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Perinatal stress moderates the link between early and later emotional skills in very preterm-born children: An 11-year-long longitudinal study

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Abstract

Background

Very preterm (VPT) birth refers to an early stressful event putting children at heightened risk for emotional difficulties. However, there is an important individual variability, leaving unexplained why some VPT children do not develop emotional difficulties, while others develop such difficulties in the early years or later in life.

Aim

In this study, we examined whether perinatal stress is a risk factor explaining heterogeneities in emotional problems in VPT children.

Methods

Thirty-six VPT children and 22 full-term born (FT) children participated in an 11 year-long study. Risk for perinatal stress was assessed at birth with the Perinatal Risk Inventory. Mothers reported children's emotional difficulties at 18 months of child age on the Symptom Checklist and at 11 years on the Child Behavior Checklist.

Results

Results indicated significant differences in emotional scores at 11 years not only between VPT and FT children but also between the low and high perinatal stress groups. More importantly, emotional scores at 18 months influenced variability in internalizing scores at 11 years *only* in VPT children with high perinatal stress.

Conclusion

Although prematurity affects the emotional abilities of preadolescents, the link between emotional skills in early and later childhood is moderated by the severity of perinatal stress. In particular, VPT children who are born with more complications, and as such experience a more stressful perinatal environment, are more likely to show emotional difficulties at preadolescence.

Keywords: prematurity, emotional problems, perinatal stress, risk factor, longitudinal design

Perinatal stress moderates the link between early and later emotional skills in very preterm-born children: An 11-year-long longitudinal study

Medical and technological advances along with improvements in neonatal care in the past 30 years have allowed for an increase in survival rate of very preterm infants (1, 2), which has opened up a field of study on the developmental outcomes of preterm children. Several cohort studies (e.g., EPIcure in the UK and Epipage in France) have now followed the outcome of children born preterm in the 1980s and 1990s through adolescence and adult life, and have sought to define the full spectrum of risk for cognitive, emotional, and social difficulties.

Whether children are born extremely preterm (<28 weeks of gestation), very preterm (28-32 weeks) or moderately preterm (33-36 weeks), the literature converges that one of the most frequent problems children face is of emotional nature (for meta-analyses, see 3, 4). Despite important methodological differences, population definitions, and age at assessment, consistencies across studies suggest a "preterm behavioral phenotype" characterized by a greater risk for emotional problems (5). The prevalence rates of emotional problems in populations of preterm children vary between 8% and 39%, depending mainly on their gestational age (GA), compared to 5-10% of prevalence in full term children (6). Specifically, across early and late childhood, studies using screening measures have found that preterm-born children are, among others, at a heightened risk for anxiety symptoms, depressive symptoms, withdrawn behavior, and somatic complaints—a constellation of emotional problems described as internalizing symptoms (7-12). Similarly, studies using diagnostic measures have found that preterm children are at a higher risk for meeting psychiatric diagnosis, with anxiety disorder being the most frequent diagnosis (13). Importantly, emotional problems tend to persist into adolescence and adulthood (14, 15) and there is evidence that a previous history of social-emotional problems is a strong predictor of current symptoms (16-18). Wiles and colleagues (19) suggest that the emotional distress observed in preterm-born individuals throughout the lifespan is not related to environmental factors but rather is due to perinatal factors.

Despite the consensus in the literature that emotional difficulties are one of the most common psychological problems in preterm children, there is a fair amount of individual differences among children born preterm (e.g., 20). Why do some children born preterm exhibit emotional problems and

others do not? Furthermore, why do some very preterm-born children develop emotional difficulties in the early years while others develop such problems later in life? The etiology underlying childhood emotional problems, including in children born very preterm, is understood to be complex and multi-factorial (21). In developmental psychiatry, emotional disturbances are most commonly associated with stressful life events, such as exposure to violence, maltreatment, or abuse (22). In particular, a positive association between stress and internalizing symptoms has been found in both community and clinic samples of children and adolescents (23, 24).

At birth, the preterm infant is physically and neurologically immature to survive outside of the adapted environment of the womb and is frequently subject to intensive care in the Neonatal Intensive Care Unit (NICU). Furthermore, many preterm-born children remain hospitalized for weeks—even for months—during which they endure painful procedures and/or heavy treatments due to medical complications. Thus, because of the many invasive painful procedures (e.g., skin-breaking procedures), sensory dystimulation (e.g., hospital noise, bright lights, medical odors), and the lack of proximity to the mother, a preterm birth puts infants at risk for *perinatal stress* (25). Here, we define perinatal stress as a combination of infant's medical characteristics at birth (e.g., GA, weight, Apgar score, head circumference) and a set of NICU-specific procedures due to infectious complications and/or intracranial hemorrhage (e.g., ventilation, electroencephalogram, anticonvulsant treatment, exchange transfusion). The degree of adversity of such perinatal experience—i.e., perinatal stress—that can sometimes last for a long time, is likely to worsen the developmental trajectory of preterm-born children.

Above and beyond GA, quantifying the adversity of the neonatal experience has been shown to reliably explain individual differences in the developmental outcome of preterm-born children. For example, a large cohort study examining risk factors associated with neurobehavioral outcomes in very preterm children (VPT) at 2 years of age found that postnatal steroid and inotrope use, and especially prolonged ventilation were associated with a lower developmental quotient, as measured by the Brunet-Lézine early childhood psychomotor development scale (26). Likewise, greater pain exposure has been negatively associated with brain development in VPT children (27, 28). In a similar vein, examining pain-related stress, Grunau and colleagues found that a greater number of skin-

breaking procedures is associated with greater internalizing symptoms in VPT children both at 18 months of corrected age (29) and at 7 years (30). Taken together these results suggest that accounting for the adversity of the experience in the NICU (i.e., perinatal stress) is important for untangling questions related to individual variability in developmental outcomes in VPT children.

In the current study, we aim at examining an important factor that might explain why some VPT children show emotional difficulties while others do not. Specifically, we ask whether medical perinatal stress affects emotional problems in VPT children. More importantly, we seek to determine whether the degree of adversity of the perinatal stress that VPT children experience in the NICU (i.e., low *vs.* high perinatal stress) acts as a moderator in the relationship between emotional scores in infancy and in preadolescence. Based on the existing literature on the influence of stress on emotional problems, we predict that—within the VPT group—children experiencing more perinatal stress would show a greater amount of emotional difficulties.

Method

Participants

The participants came from a larger longitudinal project on the psychological outcome of preterm children (31-34). Babies born ≤ 33 weeks of gestational age (GA) at the NICU of the University Hospital of Lausanne in 1998 were eligible for inclusion in this longitudinal study. Exclusion criteria were congenital malformation or chromosomal abnormalities for babies, and mental disorders, substance use or no fluent French for parents. From the 105 eligible VPT participants, 20 refused to participate and 12 were excluded after their baby's death. Further exclusion criteria were severe developmental problems and/or visual impairments (assessed by a standard pediatric examination at 6 months, $n = 4$). From 18 months corrected age to 11 years of age, 37 participants dropped out of the study (e.g., refused follow up assessment, were unable to be contacted) resulting in a sample of 36 preterm children (for socio-demographic and neonatal data, see Table 1 for included and for drop out VPT participants). Dropout rate at birth was 30%, whereas dropout rate between 6 months and 11 years was 35%; both rates are similar to previous studies on VPT children (e.g., 35).

A control group composed of FT born babies (GA > 37 weeks) was recruited during the same year at the maternity ward of the same hospital. Exclusion criteria were the following: (1) difficulties

during pregnancy or delivery, (2) somatic abnormalities in babies, (3) mental disorders, and/or (4) no fluent French in parents. The control group included 56 healthy FT babies. Among them, 14 refused to participate or were unreachable for the follow up assessments at 6 and 18 months of child age (dropout rate at birth: 25%). From 18 months to 11 years of age, 20 participants dropped out of the study (e.g., refused follow up assessment, unable to contact) resulting in a sample of 22 FT children (dropout rate at 11 years: 48%; for socio-demographic and neonatal data of FT included participants, see Table 1).

Procedure

The design, a longitudinal clinical cohort study, and the protocol were approved by the relevant ethics committee for clinical research in humans. At the child's birth, mothers were informed about the study and asked to sign a consent form for participation in the research. Socio-demographic and neonatal data were recorded at birth (see Tables 1 for specific measures). At 18 months of child age (M_{VPT}=18.4 months of corrected age, *SD*=.45; M_{FT}=18.4 months, *SD*=.51), an assessment of children's behavior problems, including emotional difficulties (see Measures section below) was performed. This age was selected because it refers to a mandatory well-child visit and an important developmental milestone corresponding to the emergence of social cognitive skills (18 months; 36). At 11 years of child age (M_{FT}=11.4 years, *SD*=1.95; M_{VPT}=11.06 years, *SD*=3.26), families were re-contacted for an assessment including a measure of psychopathological symptoms, including emotional difficulties. Written consent was obtained from all participants. Participants received a monetary compensation.

Measures

Socio-demographic data. Child gender, child nationality, and parental status data were obtained from all participants.

Socio-Economic Status. An adaptation of the Hollingshead index (37) was used to assess socio-economic status (SES). Maternal and paternal education level and professional occupation rated each on a 4-point scale (e.g., degree: 1 = compulsory school, 4 = university grade completed; occupation: 1= no job/ unqualified employee, 4 = senior banker or physician in a private practice) were taken into account. The SES index reflects the average of the four scores.

Perinatal stress. The perinatal risk inventory (PERI; 38) is an 18-item inventory assessing at birth the severity of perinatal problems on the basis of perinatal factors such as the APGAR index, gestational age, weight, head growth, seizures, electroencephalogram, ultrasonograph, ventilation, etc. Because it assesses the main characteristics of the perinatal experience, including medical complications and the respective NICU-specific procedures, PERI was used as an index of perinatal medical stress experienced by the infant. Following earlier work (33, 34), we used a clinical cutoff of 5 or more points, thereby separating VPT infants into experiencing *low perinatal stress* (50% of VPT children, *n*=18) or *high perinatal stress* (50% of VPT children, *n*=18; see Table 1 for descriptive statistics). To determine that cutoff, we considered the fact that premature infants without medical complications such as mechanical ventilation more than 24 hours after birth, infectious disease, necrotizing entero-colitis, and/or meningitis obtain PERI scores ranging between 0 and 4 points.

Emotional problems in infancy. The Symptom Check List (SCL; 39) is a 30-minute semi-structured interview with the mother that aims to explore her perception of her infant's problems. The SCL explores 4 groups of difficulties: (1) sleeping problems (trouble going to sleep, night waking, time needed to go back to sleep, and evaluation of the overall consequences of the emotional problems on the parent–child relationship), (2) eating problems (refusal to eat, appreciation of the meal as a negative experience, vomiting, and evaluation of the overall consequence of the emotional problems on parent–child relationship), (3) psychosomatic symptoms (digestion, asthma, allergies, and eczema), and (4) *emotional and behavioral disorders* (frequency and intensity of excesses of anger, opposition, aggressiveness, rituals such as body rocking and head banging, withdrawal, fears, and separation anxiety). The items were coded by the interviewer on a 1- to 5-point scale (1: absence of symptom; 5: severe disorder). In this study, we calculated the mean sum for emotional and behavioral symptoms (16 items, possible score range = 16-80) as indexing young children's emotional difficulties at 18 months of age.

Emotional problems in preadolescence. The Child Behavior Checklist (CBCL; 40) is a widely used, 120-item questionnaire identifying psychopathological symptoms in children and adolescents from 6 to18 years of age (school-age version; CBCL/6–18). Mothers made the ratings in the present study. The checklist comprises a number of statements about the child's behaviors, and

responses are coded on a 3-point Likert scale (0 = Not True, 1 = Somewhat or Sometimes True, 2 = Very True or Often True). It rates the severity of difficulties in eight syndrome subscales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviors, and aggressive behaviors. Two broader scales can be computed by summing corresponding items and transforming the result into T scores (M=50; SD=15): the internalizing (anxious/depressed, withdrawn/depressed, somatic complaints) and the externalizing problems scale (rule-breaking behavior, aggressive behavior). Internalizing symptoms scores were used in the present study as indexing emotional problems at 11 years of age.

Data analyses

Exploring the distribution of the data revealed that it fits assumptions for parametric testing. Comparisons were performed according to group (FT *vs.* VPT), perinatal stress group within the VPT group (high *vs.* low PERI group), and dropout group (included *vs.* dropout). Group differences for categorical variables were calculated with chi-square tests (χ^2), whereas differences for numerical variables were computed with a Multivariate Analysis of Variance (MANOVA) or with Student's *t*-test for independent samples.

As a first step, we examined differences on emotional scores. As a second step, Bravais-Pearson coefficients of correlations were computed in order to examine associations between variables. As a third and final step, a hierarchical regression analysis was conducted in order to determine whether the internalizing scores of VPT children at 11 years are explained by emotional scores at 18 months, perinatal stress (low *vs.* high PERI), and/or the interaction term of emotional scores at 18 months and perinatal stress. Variance inflation factors indicated no multicollinearity. Shapiro-Wilk test on both standardized and unstandardized residuals indicated that they are normally distributed (p=.836). Statistical analyses were conducted with the Statistical Package for Social Sciences v. 23; p-value significance was set, by convention, at p<.05.

Results

Group differences

Descriptive statistics are displayed in Table 1. Group difference analyses revealed that the samples of FT and VPT children were comparable in terms of gender (p=.593), nationality (p=.329),

parental status (p=.444), and maternal age (p=.946). As expected, all neonatal data showed highly significant group differences (p_s <.001). Additionally, we found group differences in terms of SES (p =.012).

We also compared VPT children according to their perinatal score (see two last columns of Table 1 for descriptive statistics) and found that VPT children with low *vs.* high perinatal stress did not differ in terms of gender (p=.502), nationality (p=.228), parental status (p=.596), nor maternal age (p=.274). As expected, compared to VPT children from the low perinatal stress group, VPT children from the high perinatal stress group showed lower birth weight, $t(34)=2.76$, p=.009, and lower head circumference, $t(34)=2.88$, p=.007, as well as a trend towards lower gestational age, $t(34)=1.74$, p=.09. Similar to the FT *vs.* VPT group comparison, we found differences between VPT with children low *vs.* high perinatal stress in terms of SES, $t(34)=3.87$, p<.001. Accordingly, SES was entered as a first step in our regression model predicting VPT children's internalizing symptoms at 11 years of age.

Moreover, we compared VPT participants who remained in the study to VPT participants who dropped out between the 18-months and the 11-years assessments. We found that VPT drop out participants had lower SES scores (p=.01), lower birth weight (p=.029), and higher perinatal stress scores (p=.008; see Table 1 for descriptive statistics).

Emotional scores

First, we examined whether emotional scores differ at 18 months and at 11 years of age (see Table 1 for descriptive statistics). When comparing FT to VPT children, we found that they differ in CBCL internalizing symptoms at 11 years, $t(55)= -2.42$, p=.019, but not in emotional scores at 18 months (p>.05). Within the group of VPT children, when comparing children at low *vs.* high perinatal stress, we found that children differ in emotional scores at 18 months, $t(34)=2.32$, p=.027, but not in internalizing symptoms at 11 years of age, $t(33)= -1.14$, p>.05. Additionally, we found that 29% of our sample of VPT children met the clinical CBCL cut off for internalizing symptoms (T score ≥ 65), whereas none of the FT children did. More importantly, within the VPT group, 44% of children with high perinatal stress showed internalizing scores above the clinical range, compared to 12% of VPT children with low perinatal stress, $\chi^2(1)=4.57$, p=.032.

Correlation analyses

Second, we correlated emotional scores at 18 months with internalizing symptom scores at 11 years. When correlations were performed separately for each group (FT and VPT), we did not find association between these two variables (p_s>.05). However, for VPT children, when we performed correlations separately for each perinatal stress group (low and high stress), we found a significant link between emotional scores at 18 months and internalizing symptoms at 11 years in the high perinatal stress group (r=.577, p=.012), but not in the low perinatal stress group (r=-.081, p>.05).

Regression analysis

Last, for children within the VPT group, we modeled a regression analysis that significantly explained 37% of the variance in VPT children's internalizing problems scores at 11 years of age, $F(4,34)=4.44$, p=.006, R^2=.37. Theoretically-based predictors included SES, the main effect of perinatal stress group (high *vs.* low PERI), and emotional scores at 18 months, as well as the interaction term of emotional scores at 18 months and perinatal stress group (see Table 2). Importantly, two variables were revealed as significant predictors of VPT children's internalizing symptoms at 11 years, namely SES (p=.034) and the interaction term between PERI stress group and emotional scores at 18 months (p=.033). Further analyses revealed that emotional scores at 18 months predicted VPT children's internalizing symptom scores at 11 years only in the high PERI stress group (β=.577, p=.012), but not in the low PERI stress group (β =-.081, p=.758; see Figure 1).

Discussion

In this study, we examined the influence of perinatal stress on the link between early and late emotional problems in children born very preterm. We defined perinatal stress as the combination of preterm newborn's basic data (e.g., GA, weight, head circumference) and the adversity of the medical experience in the NICU. More specifically, we asked whether—within children born preterm—perinatal stress moderates the link between early and later emotional difficulties. We found that VPT children with higher perinatal stress showed more internalizing difficulties at 11 years. More importantly, emotional skills at 18 months of age predicted internalizing difficulties 10 years later in VPT children with high perinatal stress, but *not* in VPT children with low perinatal stress. Our findings suggest that infant perinatal stress is a risk factor for emotional problems in very preterm-born preadolescents.

Our findings on the difference in internalizing symptoms at 11 years of age between FT and VPT children are consistent with the literature on psychological difficulties found in children born very preterm (41-43). Additionally, in line with the prevalence rate for emotional problems in VPT children that varies between 8% and 39% depending on GA *vs*. 5-10% in samples of FT children (6), it appeared that 29% of our sample of VPT children and 44% of our sample of VPT children at high perinatal stress met the clinical CBCL cut off scores for internalizing symptoms (T score ≥ 65). However, unlike previous studies (e.g., 44), we did not find differences between FT and VPT children on emotional skills at 18 months of age. One possibility is that emotional problems become evident at a more advanced age. Another possibility might stem from the difference in instruments used to assess emotional problems. Because we could not use the same measure for emotional difficulties at 18 months and at 11 years, it is likely that those instruments differ in the way they capture variability in such difficulties. In fact, SCL measures aspects specific to early development along with functional disorders, whereas CBCL assesses psychopathological symptoms. Additionally, as described in the Measures section, the SCL subscale that we used as a proxy for emotional difficulties at 18 months is a combination of emotional *and* behavioral problems, both being closely intertwined at this early age.

Why is (perinatal) stress related to emotional difficulties? When excessive amounts of stress are experienced, the demands placed on the individual—both in humans and in animals—exceed the resources for coping with the stressor (e.g., stimuli, people, situations). Despite the fact that there are different theoretical models explaining how adverse stress impacts psychological functioning (General Adaptation Theory (45); Psychological Stress Theory (46); Allostatis Theory (47), there is a general consensus that stressful experiences can precipitate emotional disturbances, including major psychiatric disorders such as anxiety disorders and depression (23, 24). Previous work has shown that preterm birth—as a highly stressful life event—puts infants at risk for emotional problems (see 3, 4). The stress that preterm-born infants experience in the neonatal environment is due, in a large part, to the invasive painful procedures and the sensitive dystimulation, such as the bright lights, the continuous hospital noise, the strong smell of medical products (48). More importantly, such dystimulation happens to a neurologically immature and highly vulnerable baby that has not yet developed protective mechanisms. In fact, the earlier an infant is born, the higher is the risk for

medical complications and for a longer hospital stay, and therefore the risk for medical perinatal stress. This suggests that accounting for NICU-specific risk factors for perinatal stress is key to explaining individual variability in preterm-born children. Beyond the classical studies comparing children in terms of GA and/or birth weight, studies recently started including other neonatal measures as stress predictors of psychological functioning throughout childhood. More specifically, it was found in a cohort of VPT children that pain-related stress is associated to internalizing symptoms both at 18 months corrected age (29) and at 7 years (30). In line with this work on the influence of stress on emotional problems in VPT children, here we measured perinatal stress related to a premature birth as the severity on a number of important perinatal indices, such as hydrocephalus, intracranial hemorrhage, ventilation, and exchange transfusion (i.e., 18 items on the PERI scale; 38). We found that the severity of perinatal stress accounted for the link between early and later emotional difficulties in VPT children. In particular, for VPT children who experienced high perinatal stress, early emotional scores predicted later internalizing symptoms. However, for VPT children with low perinatal stress, this link was not established. A possible explanation of this moderating effect might stem from the influence of the adversity of perinatal stress on children's *coping* strategies (49). Accordingly, children with high perinatal stress might be affected in their abilities to cope with difficulties and thus, might be more likely to embark on the trajectory at-risk for emotional difficulties. Conversely, children with low perinatal stress might be able to unfold coping strategies thus shifting to the resilience trajectory. Taken together, these findings suggest that perinatal stress plays an important role in the etiology of emotional problems in VPT children and that future studies on the psychological outcomes of preterm-born children should include measures of perinatal stress experienced by the preterm baby.

Importantly, another predictor of VPT preadolescents' internalizing scores was SES (p=.034). Although SES was included in the regression model in order to control for group differences, this result is consistent with the literature indicating that economically disadvantaged families are at a heightened risk both for a preterm birth (50) and for psychopathology (51), including internalizing symptoms (52). Low SES is an environmental challenge that moderates etiologic influences on susceptibility to psychopathology. In preterm-born children, the link between low SES and

internalizing symptoms has already been established (44, 53, 54). From these findings, we could hypothesize that parents who are economically preoccupied might not be as available, sensitive, and responsive to their VPT children's emotional needs and experiences, which on the long term might put VPT children at risk for emotional difficulties. In sum, accounting for the influence of SES – as a significant life challenge – is an important step in empirical efforts examining the developmental outcomes in VPT children.

Although we found that perinatal stress is an important factor interacting with emotional scores at 18 months of age, our regression model explained 37% of the variance of VPT children's internalizing symptoms at 11 years of age, leaving 63% of that variance unexplained. In other words, variability in perinatal stress and SES help explain some of the variability in internalizing problems in VPT children, suggesting that other factors remain unaccounted. In a recent review on VPT children, Montagna and Rosarti (21) proposed that several factors could contribute to the understanding of the association between preterm birth, socio-emotional difficulties, and psychopathology. More specifically, they review studies on the influence of biological vulnerability (e.g., altered neurodevelopment), early life adversities (e.g., stress), and parenting (e.g., emotional availability of parents) on psychopathological symptoms in VPT children. Consistent with this work, a previous study on the cohort presented here has found that prematurity puts children at risk for internalizing problems, but this link is moderated by maternal sensitivity during early interactions (31). More precisely, only VPT children whose mothers showed an insensitive interactive style scored higher than FT peers on internalizing symptoms. Taken together, these findings urge for an integrative model including neural maturation, psycho-social functioning, and familiar and cultural environment, which all dynamically interact in the first years of life. A preterm birth affects all these aspects of development, prompting a cascade of neurodevelopmental outcomes that affect the individual, together with the entire family and extended social systems. It is therefore essential that future empirical efforts adopt an integrative model studying bio-psycho-social influences on psychopathology in children born very preterm.

Comparing results across studies on the outcome of preterm children has been challenging for several reasons. A main reason lays in the inclusion/exclusion criteria set by authors. Whereas many

studies include preterm-born children with neurological damage (e.g., 55), the cohort presented in this study is composed of children without congenital malformations, chromosomal anomalies, foetopathy, or severe neurodevelopmental complications (e.g., cerebral palsy, mental retardation). Setting such exclusion criteria allows for studying the effects of prematurity alone, without the cumulative effects of neurological conditions. Additionally, in this study we used corrected age instead of chronological age. Corrected age takes into account the neurobiological maturation level of the central nervous system, while chronological age gives prominence to the duration of the exposure to the environmental experience after birth and thus overestimates at risk children. Furthermore, the fact that this cohort is born in the late 1990s reflects the contemporaneous outcomes relevant to current public health concerns. This is important given the substantial advances in the 1990s in neonatal care that changed fundamentally the nature of medical, nurse, and parental care for preterm-born infants. In order to allow for more straightforward links between the results of this study and other empirical efforts in the field, we placed an emphasis on well categorizing the presented cohort.

Despite our methodological efforts, this study presents a few limitations that need to be addressed in future empirical efforts. First, it included a relatively small sample size. This is not surprising given the long-term longitudinal design of the study. Second, it appears that there was a dropout bias. Compared to VPT children who remained in the study, VPT children who dropped out of the study between the 18-months and the 11-years assessments presented lower SES scores, lower birth weight, and higher perinatal stress scores (see Table 1 for descriptive statistics). These results are consistent with the literature, as families who face more socio-economic and/or psychological challenges tend to be less likely to participate in research studies (56). Importantly, despite the fact that the most at-risk subjects dropped out of the study, we found reliable significant differences in emotional functioning. Last, in this study we relied only on parental report, which may have yielded a nuanced view of children's emotional problems. This is particularly noteworthy given the differences found between preterm-born adolescents' perception of themselves and parental perceptions of their child, with children tending to self-report fewer problems (43, 57).

In this study, we present findings that help understand a portion of the inter-individual variability in emotional problems found in VPT children. Specifically, our results showed that, within

children born very preterm, it is the association between the severity of perinatal stress and early emotional problems that helps predict internalizing symptoms in VPT children at preadolescence. In other words, VPT children who are born with more perinatal complications, experience more stress in the perinatal period, and are more likely to show emotional difficulties in preadolescence.

Conflict of interest: none

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Table 1.

Descriptive statistics for socio-demographic and neonatal data for full-term (FT; first column) and very preterm (VPT; second column) children; two last two columns brake down VPT children into low and high stress groups.

	Full-term (FT)	**Very preterm (VPT)**			
	Total (n = 22)	Total (n=36)	Low perinatal stress (n=18)	High perinatal stress (n=18)	Drop out (n=69)
Socio-demographic data	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Gender (boys)	8 (36)	16 (44)	9 (50)	7 (39)	46 (67)
Nationality (CH)	18 (82)	25 (69)	14 (78)	11 (61)	32 (46)
Parental status (married)	14 (64)	29 (81)	15 (83)	14 (78)	63 (91)
	M (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	
Maternal age at child's birth (yrs)	32.00 (4.21)	32.08 (4.66)	31.22 (3.84)	32.94 (5.33)	30.16 (5.12)
SES	2.93 (0.58)	2.55 (0.52)	2.83 (0.44)	2.27 (0.44)	2.21 (.69)
Neonatal data	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	
Gestational Age (wks)	39.99 (1.26)	30.46 (2.07)	31.04 (1.64)	29.87 (2.33)	29.73 (2.25)
Birth weight (gr)	3316.82 (519.27)	1451.25 (382.28)	1612.50 (318.00)	1290.00 (379.50)	1247.97 (474.65)
Head circumference at birth (cm)	34.53 (0.97)	28.11 (2.35)	29.16 (1.65)	27.06 (2.51)	27.15 (3.15)
Perinatal Risk (PERI)	0.18 (0.50)	5.03 (3.17)	2.72 (0.96)	7.33 (2.93)	7.52 (5.00)
Emotional scores	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	
At 18 months (SCL)	32.21 (8.61)	34.47 (9.84)	38.06 (9.64)	30.89 (8.90)	-
At 11 years (CBCL)	50.64 (9.42)	57.11 (10.10)	55.12 (7.73)	59.00 (11.83)	-

Note. CBCL=child behavior checklist; CH= Switzerland (Confoederatio Helvetica); cm=centimeters; gr=grams; M=mean; PERI=perinatal risk inventory;
SCL=symptom checklist; SD=standard deviation; SES=socio-economical status; wks=weeks.

Table 2.

Regression model explaining internalizing symptoms scores (CBCL) in VPT children at 11 years.

Variables	B	S.E.	*β*	t	*p*-value
Intercept	81.02	13.59		5.96	.000
SES	**-7.78**	**3.50**	**-.40**	**-2.22**	**.034**
PERI (low stress=0, high stress=1)	0.92	3.77	.05	.245	.808
Emotional problems (SCL at 18 months)	-0.11	0.22	-.10	-.472	.640
PERI x Emotional prob. (18 months)	**0.73**	**0.33**	**.46**	**2.237**	**.033**

Note: β=standardized beta coefficient; B=un-standardized beta coefficient; CBCL=child behavior checklist; PERI=perinatal risk inventory; S.E.=standard error; SCL=symptom checklist; SES=socio-economical status; t=t-test statistic; *p*-value=significance value.

Highlights:

- A very premature birth puts children at risk for emotional difficulties.
- It remains unclear why some children born very preterm (VPT) develop emotional problems while other do not.
- Perinatal stress (i.e., various invasive procedures) might explain individual variability in the development of emotional problems in VPT children.
- VPT children with higher perinatal stress are more likely to show emotional difficulties later on.

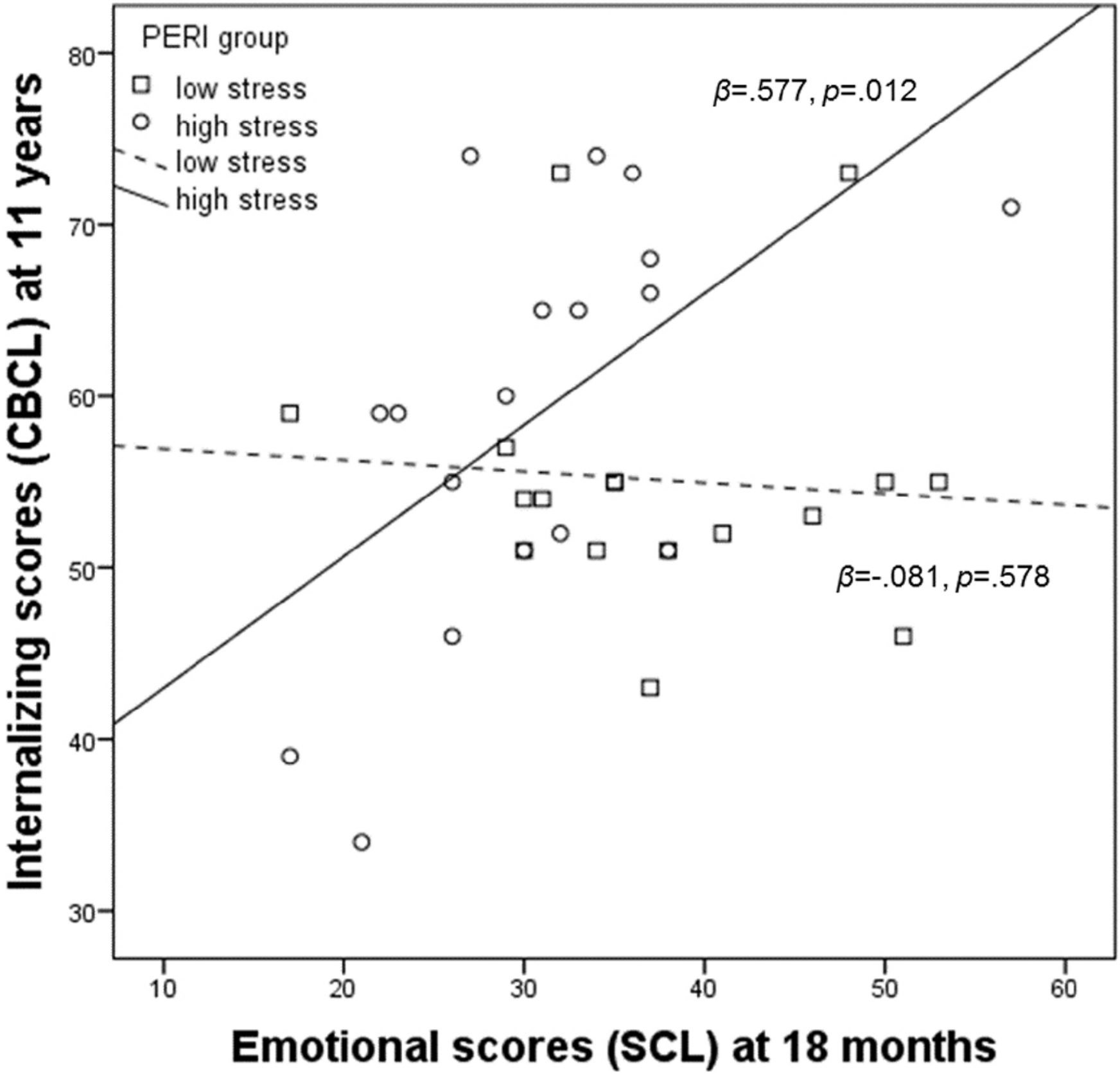
PERI group
low stress
high stress
low stress
high stress
β=.577, p=.012
β=-.081, p=.578
Internalizing scores (CBCL) at 11 years
80
70
60
50
40
30
10
20
30
40
50
60
Emotional scores (SCL) at 18 months

Figure 1