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Original Article

Co-occurrence and Severity of Neurodevelopmental Burden (Cognitive Impairment, Cerebral Palsy, Autism Spectrum Disorder, and Epilepsy) at Age 10 Years in Children Born Extremely Preterm

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ABSTRACT

BACKGROUND: This study aims to determine the prevalence of neurodevelopmental impairments at age ten years among children born extremely preterm (less than 28 weeks gestational age) and to offer a framework for categorizing neurological limitations. **METHODS:** A multicenter, prospective cohort follow-up study recruited 889 ten-year-old children born from 2002 to 2004. We assessed prevalence of cognitive impairment, measured by intelligent quotient and tests of executive function, cerebral palsy (CP), autism spectrum disorder (ASD), and epilepsy singly and in combination. The three levels of impairment severity were: category I—no major neurodevelopmental impairment; category II—normal cognitive ability with CP, ASD, and/or epilepsy; and category III—children with cognitive impairment. **RESULTS:** A total 214 of 873 children (25%) had cognitive impairment, 93 of 849 children (11%) had CP, 61 of 857 children (7%) had ASD, and 66 of 888 children (7%) had epilepsy. Further, 19% of all children had one diagnosis, 10% had two diagnoses, and 3% had three diagnoses. Decreasing gestational age was associated with increasing number of impairments ($P < 0.001$). Half the children with cognitive impairment and one third of children with CP, ASD, or epilepsy had a single impairment. Six hundred one (68% [95% CI, 64.5%-70.7%]) children were in

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category I, 74 (8% [95% CI, 6.6%-10.3%]) were in category II, and 214 (24% [95% CI 21.7%-27.4%]) were in category III. **CONCLUSIONS:** Three quarters of children had normal intellect at age ten years; nearly 70% were free of neurodevelopmental impairment. Forty percent of children with impairments had multiple diagnoses.

Keywords: extremely preterm, neurological, follow-up, multiple disabilities

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Introduction

Over the past two decades, studies of children born extremely preterm (EP) have found that the prevalence of major adverse neurodevelopmental disorders ranges from 15% to 40% for deficient intelligent quotient (IQ),[1-7] from 5% to 18% for cerebral palsy (CP),[8-13] from 7% to 8% for autism spectrum disorder (ASD),[14,15] and from 2% to 10% for epilepsy.[16,17] Prevalence data such as these usually do not account for multiple disorders occurring in the same child. Yet, disorders of development occur together more often than expected by chance. For example, one third to half of children with CP have deficient IQ[18] but only 1%-3% of children in the general population without CP have deficient IQ.[19]

Children born EP are at particularly increased risk of having multiple neurodevelopmental disorders, including deficient IQ, impaired executive function (EF), CP, ASD, and epilepsy. In the Extremely Low Gestational Age Newborn (ELGAN) cohort, the prevalence of CP at age two years was 11%.[20] In the same cohort, at age ten years, the prevalence of IQ less than 70 was 15%,[1] cognitive impairment as assessed by a summary categorization of IQ and EF ability was 25%,[21] ASD was 7%,[22] and epilepsy was 7%.[22] Here we report the frequency with which these disorders occur in isolation and in combination.

Beyond whether children born EP have single or multiple impairments is the question of how to understand the severity of the neurological burden carried by the child. Most often, overall impairment is determined either by specific criteria for each neurological disorder or, less commonly, by assigning a composite descriptive designation based on a combination of findings.[3,6,7,23,24] Studies of EP cohorts born in the past 20 years largely using such combinations estimate rates for moderate to severe overall impairment ranging from 19% to 45%.[2,3,5-7,23,24] We propose a conceptual framework for categorizing neurodevelopmental impairment based on four of the most common neurological impairments in children born EP that we reason will impact the ability to live independent adult lives—cognitive impairment, cerebral palsy, autism, and epilepsy.[25]

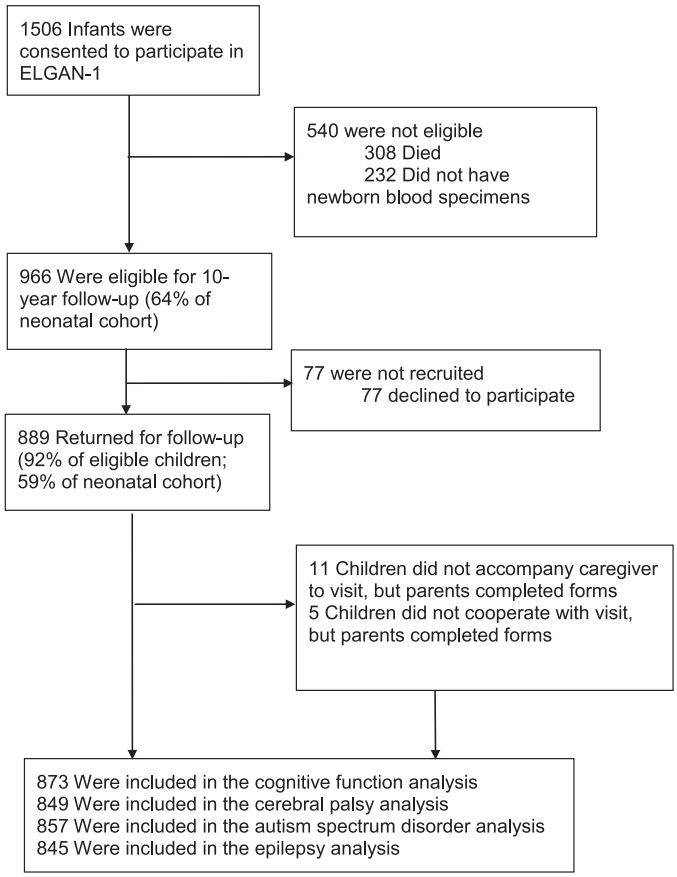

FIGURE.
Enrollment.

Methods

Participants

The ELGAN study is a multicenter observational study of the risk of structural and functional neurologic disorders in EP infants. One thousand two hundred forty-nine mothers delivering 1506 live-born infants before 28 weeks' gestation were enrolled between 2002 and 2004 (Figure). From the 1198 ELGAN study children who survived until ten years of age, we actively recruited the 966 surviving members of the ELGAN cohort from whom we had collected blood spots during the first postnatal month for the measurement of inflammation-related proteins. The institutional review boards of all participating institutions approved the study. Because of a combination of severe motor, visual, and cognitive disability, 40 children were assigned the lowest score on some or all tests. Eleven children did not accompany the caregiver during the follow-up visit, and five children could not complete the assessment,[1] leaving 873 children available for analyses.

Procedures

Cognitive evaluations were administered by certified child psychologists and all examiners underwent in-person training and verification of competency for administration of the test battery. Further, all autism evaluators participated in research-level training in administration and scoring of the Autism Diagnostic Interview—Revised (ADI-R)[26] and Autism Diagnostic Observation Schedule-2 (ADOS).[27] In this article, we use the term deficient IQ when talking about an IQ less than 70, and restrict the use of the terms cognitive ability and/or cognitive impairment to children who have deficiencies in the latent profile analysis (LPA) construct of IQ and EF (see below).