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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



Nevena Dimitrova^{*}, Hélène Turpin, Ayala Borghini, Mathilde Morisod Harari, Sébastien Urben¹, Carole Müller-Nix¹

University Service of Child and Adolescent Psychiatry, University Hospital of Lausanne, Lausanne, Switzerland

ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Prematurity Emotional problems Perinatal stress Risk factor Longitudinal design	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.

1. Introduction

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 such as population definitions or 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

* Corresponding author at: University Service of Child and Adolescent Psychiatry, University Hospital of Lausanne, Avenue d'Echallens 9, 1004 Lausanne, Switzerland. E-mail address: Nevena.Dimitrova@chuv.ch (N. Dimitrova).

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¹ Both authors contributed equally as senior authors.

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 multifactorial [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., skinbreaking 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 are 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.

2. Method

2.1. Participants

The participants came from a larger longitudinal project on the psychological outcome of preterm children [31-34]. Babies born \leq 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).

2.2. 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 $(M_{\rm VPT} = 18.4 \text{ months of corrected age}, SD = 0.45; M_{\rm FT} = 18.4 \text{ months},$ SD = 0.51), 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 $(M_{\rm FT} = 11.4 \text{ years}, SD = 1.95; M_{\rm VPT} = 11.06 \text{ years}, SD = 3.26), \text{ fa-}$ milies 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.

2.3. Measures

2.3.1. Socio-demographic data

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

2.3.2. 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: Download English Version:

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