



Neurobehavioral development prior to term-age of preterm infants and acute stressful events during neonatal hospitalization



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ARTICLE INFO

Article history:

Received 28 July 2015

Received in revised form 2 September 2015

Accepted 4 September 2015

Keywords:

Preterm infants

Early neurodevelopment

Neonatal distress

Pain

ABSTRACT

Background: Neonatal Intensive Care Units (NICUs) protect preterm infants; otherwise, this is a stressful environment including painful stimuli.

Aims: To compare early neurobehavioral development prior to term-age in preterm infants at 34–36 weeks of post-conceptual age in different gestational ages, and to examine the effects of prematurity level and acute stressful events during NICU hospitalization on neurobehavioral development.

Study design: Cross-sectional design.

Subjects: Forty-five preterm infants, 34–36 weeks of post-conceptual age, were distributed into groups: extreme preterm (EPT; 23–28 weeks of gestational age; $n = 10$), moderate preterm (MPT; 29–32 weeks of gestational age; $n = 10$), late preterm (LPT; 34–36 weeks of gestational age; $n = 25$).

Outcome measures: All of the neonates were evaluated using the Neurobehavioral Assessment of Preterm Infant (NAPI) prior to 37 weeks of post-conceptual age. The Neonatal Infant Stressor Scale (NISS) was applied for EPT and MPT infants during NICU hospitalization, and medical charts were analyzed.

Results: The EPT group experienced significantly more acute stressful events during NICU hospitalization than the MPT group. The MPT group had lower scores in motor development and vigor than the EPT and LPT group, and they exhibited poorer quality crying than the LPT group. Motor development and vigor and alertness and orientation in preterm infants were predicted by prematurity level and acute stressful events.

Conclusion: The extreme preterm was exposed to higher stressful experiences than moderate and late preterm infants. However, the moderate preterm infants presented more vulnerable than the other counterparts in motor and vigor outcomes.

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1. Introduction

Preterm birth is a remarkable risk factor for behavioral problems, poor academic achievement, and poor social development in childhood [1–3]. Children who are born extremely preterm present more motor [4], language [4,5], and cognitive impairments [4], and behavioral and emotional problems [6,7] compared with children born moderate

preterm, late preterm, or full term. A lower gestational age is associated with a higher risk for developmental problems, demonstrating the impact of the organism's immaturity in the neonatal phase on later developmental outcomes [6,8].

Neonatal contextual variables should be considered to better understand the pathway of child development. The early micro-context of the Neonatal Intensive Care Unit (NICU) is a relevant protective environment. Infants' physiological functions are not yet sufficiently mature to survive independently in the external environment [9]. Paradoxically, NICUs represent a risk factor for infants' development because of multiple painful, distressful, and uncomfortable stimuli [10,11]. For example, preterm neonates who were hospitalized in a NICU were found to be exposed to at least 44 acute stressful events and 24 chronic stressful events that were related to examinations and medical treatments [12].

Neonatal Intensive Care Units are characterized by a highly stressful environment for vulnerable immature infants, which could be fairly described as a chaotic context. The chaos is characterized by a physical and human environment of great instability daily without temporal or

Abbreviations: NICU, Neonatal Intensive Care Unit; EPT, extreme preterm; MPT, moderate preterm; LPT, late preterm; NAPI, Neurobehavioral Assessment of Preterm Infant; NISS, Neonatal Infant Stressor Scale; CRIB, Clinical Risk Index for Babies; NMI, Neonatal Medical Index; INCU, Intermediary Neonatal Care Unit; VIF, variance inflation factor; SPSS, Statistical Package for Social Sciences; CNPq, National Council for Development Science and Technology; CAPES, Coordination for the Improvement of Higher Level or Education Personnel.

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structural regularity, variability of caregivers, noise, and highly complex visual and excessive stimulation, which may directly affect the regulatory development of individual processes [13]. Moreover, concerning the developmental approach, the chaotic contexts negatively interfere with individual self-regulation and co-regulation processes [14], which are fundamental for adaptive behavior throughout development.

Consequently, the follow-up of preterm infants is highly recommended to examine the impact of both early biological and contextual factors on later outcomes. Developmental assessments are usually performed after discharge before 2 years of age [15,16], during childhood [17,18], during adolescence [19], and even in adulthood [20].

Few studies have examined very early neurodevelopment prior to term-age [21–24]. The Neurobehavioral Assessment of Preterm Infants (NAPI) evaluates the neurodevelopment of preterm infants at <37 weeks of post-conceptual age, with predictive power for later development until the first 3 years of age and the early detection of cerebral palsy in combination with magnetic resonance imaging [22,25]. The NAPI was predictive of development at 18 months of age, which in turn predicted child development at preschool age [26] and school age [27,28]. The NAPI is also predictive of different outcomes between very low birthweight and early very low birthweight preterm infants, showing that this latter group presents worse neurobehavioral development [21].

To better understand the impact of preterm birth on child development, we need to consider the relationships between the immaturity and clinical status of infants and the distressful and painful events that are experienced within the early developmental micro-context of the NICU. The present study compared very early neurobehavioral development prior to term-age in preterm infants at 34–36 weeks of post-conceptual age in different gestational age groups and examined the effects of prematurity level and acute stressful events in the NICU on neurobehavioral development.

The two main hypotheses of the present study were the following: (i) extreme preterm infants present more early neurobehavioral problems prior to term-age compared with moderate and late preterm infants, and moderate preterm infants present more early neurobehavioral problems prior to term-age compared with late preterm infants; and (ii) prematurity status (extreme preterm) and acute stressful and painful events in the NICU in preterm infants together comprise high risk factors that predict negative impacts on early neurobehavioral development prior to term-age.

2. Methods

2.1. Participants

The sample in the present study consisted of 45 preterm neonates of both sexes (44% females) who were born in the Hospital of Clinics of Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil. The neonates were distributed into three groups: neonates born extremely preterm from 23 to 28 weeks of gestational age (EPT group; $n = 10$), neonates born moderately preterm from 29 to 32 weeks of gestational age (MPT group; $n = 10$), and neonates born late preterm from 34 to 36 weeks of gestational age (LPT group; $n = 25$). The method of evaluation of gestational age was the New Ballard, as routinely adopted in the hospital. The EPT and MPT groups were composed of critically ill neonates who were hospitalized in the NICU. The LPT group included healthy neonates who were hospitalized in the Intermediary Neonatal Care Unit (INCU). The cutoff of 32 weeks of gestational age was adopted for the first two groups by considering that this is a population of preterm infants with a high risk for morbidity and mortality [29]. Extremely preterm births represent approximately 2% of births but comprise one-third of perinatal deaths [30].

The inclusion criteria were the following: neonates < 37 weeks of gestational age, neonates whose legal guardians agreed to participate in the study, neonates with stable clinical status on the day of

neurobehavioral development assessment at 34–36 weeks of post-conceptual age, and neonates in the EPT and MPT groups with at minimum of 5 days of NICU hospitalization. The exclusion criteria were the following: neonates with III/IV level intraventricular hemorrhage, hydrocephaly, microcephaly, convulsive crisis, congenital abnormalities, and congenital syphilis.

During the period of 2011 and 2012, 109 neonates met the inclusion criteria. Of this initial sample, 18 neonates died (EPT group, $n = 15$; MPT group, $n = 3$), and seven were excluded for the following reasons: III/IV level intraventricular hemorrhage (EPT group, $n = 4$; MPT group, $n = 2$) and congenital abnormality (EPT group, $n = 1$). Of the remaining 84 neonates, 39 were not included in the study for the following reasons: discharge and transfer to another hospital (EPT group, $n = 8$; MPT group, $n = 7$), extended mechanical ventilation (EPT group, $n = 4$; MPT group, $n = 5$), hospitalization in the NICU for < 5 days (EPT group, $n = 1$; MPT group, $n = 8$), clinical discharge before the completion of data collection (EPT group, $n = 2$; MPT group, $n = 1$), absence of the legal guardian in the hospital to obtain consent to participate in the study (EPT group, $n = 1$; MPT group, $n = 1$), and no consent given by the legal guardian (MPT group, $n = 1$). The final sample of the study included 45 neonates.

2.2. Ethical approval

The study was approved by the Clinical Research Ethics Board of the Hospital of Clinics, Ribeirão Preto Medical School, University of São Paulo, and informed consent was obtained from all parents of the neonates prior to participation in the study.

2.3. Setting of the study

The study was performed in the Neonatal Service in the Hospital of Clinics, which includes 17 beds in the NICU and 25 beds in the INCU. This is a tertiary university hospital and national reference center for the low-income population in the Brazilian public health system. The Neonatal Service has expertise on neonatal intensive treatment and a trained multidisciplinary health professional team that is composed of physicians, nurses, psychologists, occupational therapists, and physical therapists. Other professionals offer support to the Neonatal Service, including neurologists, surgeons, radiologists, and anesthesiologists. In the Neonatal Service, a developmental care approach is routinely adopted, including the following daily protective measures to reduce neonates' pain and distressful experiences: light reduction at night, natural light during the day, covering the incubators to protect neonates from light stimulation, non-nutritive suctioning, sucrose for pain relief during acute painful procedures, soft rolls of flannelette to swaddle the neonates, minimal manipulations for extremely preterm neonates, psychological support for mothers and other family members, and open parental visitation to the NICU during the neonates' hospitalization.

2.4. Instruments and measures

2.4.1. Neurobehavioral Assessment of Preterm Infants [25], Brazilian version [31]

The NAPI is a standardized neurodevelopmental assessment of the progression of early neurobehavioral performance in preterm infants from 32 weeks of post-conceptual age to term age (38–40 weeks post-conceptual age, gestational age plus chronological age). This instrument includes the following seven clusters: motor development and vigor, scarf sign, popliteal angle, alertness and orientation, irritability, cry quality, and percent asleep ratings. The score in each cluster ranges from 0 to 100. Early risk for abnormal neurodevelopment is assigned when cluster scores fall more than one standard deviation below the mean [21]. The face validity and sensitivity of the NAPI were described using an index of medical complications [32]. The NAPI presents criterion validity [33]. The inter-rater reliability coefficient ranges from 0.67 to

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