Long-Term Cognitive Outcomes of Birth Asphyxia and the Contribution of Identified Perinatal Asphyxia to Cerebral Palsy

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KEYWORDS

• Neonatal encephalopathy • Hypoxic ischemic encephalopathy • Newborn
• Cognitive outcome • Cerebral palsy

KEY POINTS

- Neonatal encephalopathy (NE) contributes to significant cognitive impairment among survivors who do and do not develop cerebral palsy (CP).
- A watershed MRI pattern of brain injury may predict worse cognitive outcomes even among the nondisabled survivors of NE who manifest no functional motor deficits or evidence of CP.
- Despite therapeutic hypothermia for NE, cognitive and learning deficits continue to occur and merit comprehensive assessment through school age.
- A better understanding of the extent of brain injury as it relates to cognitive impairment may lead to targeted interventions to improve childhood outcomes.
- A common misconception is that a vast majority of infants with CP have NE attributed to hypoxic ischemic encephalopathy (HIE) and intrapartum events; evidence indicates that fewer than 12% of children who are diagnosed with CP were exposed to perinatal asphyxia.

INTRODUCTION

NE among survivors of presumed perinatal asphyxia is recognized as an important cause of CP and neuromotor impairment. Recent studies suggest that moderate to severe NE contributes to a wide range of neurodevelopmental and cognitive

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impairments among survivors with and without CP.[1–6] Neonates who have severe encephalopathy at birth more often develop disabling neurologic and cognitive deficits, whereas those who survive moderate encephalopathy typically have more variable outcomes, with milder neuromotor impairments and a wider range of lesser cognitive deficits. Nearly 1 of 4 (23%) neonates who are treated with hypothermia has or develops CP.[7] Although NE only accounts for an estimated 10% of all CP cases, it seems to play a role in 25% of those who are born at term, although in many such births there is no evidence of intrapartum perinatal sentinel events.[8,9] Although some consider hypoxia-ischemia resulting from peripartum asphyxia to be the sole cause of what is called NE,[10] single-cause attribution is inherently problematic.[11] The inability to directly measure cerebral oxygen, the limited performance of its surrogate biomarkers in discriminating children who do and do not develop NE, and evidence that multiple antecedents contribute to umbilical artery acidemia in term infants strongly suggest a multifactorial origin,[12] one that might involve subtypes in which the underlying pathobiology is not fundamentally hypoxic or ischemic[13,14] — hence, the preference for NE over the term, HIE.[12] Nevertheless, this article uses these 2 terms interchangeably. The focus of this article is to review the long-term cognitive outcomes of children presumably exposed to birth asphyxia and to describe what is known about its contribution to CP.

COGNITIVE OUTCOMES AT 18 TO 24 MONTHS AFTER PRESUMED HYPOXIC ISCHEMIC ENCEPHALOPATHY IN THE ERA OF THERAPEUTIC HYPOTHERMIA

Few data are available on the cognitive outcomes of 18-month-old to 24-month-old children after presumed HIE, in large part because earlier developmental instruments did not specifically test cognition. The major randomized controlled trials of hypothermia for HIE assessed developmental outcomes using the Bayley Scales of Infant Development, Second Edition (BSID-II).[15–21] Cognitive and language outcomes were evaluated by way of the mental developmental index (MDI) component, not separately. As in other subscales of the BSID-II, scores range from 50 to 150, with a mean of 100 and an SD of 15, and significant mental delay is denoted by a score less than 70 (representative of 2 SDs below the mean). At 18 to 24 months, the prevalence of significant mental developmental delay after hypothermia for presumed HIE ranges from 23% to 30% (**Tables 1** and **2**).[15–22] Two hypothermia trials report mean MDI scores[14,19] for neonates who were cooled, ranging between 80.2 (SD 20.2) and 90.4 (SD 25.2).[7]

Smaller observational studies explored early childhood cognitive outcomes specifically. Jary and colleagues[23] investigated 18-month neurodevelopmental outcomes for 61 term infants treated with therapeutic hypothermia and compared BSID-II and Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III), assessments among those who survived. The mean and median BSID-III cognitive scores were higher than the BSID-II MDI scores (mean 102 [SD 12.3] versus 91 [SD 17]; median 100 [range 65–125] versus 93 [range 50–121]). Severe disability cutoff thresholds less than 70 also revealed differences between the 2 assessments. Among the 10 neonates who had an MDI score less than 70, only 3 had cognitive and language composite scores less than 70. Chalak and colleagues[24] reported BSID-III outcomes in another prospective cohort study of neonates treated with whole-body hypothermia for HIE (n = 62). The median BSID-III cognitive composite score was 85 (with an interquartile range of 70–90). Only 8% of infants had scores less than 70 and 34% had scores of 70 to 84; hence, a vast majority of children scored within the reported normal range for the BSID-III. Studies comparing BSID-II and BSID-III cognitive and language