Early Human Development 95 (2016) 47–53

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Executive function relates to surface area of frontal and temporal cortex in very-low-birth-weight late teenagers

Heidi Furre Østgård [a], Anne Elisabeth Sølsnes [a,*], Knut Jørgen Bjuland [a], Lars Morten Rimol [a,h], Marit Martinussen [a,b], Ann-Mari Brubakk [a,c], Asta Kristine Håberg [d,e,f], Jon Skranes [a,g], Gro Christine Christensen Løhaugen [a,g]

[a] Department of Laboratory Medicine, Children's and Women's Health, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
[b] Department of Obstetrics, St Olav University Hospital, Trondheim, Norway
[c] Department of Pediatrics, St Olav University Hospital, Trondheim, Norway
[d] Department of Circulation and Medical Imaging, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
[e] Department of Neuroscience, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
[f] Department of Medical Imaging, St Olav University Hospital, Trondheim, Norway
[g] Department of Pediatrics, Sørlandet Hospital, Arendal, Norway
[h] Department of Medicine, University of Haw, ai'i, Honolulu, HI, USA

ARTICLE INFO

Article history:
Received 31 August 2015
Received in revised form 25 January 2016
Accepted 29 January 2016

Keywords:
Very-low-birth-weight
Preterm birth
Executive function
Attention
Cerebral MRI
Cortical surface area

ABSTRACT

Background: Being born with very low birth weight (VLBW; birth weight (BW) ≤1500 g) is associated with increased risk of maldevelopment of the immature brain which may affect neurological functioning. Deficits in attention and executive function problems have been reported in VLBW survivors compared with healthy subjects.
Aims: The aim of this study was to evaluate attention and executive functions and to relate the clinical test results to cortical morphometry findings in VLBW young adults compared with term-born controls.
Study design: Prospective follow-up study of three year cohorts of VLBW and control children from birth to adulthood.
Outcome measures: A comprehensive neuropsychological test battery was administered to 55 VLBW subjects born preterm (mean BW: 1217 g) and 81 term-born controls (mean BW: 3707 g) at age 19–20. Cerebral MRI was successfully obtained in 46 VLBW subjects and 61 controls. The FreeSurfer software package was applied for the cortical analyses based on T1-weighted MRI images.
Results: The VLBW group obtained inferior scores on 15 of the 29 neuropsychological measures assessing attention and executive function and on both the attention and executive function domain scores. We found positive correlations between the executive function domain score and cortical surface area, especially in the antero-medial frontal and the temporal lobes of the brain in the VLBW group.
Conclusion: Young adults born with VLBW show deficits in attention and executive function compared with controls. The executive problems were related to smaller cortical surface area in brain regions known to be involved in higher order cognitive functioning.

1. Introduction

Approximately 1.5% of all live births are infants born preterm with very low birth weight (VLBW; birth weight < 1500 g) [1]. Cognitive deficits without major motor problems affect up to 50% of VLBW survivors, and are considered the most prevalent neurologic sequelae in this population [1]. Very low birth weight has been associated with lower IQ scores compared with term born controls in childhood [2] and lasting into adulthood [3,4]. This may in turn lead to deficits in academic and professional achievement [4,5]. The increased survival rate and persistent cognitive, psychological and general health problems also imply that clinicians will meet this high risk group in increasing numbers in adulthood [6].

Studies published on VLBW adults have reported poorer scores on general intelligence and executive functions [3,4,7,8]. Nosarti et al. [7] reported executive function impairments, including slower processing speed, in adults (age 22) born very preterm (VP) (<33 weeks of gestation). Pyhälä et al. [8] found lower scores on

Abbreviations: VLBW, Very Low Birth Weight; IQ, Intelligence Quotient; WAIS-III, Wechsler Adult Intelligence Scale – III; GA, gestational age; SES, Socioeconomic status; WMS-III, Wechsler Memory Scale-III; ES, Effect Size; MRI, Magnetic Resonance Imaging; CP, Cerebral Palsy.

* Corresponding author at: Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Medisinsk teknisk forskningssenter, N - 7489 Trondheim, Norway.
E-mail address: anne.e.solsnes@ntnu.no (A.E. Sølsnes).

http://dx.doi.org/10.1016/j.earlhumdev.2016.01.023
0378-3782/

general IQ and tests assessing executive functions, attention and visual memory among 25 year old VLBW subjects compared with term born controls. These findings were confirmed by Eryigit Madzwamuse et al. [3] who showed that also their cohort of VP/VLBW adults (age 26) obtained lower IQ scores and poorer scores on executive functions tests than term born controls. This suggests persisting cognitive deficits in VLBW survivors.

Perinatal brain injuries are common in preterm born children and may have consequences for normal maturation and growth of the immature brain [1]. Aberrant cortical findings include less complex cortical folding [9], smaller cortical surface area [10] and deviations in cortical thickness [11,12]. Recent studies have started to explore possible cortical structure–function relationships in the preterm brain in adolescence and early adulthood. Lower IQ scores in the VLBW group have been related to cortical thinning and reduced surface area in adolescents [10] and young adulthood [9,11]. A subgroup from the study sample also completed the Behavior Rating Inventory of Executive Function Adult-version (BRIEF-A), but few correlations between self-report and test-results assessing attention/executive functions were found [12].

To our knowledge, no study has looked at the relationship between attention and executive functions and cortical measures in brain areas known to take part in higher order cognitive functions in VLBW survivors reaching early adulthood. This study therefore aimed to assess attention and executive function and to relate clinical test results to cortical morphometry findings in VLBW young adults compared with term-born controls.

We hypothesized that VLBW young adults would obtain inferior results scores on the individual neuropsychological tests and on the domain scores compared with controls, and that there would be structure–function relationships between attention and executive domain scores and surface area and cortical thickness in higher order brain regions in the frontal, parietal and temporal lobes.

2. Material and methods

This study is a hospital-based follow-up study of the long term clinical consequences of being born preterm with very low birth weight (VLBW: BW < 1500 g). Three year cohorts (born in 1986–88) of VLBW children and controls born at term appropriate for gestational age (bw > 10th percentile) were evaluated at the age of 19 to 20 years.

2.1. VLBW group

A total of 121 children with VLBW (birth weight < 1500 g) were admitted to the neonatal intensive care unit (NICU) at the University Hospital in Trondheim, Norway. Of these, 33 children died and nine were not contactable at follow-up. One child with Down syndrome and two young adults with severe cerebral palsy (CP) classified at Gross Motor Function Classification System (GMFCS) level V were excluded because they were unable to perform the neuropsychological tests. Of the remaining 76 young adults, a total of 55 (72%) agreed to participate at 19–20 years of age. These participants were also assessed at one and six years of age (one year cohort of VLBW only) and also at 14 years of age (VLBW and controls). A total of 50 VLBW subjects were examined with cerebral MRI at age 19–20. The scans of four subjects had to be rejected due to motion artifacts, leaving 46 VLBW subjects for inclusion in the MRI analysis. Neurological examinations at 14 years of age showed that four of those participating at 19–20 years of age had CP: two had spastic diplegia and were classified at GMFCS level II, and two had combined spastic diplegia and hemiplegia, of whom one was classified at GMFCS level I and one at GMFCS level IV. No participant was visually impaired (according to the World Health Organization definition) based on the 14 year follow-up visual examination.

2.2. Controls

The term born controls was recruited from the same year cohorts and living in the Trondheim region. The group originally consisted of 122 children, but two subjects with congenital malformations were excluded and 10 were not contactable at follow-up. The recruitment of the control group has been reported previously [4]. From the 110 eligible subjects, 81 (74%) met for cognitive assessment and 66 had cerebral MRI. Due to motion artifacts caused by dental braces, poor image quality or lack of concomitant cognitive assessment five MRI scans were excluded.

2.3. Non-participants

There were no significant differences between participants and non-participants in any of the groups regarding maternal age at child birth, gestational age, birth weight and socio-economic status.

2.4. Ethics

The Regional Committee for Medical Research Ethics approved the study protocol (project number 4.2005.2605). Written informed consent was obtained from each participant. All participants were offered a follow-up session about their test results with the clinical neuropsychologist.

2.5. Socio-economic status

Socio-economic status (SES) was calculated according to Hollingshead's Two Factor index of Social Position, based on the education and occupation of both parents [14]. Information regarding occupational and educational attainment in the young adults was obtained through a short interview. SES data was missing in four VLBW subjects and seven control participant and for those SES values were imputed by the multiple imputation method. Sex, age at assessment and SES were included as covariates in all analyses on group differences.

2.6. Cognitive assessment

The neuropsychological testing was performed by a trained neuropsychologist who was blind to group affiliation and medical history. Testing took place during one session with a fixed order of tasks. A comprehensive neuropsychological test battery assessing IQ, attention, executive function, language, visual/motor and memory function was administered. A detailed description of the neuropsychological tests performed in the present study is given in Supplemental Material (S1). A Confirmatory Factor Analysis was applied to extract domain scores based on the individual tests, as reported before [15]. Full IQ was assessed by the Wechsler Adult Intelligence Scale 3rd edition (WAIS-III), and results have been published earlier [5].

2.7. Neonatal variables

The following clinical variables were considered: birth weight, gestational age, head circumference at birth, birth length, Apgar scores at 1 and 5 min, days in the NICU, days on mechanical ventilator, days to regain birth weight and maternal age at child birth.

2.8. MR imaging

2.8.1. Image acquisition

Cerebral MRI was performed on a 1.5 T Siemens Magnetom Symphony Sonata System with Quantum gradients (30 mT/m) and a quadrature head coil. We used a structural T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence with: TR = 7100 ms,