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Social Variables Predict Gains in Cognitive Scores across the Preschool Years in Children with Birth Weights 500 to 1250 Grams

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Objective To determine the extent that social variables influence cognitive development of very low birth weight (VLBW) infants across the preschool years.

Study design Participants were VLBW (500-1250 g) children enrolled in the Caffeine for Apnea of Prematurity randomized trial between 1999 and 2004. We investigated the relationships between 4 potential social advantages: higher maternal education, higher paternal education, caregiver employment, and 2 biologic parents in the same home—and gain in cognitive scores. Cognitive assessments were performed at the corrected ages of 18 months (Mental Development Index score on the Bayley Scales of Infant Development II) and 5 years (Full Scale IQ on the Wechsler Preschool and Primary Scale of Intelligence III). Cognitive gain was computed by subtracting each individual 18-month Mental Development Index score from the corresponding Full Scale IQ at 5 years.

Results Data were available for 1347 children. Mean (SD) cognitive scores were 90.8 (15.7) at 18 months and 98.9 (14.5) at 5 years. Multivariable regression showed that higher maternal education, higher paternal education, and caregiver employment had independent and additive effects of similar size on cognitive gain ($P < .001$); the mean cognitive gain between 18 months and 5 years increased by 3.6 points in the presence of each of these advantages. When all 3 were present, cognitive scores improved on average by 10.9 points compared with children without any of these advantages.

Conclusion In VLBW children, a count of 3 social advantages strongly predicts gains in cognitive scores across the preschool years. *(J Pediatr 2015;166:870-6)*.

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Preterm birth is a leading cause of infant morbidity and mortality in industrialized countries.[1] Infants who are born very preterm (<32 weeks) or with very low birth weight (VLBW, <1500 g) are at greater risk of poor neurobehavioral outcomes.[2,3] The Caffeine for Apnea of Prematurity (CAP) trial is a large, international, randomized controlled trial of the safety and efficacy of neonatal caffeine therapy in children with birth weights of 500-1250 g.[4,5] The primary outcome was a composite of death, cerebral palsy, cognitive delay, deafness, or blindness at a corrected age of 18 months. Caffeine reduced the rates of this composite outcome and 2 of its components, cerebral palsy and cognitive delay. These treatment benefits were attenuated at a corrected age of 5 years, although secondary motor outcomes were still improved in children who had been assigned randomly to neonatal caffeine therapy.[6]

The frequency of cognitive scores less than 2 SDs below the mean in the CAP trial cohort was lower and the mean cognitive scores were greater at 5 years than at 18 months.[6] These cognitive scores were measured with different instruments

Bayley-III	Bayley Scales of Infant and Toddler Development, 3rd Edition
BSID-II	Bayley Scales of Infant Development II
CAP	Caffeine for Apnea of Prematurity
FSIQ	Full Scale IQ
MDI	Mental Development Index
VLBW	Very low birth weight
WPPSI-III	Wechsler Preschool and Primary Scale of Intelligence III

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but both are age-standardized to have a mean of 100 and SD of 15. However, not all children experienced the same degree of cognitive improvement. The relationship between cognitive gain at 5 years and Mental Development Index (MDI) scores at 18 months was linear but with a downward slope such that the greatest gains were seen in those who performed the worst at 18 months.[6] This observation may be partly due to the statistical phenomenon of "regression to the mean": by chance those who scored low at 18 months would be expected to score higher at 5 years, and vice versa. However, other factors may have influenced the magnitude of the observed changes in cognitive scores over time.

As a child grows, the environment plays a progressively larger role in cognitive development compared with the child's genetic make-up and early health problems. In the general population, social variables are positively associated with general intelligence[7-9] and with more specific cognitive domains such as language and executive function.[10-12] In relation to more distal social-environmental factors, parenting practices that provide for a stimulating home environment are associated with improved cognitive development.[13]

Social disadvantage is also a risk factor for poorer developmental outcomes in preterm infants.[14] Yet, the extent to which social variables affect the rate of change in cognitive development over the preschool years in preterm children has not been adequately described. Social variables that have been associated with cognitive development include maternal education, paternal education, and family income.[8,15-17] We undertook this study to examine the effect of social variables on cognitive gains and losses across the preschool years in this international cohort of VLBW infants.

Methods

Infants with birth weights of 500-1250 g were enrolled in the CAP trial between October 11, 1999, and October 22, 2004, and followed to a corrected age of 18 months.[4,5] All but 4 of the original 35 study centers performed further follow-up to a corrected age of 5 years. These 31 academic hospitals were located in Canada, Australia, Europe, and Israel and had enrolled 1932 (96.3%) of the 2006 CAP trial participants.[6] We have previously demonstrated the importance of correcting for prematurity at follow-up testing to avoid bias in cognitive test scores.[18,19]

The research ethics boards of the 31 study centers approved the original and the 5-year follow-up protocols. Written informed consents were obtained from a parent or guardian of each study participant at entry into the trial and before the 5-year follow-up assessments.

The MDI score on the Bayley Scales of Infant Development II (BSID-II) was our measure of cognitive development at 18 months.[20] Children who were too cognitively impaired to be tested were assigned an "imputed" score of 49, because 50 is the lowest MDI score on the BSID-II.

The Full Scale IQ (FSIQ) on the Wechsler Preschool and Primary Scale of Intelligence III (WPPSI-III) was the measure of general cognitive ability at age 5 years.[21] Children who were too cognitively impaired to be tested were assigned an "imputed" score of 39, because 40 is the lowest FSIQ on the WPPSI-III. A total of 44 children were tested with other standardized intelligence tests because a national version of the WPPSI-III was not available or because it was no longer appropriate for the age of the child at the time of the assessment.

Demographic data collection at both follow-up visits included the following information for maternal and paternal caregivers: their level of education, current employment status, relationship to the child, and whether both parents lived in the same home.

Statistical Analyses

Linear regression was used to investigate the relationships between prespecified social variables and the change in standardized cognitive scores between ages 18 months and 5 years. Because the cognitive scores of most—although not all—children improved during this period, we refer to this difference as "cognitive gain," defined as the WPPSI-III FSIQ minus the BSID-II MDI score. We excluded children who were not tested with the BSID-II at 18 months or with the WPPSI-III at 5 years and those who had imputed cognitive scores at either age. The 4 prespecified social advantage variables were: (1) higher maternal education (ie, started or completed college or university); (2) higher paternal education (ie, started or completed college or university); (3) parental employment (at least 1 employed or self-employed caregiver at both 18 months and 5 years); and (4) 2 biologic parents in the same home at 18 months and 5 years.

These social advantage variables were categorized as "present" (coded as 1) or "absent" (coded as 0). A small number of missing values (<1%) also were included as "absent." Because the dependent variable "cognitive gain" decreased with increasing values of the 18-month MDI, this score was included as an explanatory variable in all models.

The separate effect of each social advantage variable on cognitive gain was estimated by fitting a series of regression models (Models 1 to 4 in Table I) that contained the 18-month MDI score and an indicator variable for the presence or absence of the respective social advantage. This model incorporates a common linear trend of cognitive gain with MDI score but allows the position of the trend line to vary depending on the presence or absence of the social advantage being considered. An interaction term (the product of the social advantage variable and the MDI score) was included in a secondary analysis to explore the possibility that the social advantage variables may affect the slope of the relationship between cognitive gain at 5 years and MDI score at 18 months. The fitted regression coefficient associated with each social variable estimated the mean difference in cognitive gain between children with, as opposed to without, the social advantage. Statistical significance was derived from the ratio of this coefficient and its SE.

The presence or absence of the 4 social advantages may be correlated and thus their effects, analyzed separately, may overlap. To eliminate this potential overlap, the combined