The longitudinal negative impact of early stressful events on emotional and physical well-being: The buffering role of cardiac vagal development.

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Conflict of interest

The authors have no conflicts of interest to declare

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Abstract

Early stressful events negatively affect emotional and physical well-being. Cardiac vagal tone (CVT), which is associated with better emotional and physical well-being, have also been shown to increase gradually in early childhood. Nonetheless, children's CVT developmental trajectories are greatly variable, such that CVT can increase or decrease across the years. The present study examines the longitudinal effects of early stressful events and the role of 4-years CVT developmental trajectory on children's emotional and physical well-being.

Forty-two 4-year-old children were enrolled in the study. Number of stressful events and resting electrocardiogram (ECG) were collected at T1. ECG was registered again after one (T2), two (T3) and three (T4) years. Also, children's emotional and physical well-being were assessed at T4. CVT development was calculated as the angular coefficient, reflecting the developmental trajectory of CVT across the four timepoints.

Results showed that higher numbers of experienced stressful events (T1) predicted poorer emotional and physical well-being after 4 years (T4). The interaction between the number of stressful events and CVT development emerged on physical well-being. Early stressful events negatively affect long-term children's emotional and physical well-being while a positive CVT development seems to mitigate the negative effects of early stressful events on physical well-being.

Keywords

Early stressful events, Heart Rate Variability, Cardiac vagal tone, Emotional Well-being, Physical Well-being

Introduction

Early stressful events have been shown to have a lifelong cost on child development, directly influencing learning abilities, behaviours and both physical and emotional health (Flaherty et al., 2006; Shonkoff et al., 2012). Several longitudinal studies have documented the consequences of early stressful events on educational achievement, economic productivity, health status and longevity (Felitti et al., 2019; Flaherty et al., 2006, 2009; Koenen et al., 2007). Physiologic responses to stress include the activation of the hypothalamic-pituitary-adrenocortical axis and the sympathetic-adrenomedullary system, that determines a rise in the levels of corticotropin-releasing hormone, cortisol, norepinephrine and adrenaline. While the stress response is protective and essential for survival, excessive or prolonged activation of these biological systems can be quite harmful (McEwen & Seeman, 1999) and the dysregulation of this network may affect multiple organs. The negative impact of stressful events on children's emotional and physical well-being can be modulated by adverse and protective factors (McEwen, 2006; Shonkoff et al., 2012). Protective factors are of considerable relevance since they can temper the negative effects of stressful events. For example, given a range of stressful events that can differ according to duration and magnitude, such as the first day of school, an illness or parents' divorce, the presence of a protective factor, such as supportive adults will buffer the impact of the experienced situations (Shonkoff et al., 2012). Protective factors include environmental factors as well as biological factors such as responses of the physiological systems. Among physiological indexes, cardiac vagal tone (CVT), measured through the root mean square of the successive differences between adjacent heartbeats (RMSSD), has been shown to reflect the activity of the parasympathetic vagus nerve on the sinoatrial node (Berntson et al., 1997; Malik et al., 1996). CVT is a reliable cardiac measure reflecting the ability to deal with stressful situations (Kim et al., 2018; Thayer et al., 2012) and could represent a physiological protective factor in the relationship between early stressful events and the individual's well-being

(Beauchaine & Thayer, 2015). CVT has been associated with the ability to cope with stressful situations in both adults and children (Kim et al., 2018; Thayer et al., 2012). In response to stressful stimuli, a transient reduction in CVT has been consistently reported in adults (Kim et al., 2018), in toddlers (Calkins & Johnson, 1998) and in preschool children (Calkins & Dedmon, 2000; Scrimin, Patron, et al., 2019). While CVT has been shown to be a good indicator of the ability to self-regulate in response to stressful situations, high CVT levels have been correlated with increased positive emotions (Kok & Fredrickson, 2010; Oveis et al., 2009) and emotional well-being, while reduced CVT is associated with greater psychopathology (Beauchaine & Thayer, 2015) symptoms of both internalizing and externalizing psychopathology (Beauchaine, 2015) and depression (Rottenberg et al., 2007). Also, high CVT has been related to better physical health in children (Gutin et al., 2005) and well-being in adults (Kemp & Quintana, 2013), while lower CVT has been associated with different negative outcomes such as anger, anxiety and sadness in young children (Michels et al., 2013), and chronic fatigue and asthma in adolescents (Rimes et al., 2017). Intriguingly, CVT modification during laboratory stress, together with other psychophysiological responses, have been shown to moderate the longitudinal effects of marital conflict on psychological and behavioral maladjustment among adolescents (Philbrook et al., 2018). It has to be noted that during child development sympathetic and parasympathetic branches sustain a maturation process, similar to several other biological systems, that lay the foundation for self-regulation abilities (Calkins & Keane, 2004). While there is a growing body of literature on how CVT is related to child adaptation and self-regulation, very few longitudinal investigations have focused on CVT development showing that CVT increases gradually in early childhood (up to 7 years of age; Alkon et al., 2003; Calkins and Keane, 2004; Marshall and Stevenson-Hinde, 1998), and level off by late childhood or adolescence (El-Sheikh, 2005; Hinnant et al., 2011). Most importantly, a great variability has been reported in children's CVT developmental trajectories, with CVT increasing in some children while decreasing in others across the years (Hinnant et al., 2011). No study to date focused on CVT development as a protective factor for early stressful events in child adjustment. In fact, while early stressful events can have a dangerously negative effect on both emotional and physical well-being, it could be hypothesized that appropriate maturation of the ANS, as reflected by a positive CVT development during early childhood, could buffer the effects of stress, reducing the risk for future poor emotional and/or physical health.

The present study investigates the effects of early stressful events (experienced before entering the second year of pre-school) and the moderating role of CVT development across four years on children's emotional and physical well-being. We expect a higher number of early stressful events to predict later worse emotional and physical well-being. Here it was hypothesized that a positive CVT development across the 4 years could mitigate the effects of early stressors on emotional and physical well-being, acting as a protective factor especially in those children who experienced a higher number of negative events.

Method

Participants

Forty-two children (22 boys, 52%) attending pre-school were enrolled in the study. Children had a mean age of 4.74 years (56.88 $\pm$ 6.71 months). All children were attending public pre-schools in the northeast of Italy and were from low- to middle-class families. Descriptive data have been reported in Table 1. Before the beginning of data collection, trained researchers spent three months (at the beginning of the school year) participating in classroom activities and organizing games with children in order to familiarize and obtain pre-schoolers' total trust. Subsequently, children were tested individually during 4 separate sessions.

Parental written permission and children's verbal assent were required for participation; in addition, written informed consent was obtained from the school principal and from the Ethical Committee of the Psychology section of the University of Padova," (protocol number: 89ADC65ECC5E40203FF0079D9D6CDB53). Children were given the opportunity to decline participation at any time between the four sessions as well as during every single session. In the present study, we report on the data collected in four longitudinal assessment sessions, which took place between September 2015 and December 2018.

"Table 1 here"

Procedure

Data reported in this study were collected as part of a larger study aimed at investigating the links between self-regulation and psychological functioning in primary school students (Scrimin et al., 2017; Scrimin, Moscardino, et al., 2019; Scrimin, Patron, et al., 2019). In the present study, we report on the data collected in four of the six sessions, which took place between September 2015 and December 2018. In order to establish a friendly relationship with children, researchers spent three months by weekly joining the classroom and interacting with children, organizing several short lessons and games. This familiarization phase was repeated each year before each data collection. The assessment took place at four different time points (see Figure 1) across 4 years and always at the beginning of each academic year (October-November). Specifically, children were assessed during 1) the second year of pre-school (T1); 2) the third year of pre-school (T2); 3) the first year of primary school (T3), and 4) the second year of primary school (T4). At each assessment session, children were invited to follow the researcher, that they knew well, in a schoolroom set up for the purpose of the study. Here, after a short warm-up talk, resting electrocardiography (ECG) was recorded for 4 minutes. All the recordings took place in the morning (between 9 a.m. and 12 p.m.) in the same quiet room of the school's building. After attaching the sensors, the researcher invited the child to sit comfortably and rest for 15 minutes (adaptation period). Subsequently, children were asked to watch a relaxing video on the computer screen in front of them. Moreover, before the first assessment session (T1), parents were interviewed in order to collect sociodemographic information and number of stressful events experienced by the child and family. Whereas, during the last assessment session (T4) children were interviewed on their self-reported physical and emotional well-being. This interview took place immediately after the ECG recording during the same session. It is important to note that all children were happy to take part in the study and joined the researchers for all the assessment sessions.

Measures

Sociodemographic information, and the number of stressful events

Caregivers were asked to provide sociodemographic information, including socioeconomic status (SES), employment status of both parents, educational level, number of siblings, target child's date of birth, weight and gestational age at birth, as well as relevant health-related issues. Then, they were asked to complete a checklist containing a number of stressful events that a family might experience (Scrimin et al., 2018) such as relocation, divorce, loss of a family member, accident of a family member or close friend, severe illness, arguments between parents, arguments with children, economic problems, new person lives in the family. Parents were asked to report whether each event had occurred, and at what age of the child it took place. A total stressful events score was then computed by summing up all the early stressful events.

Child well-being

The Child Health and Illness Profile – Child Edition (CHIP–CE) (Riley et al., 2004) is a 45-item questionnaire that can be administered as an interview to the child. It is designed to evaluate the well-being of children ages 6 through 11 years and examines aspects of health and well-being that can be influenced by health systems, school systems, and health promotion efforts. The CHIP–CE targets health-related quality-of-life aspects that are of special interest to the school-aged group. In the present study, the Emotional and Physical comfort subscales were employed (experience of emotional and physical symptoms and observed activity limitations). Frequency of symptoms in the past four weeks was assessed using a 5-point Likert scale (see appendix in the Supplementary material). The measure has excellent psychometric properties (Riley et al., 2004). In the present study, both subscales had good internal consistency (Cronbach Alphas range .79 to .81).

Electrophysiological data recording and processing

Electrocardiogram (ECG) was recorded by means of a POLAR sensor placed on the child's thorax using a multimodality physiological monitoring device that encodes biological signals in real-time (ProComp Infiniti; Thought Technology, Montreal, Canada). The ECG signal was recorded continuously via a 12-bit analogue-to-digital converter with a sampling rate of 256 Hz and stored sequentially for analysis. The raw ECG signal was then exported in Kubios HRV Analysis Software 2.2 (The Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland) to estimate the occurrence of each heartbeat and derive the series of inter-beat intervals (IBIs), calculated as the difference in msec between successive R-waves. First, the ECG signal was visually inspected, and artefacts were corrected by means of a piecewise cubic splines interpolation method that generates values for missing or corrupted values into the IBIs series. Then, average resting HR was calculated, as well as the square root of the mean squared differences of successive

NN intervals (RMSSD)[1]. While HR is affected by both the sympathetic and parasympathetic branches of the autonomic nervous system, RMSSD is sensitive to short-term heart period fluctuations (Malik et al., 1996) thus, it is thought to specifically reflect parasympathetic activity through the influence of the vagus nerve on the sinoatrial node (Berntson et al., 1997; Malik et al., 1996) independently of respiratory interferences (Hill et al., 2009). For a recent comprehensive review regarding the interpretation, adjustment, and reporting of HRV metrics, see (de Geus et al., 2019).

All physiological signals were recorded through a FlexComp Infiniti™ encoder (Thought Technology Ltd, Montreal, Canada) which is a computerized recording system approved by the U.S. Food and Drug Administration (FDA) and considered a gold standard measurement system (Menghini et al., 2019).

Data reduction and statistical analysis

Cardiac vagal tone (CVT) development index was calculated as the angular coefficient in RMSSD from the first to the fourth evaluation, that reflects the development trajectory across the four timepoints (see Figure 1). To determine whether the number of stressful events at T1 influenced emotional and/or physical well-being, a median split procedure was applied to individuate participants who experienced a high vs low number of early stressful events. To verify whether physical and emotional well-being at T4 where differently predicted by early stressful events at T1, by CVT development across the 4 years or by their interaction, two hierarchical linear

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[1] RMSSD was obtained according to the formula (Malik et al., 1996):

$$RMSSD = \sqrt{\frac{1}{1-N}\sum_{i=1}^{N-1}(RR_{i+1} - RR_i)^2}$$

regressions were run with physical and emotional well-being as the dependent variable, respectively, and high vs low number of stressful events at T1, vagal growth index and their interaction as predictors. All analyses were performed using R (version 3.6.1, R Development Core and Team, 2011). A *p*-value < .05 was considered statistically significant.

Results

With respect to the number of stressful events, a mean number of 3.52 (SD= 1.97, range = 1-8) stressful events were reported by parents before the recording of the first year (T1). The median corresponded to 3 stressful events at T1, therefore, after the median split procedure 19 children experienced a high number of stressful events (> 3) and 23 a low number of stressful events (≤ 3).

The first step of the hierarchical linear regression on emotional well-being showed that a high number of stressful events at T1 significantly predicted lower reported emotional well-being at T4 ($\beta = -0.55$, $p = .017$) while vagal growth did not predict subsequent emotional well-being ($p = .879$; see Table 2 and see Figure 2a). In the second step of the hierarchical linear regression the number of stressful events ($p = .052$) did not significantly predict emotional well-being, and neither did vagal growth and the interaction between the number of stressful events and vagal growth (all *p*'s > .475).

The first step of the hierarchical linear regression on physical well-being showed that a high number of stressful events at T1 significantly predicted lower reported physical well-being at T4 ($\beta = -0.87$, $p < .001$) while vagal growth did not predict subsequent physical well-being ($p = .397$; see Table 3). Therefore, a high number of stressful events during the first five years of the child was associated with lower reported physical well-being four years later (when the children are around age 9). A significant interaction between the number of stressful events at T1 and vagal growth emerged ($\beta = 0.05$, $p = .006$). Therefore, those children who suffered a lower number of stressful events reported high physical well-being independent of the vagal growth. On the contrary, children who suffered a higher number of stressful events showed a relation between vagal growth index and physical well-being, such that those who had a higher index of vagal growth reported a good level of physical well-being, while children with a high number of stressful events at T1 and low vagal growth reported the lowest level of physical well-being at T4 (see Figure 2b).

"Table 2 here"

"Table 3 here"

Discussion

The main aim of the present longitudinal study was to evaluate the role of cardiac vagal tone development in modulating the relationship between early stressful events and children's emotional and physical well-being. Most importantly, the multiple measures of CVT in a critical age period, characterized by the transition from pre-school to primary school, allowed us to study the cardiac vagal development trajectory as well as whether it could act as a positive moderator buffering the effect of early stressful events on children's well-being.

The longitudinal data on CVT showed a pattern characterized by a gradual and steady increase in CVT together with a reduction in HR, in line with previous studies (Alkon et al., 2003; Calkins & Keane, 2004; Marshall & Stevenson-Hinde, 1998). This trajectory of cardiac vagal development may reflect the physiological maturation process of the parasympathetic nervous system (Calkins & Keane, 2004; Porges et al., 1996).

As expected, results showed that children who experienced a higher number of early stressful events (before entering the second year of pre-school) reported significantly lower emotional and physical well-being 4 years later. However, despite the negative direct link between early stressful events and later emotional well-being, no direct association emerged with CVT development nor interaction between stressful events and CVT development. Regarding physical well-being, a direct negative association with early stressful events was found; in addition, this relation was also moderated by CVT development. Specifically, while children who experienced a low number of stressful events reported higher physical well-being independently of CVT development, in children who experienced a higher number of early stressful events CVT development acted as a protective factor. Children that showed an improvement in CVT across the years (i.e., positive CVT development) reported higher physical well-being while children who show no improvement or a reduction in CVT across the years showed the lowest levels of reported physical well-being.

As hypothesized, the present results bolster the predominant negative role of early stressful events on emotional well-being (Flaherty et al., 2006, 2009). On the contrary, the expected protective role of CVT development in buffering the effects of early stressful events on children's emotional well-being is not supported. Previous studies have shown how cardiac vagal tone is widely associated with emotional reactivity and regulation in children (Appelhans & Luecken, 2006; Fabes et al., 1994). It has to be noted that while children in the first years of primary school can reliably report on their well-being (Riley, 2004; Varni et al., 2007) they can have difficulties in focusing and reporting their own emotional states (Harris, 1989) and tend to express their discomfort more in terms of physical symptoms. This could help to better understand why, in the present study, no moderation of cardiac vagal development emerged between early stressful events and emotional well-being.

As hypothesized, the negative effect of early stressful events on physical well-being was mitigated by a positive development trajectory in CVT across 4 years. Specifically, among those children who experienced a higher number of early stressful events, a positive CVT development trajectory (reflecting an increase in CVT across four years) was associated with better physical well-being, while a negative or flat CVT development trajectory (reflecting a reduction or no improvement in CVT across four years) was linked to the lowest physical well-being. The maturation of different biological systems, including the parasympathetic branch of the autonomic nervous system (indexed by CVT), sets the basis for self-regulation abilities. Individual differences in the maturation of the parasympathetic system might modulate later self-regulation abilities (Calkins & Keane, 2004; Porges et al., 1994). The mechanism by which a positive CVT development modulates the effect of early stressful events on perceived physical wellbeing could be related to a better ability to face stressful events and cope with them (Fabes et al., 1994) and to adapt constructively to stressful environments (Fox, 1989).

To date, the present study is the first longitudinal study to show the role of cardiac vagal developmental trajectory in mitigating the negative effects of early stressful events on physical well-being in children. The present study has limitations that must be acknowledged. First, the sample size is limited and hence is difficult to generalize the findings. Second, children's emotional and physical well-being were not assessed at T1, making it impossible to evaluate changes in children's perceived emotional and physical well-being across evaluations. Third, similarly the occurrence of successive stressful events during T2, T3 and T4 were not assessed, therefore possible effects of successive stressful events on emotional and physical well-being cannot be evaluated. Fourth, only CVT during resting conditions was recorded in the present study. Some authors proposed that cardiac vagal response to a stressful situation (vagal withdrawal) may be more directly related to self-regulation abilities (Calkins & Keane, 2004). Nonetheless, resting CVT has been consistently associated with better emotion regulation and physical well-being (Kemp & Quintana, 2013; Thayer et al., 2010) as well as self-regulation (Koenig et al., 2016; Kok & Fredrickson, 2010).

Despite these limitations, taken together the present results support the hypothesis that early stressful events have a high impact on long term emotional and physical children's well-being and that cardiac vagal development may act as a protective mechanism that mitigates the negative effects of early stressful events on physical well-being. The identification of modifiable protective factors could help the recognition and shaping of intervention strategies for children who experienced early stressful events. To date, early childhood policy focuses mainly on educational objectives (Shonkoff et al., 2012), nonetheless, there is growing evidence for interventions to reduce negative outcomes and to prepare children to cope with stressful situations to enhance emotional and physical health and well-being, which would generate even larger returns to all of society. For example, CVT can be boosted through early psychophysiological interventions such as HRV biofeedback (Gevirtz, 2013) targeting CVT directly, which have been shown to have positive effects in children with conduct, anxious and somatoform disorders (Pop-Jordanova & Nada, 2009).

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1 Sociodemographic variables

	N=42 M (SD)
Age (months)	56.88 (6.71)
Males (N, %)	22 (52)
Immigrants (N, %)	21 (50)
Socioeconomic Status (N, %)	
Low	15 (36)
Medium	11 (26)
High	16 (38)

Table 2 Regression model on Emotional Well-being

Predictors of Emotional Well-being						
Block 1						
Predictors	**Estimate**	**SE**	**95% C.I.**		**t**	***p***
			Lower	**Upper**		
Intercept	4.23	0.18	3.86	4.60	23.10	< .001
Stressful events (High-Low) (T1)	-0.55	0.22	-0.99	-0.11	-2.50	0.017
CVT development	0.00	0.01	-0.02	0.02	0.15	0.879
Block 2						
Predictors	**Estimate**	**SE**	**95% C.I.**		**t**	***p***
			Lower	**Upper**		
Intercept	4.29	0.21	3.87	4.71	20.69	< .001
Stressful events (High-Low) (T1)	-0.78	0.39	-1.56	0.01	-2.01	0.052
CVT development	-0.005	0.01	-0.03	0.02	-0.34	0.737
Stressful events × CVT development	0.02	0.02	-0.03	0.06	0.72	0.475

Note: T1 = first evaluation during the second year of pre-school; CVT= cardiac vagal tone.

Table 3 Regression model on Physical Well-being

Predictors of Physical Well-being						
Block 1						
Predictors	**Estimate**	**SE**	**95% C.I. Lower**	**95% C.I. Upper**	**t**	***p***
Intercept	4.33	0.15	4.03	4.64	28.51	< .001
Stressful events (High-Low) (T1)	-0.87	0.18	-1.24	-0.51	-4.80	< .001
CVT development	0.01	0.01	-0.01	0.03	0.86	0.397
Block 2						
Predictors	**Estimate**	**SE**	**95% C.I. Lower**	**95% C.I. Upper**	**t**	***p***
Intercept	4.54	0.16	4.23	4.86	28.90	< .001
Stressful events (High-Low) (T1)	-1.57	0.29	-2.17	-0.98	-5.35	< .001
CVT development	-0.01	0.01	-0.03	0.01	-1.11	0.275
Stressful events × CVT development	0.05	0.02	0.01	0.08	2.89	0.006

Note: T1 = first evaluation during the second year of pre-school; CVT= cardiac vagal tone.

Figure legend

Figure 1.a Descriptive statistics on HR across the four-time evaluations; **Figure 1.b** Descriptive statistics on RMSSD across the four evaluations. Each participant is represented by a grey dot, the violin plots around the dots represent the smoothed data distribution, the black dots represent the average during each evaluation.; RMSSD = Root Mean Square of the Successive Differences; T1 = first evaluation during the second year of pre-school; T2 = second evaluation during the third year of pre-school; T3 = third evaluation during the first year of primary school; T4 =fourth evaluation during the second year of primary school.

Figure 2.a Effect of the number of early stressful events at T1 on reported emotional well-being at T4. T1 = first evaluation during the second year of pre-school; T4 =fourth evaluation during the second year of primary school. **Figure 2.b** Interaction effect of the interaction between the number of early stressful events at T1 and cardiac vagal tone development across four years in predicting reported physical well-being at T4. CVT = cardiac vagal tone. T1 = first evaluation during the second year of pre-school; T4 =fourth evaluation during the second year of primary school. Grey and black lines represent estimated regression for low and high number of early stressful events respectively; the grey area represents 95% confidence interval.