Neurocognitive outcome in young adults born late-preterm

Kati Heinonen, PhD[1*] Jari Lahti, PhD [1,2, 3] Sara Sammallahti, M.A.[1, 4,5] Dieter Wolke, PhD[6] Aulikki Lano,MD, PhD[5] Sture Andersson, MD, PhD [5] Anu-Katriina Pesonen,PhD [1] Johan G. Eriksson, MD, DMSc [2,7,8] Eero Kajantie, MD, PhD[2,5,9] and Katri Raikkonen, PhD[1]

Affiliations:

1. Department of Psychology and Logopedics, University of Helsinki, Helsinki, Finland
2. Folkhälsan Research Center, Helsinki, Finland
3. Helsinki Collegium for Advanced Studies
4. National Institute for Health and Welfare, Helsinki, Finland
5. Children's Hospital, University of Helsinki, and Helsinki University Hospital, Helsinki, Finland
6. Department of Psychology, University of Warwick, Coventry, UK
7. Department of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
8. Vasa Central Hospital, Vasa, Finland
9. Department of Obstetrics and Gynaecology, Oulu University Hospital and University of Oulu, Oulu, Finland

***Corresponding author**: Kati Heinonen, Department of Psychology and Logopedics, P.O. Box 9, 00014 University of Helsinki, Helsinki, Finland, kati.heinonen@helsinki.fi, Tel: +358-2941 29514

WORD COUNT: 2997

ABSTRACT

Aim
This study examined if late-preterm birth (34+0–36+6 weeks+days of gestation) was associated with neurocognitive deficit in young adulthood, and if small for gestational age (SGA) birth amplified any adversity.

Method
Participants derived from the prospective regional cohort study, the Arvo Ylppö Longitudinal Study (n=786; n=388 men) (mean=25 years, 4 months, standard deviation=8 months), born 1985–1986 late-preterm (n=119; n=21 SGA, <-2 standard deviation) and at term (37+0–41+6, n=667; n=28 SGA) underwent tests of intelligence, executive functioning, attention and memory, and reported their education.

Results
Those born late-preterm scored -3.71 (95% confidence interval -6.71, -0.72) and -3.11 (-6.01, -0.22) points lower on full and verbal intelligence quotient (IQ) than term peers. In comparison to those born at term and appropriate for gestational age (≥-2 to <+2 standard deviation) full, verbal and performance IQ scores of those born late-preterm and SGA were -9.45 to -11.84 points lower. After adjustments, differences were rendered non-significant, except that scores in full and performance IQ remained lower among those born late-preterm and SGA.

Interpretation
Late-preterm birth, *per se*, may not increase the risk of poorer neurocognitive functioning in adulthood. The double burden of being born late-preterm and SGA seems to increase this risk.

Running title: Neurocognitive outcome in adults born late-preterm

What this paper adds?

1) The late-preterm birth did not *per se* increase the risk of poorer neurocognitive functioning in adulthood.

2) The double burden of being born late-preterm and SGA increased this risk.

Approximately 7% of all births and over 70% of preterm births (<37+0 weeks+days of gestation) worldwide are late-preterm, defined as a birth at 34+0 through 36+6 weeks+days of gestation.[1] Compared to infants born at term (37+0-41+6 weeks+days of gestation) those born late-preterm are less mature at birth and more likely to develop medical complications that result in increased morbidity and mortality.[2] The last weeks of gestation represent a critical period of brain development, including rapid increases in brain weight, and cortical, grey and white matter volumes.[3] It is thus not surprising that children born late-preterm perform poorer than children born at term in tests of cognitive ability and executive functioning,[4–7] reported by some, but not by some other studies.[8]

Whether those born late-preterm outgrow their neurocognitive problems by adulthood remains largely unknown. The existing studies have reported mixed findings. Late-preterms, born between 1934-44 in Finland, had poorer memory function in late adulthood, especially if they had only attained low level of education,[9] and they also had lower lifetime educational attainments.[10] Population-based registry studies in Scandinavian male conscripts have also consistently shown that lower gestational age at birth was associated with poorer intellectual performance[e.g.,11] However, only one of these registry studies has assessed intellectual performance of late-preterms separately. The study showed that late-preterms, born between 1967-79 in Norway, had lower general intelligence test scores at the age of 18 years.[12] One other registry study, focusing on education, showed that late-preterms, born between 1967-83 in Norway, had attained similar educational levels at the age of 20 to 36 years compared to those born at term.[13] These cohorts were mainly born before the era of modern neonatal intensive care, in an era when low birth weight was a major perinatal

problem, but little distinction was made between slow fetal growth and preterm birth, in part because determination of length of gestation was not considered accurate enough. Therefore, the evidence from these prior studies do not necessarily translate to more recent cohorts born late-preterm.

We report here the findings from a Finnish study of infants born late-preterm between 1985-1986 and followed up to young adulthood when they underwent neuropsychological tests of intelligence, executive function, attention and memory, and reported their educational attainment. Many of these late-preterm infants had encountered adverse conditions in utero, manifesting as a small for gestational age at birth (SGA; birth weight for sex and gestational age <-2 standard deviations [SD]). Those born late-preterm and SGA have a double burden of prenatal and postnatal adversity, and may thus be more vulnerable to adverse neurocognitive outcomes than those born late-preterm and appropriate for gestational age (AGA;-2SD to +2SD). Also those born at term and SGA may fare worse in neurocognitive tests than peers born at term and AGA. Thus, we also report if the risk for poorer neurocognitive outcome in young adulthood would be higher for those born SGA either late-preterm or at term.

METHOD

The participants come from Arvo Ylppö Longitudinal Study (AYLS; the Finnish arm of the Bavarian-Finnish Longitudinal Study).[14] We identified all 1,535 infants (863 boys, 56.2%) born alive in the county of Uusimaa, Finland, between March 15, 1985 and March 14, 1986, admitted to neonatal wards in obstetric units, or transferred to the Neonatal Intensive Care Unit of the Children's Hospital, Helsinki University

Central Hospital within ten days of birth. Additionally, after every second hospitalized infant a healthy, not-hospitalized, infant was identified from maternity hospitals in the study area (n=658; 328 boys, 49.8%).

As shown in supplemental Figure 1, of the 2,193 infants of the original cohort 1,932 were born either late-preterm (n=315) or at term (n=1,617). 1,710 of these 1,932 were invited for a clinical and psychological follow-up in adulthood between 2009-2012 (for 66 participants personal identification number was not available, and for 156 the address was not traceable, they lived abroad or would have needed accommodation); 1,020 participated, and 986 underwent neuropsychological testing and/or reported educational attainment. 200 were further excluded; one whose test results were unreliable, n=193 with unverified gestational age, and six who had intellectual developmental disability, severe congenital malformations, or chromosomal abnormality potentially affecting neurocognitive development. The final sample comprised 786 participants (n=119 late-preterm; n=667 term) (mean age at neuropsychological testing mean=25 years 4 months, SD=8 months).

Within members of the original cohort who were born late-preterm or at term and invited to the adulthood follow-up, we compared those 786 who participated and were not excluded for any of various reasons to those 924 who did not participate and were not otherwise excluded. The participants were more often women (50.6% vs 41.2%, $p<0.001$), had higher birth weight SD score (Mean difference [MD]=0.18, $p=0.03$), were less often hospitalized (60.7% vs 71.2%, $p<0.001$), had older mothers (MD=0.70 years, $p=0.02$), who had smoked less often during pregnancy (14.1% vs 25.8%, $p<0.001$), and more often had parents with a higher level of education (8.7%

vs 16.0% lower secondary, 21.5% vs 29.7% vocational, 36.4% vs 33.8% general upper secondary or lower tertiary, 33.5% vs 20.4% upper tertiary, $p<0.001$); The groups did not differ in gestational age ($p=0.24$) or in Apgar score ($p=0.24$).

Further, we compared those included in the current study (n=786) with those excluded due to unverified, but existing, information on gestational age (n=193). These groups did not differ in gestational age or in IQ estimates (all p's>0.07).

The study protocol at birth was approved by the ethics committees of Helsinki City Maternity Hospital, Helsinki University Central Hospital, and Jorvi Hospital and in adulthood by the Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District. An informed consent was obtained from parents (childhood) and participants (adulthood).

Gestational Age and Fetal Growth

Gestational age was extracted from birth records. It was based on fetal ultrasound, performed before 24+0 weeks of gestation, in 82 (68.9%) of late-preterm and 432 (64.8%) of term born participants, or, if unavailable, calculated using the mother's last date of menstruation. Birth weight, extracted from birth records, was categorized into SGA (<-2SD) or AGA (≥-2SD and <+2SD) according to Finnish growth charts.[15]

Neurocognitive outcomes

Intelligence was estimated using seven subtests of the Wechsler Adult Intelligence Scale (WAIS)-III: Information, Similarities, Arithmetic, Digit span, Matrix reasoning, Picture completion, and Digit-symbol coding. Verbal intelligence quotient (IQ) was

estimated using the first four and performance IQ using the last three subtests according to the norms presented in manual,[16] and full IQ was estimated using the verbal and performance IQ.

Executive function, attention, and memory were assessed using five tests: The Trail-Making Test (TMT), The Stroop Test, Verbal fluency, The Conner's Continuous Performance Test (CPT)-II, and the Wechsler Memory Scale (WMS)-III. The TMT[17] consists of two parts (A and B) requiring psychomotor speed, focused attention, and visual-spatial ability. Part B further requires working memory, cognitive flexibility, and shifting alternation. The B-A difference score was also used. The Stroop Test (Bohnen modification) comprises two tasks[18] measuring speech motor function (baseline) and selective attention, ability to inhibit a dominant response, cognitive flexibility, working memory, and processing speed (incongruence). The difference score was also used. Verbal fluency measuring expressive-language abilities, particularly speed and flexibility of verbal thought processes was tested using the mean of the number of words produced within 60 seconds beginning with the letters "S" and "P" and words of vegetables or fruits and animals. The CPT-II measures sustained attention and ability to inhibit impulsive responses[19]: The Omission score reflect slow response style (categorized: into 0, 1-2, and >2 omissions), the Commission reflect inattention, Hit reaction time indicates slow response style, the Attentiveness (d') score reflect poor attentiveness. On the WMS-III we used logical memory, verbal paired associates and faces subtests. Immediate and general memory summary indices were calculated.[20] For a more detailed description see supplemental file 1.

Educational attainment

Participants reported their highest completed or on-going education: lower secondary, upper secondary, lower tertiary, and upper tertiary.

Covariates and Confounders

Variables known to be related to gestational age and/or to neurocognitive development extracted from birth records included sex, multiple pregnancy (singleton/multiple), parity (primiparous vs multiparous), maternal pre-pregnancy body-mass-index (BMI:kg/m^2), hypertensive disorder (hypertension, pre-eclampsia), diabetes (gestational diabetes, type 1 diabetes) and smoking during pregnancy (0, 1–10, or >10 cigarettes/day), and age at delivery (<20, 20-40, >40 years); highest educational attainment of either parent (lower secondary, vocational, general upper secondary/lower tertiary, higher tertiary) was documented from an interview during childhood.

Statistical Analysis

Variable transformations were made when necessary to attain normality and to improve linear model fitting. Intelligence test scores were standardized to a mean=100 and SD=15 and executive functioning, attention and memory test scores to a mean=0 and SD=1 using the term born group with no chromosomal abnormalities or intellectual developmental disability as the referent. Descriptive statistics of the sample were analysed with analysis of variance and χ^2-tests. Group differences in neurocognitive outcomes were tested using multiple linear (continuous outcomes), logistic (dichotomous outcomes), and multinomial (outcomes with more than two categories) regression analyses. We tested differences between those born late-

preterm and at term, and then compared those born at term and AGA with those born late-preterm and SGA, late-preterm and AGA, and at term and SGA.

In tests of general intelligence adjustments were made for sex and age at testing, (model 1). Thereafter adjustments were made for all covariates and confounders, except for highest educational attainment of either parent (model 2), which was adjusted for use in a full model (model 3). In tests of executive functioning, attention, and memory after model 1 the full IQ was also added to exclude the effect of general intelligence (models 2 and 3). We considered two-tailed p-values<0.05 statistically significant. Analyses were performed using SPSS 24.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY).

RESULTS

Table 1 shows characteristics of the sample. Those born late-preterm were hospitalized for a longer period, were more often born SGA, from multiple pregnancy, after Caesarean section, and their mothers had more frequently hypertensive disorders and diabetes, and they were breastfed for a shorter period than those born at term. Characteristics of late-preterm and term groups born SGA and AGA are presented in supplementary eTable1.

Differences between late-preterm and term groups

Figure 1 shows that those born late-preterm scored -3.71 (95% confidence interval [CI] -6.71, -0.72, p<0.02) and -3.11 (95%CI -6.01, -0.22, p=0.04) points lower than those born at term on estimated full and verbal IQ, and -3.47 (95%CI -6.39, -0.55, p

0.02), -.3.15 (95%CI -6.07, -0.22, p=0.04) and -3.07 (95%CI -6.13, -0.01, p<0.05) points lower on information, arithmetic, and matrix reasoning subtests, respectively, after adjustments for sex and age (model 1) (Figure 1). The group differences on full IQ, and on information and matrix reasoning scores remained significant after further adjustments for prenatal adversities (model 2), but when adjusted for parental education (model 3) all group differences were rendered non-significant.

Those born late-preterm and at term did not differ from each other in the other neurocognitive outcomes (p-values>0.09, Table 2), or in current/ongoing level of education (p-values>0.19, models 1-3, see also Table 1).

Differences between late-preterm and term groups born SGA and AGA

Compared to those born at term and AGA, those born late-preterm and SGA scored -11.84 (95%CI -18.33, -5.36, p<0.001), -9.45 (95%CI -15.77, -3.12, p=0.003), and -11.45 (95%CI -18.09, -4.81, p=0.001) points lower on full, verbal and performance IQ estimates (Figure 2). The late-preterm SGA group scored also lower on information, arithmetic, matrix reasoning and picture completion subtests (supplemental eFigure2). The group differences on full and performance IQ estimates, and on arithmetic and matrix reasoning subtests, remained significant even after controlling for prenatal adversities (model 2) and parental education (model 3) (p's<0.05). Test scores of term SGA and late-preterm AGA groups did not differ from those of term AGA group (p's>0.23).

In additional analyses we also found that those late-preterms who were born only slightly growth restricted, defined as <-1SD birth weight for sex and gestational age (n=45), scored lower on full, verbal and performance IQ estimates (supplemental eFigure3), and on arithmetic and matrix reasoning subtests (supplemental eFigure4) than those born at term and AGA (models 1-3).

The term AGA group did not differ from late-preterm SGA, late-preterm AGA and term SGA groups on executive function, attention and memory (*p*'s>0.05), but the trail making test difference score was higher (MD=0.84, 95%CI 0.34, 1.34, *p*=0.001, model 1; *p*=0.02 model 2), and immediate (MD=-0.42, 95%CI -0.83, -0.002, *p*=0.049, model 1) and general (MD=-0.53, 95%CI 0.95, -0.11, *p*=0.01, model 1) memory indices lower in the late-preterm SGA group than in term AGA group (MD=0.84, 95%CI 0.34, 1.34, *p*=0.001, model 1). However, these became non-significant after further adjustments (*p*>0.14, models 2,3).

DISCUSSION

A novel finding of our study of young adults born late-preterm during an era of modern neonatal intensive care, is that poorer performance on the IQ tests is not characteristic of all of them, but is rather confined to those born SGA. This group had -9.5 to -11.8 IQ points lower total, verbal and performance IQ estimates. When those born late-preterm were analyzed as a one group, young adults born late-preterm achieved over -3 points lower scores on full and verbal IQ estimates compared to those born at term after adjustment for age and sex. Yet, groups no longer differed significantly from each other after adjustments for parental education. This is in

contrast to what we found when term AGA and late-preterm SGA groups were compared, where the majority of the significant associations remained even after adjustments. Our findings thus suggest that improvement in prenatal and neonatal care up to the mid 1980's, does not seem to offer equal long-term neuroprotection for all individuals born late-preterm. This lack of neuroprotection appears especially true for a relatively large group, 17.6%, born late-preterm and SGA, and for an even larger group, 37.8%, born late preterm and moderately SGA. These groups have in addition to being born immature, likely suffered from intrauterine adversities as reflected in their suboptimal fetal growth.

We are aware of only one previous study that reported an average difference of 1.3 IQ points between individuals born late-preterm and at term in adulthood.[12] Yet, the cohort included only men who were born 6-18 years earlier than our cohort.

Our study also showed that executive functioning, memory and attention were mainly unaffected, suggesting that 'higher-level' cognitive functioning may resist the impact of late-preterm birth. In a group of those further complicated by SGA birth there were some evidence of poorer memory functioning and cognitive flexibility, although these association were non-significant after adjusting for full IQ and prenatal adversities. The only existing study on adults showed poorer memory and executive functioning in those born late-preterm than at term.[9] Yet, the participants in that study were in their late adulthood and born at a time when neonatal care differed significantly from that of the mid 1980's.

Although current study is not directly comparable to studies focusing on childhood outcomes and using more contemporary cohorts, current results are in line with the ones showing that the differences between late-preterms and terms diminish when focusing on healthy late-preterms.[5,8]

We did not find differences in educational attainments between those born late-preterm and at term. This is in line with a Norwegian register study on young adults,[13] but in disagreement with a Finnish register study showing that those born late-preterm were more likely to have attained only basic or upper secondary education.[10] It is likely that not all young adults have yet achieved their maximum lifetime educational level.

Potential mechanisms

Lower IQ scores likely result from deficits in brain development observed among those born late-preterm[21] or SGA.[22] Last weeks of pregnancy are critical for brain development[3] and late-preterm birth and/or fetal growth restriction interrupt neurodevelopmental processes. Also, potential underlying causes of preterm or SGA birth (e.g., pregnancy disorders) or increased neonatal morbidity (e.g., sepsis) may increase the risk for adverse brain developmental sequelae.[23,24] Also, potential differences in mode of delivery, breastfeeding, and postnatal growth may be underlying factors. Neither can we rule out potential epigenetic changes. Further, early family environment, including socioeconomic status, may affect neurocognitive development through cognitive stimulation and experiences of stress.[25] Parental education also may reflect a genetic basis for neurocognitive abilities.

Strengths and limitations

Strengths of our study include a long follow-up and the use of standardized measurements. Further, we had verified information on gestational age and were able to account for potential covariates and confounders. Limitations also exist. Hospitalized infants are overrepresented. However, in Finland in the mid-1980s, newborns were more likely than nowadays to be admitted to a neonatal ward due to problems of transient nature. Many of the admitted infants had no diagnosed illnesses and were admitted for a short observation period. Moreover, those with congenital malformations or chromosomal abnormalities were excluded. Further, SGA was based only on birth weight and some infants may be constitutionally small and not growth restricted, though we made adjustments for maternal size. Further, the sample size of those born late-preterm and SGA was small. Yet, we had power to detect significant differences, and the results remained similar also in the sample of slightly growth restricted participants. The small sample size also restricted the analyses of sex differences. Male gender has been shown increase the risk for adverse outcomes among late-preterms.[5] In our study 61.9% of the late-preterm SGA participants were male, and the found results may thus reflect generally poorer male outcomes.

Loss to follow-up may impact generalizability of the findings. Those included in our analytical sample were more often born healthy, and had grown-up in more advantageous pre- and postnatal environments than those who did not participate. This would be expected to reduce the impact of preterm SGA birth, however, and potentially reinforces the strength of our findings. Finally, our findings may not generalize to cohorts born recently or to those not receiving advanced medical care.

CONCLUSIONS

Late-preterm birth, *per se,* may not increase the risk of poorer neurocognitive functioning in adulthood. Instead, the double burden of being born late-preterm and SGA seems to increase this risk. If other studies confirm our findings, efforts to support neurodevelopment should be targeted especially towards the late-preterm group born SGA.

A**cknowledgements**:

Sources of funding:
Childhood follow-up was financially supported by the Bundesministerium für Forschung und Technik (Federal Goverment of Germany, Ministry of Science and Technology) program grants PKE 4 and JUG 14 (FKZ's 0706224, 0706564, and 01EP9504) to Drs Klaus Riegel, Dieter Wolke, and Barbara Ohrt; Adulthood follow-up was financially supported by the Academy of Finland program grants (to Drs Eriksson, Raikkonen and Kajantie); The work by Aulikki Lano was supported by Foundation of Pediatric Research; The work by Dr Heinonen and Dr. J. Lahti was supported by Academy of Finland post-doctoral grant; The work by S. Sammallahti was supported by the Doctoral School of Clinical Research; Dr Eriksson was supported also by grant from Samfundet Folkhälsan; Dr Andersson from Päivikki and Sakari Sohlberg Foundation and Finska Läkaresällskapet; and Dr Kajantie by Foundation for Pediatric Research, Juho Vainio Foundation, Novo Nordisk Foundation, Signe and Ane Gyllenberg Foundation, Sigrid Jusélius Foundation. Funders did not have any role in study design, data collection, data analysis, manuscript preparation and /or publication decisions.

Special thanks are due to Juha Peltola, Timo Vartia and the numerous other persons who carried out the data collection and kept the sample intact in childhood and adulthood follow-ups.

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Table 1. Characteristics of the study sample by gestational age

Variable	Late-preterm (n=119) n (%)/mean(SD)	Term (n=667) n (%)/mean(SD)	chi2 / ANOVA *P*-value
Sex (men)	65 (54.6%)	323 (48.4%)	0.21
Pre- and neonatal period			
Birth weight for gestational age			<0.001
SGA	21 (17.6%)	28 (4.2%)	
AGA	92 (77.3%)	614 (92.1%)	
LGA	6 (0.5%)	25 (3.7%)	
Multiple pregnancy	17 (14.3%)	16 (2.4%)	<0.001
Parity (Primiparous)	67 (56.3%)	329 (49.3%)	0.16
Maternal prepregnancy BMI	21.9 (2.59)	22.3 (3.35)	0.21
Maternal hypertensive disorder			<0.001
Hypertension	11 (9.2%)	113 (16.9%)	
Pre-eclampsia	17 (14.3%)	14 (2.1%)	
Normotension	91 (76.5%)	540 (81.0%)	
Maternal diabetes			<0.001
no OGTT	88 (73.9%)	530 (79.5%)	
normal OGTT	17 (14.3%)	91 (13.6%)	
gestational diabetes	3 (2.5%)	35 (5.2%)	
Type 1 diabetes	11 (9.2%)	10 (1.5%)	
Type 2 diabetes	0 (0.0%)	1 (0.1%)	
Maternal smoking during pregnancy			0.06
No	97 (81.5%)	578 (86.7%)	
1-10 cigarettes/ day	20 (16.8%)	66 (9.9%)	
>10 cigarettes/ day	2 (1.7%)	23 (3.4%)	
Maternal age at delivery			0.84
< 20 years	1 (0.8%)	10 (1.5%)	
20 to 40 years	116 (97.5%)	644 (96.6%)	
> 40 years	2 (1.7)	13 (1.9%)	
Labor type [a]			<0.001
Spontaneous birth	57 (48.3%)	520 (79.6%)	
Elective caesarian section	25 (21.2%)	47 (7.2%)	
Other caesarian section	36 (30.5%)	86 (13.2%)	
Apgar score 5 minutes [b]			0.66
0-7	10 (8.7%)	49 (7.5%)	
> 7	105 (91.3%)	604 (92.5%)	
Breastfeeding at 5 months [c]			<0.001
Never	10 (8.8%)	18 (2.85)	
Finished	67 (59.3%)	308 (47.3%)	
Partial	32 (28.3%)	232 (35.6%)	
Full	4 (3.5%)	93 (14.3%)	
Length of stay in hospital/ days			<0.001
no hospitalization	8 (6.7%)	301 (45.1%)	

up to 7 days	95 (79.8%)	340 (51.0%)	
> 7 days	16 (13.4%)	26 (3.9%)	

Table 1. Characteristics of the study sample by gestational age (continued)

Childhood			
Parental education			0.37
lower secondary	12 (10.1%)	56 (8.4%)	
vocational education	32 (26.9%)	137 (20.5%)	
general upper secondary or lower tertiary	39 (32.8%)	247 (37.0%)	
upper tertiary	36 (30.3%)	227 (34.0%)	
Academic performance			
Grade point average at the end of comprehensive school (scale 4-10)[d]	8.2 (0.9)	8.3 (0.8)	0.89
Remedial education (yes)[e]	36 (33.0%)	185 (29.3%)	0.43
Own completed or on-going education [f]			0.87
lower secondary	8 (7.0%)	35 (5.4%)	
upper secondary	39 (33.9%)	208 (32.0%)	
lower tertiary	29 (25.2%)	172 (26.5%)	
upper tertiary	39 (33.9%)	235 (36.2%)	
Young adulthood			
Age at testing	25.2 (0.60)	25.3 (0.63)	0.03
Full IQ estimate [g]	106.8 (10.9)	109.0 (10.9)	0.05
Verbal IQ estimate [h]	103.5 (13.3)	105.2 (12.7)	0.18
Performance IQ estimate [i]	110.4 (10.4)	112.6 (10.9)	0.05

Note. a Data missing from 1 late-preterm and 14 term. b Data missing from 4 late-preterm and 14 term. c data missing from 6 late-preterm and 16 term. d Data missing from 23 late-preterm, 102 term. e data missing from 10 late-preterm and 35 term. f data missing from 4 late-preterm and 17 term. g data missing from 7 late-preterm and 47 term. h data missing from 5 late-preterm and 37 term. i data missing from 7 late-preterm and 46 term.

AGA = appropriate for gestational age; BMI = body-mass-index; IQ = intelligence quotients, LGA = large for gestational age; n = number of participants; OGTT = Oral glucose tolerance test; SD = standard deviation; SGA = small for gestational age

Table 2. Group differences in executive functioning, attention and memory.

	n late-preterm/ term	**Model 1 B (95%% CI), *P***	**Model 2, *P***	**Model 3, *P***
Trail Making Test				
A	113/628	-0.07 (-0.13 to 0.27), 0.51	0.85	0.88
B	113/629	-0.12 (-0.09 to 0.32) , 0.27	0.97	0.88
B-A	113/628	0.16 (-0.07 to 0.39), 0.17	0.62	0.67
Stroop Test				
Baseline	111/621	-0.01 (-0.22 to 0.20), 0.93	0.34	0.38
Incongurence	111/621	-0.10 (-0.11 to 0.31), 0.35	0.59	0.60
Incongurence-Baseline	111/621	0.17 (-0.03 to 0.38), 0.09	0.09	0.10
Verbal fluency	114/633	-0.01 (-0.21 to 0.18), 0.89	0.24	0.21
CPT-II				
Commission	117/625	0.14 (-0.06 to 0.34), 0.16	0.14	0.14
Hit reaction time	117/625	-0.03 (-0.23 to 0.17), 0.75	0.44	0.41
Attentiveness (d')	117/625	-0.11 (-0.23 to 0.19), 0.85	0.26	0.25
WMS-III				
General	114/626	-0.10 (-0.30 to 0.09), 0.29	0.79	0.85
Immediate	114/626	-0.08 (-0.27 to 0.11), 0.42	0.91	0.85

Note. B unstandardized coefficient (=mean difference between late-preterm and term), CI confidence interval; Model 1, adjusted for sex and age at testing, Model 2 further adjusted for estimated full IQ, multiple pregnancies, parity, maternal pre-pregnancy BMI, hypertensive disorder during pregnancy, diabetes during pregnancy, smoking during pregnancy, maternal age at delivery; Model 3, further adjusted for highest educational attainment of either parent; CPT: Conner's continuous performance test; WMS: Wechsler Memory Scale.

Figure Legends

Figure 1. Forest plot of the differences between late-preterm (n=119) and term born (n=667) group in intelligence test scores (WAIS-III)

Figure 2. Estimated marginal means and 95 % confidence intervals of estimated IQ scores in those born late-preterm and SGA, late-preterm and AGA, at term SGA, and at term SGA, and statistical differences in comparison to those born at term and AGA. The estimated marginal means are adjusted for sex and age.