



Very preterm adolescents show impaired performance with increasing demands in executive function tasks[☆]



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ARTICLE INFO

Article history:

Received 26 June 2015

Received in revised form 29 September 2015

Accepted 26 October 2015

Keywords:

Very preterm birth
executive function
task demand
child development

ABSTRACT

Background: Very preterm birth is often associated with executive function deficits later in life. The transition to adolescence increases personal autonomy, independence and, in parallel, the demands placed on executive functions at home and in school.

Aim: To assess the impact of increasing demands on executive function performance in very preterm children and adolescents with normal intellectual and motor functions.

Methods: Forty-one very preterm children and adolescents with normal intellectual and motor functions and 43 healthy term-born peers were assessed at a mean age of 13.0 years (SD: 1.9; range: 10.0–16.9). A comprehensive battery of performance-based executive function measures with different demand levels as well as a parent-rating questionnaire evaluating executive functions relevant for everyday life was applied. Standardized mean differences between groups of $d \geq .41$ were regarded as clinically relevant.

Results: No group differences were found at the lowest demand levels of working memory ($d = .09$), planning ($d = -.01$), cognitive flexibility ($d = -.21$) and verbal fluency ($d = -.14$) tasks, but very preterm participants scored significantly below their term-born peers in the most demanding levels ($d = -.50, -.59, -.43$ and $-.55$, respectively). These differences were clinically relevant. Executive functions relevant for everyday life were strongly impaired in very preterm participants, e.g., global executive composite ($d = -.66$).

Conclusion: Very preterm children and adolescents with normal intellectual and motor functions are at high risk for executive function deficits that may only become apparent with increasing demands, potentially leading to academic and other deficits.

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Abbreviations: ANCOVA, analysis of covariance; BRIEF, Behavior Rating Inventory of Executive Function; CANTAB, Cambridge Neuropsychological Test Automated Battery; CI, confidence interval; IES, intra-/extradimensional shift; IQ, intelligence quotient; SES, socio-economic status; SOC, Stockings of Cambridge; SMD, standardized mean difference; SWM, spatial working memory; TB, term-born; VPT, very preterm; WISC-IV, Wechsler Intelligence Scale for Children 4th edition.

[☆] Competing interests: none.

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1. Introduction

Many very preterm children and adolescents experience behavioral, social and academic problems in the absence of major motor and cognitive disabilities [1–4], resulting in a high need for support and special care [2,4]. Executive functions, that is higher-order cognitive processes such as working memory, cognitive flexibility, verbal fluency or planning [5,6] are also often impaired in very preterm children [7–11] and adolescents [12–15]. Importantly, these executive functions have been shown to be involved in the development of the social, behavioral and academic difficulties which very preterm children and adolescents frequently encounter [12,16–18].

These difficulties in academic performance and other aspects of everyday life often increase or only become apparent as very preterm

children become older and reach secondary school level [2]. This transition to secondary school is accompanied by increasing demands placed on executive functions both at home and school as personal autonomy, independence and planning responsibilities grow [19,20]. It could therefore be hypothesized that the rising incidence of academic and other difficulties in very preterm children and adolescents is associated with the increased demands placed on executive functions during this age period and, thus, that very preterm children may have difficulties in coping with these increasing demands.

However, the effect of increasing demands on executive function performance in very preterm children and adolescents is not yet clear. To date, no study has systematically investigated how the level of demands placed on executive functions impacts task performance in very preterm children at the transition to adolescence. Specifically, it is not clear whether very preterm children and adolescents with normal intellectual and motor functions perform differently from their term-born peers in response to increasing demands.

Hence, the current study investigated the impact of increasing task demands on executive function performance in a group of very preterm children and adolescents with normal intellectual and motor functions by applying a comprehensive battery of executive function tasks with different demand levels in parallel with a parental questionnaire evaluating executive functioning in everyday life. The aim was to clarify whether increasing demands have a greater impact on executive function performance in those born very preterm compared to those born at term, and whether everyday functional impairments are different between the two groups. We expected that the level of demands placed on executive function abilities has a greater impact on task performance and that everyday functional abilities are more strongly impaired in very preterm children and adolescents compared to healthy term-born peers.

2. Material and methods

2.1. Participants and study procedure

Former patients of the Department of Neonatology, University Hospital Zurich, Switzerland who fulfilled the following inclusion criteria were recruited for the current study 1) born ≤ 32 weeks of gestation; 2) no evidence of cystic periventricular leukomalacia or hemorrhagic infarction on neonatal ultrasound; 3) no cerebral palsy or developmental delay ($IQ < 85$) at the routine follow-up consultations at the Child Development Center, University Children's Hospital Zurich, Switzerland between the ages of four and eight years; and 4) at the time of the assessment, they were between ten and sixteen years old. A total of 175 children fulfilled all inclusion criteria and were contacted by letter. Of these, 41 children and adolescents and their parents accepted the invitation to participate (23.4%). Those who participated did not differ from those who did not participate with regard to gestational age, birth weight, perinatal complications and IQ assessed at the follow-up consultation (all $p > .05$). Friends and siblings of very preterm participants and children and adolescents from local schools were recruited for the control group. Inclusion criteria were term birth (≥ 37 weeks gestation), no perinatal complications and no neurodevelopmental illnesses (e.g., attention-deficit-hyperactivity-disorder). Forty-three term-born (TB) participants were included and group-matched to the very preterm (VPT) participants with regard to gender and age at assessment.

Over the course of an afternoon, an examiner trained in cognitive testing administered various computerized and paper-pencil tests in a pseudo-randomized order. Participants were compensated with a gift certificate.

All data were collected between January and December 2013. The study was approved by the ethical committee of the Canton of Zurich, Switzerland. Written informed consent was obtained from a parent as well as from participants older than 15 years. Younger participants provided oral consent.

2.2. Measures

For VPT participants, perinatal data were collected from the hospital's medical records. Socio-economic status (SES) was estimated using a six-point scale based on maternal education and paternal occupation [21]. IQ was estimated with a 4-subtest combination of the *Wechsler Intelligence Scale for Children* (WISC-IV, German version [22]): Block design, vocabulary, letter-number-sequence, and symbol search. This subtest combination has been shown to correlate highly with the full version ($r = .95$) [23]. In a subset of 63 children and adolescents (33 VPT and 32 TB participants), the pegboard subtest of the Zurich Neuromotor Assessment (ZNA [24]) was applied. In this task, brass pegs are placed in twelve holes in a board and need to be inverted and replaced in turn using only one hand. Two runs per hand are timed and the average performance time (in seconds) of all runs is used as a measure of fine motor abilities.

2.2.1. Executive functions measures

A variety of performance-based and rating scale measures were applied for a comprehensive understanding of executive function abilities [25].

Three executive function tasks of the *Cambridge Neuropsychological Test Automated Battery* (CANTAB [26]) were randomly administered on a 12.1-inch touch screen tablet: Spatial working memory was assessed with the Spatial Working Memory (SWM) task, planning abilities were assessed with the Stockings of Cambridge (SOC) task, and cognitive flexibility was assessed with the intra-/extradimensional shift (IES) task. Detailed descriptions of the tasks and outcome measures are provided in Table 1. Due to technical problems, data for one TB participant were lost for the SOC task.

Verbal fluency was assessed using the *Regensburger Wortflüssigkeits-Test* (RWT [27]), a German-language verbal fluency test which requires participants to produce words in accordance with specific rules: In the phonetic and semantic fluency subtests, words starting with the letter 'S' or types of animals have to be generated, respectively. In the category-switching subtests, words starting with the letters 'G' and 'R' (phonetic switching) or types of fruits and sports (semantic switching) have to be named in an alternating manner. Verbal responses were recorded and later transcribed by the examiner. An additional minute of testing was added to the standard test length of one minute as the increased assessment duration of two minutes has been shown to place higher demands on verbal fluency abilities compared to one minute [27,28]. The number of words produced in the first (low demands) and the second minute (high demands) were used as dependent variables. One TB participant was not tested as German was not his first language. Data for another TB participant are missing for two subtests due to a failure of the recording device. For two VPT and two TB participants, performance was not separated in the first and second minutes, thus, only the total number of words produced within two minutes was available.

The *Behavior Rating Inventory of Executive Function* (BRIEF, German version [29]) was used to investigate whether executive function deficits translate into daily life. In this questionnaire, parents rate 86 statements regarding their children's executive functions relevant to everyday life. Eight individual subscales may be summarized in a behavioral and a cognitive regulation index. Taken together, the two index scales form the global executive composite. The individual subscales, the indices, and the composite score were used as dependent variables. For all but one VPT participant, at least one parent completed the questionnaire. If both parents completed a questionnaire separately ($n = 45$), mean values were used for the analyses.

2.3. Statistical analyses

To compare groups, univariate analyses of covariance (ANCOVAs) with SES and age at assessment as covariates were applied for all continuous variables. To assess whether performance differences between

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