Head growth and intelligence from birth to adulthood in very preterm and term born individuals

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Abstract

Objective: To investigate the effects of infant and toddler head growth on intelligence scores from early childhood to adulthood in very preterm (<32 weeks gestational age; VP) and/or very low birth weight (<1500g; VLBW) and term born individuals.

Method: 203 VP/VLBW and 198 term comparisons were studied from birth to adulthood as part of the prospective geographically defined Bavarian Longitudinal Study (BLS). Head circumference was assessed at birth, 5, 20 months, and 4 years of age. Intelligence was assessed with standardized tests in childhood (6 and 8 years: K-ABC) and at 26 years (Wechsler Adult Intelligence Scale, WAIS). Structural equation modeling (SEM) was used to model the effect of head growth on IQ.

Results: On average, VP/VLBW had lower head circumference at birth (27.61cm versus 35.11cm, mean difference 7.49, 95% CI [7.09 – 7.90]) and lower adult intelligence scores (88.98 versus 102.54, mean difference 13.56 [10.59 - 16.53]) than term born comparison individuals. Head circumference at birth (e.g., total effect β=.48, p<.001 for adult IQ) and head growth in childhood predicted intelligence development from age 6 to 26 years in both VP/VLBW and term born individuals (70% of variance in adult IQ explained by full model). Effects of gestation and birth weight on intelligence were fully mediated by head circumference and growth.

Conclusions: This longitudinal investigation from birth to adulthood indicates head growth as a proxy of brain development and intelligence. Repeated early head circumference assessment adds valuable information when screening for long-term neurocognitive risk.

Key words: early childhood; gestational age; prospective longitudinal study; brain development; birth weight; Wechsler Adult Intelligence Scale; RECAP preterm

Introduction

Very preterm (<32 weeks gestational age; VP) and very low birth weight (<1500g, VLBW) infants grow up with life-long risks for neurocognitive impairment (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015; Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015). Early identification allows timely provision of resources. Follow-up after VP/VLBW birth is a general standard in many Western countries (Doyle et al., 2014). However, assessing cognitive development through descriptive behavioral data is time consuming and expensive (Aslin & Fiser; Hack et al., 2005). Repeated head circumference assessments may be a cost-effective indicator of brain development (Bartholomeusz, Courchesne, & Karns, 2002; Cheong et al., 2008; Garcia-Alix, Saenz-de Pipaon, Martinez, Salas-Hernandez, & Quero, 2004). Regional brain and cortical growth is significantly associated with brain maturation (Makropoulos et al., 2016), generally indicating that size matters.

Head circumference is measured in infancy in most countries, but its predictive validity remains controversial (Wright & Emond, 2015). At term, preterm infants have smaller whole brain volumes than term born infants (Ball et al., 2012; Makropoulos et al., 2016). Researchers argue that head growth between birth and 2 years is critical for intellectual development (Räikkönen et al., 2009) and studies of preterm populations have documented the value of head growth as a predictor of long-term neurocognitive abilities (Sammallahti et al., 2017; Sammallahti et al., 2014). Accelerated postnatal head growth suggests catch up after prenatal restraint (Cockerill, Uthaya, Doré, & Modi, 2006), but may not compensate for poor earlier growth after infancy (Gale, O'Callaghan, Bredow, & Martyn, 2006). Thus, it is important to investigate whether there are certain time windows of head growth that matter most for later IQ development.

In clinical practice, individual head growth is usually documented by plotting raw head circumference values on age-standardized growth chart curves, by converting raw values into standard scores, or by categorizing scores (Fenton & Kim, 2013). This is done to (clinically) identify individuals who grow at a substantially slower than average rate. Instead, growth over time assessed with latent class growth curve analyses to identify how the growth rate across all individuals (i.e., head growth) affects growth in another dimension (i.e., IQ). Structural equation modeling (SEM) has been proposed as the most appropriate in the context of additional factors (e.g., gestational age, birth weight) (Usami, Hayes, & McArdle, 2017).

Our aims were (1) to investigate VP/VLBW and term born individuals' head growth from birth to 4 years and intelligence in childhood and adulthood, and (2) to determine the specific timing of head growth that matters for intelligence development.

Method

Design

Participants were all VP and/or VLBW infants and an equally sized group of healthy term comparisons born in a geographically defined area of South Bavaria (Germany) between January 1985 and March 1986 as part of the prospective whole population Bavarian Longitudinal Study (BLS). The current study uses data collected at birth, term and at 5 and 20 months, and at 4, 6, 8, and 26 years of age.

Standard Protocol Approvals and Patient Consents. This research was completed in accordance with the Helsinki Declaration. Original ethical approval was obtained from the University of Munich Children's Hospital and the Landesärztekammer Bayern. Ethical approval for the adult follow-up was granted by the Ethical Board of the University Hospital Bonn (reference 159/09).

Informed written consent was provided by parents within 48 hours of their child's birth and all participants gave fully informed written consent for the adult assessment.

Participants. This study assesses a whole population sample of 682 VP/VLBW individuals (Wolke & Meyer, 1999). Of this cohort, 411 VP/VLBW were presumed alive, living in Germany, and eligible for inclusion at 26 years of age, and 260 (63.3%) participated in the adult assessment (see Appendix Figure 1). The BLS VP/VLBW participants did not differ from VP/VLBW adults who dropped out in terms of GA, BW, duration of hospitalization, gender, maternal age, parental marital status, and childhood cognitive scores, but had fewer prenatal complications and were of higher socioeconomic status (SES) (Eryigit Madzwamuse et al., 2015).

Of 916 healthy term-born comparison infants at birth, 350 were selected and stratified to match the VP/VLBW participants at the 6 years follow-up assessment. Of these, 308 individuals were eligible for inclusion and 229 (74.4%) participated at 26 years (Eryigit Madzwamuse et al., 2015). Only participants who had complete childhood and adulthood IQ data (203 VP/VLBW and 198 term comparisons) were included in the current analyses.

Head Circumference. Head circumference (cm) was assessed by trained research nurses during clinical assessments at birth, 5, and 20 months, and at 4, 6, and 8 years of age. At 5 and 20 months, examination ages were corrected for gestational age at birth. HC was measured twice at each assessment and the average score was recorded. Raw HC scores and standardized scores are reported in Table 1. Raw scores are used in main analyses in order to investigate separate contributions of gestation and birth weight in our statistical models.

Biological and Demographic Characteristics. Gestational age (weeks, range: VP/VLBW=25-36, term comparisons=37-42) and birth weight (grams, range: VP/VLBW=630-2590g, term

comparisons=2120-5050g) were coded from Bavarian perinatal survey forms at birth (Zander, Holzmann, & Selbmann, 1989). Family SES at birth was assessed as a weighted composite score of parents' education and occupation (Bauer, 1988).

Neurocognitive Assessments. Cognitive development (i.e., intelligence) was assessed longitudinally by psychologists with standardized tests in childhood and adulthood (Breeman et al., 2015). At age 20 months, children were administered the Griffiths' Mental Development Scales Developmental Quotient (DQ) items (Brandt, 1983). At 6 and 8 years, IQ was assessed with the German version of the Kaufman Assessment Battery for Children (K-ABC) (Melchers & Preuss, 1991). Reliability and construct validity of the K-ABC are high (e.g., 0.70 correlation with the Wechsler Intelligence Scale for Children-Revised (WISC-R) total score) (Melchers & Preuss, 1991). At 26 years, age-normed Full-Scale IQ was assessed with a short German version of the Wechsler Adult Intelligence Scale (WAIS III) (Von Aster, Neubauer, & Horn, 2006). In our models, VP/VLBW individuals' DQ and IQ data from different ages are directly compared to healthy term born comparison individuals' DQs and IQs at each assessment point.

Statistical Approach. Data were analyzed with SPSS 23 and Amos 24 (Armonk, NY: IBM Corp.). Structural Equation Modeling (SEM) was used to simultaneously test direct and indirect associations between head circumference and growth, and intelligence to 26 years of age. Gestational age, birth weight, and family SES were included as additional predictors of interest. In the initial, full model, all variables and the potential paths between each measure were included (see Appendix Figure 2). Model fit values were then used to identify the best fitting and most parsimonious final model, indicating the timing of head growth that matters most for

intelligence development. Final model results are presented combined for VP/VLBW and term comparisons (Model 1), and as separate multiple-group models (Models 2 and 3).

Results

On average, VP/VLBW had lower head circumference at birth, lower head growth from 20 months to 4 years, and lower intelligence scores than term born comparison individuals (Table 1). However, VP/VLBW had higher head growth from birth to 5 months and, on average, from birth to 20 months than term born comparison infants, both assessments were scheduled corrected for gestational age.

- Table 1 and Figure 1 about here -

The initial, full model did not have sufficient fit (χ^2=80.44(df=16), p<0.001, CFI=.983, $RMSEA$=1.00 (90% CI=.079 to .123), $PCLOSE$=.000; Appendix Figure 2) and was thus reduced to the best fitting, most parsimonious Model 1 (Figure 1). In particular, there was no added value in assessing head growth from birth to five months and then from five to 20 months separately, thus growth from birth to 20 months was collapsed into one variable. Moreover, cognitive development at 20 months was less accurately predicted by infants' head growth than IQ at 6+ years. Model 1 showed that head circumference at birth and head growth in childhood predicted intelligence development from age 6 to 26 years in both VP/VLBW and term born individuals. Effects of gestation and birth weight on intelligence were found to be fully mediated by head circumference and growth (i.e., indirect effects) while family SES directly predicted intelligence. Table 2 shows detailed direct, indirect, and total effects for all variables in the model. The total variance explained (R^2) in intelligence was 29% at 6 years, 73% at 8 years, and

70% at 26 years of age. Overall model fit was excellent with χ^2=19.85(df=16), p<0.227, *CFI*=.999, *RMSEA*=.025 (*90% CI*=.000-.055), *PCLOSE*=.907.

- Table 2 about here -

Since part of the explained variance in adult IQ was carried by childhood IQ (i.e., longitudinal stability of IQ), we also explored how much variance was explained if only the isolated effects of HC at birth and head growth were used to predict adult IQ. A substantial R^2=.24 were explained just by HC at birth and early head growth in the total sample (R^2=.22 in VP/VLBW and R^2=.02 in healthy term control individuals, respectively).

To test if the associations between head growth and intelligence were different among VP/VLBW compared with term comparison individuals, we ran the same SEM separately as a multiple-group model. As before, head circumference at birth, head growth from birth to 20 months, and from 20 months to 4 years predicted intelligence development from age 6 to 26 years in VP/VLBW and term born individuals, but the path coefficients were slightly different (Figures 2 and 3).

- Figures 2 and 3 about here -

Model 2 shows that among VP/VLBW, head circumference at birth and head growth in early childhood directly predicted intelligence at age 6, while there were only indirect effects on intelligence at 8 and 26 years. The total variance explained in intelligence was 22% at 6 years, 79% at 8 years, and 73% at 26 years.

Model 3 shows that among term comparisons, only head growth from birth to 20 months directly predicted intelligence at age 26. The total variance explained in term comparison individuals' intelligence was lower with 9% at 6 years, 53% at 8 years, and 53% at 26 years.

As before, model fit was excellent with χ^2=19.78(df=16), p<0.230, CFI=.999, $RMSEA$=.024 (90% CI=.000-.053), $PCLOSE$=.924; and effects of gestation and birth weight on intelligence were fully mediated by head circumference and growth while family SES directly predicted intelligence.

Discussion

This longitudinal investigation from birth to adulthood confirms that early head growth as a proxy of brain development predicts later intelligence in VP/VLBW but also in term born individuals. Larger head circumference at birth and higher head growth during the first four years predicted IQ from age 6 to 26 years in both VP/VLBW and term born individuals while effects of gestation and birth weight on intelligence were fully mediated by head circumference and growth. These findings add to previous evidence about the value of repeated head circumference assessments in early childhood, in particular in VP/VLBW children, as a proxy of brain volume and screening for later intellectual impairments (Kapellou et al., 2006).

Head growth is driven by brain growth and thus an indicator of brain development (Kiesler & Ricer, 2003). Researchers have suggested that the same genetic factors have an effect on physical (i.e., head) growth and cognitive development (Silventoinen, Iacono, Krueger, & McGue, 2012). However, postnatal brain growth is the product of complex mechanisms, including gray matter maturation (i.e. axon and dendrite sprouting, synapse formation, cortical gyrification) and white matter formation (i.e. glial cell proliferation, myelination). Anatomically, the cranium surrounds and protects the brain and brainstem, and two thirds of its growth occur

by two years of age (Kiesler & Ricer, 2003). In healthy term born infants, cortical thickness reaches 97% of adult size by age two (Lyall et al., 2015) and cortical gyrification also happens during the first two years (Li et al., 2014), whereas cortical surface area expansion mainly drives brain growth after two years of age (Lyall et al., 2015). Lower gestation at birth is associated with smaller whole brain volume and growth at term-equivalent age (Kidokoro et al., 2014; Padilla, Alexandrou, Blennow, Lagercrantz, & Ådén, 2015) and age three months (Holland, Chang, Ernst, & et al., 2014). Additionally, premature birth is associated with regional brain alterations, particularly in subcortical structures such as the thalamus and striatum as well in lateral temporal and parietal cortices (Ball et al., 2012; Meng et al., 2016). These alterations persist into adulthood and are not only accompanied by widespread changes in cerebral white matter (Bäuml et al., 2014; Meng et al., 2016) but also associated with impairments in neurocognitive and behavioral development (Kidokoro et al., 2014; Parker et al., 2008).

Head circumference is an excellent indicator of cerebral volume measured with MRI in one to six year old children (r=0.59-0.93), but its predictive validity is weaker in typically developing older children, adolescents, and adults (r=0.45 to 0.69) (Bartholomeusz et al., 2002; Lange, Froimowitz, Bigler, & Lainhart, 2010). Accordingly, head circumference may present an easily assessable proxy of overall brain volume, but only during the first years of life, and prediction from HC measurement alone is similar to that of term MRI (Anderson et al., 2017).

With regard to the timing of head growth, SEM indicated that the period from birth to 20 months of age mattered most for _directly_ predicting later IQ development, but _indirect_ effects of head growths from 20 months to 4 years of age were also relevant. This suggests that accelerated brain growth during the first 20 months after preterm birth may be most beneficial

for age-appropriate IQ development later in life, in particular for infants born VP/VLBW.

Moreover, and in accordance with studies of normative brain growth (Li et al., 2014; Lyall et al., 2015), the significant direct effect of head growth from birth to 20 months on term adults' IQs suggests that the first two years of postnatal life may represent a critical window for healthy brain growth and development. Thus, regular head circumference measurements, used in conjunction with other neurodevelopmental tools, may be recommended until at least 2 years of age in order to screen for potential brain growth delay. As a result, clinicians may need additional training to correctly administer this effective and inexpensive screening tool (James, Perszyk, MacGregor, & Aldana, 2015).

Children's IQ development is influenced by genetic (Marioni et al., 2014) and environmental factors, such as parents' socioeconomic status (Sameroff, Seifer, Barocas, Zax, & Greenspan, 1987), children's home literacy environments (Jaekel, Schölmerich, Kassis, & Leyendecker, 2011), and preschool quality (Melhuish, 2011). Accordingly, environmental stimulation may promote cognitive development of both VP/VLBW and full term children (Wolke, Jaekel, Hall, & Baumann, 2013), thus early identification of those children who are at-risk for low IQ would allow timely provision of resources and intervention. Our observational study results substantiate the validity of studies that aim to improve preterm infants' long-term cognitive outcomes by supporting early head growth. Such strategies may target individualized neonatal nutrition, adaptive feeding, and breastfeeding to stimulate growth and neurodevelopmental outcomes (Belfort et al., 2016; Christmann et al., 2017). Recently, the microbiome-gut-brain axis has also received attention due to its potential for neuroprotection against white matter injury (Keunen, van Elburg, van Bel, & Benders, 2015). Other avenues towards intervention may target

'nutrition for the brain' via environmental stimulation (e.g., the NICU environment (Pineda et al., 2014), sensitive parenting (Milgrom et al., 2010; Wolke et al., 2013), preschool education (McCormick et al., 2006), and family psychosocial support (Benzies, Magill-Evans, Hayden, & Ballantyne, 2013)).

Our sample represents one of the largest whole-population longitudinal studies of neurocognitive development after VP/VLBW birth. In total, 68% of the eligible VP/VLBW and term comparisons recruited at birth were assessed at 26 years, however, the dropout was not random, as low SES families were less likely to continue participation. Social factors are a major reason for dropout in most longitudinal studies (Hille, Elbertse, Gravenhorst, Brand, & Verloove-Vanhorick, 2005) and analyses were controlled for SES at birth. Participants were born in Germany in 1985/1986, before the introduction of pioneering new treatments such as surfactant administration, which significantly improved high risk infants' survival rates. However, studies have shown that increased survival may not result in equivalent improvement of long-term neurocognitive outcomes (Cheong et al., 2017; Moore et al., 2012; Wolke et al., 2015), thus the current findings may be as relevant to infants born today as to those born 30 years ago.

Changes of absolute measurements of head circumference according to postnatal age (adjusted for gestation at birth at the 5 and 20 months assessments) were included in our models. From a clinical perspective, it might be preferable to use standardized *z*-scores, however, our aim was to investigate the effect of head growth on intelligence growth, while simultaneously assessing the effects of gestational age and birth weight on these growth trajectories. Our results show that the relationship between head growth and IQ development is very similar in both VP/VLBW

and term individuals, but gestational age and birth weight are important factors to predict these trajectories. Standardized head circumference scores would control for gestational age but take away the variation in IQ development explained by this important factor, thus we used raw values to model head growth over time, while timing of assessments at 5 and 20 months was adjusted for gestational age at birth as recommended in clinical practice (Wilson-Ching, Pascoe, Doyle, & Anderson, 2014).

We were able to explain >70% of the variation in adult intelligence, however the majority of this was due to the longitudinal stability of IQ prediction from 6 years of age, not head circumference directly. Nevertheless, a considerable 24% of variance was explained in adult IQ if only the isolated effects of HC at birth and head growth were included in the model (however this percentage of variance explained was mainly due to the VP/VLBW individuals in the sample). Intelligence is a multidimensional construct that develops through cascades (Bornstein, Hahn, & Wolke, 2013). This is reflected in our models, with early development directly and indirectly affecting what comes later, i.e., long-term effects of early head growth as marker for brain volume and function on adult IQ. Full scale IQs are relatively stable over time (Schneider, Niklas, & Schmiedeler, 2014), but VP/VLBW children often have limited neurocognitive resources (Jaekel, Baumann, & Wolke, 2013) and, as a result, their average low IQs remain relatively stable from early childhood onwards. Indeed, moderate prediction of adult intelligence is possible from toddler age in VP/VLBW or extremely preterm, but only from 6 years in healthy term comparison children (Breeman et al., 2015). This is reflected in our multi-group models, as VP/VLBW individuals' head circumference and growth had their strongest effects on 6 year IQ and from there on indirectly into adulthood, suggesting a rather fixed

neurocognitive trajectory (Breeman et al., 2015; Eryigit Madzwamuse et al., 2015). Similarly, the effects of family SES at birth on later IQ were larger in the healthy term born group than in VP/VLBW (e.g., .26 versus .06 at 6 years), indicating differences in developmental plasticity. Family SES affects cognitive development via both genetic and environmental pathways, but VP/VLBW may be more strongly affected by neonatal factors (Jaekel et al., 2013) that affect brain and head growth. Intelligence is only one marker of cognitive function, and while VP/VLBW individuals may achieve IQ test results within the average range, their daily performance in school and at work may be affected by other cognitive problems such as attention, executive function, or processing speed.

Finally, IQ assessments changed from childhood to adulthood but our instruments have been shown to deliver reliable and consistent age-appropriate estimations of intelligence (Melchers & Preuss, 1991). Moreover, potential variations in IQ estimates across different tests (e.g., Griffiths versus Bailey Scales) were not of concern due to the prospective inclusion of a matched healthy term comparison group with the same measures taken at all assessment points.

Model fit values indicated that the developmental pathways included in this study accurately reflect the true neurodevelopmental mechanisms in the two populations studied. Thus, our results confirm previous evidence suggesting that repeated early head circumference measurements are a valuable and easy screening tool for long-term neurocognitive risk assessment after preterm birth, in particular in light of recent findings refuting the diagnostic benefits of routine MRI on preterm infants (Edwards et al., 2018; Hintz et al., 2018). Considering specific neurocognitive mechanisms, however, overall head circumference and brain volume are rather broad markers for cognitive functioning, thus clinical assessments should always include

other tools and a thorough review of known risk factors associated with cognitive impairment. Additional variance in individual IQ development may be explained by regional rather than global differences as well as by alterations in brain connectivity.

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Table 1. Descriptive characteristics of the VP/VLBW and term participants from birth to age 26 years

	VP/VLBW (n = 203)	Term comparisons (n = 198)	Mean difference (95% CI)	p
Birth weight (g)	1318 (320)	3368 (453)	2050 (1973 –2127)	<.001
Gestational age (weeks)	30.40 (2.05)	39.65 (1.19)	9.25 (8.92 – 9.58)	<.001
Sex (% male)	53.2	47.9	1.09[a]	.296
Family SES (1= lowest, 6=highest)	2.61 (1.42)	2.85 (1.54)	0.24 (0.05 – 0.54)	.100
Head circumference at birth (cm)	27.61 (2.39)	35.11 (1.34)	7.49 (7.09 – 7.90)	<.001
Head growth, birth to 5 months (cm)	14.57 (2.57)	7.71 (1.21)	-6.86 (-7.28-(-6.44)	<.001
Head growth, 5 to 20 months (cm)	5.68 (1.43)	5.72 (0.94)	0.05 (-0.30 – 0.20)	.722
Head growth, birth to 20 months (cm)	20.24 (2.45)	13.44 (1.48)	-6.81 (-7.23 -(-6.39))	<.001
Head growth, 20 months to 4 years (cm)	2.21 (1.01)	2.64 (0.96)	0.43 (0.22 – 0.63)	<.001
Standardized head circumference, birth[b]	-5.35 (2.00)	0.77 (1.06)	6.12 (5.79 – 6.45)	<.001
Standardized head circumference, 5 months[b]	0.12 (1.39)	0.67 (0.83)	0.56 (0.32 – 0.79)	<.001
Standardized head circumference, 20 months[b]	0.51 (1.24)	1.05 (0.93)	0.54 (0.32 – 0.77)	<.001
Standardized head circumference, 4 years[b]	-0.09 (1.16)	0.71 (0.94)	0.80 (0.58 – 1.02)	<.001
DQ at 20 months	95.37 (17.82)	107.02 (6.47)	11.65 (14.33 – 8.96)	<.001

IQ at 6 years	89.74 (14.15)	102.32 (11.27)	12.58 (9.93 – 15.23)	<.001
IQ at 8 years	92.31 (15.22)	102.91 (9.66)	10.60 (8.01 – 13.20)	<.001
IQ at 26 years	88.98 (17.33)	102.54 (12.60)	13.56 (10.59 - 16.53)	<.001

Please note: Data are presented as mean (standard deviation) if not indicated otherwise; all assessments at 5 and 20 months were adjusted for gestational age at birth; [a] χ^2-value; [b] standardized according to current international World Health organization (WHO) child growth standard scores (WHO, 2007)

Table 2. Standardized <u>direct</u>, *indirect*, and total effects (i.e., path coefficients) of the predictors in the final overall Model 2 (*N*=401)

	HC at birth	HG birth-20 months	HG 20 months – 4y	IQ 6y	IQ 8y	IQ 26y
Birth weight	<u>.66</u>/*.00*/.66	<u>.00</u>/*-.45*/-.45	<u>.49</u>/*-.12*/.38	<u>.00</u>/*.41*/.41	<u>.00</u>/*.35*/.35	<u>.00</u>/*.37*/37
Gestational age	<u>.30</u>/*.00*/.30	-<u>.27</u>/*- .20*/-.48	-<u>.34</u>/*.18*/-.16	<u>.00</u>/*.05*/.05	<u>.00</u>/*.04*/.04	<u>.00</u>/*.04*/.04
Family SES	<u>.00</u>/*.00*/.00	<u>.00</u>/*.00*/.00	<u>.00</u>/*.00*/.00	<u>.16</u>/*.00*/.16	<u>.07</u>/*.13*/.21	<u>.16</u>/*.14*/.30
HC at birth	-/-/-	-<u>.68</u>/*.00*/-.68	-<u>.76</u>/*.58*/-.18	<u>.75</u>/*-.24*/.51	<u>.00</u>/*.43*/.43	<u>.21</u>/*.27*/.48
HG birth-20 months	-/-/-	-/-/-	-<u>.85</u>/*.00*/-.85	<u>.31</u>/*-.13*/.18	<u>.00</u>/*.15*/.15	<u>.12</u>/*.13*/.25
HG 20 months – 4y	-/-/-	-/-/-	-/-/-	<u>.15</u>/*.00*/.15	<u>.00</u>/*.13*/.13	<u>.00</u>/*.11*/.11
IQ 6y	-/-/-	-/-/-	-/-/-	-/-/-	<u>.84</u>/*.00*/.84	<u>.28</u>/*.41*/.69
IQ 8y	-/-/-	-/-/-	-/-/-	-/-/-	-/-/-	<u>.49</u>/*.00*/.49

Please note: HC = head circumference, HG = head growth, IQ = intelligence quotient

Figure 1. Final Structural Equation Model 2. Neurocognitive cascades of head growth and

intelligence from birth to adulthood in VP/VLBW and term born individuals (*N*=401)

Figure 2. Multigroup Structural Equation Model 3. Neurocognitive cascades of head growth and

intelligence from birth to adulthood in <u>VP/VLBW individuals only</u> (*n*=203)

Please note: Solid lines represent significant paths, dotted lines represent non-significant paths

that were freely estimated in the model

Figure 3. Multigroup Structural Equation Model 4. Neurocognitive cascades of head growth and

intelligence from birth to adulthood in term born individuals only (*n*=198)

Please note: Solid lines represent significant paths, dotted lines represent non-significant paths

that were freely estimated in the model