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Functional outcome at school age of neonatal post-hemorrhagic ventricular dilatation☆,☆☆

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ABSTRACT

Background: Specific knowledge about the functional outcome of preterm born children with post-hemorrhagic ventricular dilatation (PHVD) is lacking.
Objectives: To determine functional outcome at school age in children with post-hemorrhagic ventricular dilatation and to identify whether PHVD characteristics increased the risk for deficits.
Methods: Single-center case–control study. Included were preterm children born between 1996 and 2003 who had PHVD in their neonatal period. The controls were children matched for gestation, gender, and year of birth. At school age, using standardized tests and questionnaires, we assessed intelligence, attention, verbal memory, executive functioning, visual perception, visuomotor integration, motor skills, and behavior.
Results: Of 34 children with PHVD 28 survived, three of whom could not be tested at school age (one child's parents declined and two were lost to follow-up). At a mean age of 10 years (6–14 years) the total and verbal IQs of the remaining 25 children (17 boys, 8 girls) were significantly lower compared to controls (difference in total IQ—14 points, verbal IQ—9 points, $P = 0.001$and $P = 0.009$, respectively). After adjustment for possible confounders, the performance of the PHVD group was poorer on visual perception and attention tests. Selective attention showed a trend toward risk of borderline and abnormal scores (OR 4.03, 95%-CI 0.84–19.2). Within the PHVD group, total IQ was significantly lower ($P = 0.048$) in those who had undergone surgical intervention ($n = 12$).
Conclusion: At school age, intelligence, attention, and visual perception were more affected in the PHVD group than in the matched controls. Surgical intervention was associated with lower IQ scores.

1. Introduction

Bleeding into the ventricles due to germinal matrix hemorrhage–intraventricular hemorrhages (GMH-IVH) is one of the major causes of hydrocephalus in preterm infants, leading to posthemorrhagic ventricular dilatation (PHVD) in up to 25% [1,2]. PHVD increases the risk of poor outcome, e.g. cerebral palsy (CP), developmental delay, and hearing and visual deficits [3,4]. Large decreases in mortality were seen after shunt surgery was introduced, but more functional deficits were also reported [5–7].

Current studies on the outcome of children who had PHVD as neonates have limitations. Three studies assessed the children at preschool age [6,8,9] when the results of developmental and neuropsychological tests are less reliable. By testing children at school age it is possible to assess a larger array of neuropsychological domains. The few outcome studies on PHVD children at school age, however, focus mainly on intelligence. They report a lower overall IQ characterized by a poorer performance IQ rather than verbal IQ [10–13] although some studies do not support this finding [7]. Finally, none of these studies corrected for perinatal characteristics, which possibly confounded the impact of

Abbreviations: AVLT, Auditory Verbal Learning Test; BRIEF, Behavior Rating Inventory of Executive Function; CBCL, Child Behavior Checklist; CP, Cerebral palsy; CSF, Cerebrospinal fluid; GMFCS, Gross Motor Function Classification System; GMH-IVH, Germinal matrix hemorrhage–intraventricular hemorrhage; IQ, Intelligence quotient; MACS, Manual Ability Classification System; Movement-ABC, Movement Assessment Battery for Children; NEPSY-II, Developmental Neuropsychological Assessment; NICU, Neonatal intensive care unit; PHVD, Post-hemorrhagic ventricular dilatation; TEA-Ch, Test of Everyday Attention in Children; WISC-III^{NL}, Wechsler Intelligence Scale for Children, Dutch version.

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PHVD on outcome. Consequently, it is unclear whether school aged children who had PHVD show other deficits apart from intelligence, and whether these deficits are related to PHVD or to other perinatal characteristics.

The primary aim of our study was to compare cognitive, motor, and behavioral functioning of children at school age, who had PHVD as neonates, with controls without PHVD but matched for gestational age, year of birth, and gender. Our second aim was to determine whether factors associated with PHVD, e.g. surgical interventions to treat PHVD or drain infections, were associated with functional outcome.

2. Methods

2.1. Patients

This was a case–control study. From our database we retrieved 34 infants born preterm between 1996 and 2003, who had been admitted to the neonatal intensive care unit (NICU) of University Medical Center Groningen (UMCG), and who had developed PHVD following GMH-IVH. PHVD was diagnosed on coronal cerebral ultrasound scans and defined as Evans' index >0.33, calculated as the right and left lateral horn width together, divided by the maximum of the internal skull width [14]. If the diameter of the lateral ventricle reached a cutoff point of more than 4 mm above the 97th percentile, in compliance with reference values of ventricular width [15], intervention was performed in accordance to our local protocol. Intervention consisted of serial lumbar punctures for 2 weeks with assessment of ventricular size through cerebral ultrasound scans. When ventricular size did not decrease, or was progressive, temporarily or definitive drainage was performed by means of Ommaya reservoir or ventriculoperitoneal shunt insertion.

Five infants died during the neonatal period, and one child died of pneumonia at the age of three (18%). Of the 28 surviving children, one set of parents declined to participate and two children were lost to follow-up, leaving 25 (89%) children who participated in the study. Three children in the PHVD group were unable to participate in our testing procedure due to learning problems. In these cases, we used the total IQs provided by the medical day-care centers they attended.

For each PHVD child selected we included a control without PHVD from the same database, matched for gestational age, year of birth, and gender. We excluded infants with major chromosomal or congenital anomalies. Table 1 contains the characteristics of the 25 children in the PHVD group and the 25 matched controls.

2.2. Follow-up

The children and their parents were invited to participate in an extension of the UMCG's routine follow-up program. School performance was also assessed. Parents gave their informed consent for their child to participate. The program entailed assessment of cognitive, motor, and behavioral functioning at school age. For those children who were unable to participate in the entire follow-up program due to learning problems, we obtained test results from their special school or medical day-care center, if such information was available.

We used a shortened version of the Wechsler Intelligence Scale for Children, 3rd Edition, Dutch version (WISC-III^{NL}) [16,17] to assess total, verbal, and performance intelligence quotients (IQ). We present the contents of the neuropsychological testing battery, functions and referring names in Table 2 [16–22,26,27]. The study was approved by the UMCG's Medical Ethical Committee.

2.3. Motor outcome

We determined the presence or absence of CP following Bax' criteria [23]. Children who developed CP were classified by a physiatrist using the Gross Motor Function Classification System (GMFCS) [24]. We used the Manual Ability Classification System (MACS) to classify the children's manual abilities [25]. High levels on MACS and GMFCS indicate serious impairment of functional abilities.

In the children with PHVD, we used Touwen's neurological examination to determine the neurological status of the children without CP and

Table 1
Patient demographics.

	PHVD ($n = 25$)	Controls ($n = 25$)	P
Males/Females	17/8	17/8	1.0
Gestational age (weeks)	28 (25–36)	29 (25–37)	0.63
Small for gestational age	1 (4)	5 (20)	0.19
Birth weight (g)	1290 (870–3017)	1240 (480–2745)	0.62
Apgar at 5 min	8 (3–10)	9 (2–10)	0.18
Resuscitation	4 (16)	1 (4)	0.35
Ventilatory support	20 (80)	17 (68)	0.52
Cerebral pathology			
Mild GMH-IVH	12 (48)	9 (36)	0.57
Severe GMH-IVH	13 (52)	None	0.0001
Periventricular venous infarction	5 (20)	2 (8)	0.42
Periventricular leukomalacia	10 (40)	6 (24)	0.36
Cystic periventricular leukomalacia	2 (8)	None	0.49
Evans' index	0.46 (0.36–0.60)	–	–
Intervention	12 (48)	none	0.0001
SES low $n = 23/21$	15 (65)	11 (52)	0.541
Late onset morbidity			
Meningitis	5 (20)	0 (0)	0.05
Bronchopulmonary dysplasia	7 (28)	8 (32)	1.0

Data is presented as median (range) or as number (percentage).
Resuscitation was defined as administration of inotropics and/or chest compressions.
Mild GMH-IVH was defined as grades I and II, severe GMH-IVH as grades III and IV.
PVL defined as periventricular echodensities for more than 1 week as seen on ultrasound.
Evans' index was defined as highest index measured as seen on ultrasound.
Sepsis and/or meningitis was defined when proven on culture.
SES (socio-economic status) was based on the mothers' educational level and profession.

Table 2
Contents of neuropsychological testing battery, functions and referring names in text.

Test/Scale names	Functions	Referring name
WISC-III-NL [16,17]	Short version of intelligence test	Intelligence
Total IQ	Global intellectual level	Total IQ
Verbal IQ	Verbal intelligence	verbal IQ
Performance IQ	Performance intelligence	performance IQ
AVLT [18]	Immediate verbal memory	verbal memory
Delayed recall	Active long-term memory	Delayed recall
Recognition	Passive long-term memory	Recognition
NEPSY-2 design copying [19]	Visuomotor functioning	Visuomotor integration
NEPSY-2 geometric puzzles	Central visual perception	Visual perception
TEA-Ch-NL map mission [20]	Selecting targets from distractors	Selective attention
TEA-Ch-NL opposite world	Attention shifting	Aattention control
BRIEF[21]	Executive function in everyday life	Executive function
CBCL total problems [22]	Total behavioral outcome	Total behavioral problems
CBCL internalizing problems	Internalizing behavior problems	Internalizing behavioral problems
CBCL externalizing problems	Externalizing behavior problems	Externalizing behavioral problems
Touwen's neurological examination [26]	Neurological status	Touwen's neurological examination
Movement Assessment Battery for Children [27]	Motor skills	Movement-ABC

WISC-III-NL, Wechsler Intelligence Scale, third edition, Dutch version; ALVT, Rey Auditory Verbal Learning Test; NEPSY-2, Developmental Neuropsychological Assessment; TEA-Ch-NL, Test for Everyday Attention for Children Dutch version; BRIEF, Behavior Rating Inventory of Executive Function parent form; CBCL, Child Behavior Checklist parent report form.