Published in final edited form as:
J Obstet Gynecol Neonatal Nurs. 2010 September ; 39(5): 536–549. doi:10.1111/j.1552-6909.2010.01171.x.

Effects of Gender on the Health and Development of Medically At-Risk Infants

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Abstract

Objectives—To examine gender-differentiated health and cognitive/motor/language developmental outcomes among medically at-risk infants.

Design—Longitudinal descriptive and comparative secondary analysis.

Setting—Neonatal intensive care unit, intermediate care unit, and infectious disease clinic of the tertiary medical centers in the Southeast and East United States.

Participants—One hundred eight (108) premature infants, 67 medically fragile infants, and 83 infants seropositive for HIV.

Methods—Neonatal and later health variables were obtained from the medical record to determine the technology dependence scores and frequency of common health problems. Data for physical growth and cognitive/motor/language development were obtained through the physical measurement, including the Bayley Scales of Infant Development–Second Edition, the Vineland Adaptive Behavior Scale, the Toll Control Developmental Checklist, and the Preschool Language Scale–3 during home visits between 6 to 27 months corrected ages.

Results—Fewer effects on health and developmental outcomes related to gender were observed with medically fragile infants than the other two groups of infants. The cognitive/motor/language scores were decreased with increasing age of the infants in all groups.

Conclusion—Male gender can be considered a significant biological risk factor for infants' cognitive and motor development, especially for premature infants. Because of their increased risk, it is recommended that male infants who are born prematurely or seropositive for HIV have early and advanced developmental screening tests by trained personnel through periodic pediatric clinic.

Keywords

Gender; Health and Development; Premature Infants; Medically Fragile Infants; Infants Seropositive for HIV

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Gender has been found to be a significant predictor of health and development in childhood, with boys usually showing greater vulnerability (Gissler, Järvelin, Louhiala, & Hemminkj, 1999; Hintz et al., 2006; James, 2000; Nuñez & McCarthy, 2003; Stevenson et al., 2000; Tioseco, Aly, Essers, Patel, & El-Mohandes, 2006). Gender differences in health appear early; boys are more likely to be born prematurely than are girls and tend to have more neonatal complications (Cooperstock, Bakewell, Herman, & Schramm, 1998; Gissler et al.; Hintz et al.; James, 2000). The higher rate of male preterm births occurs in both singleton and multiple births (Cooperstock et al.) as well as in White and Black births (Cooperstock & Campbell, 1996). In comparison with girls, boys also are more likely to be intubated, receive more resuscitation medications, and have an approximately 20% higher risk for low 1- and 5-min Apgar scores (Bekedam, Engelsbel, Mol, Buitendijk, & Pal-de Bruin, 2002; Gissler et al.; James; Stevenson et al.). As a result, the risk for neonatal and perinatal mortality is 20% higher for boys than for girls (Bekedam et al., 2002; Gissler et al.; Stevenson et al.).

Boys are also known to be more vulnerable to neonatal illnesses than are girls. Boys have higher rates of respiratory distress syndrome (RDS) and chronic lung disease (CLD) (Bartels, Kreienbrock, Dammann, Wenzlaff, & Poets, 2005; Friedrich, Stein, Pitrez, Corso, & Jones, 2006). As a result, in comparison with prematurely born girls, prematurely born boys are more likely to be exposed to medications, including surfactants and antibiotics and to receive mechanical ventilation (Sandri et al., 2004; Warrier, Du, Natarajan, Salari, & Aranda, 2006). Boys are more likely to be diagnosed with intraventricular hemorrhage (IVH), IVH Grades III-IV, and periventricular leucomalacia (PVL) (Bartels et al.; Nuñez & McCarthy, 2003; Tioseco et al., 2006).

CALLOUT 1

These gender differences in health continue into late infancy and early childhood. In comparison with girls, boys are usually found to have longer average hospital stays and receive more medication (Gissler et al., 1999). When boys have been found to have shorter hospitalization stays, this finding can be attributed to higher mortality in boys than in girls (Stevenson et al., 2000). Boys between 4 and 8 years and between 17 to 18 years averaged poorer neuropsychological function than girls in the same age groups (Allin et al., 2006). The higher rates of neurological abnormalities such as IVH and PVL in boys may be one cause of the higher prevalence of neurodevelopmental delays in boys than in girls (Gissler et al.; Morris, Smith, Swank, Denson, & Landry, 2002; Nuñez & McCarthy, 2003; Tioseco et al., 2006).

Despite these health and developmental problems, boys on average develop several motor skills earlier than girls, including the ability to lift the head while lying on the stomach, stand with support, and crawl independently (Reinisch & Sanders, 1992). Boys are more active than girls (Campbell & Eaton, 1999), and these gender differences increase with age (Campbell & Eaton). Moreover, motor development patterns differ: boys spend longer in the transition from crawling independently to walking with support, whereas girls require more time between sitting without support and standing with support (Reinisch & Sanders). The male superiority in motor development may not occur in medically at-risk infants because of motor delays caused by respiratory problems and neurological insults (Anderson, Swank, Wildin, Landry, & Smith, 1998; Keller, Ayub, Saigal, & Bar-Or, 1998; Taylor, Klein, Schatschneider, & Hack, 1998).

Gender also affects physical growth in infancy. Weight, length, and head circumference are greater in boys than in girls throughout the first year of life (Geary, Pringle, Rodeck,

Callout: Male gender has been found to be a biological risk factor of health and developmental problems in childhood.

Kingdom, & Hindmarsh, 2003). These growth differences are related to hormonal differences between boys and girls. The level of growth hormone (GH) was found to be higher in boys than in girls (Ogilvy-Stuart et al., 1998). In addition to positive correlation between free triiodothyronine (T3) and physical growth, negative correlations between GH and growth and between testosterone and physical growth were found only in girls (Tan, Pence, & Tan, 1998). Leptin, a 16-kDa adipocyte-specific peptide hormone (Toprak et al., 2004), is positively related to birthweight, weight-to-length ratio, and body mass index in both genders (Ambrosius, Compton, Bowsher, & Pratt, 1998; Ertl et al., 1999); however, the levels of leptin were lower in boys than in girls (Ambrosius et al.; Ertl et al.; Matsuda et al., 1997; Wabitsch et al., 1997).

Gender differences in health and development are sometimes reported in medically at-risk infants (Bartels et al., 2005; Friedrich et al., 2006; Stevenson et al., 2000). Hindmarsh, O'Callaghan, Mohay, and Rogers (2000) reported that, at 2 years of age, very low birthweight (VLBW) boys were more likely than VLBW girls to show cognitive delays, especially in language and social skills but not motor delays. Slower motor and cognitive development by 3 years of life was predicted by the presence of respiratory problems such as bronchopulmonary dysplasia (BPD) and neurological insults (Singer, Yamashita, Lilien, Collin, & Baley, 1997), which occur more commonly in boys.

The gender differences in health outcomes may be related to gender differences in immunological and central nervous system (CNS) development. According to Geschwind and Galaburda (1987), a high level of prenatal testosterone diminishes the size of the developing thymus gland, and the result is more health problems associated with the immune system in male fetuses and neonates. In addition, a high level of perinatal testosterone is related to greater cerebral lateralization, smaller corpus callosum, and decreased interhemispheric connectivity in boys (Hines & Shipley, 1984; Witelson, 1985). Gonadal steroid hormones also trigger different neural development in the brains of boys and girls (Arnold, 1996; Hindmarsh et al., 2000). Specific cells in the brain express enzymes that can convert testosterone into active metabolites such as estradiol and 5α-dihydrotestosterone (5α-DHT) or into inactive metabolites such as 5β-DHT (Arnold). The absence of androgenic hormones during critical periods of CNS development leads to formation of different neural circuits within the female brain (Kirn & Lombroso, 1998). The male-type brain outperforms the female type in visuospatial abilities (Hyde, 1990; Williams & Meck, 1991), whereas the female-type brain is better in verbal and linguistic abilities (Hindmarsh et al.; Hyde). A high level of prenatal testosterone not only decreases neuronal development in the left hemisphere, but also increases cognitive anomalies in the right hemisphere such as dyslexia and stuttering (Halpern, 2000). Language functions are more asymmetric in the brains of males, and the result is poorer fine motor and language skills in boys. On the other hand, visuospatial functions are more asymmetric in the brains of females, and the result is poorer gross motor and visuospatial skills in girls (Galliano, 2003; Halpern, 2000).

Social expectations and learning also affect the developmental outcomes of girls and boys (Halpern, 1997). The expectations of parents could lead girls to perform better on language tests and boys to perform better on visuospatial tests (Galliano, 2003). Girls are rewarded more frequently by parents when they show language skills, whereas boys are more frequently rewarded when they perform visuospatial tasks (Reinisch & Sanders, 1992).

Although evidence exists that health and development outcomes may differ by gender, gender effects on infant health and development have only rarely been investigated in medically at-risk infants. To examine effects of gender on health and developmental outcomes, we compared outcomes of boys and girls within three groups of medically at-risk

infants: prematurely born infants, medically fragile infants (technologically dependent and chronically critically ill preterm and full-term infants), and infants seropositive for HIV (infants who carry HIV antibodies as a result of prenatal HIV exposure). Health outcomes studied were birthweight; gestational age; medical diagnoses; degree of neurological insults; physical growth patterns; and severity of illness as measured with technology dependence, presence of common health problems, and HIV infection. Development outcomes studied were motor, cognitive, and language abilities.

The three groups of medically at-risk infants were studied to examine the effects of infant gender at different levels of illness severity. All infants studied were medically at risk, but the infants seropositive for HIV were at relatively low risk. The medically fragile infants were considered to be at extreme medical risk because they had a medical diagnosis that necessitated extended hospitalization, were dependent on technology to replace bodily functions, or had a chronic life-threatening illness that would lead to repeated exacerbations during the first year of like. Thus, the comparison of three groups of infants at different levels of medically risk, rather than studying only one group of medically at risk infants, was used to provide better understanding of the effects of gender on infant health and development. The findings; however, were generalized to the effects of gender on infant health and development across three different groups of infants with highly varied medical/health care needs.

CALLOUT 2

Method

This study used a descriptive, longitudinal research design. Three secondary data sets of medically at-risk infants were included: prematurely born infants, medically fragile infants, and infants seropositive for HIV.

Participants

The participants studied were from three earlier studies: 108 prematurely born infants (Holditch-Davis, Scher, & Schwartz, 2004), 67 medically fragile infants (Holditch-Davis, Tesh, Goldman, Miles, & D'Auria, 2000), and 83 infants seropositive for HIV (Holditch-Davis et al., 2001). Fifty-three percent of the premature infants, 63% of the medically fragile infants, and 54% of the infants seropositive for HIV were boys. All premature infants, 58% of the medically fragile infants, and 13% of the infants seropositive for HIV were born prematurely. The mean birthweight of the premature infant group (1,230 g) was smaller than that of medically fragile infants (2,061 g). During the study, seven infants seropositive for HIV were found to be infected with HIV.

Measures (see Table 1)

Infant health—Because differences existed in the original studies, different neonatal and later health variables were analyzed for each group of infants. The neonatal health variables were obtained from the medical record: birthweight (premature and medically fragile infants), gestational age (all three groups), and medical diagnoses (CLD [premature and medically fragile infants], IVH [premature infants], multisystem anomalies [medically fragile infants], and neurological anomalies [medically fragile infants]). Diagnoses were obtained from the infants' medical records. Multisystem anomalies and neurological anomalies of medically fragile infants were determined from the primary diagnosis and

Callout: Male vulnerability in cognitive and motor development appeared in infancy and increased over time regardless of the health status of the infant.

additional diagnoses from the progress notes (Miles, Holditch-Davis, Burchinal, & Nelson, 1999).

The number of neurological insults experienced by premature infants was assessed with the use of the total score of the Neurobiologic Risk Score (NBRS) (Brazy, Goldstein, Oehler, Gustafson, & Thompson, 1993; Oehler, Goldstein, Catlett, Boshkoff, & Brazy, 1993). The NBRS was developed to identify potential CNS-tissue insults that are caused by direct injury, inadequate blood flow, poor oxygenation, and metabolic disturbances (Brazy et al., 1993; Oehler et al.). Seven possible neurological insults--mechanical ventilation, acidosis, seizures, IVH, PVL, infection, and hypoglycemia--were rated as 0, 1, 2, or 4 on the basis of the severity and duration of the condition (Thompson et al., 1997). The total NBRS score is the sum of the seven item scores and ranges from 0 to 28, with higher scores indicating more severe insults. The NBRS has good psychometric properties. The instrument has correlations of -.37 and -.65 with the Bayley Mental and Psychomotor Indexes at 6 and 24 months corrected age and a correlation of .60 with neurological examination at 6, 15, and 24 months corrected age (Brazy et al.). Internal consistency of the NBRS in this sample was 0.72 (Holditch-Davis et al., 2004).

Later health was assessed through technology dependence score (medically fragile infants), neurological examination scores (medically fragile infants), and frequency of common health problems reported by the mothers (premature infants, infants seropositive for HIV). The technology dependence score was developed to measure the severity of medically fragile infants' illnesses (Miles et al., 1999). This score was a count of the types of technology and medications that the infant needed at each contact. These technologies were grouped into 19 categories (e.g., parenteral and intravenous lines, elimination technology) and 10 classes of medications (Miles et al., 1999). Each category of technologies and class of medications was scored 0 if no items in that category or class were used by the infant and 1 if one or more items were used. The total technology dependence score was the sum of the scores for all categories and classes.

A neurological examination that included assessment of 15 reflexes, eye movements, quality of movements, muscle tone, and developmental milestones developed to study medically fragile infants was conducted at 6 months and 12 months corrected age (CA) by master's-prepared nurses (Holditch-Davis et al., 2000). The examiners assessed each item and then rated the overall performance as normal if infants were rated as normal on all items including developmental milestones and did not differ from what would be expected from healthy infants, as suspect if infants had minor abnormalities, and as abnormal if infants showed definite neurological abnormalities.

The Common Infant Health Problem Questionnaire was developed by Miles and Holditch-Davis to study infants seropositive for HIV and premature infant (Holditch-Davis et al., 2001; Holditch-Davis, Schwartz, Black, & Scher, 2007). This questionnaire assessed the frequency of hospitalizations, health problems, and immunizations. The occurrence of five health variables between each contact (diarrhea, vomiting, ear infections, upper respiratory infection, and wheeze) was used in analyses. Mothers reported on the presence of five health problems for the premature infants at 2, 13, and 22 months by mailed questionnaires and at 6, 9, 18, and 27 months by questionnaires completed during in-person contacts. Data were collected for the infants seropositive for HIV during in-person contacts at 6, 12, 28, and 24 months.

Physical growth—This parameter was assessed for the premature infants and for the infants seropositive for HIV. During home visits at 6 and 18 months, study personnel weighed the premature infants on a battery-operated electronic scale with a capacity of 20

kg and accurate within 10 g. Height was determined with the use of a height-measuring board that measures to the nearest 0.1 cm and is collapsible. Head circumference was measured with a disposable tape accurate to the nearest 0.1 cm. The equipment was taken into the home. Research assistants measured dolls and volunteer children until they agreed within 5% at least 95% of the time. Height, weight, and head circumferences were obtained from clinic records for the premature infants at 9 and 27 months and for the infants seropositive for HIV at 6, 12, 18, and 24 months.

Infant development—Motor and cognitive development data for the premature infants and for the infants seropositive for HIV were obtained through the scores of Bayley Scales of Infant Development–Second Edition (BSID-II; Bayley, 1993), which consists of a Mental Development Index (MDI) and a Psychomotor Development Index (PDI) and administered by a certified child psychologist or registered nurses who were trained by the psychologist. The MDI measures specific aspects of infant cognitive abilities, including memory, habituation, problem solving, early number concepts, generalization, classification, vocalization, language, social skill, and visual/fine motor coordination. The PDI measures gross and fine motor abilities. The means on the MDI and PDI are 100, with standard deviations of ±15 (Black & Matula, 2000). The BSID-II was revised in 1993 and was standardized on a national random sample representative of the U.S. population and consisting 1,700 infants 1-42 months of age who were stratified by gender, race/ethnicity, geographic region, and level of parent education (Bayley, 1993). The MDI and PDI of the BSID-II demonstrated reliability coefficients of .88 and .84, respectively. The MDI was correlated at .79 with the General Cognitive Index of the McCarthy Scales of Children's Abilities, and the PDI was correlated at .59 with the McCarthy Motor Scale (Bayley, 1993).

Language development data were obtained through the scores of the Vineland Adaptive Behavior Scale (VABS; Sparrow, Balla, & Cicchetti, 1984) and the Toll Control Developmental Checklist (TOLL; Brandon, Frauman, Huber, Lucas, & Levine, 1989) for the medically fragile infants and through the scores of the Preschool Language Scale–3 (PLS-3; Zimmerman, Steiner, & Pond, 1992) for the premature infants and for the infants seropositive for HIV. The VABS assesses the domains of communication, daily living skills, socialization, and motor development in handicapped and nonhandicapped individuals (Sparrow, Balla, & Cicchetti). It is administered in about 20 min through an interview of a parent or other primary caregiver. The communication domain was chosen for determining the language development of medically fragile infants at 6 and 16 months of corrected age. The VABS showed good psychometric properties in that split-half reliability coefficients ranged from .83 to .94, test-retest coefficients ranged from .76 to .93, and inter rater reliability coefficients ranged from .62 to .78 (Miles, 1998). The VABS has moderately high correlations with other measures of adaptive behavior (Miles, 1998).

The TOLL was designed to assess areas of potential developmental delay in children with chronic illness (Brandon et al, 1989). Five domains of infants' developmental progress can be assessed; movement, visual, language, cognitive, and social/emotional. Items were adapted from existing standardized instruments based on clinical judgments of the primary investigators and the input of experts in early childhood development, psychology, special education, speech and language and pediatric nursing. The percent agreement regarding appropriateness of the items was reported as equal to or greater than 83% (Brandon et al., 1989). The language domain was used to examine the language developmental patterns of medically fragile infants because infants who were identified as at risk or at high risk need to be tested early and because the language domain could identify medically fragile infants' early communication problems. Ratings were based on interviews with the mothers and on direct observation.

The PLS-3 assesses prelinguistic skills, social communication, and language skills (Zimmerman, Steiner, & Pond, 1992). This instrument was standardized with the use of a sample of 1,200 children aged 2 weeks to 6 years 11 months. The sample was balanced for gender and stratified according to the 1986 U.S. Census update by education, geographic region, and race (Zimmerman et al.). The PLS-3 has good reliability and validity. The median internal consistency is .88, and test-retest reliability and inter rater reliability are above .90. With good construct and discriminant validity, the PLS-3's concurrent validity ranges from .82 to .88. The scale has an administration time of 15 to 40 min.

Procedures

The mothers of premature infants were contacted when the infants were no longer critically ill (e.g., respiratory acidosis, severe sepsis), and the mothers of the medically fragile infants were contacted once the infant's medically fragile status (e.g., dependent on technology, extended hospitalization) was confirmed if the infant was not experiencing a medical crisis (e.g., CPR, emergent surgery). The primary caregiver, either a biological mother or a legal guardian, of the infants seropositive for HIV was initially contacted when the infant was about 3 months of age by a member from the pediatric infectious-disease team in the clinic and then was referred to the data collection team. If the infant seropositive for HIV was in foster care, the appropriate county social-service agency was asked for permission to enroll the infant. In all three studies (Holditch-Davis, Scher, & Schwartz, 2004; Holditch-Davis et al., 2000; Holditch-Davis et al., 2001), the purpose of the study was explained, and written consent was obtained. Data for neonatal health (birthweight and gestational age, NBRS scores, and presence of medical diagnosis) were obtained through a medical record review.

The data for later health (neurological examination scores, technology dependence scores, and frequency of common health problems), physical growth, and maternal assessment of infant development were obtained during home visits. Home visits for premature infants were conducted at 6 and 18 months CA. Home visits for medically fragile infants were scheduled at 6, 12, and 16 months CA; and infants seropositive for HIV experienced home visits at 12, 18, and 24 months. The mothers or primary caregivers were contacted by telephone to schedule a convenient time to visit. Cognitive, motor, and language assessments were done at the clinic for premature infants at 9 and 27 months CA; at home for medically fragile infants at 6 and 12 or 16 months CA; and at the clinic for infants seropositive for HIV at 6, 12, and 18 or 24 months (for more details, see Holditch-Davis et al., 2000, 2001; Holditch-Davis et al., 2007; Miles et al., 1999; Miles, Gillespie, & Holditch-Davis, 2001).

Data analysis

To determine whether gender affected the neonatal health (birth characteristics, presence of medical diagnosis, degree of neurological insults during the neonatal period, and technology dependency at enrollment), *t*-tests were used. Generalized estimating equations (GEEs) and general linear mixed models were used to examine the genders differed over time in later health (presence of common health problems, neurological problems, and technology dependence during the infancy), growth (weight, length, and head circumference), and development (motor, cognitive, and language abilities). Descriptive analyses were used to determine the percentage of motor and cognitive impairment. To examine gender differences in developmental status in the three groups of medically at-risk infants, *t*-tests were used.

Results

Effects of Gender on Neonatal Health of Medically At-Risk Infants

As shown in Table 2, neonatal health problems of medically at-risk infants did not differ by gender. Premature infants' birthweight, gestational age, presence of CLD and IVH, and NBRS scores did not differ by gender. During the neonatal period, medically fragile infants' birthweight, gestational age, presence of CLD, multisystem anomalies, and neurological anomalies, as well as these infants' technology dependence score, also did not differ between genders. Gestational age of infants seropositive for HIV was not significantly affected by gender.

Effects of Gender on Later Health of Medically At-Risk Infants

As shown in Table 3, most later health outcomes were not influenced by gender. In comparison with prematurely born boys, prematurely born girls were more likely to experience diarrhea, and this difference did not change with age. No other later health problem variables differed by gender. Medically fragile infants showed less dependence on technology over time. The prevalence of vomiting in infants seropositive for HIV significantly decreased over time.

Effects of Gender on Growth and Development of Medically At-Risk Infants

As shown on Table 4, gender affected premature infant growth over time. In comparison with prematurely born girls, prematurely born boys were significantly heavier and longer and had larger head circumferences. On the other hand, no significant difference in growth patterns was found by gender among infants seropositive for HIV.

Tables 4 and 5 show that gender also affected infant developmental outcomes. Longitudinal analyses (Table 4) indicated that prematurely born girls showed significantly higher scores than prematurely born boys on the cognitive development test (BSID-II MDI) and that both the cognitive and motor scores decreased with increasing age. Maternal demographics and degree of prematurity were not controlled for in these analyses because there were no differences between genders within and across the three groups (Cho, Holditch-Davis, Miles, & Belyea, 2009). In the cross-sectional analyses (Table 5), prematurely born girls showed higher MDI scores at 9 months postmenstrual age (PMA) and higher PDI scores at 27 months PMA. Male and female premature infants did not differ on PLS-3 scores at 27 months. The developmental scores did not differ between the medically fragile boys and girls. The medically fragile infants showed a significant decrease on the language test (VABS) over time.

In the longitudinal analyses, girls seropositive for HIV showed better motor development (BSID-II PDI) than boys in this group (Table 4). The infants seropositive for HIV also showed a significant decrease on the cognitive scores (BSID-II MDI) over time. In the cross-sectional analyses (Table 5), girls seropositive for HIV showed significantly higher scores than boys in this group on the motor development test (BSID-II PDI) at 6 months.

Discussion

The present study examined gender differences in health, physical growth, and development in early childhood in three groups of medically at-risk infants. No gender differences were found on the neonatal health outcomes (CLD, IVH, multisystem anomalies, and neurological anomalies), except that boys were more likely to be medically fragile than were girls. In addition, fewer gender differences in later health outcomes (diarrhea, vomiting, ear infection, upper respiratory infections, and wheezing) were found than what would be

expected to occur by chance. In comparison with prematurely born boys, prematurely born girls were more likely to experience diarrhea. Results of other studies (Elsmén, Pupp, & Hellström-Westas, 2004; Hoekstra, Ferrara, Couser, Payne, & Connett, 2004) have revealed that male neonates tended to have more respiratory, circulatory, and neurological morbidity than female neonates. Like our study, these studies found a greater rate of medical fragility in boys; however, in the healthier premature infants and in infants seropositive for HIV, we did not find any gender differences in health.

We also found that growth in weight, length, and head circumference seemed to be affected by gender. In comparison with prematurely born girls, prematurely born boys were heavier and longer, and had larger head circumferences. At birth (Tioseco et al., 2006) and after birth (Geary et al., 2003), boys were expected to be heavier and longer than were girls. However, this male tendency was confirmed only in the premature infant group. Physical growth patterns of infants seropositive for HIV did not differ between genders.

Results from this study revealed a few gender effects in cognitive and motor development. Prematurely born girls showed better cognitive development outcomes at 9 months PMA and better motor development outcomes at 27 months PMA than prematurely born boys. Girls seropositive for HIV showed better motor development outcomes at 6 months of age than boys in this group. However, the reasons for female advantage in development are unclear because the proportion of neonatal and later health problems did not differ between genders. Although Singer et al. (1997) suggested that better cognitive and motor development outcomes result from girls' having fewer medical problems, Piecuch et al. (1997) found that female gender was associated with better cognitive development despite there being no relationship between gender and neurologic outcomes. In addition, girls are usually found to be superior at tasks that require fine motor skills, rapid perception, and perceptual-motor skills (Jensen, 1998; Nicholson & Kimura, 1996; O'Boyle, Hoff, & Gill, 1995); this finding implies that biological and social factors beyond health problems might explain male disadvantage in infant cognitive and motor development.

Infants seropositive for HIV are usually exposed to highly active antiretroviral therapy in utero and receive oral zidovudine for the first 6 weeks of life (Alimenti, Burdge, Ogilvie, Money, & Forbes, 2003; Lyall et al., 2001). In comparison with infant girls seropositive for HIV, infant boys in this group might have different susceptibility to these medications and their complications such as mitochondrial and hematological toxicity (Bunders, Thorne, & Newell, 2005). Bunders et al. (2005) reported that after antiretroviral treatment total counts of lymphocytes, CD4 cells, and CD8 cells were significantly lower in boys than in girls. Although boys are usually reported (Reinisch & Sanders, 1992; Campbell & Eaton, 1999) to show better motor development, the difference in drug susceptibility may affect their motor development.

More significant gender differences in physical growth and developmental outcomes were found in the prematurely born infants than were found in the medically fragile infants or in the infants seropositive for HIV. This difference was probably due to differences in the health status of the three groups of infants. The infants seropositive for HIV were the healthiest of the three groups but also had the most social risk because most of their mothers were African American and poor (Holditch-Davis et al., 2001; Miles et al., 2001). These factors may have worked against finding gender differences in this group of infants. By contrast, the medically fragile infants were the least healthy of the three groups. Unlike the premature infants and the infants seropositive for HIV who were selected from a heterogeneous population of infants, the medically fragile infants were deliberately chosen because they were the sickest premature and full-term infants. There was already a strong male predominance in this group because in comparison with female infants, male infants

were more likely to be medically fragile; this male predominance may have prevented other gender differences from being apparent. The premature infants who were the moderately ill group were then the group in which gender differences were most obvious. If male gender is considered a possible predictor of infant cognitive and motor developmental delays, prematurely born low-birthweight male infants should receive closer attention from families and health care providers (HCPs).

In addition findings about gender differences, a few other findings resulted from this study. The prevalence of technology dependence in medically fragile infants and the incidence of vomiting in infants seropositive for HIV decreased over time. The decrease in technology dependence in medically fragile infants indicates that their health problems improve over time. Talmaciu, Ren, Kolb, Kickey, & Panitch (2002) also showed that many medically fragile infants were able to become independent from their medical technologies when they became older; in addition, Glendinning, Kirk, Guiffrida, & Lawton (2001) found that 24% of infants were technology dependent before 1 year, 11% of infants needed the medical technologies between 1 and 2 years, and 4% of children were still technologically dependent between 3 and 4 years.

One of the most significant findings from this study was the decrease in developmental status over time in medically at-risk infants. As has been previously reported for the infants seropositive for HIV (Holditch-Davis et al., 2001), cognitive, motor, and language abilities showed a significant decrease over time in all three groups of infants. Similar findings of decreases in cognitive and motor development over time have been found in other studies (Culnane et al., 1999; Holditch-Davis, Belyea, & Edwards, 2005; Singer et al., 1997) of premature infants with and without BPD. Singer et al. reported that the percentage of premature infants who had cognitive and motor impairment also increased over time. Because they are required to display more complex behaviors at older ages, medically at-risk infants may display more cognitive and motor problems as they age (Black & Matula, 2000).

CALLOUT 3

In addition, the developmental decline may have been affected by the poverty of the infants seropositive for HIV. On the average, the HIV-positive mothers were more likely to be younger, to have fewer years of education, and to be single parents than were the mothers of the premature infants or the mothers of medically fragile infants. However, it must be noted that these maternal demographics did not differ between genders within and across the three groups (Cho et al., 2009). The developmental decline may also have been affected by mother-infant interactions, which have been found to be less positive between mothers and premature infants than between mothers and healthy full-term infants (Keilty & Freund, 2005; Muller-Nix et al., 2004; Schmucker et al., 2005). These environmental effects may have had a greater effect on language and other cognitive skills in the second year than on the developmental skills in infancy that depend more on visual-fine motor coordination (Bendersky & Lewis, 1994; Engelke, Engelke, Helm, & Holbert, 1995; Liaw & Brooks-Gunn, 1993).

Limitations

This study has several limitations. First, the effect sizes for the repeated-measures analyses were smaller than .80, in particular, a power of .64 was found for 67 medically fragile infants. A small effect size might lead to a failure to detect differences in health outcomes

Callout: Health care providers encourage families of medically at-risk infants, especially males, to be vigilant about ensuring that they meet cognitive and motor developmental outcomes.

between genders. Second, the infants might have been too young for the influence of gender on the language development to be detectable, although this development has been reported to be greater in the female gender (Galliano, 2003). Third and perhaps most important, the different data collection times and measures for health and language development might have led to difficulty in comparing the results across the three groups of infants in this study. Also, changes in care practice over the different time periods covered by the three studies may have affected the infant health and developmental outcomes in the three studies.

Implications for Practice and Research

Because of these limitations, this study needs confirmation using a large-scale longitudinal database that includes both ill infants and healthy, normal birthweight infants to establish gender differences in infant cognitive/motor/language development across different gestational ages and birthweights after characteristics of infant and mother are statistically adjusted. Other future studies may explore potential biological factors that could explain male vulnerability in infant cognitive/motor/language development.

Because male vulnerability in cognitive and motor development appeared in infancy and increased over time regardless of the health status of the infant, HCPs should encourage families of medically at-risk infants, especially prematurely born low-birthweight male infants, to be vigilant about infant cognitive and motor developmental outcomes by ensuring periodic visits to a newborn follow-up clinic, as well as to a pediatric clinic. Because U.S. society has been familiar with the concept of male superiority, it may not be easy to explain the concept of male disadvantage when HCPs discuss families of prematurely born low-birthweight male infants.

A recent study (Scarborough, Hebbeler, & Spiker, 2006) using a large-scale database found that, up to 3 years of age, more boys than girls were enrolled in the early intervention programs; this difference resulted from a rate of developmental delays that was higher in boys than in girls. Although male gender is known to be a biological risk factor for poor health and developmental outcomes during childhood, gender has not been taken seriously as a possible eligibility criterion for early intervention. As the results from this study indicate, gender-differentiated cognitive and motor developmental outcomes are apparent even before the first year of life. Thus, HCPs need to consider gender a potential predictor of developmental outcomes and of subsequent school readiness.

The mothers of medically at-risk infants, especially male infants, may also need guidance from HCPs on seeking emotional and psychological support (Cho, Holditch-Davis, & Miles, 2008). As part of their discharge plan, HCPs may suggest that mothers periodically check their emotional and mental status and contact social services or their physicians if they feel stressed and overwhelmed with child care (Cho et al., 2008). If possible, HCPs should provide some self-assessment tools and referral information about clinic personnel or mental health counseling (Cho et al., 2008). In addition, HCPs can discuss interventions for families, such as a group intervention consisting of families of male infants.

Conclusion

In conclusion, designing gender-specific and sensitive nursing interventions for mothers of medically at-risk infants and measuring the effectiveness of nursing interventions remain as challenging tasks. The nursing interventions may be designed from the associations among biological (e.g., biological factors beyond gender) - environmental (e.g., mother-infant interactions) - developmental (e.g., infant cognitive/motor/language skills) factors. Designing the nursing interventions and measuring the effectiveness of the nursing

interventions may also be guided by scientifically sound theories including theories of sex differences.

Acknowledgments

Funded by National Institute of Nursing Research grants NR01894, NR02868, MH51019, and NR0709. The authors thank T. Schwartz, M. Belyea, and L.C. Chien for statistical consultation.

References

Alimenti A, Burdge DR, Ogilvie GS, Money DM, Forbes JC. Lactic acidemia in human immunodeficiency virus-uninfected infants exposed to perinatal antiretroviral therapy. Pediatric Infectious Disease Journal. 2003; 22:782–788. [PubMed: 14506368]

Allin M, Rooney MAM, Griffiths T, Cuddy M, Wyatt J, Rifkin L, et al. Neurological abnormalities in young adults born preterm. Journal of Neurology, Neurosurgery, and Psychiatry. 2006; 77:495–499.

Ambrosius WT, Compton JA, Bowsher RR, Pratt JH. Relation of race, age, and sex hormone differences to serum leptin concentrations in children and adolescents. Hormone Research. 1998; 49:240–246. [PubMed: 9568809]

Anderson A, Swank P, Wildin S, Landry S, Smith K. Modeling analysis of change in neurologic abnormalities in children born prematurely: A novel approach. Journal of Child Neurology. 1998; 14(8):502–508. [PubMed: 10456759]

Arnold AP. Genetically triggered sexual differentiation of brain and behavior. Hormones and Behavior. 1996; 30:495–505. [PubMed: 9047274]

Bartels DB, Kreienbrock L, Dammann O, Wenzlaff P, Poets CF. Population based study on the outcome of small for gestational age newborns. Archives of Disease in Childhood: Fetal and Neonatal Edition. 2005; 90(1):F53–F59. [PubMed: 15613577]

Bayley, N. Manual for the Bayley Scales of Infant Development. 2nd. San Antonio, TX: Psychological Press; 1993.

Bekedam DJ, Engelsbel S, Mol BWJ, Buitendijk SE, van der Pal-de Bruin KM. Male predominance in fetal distress during labor. American Journal of Obstetrics and Gynecology. 2002; 187:1605–1607. [PubMed: 12501071]

Bendersky M, Lewis M. Environmental risk, biological risk, and developmental outcome. Developmental Psychology. 1994; 30:484–494.

Black, MM.; Matula, K. Essentials of Bayley Scales of Infant Development–II assessment. New York: Wiley; 2000.

Brandon, D.; Frauman, AC.; Huber, C.; Lucas, T.; Levine, M. The TOLL Control System for surveillance of chronically ill children. Chapel Hill, NC: Colonial Press; 1989.

Brazy JE, Goldstein RF, Oehler JM, Gustafson KE, Thompson RJ. Nursery neurobiologic risk score: Levels of risk and relationships with nonmedical factors. Developmental and Behavioral Pediatrics. 1993; 14(6):375–380.

Bunders M, Thorne C, Newell ML. for the European Collaborative Study. Maternal and infant factors and lymphocyte, CD4 and CD8 cell counts in uninfected children of HIV-1-infected mothers. AIDS. 2005; 19:1071–1079. [PubMed: 15958839]

Campbell DW, Eaton WO. Sex differences in the activity level of infants. Infant and Child Development. 1999; 8:1–17.

Cho J, Holditch-Davis D, Miles M. Effects of maternal depressive symptoms and infant gender on the interactions between mothers and their medically at-risk infants. Journal of Obstetric, Gynecologic, and Neonatal Nursing. 2008; 37:58–70.

Cho J, Holditch-Davis D, Miles M, Belyea M. Effects of gender on the interactions between mothers and their medically at-risk infants. Journal of Reproductive and Infant Psychology. 2009; 27(1): 89–105.

Cooperstock MS, Bakewell J, Herman A, Schramm F. Effects of fetal sex and race on risk of very preterm birth in twins. American Journal of Obstetrics and Gynecology. 1998; 179(3):762–765. [PubMed: 9757986]

Cooperstock M, Campbell J. Excess males in preterm birth: Interactions with gestational age, race, and multiple birth. Obstetrics and Gynecology. 1996; 88:189–193. [PubMed: 8692499]

Culnane M, Fowler M, Lee SS, McSherry G, Brady M, O'Donnell K, et al. Lack of long-term effects of in utero exposure to zidovudine among uninfected children born to HIV-infected women. Journal of American Medical Association. 1999; 281(2):151–157. for the Pediatric AIDS Clinical Trials Group Protocol 219/076 Teams.

Elsmén E, Pupp IH, Hellström-Westas L. Preterm male infants need more initial respiratory and circulatory support than female infants. Acta Pædiatrica. 2004; 93:529–533.

Engelke SC, Engelke MK, Helm JM, Holbert D. Cognitive failure to thrive in high-risk infants: The importance of the psychosocial environment. Journal of Perinatology. 1995; 15:325–329. [PubMed: 8558343]

Ertl T, Funke S, Sarkany I, Szabo I, Rascher W, Blum WF, et al. Postnatal changes of leptin levels in fullterm and preterm neonates: Their relation to intrauterine growth, gender, and testosterone. Biology of the Neonate. 1999; 75(3):167–176. [PubMed: 9925904]

Friedrich L, Stein RT, Pitrez PM, Corso AL, Jones MH. Reduced lung function in healthy preterm infants in the first months of life. American Journal of Respiratory and Critical Care Medicine. 2006; 173(4):442–447. [PubMed: 16322648]

Galliano, G. Gender: Crossing boundaries. Belmont, CA: Thomson; 2003.

Geary MPP, Pringle PJ, Rodeck CH, Kingdom JCP, Hindmarsh PC. Sexual dimorphism in the growth hormone and insulin-like growth factor axis at birth. Journal of Clinical Endocrinology and Metabolism. 2003; 88(8):3708–3714. [PubMed: 12915659]

Geschwind, N.; Galaburda, AM. Cerebral lateralization: Biological mechanisms, associations, and pathology. Cambridge, MA: MIT Press; 1987.

Gissler H, Järvelin MR, Louhiala P, Hemminkj E. Boys have more health problems in childhood than girls: Follow-up of the 1987 Finnish Birth Cohort. Acta Paediatrica. 1999; 88:310–314. [PubMed: 10229043]

Glendinning C, Kirk S, Guiffrida A, Lawton D. Technology-dependent children in the community: Definitions, numbers and costs. Child: Care, Health, and Development. 2001; 27(4):321–334.

Halpern DF. Sex differences in intelligence: Implications for education. American Psychologist. 1997; 52(10):1091–1102. [PubMed: 9329293]

Halpern, DF. Sex differences in cognitive abilities. 3rd. Mahwah, NJ: Erlbaum; 2000.

Hindmarsh GJ, O'Callaghan MJ, Mohay HA, Rogers YM. Gender differences in cognitive abilities at 2 years in ELBW infants. Early Human Development. 2000; 60:115–122. [PubMed: 11121674]

Hines M, Shipley C. Prenatal exposure to diethylstilbestrol (DES) and the development of sexually dimorphic cognitive abilities and cerebral lateralization. Developmental Psychology. 1984; 20:81–94.

Hintz SR, Kendrick DE, Vohr BR, Poole WK, Higgins RD. for the NICHD Neonatal Research Network. Gender differences in neurodevelopmental outcomes among extremely preterm, extremely-low-birthweight infants. Acta Pædiatrica. 2006; 95:1239–1248.

Hoekstra, RE.; Ferrara, B.; Couser, RJ.; Payne, NR.; Connett, JE. Survival and long-term neurodevelopmental outcome of extremely premature infants born at 23-26 weeks' gestational age at a tertiary center; Pediatrics. 2004. p. e1-e6.Retrieved March 21, 2008, from http://www.pediatrics.org/cgi/content/full/113/1/e1

Holditch-Davis D, Belyea M, Edwards L. Prediction of 3-year developmental outcomes from sleep development over the preterm period. Infant Behavior and Development. 2005; 28(2):118–131.

Holditch-Davis D, Miles MS, Burchinal M, O'Donnell K, McKinney R, Lim W. Parental caregiving and developmental outcomes of infants of mothers with HIV. Nursing Research. 2001; 50(1):5–14. [PubMed: 19785240]

Holditch-Davis D, Scher M, Schwartz T. Respiratory development in preterm infants. Journal of Perinatology. 2004; 24:631–639. [PubMed: 15175629]

Holditch-Davis D, Schwartz T, Black B, Scher M. Correlates of mother-premature infant interactions. Research in Nursing and Health. 2007; 30:333–346. [PubMed: 17514707]

Holditch-Davis D, Tesh EM, Goldman BD, Miles MS, D'Auria J. Use of the HOME Inventory with medically fragile infants. Children's Health Care. 2000; 29:257–277.

Hyde JS. Meta-analysis and the psychology of gender differences. Signs: Journal of Women in Culture and Society. 1990; 16(1):55–73.

James WH. Why are boys more likely to be preterm than girls? Plus other related conundrums in human reproduction. Human Reproduction. 2000; 15(10):2108–2111. [PubMed: 11006182]

Jensen, AR. The g factor: The science of mental ability. New York: Praeger; 1998.

Keilty B, Freund M. Caregiver-child interaction in infants and toddlers born extremely premature. Journal of Pediatric Nursing. 2005; 20:181–189. [PubMed: 15933653]

Keller H, Ayub BV, Saigal S, Bar-Or O. Neuromotor ability in 5- to 7-year-old children with very low or extremely low birthweight. Developmental Medicine and Child Neurology. 1998; 40:661–666. [PubMed: 9851234]

Kirn J, Lombroso PJ. Development of the cerebral cortex: XI. Sexual diamorphism in the brain. Development and neurobiology. Journal of American Academy of Child and Adolescent Psychiatry. 1998; 37(11):1228–1230.

Liaw FR, Brooks-Gunn J. Patterns of low-birth-weight children's cognitive development. Developmental Psychology. 1993; 29:1024–1035.

Lyall EGH, Blott M, de Ruiter A, Hawkins D, Mercy D, Mitchla Z, et al. Guidelines for the management of HIV infection in pregnant women and the prevention of mother-to-child transmission. HIV Medicine. 2001; 2:314–334. [PubMed: 11737411]

Matsuda J, Yokota I, Iida M, Murakami T, Naito E, Ito M, et al. Serum leptin concentration in cord blood: Relationship to birth weight and gender. Journal of Clinical Endocrinology and Metabolism. 1997; 82(5):1642–1644. [PubMed: 9141565]

Miles MS. Parental role attainment with medically fragile infants (Grant No RO1 NR 02868). Report to the National Institute of Nursing Research, National Institutes of Health. 1998

Miles MS, Gillespie JV, Holditch-Davis D. Physical and mental health in African American mothers with HIV. Journal of the Association of Nurses in AIDS Care. 2001; 12(4):42–50. [PubMed: 11486719]

Miles MS, Holditch-Davis D, Burchinal M, Nelson D. Distress and growth in mothers of medically fragile infants. Nursing Research. 1999; 48:129–140. [PubMed: 10337844]

Morris BH, Smith KE, Swank PR, Denson SE, Landry SH. Patterns of physical and neurologic development in preterm children. Journal of Perinatology. 2002; 22:31–36. [PubMed: 11840240]

Muller-Nix C, Forcada-Guex M, Pierrehumbert B, Jaunin L, Borghini A, Ansermet F. Prematurity, maternal stress and mother-child interactions. Early Human Development. 2004; 79:145–158. [PubMed: 15324994]

Nicholson KG, Kimura D. Sex differences for speech and manual skill. Perceptual and Motor Skills. 1996; 82:3–13. [PubMed: 8668494]

Nuñez JL, McCarthy MM. Sex differences and hormonal effects in a model of preterm infant brain injury. Annals of the New York Academy of Science. 2003; 1008:281–284.

O'Boyle MW, Hoff EJ, Gill HS. The influence of mirror reversals on male and female performance in spatial tasks: A componential look. Personality and Individual Differences. 1995; 18(6):693–699.

Oehler JM, Goldstein RF, Catlett A, Boshkoff M, Brazy JE. How to target infants at highest risk for developmental delay. Maternal-Child Nursing Journal. 1993; 18:20–23.

Ogilvy-Stuart AL, Hands SJ, Adcock CJ, Holly JMP, Matthews DR, Mohamed-Ali V, et al. Insulin, insulin-like growth factor I (IGF-I), IGF-binding protein-1, growth hormone, and feeding in the newborn. Journal of Clinical Endocrinology and Metabolism. 1998; 83(10):3550–3557. [PubMed: 9768663]

Piecuch RE, Leonard CH, Cooper BA, Kilpatrick SJ, Schlueter MA, Sola A. Outcome of infants born at 24-26 weeks' gestation: II. Neurodevelopmental outcome. Obstetrics and Gynecology. 1997; 90:809–814. [PubMed: 9351769]

Reinisch, JM.; Sanders, S. Prenatal hormonal contributions to sex differences in human cognitive and personality development. In: Gerall, AA.; Moltz, H.; Ward, IL., editors. Handbook of behavioral neurobiology. Vol. 2. New York: Plenum Press; 1992. p. 221-243.

Sandri F, Ancora G, Lanzoni A, Tagliabue P, Colnaghi M, Ventura ML, et al. Prophylactic nasal continuous positive airway pressure in newborns of 28-31 weeks gestation: Multicentre

randomized controlled clinical trial. Archives of Disease in Childhood: Fetal and Neonatal Edition. 2004; 89:F394–F398. [PubMed: 15321956]

Scarborough A, Hebbeler KM, Spiker D. Eligibility characteristics of infants and toddlers entering early intervention services in the United States. Journal of Policy and Practice in Intellectual Disabilities. 2006; 3:57–64.

Schmucker G, Brisch KH, Kohntop B, Betzler S, Osterle M, Pohlandt F, et al. The influence of prematurity, maternal anxiety, and infants' neurobiological risk on mother-infant interactions. Infant Mental Health Journal. 2005; 26:423–441.

Singer L, Yamashita T, Lilien L, Collin M, Baley J. A longitudinal study of developmental outcome of infants with bronchopulmonary dysplasia and very low birth weight. Pediatrics. 1997; 100(6):987–993. [PubMed: 9374570]

Sparrow, SS.; Balla, DA.; Cicchetti, DV. A revision of the Vineland Social Maturity Scale. Circle Pines, MN: American Guidance Service; 1984.

Stevenson DK, Verter J, Fanaroff AA, Oh W, Ehrenkranz RA, Shankaran S, et al. Sex differences in outcomes of very low birthweight infants: The newborn male disadvantage. Archives of Disease in Childhood: Fetal and Neonatal Edition. 2000; 83(1):F182–F185. [PubMed: 11040165]

Talmaciu I, Ren CL, Kolb SM, Kickey E, Panitch HB. Pulmonary function in technology-dependent children 2 years and older with bronchopulmonary dysplasia. Pediatric Pulmonology. 2002; 33:181–188. [PubMed: 11836797]

Tan Ü, Pence S, Tan M. The prenatal attenuation of brain/body development through interactions between growth hormone, triiodothyronine and testosterone during prenatal development of female neonates. International Journal of Neuroscience. 1998; 95:237–245. [PubMed: 9777441]

Taylor HG, Klein N, Schatschneider C, Hack M. Predictors of early school age outcomes in very low birth weight children. Developmental and Behavioral Pediatrics. 1998; 19(4):235–243.

Thompson RJ, Gustafson KE, Oehler JM, Catlett AT, Brazy JE, Goldstein RF. Developmental outcome of very low birth weight infants at four years of age as a function of biological risk and psychosocial risk. Developmental and Behavioral Pediatrics. 1997; 18(2):91–96.

Tioseco JA, Aly H, Essers J, Patel K, El-Mohandes AAE. Male sex and intraventricular hemorrhage. Pediatric Critical Care Medicine. 2006; 7(1):40–44. [PubMed: 16395073]

Toprak D, Gökalp AS, Hatun S, Zengin E, Arisoy AE, Yumuk Z. Serum leptin levels of premature and full-term newborns in early infancy: Metabolic catch-up of premature babies. Turkish Journal of Pediatrics. 2004; 46:232–238. [PubMed: 15503476]

Wabitsch M, Blum W, Muche R, Braun M, Hube F, Rascher W, et al. Contribution of androgens to the gender difference in leptin production in obese children and adolescents. Journal of Clinical Investigation. 1997; 100(4):808–813. [PubMed: 9259579]

Warrier I, Du W, Natarajan G, Salari V, Aranda J. Patterns of drug utilization in a neonatal intensive care unit. Journal of Pharmacology. 2006; 46:449–455.

Williams CL, Meck WH. The organizational effects of gonadal steroids on sexually dimorphic spatial ability. Psychoneuroendocrinology. 1991; 16(1-3):155–176. [PubMed: 1961837]

Witelson SF. The brain connection: The corpus callosum is larger in left-handers. Science. 1985; 219(4714):665–668. [PubMed: 4023705]

Zimmerman, I.; Steiner, V.; Pond, P. Preschool Language Scale–3. San Antonio, TX: Psychological Press; 1992.

Table 1

Summary of Measures Used in the Groups of Medically At-Risk Infants

Construct	Measure	Variable
Group		
Infant health		
Neonatal health	Chart review	Birthweight
Premature and HIV	Chart review	Gestational age
Premature, MF, and HIV	Chart review Premature and MF	CLD
	Chart review Premature	IVH
	Chart review MF	Multisystem anomalies
	Chart review MF	Neurological anomalies
	NBRS Premature	Degree of neurological insults
Late health MF	Neurological exam	Degree of neurological insults
Premature and HIV	Health history	Frequency of common health problems
Physical development	Physical growth	Weight, height, and head circumference
Premature and HIV		
Infant development		
Cognitive development	BSID-II MDI	Cognitive development
Premature and HIV		
Motor development	BSID-II PDI	Motor development
Premature and HIV		
Language development	PLS-3	Language development
Premature and HIV		
MF	VABS	Language development
MF	TOLL	Language development

Note.; HIV = infants seropositive for HIV; MF = medically fragile infants; CLD = chronic lung disease; IVH = intraventricular hemorrhage; NBRS = Neurobiologic Risk Score (Brazy, Goldstein, Oehler, Gustafson, & Thompson, 1993); BSID-II MDI = Bayley Scales of Infant Development–Second Edition Mental Development Index (Bayley, 1993); BSID-II PDI = Bayley Scales of Infant Development–Second Edition Psychomotor Development Index (Bayley, 1993); PLS-3 = Preschool Language Scale–3 (Zimmerman, Steiner, & Pond, 1992), VABS = Vineland Adaptive Behavior Scale (Sparrow, Balla, & Cicchetti, 1984); TOLL = Toll Control Developmental Checklist (Brandon, Frauman, Huber, Lucas, & Levine, 1989).

Table 2

Effects of Gender on Neonatal Health Outcomes of the Medically At-Risk Infants

	Girls		Boys			
Variable	***n***	***M***	***n***	***M***	***t(df)***	χ^2**(2)**
Premature infants						
Birthweight (g)	51	1,229.40	57	1,229.90	-0.01(106)	
Gestational age (week)	51	29.24	57	28.51	1.42(106)	
Chronic lung disease (%)	51	33.00	57	40.00		0.57
Intraventricular hemorrhage (%)	51	0.16	57	0.23		0.86
Neurobiologic Risk Score	51	2.75	57	2.70	0.08(106)	
Medically fragile infants						
Birthweight (g)	25	2,286.10	42	1,927.00	1.38(65)	
Gestational age (wk)	25	34.84	42	32.91	1.37(65)	
Chronic lung disease (%)	25	28.00	42	31.00		0.21
Multisystem anomalies (%)	25	36.00	42	33.00		0.05
Neurological anomalies (%)	25	32.00	42	31.00		0.01
Technology dependency	25	5.04	42	5.88	-1.34(65)	
Infants seropositive for HIV						
Gestational age (weeks)	38	37.68	45	38.76	-1.81(81) #	

# $p < .10$.

Table 3

Effects of Gender on Later Health Outcomes of Medically At-Risk Infants

	Gender			Time			Gender × Time		
Variable	**ß *(Girl)***	***Z***	***F(df)***	**ß**	***Z***	***F(df)***	**ß**	***Z***	***F(df)***
Premature infants at 2, 6, 9, 12, 18, 23, and 27 months									
Diarrhea	0.51	2.55*		0.02	0.66		-0.08	-1.89	
Vomiting	0.01	0.05		0.02	0.80		0.01	0.16	
Ear infection	0.00	0.00		0.03	0.91		0.01	0.15	
URI	-0.03	-0.17		0.01	0.55		0.01	0.38	
Wheezing	-0.06	-0.32		-0.02	-0.80		0.02	0.59	
Infants seropositive for HIV at enrollment, 6, 12, 18 and 24 months									
Diarrhea	1.88	1.09		0.25	0.76		-0.50	-0.97	
Vomiting	-1.24	-0.65		-1.01	3.29**		0.33	0.63	
Ear infection	1.72	1.06		-0.62	-2.01		-0.33	-0.70	
URI	0.42	0.22		-0.39	-0.90		-0.07	-0.12	
Wheezing	-1.94	-1.04		-0.48	-1.22		0.50	0.95	
Medically fragile infants at 6 and 12 months									
Neuro exam	-0.03		*0.01(65)*	-0.14	*2.17(54)*		-0.01		*0.00(54)*
TD	-0.37		*0.20(64)*	-0.89	*13.94(53)***		0.23		*0.30(53)*

Note. From Generalized Estimating Equations (Z Statistic for the groups of premature infants and infants seropositive for HIV) and General Linear Mixed Models (F Statistic for the medically fragile infants.

URI = upper respiratory infection; Neuro Exam = neurological examination; TD = technology dependence score.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 4

Effects of Gender on Growth and Developmental Outcomes of Medically At-Risk Infants Over Time From General Linear Mixed Models

	Gender		Time		Gender × Time	
Variable	**ß *(Girl)***	***F(df)***	**ß**	***F(df)***	**ß**	***F(df)***
Premature infants at 6, 9, 18, and 27 months						
Weight	-0.54	8.96(177)**	1.92	893.64(107)***	-0.08	0.42(177)
Height	-2.46	6.10(159)*	8.29	1,070.16(105)***	0.31	0.37(159)
Head circumference	-1.34	10.54(133)**	2.38	412.85(104)***	0.09	0.15(133)
Premature infants at 9 and 27 months						
MDI	8.83	17.21(83)**	-10.36	23.08(76)***	-1.27	0.08(83)
PDI	2.69	0.80(83)	-11.75	8.48(74)**	9.24	3.56(83)#
Medically fragile infants at 6 and 12 months						
TOLL	-0.67	0.08(65)	1.07	2.96(48)#	0.78	0.21(48)
Medically fragile infants at 6 and 16 months						
VABS	2.77	1.28(65)	-5.32	21.75(49)***	0.74	0.12(49)
Infants seropositive for HIV at enrollment, 6, 12, and 18 months						
Weight	-383.66	2.09(57)	3371.80	803.14(38)***	180.61	0.55(57)
Height	-0.46	0.12(33)	11.47	563.34(38)***	0.52	0.27(33)
Head circumference	-0.44	0.09(28)	4.21	102.07(38)**	0.28	0.11(28)
Infants seropositive for HIV at 6, 12, and 18 or 24 months						
MDI	0.91	0.05(113)	-4.78	11.42(75)**	2.00	0.80(113)
PDI	10.17	6.26(103)*	2.58	0.92(75)	-2.74	1.18(103)
Infants seropositive for HIV at 18 and 24 months						
VABS	-1.58	0.51(71)	-4.10	1.78(61)	4.71	3.22(71)#
PLS-3	0.70	0.04(66)	0.27	0.21(58)	1.25	0.10(66)

Note. MDI = Bayley Mental Development Index; PDI = Bayley Psychomotor Development Index; TOLL = Toll Control Developmental Checklist; VABS = Vineland Adaptive Behavior Scale; PLS-3 = Preschool Language Scale–3.

$^{\#}p < .10$.

$^{*}p < .05$.

$^{**}p < .01$.

$^{***}p < .001$.

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Table 5

Gender Differences in Developmental Outcomes by Group of Medically At-Risk Infants

	Girls		Boys		
Variable	***n***	***M***	***n***	***M***	***t(df)***
Premature infants					
MDI at 9 month	40	102.08	45	93.24	4.15(83)***
MDI at 27 month	36	90.44	42	82.88	1.87(76)#
PDI at 9 month	40	91.25	45	88.56	0.90(83)
PDI at 27 month	35	88.74	41	76.81	3.09(74)*
PLS-3 at 27 month	32	99.31	35	92.69	1.64(65)
Medically fragile infants					
MDI at 16 month	22	80.55	38	79.90	0.15(58)
VABS at 6 month	20	101.05	38	98.13	1.09(56)
VABS at 16 month	21	96.00	39	92.72	0.91(58)
Infants seropositive for HIV					
MDI at 6 month	33	95.49	29	94.21	0.28(60)
MDI at 12 month	29	94.93	36	94.57	0.10(63)
MDI at 18 or 24 month	30	89.62	35	84.63	1.31(63)
PDI at 6 month	31	93.68	29	83.31	2.24(58)*
PDI at 12 month	29	96.26	34	88.56	1.97(61)
PDI at 18 or 24 month	28	93.04	31	92.16	0.20(57)
PLS-3 at 18 month	31	89.65	37	89.19	0.13(66)
PLS-3 at 24 month	29	91.45	31	89.29	0.62(58)
VABS at 18 month	34	86.53	39	88.18	-0.74(71)
VABS at 24 month	30	87.17	33	84.12	1.32(61)

# $p < .10$.

* $p < .05$.

** $p < .01$.

*** $p < .001$.