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Autonomic arousal in children of parents with and without social anxiety disorder: a high-risk study

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Objective: Autonomic hyperarousal in social situations is considered a genetic vulnerability factor for social anxiety disorder (SAD), but so far it is unstudied in children at risk for developing SAD. We examined autonomic activity during socially stressful tasks in children of mothers and fathers with and without lifetime SAD to reveal possible biological mechanisms of intergenerational transmission of SAD. **Methods:** One hundred ten children aged 4.5 years were asked to sing a song in front of an audience and watch back their performance in the presence of that audience. Heart rate (HR), heart rate variability (HRV), electrodermal activity (EDA), and blushing (cheek blood flow and temperature) were measured in anticipation of, during, and after the tasks. Both parents' lifetime SAD status was assessed, and both parents reported about their own and their child's social anxiety symptoms. **Results:** Children of parents with lifetime SAD blushed more during the socially challenging tasks than children of parents without SAD. Moreover, children of parents with more social anxiety symptoms showed increased EDA throughout the tasks. Finally, more blushing, increased EDA, and reduced HRV were associated with greater child social anxiety. **Conclusions:** This study adds to the current knowledge on the intergenerational transmission of SAD by providing evidence that children at risk for SAD are characterized by excessive blushing in socially challenging situations. The findings also demonstrate that heightened autonomic activity is a characteristic of social anxiety already during early childhood. Hence, autonomic hyperarousal, and blushing in particular, is likely to play an etiological role in the development of SAD. **Keywords:** Social anxiety disorder; autonomic arousal; blushing; intergenerational transmission; high-risk design.

Introduction

Extant data continuously support the concept of familial resemblance for social anxiety disorder (SAD) (Stein, Chartier, Lizak, & Jang, 2001). Children of parents with SAD are at higher risk for developing SAD themselves through both genetic and environmental factors and their interaction (Beidel, 1988). A recent meta-analysis on genetic and environmental contributions to SAD found that genetic factors highly contribute to the development of SAD (with an estimated 0.41 proportion of variance), and therefore, the authors suggested that the familial transmission of SAD may be explained primarily by genetic factors (Scaini, Belotti, & Ogliari, 2014).

Autonomic hyperarousal typically measured as elevated heart rate (HR), reduced heart rate variability (HRV), and increased electrodermal activity (EDA) is considered to be a marker of genetic vulnerability to anxiety disorders (Kagan, 1994; Turner, Beidel, & Epstein, 1991). Autonomic hyperarousal in social situations plays a key role in cognitive models of SAD (Clark & Wells, 1995; Rapee & Heimberg, 1997) and is part of the diagnostic criteria for SAD (American Psychiatric Association, 2013). It is thought to be an important maintaining factor in SAD (Bögels & Lamers, 2002; Clark & Wells, 1995); however, the evidence regarding its role in the etiology of SAD is currently lacking. Thus, it is not yet clear if

autonomic hyperarousal in social situations is only a consequence of already developed SAD or if it is as well a presyndromal indicator of SAD. Cognitive models of SAD propose that anxiety-prone individuals are sensitive to interoceptive cues which they appraise in a dysfunctional way (e.g., catastrophizing) (Bögels, Mulkens, & De Jong, 1997; Domschke, Stevens, Pfeiderer, & Gerlach, 2010). The experience of autonomic arousal, such as a feeling of heat in the cheeks may, therefore, lead individuals to become aware of their blushing, which may give rise to dysfunctional thoughts (e.g., people will notice that I am blushing and they will think I am stupid, see Bögels & Reith, 1999). These thoughts, in turn, can lead to fear and avoidance of social situations in which autonomic arousal has been experienced and bring about constant fear of negative evaluation in similar social situations, which is the hallmark of SAD (Bögels et al., 2010). Thus, it is possible that autonomic hyperarousal plays an important role not only in the maintenance of SAD but also in its development.

In order to better understand the developmental role of autonomic hyperarousal in SAD, studies investigating autonomic activity in children are much needed. Moreover, to be able to investigate if autonomic hyperarousal is a premorbid factor of SAD and not only a symptom of already developed SAD, studies investigating children at risk for SAD are required. A few studies that investigated autonomic activity in socially anxious children found the patterns of autonomic basal hyperarousal as

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indicated by elevated sympathetic activation and/or reduced parasympathetic activation during baseline (Schmitz, Krämer, Tuschen-Caffier, Heinrichs, & Blechert, 2011; Schmitz, Tuschen-Caffier, Wilhelm, & Blechert, 2013) and autonomic hyperresponsiveness as indicated by elevated sympathetic activation and/or reduced parasympathetic activation during a stressful task compared to baseline (Beidel, 1988). However, several studies failed to find heightened autonomic activity in terms of basal hyperarousal and hyperresponsiveness in socially anxious children and hyperresponsiveness in socially anxious children (Alkozei, Creswell, Cooper, & Allen, 2015; Anderson & Hope, 2009; Anderson, Veed, Inderbitzen-Nolan, & Hansen, 2010). Furthermore, some studies found blunted rather than increased physiological response (e.g., Schmitz et al., 2013), and some studies found slower autonomic recovery after a stressful task in combination with basal hyperarousal in socially anxious children (Schmitz et al., 2011).

Inconsistent findings regarding autonomic basal hyperarousal and hyperresponsiveness in socially anxious children reflect similar findings found in the literature about socially anxious adults (e.g., Edelmänn & Baker, 2002; Mauss, Wilhelm, & Gross, 2004; McTeague et al., 2009; Voncken & Bögels, 2009). Thus, although theoretical models propose autonomic hyperarousal as an important characteristic of individuals with SAD, incoherent empirical findings in adults and children do not always support this assumption. It is, therefore, important to further investigate autonomic activity in relation to SAD.

Studies investigating autonomic arousal in socially anxious children mostly assessed children within 7–18 years. However, social anxiety symptoms may occur already at preschool age (Colonnesi, Engelhard, & Bögels, 2010; Edwards, Rapee, Kennedy, & Spence, 2010). From a developmental perspective, a concept of the self as an object appears in the second year of life (Lewis, 1995). At this age, children may experience heightened self-consciousness and fear as a consequence of being in the center of attention (Lewis, 1995). Between the age of 3 and 4, children also develop internal standards against which they can judge their own behaviors (Lewis, 2003) and the capacity for perspective taking (Newman, 1986) and may experience social fear when they think they may be judged negatively by other people (Lewis, 2003). Increased physiological arousal may be present very early in development as well (Siess, Blechert, & Schmitz, 2014). For example, studies on behavioral inhibition found patterns of physiological hyperarousal already in children aged 1–3 years (Kagan, Reznick, & Snidman, 1987). Because heightened autonomic arousal seems to be an early risk factor for later SAD, it is particularly important to study autonomic activity in young children who are at risk for developing SAD and to investigate the association

between physiological arousal and social anxiety symptoms already during early childhood.

Employing a high-risk study design and comparing offspring of parents with and without anxiety disorders is a particularly powerful way of identifying whether autonomic hyperarousal is a premorbid vulnerability factor for anxiety disorders and a possible biological mechanism of its transmission from parents to their offspring (Merikangas, Avenevoli, Dierker, & Grillon, 1999). Up to date, only a few high-risk studies have compared the psychophysiology in offspring of parents with and without anxiety disorders, and no high-risk study has investigated offspring at risk for SAD in particular. These studies typically measured hyperarousal in situations known to elicit general, and not social fear, such as loud noise or a picture of an animal (Grillon, Dierker, & Merikangas, 1997; Merikangas et al., 1999; Turner, Beidel, & Roberson-Nay, 2005), whereas no study has investigated physiological arousal in situations that are typically fearful for socially anxious people (e.g., performance in front of an audience) (American Psychiatric Association, 2013).

Previous studies on the transmission of anxiety disorders found that children of parents with anxiety disorders are generally characterized by autonomic hyperarousal compared with children of parents without anxiety disorders (Grillon et al., 1997; Merikangas et al., 1999; Turner et al., 2005). For example, both basal autonomic hyperarousal and hyperarousal during a fearful task indexed as more spontaneous skin conductance fluctuations were found in children of parents with anxiety disorders compared with children of parents with no mental disorders (Turner et al., 2005). Furthermore, elevated skin conductance during baseline as well as increased startle reflex reactivity was found to be greater in offspring of anxious parents compared with offspring of nonanxious parents (Merikangas et al., 1999). In the study investigating offspring of patients with panic disorder, higher resting HR and HR increases during fearful stimuli were found in children of parents with panic disorder compared with the control (Battaglia et al., 1997).

Although the basic emotion that underlies social anxiety is fear which activates the fight-flight system in socially threatening situations, socially anxious individuals also experience embarrassment and shyness as a consequence of social exposure (Gerlach, Wilhelm, & Roth, 2003). Some empirical studies suggested that autonomic responses of embarrassment and shyness are distinct from those of related emotions, such as fear (Keltner & Buswell, 1997). Blushing, the most prominent physiological response of shyness and embarrassment (Gerlach et al., 2003; Leary & Meadows, 1991), is also known to be a 'hallmark' physiological reaction of SAD (American Psychiatric Association, 2013; Bögels et al., 2010). Although there is a lack of empirical evidence, in theory, blushing has been assumed to

be a physiological response specific of SAD and not of other anxiety disorders (de Vente, Majdandžić, & Bögels, 2014). Furthermore, it has been hypothesized that blushing may be an etiological factor of SAD development (Voncken & Bögels, 2009). A recent meta-analysis on blushing and social anxiety confirmed that socially anxious adults blush more than low socially anxious individuals (Nikolić, Colonnese, de Vente, Drummond, & Bögels, 2015). In a recent study, blushing was also found in socially anxious children who do not adaptively regulate their arousal in social situations (Nikolić, Colonnese, de Vente, & Bögels, 2016). Examining the blushing response in young children at risk for developing SAD may, therefore, contribute to the existing knowledge of vulnerability factors for developing SAD.

This study

The purpose of this study was to examine autonomic arousal as represented by HR, HRV, EDA, and blushing among children at high risk for developing SAD. A high-risk sample of young children was identified in the context of parental psychopathology. In this study, autonomic arousal was compared between children of parents with and without lifetime SAD. Blushing was measured for the first time next to HR, HRV, and EDA in children at risk for SAD. Furthermore, physiological activity of children was measured during two socially stressful tasks: performance in front of an audience and watching the performance back – situations that are typically threatening for socially anxious individuals (American Psychiatric Association, 2013). By adopting a high-risk design and the concept of investigating autonomic hyperarousal in socially threatening situations, we aimed to shed more light on the possible biological mechanisms of SAD development. We hypothesized that children of parents with SAD would show heightened autonomic activity measured as elevated HR, reduced HRV, increased EDA, and increased blushing compared with children of parents without SAD. Finally, to clarify the patterns of physiological activity in relation to early social anxiety, we tested whether autonomic hyperarousal marks heightened social anxiety already in early childhood.

Methods

Participants

One hundred ten children (54 boys) with an average age of 53.26 months ($SD = 0.63$) who took part in an ongoing longitudinal study on the development of anxiety participated in this study (for the detailed description of the sample see de Vente, Majdandžić, Colonnese, & Bögels, 2011). Families were recruited during the pregnancy with a first child through midwives, advertisements, and leaflets. Parents were mostly Caucasian (93%) with a relatively high educational level ($M = 6.97$, $SD = 1.17$ on the scale 1–8). The study was

approved by the ethics committee of the University of Amsterdam. Parents provided informed consents prior to the participation.

In this study, data of the children's visit to the laboratory with their father, when they were 4.5 years old, were used. All children were rated as having normal weight on the 4-point scale based on US Center for Diseases Control and Prevention standards (1, underweight; 2, normal/healthy weight; 3, overweight; and 4, obese) by two independent coders (inter-rater reliability $r = 1.00$), and no child was rated as underweight, overweight, or obese. The families who were included in this study when the children were 4.5 years old ($n = 118$) and the families who withdrew from the study at any point after the prenatal measurement ($n = 33$) were compared on personal characteristics (SAD, SAD severity, and social anxiety symptoms) and demographic characteristics (education level, income, and work situation). The comparisons revealed that there were no differences between the families ($p > .05$) except for their educational level for mothers and for educational level and lifetime SAD for fathers. Mothers and fathers included in the study had significantly higher educational level than parents of children who withdrew from the study, $t_{(144)} = 2.60$, $p = .010$ and $t_{(148)} = 2.00$, $p = .047$, respectively. Fathers who withdrew from the study had more frequently lifetime SAD compared with fathers whose children were included in this study, $\chi^2_{(1)} = 5.77$, $p = .020$.

Setting and procedure

Two socially stressful tasks were conducted during a laboratory visit of the child with the father: a performance and a watching-back task. Children were asked to sing a song of their own choice. The child could dress up, for example, in a shiny blouse. During the baseline phase, the child sat on the podium for 2 min. Following the baseline, the child was asked to stand on the podium and sing a song of his/her choice on stage in front of three audience members: a test leader, his/her father, and an unknown woman who was recording the performance. After the child stood up and the test leader announced the child's performance, the performance phase started. During the performance, children did not excessively move (e.g., dance or walk), but were standing in front of the microphone and singing a song. The test leader was instructed to encourage the child to sing further if the child sang for <60 s. Following the performance, the child was invited to sit on the podium after which the recovery phase started. After recovering for 1 min, the child was asked to watch his/her recorded performance (if the child sang a song) with the father and the test leader on a television screen while sitting on the podium.

Measures

Physiological data recording. All measures were recorded and analyzed with the Vsrp98 software (Molenkamp, 2011) on a personal computer running Windows 7. The actual data acquisition in the program was performed by a National Instruments NI6224 data acquisition card sampling at a rate of 200S/s per channel. All physiological measures were computed for each task phase: 2-min baseline; 30-s social performance; 1-min recovery and 30 s of watching back the performance. Because not all children sang for 60 s or more ($n = 14$), 30-s periods for the performance and watching back were used in the analyses. We excluded the task phases shorter than 60 s in the analyses of HRV because of the recommendation to use a minimum of 60-s periods for measuring HRV in a reliable way (Task Force of the European Society for Cardiology, 1996). All other 30-s autonomic measures showed very strong correlations with 60-s autonomic measures (r ranged from .97 to 1.00, all $p < .001$), indicating that they were measured in a reliable way in 30-s periods.

Blush response. Blushing response was measured with an infrared-reflective photoplethysmograph device that was both DC and AC coupled. The DC component of the signal represents blood volume, while the AC component is a measure for the blood pulse amplitude. The plethysmograph output signal was amplified and filtered (low-pass, 0.75 Hz, 12 dB/oct for the 'DC' signal; high-pass, 0.5 Hz, 36 dB/oct for 'AC' signal). The DC and AC output signals were converted to arbitrary values in the range of 0–65535 (16-bit ADC) at a speed of 200 S/s. Because the absolute values of photoplethysmographic output may be influenced by individual differences in skin characteristics (Drummond et al., 2007), percentage increases from baseline to performance, to recovery, and to watching back in blood pulse amplitude (AC reactivity) and blood volume (DC reactivity) were computed.

Cheek temperature was monitored unilaterally with a platinum PT1000 temperature sensor fastened to the skin on the cheekbone of the left cheek, next to the infrared probe of the plethysmograph transducer. Relative changes (raise) in cheek temperature (i.e., temperature reactivity) were computed. Additionally, because raise in the temperature may be influenced by the starting (baseline) values of temperature (Schandry & Poth, 1983), we controlled for the baseline values of temperature in the analyses with temperature reactivity. Higher values in the performance and watching-back reactivity index indicate more blushing, whereas higher values during recovery index indicate less recovery after the performance task.

Cardiovascular measures. ECG was recorded using a standard Lead-II configuration. R-waves were automatically detected and corrected for artifacts. Two parameters were computed: HR was calculated as the number of R waves per minute and HRV was calculated as the square root of the mean squared differences (RMSSD) of successive normal-to-normal (NN) intervals – a commonly used HRV measure (Malik, 1996).

Electrodermal measures. Electrodermal activity was recorded with two curved Ag/AgCl electrodes placed on the middle phalanx of the middle and index finger of the child's left hand. Two parameters were calculated: skin conductance level reported in micro-Siemens and the number of spontaneous skin conductance responses (a number of fluctuations from a baseline exceeding .05 micro-Siemens). These two measures were significantly correlated throughout the task phases, $r(n = 84) = .55, p < .001$ for baseline, $r(n = 81) = .50, p < .001$ for performance, $r(n = 81) = .36, p = .001$ for recovery, and $r(n = 67) = .41, p < .001$ for watching back, and were z-transformed and averaged into a composite measure of EDA.

Parents' social anxiety disorder. The parent's diagnostic status was determined by the Anxiety Disorders Interview Schedule for adults (adult ADIS-A) (Brown, Barlow, & Di Nardo, 1994), a semi-structured clinical interview assessing anxiety disorders and other psychopathology. Interviewers made ratings on the ADIS Clinician Severity Rating (CSR; 0 = not at all, 8 = very, very much). Diagnoses with ratings of ≥ 4 are considered to be of a clinical level. The interview was conducted twice: at the prenatal measurement (current SAD status and lifetime SAD status were assessed) and when the child was 4.5 years old (past 5-year SAD status and current SAD status were assessed) by four trained and experienced interviewers. A trained psychologist recoded 10% of the interviews conducted at the prenatal measurement and 14% of the interviews conducted when the child was 4.5 years old. The percentage inter-interviewer agreement for SAD diagnoses was 95% for the prenatal measurement and 100% for the follow-up measurement. Past and current SAD diagnoses were combined into lifetime SAD diagnosis. The child was considered to be at risk for SAD if one or both parents had lifetime SAD.

Accordingly, children were divided into two groups: (1) children at high risk for SAD with at least one parent with SAD and (2) children at low risk for SAD with parents without SAD.

Parents' social anxiety symptoms. The abbreviated version of the Social Phobia and Anxiety Inventory (SPAI; Turner, Beidel, Dancu, & Stanley, 1989), the SPAI-18 (de Vente, Majdandžić, Voncken, Beidel, & Bögels, 2014), was used to assess social anxiety symptoms in parents. The SPAI-18 is a short version of SPAI questionnaire that has been shown to be highly reliable (Bögels & Reith, 1999; de Vente, Majdandžić, Voncken, et al., 2014). Internal consistency in the current sample was excellent ($\alpha = .98$ for both mothers and fathers). Parents filled in the questionnaire at the prenatal measurement and their scores were averaged into a composite measure.

Children social anxiety symptoms. The Social Anxiety subscale of the revised Preschool Anxiety Scale (Edwards et al., 2010) filled out by both parents was used to measure children's social anxiety symptoms at the age of four-and-a-half years. The subscale has good construct validity and internal consistency (Edwards et al., 2010). Internal consistency in the current sample was good ($\alpha = .87$ for mothers and $\alpha = .88$ for fathers). Mothers' and fathers' ratings of their child's social anxiety were correlated, $r(n = 96) = .50, p < .001$, z-transformed, and averaged into a composite score.

Statistical analyses. Physiological variables were repeatedly measured during separate task phases (i.e., baseline, performance, recovery, and watching back). Because task phases were nested within individuals, we used multilevel modeling to analyze the data. For each physiological measure, a two-level model with restricted maximum likelihood estimation was constructed. These two-level mixed-effects models were fitted separately with parents' SAD diagnosis, parents' SA symptoms, and child social anxiety symptoms predicting autonomic arousal of the child. Initially, we tested the models with 'predictor x', 'task phase', and the 'predictor x–task phase' interaction predicting children's autonomic arousal. Interactions were kept in the model or removed from the model based on *t*-tests. The significance of effects was evaluated at $\alpha < .05$. When no variance was explained by the two-way interactions, the interaction effects were excluded from the final models. Effect sizes (partial eta squared) were reported next to the tests of significance in the multilevel models and interpreted as follows: small = 0.01, medium = 0.06, and large = 0.14 (Cohen, 1988).

Results

Preliminary analyses

One hundred two children took part in the social performance task, and eight children refused to take part in the task. One child was excluded from the analyses due to fussiness she displayed during the social performance evoked by specific fear of doctors (and electrodes). Children who refused to take part in the social performance task did not significantly differ in their social anxiety levels and parents' SAD from children who carried out the social performance task, $t_{(101)} = 0.85, p = .398$ and $\chi^2_{(1)} = 2.12, p = .145$, respectively. Physiological equipment failed for 11 children who carried out the tasks. Consequently, these children did not have any of the physiological variables measured and were excluded

from the following analyses. These children did not significantly differ in their social anxiety levels and parents' SAD from children whose physiological activity was recorded, $t_{(93)} = 1.61$, $p = .111$, and $\chi^2_{(1)} = 0.27$, $p = .745$, respectively. Although the majority of children sang a song ($n = 81$), some children ($n = 21$) did not sing. The two groups of children did not differ on any of the autonomic measures during the performance (all $p > .05$), except on EDA, $t_{(82)} = 2.65$, $p = .010$ with higher EDA in children who did not sing. However, differences in EDA between these two groups of children were present already during baseline, $t_{(85)} = 2.04$, $p = .045$, indicating that the differences in this physiological measure did not occur due to different activity levels during the performance (singing vs. not singing), but were present earlier, during the baseline phase. Fifty-two mothers and 45 fathers were diagnosed with lifetime SAD accounting for 70 families (64%) in which at least one parent had a lifetime SAD. The higher prevalence of SAD in our sample compared with the general population is likely a result of self-selection of the sample. Our study entitled 'Development of shyness and self-confidence' for recruitment seemed to attract parents with a history of social anxiety.

Table S1 reports descriptive statistics and raw correlations/ t -test differences for children's physiological measures during the task procedure, parents' SAD, SA symptoms, and child social anxiety. Table S2 reports descriptive statistics of autonomic measures for all task phases for children of parents with and without SAD. Greater child social anxiety was related to more parents' social anxiety symptoms. Reduced HRV and increased EDA were associated with more children's social anxiety throughout the task. Higher temperature reactivity during the watching back and less temperature recovery was also associated with more social anxiety in children. DC reactivity during the watching back and DC recovery was higher in children of parents with SAD.

Multilevel models

Task phase. The main effect of task phase was significant for all measures ($p < .05$), indicating that the manipulation used in the task was successful and that children were physiologically aroused during the socially stressful tasks.

Parents' social anxiety. Models in which parents' SAD status and social anxiety symptoms were predictors of child physiological activity are reported in Table 1. Parents' lifetime SAD diagnosis (no = reference) was significantly associated with blushing in children, $F_{(1,45)} = 4.04$, $p = .050$, $\eta_p^2 = 0.08$ for DC reactivity (Figure 1A). Children of parents with lifetime SAD had higher DC reactivity during the performance and watching-back tasks relative to baseline and recovered less during the recovery

Table 1 Parameter estimates of the multilevel models of child physiological activity regressed on parents' SAD and social anxiety (SPAI)

	SAD			SPAI		
	β	SE	p	β	SE	p
HR	-.02	.23	.943	-.04	.12	.767
HRV	.01	.20	.951	-.06	.10	.566
EDA	.13	.17	.445	.19	.09	.047
AC reactivity	-.01	.20	.969	.02	.12	.895
DC reactivity	.47	.24	.050	-.11	.18	.530
Temperature reactivity						
1	-.09	.25	.715	-.07	.13	.587
2	.28	.25	.268			
3	-.16	.26	.149			

For SAD, 2 (no lifetime SAD) = reference. Task phase: 1, reactivity during the performance; 2, recovery; 3, reactivity during the watching back. EDA, electrodermal activity; HR, heart rate; HRV, heart rate variability; SAD, social anxiety disorder.

phase than children of parents without lifetime SAD. Furthermore, an interaction effect with task phase was found for temperature reactivity, $F_{(2,101)} = 3.22$, $p = .044$, $\eta_p^2 = 0.06$. Children of parents with SAD recovered less after the performance compared with children of parents without SAD, although they reacted less during the watching-back task (Figure 1B). Of note, post hoc analyses of the interaction showed no significant differences in any of the phases. The findings remained after controlling for the temperature level during baseline.

Self-reported parents' social anxiety symptoms significantly predicted children's EDA activity, $F_{(1,72)} = 4.10$, $p = .047$, $\eta_p^2 = 0.05$. Children of parents with more social anxiety symptoms had elevated EDA throughout the task procedure (Table 1). Heart rate and HRV were not associated to parents' SAD status and social anxiety symptoms ($p > .05$).

Child social anxiety. In the models with blushing measures as outcomes, a significant main effect of child social anxiety was found for cheek temperature reactivity, $F_{(1,52)} = 5.69$, $p = .021$, $\eta_p^2 = 0.10$. The result remained after controlling for temperature baseline values. Children with elevated levels of social anxiety were found to have higher temperature reactivity during the performance and watching-back tasks and to recover less during the recovery phase. Furthermore, significant main effects of child social anxiety were found for HRV, $F_{(1,79)} = 9.24$, $p = .003$, $\eta_p^2 = 0.10$ and EDA, $F_{(1,80)} = 5.18$, $p = .026$, $\eta_p^2 = 0.06$, but not for HR, $F_{(1,76)} = 0.19$, $p = .666$, $\eta_p^2 = 0.00$. As shown in Table 2, more child social anxiety was significantly associated with increased EDA and reduced HRV.

Discussion

This study assessed autonomic hyperarousal in children as a potential etiological factor in the

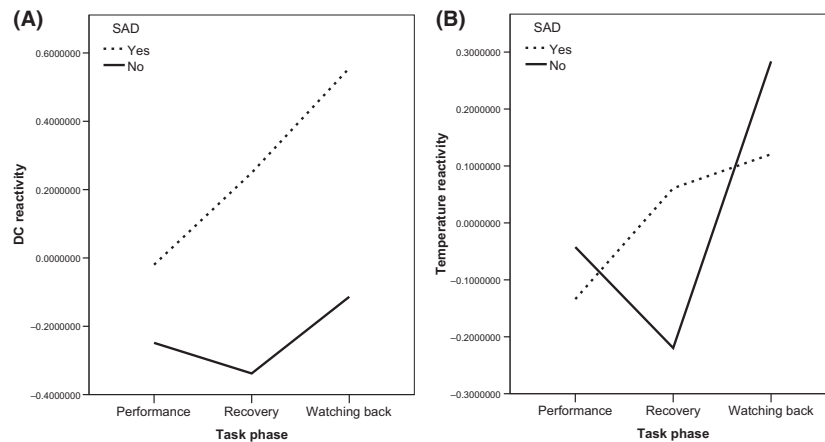


Figure 1 Predicted by the model (A) DC reactivity and (B) temperature reactivity in children of parents with and without lifetime social anxiety disorder

development of SAD. Therefore, we examined whether young children at risk for developing SAD, because their parent(s) have/had SAD, displayed autonomic hyperarousal during socially stressful tasks compared with children of parents without lifetime SAD. Moreover, we examined children’s autonomic arousal in relation to their own social anxiety symptoms. We found evidence that physiological hyperarousal, and blushing in particular, is a characteristic of children at risk for SAD. Children of parents with lifetime SAD showed stronger blushing response, as indicated by an increase from baseline in cheek blood volume during singing, recovery, and watching-back (DC reactivity) compared with children of parents without SAD. We also found autonomic hyperarousal indexed as increased EDA during baseline and socially fearful tasks in children of parents with more social anxiety symptoms, but not in children of parents with lifetime SAD. Our findings also revealed that elevated EDA throughout the task procedure and an increase in the blushing response during the tasks is related to greater children’s social anxiety. Finally, reduced HRV during baseline and recovery was found in children with greater social anxiety.

This is the first study to provide evidence that children at risk for SAD blush more during socially

challenging tasks and recover less after the task compared with children who are at low risk for SAD. Past studies reported that socially anxious adults and adults with SAD blush more than normal controls (Bögels, Rijsemus, & De Jong, 2002; Gerlach et al., 2003; Nikolić et al., 2015). This study adds to the growing body of research on blushing and SAD by demonstrating that higher blushing reactivity is also found in children whose parents have lifetime SAD. Therefore, blushing may be a biological mechanism of intergenerational transmission of SAD, and thus a biomarker for SAD.

The finding that children of parents with more social anxiety symptoms displayed elevated EDA during baseline and socially stressful tasks indicates elevated sympathetic activity throughout the task procedure in these children. This finding supports the previous findings on heightened EDA during baseline and fearful tasks in children at risk for developing anxiety disorders (Merikangas et al., 1999; Turner et al., 2005). Elevated HR and reduced HRV were not found in children at risk for SAD in this study. A similar pattern of increased EDA, but not elevated HR, has been reported previously in a sample of children at risk for anxiety disorders (Turner et al., 2005). It is possible that EDA is a more sensitive measure of autonomic activity than cardiovascular measures (Turner et al., 2005).

With respect to the analyses with children’s social anxiety symptoms, more blushing was found in children with greater social anxiety. These children responded with an increase in cheek temperature during the performance and watching-back task and recovered less after the performance. In a previous study, using the same child sample, we also found that blushing during the social performance task is related to more social anxiety, only when the child does not adaptively cope with the stressful social situation (Nikolić et al., 2016). Although the evidence regarding blushing in children is still scarce, these studies provide initial evidence that blushing

Table 2 Parameter estimates of the multilevel models of child physiological activity regressed on child social anxiety

	Child social anxiety		
	β	SE	p
HR	.05	.12	.666
HRV	-.28	.09	.003
EDA	.20	.09	.026
AC reactivity	.13	.11	.226
DC reactivity	-.04	.13	.774
Temperature reactivity	.28	.12	.022

EDA, electrodermal activity; HR, heart rate; HRV, heart rate variability.

plays an important role in social anxiety already in early childhood.

Reduced HRV activity during baseline and recovery and elevated EDA throughout the task procedure were found in children with more social anxiety symptoms. These findings confirm the results of previous studies in older children with SAD (Schmitz et al., 2011) and are in line with findings on children with BI (Schwartz, Snidman, & Kagan, 1999). Differences in HR were, however, not found in this study. Null findings regarding increased HR were also previously reported in older socially anxious children and children with SAD (Alkozei et al., 2015; Schmitz et al., 2011). Children with greater social anxiety displayed heightened basal autonomic activity which was also elevated during the socially challenging tasks. However, no interaction effects occurred, indicating that children with greater social anxiety did not react differently to socially challenging tasks, but rather had elevated levels of physiological measures throughout the procedure.

Of note, except for stronger blushing response (which is thought to be specific of SAD) in children of parents with lifetime SAD and elevated EDA in children of parents with more social anxiety symptoms, we did not find evidence for more general autonomic hyperarousal in children at risk for SAD compared with children at low risk for SAD. Considering that the effect of task phase was significant for all the autonomic measures, it is likely that children at high and low risk for SAD had similar patterns of basal arousal and reactivity for cardiovascular measures. Also, the effect sizes found in the analyses with parents' SAD were small to medium. With respect to the analyses with child social anxiety, medium effect sizes were found for both sympathetic and parasympathetic activities. However, it should be noted that all the effects occurred in the context of multiple-variable testing.

The study findings should be considered in view of some limitations. First, the sample comprised mostly Caucasian families with high educational level limiting the generalizability of our findings. Second, although the baseline and the recovery phases lasted for 120 and 60 s, the autonomic measures during the performance and watching-back tasks were analyzed for the first 30 s. Longer autonomic assessment (especially regarding cardiovascular measures) during these task phases could possibly provide more accurate assessment of changes in children at high and low risk for SAD. Furthermore, we did not control for respiration when measuring HRV in children. Although respiration does not dramatically influence the time-domain short-term RMSSD (Schipke, Arnold, & Pelzer, 1999), it is possible that the HRV differences that occurred in our study were not only a consequence of parasympathetic activity but also of different respiration rates. Third, it is not known how specific our findings are to SAD and to what degree these findings may apply to children at risk for other anxiety disorders as well. Because of the limited

sample size in this study, we did not investigate differences between groups of children with parents with only SAD and groups of children with parents with comorbid diagnoses. Future studies should address this question by investigating children of parents with only SAD compared with children of parents with comorbid anxiety disorders and no anxiety disorders. Another suggestion for future research is conducting a longitudinal study that would investigate autonomic arousal in children at risk for SAD in relation to their later SAD diagnosis in order to reveal whether children at risk who display autonomic hyperarousal indeed develop SAD, and in which cases they do not develop the disorder.

Our findings of autonomic hyperarousal in children at risk for SAD and socially anxious children bear implication for the prevention and treatment of SAD. First, early identification of children at risk for SAD may be improved, and consequent prevention programs for these children may be developed. Also, because autonomic hyperarousal, and blushing in particular, seems to be an etiological marker of SAD, procedures focusing on bodily symptoms may be incorporated in the treatment of SAD (e.g., task concentration training) (Bögels, 2006).

In summary, this study adds to the current knowledge on the intergenerational transmission of SAD. It indicates that blushing is a biological vulnerability factor for SAD. Finally, the findings that parental lifetime SAD is related to children's autonomic hyperarousal and that socially anxious children are characterized by heightened autonomic activity already in early childhood suggest that autonomic hyperarousal is an etiological factor of SAD.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Means, SDs, and correlations of physiological measures and parents' and children's social anxiety symptoms.

Table S2. Means and SDs of physiological measures for children of parents with and without SAD.

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Key points

- Autonomic hyperarousal is hypothesized to be a biological mechanism through which SAD accumulates in families, but so far unstudied in children at risk for SAD.
- Blushing, a typical physiological response of SAD, is also a possible etiological factor of the development of SAD, which has never been studied in children at risk for SAD.
- Blushing seems to be a biomarker of SAD because it was found to be a characteristic of socially anxious children and children at risk for developing SAD (because of parental lifetime SAD).
- Autonomic hyperarousal was found to be a characteristic of young socially anxious children.
- Because autonomic hyperarousal seems to be an etiological marker of SAD, treatments focusing on bodily symptoms may be incorporated in the prevention and treatment of SAD.

References

- Alkozei, A., Creswell, C., Cooper, P.J., & Allen, J.J. (2015). Autonomic arousal in childhood anxiety disorders: Associations with state anxiety and social anxiety disorder. *Journal of Affective Disorders, 175*, 25–33.
- American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders: DSM-5™* (5th edn). Arlington, VA: American Psychiatric Publishing Inc.
- Anderson, E.R., & Hope, D.A. (2009). The relationship among social phobia, objective and perceived physiological reactivity, and anxiety sensitivity in an adolescent population. *Journal of Anxiety Disorders, 23*, 18–26.
- Anderson, E.R., Veed, G.J., Inderbitzen-Nolan, H.M., & Hansen, D.J. (2010). An evaluation of the applicability of the tripartite constructs to social anxiety in adolescents. *Journal of Clinical Child & Adolescent Psychology, 39*, 195–207.
- Battaglia, M., Bajo, S., Strambi, L.F., Brambilla, F., Castronovo, C., Vanni, G., & Bellodi, L. (1997). Physiological and behavioral responses to minor stressors in offspring of patients with panic disorder. *Journal of Psychiatric Research, 31*, 365–376.
- Beidel, D.C. (1988). Psychophysiological assessment of anxious emotional states in children. *Journal of Abnormal Psychology, 97*, 80.
- Bögels, S.M. (2006). Task concentration training versus applied relaxation, in combination with cognitive therapy, for social phobia patients with fear of blushing, trembling, and sweating. *Behavior Research and Therapy, 44*, 1199–1210.
- Bögels, S.M., & Reith, W. (1999). Validity of two questionnaires to assess social fears: The Dutch Social Phobia and Anxiety Inventory and the Blushing, Trembling and Sweating Questionnaire. *Journal of Psychopathology and Behavioral Assessment, 21*, 51–66.
- Bögels, S.M., & Lamers, C.T.J. (2002). The causal role of self-awareness in blushing-anxious, socially-anxious and social phobics individuals. *Behaviour Research and Therapy, 40*, 1367–1384.
- Bögels, S.M., Mulken, S., & De Jong, P.J. (1997). Practitioner task concentration report training and fear of blushing. *Clinical Psychology and Psychotherapy, 4*, 251–258.
- Bögels, S.M., Rijsemus, W., & De Jong, P.J. (2002). Self-focused attention and social anxiety: The effects of experimentally heightened self-awareness on fear, blushing, cognitions, and social skills. *Cognitive Therapy and Research, 26*, 461–472.
- Bögels, S.M., Alden, L., Beidel, D.C., Clark, L.A., Pine, D.S., Stein, M.B., & Voncken, M. (2010). Social anxiety disorder: Questions and answers for the DSM-V. *Depression and Anxiety, 27*, 168–189.
- Brown, T.A., Barlow, D.H., & Di Nardo, P.A. (1994). *Anxiety Disorders Interview Schedule for DSM-IV*. Albany, NY: Graywind Publications.
- Clark, D.M., & Wells, A. (1995). A cognitive model of social phobia. *Social Phobia: Diagnosis, Assessment, and Treatment, 41*, 00022–00023.
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. New York: Routledge Academic.
- Colonna, C., Engelhard, I.M., & Bögels, S.M. (2010). Development in children's attribution of embarrassment and the relationship with theory of mind and shyness. *Cognition and Emotion, 24*, 514–521.
- Domschke, K., Stevens, S., Pfeiderer, B., & Gerlach, A.L. (2010). Interoceptive sensitivity in anxiety and anxiety disorders: An overview and integration of neurobiological findings. *Clinical Psychology Review, 30*, 1–11.
- Drummond, P.D., Back, K., Harrison, J., Helgadottir, F.D., Lange, B., Lee, C., ... & Wheatley, L. (2007). Blushing during social interactions in people with a fear of blushing. *Behaviour Research and Therapy, 45*, 1601–1608.
- Edelmann, R.J., & Baker, S.R. (2002). Self-reported and actual physiological responses in social phobia. *British Journal of Clinical Psychology, 41*, 1–14.
- Edwards, S.L., Rapee, R.M., Kennedy, S.J., & Spence, S.H. (2010). The assessment of anxiety symptoms in preschool-aged children: The revised Preschool Anxiety Scale. *Journal of Clinical Child & Adolescent Psychology, 39*, 400–409.
- Gerlach, A.L., Wilhelm, F.H., & Roth, W.T. (2003). Embarrassment and social phobia: The role of parasympathetic activation. *Journal of Anxiety Disorders, 17*, 197–210.
- Grillon, C., Dierker, L., & Merikangas, K.R. (1997). Startle modulation in children at risk for anxiety disorders and/or alcoholism. *Journal of the American Academy of Child & Adolescent Psychiatry, 36*, 925–932.
- Kagan, J. (1994). *Galen's prophecy*. New York: Basic.
- Kagan, J., Reznick, J.S., & Snidman, N. (1987). The physiology and psychology of behavioral inhibition in children. *Child Development, 58*, 1459–1473.
- Keltner, D., & Buswell, B.N. (1997). Embarrassment: Its distinct form and appeasement functions. *Psychological Bulletin, 122*, 250.
- Leary, M.R., & Meadows, S. (1991). Predictors, elicitors, and concomitants of social blushing. *Journal of Personality and Social Psychology, 60*, 254.
- Lewis, M. (1995). Self-conscious emotions. *American Scientist, 83*, 68–78.
- Lewis, M. (2003). The emergence of consciousness and its role in human development. *Annals of the New York Academy of Sciences, 1001*, 104–133.
- Malik, M. (1996). Heart rate variability. *Annals of Noninvasive Electrocardiology, 1*, 151–181.

- Mauss, I., Wilhelm, F., & Gross, J. (2004). Is there less to social anxiety than meets the eye? Emotion experience, expression, and bodily responding. *Cognition and Emotion*, *18*, 631–642.
- McTeague, L.M., Lang, P.J., Laplante, M.C., Cuthbert, B.N., Strauss, C.C., & Bradley, M.M. (2009). Fearful imagery in social phobia: Generalization, comorbidity, and physiological reactivity. *Biological Psychiatry*, *65*, 374–382.
- Merikangas, K.R., Avenevoli, S., Dierker, L., & Grillon, C. (1999). Vulnerability factors among children at risk for anxiety disorders. *Biological Psychiatry*, *46*, 1523–1535.
- Molenkamp, B. (2011). *VSRRP98 Manual, Version 8.0*. University of Amsterdam, The Netherlands.
- Newman, D. (1986). The role of mutual knowledge in the development of perspective taking. *Developmental Review*, *6*, 122–145.
- Nikolić, M., Colonnese, C., de Vente, W., Drummond, P., & Bögels, S. (2015). Blushing and social anxiety: A meta-analysis. *Clinical Psychology: Science and Practice*, *22*, 177–193.
- Nikolic, M., Colonnese, C., de Vente, W., & Bögels, S.M. (2016). Blushing in early childhood: Feeling coy or socially anxious. *Emotion*, *16*, 475–487.
- Rapee, R.M., & Heimberg, R.G. (1997). A cognitive-behavioral model of anxiety in social phobia. *Behaviour Research and Therapy*, *35*, 741–756.
- Scaini, S., Belotti, R., & Ogliari, A. (2014). Genetic and environmental contributions to social anxiety across different ages: A meta-analytic approach to twin data. *Journal of Anxiety Disorders*, *28*, 650–656.
- Schandry, R., & Poth, E. (1983). Eine experimentelle Untersuchung zur Psychologie und Physiologie des Errötens. *Psychologische Beiträge*, *25*, 503–514.
- Schipke, J.D., Arnold, G., & Pelzer, M. (1999). Effect of respiration rate on short-term heart rate variability. *Journal of Clinical and Basic Cardiology*, *2*, 92–95.
- Schmitz, J., Krämer, M., Tuschen-Caffier, B., Heinrichs, N., & Blechert, J. (2011). Restricted autonomic flexibility in children with social phobia. *Journal of Child Psychology and Psychiatry*, *52*, 1203–1211.
- Schmitz, J., Tuschen-Caffier, B., Wilhelm, F.H., & Blechert, J. (2013). Taking a closer look: Autonomic dysregulation in socially anxious children. *European Child & Adolescent Psychiatry*, *22*, 631–640.
- Schwartz, C.E., Snidman, N., & Kagan, J. (1999). Adolescent social anxiety as an outcome of inhibited temperament in childhood. *Journal of the American Academy of Child & Adolescent Psychiatry*, *38*, 1008–1015.
- Siess, J., Blechert, J., & Schmitz, J. (2014). Psychophysiological arousal and biased perception of bodily anxiety symptoms in socially anxious children and adolescents: A systematic review. *European Child & Adolescent Psychiatry*, *23*, 127–142.
- Stein, M.B., Chartier, M.J., Lizak, M.V., & Jang, K.L. (2001). Familial aggregation of anxiety-related quantitative traits in generalized social phobia: Clues to understanding ‘disorder’ heritability? *American Journal of Medical Genetics*, *105*, 79–83.
- Task Force of the European Society of Cardiology (1996). Heart rate variability standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, *17*, 354–381.
- Turner, S.M., Beidel, D.C., Dancu, C.V., & Stanley, M.A. (1989). An empirically derived inventory to measure social fears and anxiety: The Social Phobia and Anxiety Inventory. *Psychological Assessment: A Journal of Consulting and Clinical Psychology*, *1*, 35.
- Turner, S.M., Beidel, D.C., & Epstein, L.H. (1991). Vulnerability and risk for anxiety disorders. *Journal of Anxiety Disorders*, *5*, 151–166.
- Turner, S.M., Beidel, D.C., & Roberson-Nay, R. (2005). Offspring of anxious parents: Reactivity, habituation, and anxiety-proneness. *Behaviour Research and Therapy*, *43*, 1263–1279.
- de Vente, W., Majdandžić, M., Colonnese, C., & Bögels, S. (2011). Intergenerational transmission of social anxiety: The role of paternal and maternal fear of negative child evaluation and parenting behaviour. *Journal of Experimental Psychopathology*, *2*, 509–530.
- de Vente, W., Majdandžić, M., & Bögels, S. (2014). The Pathophysiology of Social Anxiety. In J.W. Weeks (ed.), *The Wiley Blackwell handbook of social anxiety disorder* (pp. 90–110). Chichester, UK: John Wiley & Sons, Ltd.
- de Vente, W., Majdandžić, M., Voncken, M.J., Beidel, D.C., & Bögels, S.M. (2014). The SPAI-18, a brief version of the Social Phobia and Anxiety Inventory: Reliability and validity in clinically referred and non-referred samples. *Journal of Anxiety Disorders*, *28*, 140–147.
- Voncken, M.J., & Bögels, S.M. (2009). Physiological blushing in social anxiety disorder patients with and without blushing complaints: Two subtypes? *Biological Psychology*, *81*, 86–94.

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