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# Parent behaviors moderate the relationship between neonatal pain and internalizing behaviors at 18 months corrected age in children born very prematurely

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ABSTRACT

Children born very preterm (⩽32 weeks gestation) exhibit greater internalizing (anxious/depressed) behaviors compared to term-born peers as early as 2 years corrected age (CA); however, the role of early stress in the etiology of internalizing problems in preterm children remains unknown. Therefore, we examined the relationship between neonatal pain and internalizing behavior at 18 months CA in children born very preterm and examined whether parent behavior and stress moderated this relationship. Participants were 145 children (96 very preterm, 49 full term) assessed at 18 months CA. Neonatal data were obtained from medical and nursing chart review. Neonatal pain was defined as the number of skin-breaking procedures. Cognitive ability was measured with the Bayley Scales of Infant Development II. Parents completed the Parenting Stress Index III, Child Behavior Checklist 1.5–5, and participated in a videotaped play session with their child, which was coded using the Emotional Availability Scale IV. Very preterm children displayed greater Internalizing behaviors compared to full-term control children ($P = .02$). Parent Sensitivity and Nonhostility moderated the relationship between neonatal pain and Internalizing behavior (all $P < .05$); higher parent education ($P < .03$), lower Parenting Stress ($P = .001$), and fewer children in the home ($P < .01$) were associated with lower Internalizing behavior in very preterm children, after adjusting for neonatal medical confounders, gender, and child cognitive ability (all $P > .05$). Parent Emotional Availability and stress were not associated with Internalizing behaviors in full-term control children. Positive parent interaction and lower stress appears to ameliorate negative effects of neonatal pain on stress-sensitive behaviors in this vulnerable population.



## 1. Introduction

The majority of infants born very preterm (⩽32 weeks gestational age [GA]) now survive as a result of advances in medical care; however, their long-term neurodevelopmental outcomes, including problems with behavior, have not improved [34,35,43,67]. Very preterm infants are exposed to numerous skin-breaking procedures in the neonatal intensive care unit (NICU). Greater procedural pain exposure has been associated with altered stress hormone (cortisol) regulation in children born at extremely low gestational age (ELGA; 24 to 28 weeks) compared to very low gestational age (VLGA; 29 to 32 weeks) [31,33]. Furthermore, ELGA children demonstrate higher associations between cortisol expression and internalizing (anxious/depressed) behaviors at 18 months corrected age (CA) relative to VLGA children [15]. Greater internalizing behaviors in preterm children compared to full-term control children have been reported as early 2 years CA, persist to late adolescence, and seem to be independent of cognitive ability [1,5,9,35,45,66]. Experimental animal models have also demonstrated that early stress can permanently reorganize hormonal, physiological and behavioral systems [47,48,54,58]. While rat pups exposed to neonatal pain demonstrated increased anxiety-mediated behavior during adulthood [4], the role of neonatal pain in the etiology of internalizing problems in preterm children is unknown.

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Parents play a vital role in the regulation of stress and development of their infant [36]. However, the birth of a preterm infant is a highly stressful experience for parents [49,50,72]. Parenting stress in families with preterm infants has been found to be high during infant hospitalization [27,57,68], persisting well beyond discharge from the NICU [14,26,38,63]. Moreover, parenting stress was found to be a significant and independent predictor of child internalizing behavior [73] and was associated with decreased parent emotional availability at 2 years CA in preterm children [74]. Emotional Availability (EA) is a construct characterizing a supportive caregiver whose authenticity of affect, appropriate responding (sensitivity/nonhostility/nonintrusiveness), and provision of guidance (structuring) increases their child's autonomy [10]. It is important to consider parental level of stress together with parental emotional availability when examining behavior in preterm children.

Parent support to promote sensitive and responsive interactions during hospitalization appears to improve white matter maturation in infants born preterm [53]. This is important given that early alterations of white matter development have been associated with deficits in social-emotional behaviors at age 5 in preterm children [61]. Although more positive parent interaction was found to buffer the relationship between neonatal pain and poorer focused attention at 8 months CA [70], the extent that parent EA moderates the relationship between neonatal pain and internalizing behavior remains unknown.

Therefore, we examined whether neonatal pain (adjusted for neonatal and medical confounders) is related to parent report of internalizing behaviors at 18 months CA, and whether parent EA (adjusted for parenting stress), moderates the relationship between neonatal pain and internalizing behaviors (adjusted for child cognition) in children born very preterm. Further, we examined the relationship between parent EA and internalizing in children born full term. We hypothesized that greater parent EA would be associated with fewer internalizing behaviors at 18 months CA in children born very preterm exposed to greater neonatal pain.

## 2. Methods

This study was approved by the University of British Columbia/Children's and Women's Health Centre of British Columbia Research Ethics Board, and parents provided written informed consent.

### 2.1. Participants

Ninety-six infants born very preterm (⩽32 weeks GA) and 49 full-term control infants born at the B.C. Children's & Women's Hospitals between February 2001 and July 2004 were recruited as part of a larger ongoing study of the effects of neonatal pain on the neurodevelopment of infants born very preterm [15,31,32,70]. Infants were excluded if they were born small or large for GA; if they had a major congenital anomaly, major neurosensory impairment (legally blind, nonambulatory cerebral palsy, sensory-neural hearing impairment), or severe brain injury evident on neonatal ultrasound (periventricular leukomalacia and/or grade 3 or 4 intraventricular hemorrhage); or if the mother reported use of illicit drugs during pregnancy. All full-term infants in our study were born healthy, and none was under observation for medical complications. Ninety-four mothers and 2 fathers of children born very preterm, and 47 mothers and 2 fathers of children born full term participated in the study at 18 months CA (Fig. 1).

### 2.2. Measures

#### 2.2.1. Demographics

Parent information was obtained by questionnaire. Because parent's years of education is the most important socioeconomic status (SES) indicator in relation to child development [12,59], we used parent's years of education as the index of SES for statistical analysis.

#### 2.2.2. Neonatal medical chart review

A neonatal research nurse carried out medical and nursing chart review from birth to term-equivalent age, as described previously [15,31]. Data included but were not limited to GA, gender, illness severity on day 1 (Score for Neonatal Acute Physiology II [SNAP-II]) [60], number of skin-breaking procedures, days of mechanical ventilation, and cumulative morphine exposure adjusted for weight. Neonatal pain was defined as the number of skin-breaking procedures, adjusted for illness severity on day 1, days of mechanical ventilation, and cumulative morphine exposure.

#### 2.2.3. Cognitive development

At 18 months CA, child development was assessed with the Bayley Scales of Infant Development II [8]. We used the Bayley Mental Development Index (MDI) to adjust our statistical models for child cognitive function. The Bayley MDI measures language, memory and problem-solving abilities in infants and toddlers aged 1 to 42 months. The Bayley MDI is a standardized score for overall cognitive development, with a mean of 100 and standard deviation of 15.

#### 2.2.4. Parenting stress

Parent's completed the Parenting Stress Index III (PSI) [2], which includes 120 items rated on a 6-point Likert scale from 1 (strongly agree) to 6 (strongly disagree). The PSI yields a Total Score and 2 domain scores: Child Domain (concern about the child) and Parent Domain (concern about their own parenting ability). Given that the Child Domain reflects parent's concerns about the child's behavior, including internalizing behaviors, we only included the Parent Domain in the statistical analysis because our focus was on how parental factors may influence child behavior.

#### 2.2.5. Child internalizing behavior

Parent's rated their child's behavior with the Child Behavior Checklist for children ages 1½ to 5 years (CBCL) [3], a widely used questionnaire for identifying problem behaviors in children. Ninety-nine items are rated on a Likert scale ranging from 0 (not true) to 2 (very true or often true). Seven syndrome scales (Emotionally Reactive [eg, moody, whining], Anxious/Depressed [eg, nervous, sad], Somatic Complaints [eg, does not eat well, stomachaches], Withdrawn [eg, avoids eye contact, unresponsive to affection], Sleep Problems [eg, nightmares, wakes often], Attention Problems [eg, cannot concentrate, cannot sit still], and Aggressive Behavior [eg, hits others, easily frustrated]) are empirically derived and form 2 broad domains, Internalizing and Externalizing Problems. The Internalizing scale encompasses the Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn Behaviors, whereas the Externalizing scale includes Attention Problems and Aggressive Behaviors. However, only the Internalizing domain was used, given that Internalizing, not Externalizing, problems are associated with prematurity [1,35]. Reliability for the Internalizing subscale is high (test–retest Pearson $r = 0.90$; Cronbach's alpha 0.92) [3].

#### 2.2.6. Emotional availability

The primary caregiver participated in a 5-min videotaped semi-structured teaching scenario with their child. This involved the caregiver trying to teach her child to perform tasks of varying difficulty. The easier and more familiar task involved stacking or nesting colored cups of varying sizes. The novel and more difficult task involved sorting plastic pigs and cows into separate containers. Parent behavior during this interaction was later scored from videotape using the Emotional Availability Scale IV [10].