Early EEG Grade and Outcome at 5 Years After Mild Neonatal Hypoxic Ischemic Encephalopathy

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OBJECTIVE: More than half of all infants with neonatal hypoxic ischemic encephalopathy (HIE) are graded as mild and do not meet current criteria for therapeutic hypothermia. These infants are often not enrolled in follow-up, and hence our knowledge of their long-term outcome is sparse. We wished to compare 5-year outcomes in a group of infants with mild, moderate, and severe HIE, graded with both early EEG and clinical assessment, none of whom were treated with therapeutic hypothermia.

METHODS: Term infants with HIE and a healthy comparison group were recruited at birth. Both groups had early continuous EEG recordings. Cognitive and motor outcome was assessed at 5 years.

RESULTS: Outcome was available in 53 infants with HIE and 30 infants in the comparison group at 5 years. Infants with mild HIE at birth (n = 22) had significantly lower full-scale IQ, verbal IQ, and performance IQ than comparison infants (n = 30) at 5 years (P = .001, .001, and 0.004, respectively). No difference in cognitive measures was seen between infants with mild and moderate grades HIE. Intact survival at 5 years varied across EEG grade HIE at 6 hours after birth; 75% in mild, 46% in moderate, 43% in major abnormalities, and 0% with inactive EEGs, compared with 97% in the comparison group.

CONCLUSIONS: Survivors of mild HIE, graded clinically or by early EEG, have higher rates of disability than their peers and have cognitive outcomes similar to that of children with moderate encephalopathy in an uncooled HIE cohort.

WHAT’S KNOWN ON THIS SUBJECT: Neonatal hypoxic ischemic encephalopathy (HIE) continues to be a major cause of neonatal death and long-term disability. Severity is graded using clinical and electroencephalographic signs. Outcomes for moderate and severe HIE are well understood and improve after therapeutic hypothermia.

WHAT THIS STUDY ADDS: Children at 5 years after mild HIE have lower IQ scores than peers with uneventful perinatal periods and have similar cognitive outcomes to those with uncooled moderate HIE. Children with EEG-graded mild HIE have reduced intact survival rates.

Neonatal hypoxic ischemic encephalopathy (HIE) remains a leading cause of newborn death and long-term neurodisability. It causes 23% of global neonatal deaths, totaling 1 million annually. Twenty-five percent of surviving children, are left with significant long-term neurologic disability, placing HIE in the top 10 diseases with the highest lifelong global burden. The significance of nonmotor disability is increasingly recognized, with reported rates of learning and neuropsychological difficulties, autism, epilepsy, and sensory loss contributing to adverse long-term quality of life. The more subtle disabilities may not be apparent in early childhood where assessment is focused on developmental milestones.

Outcome is generally aligned with clinical grading, with moderate and severe grades having the highest rates of motor deficit and mortality. The outcome in mild HIE is generally considered to be normal. Due to a fear of serious adverse events, before the establishment of the safety profile of induced hypothermia, infants with mild HIE were not enrolled in trials of therapeutic hypothermia and therefore do not meet current criteria for therapeutic intervention. Few prospective cohorts have included infants with mild encephalopathy; research has instead focused on moderate and severe grades. We wished to determine the cognitive and motor outcome of a prospective cohort of infants across all grades of HIE, with both clinical and early continuous EEG grading.

**METHODS**

**Initial Recruitment**

This prospective study was conducted in a maternity service with 6000 deliveries per year. Ethical approval was obtained from the clinical research ethics committee of the Cork Teaching Hospitals.

Between May 2003 and December 2005, term infants (≥37 weeks of gestation) with HIE were recruited if they fulfilled 2 of the following criteria: initial capillary or arterial pH of <7.1, Apgar score at 5 minutes of <5, initial capillary or arterial lactate level of <7 mmol/L, and abnormal neurologic features/clinical seizures. Broad inclusion criteria were used to ensure recruitment of all grades (mild, moderate, and severe) of HIE. Neurologic condition was assessed by a research pediatrician (D.M.), not involved in the clinical care of the infants within the first 6 hours and was performed by using a standardized method. Infants were excluded if alternative diagnoses were suspected (ie, sepsis, intracerebral infarction, congenital abnormalities, or metabolic encephalopathy).

The parents of infants fulfilling the criteria were approached and written informed consent was obtained within 6 hours of birth or with the onset of clinical seizures. After recruitment, silver-chloride EEG electrodes were applied to the scalp at F3, F4, C3, C4, T3, T4, O1, O2, and CZ (according to the international 10-20 system of electrode placement, as modified for neonates). A Viasys NicoletOne EEG monitor (Viasys International, Madison, WI) was used to record continuous video-EEG recording for 24 to 72 hours’ duration. Recordings were commenced as soon as possible after birth, generally within 6 hours. Measurements of heart rate, respiration, and oxygen saturation, were also recorded. A modified Sarnat encephalopathy grade was assigned at 24 hours as described by Levene in 1985. All EEGs were assigned a grade based on background activity, which has been previously described (see Table 1). All seizures in each EEG recording were annotated visually by an experienced neonatal neurophysiologist (G.B.B.).

Electrographic seizure was defined as a sudden repetitive, stereotyped discharge of minimum 10 seconds’ duration on ≥1 EEG channels with evolving frequency, amplitude, and morphology.

**Outcome Assessment**

Outcome assessment was performed at 6, 12, 24, and 60 months. The 24-month outcome was previously reported. Outcome at 5 years was assessed by a clinical psychologist (C.O.C.) blinded to the neonatal clinical course, EEG findings, and early outcome assessments of the HIE group. Attendance at early intervention services (physiotherapy, speech therapy, psychology, and/or occupational therapy) were also recorded.

A parental questionnaire was designed to capture relevant medical, clinical and demographic information. Intellectual ability was assessed by using the Wechsler Preschool and Primary Scale of Intelligence, 3rd edition (UK version.

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**TABLE 1 Classification of EEG Background Activity**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Findings</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal EEG findings</td>
<td>Continuous background pattern with normal physiologic features such as anterior slow waves</td>
</tr>
<tr>
<td>1</td>
<td>Normal/mild abnormalities</td>
<td>Continuous background pattern with slightly abnormal activity (eg, mild asymmetry, mild voltage depression, or poorly defined sleep-wake cycle)</td>
</tr>
<tr>
<td>2</td>
<td>Moderate abnormalities</td>
<td>Discontinuous activity with interburst interval of &lt;10 s, no clear sleep-wake cycle, or clear asymmetry or asynchrony</td>
</tr>
<tr>
<td>3</td>
<td>Major abnormalities</td>
<td>Discontinuous activity with interburst interval of 10–60 s, severe attenuation of background patterns, or no sleep-wake cycle</td>
</tr>
<tr>
<td>4</td>
<td>Inactive EEG findings</td>
<td>Background activity of &lt;10 µV or severe discontinuity with IBI of &gt;60 s</td>
</tr>
</tbody>
</table>
The Full-Scale IQ (FSIQ), Verbal IQ (VIQ), Performance IQ (PIQ), Processing Speed Quotient (PSQ), and General Language Composite (GLC) were calculated. All quotients are standardized with a mean (SD) of 100 (15). The children were then administered the Numbers subtest from the Children’s Memory Scale to include an additional measure of short-term auditory memory because of the known vulnerability of infants with hippocampal injury. The Numbers subtest has a mean (SD) of 10 (3).

Comparison Group

Comparison infants were recruited from a prospective study examining normal newborn EEG in healthy term infants, born between October 2005 and August 2007, who were recruited in the first postnatal day after delivery, with Apgar scores >8 at 5 minutes and a normal result from standardized neurologic examination. A baseline EEG was recorded for a maximum of 2 hours in each infant. Seven scalp electrodes were positioned over the frontal, central, temporal, and parietal areas using the 10-20 system of electrode placement, modified for neonates (F4, F3, Cz, T4, T3, P4, P3). Exclusion criteria were maternal epilepsy or diabetes, birth weight <2.5 kg, congenital anomalies, or admission to neonatal unit for special or intensive care. Parents/carers whose children were currently aged between 60 and 78 months (n = 41) were sent an information letter and a follow-up telephone call to describe the study.

Statistical Analysis

Statistical analysis was completed by using IBM SPSS Statistics 22.0 for MS Windows (IBM Corporation, Armonk, NY) and VassarStats: Website for Computational Statistics (Lowry, R 1998–2012, Vassar College, NY). The between-group differences of clinical and demographic data for the HIE and comparison groups were explored by using independent samples t test (Cohen’s d for effect size) for continuous variables, and χ² test for independence (Φ coefficient and Cramer’s V for effect size) for categorical variables. Kruskal-Wallis and post hoc Mann-Whitney U tests, positive predictive values (PPVs), and negative predictive values (NPVs) were analyzed to explore differences between neonatal clinical HIE and EEG grades and outcome. Effect sizes for Mann-Whitney U tests were calculated by using the formula

\[ r = z / \sqrt{N}, \]

where \( N \) is number of cases.

RESULTS

In total 95 children were recruited to the study: 65 children with neonatal HIE and 30 comparison infants. Of the 65 children with HIE recruited at birth, 2 were excluded from outcome analysis due to coexisting diagnoses: 1 (mild) with congenital diaphragmatic hernia and 1 (moderate) with unexplained dysmorphic features. Of the remaining 63 infants, 7 (5 mild, 2 moderate) were lost to follow-up, and 3 (2 mild, 1 moderate) withdrew from the study resulting in outcome data for 53 children at 5 years of age. Of these, 6 children (all severe) had died either in the neonatal period or early childhood. The remaining 47 children were assessed at 5 years. In the comparison group, 42 children were contacted, and 12 were lost to follow-up or withdrew.

Clinical and demographics characteristics of the HIE and comparison cases seen at 5 years are displayed in Table 2. No significant difference in socioeconomic status was evident between the groups.

Cognitive Outcome

Clinical Sarnat Grade

Of the 47 children with HIE who were assessed at 60 months, 3 children with severe CP were unable to complete the assessment. On the basis of available psychological, medical, and educational placement information, 2 were assigned the basal IQ score, and the third was inconclusive. Cognitive assessment was therefore available for 46 children with HIE and in all 30 comparison children. The median FSIQ, VIQ, PIQ, PSQ, and GLC scores for each grade of HIE are displayed in Fig 1 and Table 3.

There were statistically significant differences in all WPPSI-III cognitive domains across Sarnat grades (Comparison, n = 30; Mild, n = 22; Moderate, n = 19; Severe, n = 5). For FSIQ, χ² (3, n = 76) = 21.93 (P < .001). Median FSIQ, VIQ, PIQ, PSQ, and GLC differed significantly between comparison and mild infants (P < .001, <.001, .004, .048, and .01, respectively). Median FSIQ, VIQ, PIQ, and GLC differed significantly between comparison and moderate infants (P = .001, <.001, .02, and .01, respectively), with PSQ at .06. No significant difference was seen between mild and moderate HIE infants in any of the WPPSI-III outcome parameters measured. Surviving infants with severe
encephalopathy who were able to complete assessments had a variable outcome. The 3 children with CP had FSIQ indicating intellectual disability (68, 43, and 43), and those without CP (n = 2) had scores in the normal range. Similarly, for the Children’s Memory Scale Numbers subtest, children with mild HIE had significantly lower scores compared with comparison children (P = .004).

EEG Grades at 6 and 24 Hours

In all cases, EEG grades either remained constant or improved between 6 and 24 hours. All comparison infants had grade 0 baseline EEGs recorded, at a median age of 9.00 (interquartile range 6.75–12.25) hours. EEG grades and Sarnat grading are displayed in Fig 2.

A Kruskal-Wallis Test revealed statistically significant differences in all WPPSI domains across EEG grades 0 to 4. For the FSIQ, χ² (4, n = 68) = 23.32 (P < .001) at 6 hours, and χ² (4, n = 74) = 18.76 (P < .001) at 24 hours. At both 6 and 24 hours, those infants with grade 0 EEG readings had the highest median IQ scores, and FSIQ scores decreased as EEG abnormalities worsened, but did not differ significantly between EEG grades 1 to 3; see Table 4 for median (interquartile range) IQ scores and Supplemental Table 5 for IQ differences between grades 1 and 3). Infants with grade 4 EEGs at either time point who survived had severe to profound developmental delay; due to very low numbers, they were excluded from further analysis.

Infants with a normal (grade 0) EEG reading within the first 24 hours had significantly higher FSIQ, VIQ, and PIQ than infants with abnormal (grades 1–3) recordings at either 6 or 24 hours.

Overall Outcome

A detailed picture of overall outcome at 5 years is displayed in Fig 3. When all types of disability and/or clinical requirement for multidisciplinary early intervention team support are examined, infants with a grade 1 EEG at 6 hours had a 75% chance of intact survival. Those with grade 2 EEG abnormalities had a 46% chance of intact survival, and those with EEG grade 3 or 4 at 6 hours had only 21% intact survival. Overall, at 6 hours a moderate/major/inactive EEG (grade ≥2) had a PPV of 68% and a NPV of 75%, area under the receiver

### TABLE 2 Clinical and Demographic Characteristics of the Children Included at 5 Years

<table>
<thead>
<tr>
<th>Clinical and Demographic Characteristics of the Children Included at 5 Years</th>
<th>HIE Group (n = 47)</th>
<th>Comparison Cohort (n = 30)</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perinatal data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight, g, mean (SD)</td>
<td>3431.02 (618.26)</td>
<td>3567.67 (423.71)</td>
<td>.29</td>
<td>0.12</td>
</tr>
<tr>
<td>Gestational age, wk, mean (SD)</td>
<td>40.13 (1.48)</td>
<td>40.05 (1.17)</td>
<td>.82</td>
<td>0.03</td>
</tr>
<tr>
<td>Firstborn, n (%)</td>
<td>36 (78)</td>
<td>11 (37)</td>
<td>.001*</td>
<td>0.42</td>
</tr>
<tr>
<td>Mode of delivery, n (%)</td>
<td>—</td>
<td>—</td>
<td>&lt;.001*</td>
<td>0.58</td>
</tr>
<tr>
<td>Normal vaginal delivery</td>
<td>8 (17)</td>
<td>22 (73)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Instrumental</td>
<td>22 (47)</td>
<td>2 (7)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Elective cesarian delivery</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Emergency cesarian delivery</td>
<td>17 (36)</td>
<td>4 (13)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>28 (60)</td>
<td>13 (43)</td>
<td>.25</td>
<td>0.16</td>
</tr>
<tr>
<td>First documented pH (venous), mean (SD)</td>
<td>6.99 (0.18)</td>
<td>n/a</td>
<td>n/a</td>
<td>—</td>
</tr>
<tr>
<td>First documented BD (venous), mean (SD)</td>
<td>−15.8 (4.8)</td>
<td>n/a</td>
<td>n/a</td>
<td>—</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age assessed, mo, mean (SD)</td>
<td>64.11 (5.75)</td>
<td>67.57 (6.80)</td>
<td>.03*</td>
<td>0.30</td>
</tr>
<tr>
<td>Has sibling(s), n (%)</td>
<td>32 (73)</td>
<td>29 (97)</td>
<td>.02*</td>
<td>−0.31</td>
</tr>
<tr>
<td>Commenced primary schooling, n (%)</td>
<td>36 (78)</td>
<td>20 (69)†</td>
<td>.53</td>
<td>0.10</td>
</tr>
<tr>
<td>Maternal education level, n (%)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Primary or lower secondary</td>
<td>9 (21)</td>
<td>5 (17)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Secondary school completed</td>
<td>19 (43)</td>
<td>11 (37)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Third level qualification</td>
<td>16 (36)</td>
<td>14 (47)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hollingshead occupation criteria, n (%)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Professional/managerial (codes 7–9)</td>
<td>15 (34)</td>
<td>12 (40)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Semiprofessional/technician/clerical (codes 5–6)</td>
<td>8 (18)</td>
<td>8 (27)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Skilled manual (code 4)</td>
<td>8 (18)</td>
<td>5 (17)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Semiskilled/unskilled manual (codes 1–3)</td>
<td>13 (30)</td>
<td>5 (17)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Race: white, n (%)</td>
<td>43 (92)</td>
<td>30 (100)</td>
<td>.15</td>
<td>−0.19</td>
</tr>
<tr>
<td>Region, n (%)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Urban</td>
<td>15 (32)</td>
<td>7 (23)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Small town</td>
<td>20 (43)</td>
<td>14 (47)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rural</td>
<td>12 (26)</td>
<td>9 (30)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

BD, base deficit; n/a, not available; —, P value calculated across all categories.

* R = correlation with FSIQ at 5 y.

** Based on Hollingshead Occupational Scale.13

† Significant P value.
operating characteristic curve = 0.712 (95% confidence interval 0.558–0.867) in predicting an abnormal outcome at 5 years. At 24 hours, the ability of an EEG grade of ≥2 to predict abnormal outcome was PPV 74%, NPV 68% and area under the receiver operating characteristic curve 0.696 (95% confidence interval 0.546–0.845). The improved PPV at 24 hours was due to the natural evolution of HIE, with normalization between 6 and 24 hours. Thus, EEG recordings that remained abnormal at 24 hours held a worse prognosis (Fig 3).

**DISCUSSION**

We have shown significant reductions in FSIQ, VIQ, PIQ, PSQ, and GLC at 5 years in children who had mild HIE at birth compared with a contemporaneous comparison group. Although children with mild HIE had higher rates of overall intact survival, on detailed IQ assessments, children with a history of mild HIE did no better than children with moderate HIE at birth. Greater differences were evident between the mild and moderate grades when a detailed analysis of outcome was examined. Intact survival after mild EEG abnormalities at 24 hours was 65% and 57% with moderate HIE. Both groups compared poorly to the comparison groups, in which 97% had an intact survival.

Current care strategies are based on the premise that outcome in infants with mild encephalopathy is normal, with studies reporting good outcome. However, a number of retrospective studies have recently shown rates of memory and learning impairment to be greater than expected and somewhat closer to that of infants after moderate HIE. In the era of hypothermia, studies have shown that infants classified as mild on clinical scoring alone have higher rates of morbidity in the neonatal period, but direct

**FIGURE 1**

Boxplot representations of WPPSI-III FSIQ and subquotient scores for the HIE Sarnat grade groups and the comparison group. GLIQ, general language IQ; PSIQ, processing speed IQ. Horizontal lines set at mean (SD) expected = 100 (15).
comparison with uncooled, moderate grade infants is no longer possible because of universal introduction of hypothermia in high-income countries. Our finding builds on growing evidence that children with mild HIE do not follow a normal developmental trajectory. Significant, subtle disability can become more frequent with age as children “grow into” their deficits.15, 16 Recent retrospective cohorts suggest that up to 70% of adolescents have learning and behavioral difficulties that affect their everyday lives.18–20 Unfortunately, most long-term follow-up studies either exclude those with mild HIE or do not have local contemporary control populations.

Management of infants with mild HIE remains supportive. Current protocols for therapeutic hypothermia include infants with moderate to severe HIE only.3 These protocols are based on clear data from large randomized controlled trials of efficacy in moderate and severe HIE showing improved rates of intact survival.3,21,22 Even within these grades, benefit is not universal with a number needed to treat of 7 to 8 infants for 1 intact survival.23 In infants with mild HIE, the risk-to-benefit ratio is likely to be even less balanced in favor of aggressive intervention. However, although the economic cost of NICU care and cooling is high, it may not be so when compared with lost academic achievement. Furthermore, preliminary indications from the rollout of hypothermia in clinical settings report that infants with mild HIE are being treated in many centers.24 Recent studies highlight the difficulty in assigning HIE grade with many infants misclassified based on clinical grading alone.17

We have confirmed the accuracy of our clinical grading at 24 hours by assessing simultaneous EEG recordings. This has allowed us to examine the ability of both clinical and EEG grade to predict long-term outcome. Our data support the need for future clinical trials of neuroprotective agents to include infants with mild HIE, both to ascertain the effect of cooling and to examine adjunct low-cost medical therapies.25,26 Because 50% of infants with HIE have mild grade encephalopathy, the burden of disability with loss of academic potential and decreased employment prospects may be greater on a global scale, with greater numbers but similar cognitive outcomes to that of moderate HIE.27 Predicting which infants with clinically mild HIE might benefit most from intervention is a challenge. Early EEG may help, because, in our cohort, normalization of the EEG in the first 24 hours was associated with a normal outcome at 5 years.

It remains unclear why such an apparently mild injury may lead to adverse outcome. The answer may lie in vitro and animal studies suggesting that an initial insult permanently alters the brain’s ability to repair and develop. This “tertiary brain injury” appears to initiate an altered inflammatory or epigenetic response within the brain that affects...
Our data shows the heterogenous profile of disability after HIE and the need for multidisciplinary early intervention. Additional multidisciplinary developmental support was required in 35% of children with mild EEG abnormalities at 24 hours, compared with 3% in the comparison group. Although previous reports have estimated an increased rate of autistic spectrum disorder in HIE. Our rates of autistic spectrum disorder and attention-deficit/hyperactivity disorder were not higher than expected. Our data confirms the importance of long-term follow-up to school age and the use of contemporaneous local controls. At our 2-year outcome assessment, these children were compared with standardized norms, and almost all mild infants scored within normal ranges. Unfortunately, we did not assess a comparison group at this stage. Longer term follow-up, with the availability of a comparison group has revealed significant differences at school age. Our comparison group performed better than expected on WPPSI-III assessment. This level of attainment has been recorded in control groups of children in other studies using the WPPSI-III.
may be due to local population differences, the socioeconomic profile of the group, or the Flynn effect of IQ drift over time, estimated by the test publishers to be a 0.33 score increase per annum. This would equate to a 2.3- to 3.6-point increase for our study. In addition, our comparison group was used because of the availability of neonatal EEG for them and were recruited on the basis of an uneventful perinatal course. However, this group may be “healthier” than children chosen from the normal population. No significant differences in socioeconomic status or maternal education existed between our case and comparison groups.

The major limitation of the study is the small numbers available with outcome at 5 years. However, recruitment of infants with HIE is difficult, and few cohorts are studied prospectively from birth. Fewer still include children with mild HIE. Our cases have been carefully categorized using both EEG and Sarnat grading, and our comparison group uniquely had early EEG and clinical assessment of their neurologic status at birth. Follow-up was detailed and blinded to neonatal data in both the cases and the comparison group. Few prospective data on noncooled cohorts comparing mild to moderate HIE are available. Although rates of disability in infants with moderate HIE will now be altered due to therapeutic hypothermia, there are no approved and effective therapies for those with mild or severe HIE. Our data indicate that significant disability occurs within these grades at 5 years and support continued research in these cohorts to develop adjunct therapies that are suitable and effective in all grades of HIE.

**CONCLUSIONS**

We have shown that cognitive outcome, measured by the WPPSI-III is significantly reduced after mild, moderate, or severe HIE compared with a contemporaneous comparison group, whether graded by EEG or clinical Sarnat grade. Although mild HIE had the highest rates of intact survival, no difference in cognitive ability was evident between mild and moderate grades of HIE. Our data support the need for future studies of neuroprotection to include infants with mild HIE.

**ACKNOWLEDGMENTS**

We thank Drs Louise Gibson and Evonne Low for assisting with the neurologic assessments at 5 years. We also thank all of the children and their parents and carers for giving their time so willingly to this project.

**ABBREVIATIONS**

CP: cerebral palsy  
FSIQ: full scale intelligence quotient  
GLC: general language composite  
HIE: hypoxic ischemic encephalopathy  
NPV: negative predictive values  
PIQ: performance intelligence quotient  
PPVs: positive predictive values  
PSQ: processing speed quotient  
VIQ: verbal intelligence quotient  
WPPSI: Wechsler Preschool & Primary Scale of Intelligence


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Pediatrics originally published online September 20, 2016;
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