High Incidence of Multi-Domain Disabilities in Very Preterm Children at Five Years of Age

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Objectives To describe the prevalence and co-occurrence of disabilities and their association with parental education in preterm children and term control subjects.

Study design In a prospective study, preterm children (n = 104), born at <30 weeks' gestation or birth weight <1000 g, and term children (n = 95) were assessed at corrected age 5 with an intelligence quotient (IQ) test, behavior questionnaires for parents and teachers, and motor and neurologic tests. A disability was defined as results in the mild abnormal range of each test or below. Associations of outcomes with parental education were studied.

Results Of the preterm children, 75% had at least one disability and 50% more than one, compared with 27% and 8%, respectively, of term control subjects ($P < .01$). The preterm-term difference in full scale IQ increased from 5 IQ points if parental education was high to 14 IQ points if it was low, favoring the term children in both groups. A similar pattern was found for behavior, but not for motor and neurologic outcome.

Conclusions Disabilities occur frequently after very preterm birth and tend to aggregate. Neurologic and motor outcomes are mostly influenced by biologic risk, and social risks contribute to cognitive and behavioral outcome. *(J Pediatr 2011;159:79-85)*.

Very preterm born children are at risk for disabilities on a range of developmental domains.[1-5] Multidisciplinary follow-up assessment is important for optimal patient care, research purposes, and evaluation of neonatal intensive care. There are an extensive number of articles available on developmental outcomes of preterm-born children. Mild problems, such as intelligence quotient (IQ) scores between –1 SD and –2 SD are not always considered problematic,[6] although these can have a significant influence on school performance.[1,7]

Studies that evaluated mild disabilities differ in the developmental domains studied.[1-4] In all these studies, neurologic, as well as cognitive, functioning is assessed. Although behavior questionnaires are included, usually the teacher is not asked as an informant, and motor development may not be evaluated. [1,4] In studies that focus on multiple domains and mild disabilities, the percentage of children with disabilities is around 60%.[1-4]

Global IQ scores are usually the gold standard for evaluating a child's cognitive functioning. Although verbal and performance IQ and processing speed are clinically important separate indicators of cognitive functioning,[8-10] it is not customary to distinguish such factor scores of intelligence in definition of a developmental disability.

This cohort study was designed to investigate multidomain developmental outcome in 5-year-old children born very preterm, in comparison with term-born control subjects. We focus on the occurrence of both mild and severe disabilities and consider factor scores of intelligence. The main aim was to describe how many preterm-born children had developmental disabilities in comparison with term-born control subjects.

Low socioeconomic status is a risk factor for preterm birth[11] but also for less-optimal developmental outcomes in preterm children.[12,13] A second aim was to investigate the association between outcomes on different domains and parental education as a marker of socioeconomic status.

BW	Birth weight
CP	Cerebral palsy
FSIQ	Full-scale intelligence quotient
IQ	Intelligence quotient
M-ABC	Movement Assessment Battery for Children
NICU	Neonatal intensive care unit
PIQ	Performance intelligence quotient
SDQ	Strengths and Difficulties Questionnaire
VIQ	Verbal intelligence quotient
WPPSI	Wechsler Preschool and Primary Scale of Intelligence

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Methods

This study is a single-center prospective cohort study has been approved by the Medical Ethics Commission of the Academic Medical Centre, Amsterdam, The Netherlands. In the Netherlands, care in the neonatal intensive care unit (NICU) is regionalized.

Two groups of children participated in this study. The preterm group consisted of children born at <30 weeks' gestation or with birth weights (BW) <1000 g, who reached the corrected age of 5 between December 2007 and June 2009. Inclusion criteria were (1) hospitalization in our NICU; (2) participation at least once in our neonatal follow-up program; and (3) resident in the Netherlands. Exclusion criteria were as follow: (1) participation in one of two other studies (Preeclampsia-Eclampsia Trial Amsterdam[14] or Stedelijk Interventie Project Prematuren (Urban Intervention Project Preterm Born Children)[15]) because of the use of different instruments and different timing of follow-up; (2) a genetic syndrome; or (3) being too handicapped to undergo an age-appropriate IQ test.

The control group included children born after 37 weeks' gestation, with BW >2500 g, who reached age 5 in the same time period, and who were attending mainstream schools. Exclusion criterion was a planned or current referral for learning or behavioral problems.

All parents of eligible preterm children fulfilling our inclusion criteria received an invitation letter. They were asked to participate and to help recruit a term-born control child. To recruit children for the control group, we first approached schoolmates of the preterm children, or secondly, members of the social network of the participating family. Finally, we tried to recruit control subjects via schools in the neighborhood of our hospital.

The assessment protocol was similar for both groups. At the first appointment, shortly after the child reached the corrected age of 5, IQ was assessed by a trained child psychologist, and the parents filled out a questionnaire about the child's behavior. At the second visit, in 90% of the cases within 3 months after the first visit, neurologic and motor tests were performed by a trained pediatrician or child physiotherapist. Investigators were not blinded to birth status. For the preterm group, all test scores were based on the corrected age. Decisions about (ab)normality of test scores of individual children were based on normative test data.

Measures

Intelligence. IQ was assessed with the Dutch translation of the third version (2009) of the Wechsler Preschool and Primary Scale of Intelligence (WPPSI).[16] The seven core subtests were administered, and in addition the subtest Symbol Search. The full-scale intelligence quotient (FSIQ), verbal intelligence quotient (VIQ), performance intelligence quotient (PIQ) and processing speed quotient were calculated. These were considered mildly or severely abnormal if more than 1 SD or 2 SD below the mean, respectively.

Behavior. Behavioral, emotional, and social functioning were assessed with the Strengths and Difficulties Questionnaire (SDQ), parent and teacher form.[17] Only a total problem score was used for this study. According to the test manual, a score was mildly abnormal if higher than the 80th percentile, and severely abnormal if higher than the 90th percentile.

Neurologic development. Neurologic development was qualitatively assessed with the Touwen neurologic examination.[18,19] Posture, reflexes, sensory deficits, cranial nerve dysfunction, and involuntary and associated movements were examined. Neurologic development was classified as normal, simple, or complex minor neurologic dysfunction, or cerebral palsy (CP).[19]

Motor development. Motor development was assessed with the Movement Assessment Battery for Children, Second Edition (M-ABC).[20] For some children of the preterm group (n = 19) who also participated in the Caffeine for Apnea of Prematurity-trial,[21] the first edition of the M-ABC was administered. The total score was considered mildly or severely abnormal if equal to or less than the 15th percentile or 5th percentile, respectively.

Composite Outcome

As a primary endpoint of this study, two composite outcome scores of the disabilities on all four developmental domains were calculated. One composite score included all disabilities (mild and severe) and the other only severe disabilities.

On the first composite outcome score, all mild disabilities and severe disabilities were counted as one disability and were added to a sum score reflecting the total number of mild-to-severe disabilities. Children without any disability received a composite score of zero.

If a child had one or more abnormal factor scores (VIQ, PIQ, processing speed quotient, or FSIQ), the cognitive outcome was regarded as abnormal and counted as one disability. On the behavioral domain, a (mildly) abnormal score on the SDQ of either parent or teacher (or both), was counted as one disability. On the motor domain an abnormal score on the M-ABC (≤P15), and on the neurologic domain a diagnosis of simple or complex minor neurologic dysfunction or CP was counted as one disability.

Children were included in the composite score if test results in at least two different domains were available. A missing test result was then taken into the calculation as zero.

A second composite outcome score was calculated by adding all severe problems of a child (a WPPSI factor-score of <2SD, a SDQ-score of >P90, a diagnosis of CP, and a M-ABC-score of ≤P5).

Baseline Characteristics

Perinatal data were abstracted from an ongoing prospective database that is used for all infants admitted to our NICU (Table I). Perinatal data of term control subjects were collected by parental questionnaire.