage. A polyvagal theory. *Psychophysiology* 32, 301–318.
- Porges, S.W., 2007. The polyvagal perspective. *Biological Psychology* 74 (2), 116–143.
- Porges, S.W., Doussard-Roosevelt, J.A., Maiti, A.K., 1994. Vagal tone and the physiological regulation of emotion. *Monographs of the Society for Research in Child Development* 59, 167–186.
- Porges, S.W., Doussard-Roosevelt, J.A., Portales, A.L., Greenspan, S.I., 1996. Infant regulation of the vagal “brake” predicts child behavior problems: a psychobiological model of social behavior. *Developmental Psychobiology* 29, 697–712.
- Putnam, S.P., Ellis, L.K., Rothbart, M.K., 2001. The structure of temperament from infancy through adolescence. In: Elias, A., Angleitner, A. (Eds.), *Advances and proceedings in research on temperament*. Pabst Scientist Publisher, Berlin, Germany, pp. 165–182.
- Puttonen, S., Elovainio, M., Kivimäki, M., Koskinen, T., Pulkki-Raback, L., Viikari, J.S., Raitakari, O.T., Keltikangas-Järvinen, L., 2008. Temperament, health-related behaviors, and autonomic cardiac regulation: the cardiovascular risk in young Finns study. *Biological Psychology* 78, 204–210.
- Raine, A., 1996. Autonomic nervous system factors underlying disinhibited, antisocial, and violent behaviour. *Biosocial perspectives and treatment implications*. *Annals of the New York Academy of Sciences* 794, 46–59.
- Raine, A., 2002. Biosocial studies of antisocial and violent behavior in children and adults: a review. *Journal of Abnormal Child Psychology* 30, 311–326.
- Raine, A., Venables, P.H., Mednick, S.A., 1997. Low resting heart rate at age 3 years predisposes to aggression at age 11 years: evidence from the Mauritius Child Health Project. *Journal American Academy Child Adolescent Psychiatry* 36, 1457–1464.
- Raine, A., Reynolds, C., Venables, P.H., Mednick, S.A., Farrington, D.P., 1998. Fearlessness, stimulation-seeking, and large body size at age 3 years as early predispositions to childhood aggression at age 11 years. *Archives of General Psychiatry* 55, 745–751.
- Ravaja, N., 2004. Effects of a small talking facial image on autonomic activity: the moderating influence of dispositional BIS and BAS sensitivities and emotions. *Biological Psychology* 65, 163–183.
- Reznick, J.S., Kagan, J., Snidman, N., Gersten, M., Baak, K., Rosenberg, A., 1986. Inhibited and uninhibited children: a follow-up study. *Child Development* 57, 660–680.
- Richards, J.E., Cameron, J.D., 1989. Infant heart-rate variability and behavioral developmental status. *Infant Behavior and Development* 12, 45–48.
- Rothbart, M.K., Derryberry, D., 1981. Development of individual differences in temperament. In: Lamb, M., Brown, A. (Eds.), *Advances in Developmental Psychology*. Erlbaum, Hillsdale, NJ, pp. 37–86.
- Scarpa, A., Raine, A., Venables, P.H., Mednick, S.A., 1997. Heart rate and skin conductance in behaviorally inhibited Mauritian children. *Journal of Abnormal Psychology* 106, 182–190.
- Schmidt, L.A., Fox, N.A., Schulkin, J., Gold, P.W., 1999. Behavioral and psychophysiological correlates of self-presentation in temperamentally shy children. *Developmental Psychobiology* 35, 119–135.
- Schwartz, C.E., Wright, C.I., Shin, L.M., Kagan, J., Rauch, S.L., 2003. Inhibited and uninhibited infants “grown up”: adult amygdalar response to novelty. *Science* 300, 1952–1953.
- Strelau, J., 1994. The concepts of arousal and arousability as used in temperament studies. In: Bates, J.E., Wachs, T.D. (Eds.), *Temperament: Individual Differences at the Interface with Biology and Behavior*. American Psychological Association, Washington DC, pp. 117–141.
- Thayer, J.F., Brosschot, J.F., 2005. Psychosomatics and psychopathology: looking up and down from the brain. *Psychoneuroendocrinology* 30, 1050–1058.
- Thayer, J.F., Lane, R.D., 2000. A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders* 61 (3), 201–216.
- van Roon, A.M., Mulder, L.J., Althaus, M., Mulder, G., 2004. Introducing a baroreflex model for studying cardiovascular effects of mental workload. *Psychophysiology* 41, 961–981.
- Vingerhoets, A., Nyklicek, I., Denollet, J. (Eds.), 2008. *Emotion Regulation: Conceptual and Clinical Issues*. Springer, New York, pp. 3–27.
- Virtanen, R., Jula, A., Salminen, J.K., Voipio-Pulkki, L.M., Helenius, H., Kuusela, T., Airaksinen, J., 2003. Anxiety and hostility are associated with reduced baroreflex sensitivity and increased beat-to-beat blood pressure variability. *Psychosomatic Medicine* 65, 751–756.
- Watkins, L.L., Blumenthal, J.A., Carney, R.M., 2002. Association of anxiety with reduced baroreflex cardiac control in patients after acute myocardial infarction. *American Heart Journal* 143 (3), 460–466.
- Yeragani, V.K., Pohl, R., Balon, R., Ramesh, C., Clitz, D., Jung, I., Sherwood, P., 1991. Heart rate variability in patients with major depression. *Psychiatry Research* 37, 35–46.
- Zuckerman, M., 1990. The psychophysiology of sensation seeking. *Journal of Personality* 58, 313–345.