

ORIGINAL ARTICLE

Joint association of Apgar scores and early neonatal symptoms with minor disabilities at school age

D Moster, R T Lie, T Markestad

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Objective: To examine whether the combination of a low five minute Apgar score and symptoms of neonatal encephalopathy is associated with minor impairments at school age.

Design: Population based cohort study.

Setting: Norway.

Participants: All 727 children of the cohort were born between 1983 and 1987, had normal birth weights, no congenital malformations, and no major neurological abnormalities. The cohort comprised three groups with five minute Apgar scores of 0–3, 4–6, and 7–10, and were followed from birth to 8–13 years of age by combining data from The Medical Birth Registry, questionnaires, hospital discharge summaries, and the National Insurance Scheme.

Main outcome measure: Neurodevelopmental impairments such as learning, behavioural, and minor motor difficulties.

Results: Children with a five minute Apgar score of 3 or less and signs consistent with neonatal encephalopathy had a significantly increased risk of developing minor motor impairments (odds ratio (OR) 12.8, 95% confidence interval (CI) 2.6 to 63.2), epilepsy (OR 7.0, 95% CI 1.3 to 39.2), need of extra resources in kindergarten (OR 7.0, 95% CI 1.3 to 39.2) or at school (OR 3.4, 95% CI 1.8 to 6.3), and had reduced performance in reading (OR 4.6, 95% CI 2.3 to 9.5) and mathematics (OR 3.3, 95% CI 1.5 to 7.3), compared with children with normal Apgar scores and no neonatal symptoms. They also more often had problems related to tractability, aggressivity, passivity, anxiety, academic performance, and fine motor development.

Conclusion: Children with low Apgar scores and subsequent signs of cerebral depression who do not develop cerebral palsy may still have an increased risk of developing a variety of neurodevelopmental impairments and learning difficulties.

See end of article for authors' affiliations

Correspondence to:
Dr Moster, Department of Paediatrics, Barnekliviken, Haukeland University Hospital, N-5021 Bergen, Norway;
Dag.Moster@smis.uib.no

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Identification of children at risk of later impairments is difficult soon after birth. Studies have suggested that neonates with depressed vital functions after delivery will die, be severely disabled, or develop apparently normally.^{1–5} Few long term follow up studies, however, provide information on the risks of less severe disabilities.

In 1953, Virginia Apgar proposed a clinical score to improve the appraisal of an infant's clinical status after birth.⁶ The Apgar score gives the total numerical value of five clinical signs: heart rate, respiratory effort, reflex irritability, muscle tone, and colour. Each sign is given a value from 0 to 2, and a score of 7–10 is considered to be the normal range.⁷ A low Apgar score is by itself no evidence of intrapartum asphyxia, but may be related to prematurity, congenital malformations, perinatal infections, or maternal sedation or anaesthesia. The Apgar score has gained worldwide use as a marker of a child's vitality immediately after birth, but its value as a predictor of later disabilities is debated.

In 1976, Sarnat and Sarnat⁸ described newborns with an encephalopathy following fetal distress. Neonatal encephalopathy may be defined as a clinical syndrome of disturbed neurological function in the earliest days of life in the term infant, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness, and often by seizures.⁹

An association between a low Apgar score combined with neonatal encephalopathy and subsequent death or major neurological handicap is well documented.^{10–11} The purpose of this study was to evaluate the joint association of low Apgar scores and subsequent signs of cerebral depression in the first week of life, with minor impairments at school age among children without major neurological abnormalities.

SUBJECTS AND METHODS

Study design

All infants born alive in Norway during the period 1983–1987 with a birth weight of at least 2500 g and a recorded five minute Apgar score were identified in The Medical Birth Registry. Infants with birth defects were excluded. Among the remaining 235 642 children, we identified 214 children with a five minute Apgar score of 0–3, a random sample of 400 infants with scores 4–6 (132 with a score of 4, 133 with a score of 5, 135 with a score of 6), and a sample of 404 infants with a score of 7–10. The Central Population Register of Norway verified that the children were alive, and provided the names of the caregivers and their postal addresses in Norway.

When the children were 8–13 years old, a 117 item questionnaire on conditions during birth, the newborn period, later neurological diagnoses, learning difficulties, school performances, behavioural characteristics, need for follow up by hospitals, and need for extra resources in school was mailed to the carers, preferentially the mothers. Parents were also asked for written permission to obtain discharge summaries from hospitals where their children had been examined or treated as neonates or during childhood.

Every citizen in Norway is identified by a national identification number. The numbers are used by national registries and simplify record linkage. The information from The Medical Birth Registry, questionnaires, and hospitals' discharge summaries was combined with information from the National Insurance Scheme. The latter provides a basic benefit for any disability in children, which involves significant expenses and an additional attendance benefit if the disabled child needs special attention or nursing. This is granted for all children in

Norway irrespective of a family's income, and the medical reason for giving benefits is recorded.

A total of 770 (76%) of the questionnaires were adequately answered (80%, 74%, and 75% in the three subgroups of children with five minute Apgar scores of 0–3, 4–6, and 7–10 respectively). Discharge summaries were received from hospitals concerning the newborn period for 134 children and from later hospital admissions for 97 children. All hospitals that were asked for discharge summaries responded positively. Twelve children were reported by parents to have congenital malformations not previously recorded by The Medical Birth Registry. Furthermore, we identified 31 children with major neurological impairments: 29 had cerebral palsy and/or severe mental retardation; one had an injury to the spinal cord; and one still required ventilator treatment at night at the age of 13 years. There was full agreement between parents' reports and discharge summaries with regard to these diagnoses. The remaining 727 children had no recorded congenital malformations and no major neurological impairment noted from parents, discharge summaries, or the National Insurance Scheme. These 727 comprised the cohort used to study minor impairments.

The study was approved by the Norwegian Board of Health, the Norwegian Data Inspectorate, and the Regional Committee on Medical Research Ethics. For parents who initially did not respond to the questionnaire, only one reminder was allowed, and requests to hospitals for discharge summaries were only allowed after written consent from parents.

Questionnaire

From the children's first week of life, parents were asked about the presence of three different symptoms that may imply neonatal encephalopathy: neonatal seizures, feeding difficulties with or without the need for intravenous or tube feeding, and need for ventilator treatment.

From later ages, there were questions on specific medical diseases and diagnoses, need for follow up by doctors and paramedics, need for special resources in kindergarten or school, and educational and behavioural problems. Parents were also asked to judge their child's school performances in reading, writing, spelling, and mathematics by one of five alternatives for each subject: not capable; far below average; below average; average; above average.

To judge possible behavioural and academic problems, parents were asked to score 55 characteristics for the child on a scale of 1–4. These characteristics were used to classify a total of 11 scales. Eight of these 11 scales were from the Yale Children's Inventory Scales: attention, habituation, impulsivity, activity, tractability, academic learning, academic performance, and fine motor development.¹² Three other behavioural scales describing aggressivity, passivity, and anxiety were also incorporated.¹³

Statistical analysis

Each of the three Apgar score groups was divided into two subgroups depending on the presence or absence of subse-

quent signs of cerebral depression (seizures, ventilator treatment, or feeding difficulties in the first week of life). A categorical variable identifying these six subgroups was used as an independent variable in the logistic regression analyses. The category of children with a five minute Apgar score of 7–10 and without seizures, no ventilator treatment, and no feeding difficulties in the first week of life was used as the reference group in these analyses.

Firstly, outcomes in terms of neurodevelopmental impairments, need for intervention and follow up by specialised personnel, and school performances were analysed.

Secondly, the Yale Children's Inventory Scales and additional scales of pathological behaviour were analysed. Initially, each scale for each child was calculated as the mean of the individual items in that scale. For each scale the 95th centile of the score for the group of children with Apgar scores of 7–10 was used as cut off to define a pathological score. This was done for each of the 11 scales and for each sex separately. The presence of a pathological score was then used as outcome variable in logistic regression models.

Thirdly, to adjust for possible confounding variables, all analyses were repeated, including the level of education of each parent in the logistic regression models. In the analyses of learning difficulties and school performances, adjustments were also performed for known learning disabilities for close relatives. Educational levels of each of the parents were assessed on a six point scale. Learning disabilities among relatives were classified on a four point scale according to whether learning disabilities were reported by two or more relatives of first degree, one relative of first degree, at least one relative of second degree but none of first degree, and finally no known relatives with learning difficulties.

The purpose of this paper was to estimate the joint effect of Apgar score and neonatal encephalopathy on the risk of particular conditions during childhood. However, we also analysed the effect of Apgar scores irrespective of neonatal encephalopathy, and analysed the effect of neonatal encephalopathy irrespective of Apgar scores for all the outcomes studied. Finally, to judge whether one of the three signs we used as indicators of neonatal encephalopathy was more predictable than the others, all analyses were repeated by using each of these signs—that is, neonatal seizures, feeding difficulties, and need for ventilator treatment—as independent covariables in the logistic regression models. BMDP Statistical Software was used for all statistical analyses.¹⁴

RESULTS

According to the parents, nearly half of the infants with a five minute Apgar score of 0–6 and 13% with normal scores developed symptoms in the first week of life such as neonatal seizures, feeding difficulties, or ventilator treatment (table 1). The reliability of parents' information was tested against discharge summaries from the neonatal units, and there was reasonable agreement for all three symptoms ($\kappa = 0.68$ for neonatal seizures, feeding difficulties necessitating tube or intravenous feeding, and ventilator treatment separately).

Table 1 Distribution of five minute Apgar scores and neonatal symptoms in the first week of life among 727 infants with normal birth weight, no congenital malformations, and without major neurological impairments

	Apgar 0–3 (n=155)	Apgar 4–6 (n=274)	Apgar 7–10 (n=298)
Neonatal seizures	18 (11.6)	13 (4.7)	1 (0.3)
Need for intravenous or tube feeding	31 (20.0)	41 (15.0)	0 (0)
Feeding difficulties without need for intravenous or tube feeding	23 (14.8)	40 (14.6)	37 (12.4)
Ventilator treatment	50 (32.3)	67 (24.5)	5 (1.7)
Neonatal symptoms* first week of life	77 (49.7)	122 (44.5)	40 (13.4)

Values are numbers with percentages in parentheses.

*At least one of the symptoms: seizures, feeding difficulties, or ventilator treatment.

Table 2 Numbers and odds ratios (95% confidence interval) of minor neurological impairments among 727 children at 8–13 years of age related to Apgar scores five minutes after birth and symptoms that may indicate neonatal encephalopathy* (SNE)

	Apgar 0–3		Apgar 4–6		Apgar 7–10		– SNE (total=258)	
	+ SNE (total=77)	– SNE (total=78)	+ SNE (total=122)	– SNE (total=152)	+ SNE (total=40)	– SNE (total=258)		
Minor motor impairments†	7	12.8 (2.6 to 63.2)	1	1.7 (0.1 to 18.7)	2	1.7 (0.2 to 12.3)	2	1.0 (ref)
Developing skills later than usual§	13	3.3 (1.5 to 7.3)	2	0.4 (0.1 to 1.9)	10	1.5 (0.6 to 3.3)	9	1.0 (0.4 to 2.4)
ADHD related diagnoses¶	4	14.1 (1.5 to 128)	0	–†	4	8.7 (1.0 to 79.1)	3	5.2 (0.5 to 50.4)
Epilepsy**	4	7.0 (1.3 to 39.2)	0	–†	0	–†	1	0.8 (0.1 to 9.5)
Febrile seizures††	6	3.0 (1.0 to 9.3)	5	2.5 (0.8 to 8.0)	5	1.5 (0.5 to 4.9)	13	3.4 (1.3 to 8.6)
Visual impairments†††	10	2.1 (0.9 to 4.8)	9	1.9 (0.8 to 4.3)	11	1.4 (0.6 to 3.1)	20	2.2 (1.1 to 4.3)
Strabismus§§	10	2.6 (1.1 to 6.1)	6	1.5 (0.5 to 3.9)	8	1.2 (0.5 to 3.0)	12	1.5 (0.7 to 3.3)
Use of glasses¶¶	16	2.8 (1.4 to 5.7)	13	2.2 (1.0 to 4.5)	17	1.7 (0.9 to 3.4)	31	2.8 (1.5 to 5.0)
Hearing impairments***	6	1.6 (0.6 to 4.4)	4	1.0 (0.3 to 3.2)	10	1.7 (0.7 to 4.0)	7	0.9 (0.4 to 2.3)

*Symptoms that may indicate neonatal encephalopathy were defined as seizures, feeding difficulties, and/or ventilator treatment in the first week of life. Their distribution related to Apgar scores are specified in table 1; †defined as having motor impairments requiring follow up by doctors without being diagnosed as having cerebral palsy or attention deficit/hyperactivity disorder (ADHD), p=0.004; ‡none in the cell; §p=0.03; ¶p=0.04; **p=0.03; ††defined as febrile seizure without simultaneously reporting epilepsy, p=0.11; †††p=0.25; §§p=0.41; ¶¶p=0.008; ***p=0.76. Only two children used hearing aid.

Children with a five minute Apgar score of 0–3 and with symptoms indicating encephalopathy in the first week of life had about a 13-fold increased risk of later minor motor impairments, a 14-fold increased risk of an attention deficit/hyperactivity disorder related diagnosis, and a seven-fold increased risk of epilepsy compared with children with normal Apgar scores and no neonatal symptoms (table 2). If the five minute Apgar score was 3 or less and the infant had no neonatal symptoms, no increased risk of such adverse outcome could be shown. Infants with the lowest Apgar scores and neonatal symptoms had a minor but significantly increased risk of strabismus and use of glasses, and were reported by parents to develop skills later than other children of the same age.

Children with five minute Apgar scores of 0–3 and subsequent neonatal symptoms in the first week of life had about a sevenfold increased risk of need for extra resources in kindergarten, a threefold increased risk of intervention at school, nearly sixfold the need for follow up by a child psychologist, and nearly fourfold the need for follow up by the special resource centre for children with educational or behavioural problems available in all municipalities in Norway, compared with children with no known problems in the early neonatal period (table 3). Children with low Apgar scores but no early neonatal symptoms did not have increased risks of such problems.

Significantly more children with five minute Apgar scores of 0–3 and symptoms of neonatal encephalopathy were judged by their parents to perform below average in reading, writing, spelling, and mathematics compared with children with normal Apgar scores and no neonatal symptoms (table 4). Children with low Apgar scores but no symptoms in the first week of life, performed like the presumed normal group.

Also, children with five minute Apgar scores of 0–3 and subsequent neonatal symptoms more often had pathological scores related to tractability, aggressivity, passivity, anxiety, academic learning and performance, and fine motor development than children with normal Apgar scores and no neonatal symptoms (table 5). Children with five minute Apgar scores of 4–6 and neonatal symptoms significantly more often had pathological scores related to attention, tractability, passivity, anxiety, and fine motor development than children without neonatal problems (table 5).

Adjustments for educational levels of parents and for learning disabilities among family members only marginally affected the estimates of the odds ratios of the six categories of the study variable concerning Apgar scores and early neonatal symptoms, and never influenced the ranking between these categories.

In the absence of encephalopathy, the general effect of Apgar score was generally small. When the effect of Apgar scores was studied irrespective of the presence of neonatal encephalopathy, associations were shown between low five minute Apgar scores on one side and minor motor impairments, febrile seizures, use of glasses, use of psychologist, reading problems, and pathological scores on tractability, anxiety, academic performance and fine motor development on the other.

When the effect of neonatal encephalopathy was studied irrespective of Apgar score, associations were shown between symptoms of neonatal encephalopathy on one side, and minor motor impairments, late development of skills, attention deficit/hyperactivity disorder related diagnoses, need for extra resources in kindergarten and at school, help from resource centre for educational and behavioural problems, problems with reading, mathematics, and spelling, and pathological scores on tractability, aggressivity, passivity, anxiety, and fine motor development on the other.

When the three signs used as indicators of neonatal encephalopathy were studied as independent variables in the logistic regression models, feeding difficulties were more often

Table 3 Numbers and odds ratios (95% confidence interval) of need for intervention and follow up by specialised personnel among 727 children at 8–13 years of age related to Apgar scores five minutes after delivery and symptoms that may indicate neonatal encephalopathy* (SNE)

	Apgar 0–3		Apgar 4–6		Apgar 7–10	
	+ SNE (total=77)	– SNE (total=78)	+ SNE (total=122)	– SNE (total=152)	+ SNE (total=40)	– SNE (total=258)
Extra resources in kindergarten†	4 7.0 (1.3 to 39.2)	1 1.7 (0.1 to 18.7)	7 7.8 (1.6 to 38.2)	1 0.8 (0.1 to 9.5)	0 †	2 1.0 (ref.)
Intervention at school‡	23 3.4 (1.8 to 6.3)	6 0.7 (0.3 to 1.7)	19 1.5 (0.8 to 2.7)	20 1.2 (0.7 to 2.2)	9 2.3 (1.0 to 5.3)	29 1.0 (ref.)
Speech therapist¶	9 1.4 (0.6 to 3.1)	3 0.4 (0.1 to 1.4)	11 1.0 (0.5 to 2.2)	12 0.9 (0.4 to 1.8)	4 1.1 (0.4 to 3.5)	23 1.0 (ref.)
Psychologist**	5 5.9 (1.4 to 25.4)	3 3.4 (0.7 to 17.2)	1 0.7 (0.1 to 6.9)	2 1.1 (0.2 to 6.9)	1 2.2 (0.2 to 21.6)	3 1.0 (ref.)
Resource centre for educational and behavioural problems††	18 3.8 (1.9 to 7.8)	6 1.1 (0.4 to 2.7)	14 1.6 (0.8 to 3.4)	18 1.7 (0.9 to 3.3)	7 2.7 (1.0 to 6.8)	19 1.0 (ref.)

*Symptoms that may indicate neonatal encephalopathy were defined as seizures, feeding difficulties, and/or ventilator treatment in the first week of life. Their distribution related to Apgar scores are specified in table 1; †p=0.01; ‡none in the cell; §including at least one of the following: need for special school (n=2); need for special resources in ordinary school (n=101); continuation of one school year (n=2); recommended delayed start at school (n=9); p=0.001; ¶p=0.57; **p=0.12; ††p=0.007.

associated with later adverse outcome than neonatal seizures. Of the three signs used, need for ventilator treatment seemed to be least associated with later adverse outcome.

DISCUSSION

In this study of children with normal birth weight and no congenital malformations, who survived without major neurological disabilities, we show a significantly increased risk of minor impairments at school age if the child showed symptoms consistent with cerebral depression in the first week of life. The combination of a five minute Apgar score of 3 or less and subsequent signs of cerebral depression such as seizures, ventilator treatment, or feeding difficulties in the early neonatal period carried a significantly increased risk of a variety of later minor disabilities. This included minor motor impairments, delayed development of skills, attention deficit/hyperactivity disorder related diagnoses, epilepsy, strabismus, use of glasses, need for extra resources in kindergarten and at school, performances in reading, writing, spelling, and mathematics below average, and pathological scores related to tractability, aggressivity, passivity, anxiety, academic learning, academic performance, and fine motor development. Children with a low Apgar score, but without subsequent symptoms of neonatal encephalopathy, or children with such symptoms but without a preceding low Apgar score, seemed to have almost no increased risk for such deficits. An intermediate Apgar score carried an intermediate risk.

The major strengths of the study were a population based cohort, an acceptable response rate of 76%, the use of four different data sources to secure exclusion of children with congenital malformations and major neurological impairments, and a relatively large study group of 727 children. The major weaknesses were that data on subsequent symptoms of cerebral depression and on later minor impairments were based on parents' information, and that we could not perform a grading of the assumed neonatal encephalopathy. Different grading schemes of neonatal encephalopathy exist, but their ability to provide prognostic discrimination is limited.¹⁵ We chose three neonatal symptoms (seizures, ventilator treatment, and feeding difficulties) which have been reported to relate to long term outcome,¹⁶ and which we believed would be easily remembered by the parents, an assumption underscored by the agreement with the discharge summaries. Furthermore, information on follow up by different specialised resource centres implies that the actual impairments were judged to be considerable not only by parents, but also by trained personnel.

Adverse environmental factors may place a child at risk of poorer outcome.¹⁷ Possible effects of socioeconomic differences and differences in opportunities of obtaining social or educational support were reduced by the fact that health care and need for extra resources in school because of learning disabilities or behavioural problems are free of charge for all children in Norway, and that virtually all children attend the public schools. Adjustments for educational levels of the parents and for learning difficulties among close relatives only marginally affected the results, indicating that bias due to socioeconomic differences was of minor importance.

In the study we preferred to use birth weight instead of gestational age to identify presumably normal term babies. In The Medical Birth Registry, birth weight is more reliably recorded than gestational age, and data on gestational age is more often missing. However, in an emergency situation in the delivery room, an infant may not have been weighed and therefore not included in the study. This possible bias was examined using data in The Medical Birth Registry: in addition to the original sample of 235 642 infants with known birth weights of at least 2500 g, only 205 infants were recorded without a birth weight, but with a gestational age of at least 37 weeks. Twenty had Apgar scores of 3 or less, and only eight of

Table 4 Numbers and odds ratios (95% confidence interval) of parents' evaluation of their child's school performances to be below average among 727 infants at 8–13 years of age related to Apgar scores five minutes after delivery and symptoms that may indicate neonatal encephalopathy* (SNE)

	Apgar 0–3		Apgar 4–6		Apgar 7–10	
	+ SNE (total=77)	– SNE (total=78)	+ SNE (total=122)	– SNE (total=152)	+ SNE (total=40)	– SNE (total=258)
Reading†	19 4.6 (2.3 to 9.5)	4 0.8 (0.3 to 2.4)	15 2.0 (1.0 to 4.1)	20 2.2 (1.1 to 4.3)	4 1.6 (0.5 to 5.0)	17 1.0 (ref)
Writing‡	14 2.6 (1.3 to 5.5)	4 0.6 (0.2 to 2.0)	12 1.3 (0.6 to 2.8)	17 1.5 (0.8 to 3.0)	3 1.0 (0.3 to 3.4)	20 1.0 (ref)
Mathematics§	13 3.3 (1.5 to 7.3)	2 0.4 (0.1 to 1.9)	9 1.3 (0.5 to 3.0)	12 1.4 (0.6 to 3.1)	3 1.3 (0.4 to 4.8)	15 1.0 (ref)
Spelling¶	15 2.5 (1.2 to 5.0)	4 0.6 (0.2 to 1.7)	18 1.8 (0.9 to 3.4)	20 1.6 (0.8 to 2.9)	5 1.5 (0.5 to 4.1)	23 1.0 (ref)

*Symptoms that may indicate neonatal encephalopathy were defined as seizures, feeding difficulties, and/or ventilator treatment in the first week of life. Their distribution related to Apgar scores are specified in table 1; †including: below mean (n=72); far below mean (n=7); none classified as not capable. p=0.0006; ‡including: below mean (n=64); far below mean (n=5); not capable (n=1). p=0.10; §including: below mean (n=46); far below mean (n=6); not capable (n=2). p=0.03; ¶including: below mean (n=69); far below mean (n=12); not capable (n=4). p=0.05.

Table 5 Odds ratios (95% confidence interval) of pathological behavioural and academic scores among 727 infants at 8–13 years of age related to Apgar scores five minutes after delivery and symptoms that may indicate neonatal encephalopathy* (SNE)

	Apgar 0–3		Apgar 4–6		Apgar 7–10	
	+ SNE (total=77)	– SNE (total=78)	+ SNE (total=122)	– SNE (total=152)	+ SNE (total=40)	– SNE (total=258)
Attention†	1.5 (0.5 to 5.1)	1.1 (0.3 to 4.2)	2.7 (1.1 to 6.8)	1.5 (0.6 to 4.1)	1.5 (0.3 to 7.0)	1.0 (ref)
Habituation‡	3.6 (1.0 to 12.6)	2.7 (0.7 to 10.4)	2.2 (0.6 to 7.6)	1.4 (0.4 to 5.2)	2.7 (0.5 to 14.2)	1.0 (ref)
Impulsivity§	1.4 (0.5 to 4.2)	2.0 (0.8 to 5.3)	1.2 (0.5 to 3.2)	0.7 (0.2 to 2.0)	1.1 (0.2 to 5.0)	1.0 (ref)
Activity¶	2.1 (0.5 to 8.9)	3.5 (1.0 to 12.3)	2.6 (0.8 to 8.8)	1.7 (0.5 to 6.1)	2.7 (0.5 to 14.7)	1.0 (ref)
Tractability**	3.8 (1.4 to 9.9)	2.3 (0.8 to 6.8)	3.7 (1.5 to 8.7)	1.8 (0.7 to 4.5)	3.2 (0.9 to 10.8)	1.0 (ref)
Aggressivity††	4.2 (1.7 to 10.3)	1.7 (0.6 to 5.1)	2.2 (0.9 to 5.5)	1.2 (0.5 to 3.3)	2.8 (0.8 to 9.6)	1.0 (ref)
Passivity‡‡	3.6 (1.1 to 11.5)	1.1 (0.2 to 5.6)	5.1 (1.9 to 13.7)	2.1 (0.7 to 6.3)	4.8 (1.3 to 17.9)	1.0 (ref)
Anxiety§§	6.0 (1.9 to 18.8)	2.7 (0.7 to 10.5)	4.6 (1.5 to 13.7)	1.4 (0.4 to 5.3)	4.2 (1.0 to 18.4)	1.0 (ref)
Academic learning¶¶	3.0 (1.2 to 7.5)	0.9 (0.2 to 3.3)	1.6 (0.6 to 4.0)	1.1 (0.4 to 2.9)	–***	1.0 (ref)
Academic performance†††	7.6 (2.5 to 23.1)	2.8 (0.7 to 10.6)	2.6 (0.8 to 8.8)	2.8 (0.9 to 8.7)	–***	1.0 (ref)
Fine motor development‡‡‡	7.1 (2.5 to 19.9)	1.7 (0.4 to 7.0)	3.4 (1.2 to 9.7)	3.6 (1.3 to 9.9)	3.4 (0.8 to 14.2)	1.0 (ref)
Combined§§§	3.7 (2.1 to 6.3)	1.3 (0.7 to 2.4)	2.7 (1.6 to 4.3)	1.4 (0.8 to 2.2)	1.7 (0.8 to 3.6)	1.0 (ref)

*Symptoms that may indicate neonatal encephalopathy were defined as seizures, feeding difficulties, and/or ventilator treatment in the first week of life. Their distribution related to Apgar scores are specified in table 1; †p=0.42; ‡p=0.40; §p=0.61; ¶p=0.45; **p=0.03; ††p=0.04; ‡‡p=0.009; §§p=0.01; ¶¶p=0.06; ***none in the cell; †††p=0.003; ‡‡‡p=0.004; §§§defined as pathological score of at least one of the other items. p<0.00005.

them lived for more than one year. If these children had been included, it is possible that the relative risk of impairments due to low Apgar score would have been slightly higher.

In a review of follow up studies of “perinatal asphyxia”, Paneth and Stark¹⁶ concluded that these studies, despite heterogeneous designs, had consistent results in that the great majority of children develop normally and that the distinct minority who develop chronic brain impairment have three characteristics: their asphyxia is likely to be very severe and prolonged; they commonly show neurological signs in the neonatal period such as seizures, uncoordinated feeding, and difficulties with respiratory control; and the subsequent handicap is generally severe, often multiple, and virtually always involves the motor system. Possible associations between perinatal events and later minor impairments are not so well documented.^{16–18}

The National Collaborative Perinatal Project reported a slight association between low Apgar scores at five minutes and learning difficulties, hyperkinetic-impulsive behaviour, and neurological soft signs.¹⁹ In a review of 24 studies of “asphyxia” that took place before the early 1970s, Gottfried²⁰ concluded that, in survivors without frank pathology, cognitive deficits were more prevalent in preschoolers than in older children. In the present study, the need for extra resources in kindergarten had a stronger association with low Apgar scores and neonatal symptoms than the need for extra resources in school.

The academic performance of young school aged children who have experienced perinatal asphyxia has rarely been assessed.²¹ Some studies have shown no decrease in IQ in non-disabled survivors with depressed Apgar scores, but the

severity of encephalopathy has had some impact.^{3, 22–24} The St Louis study reported that 7 year old children who had been “anoxic” at birth tended to show deficits in reading.²³ Significantly more delayed skills in reading, spelling, and/or arithmetic among children with moderate than mild encephalopathy have also been shown by others.²⁴

Comparisons between the present and earlier studies are difficult because neonates with a suspected risk of later adverse outcome are selected in different ways—for example, the term “asphyxia” has been used with a variety of definitions.²⁶ In the present study, however, we wanted to avoid the term “perinatal asphyxia” as the term is poorly defined, but rather use more easily defined markers such as the five minute Apgar score in combination with symptoms compatible with neonatal encephalopathy in the first week of life, which we considered were easily observed by parents. We realise that such symptoms may have causes other than perinatal ischaemia or hypoxaemia, and that the present study therefore shows an association of neonatal depression in a wider sense with later impairments.

The most striking finding of this study is the consistently increased risk of minor impairments in children with both a low Apgar score of 0–3 and symptoms of subsequent neonatal encephalopathy, whereas a similarly depressed Apgar score without neonatal symptoms was not associated with an increased risk. Intermediate Apgar scores of 4–6 at five minutes combined with neonatal symptoms were associated with later impairments to a much lesser degree. The interpretation may be that such symptoms after a low Apgar

score may reflect underlying brain damage, while intermediate Apgar scores as well as symptoms of neonatal encephalopathy without a previous low Apgar score, or a low Apgar score without such symptoms, may reflect a variety of adaptive problems from intrauterine to extrauterine life, not necessarily associated with brain injury.

The potential for preventing the outcomes studied here may be limited even if the high risk children identified by this study could be given effective treatment. During the period of this study, only 0.1% of children without congenital malformations had a five minute Apgar score of 0–3, and 0.6% had a score of 4–6.²⁷ In our sample, about one half of the children with a score of 0–3 had symptoms of neonatal encephalopathy. As few as 0.05% of the population may therefore be assumed to have a combination of a very low Apgar score and neonatal encephalopathy. Even with a relative risk of 20 for a particular outcome, an exposure that affected as few as 0.05% of the population would account for less than 1% of the cases of that condition (calculated as the population attributable risk).

An elaborate neurological examination in the early neonatal period may possibly improve the identification of infants at risk, but early markers of later impairments with both a high sensitivity and specificity are lacking. As most children with low Apgar scores and subsequent symptoms of neonatal encephalopathy will develop normally, these criteria do not seem to be sufficient to select infants for studies of early intervention that may be harmful.

In a clinical setting, however, these criteria may be useful in identifying children in need of follow up after discharge. The study shows that these children face a significantly increased risk of later impairments, and follow up beyond excluding major handicaps should therefore be considered. On the other hand, if a child with a severely depressed Apgar score does not develop seizures, have feeding difficulties, or require ventilator treatment in the first week of life, parents and health care workers may be reasonably reassured that the child has no increased risk of later impairments compared with children who appear to be healthy at birth.

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Authors' affiliations

D Moster, T Markestad, Department of Paediatrics, Haukeland University Hospital, N-5021 Bergen, Norway
D Moster, RT Lie, Division for Medical Statistics, Department of Public Health and Primary Health Care, University of Bergen, Armauer Hansen's building, Haukeland Hospital, N-5021 Bergen, Norway
D Moster, RT Lie, Medical Birth Registry of Norway, Locus of Registry-based Epidemiology, Armauer Hansen's building

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