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Follow-up at age 10 years in ELBW children — Functional outcome, brain morphology and results from motor assessments in infancy☆,☆☆

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ABSTRACT

Background: Extremely-low-birth-weight (ELBW) children without severe brain injury or CP are at high risk of developing deficits within cognition, attention, behavior and motor function. Assessing the quality of an infant's spontaneous motor-repertoire included in Prechtl's General-Movement-Assessment (GMA) has been shown to relate to later motor and cognitive functioning in preterm children without CP.
Aims: To investigate functional outcome and cerebral MRI morphometry at 10 years in ELBW children without CP compared to healthy controls and to examine any relationship with the quality of infant-motor-repertoire included in the GMA.
Study design: A cohort-study-design.
Subjects: 31 ELBW children (mean birth-weight: 773 g, SD 146, mean gestational age 26.1 weeks, SD 1.8) and 33 term-born, age-matched controls.
Outcome measures: GMA was performed in ELBW children at 3 months corrected age. At 10 years the children underwent comprehensive motor, cognitive, behavioral assessments and cerebral MRI.
Results: The non-CP ELBW children had similar full-IQ but poorer working memory, poorer motor skills, and more attentional and behavioral problems compared to controls. On cerebral MRI reduced volumes of globus pallidus, cerebellar white matter and posterior corpus callosum were found. Cortical surface-area was reduced in temporal, parietal and anterior-medial-frontal areas. Poorer test-results and reduced brain volumes were mainly found in ELBW children with fidgety movements combined with abnormal motor-repertoire in infancy.
Conclusion: Non-CP ELBW children have poorer functional outcomes, reduced brain volumes and cortical surface-area compared with term-born controls at 10 years. ELBW children with abnormal infant motor-repertoire seem to be at increased risk of later functional deficits and brain pathology.

1. Introduction

The survival rates of children born with extremely-low-birth-weight (ELBW, BW < 1000 g) have been increasing during the last decades [1]. However, the number of ELBW children who develop disabilities like cerebral palsy (CP), cognitive impairments, and psychiatric and behavioral problems is still high compared with term-born peers [2]. Increased incidence of perinatal brain injury is the most common cause of the neurologic morbidity reported in preterm born children [3]. The brain injuries include focal periventricular white matter necrosis and diffuse white matter injury with widespread gliosis and axonal damage that may have secondary effects on development of the immature cerebral cortex, thalamus, cerebellum and basal ganglia [3,4]. A qualitative general movement assessment (GMA) in infants based on the observation

Abbreviations: ELBW, extremely low birth weight; MRI, magnetic resonance imaging; CP, cerebral palsy; GMA, general movement assessment; WISC, Wechsler Intelligence Scale for Children; IQ, intelligence quotient; MABC, Movement assessment battery for children; ADHD, attention-deficit/hyperactivity disorders; BRIEF, Behavioral Rating Inventory of Executive Function; SGA, small-for-gestational-age.

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of spontaneous movements during the early post-term period is a sensitive and non-intrusive method to predict motor disorders like CP in later childhood [5]. A recent study suggested that the quality of general movements might be an early predictor also for cognitive function in very preterm born children [6] however, that study did not include motor or behavioral outcomes. We previously reported that the assessment of infant motor repertoire in a group of high risk neonates might be an early clinical marker for a composite of later motor dysfunction and cognitive impairments in non-CP children [7]. As an extension of that study we now aimed to examine the functional outcome and brain pathology evaluated with MRI morphometry at age 10 years in a cohort of ELBW children without CP compared with healthy term-born controls. In addition, we aimed to study whether early infant motor repertoire in the ELBW children that did not develop CP was associated with functional outcome and cerebral MRI findings at age 10. We hypothesized that non-CP ELBW children would have inferior functional test results and more brain pathology than controls and that pathological outcome would be related to abnormal early motor repertoire.

2. Methods

This geographically based follow-study included three year-cohorts of ELBW children born at the Trondheim University Hospital in Norway during the years 1999–2001. Inclusion criteria were children with birth-weight below 1000 g who participated in the regular follow-up at the Trondheim University Hospital. Exclusion criteria were diagnosed congenital syndromes. A total of 74 ELBW children were born and admitted to the Neonatal Intensive Care Unit (NICU) in Trondheim during the three year period. Nine children (12%) died during the neonatal period and 30 children had follow-up at other hospitals; hence 35 ELBW children were asked to participate in the study. Parents of 31 (88.6%) children gave their written consent. At follow-up the ELBW children were assessed at a mean age of 10 years and 2 months (SD 0.8). A term-born, age-matched control group of 33 healthy children were recruited from four different schools within the Trondheim area. Mean age at examination for controls was 10 years and 6 months (SD 0.7).

2.1. General movement assessment (GMA)

At 14 weeks (SD 1.6) post-term age, all the ELBW children were videotaped at the NICU as part of a standard follow-up program for general movement assessment (GMA) including an “Assessment of Motor Repertoire” [5]. Assessment of Motor Repertoire is part of the GMA and provides a motor optimality score consisting of the parameters: fidgety movements, repertoire of co-existent movements, quality of other movements, quality of postural patterns and quality of infant motor repertoire. A certified child physiotherapist and a pediatrician reanalyzed all the video recordings at the 10-year follow-up, independently and blinded to neonatal medical history, earlier assessments and later outcome of the children. In case of disagreement of scoring (in two videos), a second evaluation was performed by each researcher independently and consensus was reached. In this study we focused on fidgety movements and motor repertoire. Fidgety movements seen as small, continuous movements of moderate speed and variable acceleration in the whole body in any direction from the age of 6 weeks to 20 weeks post-term, were classified as normal “F+” when present continuously. When the fidgety movements were completely absent, they were classified as “F−”, and when they were sporadic or not continuously present they were classified as “F+/−”. For the Assessment of Motor Repertoire a classification of concurrent motor repertoire based on the categories of Bruggink et al. [8] was used. Concurrent motor repertoire was defined as “normal” when the movements were fluent, variable and smooth, and “abnormal” when the movements were monotonous, jerky or stiff. The videotapes of two infants were of too poor quality to be analyzed, and in three children the videotapes were lost to follow-up; hence videotapes from 26 of 31 ELBW infants (84%) were analyzed with GMA.

2.2. Clinical assessments

The Wechsler Intelligence Scale for Children, version-III (WISC-III) [9] was administered to all children and full intelligence quotient (IQ) and four IQ indices were calculated. The neuropsychological assessment included the Stroop Color Word [10] to assess the ability to respond selectively to competing stimulus and selective attention. The Tower of London test [11] was included to assess planning and problem-solving ability and The Trail-Making Test [10] for assessing attention and focused attention. The Beery–Buktenica Developmental Test of Visual–Motor Integration (Beery-VMI) [12] was used to assess visual, perceptual and constructional abilities. The Movement-Assessment-Battery for Children, second-edition (MABC-2) [13] was administered to assess motor skills. For the MABC-2, higher scores indicate better performances and lower scores mean poorer performances on the test.

2.3. Questionnaires

The ADHD rating scale [14] questionnaire was completed by all parents to assess hyperactivity and inattention. Executive function was evaluated by the parental reported Behavioral Rating Inventory of Executive Function (BRIEF) [15]. Higher scores indicate poorer performance.

2.4. Cerebral MRI

Cerebral MRI was acquired on a 1.5 Tesla Siemens Avanto MR scanner (Siemens, Erlangen, Germany) with Quantum gradients 40 mT/m and a 12 channel head coil. A structural T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence was acquired. For the image analysis of brain morphology, we used the freely available FreeSurfer software version 5.1 (http://surfer.nmr.mgh.harvard.edu/). Further details about MRI acquisition and analysis can be found in the Supplemental materials. MRI was not performed in four ELBW children without CP due to anxiety and in one child the performed MRI scan had to be excluded due to movement artifacts. Hence MRI was successfully performed in 21 ELBW children without CP. In the control group, one child had braces and two children did not consent to MRI scanning, hence MRI was successfully completed in 30 control children.

2.5. Socioeconomic status

Socioeconomic status (SES) was calculated according to Hollingshead's two-factor index of social position based on mean educational levels and current employment of both or single parents [16].

2.6. Statistics

IBM SPSS Statistics, version 21 (Armonk, NY) was used for the statistical analyses. The Student t-test, Mann–Whitney U-test and Chi-squared test were used for group comparisons. A General Linear Model (GLM) was used to compare group differences in brain volumes, cortical thickness and brain surface area with SES, gender and age at MRI as covariates. The same model was used to compare group differences in clinical test results between the two groups. We used the partial correlation analysis controlled for SES, gender and age at MRI to calculate the linear correlation between different test results and brain regions of interest based on MRI results. Two-tailed p value ≤ 0.05 was considered to be statistically significant, except when looking at group comparisons of brain volumes where a p-value ≤ 0.01 was used as level of significance to adjust for multiple comparisons.