Longitudinal Growth and Neuropsychological Functioning at Age 7 in Moderate and Late Preterms

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abstract

OBJECTIVE: To determine the association between longitudinal growth measures (height, weight, head circumference, and extent of catch-up growth) and neuropsychological functioning at 7 years in moderately and late preterm children.

METHODS: This study was part of a prospective, community-based cohort study. Data on growth were obtained from records on routine assessments in well-child centers until age 4 years and in a research setting at 7 years. Neuropsychological functioning was assessed at age 7 years. We assessed associations of growth with neuropsychological functioning and determined odds ratios for impaired neuropsychological functioning. All analyses were corrected for maternal education.

RESULTS: We included 234 children. Median gestational age was 34 weeks (P25–75: 33–35 weeks), and mean birth weight was 2.2 kg (± 0.5 kg). Short stature at all ages was associated with poorer motor, IQ, and attention scores and led to increased risks of impaired motor skills and low IQ. Lower weight at 1 and 4 years was associated with poorer IQ scores. Increased weight gain between age 4 and 7 years was, however, associated with poorer motor, IQ, and attention scores. Decreased head circumference gain in the first year of life was associated with poorer motor and attention scores and led to an increased risk of impaired motor and attention skills.

CONCLUSIONS: In moderately and late preterm children, poorer growth in the first 7 years is associated with poorer neuropsychological functioning. Regarding height, short stature was also associated with a higher likelihood of clinically relevant impaired neuropsychological functioning.

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Ms Dotinga executed the study, carried out the analyses, and drafted the initial manuscript; Dr Eshuis carried out the analyses and critically reviewed the manuscript; Dr Bocca designed the data collection instruments on growth, carried out analyses, and critically reviewed the manuscript; Dr Kerstjens designed the data collection instruments, coordinated data collection at all sites, and critically reviewed the manuscript; Dr Van Braeckel designed part of the data collection instruments, coordinated and supervised data collection at all sites, and critically reviewed the manuscript; Dr Reijneveld conceptualized and designed the study, supervised the execution of the study including the statistical analyses, and critically reviewed the manuscript; Dr Bos conceptualized and designed the study, supervised the execution of the study including data collection and analyses, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Moderately and late preterm children have an increased risk of growth restraint and impaired neuropsychological functioning. The association between growth and neuropsychological functioning has been established for very low birth weight and very preterm children only.

WHAT THIS STUDY ADDS: In moderately and late preterm children, poorer growth is associated with poorer neuropsychological functioning. Regarding height, poorer growth is also associated with a higher likelihood of clinically relevant impaired neuropsychological functioning, particularly for intelligence, attention, and motor skills.

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Preterm birth is highly prevalent and frequently leads to impaired neuropsychological functioning in children. Worldwide, ~11% of all children are born preterm (defined as gestational age <37 weeks),[1] with moderate preterm birth (gestational age between 32 and 34 weeks) and late preterm birth (gestational age between 34 and 37 weeks) accounting for approximately two-thirds of this.[2,3] Most preterm infants survive, but compared with term infants, they are at increased risk of long-term morbidity, particularly with regard to neuropsychological functioning.[4,5] Major examples of neuropsychological complications are impaired learning and visual-perceptual disorders.[1] Moreover, behavioral problems and poorer neuropsychological outcomes for preterm children have been shown in several studies,[6–9] particularly for total intelligence, performance intelligence, visuospatial reasoning, attention, and executive functioning.[10]

Preterm birth is also associated with impaired growth in the first years of life. Compared with children born at term, the risk of growth restriction is 2.5 times higher in moderately and late preterm infants.[11,12] After a period of postnatal growth failure, catch-up growth for height, weight, and head circumference (HC) is seen in most preterm infants.[13,14] This catch-up growth of preterm born children has been found throughout childhood and even in adolescence.[15,16]

Growth restraint and impaired neuropsychological functioning have been shown to be associated in both very preterm infants and very low birth weight infants.[17–20] However, research exploring this association in moderately and late preterm children is lacking. Although moderately and late preterm infants are more mature than early preterm infants, they are considerably less mature than term infants, increasing the likelihood of impaired functioning. Therefore, the aim of our study was to determine the association between longitudinal growth measures (height, weight, HC, and extent of catch-up growth) and neuropsychological functioning in moderately and late preterm-born children at early school age.

METHODS

Patient Selection

This study is part of the Longitudinal Preterm Outcome Project (LOLLIPOP). LOLLIPOP is a prospective, community-based cohort consisting of 45 446 children born in the Netherlands in 2002 and 2003, investigating growth, development, and health of preterm-born children, with emphasis on moderately and late preterm birth. Children were included during routine follow-up in 13 preventive child health care organizations. Exclusion criteria were major congenital malformations, chromosomal abnormalities, and syndromes. Details regarding sampling procedures, inclusion and exclusion criteria, study conduct, participants, and nonparticipants in the LOLLIPOP study have been described elsewhere.[8,21]

For this study, all 341 moderately and late preterm children from the 3 northern provinces in the Netherlands were invited for neuropsychological testing. In total, 248 children born moderately and late preterm agreed to participate, corresponding to a response rate of 73%. In 234 children data on both growth and neuropsychological functioning were available. The Ethical Review Board of the University Medical Center of Groningen approved the study. Examinations were performed in accordance with the institutional and international (Declaration in Helsinki, 1964, European Union Council Directive 86/609/EEC) ethical standards, including written informed consent.

Measures and Procedures

Growth

Data on growth were obtained from records on routine assessments in preventive child health care organizations. Children in the Netherlands routinely have 15 well-child checkups in the first 4 years of life. Height, weight, and HC (the latter until the large fontanel is closed) are assessed during these checkups. Standardized measuring devices are used to measure height and weight (ie, an infantometer or stadiometer). Growth was measured at birth and at the ages of 0 to 4 and 7 years. Growth at age 7 years was measured in a research setting. Children were examined in supine position until they reached the age of 24 months. From 24 months, the child was standing during measurements. We only present data on growth at the ages of 1, 4, and 7 years because growth at the ages of 2 and 3 years was measured relatively less frequently.

Weight at birth was converted to *z* scores using the Dutch Kloosterman curve.[22] Small for gestational age was defined as birth weight <10th centile. Large for gestational age was defined as birth weight >90th centile. Height and HC at birth were converted to *z* scores according to Niklasson.[23] Growth measures at the ages of 1, 4, and 7 years were converted to *z* scores according to Dutch references, derived from the fourth Dutch nationwide growth study.[24] Differences between *z* scores were calculated at all ages to determine whether catch-up growth occurred.

Neuropsychological Functioning

At a mean age of 6.9 years (± 0.1 year), neuropsychological functioning was assessed. Neuropsychological outcomes concerned intelligence, visuomotor integration, memory, and attention. We assessed total, verbal, and performance intelligence using a shortened version of the Wechsler Intelligence Scale for Children, Third

TABLE 1 Growth and Neuropsychological Functioning, Presented as Raw Scores and *z* Scores

	Raw Score, Mean (SD)	*z* Score, Mean (SD)
Height, cm		
1 y	74.1 (2.6)	−0.443 (1.4)
4 y	103.7 (4.0)	−0.123 (1.0)
7 y	124.8 (5.4)	−0.212 (1.0)
Height gain, cm		
0–1 y	29.0 (3.2)	−0.108 (2.0)
1–4 y	29.5 (2.9)	0.380 (0.7)
4–7 y	21.1 (2.7)	0.079 (0.5)
0–7 y	79.7 (5.3)	0.010 (2.0)
Wt, kg		
1 y	9.4 (1.1)	−0.387 (1.4)
4 y	16.6 (2.3)	−0.203 (1.0)
7 y	24.4 (4.8)	−0.116 (1.3)
Wt gain, kg		
0–1 y	7.1 (0.9)	−0.536 (1.3)
1–4 y	7.2 (1.9)	0.212 (0.8)
4–7 y	7.8 (2.9)	0.105 (0.7)
0–7 y	22.2 (4.7)	−0.251 (1.4)
HC, cm		
1 y	46.5 (1.4)	−0.044 (0.9)
HC gain, cm		
0–1 y	14.9 (1.7)	0.041 (1.0)
IQ		
Verbal	103.7 (10.5)	0.246 (0.7)
Performance	98.6 (12.0)	−0.091 (0.8)
Total	101.2 (9.4)	0.080 (0.6)
Attention		
Divided visual attention	12.0 (4.7)	−0.046 (0.9)
Response inhibition	49.6 (19.9)	0.078 (1.2)
Sustained auditory attention	6.4 (2.5)	0.032 (1.2)
Visuomotor integration		
Design copying	64.2 (9.9)	−0.098 (1.1)
Auditory-verbal memory		
Immediate recall	34.3 (8.4)	0.148 (1.1)
Delayed recall	7.5 (2.5)	−0.010 (1.1)
Recognition[a] (P25–75)	29.0 (27.0–30.0)	
Executive functioning		
Behavior-regulation index	40.2 (10.0)	0.323 (1.0)
Meta-cognition index	64.3 (14.5)	0.390 (1.0)
Global executive composition	104.5 (22.4)	0.391 (1.0)
Motor skills		
Manual dexterity[a] (P25–75)	0.5 (0.0–1.5)	
Ball skills[a] (P25–75)	1.0 (0.0–3.0)	
Static and dynamic balance[a] (P25–75)	0.5 (0.0–2.0)	
Total score	4.8 (5.0)	−0.034 (1.0)

Higher scores represent better performance on the subtests, except for response inhibition, all executive functioning, and all motor skills, where higher scores indicate poorer performance.

[a] No *z* scores available.

Edition, Dutch version.[25] The score for verbal IQ was based on scores for subtests of abstract reasoning (ie, Similarities) and comprehension of words (ie, Vocabulary). The score for performance IQ was based on scores for subtests of chronological sequencing (ie, Picture Arrangement) and visual-perceptual reasoning (ie, Block Design). The score for total IQ was determined by the average of verbal IQ and performance IQ. We assessed visuomotor integration using the subtest Design Copying of the Neuropsychological Test Battery for Children.[26] We assessed verbal memory using a standardized Dutch version of the Rey Auditory Verbal Learning Test (AVLT).[27] This test evaluates immediate recall, delayed recall, and recognition. Divided visual attention, sustained auditory attention, and response inhibition were assessed using the subtests Map Mission, Score!, and Opposite World from the Test of Everyday Attention for Children, respectively.[28]

We used the Behavior Rating Inventory of Executive Function, filled out by parents, to assess executive functioning in daily life. Executive functioning is described as well-organized, purposeful, goal-directed, and problem-solving behavior.[29] Two subscales of this questionnaire are the behavior regulation index and the meta-cognition index. The score for global executive composition is the sum of these subscales.

We assessed motor outcomes using the Movement Assessment Battery for Children. This standardized test of motor skills for children provides scores for manual dexterity, ball skills, and static and dynamic balance. From these 3 domains a total motor performance score is calculated.[30]

We excluded scores in cases in which the child was too tired and/or uncooperative (as assessed by the trained experimenter) and when questionnaires were incomplete.

We converted all raw scores into *z* scores by using the centiles according to the manuals. Because standardization in centiles or *z* scores lacked for the subdomains of the Movement Assessment Battery for Children and the Recognition subtest of the AVLT, we used raw scores for these subtests. Based on the *z* scores of the tests, we classified the children into normal or abnormal for each neuropsychological domain. Scores below −1 SD were classified as abnormal, and all other scores were classified as normal. If no *z* scores could be calculated, we used the cutoff scores from the manual; that is, for the subdomains of the Movement Assessment Battery for Children, scores below the 15th centile were classified as abnormal, and for the

TABLE 2 Associations of Height and Height Gain Between Birth and Age of 7 Years With Neuropsychological Functioning, Corrected for Maternal Education: β Coefficients

	Height				Height Gain			
	0 y	1 y	4 y	7 y	0–1 y	1–4 y	4–7 y	0–7 y
	n = 182	*n* = 152	*n* = 201	*n* = 203	*n* = 125	*n* = 136	*n* = 185	*n* = 168
IQ								
Verbal	0.005	0.166*	0.157*	0.150*	0.190*	0.081	−0.049	0.086
Performance	0.023	0.162*	0.071	0.033	0.050	0.083	−0.065	0.012
Total	0.016	0.192*	0.132	0.100	0.140	0.097	−0.070	0.060
Attention								
Divided visual attention	−0.233*	−0.049	0.069	0.132	0.169	0.108	0.088	0.294**
Response inhibition	−0.018	0.131	0.117	0.110	0.029	0.193*	−0.063	0.094
Sustained auditory attention	0.061	0.126	0.151*	0.150*	−0.053	−0.010	−0.019	0.069
Visuomotor integration								
Design copying	−0.041	0.134	0.164*	0.120	0.143	0.152	−0.129	0.125
Auditory-verbal memory								
Immediate recall	−0.038	0.056	0.112	0.124	0.111	0.122	0.018	0.114
Delayed recall	0.110	0.002	0.013	−0.002	−0.104	0.078	−0.054	−0.095
Recognition[a]	0.033	−0.088	0.041	0.008	−0.154	0.070	0.049	−0.046
Executive functioning								
Behavior-regulation index	0.046	−0.045	−0.066	−0.012	−0.121	0.029	0.048	−0.046
Meta-cognition index	0.051	−0.019	−0.055	−0.075	−0.153	0.012	−0.049	−0.071
Global executive composition	0.050	−0.032	−0.059	−0.050	−0.151	0.034	−0.008	−0.060
Motor skills								
Manual dexterity[a]	0.054	0.195*	0.108	0.120	0.078	0.027	−0.074	−0.006
Ball skills[a]	−0.040	0.194*	0.185**	0.153*	0.098	0.019	−0.045	0.083
Static and dynamic balance[a]	−0.010	0.017	0.053	−0.008	0.011	0.132	−0.123	−0.004
Total score	0.031	0.144	0.158*	0.084	0.044	0.121	−0.151*	0.041

[a] Raw scores were used. Spearman correlation coefficients are presented without adjustment for maternal education.
* $P < .05$.
** $P < .01$.

Recognition subtest of the AVLT, a score below 28 was classified as abnormal.

We considered socioeconomic status of the parents to be a potential confounder, which was measured by maternal education.

Statistical Analysis

First, we assessed background characteristics of the sample. Second, we assessed associations between growth and neuropsychological functioning, by determining β coefficients between *z* scores for height, weight, HC, and catch-up growth and *z* scores for outcome measures (motor and neuropsychological functioning) by using linear regression analyses. Regarding ordinal outcomes, we used the Spearman Rank correlation coefficients between the z scores for height, weight, HC and catch-up growth and scores on the Recognition subtest and the subdomains of the Movement Assessment Battery for Children. Variables were recoded so that the β coefficients between growth and neuropsychological test scores were positive in case of better growth associated with higher scores, and negative if better growth was associated with lower scores. Third, for all growth measures, we performed logistic regression analyses leading to odds ratios for abnormal scores on a specific neuropsychological outcome.

Throughout the analyses, $P < .05$ was considered statistically significant. IBM SPSS version 22.0 (IBM Corp, Armonk, NY) was used for the statistical analyses.

RESULTS

Characteristics of the Sample

A total of 234 children were included, 128 boys and 106 girls. Median gestational age was 34 weeks (P25–75: 33–35 weeks) and mean birth weight 2.2 kg (SD 0.5 kg). Our sample contained 28 children who were small for gestational age (12.0%) and 30 children who were large for gestational age (12.8%); the others were appropriate for gestational age (75.2%). In our study, 53 multiples were included (22.6%), of whom 96.2% were twins; the others were triplets and quadruplets. Of the singletons, 13.9% were small for gestational age, for multiples this was 12.8%.

We present mean height, weight, and HC and corresponding *z* scores at the ages of 1, 4, and 7 years as well as data on growth, that is, change of *z* scores between birth and age 7 years, in Table 1. We also show mean scores (SD) for motor and neuropsychological tests at age 7 years in Table 1. Moderately and late preterm born children had higher scores on executive functioning

TABLE 3 Associations of Weight and Weight Gain Between Birth and Age 7 Years With Neuropsychological Functioning, Corrected for Maternal Education: β Coefficients

	Weight				Weight Gain			
	0 y	1 y	4 y	7 y	0–1 y	1–4 y	4–7 y	0–7 y
	n = 225	*n* = 152	*n* = 201	*n* = 201	*n* = 152	*n* = 136	*n* = 184	*n* = 201
IQ								
Verbal	0.089	0.154	0.197**	0.058	0.092	0.131	−0.150*	−0.022
Performance	0.132*	0.219**	0.126	0.033	0.053	0.053	−0.134	−0.075
Total	0.128*	0.225**	0.187**	0.047	0.093	0.105	−0.174*	−0.061
Attention								
Divided visual attention	−0.082	−0.030	0.123	0.119	−0.040	0.108	0.013	0.169*
Response inhibition	0.079	0.151	0.077	0.015	−0.022	0.027	−0.144	−0.031
Sustained auditory attention	0.045	0.122	0.136	0.002	0.022	−0.074	−0.176*	−0.031
Visuomotor integration								
Design copying	0.064	0.138	0.048	−0.015	0.055	−0.081	−0.109	−0.038
Auditory-verbal memory								
Immediate recall	−0.044	0.029	0.076	0.021	0.054	0.074	−0.015	0.058
Delayed recall	−0.085	−0.092	−0.020	0.066	0.057	0.009	−0.037	0.006
Recognition[a]	−0.085	−0.026	0.024	0.037	0.054	−0.055	0.131	0.101
Executive functioning								
Behavior-regulation index	0.075	0.026	0.009	0.076	−0.090	0.020	0.058	0.014
Meta-cognition index	0.062	0.027	−0.040	−0.011	−0.095	−0.051	−0.034	−0.047
Global executive composition	0.068	0.030	−0.020	0.027	−0.100	−0.013	0.007	−0.020
Motor skills								
Manual dexterity[a]	0.020	0.094	0.033	0.033	0.087	0.009	−0.064	−0.028
Ball skills[a]	−0.051	0.039	0.047	−0.056	0.127	−0.006	−0.152*	0.017
Static and dynamic balance[a]	−0.030	−0.034	−0.054	−0.084	0.028	0.044	−0.065	−0.039
Total score	0.008	0.061	−0.009	−0.161*	0.028	−0.021	−0.228**	−0.142*

[a] Raw scores were used. Spearman correlation coefficients are presented without adjustment for maternal education.
* $P < .05$.
** $P < .01$.

measures compared with the norm. Scores for verbal IQ were slightly higher than the norm. All other scores were comparable with the norms.

Growth and Neuropsychological Functioning: Correlation Coefficients

Growth correlated positively with several aspects of neuropsychological functioning, as presented in Tables 2, 3, and 4. Height correlated positively with motor, IQ, and attention scores. Associations between height gain and neuropsychological domains were alternating positive and inverse. Without correction for maternal education, we also found that height gain in the first year of life correlated inversely with meta-cognition index and global executive composition. Association measures of height and height gain with the outcomes are shown in Table 2.

Weight correlated positively with IQ scores and inversely with motor skills. Weight gain between ages 4 and 7 years correlated inversely with most neuropsychological outcomes. Association measures of weight and weight gain with the outcomes are shown in Table 3.

HC gain in the first year of life correlated positively with motor and attention scores. Association measures of HC and HC gain with the outcomes are shown in Table 4.

Growth and Dichotomized Neuropsychological Functioning: Odds Ratios

Decreased growth increased the likelihood of clinically relevant impaired neuropsychological functioning, as presented in Tables 5, 6, and 7. Short stature was associated with an increased risk of impaired motor skills and IQ. Decreased height gain between birth and age 7 years increased the risk of impaired attention.

Decreased HC gain in the first year of life increased the probability of impaired motor skills and attention. The latter was not significant without correction for maternal education.

We found no statistically significant increased or decreased odds ratios for weight and neuropsychological outcomes.

DISCUSSION

We found some measures for poorer growth in moderately and late preterm children (gestational age between 32 and 36 weeks) to be associated with poorer neuropsychological outcomes on several domains. We found inverse associations between height gain from 4 to 7 years and motor skills, as well as between weight gain from 4 to 7 years and most neuropsychological domains. Regarding height, poorer growth

TABLE 4 Associations of HC and HC Gain Between Birth and Age 1 Year With Neuropsychological Functioning, Corrected for Maternal Education: β Coefficients

	HC		HC Gain
	0 y	1 y	0–1 y
	n = 160	*n* = 164	*n* = 123
IQ			
Verbal	−0.084	0.070	0.091
Performance	−0.046	0.044	0.059
Total	−0.078	0.070	0.095
Attention			
Divided visual attention	−0.131	−0.012	0.192*
Response inhibition	−0.018	0.047	0.081
Sustained auditory attention	−0.014	0.069	0.110
Visuomotor integration			
Design copying	−0.087	−0.012	0.084
Auditory-verbal memory			
Immediate recall	−0.144	−0.053	0.096
Delayed recall	−0.140	−0.076	0.065
Recognition	−0.201**	−0.089	0.097
Executive functioning			
Behavior-regulation index	0.061	0.008	−0.083
Meta-cognition index	−0.015	0.076	0.043
Global executive composition	0.012	0.040	−0.017
Motor skills			
Manual dexterity	−0.106	−0.043	0.024
Ball skills[a]	−0.103	0.075	0.178*
Static and dynamic balance[a]	−0.158*	−0.013	0.082
Total score	−0.112	0.042	0.107

[a] Raw scores were used. Spearman correlation coefficients are presented without adjustment for maternal education.
* $P < .05$.
** $P < .01$.

was also associated with a higher likelihood of clinically relevant impaired neuropsychological outcomes.

In our study, decreased height was associated with poorer motor skills, lower IQ, and lower scores on attention. Additional evidence on the relation between height and neuropsychological functioning is limited. A recently published review shows that most studies focus on gains of weight and HC in relation to neuropsychological outcomes, without reporting on height gain.[20] None of these studies were limited to moderately and late preterm children like ours, but they included all preterm children or had inclusion criteria based on birth weight. Moreover, few studies report on school age outcomes of IQ in relation to growth in only early preterm groups, and none in relation to other neuropsychological domains.[20]

Leppänen et al studied the association between height and IQ at 5 years in a Finnish cohort of very preterm children.[17] They could not demonstrate a significant association between height gain (ie, a difference in *z* scores) and full-scale IQ. This is more or less in line with our study. We found that poor height gain was associated with lower IQ, but only between 0 and 1 year. Leppänen et al further reported to have found more associations between height and neuropsychological measures; however, they did not report actual height but only changes in height.[17] We now add to their results that, in moderately and late preterm children, shorter height at 1 year and 4 years is associated with lower scores on IQ, attention, and motor tests.

Decreased weight was also associated with decreased IQ scores in our study. This is consistent with previous studies in children with a very low birth weight and in early preterm children.[17,19] We, however, also found that increased weight gain between the ages of 4 and 7 years was associated with poorer IQ scores, poorer attention scores, and poorer motor skills. Although only significant for motor skills, we also found negative associations between height gain in the same period and IQ, attention, and motor skills. Our results thus imply that rapid growth between ages 4 and 7 years may have a negative effect on neuropsychological functioning of moderate and late preterm children. These outcomes have not previously been described in literature. Several other studies report that increased weight gain is associated with better IQ scores, but this concerns weight gain between birth and 2 to 3 years.[20,31] Our study adds to the existing literature that, in moderately and late preterm-born children, weight gain between 4 and 7 years is associated with poorer scores on IQ, attention, and motor skills. Even so, mean weight at 4 and 7 years was still 0.1 to 0.2 SD lower than the norm for the whole group.

Increased gain of HC in the first year of life was associated with better motor and attention skills, a finding supported by Ehrenkranz et al.[18] We did not find any associations between HC and IQ. Further evidence on the relation between HC and IQ is inconsistent. Previous studies tended to report positive associations[31,32] or could not demonstrate an association.[33,34] These studies were mainly focused on a general population, rather than preterm children. Wright et al concluded that HC is neither specific nor sensitive for detecting poorer neuropsychological outcomes because 93% of the children with impaired neuropsychological outcomes from their study had a HC within the normal range.[33]

TABLE 5 Likelihood of a Poor Neuropsychological Outcome in Case of Poor Height and Height Gain, Corrected for Maternal Education: Odds Ratios With 95% Confidence Intervals

	Height				Height Gain			
	0 y	1 y	4 y	7 y	0–1 y	1–4 y	4–7 y	0–7 y
	n = 181	*n* = 152	*n* = 200	*n* = 203	*n* = 125	*n* = 135	*n* = 185	*n* = 168
IQ								
Verbal	0.812 (0.479–1.378)	2.935 (0.934–9.226)	2.177 (0.785–6.035)	3.901 (1.414–10.77)**	2.073 (0.966–4.450)	1.615 (0.293–8.893)	1.079 (0.109–10.69)	2.126 (1.073–4.209)*
Performance	0.922 (0.709–1.199)	1.130 (0.634–2.013)	0.745 (0.443–1.252)	0.843 (0.524–1.356)	0.979 (0.695–1.379)	0.601 (0.216–1.674)	0.621 (0.208–1.852)	1.170 (0.858–1.595)
Total	0.908 (0.551–1.496)	2.304 (0.769–6.903)	1.389 (0.549–3.520)	2.504 (1.046–5.994)*	1.442 (0.616–3.378)	0.933 (0.125–6.950)	0.167 (0.007–3.831)	1.721 (0.841–3.523)
Attention								
Divided visual attention	0.812 (0.680–0.971)†	0.897 (0.701–1.147)	1.021 (0.743–1.404)	1.208 (0.875–1.669)	1.152 (0.923–1.438)	1.180 (0.673–2.069)	1.334 (0.677–2.629)	1.375 (1.117–1.693)**
Response inhibition	0.970 (0.800–1.175)	1.395 (0.885–2.199)	1.072 (9.745–1.542)	1.082 (0.741–1.580)	1.095 (0.859–1.396)	1.268 (0.655–2.453)	0.567 (0.249–1.289)	1.032 (0.829–1.286)
Sustained auditory attention	0.903 (0.728–1.120)	1.116 (0.723–1.722)	0.922 (0.627–1.357)	1.017 (0.687–1.506)	1.222 (0.905–1.650)	0.970 (0.466–2.015)	1.039 (0.442–2.439)	1.170 (0.913–1.499)
Visuomotor integration								
Design copying	0.902 (0.732–1.110)	1.306 (0.832–2.050)	1.144 (0.788–1.660)	1.020 (0.683–1.524)	1.250 (0.947–1.649)	1.725 (0.872–3.412)	0.493 (0.213–1.143)	1.199 (0.943–1.524)
Auditory-verbal memory								
Immediate recall	0.903 (0.739–1.103)	1.339 (0.839–2.139)	1.134 (0.767–1.678)	1.437 (0.961–2.150)	1.308 (0.994–1.720)	1.440 (0.718–2.886)	1.250 (0.512–3.053)	1.227 (0.971–1.550)
Delayed recall	1.014 (0.860–1.196)	1.055 (0.784–1.420)	1.186 (0.865–1.624)	1.163 (0.841–1.607)	0.980 (0.800–1.201)	1.310 (0.741–2.317)	0.746 (0.377–1.477)	0.991 (0.828–1.186)
Recognition	1.028 (0.878–1.203)	0.847 (0.645–1.113)	1.058 (0.783–1.428)	0.949 (0.698–1.291)	0.868 (0.710–1.062)	1.138 (0.659–1.966)	1.168 (0.608–2.243)	0.973 (0.820–1.156)
Executive functioning								
Behavior-regulation index	1.003 (0.863–1.166)	1.239 (0.910–1.687)	1.076 (0.805–1.438)	1.245 (0.921–1.683)	1.136 (0.939–1.374)	0.818 (0.484–1.382)	1.167 (0.629–2.166)	1.052 (0.890–1.243)
Meta-cognition index	1.158 (0.938–1.430)	1.020 (0.726–1.432)	0.831 (0.557–1.241)	0.767 (0.513–1.147)	0.819 (0.642–1.045)	0.977 (0.483–1.975)	0.850 (0.371–1.946)	0.820 (0.654–1.029)
Global executive composition	1.083 (0.855–1.372)	1.020 (0.696–1.496)	0.856 (0.536–1.369)	0.852 (0.543–1.336)	0.887 (0.678–1.161)	1.630 (0.685–3.877)	0.548 (0.208–1.444)	0.877 (0.679–1.132)
Motor skills								
Manual dexterity	1.269 (0.972–1.658)	2.024 (1.043–3.928)†	1.159 (0.676–1.988)	1.399 (0.835–2.344)	0.852 (0.643–1.130)	1.122 (0.408–3.086)	0.468 (0.123–1.780)	0.820 (0.616–1.092)
Ball skills	0.934 (0.799–1.092)	1.122 (0.833–1.512)	1.424 (1.055–1.922)†	1.367 (1.008–1.856)†	1.140 (0.928–1.400)	1.285 (0.746–2.215)	0.741 (0.395–1.387)	1.198 (1.001–1.433)*
Static and dynamic balance	1.059 (0.884–1.269)	1.174 (0.788–1.750)	1.201 (0.862–1.674)	0.969 (0.688–1.365)	0.974 (0.780–1.216)	2.234 (1.117–4.469)*	0.538 (0.266–1.085)	0.927 (0.761–1.128)
Total score	1.090 (0.900–1.321)	1.834 (1.109–3.033)*	1.444 (1.001–2.083)†	1.215 (0.837–1.762)	0.979 (0.771–1.243)	2.001 (0.953–4.200)	0.540 (0.248–1.175)	0.979 (0.795–1.205)

* $P < .05$.
† $P < .05$: β coefficients for these associations were also statistically significant.
** $P < .01$: β coefficients for these associations were also statistically significant.

TABLE 6 Likelihood of a Poor Neuropsychological Outcome in Case of Poor Weight and Weight Gain, Corrected for Maternal Education: Odds Ratios With 95% Confidence Intervals

	Weight				Weight Gain			
	0 y	1 y	4 y	7 y	0–1 y	1–4 y	4–7 y	0–7 y
	n = 224	*n* = 152	*n* = 200	*n* = 201	*n* = 152	*n* = 135	*n* = 184	*n* = 201
IQ								
Verbal	1.021 (0.407–2.579)	4.833 (1.237–18.88)*	2.572 (0.916–7.221)	1.598 (0.905–2.819)	3.009 (1.123–8.066)*	0.915 (0.194–4.316)	0.538 (0.102–2.852)	1.562 (0.900–2.710)
Performance	1.057 (0.669–1.669)	1.634 (0.879–3.038)	0.832 (0.527–1.312)	0.841 (0.598–1.183)	1.149 (0.660–2.000)	0.575 (0.268–1.238)	0.657 (0.305–1.412)	0.839 (0.604–1.165)
Total	1.033 (0.471–2.269)	2.132 (0.723–6.286)	1.935 (0.752–4.980)	1.654 (0.910–3.007)	1.947 (0.775–4.890)	1.154 (0.186–7.138)	0.704 (0.103–4.819)	1.593 (0.883–2.874)
Attention								
Divided visual attention	0.930 (0.686–1.261)	0.899 (0.700–1.156)	1.158 (0.840–1.596)	1.277 (0.958–1.702)	0.845 (0.643–1.109)	1.256 (0.749–2.107)	1.141 (0.705–1.847)	1.274 (0.988–1.642)
Response inhibition	1.294 (0.881–1.902)	1.726 (1.091–2.729)*	1.198 (0.833–1.722)	1.103 (0.811–1.500)	1.102 (0.763–1.590)	0.937 (0.543–1.616)	0.722 (0.395–1.320)	0.963 (0.735–1.263)
Sustained auditory attention	0.934 (0.642–1.360)	1.127 (0.734–1.729)	0.967 (0.674–1.388)	0.877 (0.655–1.176)	1.126 (0.737–1.719)	0.938 (0.505–1.741)	0.647 (0.349–1.199)	0.926 (0.700–1.227)
Visuomotor integration								
Design copying	1.030 (0.704–1.505)	1.363 (0.879–2.115)	1.018 (0.706–1.469)	0.968 (0.706–1.328)	1.240 (0.823–1.870)	0.937 (0.540–1.625)	0.832 (0.448–1.547)	1.011 (0.750–1.362)
Auditory-verbal memory								
Immediate recall	0.726 (0.502–1.050)	1.181 (0.784–1.779)	1.037 (0.706–1.523)	0.961 (0.705–1.311)	1.611 (1.016–2.554)*	1.267 (0.677–2.370)	0.873 (0.458–1.666)	1.166 (0.859–1.581)
Delayed recall	0.787 (0.577–1.073)	1.022 (0.772–1.352)	1.044 (0.768–1.420)	0.966 (0.750–1.245)	1.149 (0.819–1.611)	1.035 (0.638–1.678)	0.986 (0.597–1.627)	1.103 (0.867–1.404)
Recognition	0.882 (0.656–1.185)	0.949 (0.740–1.217)	1.113 (0.830–1.494)	1.045 (0.819–1.332)	0.951 (0.732–1.236)	0.829 (0.598–1.511)	1.113 (0.711–1.744)	1.123 (0.894–1.412)
Executive functioning								
Behavior-regulation index	1.097 (0.829–1.452)	1.178 (0.896–1.551)	1.100 (0.831–1.457)	1.027 (0.810–1.301)	1.280 (0.931–1.760)	0.934 (0.593–1.471)	0.871 (0.556–1.363)	0.984 (0.793–1.220)
Meta-cognition index	1.057 (0.711–1.570)	1.039 (0.728–1.484)	0.897 (0.619–1.302)	0.926 (0.684–1.254)	0.926 (0.680–1.261)	0.975 (0.534–1.782)	1.031 (0.561–1.894)	0.945 (0.713–1.252)
Global executive composition	1.361 (0.846–2.188)	1.066 (0.696–1.633)	0.886 (0.574–1.368)	0.954 (0.675–1.349)	0.872 (0.636–1.197)	1.142 (0.540–2.416)	0.713 (0.344–1.479)	0.847 (0.626–1.146)
Motor skills								
Manual dexterity	1.112 (0.660–1.873)	1.685 (0.898–3.160)	0.910 (0.549–1.508)	1.069 (0.709–1.614)	1.257 (0.710–2.226)	0.757 (0.362–1.580)	0.870 (0.352–2.148)	1.026 (0.705–1.493)
Ball skills	0.851 (0.641–1.131)	1.015 (0.788–1.309)	1.207 (0.899–1.620)	0.955 (0.753–1.211)	1.129 (0.835–1.525)	1.113 (0.691–1.791)	0.645 (0.383–1.086)	1.080 (0.866–1.348)
Static and dynamic balance	1.002 (0.723–1.390)	0.977 (0.731–1.304)	0.867 (0.628–1.198)	0.785 (0.600–1.026)	0.927 (0.696–1.234)	1.185 (0.670–2.096)	0.674 (0.386–1.183)	0.825 (0.646–1.055)
Total score	1.045 (0.730–1.497)	1.436 (0.980–2.272)	1.127 (0.780–1.630)	0.838 (0.634–1.106)	1.192 (0.785–1.811)	1.208 (0.644–2.267)	0.575 (0.312–1.060)	0.880 (0.679–1.141)

* $P < .05$.

We found only 1 association between a growth measure and visuomotor integration, and none between growth measures and executive functioning and memory. Although the associations between growth and these measures were not significant, the correlation coefficients were positive in most of the tests. This may explain why a global measure, such as IQ, in which several domains are reflected, came out significantly in a number of associations.

In the current study we found more significant associations with attained height and weight than with growth. We considered that the associations in these parameters might already be present at birth but could not confirm this for height and HC. The few associations that were significant between neuropsychological outcomes and *z* scores of birth height, birth weight, and birth HC were found in other domains than those that were significant later on, except for total IQ and performance IQ in relation to weight. Apparently, a higher *z* score of weight at birth was associated with better IQ, persisting up to 4 years, but not at 7 years. The meaning of this should be the subject of future research.

The major strengths of this study were its large sample of moderately and late preterm-born children, its community-based longitudinal design, and the assessment of a wide range of neuropsychological outcomes, using carefully selected, well-established measures. The use of retrospectively collected growth data could be considered as a limitation. Even so, we are confident that our data are reliable, because professionals who were trained in assessing children executed these assessments by using standardized equipment and techniques.

TABLE 7 Likelihood of a Poor Neuropsychological Outcome in Case of Poor HC and HC Gain, Corrected for Maternal Education: Odds Ratios With 95% Confidence Intervals

	HC		HC Gain
	0 y	1 y	0–1 y
	n = 160	*n* = 164	*n* = 123
IQ			
Verbal	0.761 (0.324–1.790)	1.621 (0.389–6.747)	2.732 (0.603–12.37)
Performance	0.780 (0.496–1.227)	1.431 (0.742–2.759)	1.537 (0.841–2.808)
Total	0.850 (0.420–1.721)	1.336 (0.538–3.317)	1.382 (0.613–3.114)
Attention			
Divided visual attention	0.812 (0.590–1.117)	1.159 (0.767–1.751)	1.526 (1.013–2.300)†
Response inhibition	1.040 (0.732–1.476)	1.107 (0.680–1.803)	0.898 (0.587–1.373)
Sustained auditory attention	0.826 (0.564–1.210)	1.253 (0.743–2.114)	1.355 (0.817–2.247)
Visuomotor integration			
Design copying	0.871 (0.589–1.288)	1.113 (0.683–1.815)	1.491 (0.891–2.495)
Auditory-verbal memory			
Immediate recall	0.737 (0.487–1.116)	0.809 (0.484–1.352)	1.196 (0.725–1.971)
Delayed recall	0.636 (0.448–0.903)*	0.751 (0.494–1.139)	1.221 (0.815–1.829)
Recognition	0.801 (0.581–1.103)	0.934 (0.634–1.378)	1.101 (0.748–1.620)
Executive functioning			
Behavior-regulation index	1.204 (0.889–1.631)	1.495 (1.013–2.208)*	1.027 (0.720–1.463)
Meta-cognition index	1.066 (0.698–1.628)	1.464 (0.777–2.757)	1.183 (0.605–2.315)
Global executive composition	1.418 (0.895–2.245)	1.184 (0.614–2.283)	0.775 (0.432–1.391)
Motor skills			
Manual dexterity	1.036 (0.650–1.651)	1.312 (0.692–2.489)	0.954 (0.558–1.632)
Ball skills	0.756 (0.553–1.035)	1.227 (0.832–1.807)	1.847 (1.206–2.829)**
Static and dynamic balance	0.928 (0.661–1.303)	0.900 (0.568–1.428)	0.956 (0.634–1.439)
Total score	0.784 (0.541–1.136)	1.340 (0.793–2.264)	1.444 (0.885–2.356)

* $P < .05$.

† $P < .05$: β coefficients for these associations were also statistically significant.

** $P < .01$: β coefficients for these associations were also statistically significant.

Our findings indicate that better growth is associated with better neuropsychological functioning in moderately and late preterm children. Further research is needed to determine whether this association is causal. If indeed it concerns a causal relation, this would have important implications for practice, as it would imply that promoting growth in moderate and late preterm children leads to better neuropsychological functioning. Growth velocity in early life is, however, associated with increased cardiovascular risk in adulthood. Although this is true for adults born with low birth weight or intrauterine growth restriction, this does not apply to adults born preterm in general, as shown in a recent review by Lapillone et al.[35] In this broader group, growth velocity between birth and expected term age, and up to 12 to 18 months after term, had no effect on later cardiovascular risk, in contrast to growth velocity after 18 months and during childhood. At present, evidence suggests that balanced height and weight gain in preterm children should be promoted in early life. Excessive weight gain should be avoided, particularly in the children born preterm with intrauterine growth restriction. Future follow-up of our cohort regarding cardiovascular risk may provide more evidence regarding this issue.

CONCLUSIONS

In moderately and late preterm children, poorer growth is associated with poorer neuropsychological functioning. Rapid growth between the ages of 4 and 7 years, however, seems to have adverse effects on neuropsychological functioning. Regarding height, short stature was associated with a higher likelihood of clinically relevant impaired neuropsychological functioning. Additional research is needed to determine whether the observed associations are causal and to provide more insight in cardiovascular risks that may accompany catch-up growth.

ABBREVIATIONS

AVLT: Rey Auditory Verbal Learning Test
HC: head circumference
LOLLIPOP: Longitudinal Preterm Outcome Project

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