Follow-up of Extremely Preterm Infants; the Long and the Short of It

Betty R. Vohr, MD

The study by Cheong et al,[1] "Changing neurodevelopment at 8 years of children born extremely preterm since the early 1990s" in this issue of *Pediatrics*, once again reminds us of the challenges and limitations of follow-up studies. The authors have done a commendable job following 3 cohorts (1991 to 1992, 1997, and 2005) of extremely preterm infants from 22 to 27 weeks' gestation to 8 years of age. Although the authors previously had shown that there was no improvement in moderate to severe disability at 8 years between 1991 to 1992 and 1997,[2] their report[3] of all 3 cohorts at 2 years of age identified a significant decrease in severe disability (15.4% to 3.7%) and severe developmental delay (14.8% to 3.7%) between 1997 and 2005 attributed to improvements in perinatal interventions. *The Bayley Scales of Infant and Toddler Development, Third Edition*,[4] however, which was first used with the 2005 cohort, is known to underestimate developmental delay. In addition, Bayley scores are not strong predictors of school-age outcomes.[5,6] The purpose of the current study was to additionally compare neurodevelopmental outcomes of the 3 cohorts at 8 years of age. The strengths of this report include the substantial sample size, comprehensive medical and social environmental data, comparison with term controls, blinded school-age assessments, and 8-year follow-up rates of 93%, 94%, and 86%.

The findings, as expected, were that preterm children had higher rates of disability and lower IQ and achievement scores than term controls at 8 years of age. The rates of disability and low IQ scores remained unchanged among preterm children across eras, whereas scores for academic achievement in reading, spelling, and mathematics were lower compared with previous cohorts. It is important to note that the Wide Range Achievement Test[7] at 8 years begins to tap into components of executive function (EF) skills used in reading and mathematics.[8] Very preterm children are known to have persisting deficits in EF.[9–14] Some of the lack of association between early Bayley scores and achievement tests at school age may well reflect the challenges that preterm children have with a spectrum of EF skills that emerge with increasing age. Preterm infants even without a history of brain hemorrhage or periventricular leukomalacia have alterations in brain microstructure and neural connectivity networks[15–18] that are associated with deficits in EF skills.

I have always been an optimist, however, when it comes to preterm infant long-term outcomes, and, in reviewing the study, I would like to note factors that may influence interpretation of the findings. First, mean test scores for preterm children were all in the average range. Second, analyses of preterm subgroups are helpful. In the Indomethacin Trial,[12,19,20] subgroups of very preterm children followed to ages 12 to 16 years attained vocabulary and block-design subtest scores that were similar to term controls. They also had clear evidence of EF deficits.[12] Children that caught up had lower rates of neurosensory impairment and mothers with higher education.[19] This finding suggests that preterm infants without

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a major neurosensory morbidity or social environmental disparities are those with the capacity to recover over time. In the Cheong et al study,[1] rates of low maternal education and lower social class were higher in the preterm groups during all eras. Although adjustments were made in the regressions for sociodemographic variables, in 2005, the preterm low social class rate was 3 times higher and the low maternal education rate was 2 times higher compared with controls.

Another finding was that the 2005 school-age children assessed were 1 year younger than the 1991 to 1992 cohort and 7 months younger than the 1997 cohort. Why might this be important? First, former preterm infants are more likely to require special services, repeat a grade, or start school later.[21,22] The Wide Range Achievement Test[7] can be scored by using either age or grade-level norms. With the age norms reported, a child is compared with peers that are his/her same age in 3-month increments (ie, 7 years, 0 months to 7 years, 3 months; 7 years, 4 months to 7 years, 7 months, etc). However, when using grade norms, a child is compared with peers in his/her same grade (fall or spring semester). A 7-year-old child in second grade whose reading and math skills are average is going to score higher than an 8-year-old child in second grade with the exact same skills with age norms. However, if second-grade norms are used for both children, their scores will be similar. It is unfair to compare the 7-year-old child who may be in the first or second grade to 7- or 8-year-old children who may be in third grade and have learned more advanced skills.

To summarize, this is an exceptional study that was difficult to conduct and provides some disconcerting data suggesting that there may be a plateauing of extremely preterm school-age cognitive and neurosensory outcomes and a deterioration of academic skills. It reminds us of the importance of school-age assessments and that there is much more to be learned about interventions, assessments, and environmental factors that impact on preterm school-age and adolescent outcomes. I remain optimistic.

ABBREVIATION

EF: executive function

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