Childhood Neglect and Cognitive Development in Extremely Low Birth Weight Infants: A Prospective Study

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ABSTRACT. ***Objective.*** **To examine the relationship between child maltreatment and cognitive development in extremely low birth weight infants, adjusting for perinatal and parental risk factors.**

Methods. **A total of 352 infants with birth weight of <1000 g were followed prospectively for 4 years. The data were analyzed with regard to perinatal and parental risk factors and referrals for suspected child maltreatment to government agencies. Perinatal risk factors included birth weight, gestation, gender, periventricular hemorrhage, ventricular dilation, home oxygen requirement, and necrotizing enterocolitis. Parental risk factors included maternal age, race, marital status, education, and hospital insurance status. Cognitive *z* scores were calculated at 1, 2, and 4 years, and head circumference *z* scores were calculated at birth, 2 years, and 4 years.**

Results. **Fifteen percent of infants were referred to child protective services for suspected child maltreatment. The adjusted general cognitive index at 4 years was significantly reduced in infants who were referred for neglect (−17.6; 95% confidence interval: −3.3, −31.9). Infants whose neglect was substantiated had a progressive decline in their cognitive function over time (cognitive *z* scores: −0.97, −1.37, and −2.05 standard deviations at 1, 2, and 4 years, respectively), compared with nonneglected infants (*z* scores: −0.04 to −0.36). They had a significantly smaller head circumference at 2 and 4 years but not at birth (adjusted *z* score at 4 years: −0.812; 95% confidence interval: −0.167, −1.458). Perinatal risk factors and physical disability were not related to maltreatment referral; only parental factors were independent predictors.**

Conclusions. **Childhood neglect is associated significantly with delayed cognitive development and head growth. Addressing risk factors antenatally and in early childhood may improve outcomes. *Pediatrics* 2001;108: 142–151; *child abuse, neglect, infant, extremely low birth weight, child development, cognition, developmental biology.***

ABBREVIATIONS. NEC, necrotizing enterocolitis; SGA, small for gestational age; SES, socioeconomic status; ELBW, extremely low birth weight; SD, standard deviation; FYCCQ, Families, Youth and Community Care Queensland; GQ, general quotient; GCI, general cognitive index; Adj OR, adjusted odds ratio; CI, confidence interval.

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There are many potential risk factors associated with cognitive delay in extremely preterm infants. These include perinatal factors such as periventricular hemorrhage, ventricular dilation,[1] periventricular leukomalacia,[2] chronic neonatal lung disease, necrotizing enterocolitis (NEC), male gender,[1] and being small for gestational age (SGA).[3] However, during recent years there has also been recognition of the association between sociodemographic factors—such as poverty, low maternal education, and single parenthood—and the cognitive development of preterm infants.[4,5]

This has led to the question of how sociodemographic variables actually influence cognitive development. A recent report of the National Research Council and Institute of Medicine of the National Academies[6] provided extensive evidence that childhood experience has a substantial impact on brain development. Child abuse and neglect—including a deprived learning environment and physical or emotional neglect or abuse—often coexist with many of these sociodemographic factors,[7] potentially confounding their association with cognitive outcomes.

More than a decade ago, Leonard et al[8] demonstrated that among very low birth weight infants who were followed to 4.5 years of age, a referral to child protective services was more significant in predicting cognitive outcome than severe intraventricular hemorrhage, chronic neonatal lung disease, or low socioeconomic status (SES). Despite this finding, few, if any, subsequent studies have included child maltreatment as a potential outcome predictor, and these results have not been replicated in other high-risk infant groups. Although Leonard's study identified child maltreatment as an important direct risk factor, it did not adjust for other potential confounders, such as ventricular dilation, NEC, maternal age, or marital status. The potential impact of different types of maltreatment, such as childhood neglect, also was not assessed.

In a review of the past decade, Kaplan et al[9] reported that child maltreatment was consistently associated with impaired cognitive ability within a childhood population. A recent population-based study showed a strong association between cognitive disability and maltreatment, including neglect, although the direction of association could not be determined.[10] The role of disability, as either a maltreatment risk factor or an outcome, is still unclear.

Although higher rates of child abuse and neglect have been reported among preterm infants,[7] no prospective studies within this group have evaluated potential risk factors. Although one study described the antecedents of abuse and neglect among neonatal intensive care graduates,[11] the mean birth weight and gestation was significantly lower in the referred group. The question of the relative contribution of perinatal and parental risk factors to the subsequent maltreatment of preterm infants has not been addressed adequately in the literature. The answer to this question is important in formulating effective intervention strategies.

The purpose of this study was to examine potential risk factors and cognitive outcomes associated with child maltreatment, within a highly vulnerable infant group—those born with extremely low birth weight (ELBW; <1000 g). With a large prospective cohort of ELBW infants, we were able to adjust for potential confounding perinatal and parental variables while measuring associated cognitive changes over time. It was hypothesized that among ELBW infants, parental risk factors—rather than perinatal factors—would predict subsequent maltreatment and that child maltreatment would be associated independently with cognitive delay.

METHODS

Patients

The study cohort consisted of 353 infants who were born at <1000 g and admitted to the Mater Mothers' Hospital, Brisbane, Australia, between 1983 and 1993 inclusive, and survived to at least 4 months' corrected age. One child with Down's syndrome was excluded. At 4 years of age, 269 (76%) of these children were cognitively assessed at the Growth and Development Research Unit of the Mater Children's Hospital (mean corrected age: 4.19 years; standard deviation [SD]: 0.57). Of the total study cohort, 314 children (89%) also had been assessed at 12 months of age and 336 (93%) had been assessed at 2 years. A comparison of those who had been cognitively assessed at 4 years with those who had not been assessed is presented in Table 1.

TABLE 1. Comparison of Cases Assessed With GCI at 4 Years and Those Not Assessed

Parameter	Cases With 4-Year GCI (n = 269)	Cases Without 4-Year GCI (n = 83)	P Value
Griffiths general quotient			
1 y (mean ± SD)	100 ± 11.6	93 ± 12.8	<.001
	(n = 257)	(n = 57)	
2 y (mean ± SD)	96 ± 12.7	90 ± 18.1	<.001
	(n = 261)	(n = 65)	
Physical disability at 2 y			
Cerebral palsy or bilateral blindness or deafness	20 (8%)	10 (15%)	.058
	(n = 262)	(n = 66)	
Perinatal risk factors			
Birth weight (g ± SD)	830 ± 123	849 ± 100	.20
Male gender	110 (41%)	43 (52%)	.08
Gestation (wk ± SD)	7.1 ± 2.1	27.0 ± 2.1	.86
SGA	50 (19%)	13 (16%)	.54
Multiple birth	67 (25%)	23 (28%)	.61
Home oxygen	43 (16%)	16 (19%)	.48
Periventricular hemorrhage (grade 3–4)	8 (3%)	11 (13%)	<.001
Ventricular dilation	12 (5%)	16 (19%)	<.001
NEC	16 (6%)	3 (4%)	.40
Retinopathy of prematurity	28 (48%)	40 (48%)	.92
Parental risk factors			
Maternal age			
16–21 y	22 (8%)	14 (17%)	
>21 y	247 (92%)	69 (83%)	.022
Marital status			
Married	216 (80%)	55 (66%)	
Cohabitating couple	29 (11%)	18 (22%)	
Single	24 (9%)	10 (12%)	.019
Maternal education*			
High school incomplete	120 (45%)	49 (60%)	
High school complete	69 (26%)	23 (28%)	
Posthigh school	79 (30%)	10 (12%)	.005
Hospital status (public)	175 (65%)	58 (70%)	.42
Maternal race			
White	250 (93%)	74 (89%)	
Aboriginal	6 (2%)	5 (6%)	
Asian/other	13 (5%)	4 (5%)	.22
Referral for child maltreatment			
All referrals	32 (12%)	20 (24%)	.006
Substantiated referrals	21 (8%)	10 (12%)	.23
Physical abuse referrals†	15 (6%)	10 (12%)	.045
Emotional abuse referrals	22 (8%)	11 (13%)	.17
Neglect referrals	21 (8%)	12 (15%)	.07

* Data missing in 2 cases. Percentages rounded.
† Not statistically significant when including only substantiated cases.

Perinatal Risk Factors

Ten perinatal risk factors, for which data were available consistently, were identified as being predictive of cognitive outcomes from a review of the literature.[1,3,8,12–14] They were assessed prospectively in relation to cognitive development, as well as maltreatment referral. These included birth weight, gestation, SGA status, gender, multiple births, the requirement for home oxygen, grade 3 to 4 periventricular hemorrhage, moderate to severe ventricular dilation, NEC (equivalent to modified Bell's staging IIA or higher[15]), and retinopathy of prematurity (any stage, as identified by an ophthalmologist). SGA was defined as birth weight less than the third percentile for gestation on standardized growth charts.[16] Periventricular hemorrhage was measured as grade 0 (nil), grade 1 (subependymal hemorrhage), grade 2 (hemorrhage filling $<$50% of ventricle), grade 3 (hemorrhage filling $>$50% of ventricle), and grade 4 (hemorrhage with parenchymal involvement).[17] Ventricular dilation was classified as nil, mild, moderate, or severe, as described previously.[17]

Apgar scores also were recorded at 1 and 5 minutes. Assessments of periventricular leukomalacia and sepsis were not included in the analysis because of incomplete data collection.

Parental Risk Factors

Identified parental risk factors included maternal age, race, marital status (married, cohabiting couple, or single ["single" included all divorced, separated, widowed, or never-married mothers]), maternal education, and hospital insurance status.[4,5,18] In Australia, public hospital care is readily available; only 48% of the population had private hospital insurance at the time of this study.[19] Maternal racial origins were classified as white, Australian aboriginal, Asian, or other. These factors also were assessed in relation to cognitive outcomes and the risk of maltreatment referral.

Referral for Child Maltreatment

Referrals for suspected child abuse or neglect between 1983 and July 1999 were obtained from the government agency, Families, Youth and Community Care Queensland (FYCCQ), and from interstate registries and overseas, where indicated. This included the date of referral, whether the referral was substantiated on subsequent investigation, and the type of maltreatment referred or substantiated (physical, emotional, sexual, and neglect). Although medical practitioners are the only mandatory reporters by law in Queensland, referrals may be received from any member of the public, after being screened by FYCCQ workers.

Substantiated referrals included cases in which, after departmental investigation, there was "reasonable cause to believe that the child had been, was being, or was likely to be abused or neglected."[20] Although these referrals were more likely to represent the more significant cases—with confirmatory evidence available—this study considered any referral to indicate a degree of risk. All referrals were used in regression analyses. Physical abuse was defined as any nonaccidental physical injury inflicted by a person who had care of the child. The definition of emotional abuse included any act resulting in a child's suffering any kind of emotional deprivation or trauma. Childhood neglect was defined as a "failure to provide conditions that were essential for the healthy physical and emotional development of a child." Finally, the definition of sexual abuse included exposing a child to or involving a child in inappropriate sexual activities.[20] Referrals that occurred before the time of the 4-year cognitive assessment were distinguished from all recorded referrals, to ensure that infants who had been born earlier in the study were not subject to reporting bias.

Confidentiality was maintained with the use of a confidential identification number. Names and dates of birth along with the confidential number were sent directly to FYCCQ, who then linked referral data to the number only, returning this data to the researchers directly. Researchers then obtained anonymous child and maternal data to link to the referral records. Thus, researchers and Growth and Development Research Unit staff had no information to link referrals to particular infants. Ethical approval was obtained from both the Mater Mothers' and Mater Children's Hospitals Research Ethics Committees.

Outcome Measures

Surviving ELBW infants were followed at the multidisciplinary Growth and Development Research Unit of the Mater Children's Hospital, where they were medically assessed and seen by a developmental psychologist. The psychologist assessed cognitive development using the Griffiths general quotient[21] (GQ; mean: 100; SD: 12) at 1- and 2-year visits and the McCarthy general cognitive index[22] (GCI; mean: 100; SD: 15) at 4 years, with *z* scores calculated to compare scores across time. "Borderline intellectual disability" was defined as IQ from -1 to -2 SD below the mean, and "intellectual disability" was defined as IQ below 2 SD. Medical assessment included the recording of clinical data by a pediatrician, as well as plotting height, weight, and head circumference on standardized growth charts at birth, 2 years, and 4 years of age. Standardized *z* scores, independent of gestation and corrected age, were calculated on the basis of the 1990 British growth data.[16] Assessment of physical disability was completed by pediatricians in consultation with physical therapists, ophthalmologists, and audiologists, as relevant. A diagnosis of cerebral palsy included diplegia, spastic hemiplegia, quadriplegia, or other related forms of motor dysfunction. All study infants had hearing assessed by brainstem evoked response before discharge and by behavioral response and tympanometry at 8 to 12 months. Deafness was defined as sensorineural hearing impairment requiring amplification. Vision was assessed by an ophthalmologist, with blindness defined as absent or minimal light perception in both eyes at last assessment.

Statistical Analysis

The χ^2 test was used to compare differences in categorical variables and analysis of variance for differences in mean scores. Multiple linear regression analysis was used to determine the independent predictors of GCI and head circumference. Logistic regression analysis was used to assess the independent predictors of referral for child maltreatment. A 2-tailed P value $<.05$ was considered significant. Statistics were performed using SPSS for Windows (Release 9.0; SPSS Inc, Chicago, IL).

RESULTS

Fifty-two (15%) of the 352 ELBW children were referred to child protective services for suspected child maltreatment; 32 children (9%) were referred before the 4-year assessment. Fifty percent of these 32 infants were referred before the age of 5.5 months (median corrected age: 7.6 months; interquartile range: 0.4, 30.0 months).

Twenty-seven (52%) of the 52 referred children were reported on $>$1 occasion, often with $>$1 type of maltreatment reported on each occasion. Thirty-one children (60% of those referred) had 1 or more substantiated report, including 19 children (37%) with substantiated neglect. Overall, 167 maltreatment reports were received on 117 occasions, of which 80 (48%) were substantiated. Neglect was the most frequently reported type of maltreatment ($N = 71$), followed by emotional abuse ($N = 51$), physical abuse ($N = 39$), and sexual abuse ($N = 6$). The impact of sexual abuse was not evaluated because of insufficient numbers. Both neglect and emotional abuse were seen in 22 children (42% of referred children), neglect and physical abuse were seen in 14 children (27% of referred children), and neglect and physical and emotional abuse were seen in 13 children (25% of referred children).

Of the 352 study infants, 269 (76%) were cognitively assessed at 4 years of age, including 32 (62%) of the 52 referred infants (Table 1). Of the 83 children without cognitive scores, just more than half were lost to follow-up ($N = 43$); almost one third of these families subsequently were reported for suspected child maltreatment (ie, 14 referred children). However, 27 of the remaining children attended the clinic appointment but were unable to be cognitively assessed because of disability ($N = 13$; none referred), behavior problems ($N = 12$; 4 referred), or being from a non–English-speaking family ($N = 2$; none referred). In addition, 1 child had died at 2 years of age (with no reports recorded), 4 had moved interstate (1 referred), and 8 were assessed at a later age with the use of other psychometric tests (1 referred). Of the 13 infants who could not be assessed because of disability, 10 had had ventricular dilation and 12 had cerebral palsy, bilateral blindness, or deafness, as determined at age 4.

Those who were not assessed at 4 years were more likely to have had lower intelligence scores on previous assessments and to have been born to young, unmarried, poorly educated mothers who were more often reported for child maltreatment. They also were more likely to have had periventricular hemorrhage and dilation and physical disability at 2 years (Table 1). Ten of the 16 infants who had moderate to severe ventricular dilation and who were not assessed had cerebral palsy, bilateral blindness, or deafness identified at 4 years, precluding their cognitive testing. All of the infants who had grade 3 to 4 periventricular hemorrhage and who were not assessed also had ventricular dilation. However, none of these medical factors was associated with a significant increase in the rate of referral (Table 2) or of referral for neglect.

Parental risk factors were far more likely to predict referral for child maltreatment than perinatal factors; only NEC and retinopathy of prematurity reached statistical significance. Physical disability at 2 years was not predictive of referral at any time. On univariate analysis, all parental risk factors were associated strongly with maltreatment referral (Table 2). The same factors also were significant in predicting referral for neglect.

To determine the independent contribution of risk factors on maltreatment referral, we included parental and significant perinatal risk factors simultaneously in a logistic regression model. Although aboriginal race was associated strongly with referral (with 82% of aboriginal families referred), because of small numbers and a strong association with other parental variables, these cases were excluded from the analysis. After adjustment for other potential confounding variables, the association between maltreatment referral and the perinatal risk factors became nonsignificant, as did maternal age, single marital status, and maternal education. The only independent predictors of referral among ELBW infants were public hospital status (adjusted odds ratio [adj OR]: 3.5; 95% confidence interval [CI]: 1.1, 10.6) and unmarried cohabitation (adj OR: 3.3; 95% CI: 1.4, 7.7). None of the factors included in the model was associated independently with referral for neglect.

In examining the perinatal predictors of GCI outcome, child maltreatment and parental risk factors were more strongly associated with cognitive delay than were perinatal factors. The only perinatal factors that were associated significantly with lowered

TABLE 2. Potential Risk Factors for Child Abuse and Neglect Referrals

Risk Factor	Cases Not Referred ($n = 300$)	Cases Referred ($n = 52$)	P Value
Physical disability at 2 y			
Cerebral palsy or bilateral blindness or deafness	27 (10%) ($n = 284$)	3 (7%) ($n = 44$)	.57
Perinatal risk factors			
Birth weight (g ± SD)	834 ± 121	842 ± 98	.63
Male gender	127 (42%)	26 (50%)	.30
Gestation (wk ± SD)	27.0 ± 2.1	27.1 ± 2.0	.86
SGA	56 (19%)	7 (14%)	.37
Multiple birth	77 (26%)	13 (25%)	.92
Home oxygen	48 (16%)	11 (21%)	.36
Periventricular hemorrhage (grade 3–4)	16 (5%)	3 (6%)	.90
Ventricular dilation	24 (8%)	4 (8%)	.94
NEC	13 (4%)	6 (12%)	.034
Retinopathy of prematurity	136 (45%)	32 (62%)	.031
Parental risk factors			
Maternal age			
16–21 y	24 (8%)	12 (23%)	
>21 y	276 (92%)	40 (77%)	.001
Marital status			
Married	248 (83%)	23 (44%)	
Cohabitating couple	30 (10%)	17 (33%)	
Single	22 (7%)	12 (23%)	<.001
Maternal education*			
High school incomplete	131 (44%)	38 (75%)	
High school complete	84 (28%)	8 (16%)	
Posthigh school	84 (28%)	5 (10%)	<.001
Hospital status (public)	185 (62%)	48 (92%)	<.001
Maternal race			
White	283 (94%)	41 (79%)	
Aboriginal	2 (1%)	9 (17%)	
Asian/other	15 (5%)	2 (4%)	<.001

* Data missing in 2 cases. Percentages rounded.

TABLE 3. Parental Risk Factors and Child GCI at 4 Years

Risk Factor	Number (n = 269)	GCI	P Value
Maternal age			
16–21 y	22	81	
>21 y	247	98	<.001
Marital status			
Married	216	98	
Cohabitating couple	29	93	
Single	24	84	<.001
Maternal education*			
High school incomplete	120	92	
High school complete	69	98	
Posthigh school	79	102	.003
Hospital status			
Private	94	102	
Public	175	93	<.001
Maternal race			
White	250	97	
Aboriginal	6	72	
Asian/other	13	87	<.001

* Data missing in 1 case.

scores were male gender (male: 93; female: 99; P = .013) and ventricular dilation (GCI: 86 vs 97; P = .037). However, all parental variables were highly predictive of reduced GCI (Table 3). Similarly, all categories of child maltreatment referral, except substantiated physical abuse, were associated strongly with cognitive delay (Table 4); the most pronounced differences were seen in cases of substantiated neglect (GCI: 98 vs 69 in maltreated infants; $P < .001$).

To control for possible confounding, we used a multiple linear regression model with GCI at 4 years as the dependent variable. Perinatal and parental

TABLE 4. Referral for Child Maltreatment and Child GCI at 4 Years

Parameter	Number (n = 269)	GCI	P Value
All referrals			
No	237	98	
Yes	32	83	<.001
All referrals (before assessment)			
No	248	98	
Yes	21	82	<.001
All substantiated referrals			
No	248	98	
Yes	21	82	<.001
Substantiated referrals (before assessment)			
No	254	97	
Yes	15	83	.003
Physical abuse referrals*			
No	254	97	
Yes	15	83	.004
Emotional abuse referrals†			
No	247	98	
Yes	22	81	<.001
Neglect referrals†			
No	248	98	
Yes	21	77	<.001

* Not statistically significant when including only substantiated cases (P = .2).
† Similar statistical significance when including only substantiated cases or those referred before 4-year assessment.

risk factors were entered simultaneously in the model, together with a single variable for all child maltreatment referrals (adjusted R^2: 0.18; $F = 4.7$ [df 16, 251]; $P < .001$). As 5 of the 11 aboriginal mothers were lost to follow-up (of whom 4 were reported), aboriginal cases were excluded from the regression analysis. The only significant independent perinatal risk factors were low birth weight (<750 g) and male gender (Fig 1). Of the parental factors, limited maternal education, public hospital status, and referral for any form of child maltreatment also were associated significantly with cognitive delay (Fig 2).

The most dramatic results were seen after adjustment for the 3 individual maltreatment subtypes (physical abuse, emotional abuse, and neglect). Factors that were found to be significant in the previous model (ie, male gender, birth weight, incomplete high school education, and public hospital status) were added to the regression model. Sexual abuse cases and aboriginal families were excluded, again because of limited numbers. After adjustment for confounding variables, neglect was found to be the only maltreatment subtype that was associated independently with cognitive delay, with a difference of −17.6 GCI points (Fig 3; adjusted R^2: 0.15; $F = 7.67$ [df 7, 249]; $P < .001$). In addition, the association between cognitive outcome and hospital insurance status was no longer statistically significant.

Cognitive assessments were evaluated from 12 months and 2 years of age with the use of the GQ. This showed a progressive decline in the mean cognitive z score in infants who were referred for neglect, reaching the level of "intellectual disability" in the substantiated group. However, IQ levels in infants who were not referred for neglect remained relatively constant (Fig 4). All differences between referred and nonreferred groups were statistically significant. This remained true after inclusion of only cases that were referred before the 4-year assessment. A similar decline also was seen in neglected infants after adjustment for perinatal and parental risk factors (as previously described in Fig 3; adjusted z scores: −0.16, −0.34, and −1.01 at 1, 2, and 4 years, respectively), in all referred cases (cognitive z scores: −0.42, −0.83, and −1.13), and in substantiated cases (cognitive z scores −0.58, −1.00, and −1.20).

Infants whose neglect was substantiated also had a significantly smaller head circumference at 2 and 4 years, after adjustment for birth weight of <750 g, SGA, ventricular dilation, Apgar score ≤5 at 5 minutes, and cerebral palsy at 2 or 4 years, respectively (adjusted R^2: 0.146; $F = 9.36$ [df 6, 288]; $P < .001$ at 4 years). This was despite having similar measurements at birth to those not referred for neglect (adjusting for factors above, except cerebral palsy; Fig 5). Other types of child maltreatment, including physical abuse, were not associated with a reduced head circumference at 4 years. There also was no significant association between neglect and infant weight or height at 2 or 4 years, even after adjustment for factors that were significant on univariate analysis (including birth weight of <750 g, gender, SGA, cerebral palsy, and multiple births).

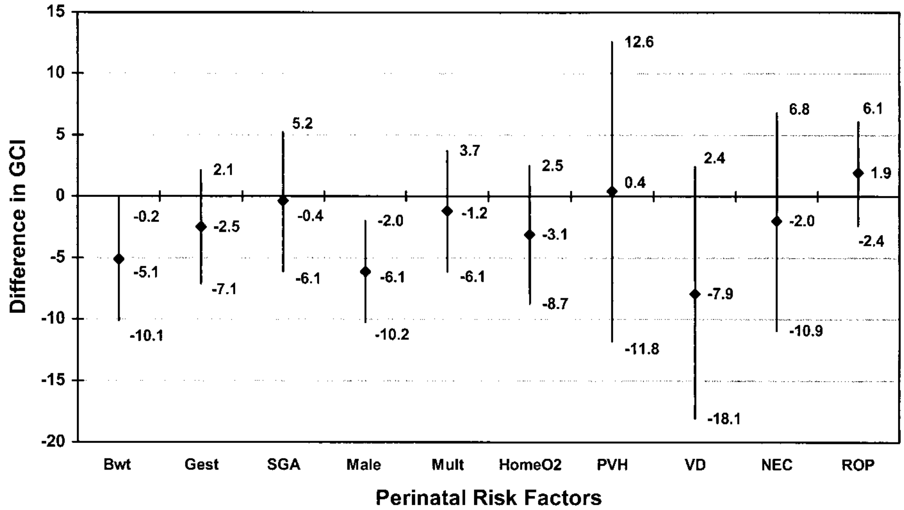

Fig 1. Comparison of adjusted GCI scores at 4 years of age, in relation to perinatal risk factors. Multiple linear regression performed, adjusting for all variables described below, plus male gender, NEC, maternal age, marital status, education, hospital insurance status, and all referrals for child maltreatment. Error bars represent 95% confidence intervals. Bwt, birth weight <750 g; Gest, gestational age <27 weeks; SGA (less than the third percentile); Mult, multiple births; $HomeO_2$, home oxygen supplied; PVH, grade 3 or 4 periventricular hemorrhage; VD, moderate to severe ventricular dilation; ROP, retinopathy of prematurity.

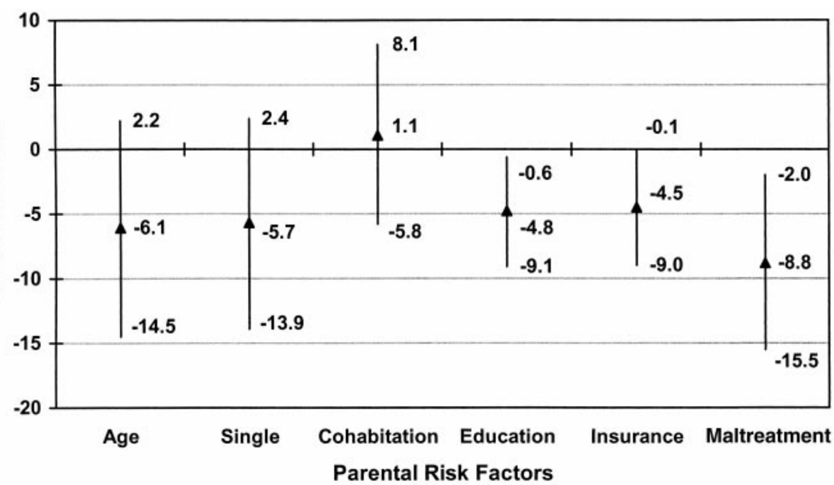

Fig 2. Comparison of adjusted GCI scores at 4 years of age, in relation to parental risk factors and referral for child maltreatment. Multiple linear regression performed, adjusting for all variables described below plus single marital status, unmarried cohabitation, birth weight <750 g, gestational age <27 weeks, SGA, requirement for home oxygen, grade 3 or 4 PVH, moderate to severe VD, and NEC. Error bars represent 95% CI. Age, maternal age 16–21 years; education, incomplete high school; insurance, no private hospital insurance; maltreatment, all referrals for maltreatment.

DISCUSSION

In assessing the relative impact of perinatal and parental variables on an ELBW infant's cognitive development, it is evident that both play an important role. However, this study also has shown that childhood neglect is a highly significant independent factor, associated with lower intellectual abilities and reduced head circumference.

Although physical disability is the most visible adverse outcome of extreme prematurity, cognitive delay is by far the most common.[23] In matching school kindergarten records with statewide birth records, Resnick et al[18] found that whereas perinatal factors were most predictive of severe disability, sociodemographic factors most strongly correlated with cognitive delay, including learning disability, emotional disability, and academic problems. The authors concluded, after considering differences in prevalence, that the impact of sociodemographic factors on 5-year educational outcomes was more than 10 times that of very low birth weight (<1500 g).

Predictors of Cognitive Delay

After adjustment for social risk, the only 2 perinatal factors that remained significantly associated with cognitive delay were low birth weight (<750 g) and male gender. Other studies also have shown that long-term cognitive delay is associated significantly with birth weight of <750 g[23,24] and male gender.[25] Ventricular dilation also has been shown to predict intellectual impairment.[1,13] Although our study demonstrated this association on univariate analysis, it was not significant after adjustment for potential confounding variables. However, more than 60% of the neonates who had ventricular dilation and who were not cognitively assessed at 4 years had cerebral palsy, blindness, or deafness, which precluded testing. It is highly likely that ventricular dilation is, in fact, a true predictor of cognitive delay.

Numerous studies[5,18,24,26] also have shown an association between cognitive delay in preterm infants and sociodemographic variables, including SES, low maternal education, single marital status, and nonwhite race—all of which were significant on univariate analysis in our study. However, after adjustment for childhood neglect and other significant factors, maternal education was the only independently significant parental risk factor. Numbers were insufficient to analyze further the observed association with aboriginal race, although this issue requires further

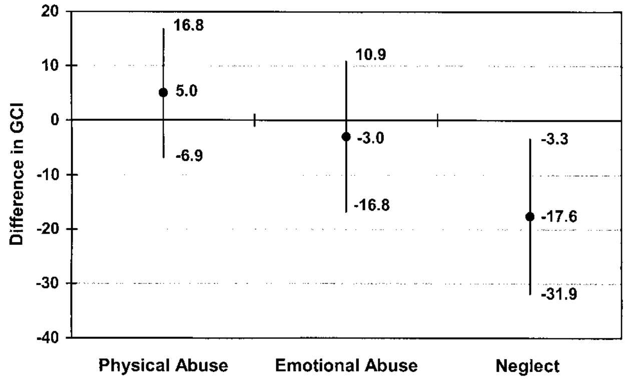

Fig 3. Comparison of adjusted GCI scores at 4 years of age, in relation to maltreatment subtypes. Multiple linear regression performed, adjusting for differing types of maltreatment, birth weight <750 g, male gender, incomplete high school education, and public hospital status (factors found to be significant in initial linear regression analysis). Error bars represent 95% CI.

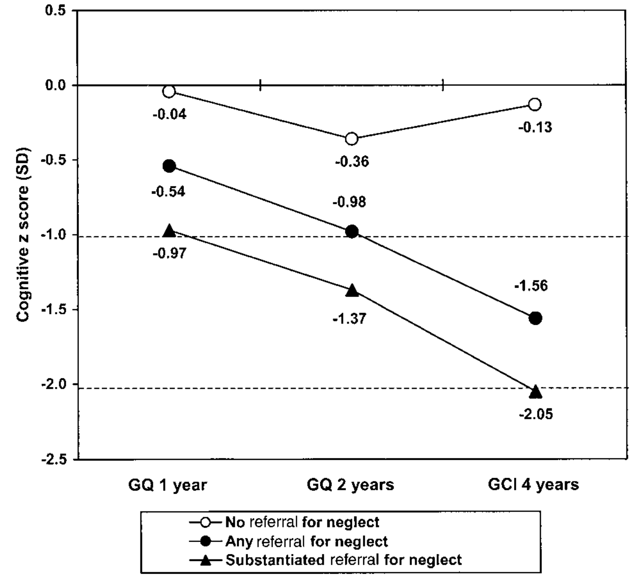

Fig 4. Comparison of cognitive z scores at 1, 2, and 4 years in infants who were referred for neglect or substantiated neglect versus those who were not referred for neglect. Dotted lines represent upper limits of "borderline intellectual disability" (−1.0 SD) and "intellectual disability" (−2.0 SD). Numbers of cases: No neglect referrals: 287, 295, and 248 at 1, 2, and 4 years, respectively; any neglect referrals: 27, 31, and 21 at 1, 2, and 4 years; substantiated neglect referrals: 16, 18, and 13 at 1, 2, and 4 years.

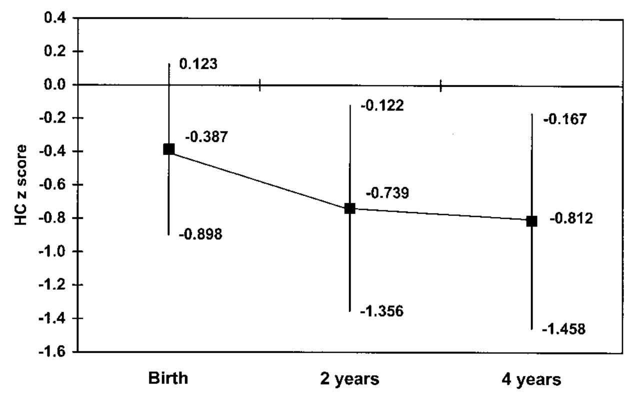

Fig 5. Comparison of adjusted head circumference z scores in infants whose neglect was substantiated: at birth, 2 years, and 4 years of age. Multiple linear regression performed, adjusting for birth weight of <750 g, SGA, Apgar score ≤5 at 5 minutes, VD, and cerebral palsy at 2 or 4 years, respectively. Error bars represent 95% CI. HC, head circumference.

investigation. Public hospital status, a broad marker of SES, was marginally below the specified level of significance.

Escalona,[26] in prospectively following a neonatal intensive care population and adjusting for SES, suggested that environmental deficits and stressors might impair early cognitive development, particularly in preterm infants. Although that study used a standardized measure of SES that was not incorporated into our study, the potential for child maltreatment was not considered. Although Leonard et al[8] found low SES to be associated with lowered cognitive outcomes, the individuals in the subgroup that was not referred for abuse were more likely to score within the normal range. Providing financial resources without recognizing issues related to child maltreatment is unlikely to have a significant impact on the problem of resource utilization, as observed elsewhere.[27]

Because families that are at social risk also are at increased risk of child maltreatment,[7] sociodemographic factors may be surrogate measures for the quality of parent–child interaction. As reviewed by Zeanah et al,[28] poverty and socioeconomic disadvantage may be associated with fewer resources, affecting nutrition, shelter, and health. Maternal education may have an impact on the mother's problem-solving abilities, material resources, or understanding of normal developmental milestones, which in turn may have an impact on the parent–child relationship. As Kalmar and Boronkai[29] demonstrated, intellectual stimulation of both preterm and term infants is associated significantly with IQ outcomes, and this persists after adjustment for other biological factors over time.

In effect, the parental risk factors may represent inadequacies in the parents' abilities to provide the physical and emotional resources required for a child's optimal development—a less identifiable but significant form of "neglect." Other studies that have measured home environment factors directly in preterm infants also have shown a significant relationship with cognitive development.[24,30,31] "Referral for child maltreatment" is an even more specific—although probably much less sensitive—marker of adverse parent–child interaction. The main disadvantage is its potential to underestimate prevalence vastly. Without a non-ELBW infant control group, however, the present study could not determine whether the parental factors measured were specific to this ELBW population or were applicable to other high-risk infants.

Another limitation of this study was that it did not examine child protective interventions, such as the provision of additional family support or out-of-home care, which may have affected cognitive outcomes. However, a majority of studies—but not all[32]—have shown improved long-term cognitive outcomes in children who receive intervention.[33–35] Without such intervention, one would expect the cognitive differences between referred and nonreferred infants to be even more pronounced.

Predictors of Maltreatment Referral

The present study also demonstrated that parental risk factors are more significant than perinatal factors in predicting which ELBW infants are at risk for being maltreated. Although disability in general has been implicated as a risk factor for child maltreatment,[10] in our study, physical disability—defined as cerebral palsy, blindness, or deafness—was not associated with a higher rate of referral. Although Sullivan and Knutson's work[10] showed that referral rates of children with physical disabilities were higher than the control population without disabilities, the rates of maltreatment were still lower than for children with cognitive-based or behavioral disabilities. With more than 80% of their study population representing children with cognitive or behavioral disability, it is possible that many cases of disability may represent an outcome of rather than a risk factor for child maltreatment. This question deserves further study.

Socioeconomic variables also have been implicated commonly as risk factors for child maltreatment.[11] Unmarried cohabitation, however, rarely has been examined; most studies have failed to distinguish this family type from married or single status. One other study demonstrated a higher relative risk for abuse in cohabiting couples compared with married or single parents, although preterm infants specifically were not examined.[36] Although the mechanisms behind this finding are uncertain, it may be related to relationship instability or characteristics of the perpetrator of abuse. More specific risk factors for child abuse and neglect, such as family violence, drug addiction, and maternal depression,[7] were not assessed. Although our data are useful in formulating intervention strategies, the findings cannot be extrapolated to the general birth population without a term infant control group.

Neglect, Cognition, and Head Growth

In seeking to understand how childhood neglect may be associated with head growth, neuroscience research provides valuable insight. During fetal development and early childhood, brain growth is regulated by genes but is critically influenced by sensory stimulation and experience. Neuronal connections are formed and modified by repetitive, patterned stimulation of the neural system in a "use-dependent" manner.[37] Forty years of animal research has demonstrated unequivocally the anatomic plasticity of the brain in response to sensory stimulation or, conversely, to deprivation. Animals that are reared in stimulus-deprived environments tend to have a reduced cerebral weight and length and cortical depth. This finding correlates with a variety of histologic changes, including decreased neuron perikaryonal and nuclear size and dendritic branching and reduced numbers of neuroglia and synaptic connections, as reviewed by Walsh[38] and Glaser.[39]

More recent human studies have shown that a small head circumference in infancy is associated with cognitive delay in very low birth weight [40,41] and ELBW[42] infants. In addition, the English and Romanian Adoptees Study Team[43] demonstrated a 2-SD reduction in the mean head circumference of late-adopted Romanian orphans who had experienced profound emotional and physical neglect. However, in contrast to our study, the authors were unable to distinguish the effects of malnutrition on head growth from those of emotional or cognitive deprivation. The present study demonstrated that a reduced head circumference and cognitive delay both are associated with childhood neglect, independent of other growth parameters, and that this association seems to become more pronounced over time and with severity of exposure (see Figs 4 and 5). Although our study did not distinguish differing types of neglect, other researchers have suggested that global sensory deprivation is more strongly correlated with head size than "chaotic" neglect.[44] Distinguishing subtypes of neglect would be useful in future research.

Using anatomic magnetic resonance imaging, De Bellis et al[45] observed significant differences in the cerebral volumes of maltreated children compared with matched controls. They postulated that this could be related to elevated catecholamine and cortisol levels often found in traumatized children[46,47] or to early sensory deprivation, both of which may result in altered neuronal differentiation and synaptic proliferation.

With these studies linking early childhood neglect, reduced head circumference, and cognitive delay, one possible causal pathway is proposed. However, without parental IQ or head circumference data, genetic factors cannot be excluded. It is conceivable that some ELBW children may have a genetic predisposition for slowing of head growth in early infancy, with associated cognitive delay. These children with developmental delay may then be more likely to come to the attention of child protection authorities.

Addressing Childhood Neglect

In 1994, the Advisory Board on Child Abuse and Neglect declared a "state of emergency" with respect to child maltreatment, because of the widening gap between the extent of the problem and resources allocated to address it.[48] The National Institutes of Health recently identified childhood neglect as a "serious public health, justice, social services, and education problem," with a paucity of research addressing the issue.[49]

Despite advances in neonatal intensive care technology, which result in increased survival,[50] extremely preterm infants remain at high risk for cognitive delay.[12,51] Our failure to recognize or address adequately the risk factors for abuse and neglect may be a contributory factor. As Rosenblatt observed, "The basic incongruity in . . . perinatal care lies in our superb ability to care for the individual patient and our dismal failure to address the problems of the larger society."[52]

One of the most promising means of addressing our "dismal failure" is through home visitation programs, focusing on parents of ELBW infants who are at the highest risk of maltreatment. Several programs have been shown to improve cognitive outcomes in preterm infants[34,53] as well as in infants with nonorganic failure to thrive, presumably related to neglect.[54] Another study[55] demonstrated that home visitation was associated with a significantly reduced incidence of child abuse and neglect. In contrast, a longitudinal study of preterm infants that focused more on center-based child intervention failed to demonstrate sustained long-term results.[56]

Although our study identified possible predictors and cognitive consequences of child maltreatment in ELBW infants, we now need to secure resources to intervene effectively. Only then can we hope to improve significantly the cognitive development—and overall quality of life—of this vulnerable infant group.

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STANDARDIZED TREATMENTS, GUIDELINES, PATHWAYS—HAVE ARRIVED

Five health plans that cover almost every resident of Minnesota will announce today that they are supporting standard treatment and prevention procedures for 50 common ailments like lower back pain, high blood pressure, diabetes, and bladder infections.

This is the first time all the major health plans in a state have collaborated to endorse a set of standard guidelines or protocols. Their support represents a major step toward the adoption of national "best practice" medical standards based on recognized scientific evidence.

The protocols, which will be continuously adjusted by panels of doctors as new medicines and procedures appear, are available on the Internet to consumers nationwide. The standards do not dictate how doctors must treat patients, but both patients and doctors will be aware of what the recommended treatments are.

The Minnesota health insurers are endorsing standards that have been developed by 21 physician groups that include 3200 doctors, 36% of all the physicians in the state.

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