# Attention Problems of Very Preterm Children Compared with Age-Matched Term Controls at School-Age

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**Objectives** To clarify the severity, specificity, and neurocognitive underpinnings of attention problems in very preterm children.

**Study design** A sample of 66 preterm (<32 weeks gestation), mean (SD) age 7.5 (0.4) years, and 66 age-matched term controls participated. Symptoms of inattention were assessed using parent and teacher-rated questionnaires, and neurocognitive measures included speed and consistency in speed of information processing, lapses of attention (tau), alerting, orienting, and executive attention, as well as verbal and visuospatial working memory. Group differences were investigated using ANOVA, and Sobel tests were used to clarify the mediating role of neurocognitive impairments on attention problems.

**Results** There was a large decrease in visuospatial working memory abilities ($P < .001$, $d = .87$), and medium increases in tau ($P = .002$, $d = 0.55$) as well as parent and teacher ratings of inattention (range $d = 0.40$-$0.56$) in very preterm children compared with term peers. Tau and visuospatial working memory were significant predictors of parent ($R^2 = .161$, $P < .001$ and $R^2 = .071$, $P = .001$; respectively) and teacher ($R^2 = .152$, $P < .001$ and $R^2 = .064$, $P = .002$; respectively) ratings of inattention, and completely explained the effects of very preterm birth on attention problems.

**Conclusions** Increased lapses of attention and poorer visuospatial working memory fully account for the attention problems in very premature children at school-age. *(J Pediatr 2012;161:824-9)*.

Improved perinatal care has increased survival rates of very preterm (<32 weeks of gestation) infants. However, very preterm birth has negative consequences on normal maturation processes in the brain,[1] which consequently result in neurocognitive and behavioral problems in very preterm children in childhood.[2-4] At school-age, attention problems are among the most prominent behavioral problems reported in very preterm children.[5,6] These attention problems may have a detrimental impact on school performance and social function in very preterm children, however, the exact nature is still poorly understood.

Attention is a multifaceted construct and involves a range of neurocognitive abilities. Besides maintaining consistent fast and accurate levels of information processing,[7] brain networks of orienting, alerting, and executive attention,[8] as well as working memory abilities are involved.[9] Brain networks of orienting, alerting, and executive attention are crucial in (1) the ability to orient to; (2) the ability to maintain focus; and (3) ability to shift attention between events, respectively, and have been extensively studied in neurobiologic research.[8] Furthermore, proper working memory abilities are essential in guiding attention by holding in mind relevant information for the task at hand.[9,10] Importantly, impairments in all these neurocognitive abilities involved in attention have been demonstrated to play a pivotal role in attention problems of children diagnosed with attention deficit/hyperactivity disorder (ADHD).[10,11] However, despite the potential for new treatment opportunities,[12-14] the roles of these neurocognitive functions in attention problems of very preterm children have not been investigated.

To elucidate the neurocognitive underpinnings of attention problems in very preterm children, we studied: (1) the severity and specificity of attention problems in very preterm children using both parent and teacher ratings of inattention at school age; (2) the differences between very preterm children and term peers on neurocognitive abilities involved in attention; and (3) the possibility that these neurocognitive functions mediate the relationship between very preterm birth and attention problems at school age.

## Methods

A sample of 66 very preterm (<32 weeks gestation) children and 66 age-matched term controls participated. All 66 very preterm children had participated in

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|---|---|
| ADHD | Attention deficit/hyperactivity disorder |
| ANT | Attention Network Test |
| CBCL | Child Behavior Checklist |
| IQ | Intelligence quotient |
| PDBD | Parent Disruptive Behavior Disorders rating scale |
| SES | Social economic status |
| TDBD | Teacher Disruptive Behavior Disorders rating scale |
| TRF | Teacher Report Form |

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Supported by an unrestricted research grant from Danone Friederichsdorf, Germany, which had no involvement in (1) study design; (2) the collection, analysis, and interpretation of data; (3) the writing of the report; and (4) the decision to submit the paper for publication. R.v.E. is an employee of Danone Research, Centre for Specialised Nutrition. The other authors declare no conflicts of interest.

 10.1016/j.jpeds.2012.05.010

a randomized controlled trial on enteral glutamine supplementation (0.3 g/kg/d) between day 3 and 30 of life.[15] For this study, all very preterm children admitted between September 2001 and July 2003 to the level III neonatal intensive care unit of the VU University Medical Center Amsterdam were eligible for inclusion, and baseline characteristics of the sample have been previously reported.[15] Of the 102 infants included in the original study, 89 infants were alive at 1-year follow-up, and 74 were participating in the 6-year follow-up. At 7-8 years of age, parents of all 74 children were contacted and invited to participate in the current study, of which 68 (92%) agreed, and 66 (89%) successfully completed all neurocognitive tasks at the mean (SD) age of 7.5 (0.4) years (Table I). The remaining 2 children were unsuccessful in completing the neurocognitive test battery. There were no differences between the glutamine and the placebo group on any of the dependent variables (all $P > .05$; all $d < 0.49$).

Age-matched, term born peers from the same classrooms as attended by the very preterm children were invited to participate in the study. Controls were required to be born >37 weeks of gestation without any perinatal complications as reported by their parents, and to attend regular classes and to be free of behavioral and academic difficulties as reported by their teacher. Using this method of recruitment, age-matched controls were recruited for 41 very preterm children. Of the remaining 25 very preterm children, 4 attended special classes and 21 schools were not willing to participate in the recruitment of age-matched controls. Additional age-matched controls (n = 25) were recruited by contacting other schools located in the same area as schools attended by the very preterm children. Social economic status (SES) was determined by classifying the highest level of education in a household on a 4-point scale, with higher scores indicating higher levels of education and corresponding higher SES.

All parents completed written informed consent prior to the study, which was approved by the medical ethical committee of the VU Medical Center. Neurocognitive assessments were at the VU University Amsterdam by qualified and trained testers using standardized instructions. Both parents and each child's teacher were asked to complete questionnaires addressing behavioral problems including attention problems at home and at school, respectively.

Parent ratings of inattention at home were derived from the Attention Problems scale of the Child Behavior Checklist (CBCL)[16] and the Inattention scale of the Parent Disruptive Behavior Disorders rating scale (PDBD).[17] Teachers completed the teacher equivalents of the parent scales, including the Teacher Report Form (TRF)[18] and Teacher Disruptive Behavior Disorders rating scale (TDBD).[17] Hyperactivity/impulsivity was measured using the Hyperactivity/Impulsivity scale of the parent-rated PDBD and teacher-rated TDBD. In addition, internalizing behavior problems and externalizing behavior problems were measured using the subscales of Internalizing Behavior and Externalizing Behavior from both the parent-rated CBCL and teacher-rated TRF. All 4 questionnaires are widely used and have excellent psychometric properties.[16-18] Scores on the CBCL and TRF were standardized using T-scores with a mean (SD) of 50 (10), and scores on the PDBD and TDBD were standardized with a mean (SD) of 10 (3), with higher scores indicating higher ratings of behavioral problems.

Intelligence quotient (IQ) was measured by a short-form of the Wechsler Intelligence Scale for Children-III,[19] including the subtests Vocabulary and Block Design. Both subtests correlate strongly ($r > .90$) with Full Scale IQ.

Orienting, alerting, and executive attention were assessed using an adapted version of the Attention Network Test (ANT)[8] suitable for the use with young children. In this task, children had to respond as fast as possible to the appearance of a target on the left side or the right side of the screen by pressing a button corresponding to the location at which the target appeared. There were 4 types of trials. Neutral trials contained a neutral cue in the middle of the screen that preceded the target. Orienting trials contained a directional cue in the middle of the screen pointing to the position of the target, which subsequently followed. Executive trials contained directional cues incongruent with the position of the

**Table I. Characteristics of very preterm children and term controls**

| | Preterm (N = 66) | Controls (N = 66) | *P* value | Effect size (*d*) |
|---|---|---|---|---|
| Age at follow-up, y (mean ± SD) | 7.5 (0.4) | 7.6 (0.5) | .41 | 0.22 |
| SES (mean ± SD) | 3.2 (0.7) | 3.2 (0.8) | .89 | 0.01 |
| Sex, male (%) | 33 (50.0) | 28 (42.4) | .39 | |
| WISC-III full scale IQ (mean ± SD) | 96.6 (17.6) | 105.8 (14.4) | **.001** | 0.92 |
| Birth weight, g (mean ± SD) | 1241 (355) | | | |
| Gestational age, wk (mean ± SD) | 29.3 (1.6) | | | |
| Small for gestational age (<10th percentile), n (%) | 18 (27.3) | | | |
| CRIB score (mean ± SD) | 3.0 (2.8) | | | |
| Apgar score after 5 min <6, n (%) | 5 (7.6) | | | |
| IVH, n (%) | 14 (21.2) | | | |
| ≥ 1 infection with positive blood culture, n (%) | 41 (62.1) | | | |
| Sepsis, n (%) | 42 (63.6) | | | |
| BPD, n (%) | 19 (28.8) | | | |
| Cesarean delivery, n (%) | 37 (56.1) | | | |
| Antenatal corticosteroid, n (%) | 53 (80.3) | | | |

*BPD*, bronchopulmonary dysplasia; *CRIB*, Clinical Risk Index for Babies; *IVH*, intraventricular hemorrhage; *WISC-III*, Wechsler Intelligence Scale for Children-III.
Bold number pertains to significant *P* value ($P < .05$).