European Child & Adolescent Psychiatry (2019) 28:377–388
https://doi.org/10.1007/s00787-018-1202-4

ORIGINAL CONTRIBUTION

Head circumference and child ADHD symptoms and cognitive functioning: results from a large population-based cohort study

Muriel Ferrer[1] · Raquel García-Esteban[1,2,3] · Carmen Iñiguez[3,4] · Olga Costa[4] · Ana Fernández-Somoano[3,5] · Cristina Rodríguez-Delhi[6] · Jesús Ibarluzea[3,7,8] · Aitana Lertxundi[3,8] · Cathryn Tonne[1] · Jordi Sunyer[1,2,3,9] · Jordi Julvez[1,2,3,9]

Received: 20 December 2017 / Accepted: 16 July 2018 / Published online: 19 July 2018

Abstract

The aim of this study is to understand the association between prenatal, newborn and postnatal head circumference (HC) and preschool neurodevelopment in a large population-based birth cohort. The INMA project followed 1795 children from 12 weeks of pregnancy to preschool years. HC measurements were carried out prospectively, and following a standardized protocol during pregnancy (12, 20 and 34 weeks), birth, and child ages of 1–1.5 and 4 years old; and *z*-scores were further estimated. Prenatal head growth was assessed using conditional *z*-scores between weeks 12–20 and 20–34. Several neuropsychological tests [MSCA (cognition), CPT (attention)] and behavioral rating scales [DSM-IV-ADHD, CAST (autism), CPSCS (social competence)] were carried out during the last follow-up (5 years old). Multivariable models adjusted for family and child characteristics were applied to analyze associations between HC and neurodevelopment. In fully adjusted models, prenatal HC and head growth showed little or no associations with the neurodevelopment outcomes. Independent associations were observed between HC *z*-scores at birth, 1–1.5 years and 4 years and MSCA global cognitive scores and DSM-IV inattention symptoms. Specifically, *z*-score at birth was positively associated with general cognitive scores [β 1.22, 95% confidence interval (CI) 0.59, 1.85], and we observed a protective association with ADHD-DSM-IV total symptoms, mean ratio (MR) 0.85 (0.75, 0.96). Prenatal HC and head growth measurements gave little information about child cognitive abilities and behavior at preschool years. However, HC at birth and early childhood was positively associated with a range of neuropsychological outcomes, including protective associations with ADHD symptoms.

Keywords Head circumference, neuropsychological development · ADHD symptoms · Cohort study

Abbreviations

ASC	Autism spectrum conditions
ASD	Autism spectrum disorder
BSID	Bayley scales of infant development
CAST	Childhood autism spectrum test

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00787-018-1202-4) contains supplementary material, which is available to authorized users.

✉ Jordi Julvez
jordi.julvez@isglobal.org

1 ISGlobal, Instituto de Salud Global de Barcelona-Campus MAR, PRBB, C. Doctor Aiguader 88, 08003 Barcelona, Catalonia, Spain

2 IMIM (Hospital del Mar Medical Research Institute), Barcelona, Catalonia, Spain

3 CIBER Epidemiologia y Salud Pública (CIBERESP), Madrid, Spain

4 Epidemiology and Environmental Health Joint Research Unit, FISABIO-Universitat, Jaume I-Universitat de València, Av. Catalunya 21, 46020 Valencia, Spain

5 Departamento de Medicina, Universidad de Oviedo, Oviedo, Asturias, Spain

6 Servicio de Pediatría, Hospital San Agustín, Avilés, Asturias, Spain

7 Public Health Division of Gipuzkoa, BioDonostia Research Institute, Gipuzkoa, San Sebastian, Spain

8 Faculty of Psychology, University of the Basque Country (UPV/EHU), San Sebastian, Spain

9 Universitat Pompeu Fabra (UPF), Barcelona, Catalonia, Spain

CI	Confidence interval
CPT	Conner's kiddie continuous performance test
CPSCS	California preschool social competence scale
CBCL	Child behavior check list
DSM-IV-ADHD	Attention-deficit/hyperactivity disorder criteria of the diagnostic and statistical manual of mental disorders, fourth edition form list
ELBW	Extremely low birth weight
FDR	False discovery rate
HC	Head Circumference
INMA	Infancia y medio ambiente [environment and childhood]
SD	Standard deviation
MSCA	McCarthy scales of children's abilities
MR	Mean ratio

Introduction

A growing body of evidence supports an association between general physical development and more specifically, head growth, with neuropsychological and behavioral development [1–9]. Head circumference (HC) has been considered a good indicator of intracranial volume as well as of cognitive development [3, 10]. Newer studies have focused on repeated HC measurements, as they are better predictors of head growth trajectories, and consequently, could be better determinants of neuropsychological and behavioral development [11, 12].

However, not all studies have observed a positive association between HC and neuropsychological development [13, 14]. A large number of individual and environmental factors could potentially confound the association between these two developmental indicators [14]. These factors include the infant's immediate environment such as breastfeeding duration, a proxy of maternal Intelligence Quotient (IQ), and parental education, socioeconomic status and mental health [1, 3, 5, 13–17].

To our knowledge, previous studies with both positive and null associations between HC and neurodevelopment outcomes have been mainly based on specific child populations with particular neuropsychiatric difficulties, prematurity or abnormal head growth [14]. Evidence of an association between head growth and neurodevelopment within the general population would be of greater public health relevance and has greater external validity.

Although several previous studies have linked fetus and brain development and physical development with ADHD [18–21], one of the most common neuropsychiatric outcomes with adverse consequences for the child's school life [22], few have investigated the association between HC and ADHD symptoms and results have been mixed [23–26]. Sta- this found no significant association between HC and head growth velocity during the first 2 years of life of 87 ELBW babies and ADHD at school age [23], Heinonen found, with a larger population ($n = 893$), that smaller HC from birth to 56 months was related to higher ADHD symptoms [24]; another similar study also found a protective association between HC and ADHD symptoms [25]; and a recent birth cohort study ($n = 3749$) with prenatal growth parameters, including birth HC measurements, found no overall association with ADHD symptoms, only when they stratified the analyses by child sex, females showed that smaller HC was positively associated with CBCL attention problems [26].

In contrast, there is a relatively large literature regarding the association between HC and autism spectrum disorder (ASD), in particular with macrocephaly and growth rate during early childhood [27–29]. However, recent results plead to caution since evidence is mixed with null associations [30]. Therefore, further research is still needed to understand the link between HC and ASD.

We previously reported no association between longitudinal measurements of intrauterine HC and cognitive and motor outcomes measured at 14 months using the Bayley Scales of Mental Development in a population-based birth cohort [14]. One possible explanation for this finding is the relatively short follow-up period, given the rapid increase of the intracranial volume during the first 2 years of life [31] as well as head circumference growth throughout childhood [32]. Building on this previous work, we investigated the association between repeated measurements of HC (from 12 weeks of gestational age to 4 years) and preschoolers' cognitive and social competences, ADHD and autism spectrum symptoms in a large population-based cohort with extensive data on potential confounders.

Methods

Study design and population

This study was based on four cohorts with prenatal, newborn and postnatal HC data (Asturias, Gipuzcoa, Sabadell and Valencia) of the larger INMA Project (Infancia y Medio Ambiente [environment and childhood]). The INMA Project was established between 2004 and 2008. Subject recruitment and follow-up procedures have been reported in detail elsewhere [33]. Briefly, mothers were considered eligible for inclusion if they were residents in the cohort area, at least 16 years old, were carrying a singleton pregnancy and were planning to give birth at the reference hospital. Mothers who had participated in an assisted fertility program and those with communication difficulties were excluded. A total of

2644 eligible pregnant women agreed to participate in the study. Women were monitored during pregnancy and their children enrolled at birth and followed-up until preschool years. After excluding women who withdrew, were lost to follow-up, or underwent abortions or fetal deaths, a total of 2506 pregnant women were monitored until delivery. The study sample included 1877 children with data on at least one HC measurement and neurodevelopment outcome at 5 years, and the population for analyses with all the covariates were 1795 (Fig. 1). Both preterm ($n=66$) and term children were included. As previously reported, women–child pairs who were excluded from the analysis due to lost to

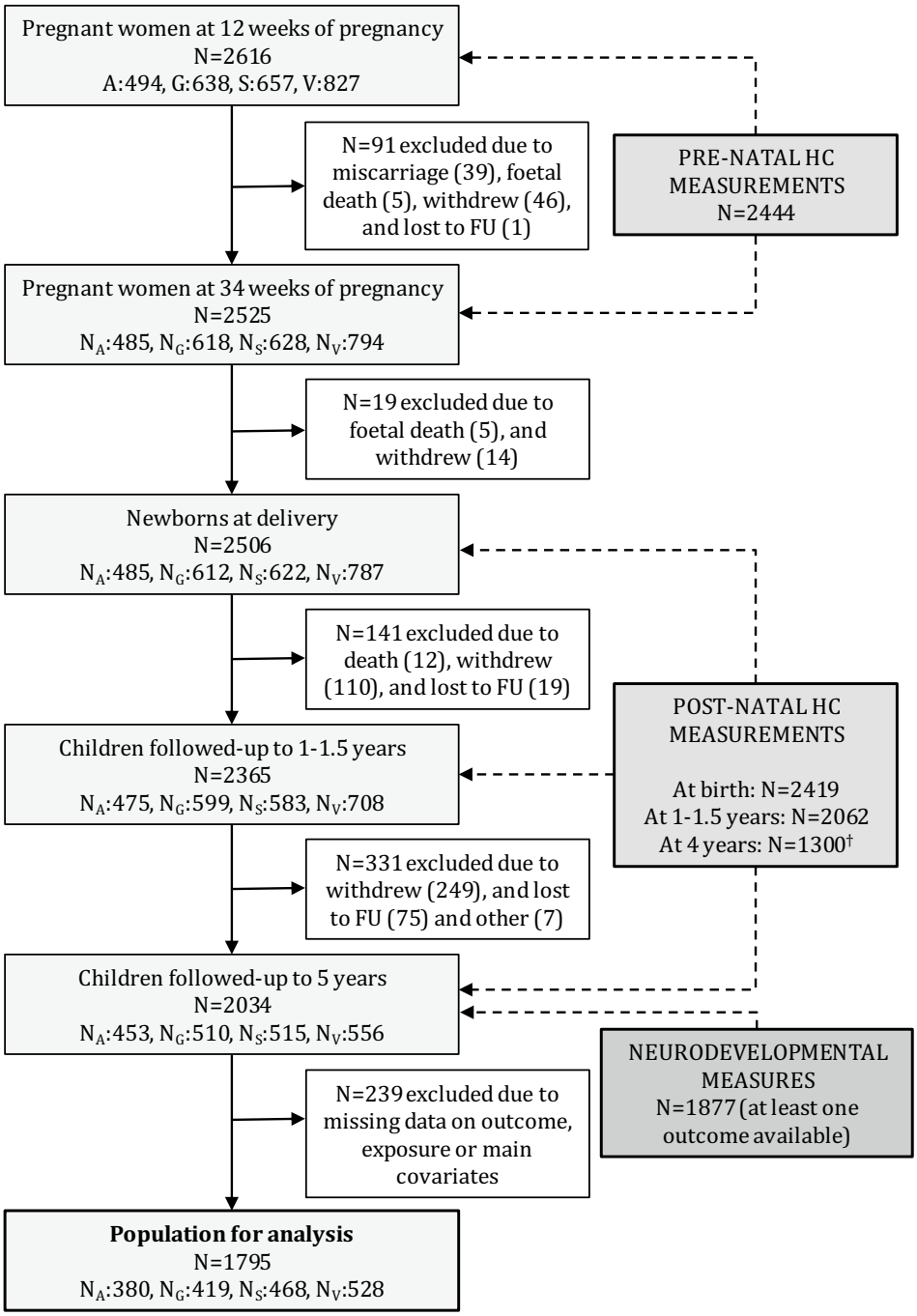

Fig. 1 Flowchart of participants included in the study

N: Number of observations, N_X : Number of observations by sub-cohort, where X = A: Astúrias, G: Gipuzkoa, S: Sabadell, and V: Valencia; FU: follow-up
† Not available for Valencia sub-cohort

follow-up had a slightly lower maternal age at birth, gestational age, and social class, and a higher parity and foreign origin prevalence [14]. All women provided written informed consent prior to participating in the study and the research protocol was approved by the ethics committees of the centers involved in the study.

Head circumference

Ultrasound scans (Voluson 730 Pro and 730 Expert; Siemens Sienna) were scheduled at 12, 20, and 34 weeks of gestation and performed by obstetricians specialized in conducting these types of examinations at the respective hospitals. Additionally, we had access to the records of any other ultrasound scan performed on women during their pregnancy, which allowed us to obtain from two to eight valid ultrasounds per woman between 7 and 42 weeks of gestation. An early crown–rump length (CRL) measurement was used for pregnancy dating. Gestational age was established using CRL when the difference with the age based on the self-reported last menstrual period was ≥ 7 days. Women with a difference of > 3 weeks ($n = 18$) were excluded to avoid a possible bias. After several training sessions, we conducted a quality control study with the sonographers involved in the assessments to determine inter-observer reliability. Intra-class correlation coefficients [34] between the examiners were in the range of 0.80–0.91 and coefficients of variation were lower than 5%. Infant HC at birth was assessed by a nurse when the newborn arrived at the hospital ward within the first 12 h of life. HC measurements at 1–1.5 and 4 years of age were carried out by trained fieldwork nurses. All newborn and postnatal HC measurements were maximum fronto-occipital circumference using a flexible tape following a standardized protocol with no inter-observer reliability measurements required due to a low degree of task complexity.

Prenatal HC

We used linear mixed models [35] to obtain growth curves for each parameter in each cohort separately. Models were adjusted for factors known to affect fetal growth: maternal age, height, parity, country of origin (as proxy of ethnicity), pre-pregnancy weight, father's height, and fetal sex. In accordance with these customized models, we calculated unconditional z-scores at 12, 20, and 34 weeks of gestation and conditional z-scores for 12–20 and 20–34 weeks of gestation based on the INMA study population as referent. An unconditional z-score describes the value of the parameter for a specific gestational age, while the conditional z-scores (conditioned on the value measured at the previous gestational age) describe the growth experienced in the respective time interval [36–38]. To reduce random error due to small deviations from the scheduled exam times, we calculated z-scores using the predicted value (by the corresponding fetal curve) at this particular time point conditioned to the nearest measure. More detailed information is in Online Appendix 1 and published elsewhere [14, 36].

Newborn and postnatal HC

Head circumference for gestational age z-scores at birth was based on the International Fetal and Newborn Growth Consortium for the twenty-first Century (INTERGROWTH-21st) standard [39]. For head circumferences at age 1–1.5 and 4 years, z-scores were based on the World Health Organization (WHO) Child Growth Standards [40]. We analyzed z-scores for head circumference based on child age and sex.

Neuropsychological and behavioral measures

Neuropsychological development was assessed at a mean age of 4.9 (SD 0.6) years using a battery of different psychometrical scales and computer-based tests. The McCarthy Scales of Children's Abilities (MCSA) [41] was used to evaluate cognitive and psychomotor development. The California Preschool Social Competence Scale (CPSCS) was used for assessment of child's social competence [42]. The childhood autism spectrum test (CAST) [43] was used to quantify autism spectrum symptoms in children (ASC); each point represents one symptom of ASC [44]. The form list of attention-deficit/hyperactivity disorder criteria of the diagnostic and statistical manual of mental disorders fourth edition (ADHD-DSM-IV) [45] was used for identification of inattention and hyperactivity/impulsivity symptoms, which is as valid for ADHD diagnosis in children from 2 to 5 years of age as it is in older children [16, 46]. Finally, the Conner's kiddie continuous performance test (K-CPT) [47], a computerized test was used to evaluate attention function, reaction time, accuracy and impulse control. Measures on K-CPT include: omission errors in which a target stimulus is presented, but the child fails to respond to it; commission errors in which the child responds to a non-target stimulus; and Hit Reaction Time Standard Error (HRT-SE) which corresponds to the variation in time of latency before a response, a measure of distractibility. These K-CPT variables have all been correlated to ADHD symptoms and have been repeatedly used for ADHD research [48].

A common protocol was followed for evaluation [16]. Trained psychologists supervised all the psychometrical assessments. MSCA and K-CPT were performed by children with the supervision of four trained psychologists (one per cohort) who also administered the CAST questionnaire to the child's parents to increase the CAST score accuracy. ADHD-DSM-IV and CPSCS were teacher-rated (for details on all tests and rating scales see Online Appendix 2).

Statistical analysis

All outcome scores were treated as continuous variables, to improve statistical power compared to dichotomized outcomes [49]. The association between HC measurements and neurodevelopment outcomes was fitted with multivariable linear regression models (quantitative outcomes) and negative binomial regression models (semi-quantitative outcomes: CPT omissions and commissions; ADHD-DSM-IV and CAST scores). The use of negative binomial regression models aimed to account for over-dispersion of the data, and results were shown as mean ratios (MR) which should be interpreted as relative risks. Results were presented as coefficients (β) or mean ratios (MR) with corresponding 95% confidence intervals (CI). First, models were adjusted for child's age at neurodevelopment test assessment (minimally adjusted models). Second, following a previous study [14], models were additionally adjusted for maternal age at birth, body mass index based on measured height at recruitment and pre-pregnancy self-reported weight, smoking during pregnancy (no versus yes), parity, country of birth (Spanish versus foreign), social class (occupation during pregnancy based on the highest social class using a widely used Spanish adaptation of the international ISCO88 coding system; I–II, managers/technicians; III, skilled; IV–V, semiskilled/unskilled) and education (primary or less, secondary, university degree); paternal body mass index and country of birth; child's sex and child's gestational age (fully adjusted models). MCSA scores were also adjusted for quality of the test performance flagged by the psychologist (good versus not-so-good). Examiners identified children whose tests were of good quality and of poor quality (e.g., due to fatigue, illness, etc.). The further exclusion of children with poor quality examinations ($n = 87$) did not change the final results (data not shown); we, therefore, included them in the analysis, adjusting for a binary indicator of exam quality.

In further sensitivity analyses, final HC models were repeated adding adjustments for: maternal verbal IQ proxy (WAIS-IV similarities subtest) [50] and mental health (SCL-R-90) [51]; child breastfeeding duration adjustment; and excluding children born preterm. We further analyzed differences in HC between participants and other members of the INMA cohort who did not participate, checked for potential interactions by child sex and included false discovery p value corrections (FDR) due to multiple statistical test comparisons.

Separate models were applied to each cohort and combined estimates were calculated with a fixed effects meta-analysis. We assessed heterogeneity in the estimates using the Cochran Q test and the I-squared statistic (I^2). Random effects model was used if $I^2 > 50\%$.

Results

The study sample included 868 female and 913 male children; the mean gestational age was 39.67 (SD 1.41) weeks and there were 66 preterm infants. Complete details of the study sample characteristics are given in Table S1. Mean prenatal HC at 12, 20 and 34 weeks was 71.90 (SD 6.37) mm, 172.43 (SD 8.06) mm and 305.93 (SD 11.00) mm, respectively. Mean HC was 34.34 (SD 1.4) cm at birth, 47.15 (SD 1.67) cm at 1–1.5 years, and 51.07 (SD 1.50) cm at 4 years of age (Table 1). There were no HC differences between included and excluded participants of the study (Table S2).

In general, we found moderate (greater than 0.4) correlations between birth and postnatal measurements and high

Table 1 Prenatal, newborn and postnatal head circumference (HC) [mean (standard deviation)] by sub-cohort location

	Asturias $n = 380$	Gipuzkoa $n = 419$	Sabadell $n = 468$	Valencia $n = 528$	Total $n = 1795$
Prenatal					
HC at week 12 (mm)	76.67 (2.57)	71.14 (6.30)	71.78 (6.71)	69.19 (6.14)	71.90 (6.37)
HC at week 20 (mm)	174.58 (7.17)	171.41 (6.99)	175.46 (8.42)	169.02 (7.62)	172.43 (8.06)
HC at week 34 (mm)	308.64 (11.14)	303.53 (11.24)	310.01 (9.38)	302.27 (10.34)	305.93 (11.00)
Newborn and postnatal					
HC at birth (cm)	34.27 (1.47)	34.75 (1.34)	34.26 (1.22)	34.14 (1.47)	34.34 (1.40)
HC-for-gestational age z-score at birth	0.34 (1.14)	0.67 (1.03)	0.28 (0.94)	0.22 (1.11)	0.36 (1.07)
HC at 1 year of age (cm)	48.42 (1.71)	47.26 (1.70)	47.09 (1.41)	46.42 (1.39)	47.15 (1.67)
HC-for-age z-score at 1 year	1.03 (1.19)	0.88 (1.19)	0.70 (0.94)	0.71 (0.93)	0.80 (1.05)
HC at 4 years of age (cm)	51.34 (1.51)	50.98 (1.46)	50.93 (1.49)	NA	51.07 (1.50)
HC-for-age z-score at 4 years	0.88 (0.97)	0.65 (0.97)	0.60 (0.96)	NA	0.70 (0.97)

NA not applicable

correlations (greater than 0.7) between postnatal HC measurements at 1–1.5 and 4 years of age. Regarding prenatal HC, correlations between measurements generally decreased with increasing time between measurements (Table 2).

Most of the results from minimally and fully adjusted regression models showed no statistically significant associations between prenatal HC and neurodevelopment outcomes, except for some inconsistent associations with *z*-score of fetal size at 12th and 20th week and fetal growth at 12–20 weeks (Table 3, Table S3). Specifically in the fully adjusted models, the larger the 12th week HC, the lower the child scored at the MCSA quantitative subscale [(β −0.72, 95% CI −1.42, −0.02) points per each HC *z*-score above the HC median of the norm sample) as well as being a slight adverse factor for omissions committed on the K-CPT test (MR 1.06, 95% CI 1.01, 1.10). However, fetal growth at 12–20 weeks showed some protective associations with ADHD scores and MCSA perceptive-performance subscale. None of the prenatal data seemed to show any association with the child scores of social competence, as measured with CPSCS, and autism spectrum symptoms, as measured with CAST.

However, results from minimally and fully adjusted regression models showed positive associations between newborn and postnatal HC measurements (birth 1–1.5 years and 4 years) and cognitive outcomes at preschool years taken from the MSCA test (Table 4, Table S4). Specifically, MSCA global cognitive scale, perceptive-performance subscale, quantitative subscale and executive subscale were associated with newborn and postnatal HC measurements. No association was found between the verbal subscale and HC measurements at any of the follow-ups.

Larger newborn and postnatal HC were protective for ADHD symptom (Table 4). HC at birth was associated with lower scores of both total symptoms (MR 0.85, 95% CI 0.75; 0.96) and inattention symptoms (MR 0.80, 95% CI 0.70; 0.92); and HC at 1–1.5 years was associated with lower inattention symptoms (MR 0.80, 95% CI 0.69; 0.94). Further, results from fully adjusted regression models showed no associations between newborn and postnatal HC and CPSCS global score, CAST global score and the K-CPT test outcomes (Table 4). However, minimally adjusted regression models showed some significant, protective associations with CPSCS, CAST and CPT-commission outcomes (Table S4).

Similar results for prenatal, newborn and postnatal HC were observed when preterm births (< 37 weeks) were excluded from final models (Tables S5 and S6). Results were similar in sensitivity analyses between newborn and postnatal HC and neurodevelopment adjusting for maternal IQ proxy and mental health (Table S7), and child breastfeeding duration (Table S8).

To correct for multiple statistical comparisons, false discovery corrected *p* values (FDR) are shown in Table S9 and Table S10; and the main findings on newborn HC measurement remained significantly associated with MSCA and ADHD outcomes.

No interactions between HC and neurodevelopment by sex were detected in most of the models (Tables S11 and S12), except for a few attention-related and CAST outcomes, in which males tended to show higher scorings and stronger associations; however, none of the interaction *p* values passed FDR corrections (data not shown).

Table 2 Spearman correlation coefficients between head circumference measurements according to age and sub-cohort location

Head circumference measurements		Spearman correlation				
		Asturias	Gipuzkoa	Sabadell	Valencia	All
Week 12	Week 20	0.733*	0.542*	0.434*	0.486*	0.510*
	Week 34	0.387*	0.202*	0.190*	0.236*	0.275*
	Birth	0.308*	0.058	0.077	− 0.012	0.061*
	1 year	0.514*	0.049	0.040	0.121*	0.250*
	4 years	0.435*	0.089	0.019	NA	0.154*
Week 20	Week 34	0.347*	0.426*	0.268*	0.379*	0.419*
	Birth	0.330*	0.187*	0.164*	0.150*	0.191*
	1 year	0.421*	0.248*	0.169*	0.250*	0.313*
	4 years	0.354*	0.238*	0.151*	NA	0.237*
Week 34	Birth	0.488*	0.454*	0.457*	0.404*	0.406*
	1 year	0.402*	0.394*	0.357*	0.417*	0.407*
	4 years	0.407*	0.380*	0.278*	NA	0.339*
Birth	1 year	0.432*	0.413*	0.515*	0.433*	0.413*
	4 years	0.409*	0.433*	0.503*	NA	0.432*
1 year	4 years	0.728*	0.725*	0.821*	NA	0.760*

*p value < 0.05

Table 3 Associations and 95% confidence intervals between fetal head circumference and neurodevelopment at 5 years of age

	Unconditional *z*-scores at			Conditional *z*-scores between	
	Week 12	Week 20	Week 34	12–20 weeks	20–34 weeks
	β (95% CI)	*β* (95% CI)	*β* (95% CI)	*β* (95% CI)	*β* (95% CI)
MCSA global cognitive scale	−0.42 (−1.08; 0.25)	0.24 (−0.41; 0.89)	0.25 (−0.38; 0.88)	0.45 (−0.20; 1.10)	0.22 (−0.41; 0.85)
MCSA verbal subscale	−0.53 (−1.23; 0.17)	−0.19 (−0.88; 0.50)	0.10 (−0.56; 0.77)	0.04 (−0.65; 0.72)	0.16 (−0.50; 0.83)
MCSA perceptive-performance subscale	0.06 (−0.62; 0.74)	0.66 (0.00; 1.32)	0.32 (−0.32; 0.96)	0.68* (0.02; 1.34)	0.18 (−0.46; 0.82)
MCSA quantitative subscale	−0.72* (−1.42; −0.02)	0.21 (−0.48; 0.90)	0.43† (−0.76; 1.61)	0.61 (−0.08; 1.29)	0.44† (−0.71; 1.59)
MCSA executive function	−0.61 (−1.29; 0.07)	0.09 (−0.58; 0.76)	0.42† (−0.52; 1.35)	0.41 (−0.26; 1.07)	0.45† (−0.51; 1.41)
CPSCS global score	−0.79 (−1.69; 0.11)	0.37 (−0.47; 1.21)	0.50 (−0.30; 1.31)	1.17† (−0.38; 2.73)	0.42 (−0.38; 1.22)
K-CPT HRT	0.54 (−5.96; 7.03)	0.02 (−6.77; 6.82)	−0.30 (−6.97; 6.37)	−0.19 (−6.95; 6.58)	−0.46 (−7.17; 6.25)
K-CPT HRT-SE	0.33 (−0.43; 1.08)	0.15 (−0.61; 0.91)	−0.24 (−0.98; 0.51)	−0.02 (−0.78; 0.74)	−0.07† (−1.19; 1.05)
	MR (95% CI)	MR (95% CI)	MR (95% CI)	MR (95% CI)	MR (95% CI)
K-CPT omissions	1.06* (1.01; 1.10)	0.98 (0.94; 1.02)	0.98 (0.94; 1.02)	0.95* (0.91; 0.99)	0.98 (0.94; 1.03)
K-CPT commissions	0.98 (0.95; 1.01)	0.99 (0.96; 1.02)	1.01 (0.98; 1.04)	1.00 (0.97; 1.03)	1.01 (0.98; 1.04)
ADHD-DSM-IV total symptoms	1.14 (1.00; 1.30)	0.94 (0.83; 1.06)	0.92 (0.81; 1.04)	0.87* (0.77; 0.99)	0.92 (0.81; 1.05)
Inattention symptoms	1.18 (0.99; 1.39)	0.92 (0.80; 1.07)	0.91 (0.78; 1.06)	0.84* (0.72; 0.98)	0.92 (0.79; 1.07)
Hyperactivity/impulsivity symptoms	1.14 (0.99; 1.32)	0.94† (0.77; 1.16)	0.94 (0.82; 1.08)	0.89 (0.78; 1.02)	0.94 (0.82; 1.08)
CAST global score	1.03† (0.98; 1.07)	1.00 (0.97; 1.02)	1.00 (0.97; 1.02)	0.99 (0.96; 1.01)	1.00 (0.97; 1.02)

Coefficient (*β* linear regression model) or mean ratio (*MR* negative binomial regression model) and 95% CI for a HC SD (*z*-score) increase estimated by meta-analysis by cohort

Models adjusted for child's sex and age at neurodevelopment test assessment, maternal smoking during pregnancy, education and social class; and paternal country of birth. Cohort-specific covariates also included: maternal age, body mass index, parity, and country of birth, and paternal body mass index (INMA-Asturias); maternal body mass index, parity (INMA-Gipuzkoa); maternal country of birth (INMA-Sabadell); maternal country of birth, parity, paternal body mass index (INMA-Valencia)

MCSA McCarthy Scales of Children's Abilities, *CPSCS* California Preschool Social Competence Scale, *K-CPT* Conners' kiddie continuous performance test, *CAST* childhood autism spectrum test, *HRT* hit reaction time, *SE* standard error

**P* value of estimated coefficient from meta-analysis was < 0.05

†Random effects models was used (I^2 statistic > 50%)

Discussion

Our results from a population-based birth cohort indicate that prenatal head growth was not associated with children's neurodevelopment assessed at preschool age. On the other hand, newborn and postnatal HC measurements taken longitudinally from birth to 4 years were positively associated with the global cognitive scale of MSCA test, particularly perceptive, quantitative and executive function subscales, but not with the verbal subscale. The study revealed other interesting associations between newborn and postnatal HC measurements and ADHD symptoms. For example, our results suggest that children with larger HC, particularly at birth, were less likely to be given high scores on inattention symptoms.

In a previous study with this sample with shorter follow-up, Álamo-Junqueras's and colleagues reported no association between prenatal HC and head growth with neurodevelopment at the age of 1–1.5 years assessed with the BSID's mental and psychomotor scores [14]. Álamo-Junquera et al. [14]. hypothesized that the lack of association could have been due to a possible lack of sensitivity to assess complex functional changes at the early age of 1–1.5 years (time of the neuropsychological assessment). We extended longitudinal follow-up with neuropsychological assessment at age 5; however, our results were similar to those of Álamo-Junqueras's et al. In general, there are very few studies with prenatal HC data and even less with a population-representative sample. The majority of those studies failed to find an association [1, 52, 53]. Whitehouse et al. found no relation between occipito-frontal HC measured using ultrasonography at 18 weeks of gestation and language neurodevelopment [52]. In 2009, a study with 41 children with spina bifida also concluded that prenatal HC

Table 4 Associations and 95% confidence intervals between newborn and postnatal head circumference and neurodevelopment at 5 years of age

	Head circumference *z*-scores at		
	Birth	1–1.5 years	4 years
	β (95% CI)	*β* (95% CI)	*β* (95% CI)
MCSA global cognitive scale	1.22* (0.59; 1.85)	1.13*† (0.10; 2.15)	0.95* (0.15; 1.75)
MCSA verbal subscale	0.70† (−0.38; 1.77)	0.73† (−0.52; 1.98)	0.51 (−0.35; 1.36)
MCSA perceptive-performance subscale	1.20* (0.55; 1.84)	1.11* (0.46; 1.77)	1.08* (0.26; 1.90)
MCSA quantitative subscale	0.96* (0.28; 1.63)	0.97* (0.28; 1.66)	0.91* (0.06; 1.76)
MCSA Executive function	1.14* (0.48; 1.79)	1.07† (−0.10; 2.25)	0.90* (0.07; 1.72)
CPSCS global score	0.80 (−0.02; 1.62)	0.83 (−0.02; 1.67)	1.55† (−0.23; 3.33)
K-CPT HRT	−1.08 (−7.65; 5.49)	−1.04 (−8.21; 6.12)	1.78 (−9.73; 13.29)
K-CPT HRT-SE	−0.31 (−1.05; 0.44)	−0.56 (−1.37; 0.25)	−0.67 (−1.85; 0.51)
	MR (95% CI)	MR (95% CI)	MR (95% CI)
K-CPT omissions	0.97 (0.93; 1.02)	0.98 (0.94; 1.03)	0.98 (0.93; 1.04)
K-CPT commissions	1.00 (0.98; 1.03)	0.98 (0.95; 1.01)	0.96 (0.92; 1.00)
ADHD-DSM-IV total symptoms	0.85* (0.75; 0.96)	0.88 (0.77; 1.01)	0.82† (0.59; 1.14)
Inattention symptoms	0.80* (0.70; 0.92)	0.80* (0.69; 0.94)	0.78† (0.56; 1.10)
Hyperactivity/impulsivity symptoms	0.90 (0.79; 1.04)	0.89† (0.68; 1.17)	0.85† (0.59; 1.23)
CAST global score	0.98 (0.96; 1.01)	1.00 (0.97; 1.02)	1.00 (0.96; 1.03)

Coefficient (*β* linear regression model) or mean ratio (*MR* negative binomial regression model) and 95% CI for a HC SD (*z*-score) increase estimated by meta-analysis by cohort

Models adjusted for maternal age at birth, body mass index, smoking during pregnancy, parity, country of birth, social class and education; paternal body mass index and country of birth; and child's sex, gestational age (except *z*-score at birth), and age at neurodevelopment test assessment

MCSA McCarthy Scales of Children's Abilities, *CPSCS* California Preschool Social Competence Scale, *K-CPT* Conners' kiddie continuous performance test, *CAST* childhood autism spectrum test, *HRT* hit reaction time, *SE* standard error

*p value of estimated coefficients from meta-analysis was < 0.05

†Random effects models was used (I^2 statistic $> 50\%$)

was not a good predictor of mental and motor function at the age of 5 years [53], and Walker et al. only found a small association between ultrasound measurements of HC at 14 weeks of gestational age and reasoning ability measured with the Raven's test at the age of 6–8 years [1].

Our results for newborn and postnatal HC and cognitive development are consistent with several previous studies. Heinonen et al. reported an association between prenatal growth (based on measurements of body size at birth) and postnatal body size, including HC, with individual cognitive differences in a Finnish population-based cohort [2]. Similar findings were reported in a recent meta-analysis by Harris [3]. Veena et al. observed a similar pattern to ours, where verbal skills were not affected by HC at birth while perceptive performance was affected [4]. However, several other studies have reported an association between HC and verbal abilities [5, 6]. Verbal skills should be further investigated since it seems that they have a different trajectory of development than perceptual skills. In particular, Raikkonen and Pesonen observed critical periods specific for verbal development, between the ages of 2 and 7 years [7]. These findings suggest the complexity of the relationship between the brain, development and cognitive abilities. This idea is supported by neuroimaging studies that correlate brain structure with function, and which have identified different brain regions relating differently to high function cognitive abilities [54]. From this, it is understandable that other factors should be considered other than total brain size. However, from a general population point of view, these results further support the idea of HC measurements as inexpensive and non-invasive health indicators that can be used to screen children at potential risk of non-optimal neurodevelopment.

In relation to ADHD symptoms, results are in accordance with the majority of previous studies that observed that smaller body size, weight and HC at birth were associated with an increase of child ADHD symptoms at preschool and school ages [24, 25, 55, 56]. Lahti et al. found that HC was a stronger predictor of hyperactivity and inattention symptoms than birth weight [25]. Similarly, Murray et al. observed an association between larger HC at birth and lower attention difficulties, but only in female children [26]. Also, Heinonen's subsample of term, normal birth weight healthy babies,

reported that HC was a better predictor of ADHD symptoms rated by their parents at the age of 56 months, than other measurements such as birth length, BMI growth between 20 and 56 months or the relative BMI at 56 months [24]. Additionally, there are studies that reported relationships between small brain volume and ADHD symptoms [18]. In accordance with our results, Portellano [57] suggested that HC was a determinant of inattention symptoms, but not of hyperactivity–impulsivity symptoms. The results in our study were significant only for the inattention symptoms while hyperactivity–impulsivity symptoms were not associated with any prenatal, newborn and postnatal HC measurements. This finding requires further confirmation, but supports the idea of anatomical distinctions between hyperactivity–impulsivity and inattention symptom disorders [57]. Previous studies regarding ADHD were mostly conducted within clinical populations; therefore, our study contributes to the literature by associating HC and ADHD symptoms following a symptom dimensional method and by being a large population-based sample.

Early life head overgrowth has been suggested to be linked to autism spectrum disorders [27–29]; however, present findings did not support this hypothesis since no significant patterns were detected in CAST scores in the fully adjusted regression models. This is probably due to the healthy characteristics of the children studied, since they tended to show low CAST symptom scorings, as expected. However, our findings are in accordance with a recent case–control study that reported no associations between early life HC measurements and autism spectrum disorders [30].

The study results support the concept of prenatal fetal programming and long-term health consequences commented in the developmental origins of health and disease hypothesis (DOHaD) [58]. Early life brain growth may be indicative of brain programming and maturation with potential long-term functional consequences. To support this theoretical framework, we assume that newborn HC measurements indicate late prenatal growth [10], and the fact they were important predictors of later child neurodevelopment in the multivariable statistical analyses.

Control for selected confounding variables, which have previously been proven to be important factors of prenatal and postnatal neurodevelopment, was a significant element of this study, which adjusted for maternal smoking during pregnancy [59], maternal IQ proxy and mental health [14], and parental social class and education [15], among others. First, in concordance to the former study, maternal education, social class and age at birth, smoking during pregnancy, parental BMI and country of birth, as well as parity, did not change results significantly. Second, the study overcame a limitation pin pointed in the antecedent study, and the role of maternal IQ proxy and mental health was explored. Once again, the results showed that the adjustment did not change findings. This supports the existing association between HC and individual differences in early neurodevelopment, as well as the proposition of making newborn and postnatal HC a valid routine measurement.

This longitudinal study recruited families during the first trimester of pregnancy and started collecting data by trained professionals with validated tools to assess anthropometrical, environmental, behavioral and cognitive variables. To our knowledge, this is one of the very few studies that have used actual prenatal HC measurements instead of estimated data from preterm births or growth charts. The majority of studies estimate fetal growth and fetal possible adversities through measurements of size at birth, including HC [10, 14, 60], therefore, the possible uncertainties due to a lack of intrauterine data have been minimized with this longitudinal cohort study with recruited women during early pregnancy.

Our study has several strengths already commented, such as the prenatal, newborn and postnatal prospective design and standardized methods used for HC and neurodevelopment measurements, data on a wide range of potential confounders, and a large population-based sample. Nonetheless, limitations to the study should be noted. There was some loss to follow-up, which was slightly biased toward less socially advantageous families. This could potentially reduce the external validity of the findings, but probably not internal validity. Finally, we had no information on parental HC, possibly a better predictor of child HC than parental BMI, to adjust for potential residual confounding due to genetics.

Neuropsychological research historically focused on neurodegenerative disorders, brain injury and rehabilitation; in the last two decades, research has started focusing on the early development of neuropsychology and its impact on actual abilities, behavior and difficulties. Modern technology allows for a better understanding of the relationship between brain development and volume with early neurodevelopment outcomes [61]. Several studies support that an easy, non-invasive and inexpensive measurement such as HC is a good predictor of brain volume, especially during childhood [62]. Evidence supporting the use of these measurements as valid indicators of neuropsychological and neuropsychiatric functioning could increase the feasibility of conducting studies in low-income countries where there is a high rate of low birth weight babies and lower HC due to poverty and malnutrition [4].

Our findings support the usefulness of HC as a newborn and postnatal measurement tool to assess possible suboptimal neurodevelopment in young children from the general population. Specifically, we observe that larger HC is associated with an improved cognitive function and lower ADHD symptoms.

Acknowledgements We would like to thank all the participants of the INMA Project for their collaboration as well as the project investigators at each cohort center as well as the coordination centers. A full roster of the INMA Project investigators can be found at http://www.PROYECTOINMA.org/. Wilma Zijlema did English edits in the manuscript.

Funding Sabadell: This work was supported by grants from the Spanish Ministry of Health [FIS-PI041436]; Instituto de Salud Carlos III [Red INMA G03/176 and CB06/02/0041 and predoctoral grant PFIS 2010, Register FI10/00399]; the Generalitat de Catalunya-CIRIT [1999SGR 00241]; the EU sixth framework project NEWGENERIS [FP6-2003-Food-3-A-016320]; Fundació Roger Torné, and Fundació La Mataró de TV3 (Project No. 090430 & No. 20162210). This study has been funded by Instituto de Salud Carlos III through the projects "CP14/00108 & PI16/00261" (co-funded by European Regional Development Fund "A way to make Europe"). Asturias: This study was funded by grants from Instituto de Salud Carlos III (Red INMA G03/176 and CB06/02/0041), FISS-PI042018, FISS-PI09/02311, FISS-PI1302429, Obra Social Cajastur/Fundación Liberbank and Universidad de Oviedo. Guipuzkoa: This study was funded by grants from Instituto de Salud Carlos III (FIS-PI06/0867 and FIS-PS09/00090), Department of Health of the Basque Government (2005111093 and 2009111069), and the Provincial Government of Gipuzkoa (DFG06/004 and DFG08/001). Valencia: This study was funded by grants from UE (FP7-ENV-2011 cod 282957 and HEALTH.2010.2.4.5-1, Instituto de Salud Carlos III (Red INMA G03/176, CB06/02/0041, FIS-FEDER 03/1615, 04/1509, 04/1112, 04/1931, 05/1079, 05/1052, 06/1213, 07/0314, 09/02647, 11/01007, 11/02591, and CP11/00178), and the Conselleria de Sanitat Generalitat Valenciana; all in Spain. FIS-DENAMIC: PI/11/02038. Jordi Julvez holds a Miguel Servet contract (MS14/00108) awarded by the Spanish Institute of Health Carlos III (Ministry of Economy and Competitiveness). This study was also funded by grants from UE (FP7-ENV-2011 cod 282957 and HEALTH.2010.2.4.5-1), Instituto de Salud Carlos III (Red INMA G03/176, CB06/02/0041, FIS-FEDER 03/1615, 04/1509, 04/1112, 04/1931, 05/1079, 05/1052, 06/1213, 07/0314, 09/02647, 11/01007, 11/02591, 17/00663, and CP11/00178), Alicia Koplowitz Foundation 2017, and the Conselleria de Sanitat Generalitat Valenciana; all in Spain.

Compliance with ethical standards

Conflict of interest None of the authors have conflicts of interest to disclose. None of the authors have financial relationships relevant to this article to disclose.

References

1. Walker SP, Thame MM, Chang SM, Bennett F, Forrester TE (2007) Association of growth in utero with cognitive function at age 6–8 years. Early Hum Dev 83(6):355–360
2. Heinonen K, Räikkönen K, Pesonen A-K et al (2008) Prenatal and postnatal growth and cognitive abilities at 56 months of age: a longitudinal study of infants born at term. Pediatrics 121(5):e1325–e1333
3. Harris SR (2015) Measuring head circumference: update on infant microcephaly. Canadian Family Physician Medecin de Famille Canadien 61(8):680–684
4. Veena SR, Krishnaveni GV, Wills AK et al (2010) Association of birthweight and head circumference at birth to cognitive performance in 9- to 10-year-old children in South India: prospective birth cohort study. Pediatr Res 67(4):424–429
5. Ivanovic DM, Leiva BP, Pérez HT et al (2004) Head size and intelligence, learning, nutritional status and brain development. Head, IQ, learning, nutrition and brain. Neuropsychologia 42(8):1118–1131
6. Räikkönen K, Forsen T, Henriksson M et al (2009) Growth trajectories and intellectual abilities in young adulthood: the Helsinki birth cohort study. Am J Epidemiol 170(4):447–455
7. Räikkonen K, Pesonen A (2009) Early life origins of psychological development and mental health. Scand J Psychol 50(6):583–591
8. Raikkonen K, Kajantie E, Pesonen AK, Heinonen K, Alastalo H, Leskinen JT, Nyman K, Henriksson M, Lahti J, Lahti M, Pyhälä R, Tuovinen S, Osmond C, Barker DJ, Eriksson JG (2013) Early life origins cognitive decline: findings in elderly men in the Helsinki birth cohort study. PLoS One 8(1):e54707
9. Scharf RJ, Rogawski ET, Murray-Kolb LE, Maphula A, Svensen E, Tofail F, Rasheed M, Abreu C, Vasquez AO, Shrestha R, Pendergast L, Mduma E, Koshy B, Conaway MR, Platts-Mills JA, Guerrant RL, DeBoer MD (2018) Early childhood growth and cognitive outcomes: findings from the MAL-ED study. Matern Child Nutr. https://doi.org/10.1111/mcn.12584
10. Fujimura M, Seryu JI (1977) Velocity of head growth during the perinatal period. Arch Dis Child 52(2):105–112
11. Coronado R, Macaya A, Giraldo J, Roig-Quilis M (2014) Concordance between a head circumference growth function and intellectual disability in relation with the cause of microcephaly. Anales de Pediatría 83:109–116 **(English edition)**
12. Leppänen M, Lapinleimu H, Lind A, Matomäki J, Lehtonen L, Haataja L, Rautava P (2014) Antenatal and postnatal growth and 5-year cognitive outcome in very preterm infants. Pediatrics 133(1):63–70
13. Raz S, Newman JB, De Bastos AK, Peters BN, Batton DG (2014) Postnatal growth and neuropsychological performance in preterm-birth preschoolers. Neuropsychology 28(2):188–201
14. Álamo-Junquera D, Sunyer J, Iñiguez C et al (2015) Prenatal head growth and child neuropsychological development at age 14 months. American Journal of Obstetrics and Gynecology 212(5):661.e1–661.e11
15. Lawlor DA, Batty GD, Morton SM, Deary IJ, Macintyre S, Ronalds G, Leon DA (2005) Early life predictors of childhood intelligence: evidence from the Aberdeen children of the 1950s study. J Epidemiol Community Health 59(8):656–663
16. Boucher O, Julvez J, Guxens M et al (2017) Association between breastfeeding duration and cognitive development, autistic traits and ADHD symptoms: a multicenter study in Spain. Pediatr Res 81(3):434–442
17. Monroy-Torres R, Naves-Sánchez J, Ortega-García JA (2012) Breastfeeding and metabolic indicators in Mexican premature newborns. Rev Invest Clin 64(6 Pt 1):521–528
18. Castellanos FX, Lee PP, Sharp W et al (2002) Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA 288(14):1740–1748
19. Linnet K, Wisborg K, Agerbo E, Secher N, Thomsen P, Henriksen T (2006) Gestational age, birth weight, and the risk of hyperkinetic disorder. Arch Dis Child 91(8):655–660
20. Hultman C, Torrång A, Tuvblad C, Cnattingius S, Larsson J, Lichtenstein P (2007) Birth weight and attention-deficit/hyperactivity symptoms in childhood and early adolescence: a prospective Swedish twin study. J Am Acad Child Adolesc Psychiatry 46(3):370–377
21. Vander Ploeg Booth K (2016) Attention-deficit/hyperactivity disorder (ADHD) in children born preterm and with poor fetal growth. NeoReviews 17(4):e213–e219
22. Julvez J, Forns M, Ribas-Fitó N, Torrent M, Sunyer J (2011) Attention behavior and hyperactivity and concurrent neurocognitive and social competence functioning in 4-year-olds from

two population-based birth cohorts. Eur Psychiatry J Assoc Eur Psychiatry 26(6):381–389
23. Stathis S, O'Callaghan M, Harvey J, Rogers Y (1999) Head circumference in ELBW babies is associated with learning difficulties and cognition but not ADHD in the school-aged child. Dev Med Child Neurol 41(6):375–380
24. Heinonen K, Räikkönen K, Pesonen A-K et al (2011) Trajectories of growth and symptoms of attention-deficit/hyperactivity disorder in children: a longitudinal study. BMC Pediatrics 11:84
25. Lahti J, Räikkönen K, Kajantie E, Heinonen K, Pesonen A-K, Järvenpää A-L, Strandberg T (2006) Small body size at birth and behavioural symptoms of ADHD in children aged five to six years. J Child Psychol Psychiatry 47(11):1167–1174
26. Murray E, Matijasevich A, Santos IS, Barros AJ, Anselmi L, Barros FC, Stein A (2015) Sex differences in the association between foetal growth and child attention at age four: specific vulnerability of girls. J Child Psychol Psychiatry 56(12):1380–1388
27. Courchesne E, Carper R, Akshoomoff N (2003) Evidence of brain overgrowth in the first year of life in Autism. J Am Med Assoc 290(3):337–344
28. Sacco R, Gabriele S, Persico A (2015) Head circumference and brain size in autism spectrum disorder: a systematic review and meta-analysis. Psychiatry Res Neuroimaging 234(2):239–251
29. Pyhälä R, Hovi P, Lahti M, Sammallahti S, Lahti J, Heinonen K, Pesonen AK, Strang-Karlsson S, Eriksson JG, Andersson S, Järvenpää AL, Kajantie E, Räikkönen K (2014) Very low birth weight, infant growth, and autism-spectrum traits in adulthood. Pediatrics 134(6):1075–1083
30. Zwaigenbaum L, Young GS, Stone WL et al (2014) Early head growth in infants at risk of autism: a baby siblings research consortium study. J Am Acad Child Adolesc Psychiatry 53:1053–1062
31. Zhang L, Thomas KM, Davidson MC, Casey BJ, Heier LA, Uluğ AM (2005) MR quantitation of volume and diffusion changes in the developing brain. AJNR Am J Neuroradiol 26(1):45–49
32. James HE, Perszyk AA, MacGregor TL, Aldana PR (2015) The value of head circumference measurements after 36 months of age: a clinical report and review of practice patterns. J Neurosurg Pediatr 16(2):186–194
33. Guxens M, Ballester F, Espada M, INMA Project et al (2012) Cohort Profile: the INMA–INfancia y Medio Ambiente–(Environment and Childhood) Project. Int J Epidemiol 41(4):930–940
34. (1982) Intraclass correlation coefficient. In: Kotz S, Johnson NL (eds) Encyclopaedia of statistical sciences, vol 4. Wiley, New York, pp 213–217
35. Pinheiro J, Bates D (2000) Mixed-effects models in S and S PLUS: statistics and computing. Springer, New York
36. Iñiguez C, Ballester F, Amorós R, Murcia M, Plana A, Rebagliato M (2012) Active and passive smoking during pregnancy and ultrasound measures of fetal growth in a cohort of pregnant women. J Epidemiol Community Health 66(6):563–570
37. Gurrin LC, Blake KV, Evans SF, Newnham JP (2001) Statistical measures of foetal growth using linear mixed models applied to the foetal origins hypothesis. Stat Med 20(22):3391–3409
38. Royston P (1995) Calculation of unconditional and conditional reference intervals for foetal size and growth from longitudinal measurements. Stat Med 14(13):1417–1436
39. Villar J, Cheikh Ismail L, Victora CG et al (2014) International fetal and newborn growth consortium for the 21st century (INTERGROWTH-21st). International standards for newborn weight, length, and head circumference by gestational age and sex: the newborn cross-sectional study of the INTERGROWTH-21st Project. Lancet 384(9946):857–868
40. de Onis M, Garza C, Onyango AW, Rolland-Cachera MF (2009) Le, Comité de nutrition de la Société française de pédiatrie. [WHO growth standards for infants and young children]. Arch Pediatr 16(1):47–53
41. McCarthy DMSCA (2009) Escalas McCarthy de Aptitudes y Psicomotricidad para Niños. TEA Ediciones, Madrid
42. Julvez J, Forns M, Ribas-Fito N, Mazon C, Torrent M, Garcia-Esteban R (2008) Psychometric characteristics of the California preschool social competence scale in a Spanish population sample. Early Educ Dev 19:795–815
43. Scott F, Baron-Cohen S, Bolton P, Brayne C (2002) The CAST (childhood Asperger syndrome test): preliminary development of UK screen for mainstream primary-school children. Autism 6(1):9–31
44. Williams J, Scott F, Stott C et al (2005) The CAST (childhood Asperger syndrome test): test accuracy. Autism 9:45–68
45. American Psychiatric Association (2002) Manual diagnóstico y estadístico de los trastornos mentales. Masson, IV. Barcelona
46. Sterba S, Egger HL, Angold A (2007) Diagnostic specificity and nonspecificity in the dimensions of preschool psychopathology. J Child Psychol Psychiatry [Internet] 48(10):1005–1013
47. Conners C, Staff M (2001) Conners' kiddie continuous performance test (K-CPT): computer program for windows technical guide and software manual. Multi-Health Systems, Inc, Toronto
48. Conners C, Epstein J, Angold A, Klaric J (2003) Continuous performance test performance in a normative epidemiological sample. J Abnorm Child Psychol 31:555–562
49. Vilor-Tejedor N, Alemany S, Forns J, Cáceres A, Murcia M, Macià D, Pujol J, Sunyer J, González JR (2016) Assessment of susceptibility risk factors for ADHD in imaging genetic studies. J Atten Disord. https://doi.org/10.1177/1087054716664408
50. Axelrod BN (2002) Validity of the Wechsler abbreviated scale of intelligence and other very short forms of estimating intellectual functioning. Assessment 9(1):17–23
51. González de Rivera JL, Derogatis L, de las Cuevas C (1989) The Spanish Version of the SCL-90-R: normative data in general population. Towson, Baltimore
52. Whitehouse AJ, Zubrick SR, Blair E, Newnham JP, Hickey M (2012) Fetal head circumference growth in children with specific language impairment. Arch Dis Child 97(1):49–51
53. van der Vossen S, Pistorius LR, Mulder EJ, Platenkamp M, Stoutenbeek P, Visser GH, Gooskens RH (2009) Role of prenatal ultrasound in predicting survival and mental and motor functioning in children with spina bifida. Ultrasound Obstet Gynecol 34(3):253–258
54. Jung RE, Haier RJ (2007) The parieto-frontal integration theory (P-FIT) of intelligence: converging neuroimaging evidence. Behav Brain Sci 30(2):135
55. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS (2002) Cognitive and behavioral outcomes of school-aged children who were born preterm. JAMA 288(6):728–737
56. Ptacek R, Kuzelova H, Paclt I, Zukov I, Fischer S (2009) ADHD and growth: anthropometric changes in medicated and non-medicated ADHD boys. Med Sci Monitor Int Med J Exp Clin Res 15(12):CR595–CR599
57. Portellano JA (2007) Trastorno por déficit de atención (TDAH). In: Portellano JA (ed) Neuropsicologia infantil. Sintesi, Madrid, pp 145–159
58. Wadhwa P, Buss C, Entringer S, Swanson M (2009) Developmental origins of health and disease: brief history of the approach and current focus on epigenetic mechanisms. Semin Reprod Med. 27(5):358–368
59. Julvez J, Ribas-Fito N, Torrent M, Forns M, Garcia-Esteban R, Sunyer J (2007) Maternal smoking habits and cognitive development of children at age 4 years in a population-based birth cohort. Int J Epidemiol 36(4):825–832

60. Schlotz W, Phillips DIW (2009) Fetal origins of mental health: evidence and mechanisms. Brain Behav Immun 23(7):905–916
61. Young JM, Powell TL, Morgan BR et al (2015) Deep grey matter growth predicts neurodevelopmental outcomes in very preterm children. NeuroImage 111:360–368
62. Bartholomeusz HH, Courchesne E, Karns CM (2002) Relationship between head circumference and brain volume in healthy normal toddlers, children, and adults. Neuropediatrics 33(5):239–241