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Body Composition Changes from Infancy to 4 years and Associations with Early Childhood Cognition in Preterm and Full-term Children

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Abstract

Background—Infants born prematurely are at risk for neurodevelopmental complications. Early growth is associated with improved later cognition. The relationship of early proportionality and body composition with later cognition is not well established.

Objectives—To assess differences in fat-free mass and adiposity (fat mass, %-body fat) changes in preterm and full-term infants through preschool age and examine associations with early childhood cognition.

Methods—This is a prospective, observational study in an appropriate for gestational age cohort of 71 patients (20 preterm and 51 full-term) from infancy through preschool age. Anthropometric and body composition measurements via air displacement plethysmography were obtained during infancy at term and 3–4 months (preterm corrected ages) and at 4 years. Cognitive testing occurred at 4 years. Associations of body composition changes between visits with cognitive function were tested using linear regression.

Results—In the preterm group, higher term to 4 month corrected age %-body fat gains were associated with lower working memory performance ($p=0.01$), and higher 4 month corrected age to 4 year fat-free mass gains were associated with higher full-scale IQ ($p=0.03$) and speed of processing performance ($p=0.02$). In the full-term group, higher 4 month to 4 year fat mass gains were associated with lower full-scale IQ ($p=0.03$).

Conclusions—Body composition gains during different time periods are associated with varying areas of cognitive function. These findings may inform interventions aimed at optimal growth.

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Declarations

The authors declare no conflicts of interest.

Keywords

body composition; premature neonates; neurodevelopmental outcome; growth; fat-free mass; adiposity; processing speed; executive function; intelligence quotient

Introduction

Children born prematurely are at risk for later cognitive deficits. Growth failure after premature birth is a risk factor for poorer neurodevelopment; better infancy growth is associated with improved cognitive and motor function. Increased gains in weight, length, and head circumference both during and after NICU hospitalization are associated with improved neurodevelopment (1, 2).

Children born prematurely are also at risk for long-term metabolic health detriments. In this population the neurodevelopmental benefits of growth can be in competition with the potential harm of rapid growth given its association with later insulin-resistance, hypertension, and obesity (3, 4). Balancing enhanced neurodevelopment with minimized metabolic risk may require interventions that track (5) and target optimal proportionality and quality of weight gain (body composition). For example, improved length gains (a lean growth marker) up to 12 months corrected age (CA) are associated with improved cognition (2), while increased BMI gain (a fat growth marker) from term CA to 18 months CA is associated with later obesity (4). Notably, however, length and BMI may not accurately reflect lean and fat compartments in infancy and childhood (6, 7).

Children born prematurely have different body composition at term CA than those born full-term: lower fat-free mass and a higher percentage of fat mass (8, 9). Comparative reports of later life body composition between children born preterm versus full-term have varying results (10, 11). Emerging evidence suggests positive associations between fat-free mass (FFM) gains, but not fat mass (FM) gains, and later improvements in neurodevelopment. Specifically, greater FFM measurements at term and 4 months CA are associated with faster speed of processing at 4 months CA (12), and greater FFM gains during NICU hospitalization are associated with improved motor and cognitive scores at 12 months CA (13).

We previously reported on differences in body composition growth patterns between term and preterm infants from infancy to preschool age (11). Associations of body composition beyond infancy with early childhood cognition in preterm infants have not yet been reported. Knowledge regarding the continued influence of growth patterns on later neurodevelopment will inform optimal growth patterns and interventions promoting these patterns.

In this paper, we aimed to test the hypothesis that cognitive function, particularly memory and executive function, are associated with fat-free body mass accretion in preterm and not full-term infants.

Methods

Subjects

Subjects were recruited during infancy from the University of Minnesota Masonic Children's Hospital (preterm, n=27; December 2008 through October 2009) and an on-going infancy body composition study (full-term, n=97; April 2009 through June 2010) (14). The initial study explored possible body composition differences between preterm and full-term infants. Preterm subjects were recruited as a convenience sample. As this was a pilot study, a power analysis was not conducted given no previous studies reporting on similar predictors and outcome variables. Included subjects were born appropriate for gestational age (AGA): birth weight between the 10th and 90th percentiles on Fenton preterm growth curves or World Health Organization full-term growth curves. Preterm infants were included if born <35 weeks GA and excluded if they were diagnosed with a condition known to affect growth (e.g. congenital viral infection, chromosomal abnormality). Further group details are in the initial report (8). The University of Minnesota Institutional Review Board approved the infancy and preschool follow-up studies. Parents gave written consent for their child's participation in each portion of the study.

Reported birth characteristics were GA, birth weight, sex, illness, and nutritional factors from the electronic medical record (preterm) or parental report (full-term). Demographics (maternal highest level of education and race) and feeding practice (breast milk and, or formula) were collected by self-report during the infancy visits.

Protocol

Subjects participated in 3 visits at our outpatient research center. The first, Visit 1, was after NICU discharge, near term post-menstrual age for preterm infants, and about 2 weeks after hospital discharge for full-term infants (39–44 weeks post-menstrual age). The next time point, Visit 2, was at 3–4 months (preterm CA). Finally, Visit 3 or "preschool visit," was at 4 years.

Anthropometrics and body composition

Study staff measured anthropometrics (weight, length or height, and head circumference) and body composition via air displacement plethysmography (ADP) at all visits. ADP was completed using the PEA POD at Visits 1 and 2 and the BOD POD with Pediatric Option at Visit 3 (Cosmed, Ltd.; Concord, CA). Body composition via ADP uses a participant's weight, length (Visits 1 and 2) or height (Visit 3), and volume measurements to calculate body density. Participant FFM, FM, and percent body fat (%BF) are derived from the body density measurement using established density values of FFM and FM (15, 16), as validated in infants and children, including those born prematurely (17–19).

Cognitive testing

Cognitive testing performed at 4 years included measurements of general intelligence plus specific domains known to be affected in the preterm population: memory, attention, and executive function. All children were able to fully participate in testing.

A trained psychometrist (SH) blinded to children's birth status administered the standardized Wechsler Preschool and Primary Scale of Intelligence Fourth Edition (WPPSI-IV; Wechsler, 2012). Age-normed results are: Full-Scale Intelligence Quotient (FSIQ), Verbal Comprehension Index, Visual Spatial Index, Fluid Reasoning Index, Working Memory Index (WMI), and Processing Speed Index (PSI).

Four tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were chosen and administered in a standard, scripted format by one of three trained researchers. Tasks chosen test executive functioning related to visual memory, working memory, and speed of processing (20). Performance differences in later childhood cohorts born preterm versus full-term have been reported (21).

Visual evoked potentials

Brain speed of processing was also assessed with pattern reversal visual evoked potentials (VEP) via event-related potentials. A previous report of the preterm portion of this cohort showed associations between speed of processing and infancy body composition (12). A 128-channel Sensor Net System was used. Event-related potential data were collected and recorded online using NetAmps Amplifiers and the NetStation software (Electrical Geodesics Incorporated, Eugene, OR). The child's visual response latency (msec), referred to as "p100," was measured at lead 76, the midline occipital active electrode (22).

Data analysis

Descriptive statistics by preterm versus full-term status were analyzed as mean (SD) or count (percentage) as appropriate for demographic, cognition, and body composition variables. Two-sample t-tests for continuous variables or Fisher's exact tests for categorical variables were run with preterm versus full-term status for all variables to calculate p-values.

To examine associations between body composition changes and children's performance on each cognitive test, a multivariable linear regression analysis was performed. Exposures were fat-free mass and percentage body fat change from term to 3–4 months (preterm CAs) and from 3–4 months (preterm CA) to 4 years. The outcome measures were WPPSI-IV, CANTAB, and VEP performance at 4 years. Covariates known to be associated with children's cognitive performance-- sex, race, and maternal education-- were included in all models. Exact age at 4-year visit was additionally adjusted for in the analysis of all the CANTAB variables, as CANTAB results are not age normative. Given our hypothesis that body composition changes would be associated with cognitive testing at 4 years of age in the preterm group, but not full-term group, the two groups were assessed separately in the regression analyses.

Analyses were performed using SAS (v9.3; SAS Institute, Cary, NC). Statistical significance was defined as $p < 0.05$.

Results

Some participants were lost to follow-up (22 of 27 preterm and 52 of 97 full-term infants participated in Visit 3). Preterm and full-term children who did versus did not complete Visit

3 had no significant group differences in birth weight, GA (13), maternal education, or race (data not shown). Three children (two preterm, one full-term) did not have body composition data collected at Visit 3 given lack of child cooperation. This analysis includes children with body composition data at all visits (preterm n=20, GA 27.0 to 34.9 weeks; full-term n=51).

Participant characteristics and preschool cognitive testing results are seen in Table 1.

Preterm infants had lower FFM and higher %BF than the full-term infants at Visit 1 but similar body composition at Visits 2 and 3 (previously reported data not shown) (8, 11). Body composition accretion from Visit 1 to Visit 2 was different for the two groups, as shown in Table 2. As compared to full-term infants, from Visit 1 to Visit 2 the premature infants gained less FM (90.7g/week versus 59.8g/week, $p=0.001$), less %BF (0.96%/week versus 0.39%/week, $p<0.001$), and similar FFM (120g/week, $p=0.96$). The groups had similar body composition changes from Visit 2 to Visit 3.

Table 3 details significant results of the regression analysis for preterm children.

Early changes in proportionality (%BF) were associated with the preterm children's performance on working memory tests at preschool age: greater gains in %BF from Visit 1 to Visit 2 were associated with a lower WPPSI-IV WMI score and a higher number of errors on CANTAB Spatial Working Memory (SWM) test. Figure 1 illustrates these significant associations found in the preterm but not full-term group. Each percentage point higher %BF per week from Visit 1 to Visit 2, was associated with a 21-point lower WPPSI-IV WMI at Visit 3 (SE 6.3, $p=0.005$) and 22 more total errors on CANTAB SWM (SE 6.1, $p=0.005$) in preterm participants.

Later body composition and proportionality changes were associated with preterm children's general cognition (WPPSI-IV FSIQ) and tests of processing speed. Higher FFM gain from infancy to early childhood (Visit 2 to Visit 3) was positively associated with preschool full-scale IQ and PSI in the preterm group, as seen in Figure 2. For a preterm participant each gram of FFM gained per week from Visit 2 to Visit 3 was associated with a 0.85-point higher WPPSI-IV FSIQ (SE 0.36, $p=0.033$) and 0.95-point higher WPPSI-IV PSI (SE 0.35, $p=0.015$). Higher FFM gain during this time period was also associated with a 244 msec lower CANTAB Delayed Match to Sample (DMS) latency for correct answer (SE 43.6, $p<0.001$), i.e. a faster time. Additionally, for each %BF gain per week from Visit 2 to Visit 3, VEP p100 latency increased by 331 msec (SE 94.8, $p=0.004$), i.e. a slower time.

Body composition changes in the preterm children were not associated with other WPPSI-IV sub-scores nor CANTAB Spatial Span or other DMS measures (data not shown).

In the full-term group later adiposity gains were negatively associated with preschool cognition. Specifically, FM gains from Visit 2 to Visit 3 were associated only in the full-term group with lower FSIQ ($\beta=-0.92$, SE 0.41, $p=0.031$), lower PSI ($\beta=-0.77$, SE 0.38, $p=0.049$), and lower maximum span length on CANTAB Spatial Span ($\beta=-0.1$, SE 0.04, $p=0.029$).

Discussion

Early growth is important for preterm children's later cognition. Concern exists regarding potential adverse metabolic consequences of excess growth (i.e. later obesity, hypertension, and insulin resistance). Evidence increasingly supports augmenting lean tissue growth to optimize the competing cognitive and metabolic outcomes (2, 4). Recent literature specifically suggests that gains in FFM, but not FM, are associated with improved infancy cognition (12, 13). To our knowledge, this is the first report relating body composition changes beyond infancy with preschool age cognition.

As compared to full-term infants, this heterogeneous group of AGA preterm infants had less FFM and higher % body fat at term CA (8). Then the preterm group gained significantly less FM and less %BF but similar FFM from term CA to 3–4 months CA (see Table 2), and the groups had similar body composition (8). The groups were also similar at 4 years (11). Except for slightly lower WPPSI-IV Processing Speed Index in the preterm group, cognitive testing results including general cognition were normal and similar for both groups, demonstrating a preterm group relatively unaffected by major neurodevelopmental disability.

In the preterm cohort, greater %BF gain (greater FM gain relative to less FFM gain) from term CA to 4 months CA (Visit 1 to Visit 2) was negatively associated with preschool working memory. Poorer working memory performance has been described in very low birth weight and late preterm infants (21, 23). These tasks are a function of the dorsolateral prefrontal cortex and hippocampus (21). Structural changes in these areas are associated with working memory performance in preterm children (24). These brain areas undergo rapid structural and functional changes during infancy and are vulnerable to stress-related injury including nutritional deprivation (25). Infancy growth patterns in association with working memory performance have not been previously reported.

Our findings infer that higher adiposity and/or lack of appropriate FFM growth from term to 4 months CA may be detrimental to developmental trajectories in these brain areas and preterm children's on-going working memory performance. Weight and length growth during the early infancy/post-NICU discharge time period are recognized as important for later neurodevelopment (4). Therefore, we suggest that targeting overall growth while minimizing FM and %BF gains may promote improved working memory function development. Working memory and other executive functioning continue to develop beyond preschool age. Longer-term studies are needed to determine persistence of these findings.

Greater infancy to preschool age (Visit 2 to Visit 3) FFM gains, but not adiposity gains, were associated with improved overall cognition (FSIQ) and processing speed task performance (WPPSI-IV PSI, CANTAB DMS latency, VEP p100 latency) among the preterm cohort. Differences in processing speed between preterm and full-term children are well known, and our study confirms these findings. Processing speed and general cognition are associated with brain imaging changes. FFM is a reflection of overall protein accretion, which along with growth factors such as IGF-1, is necessary for overall brain growth and myelination (25). Soria-Pastor et al. studied a group of adolescents born prematurely and found both overall intelligence and processing speed were correlated with decreased brain white matter

on MRI (26). Murray et al. also reported in a group of 7-year-olds born prematurely that decreased processing speed was associated with global brain and white matter abnormalities on MRI (27).

Our findings indicate that specific body composition changes continue to incur neurodevelopmental benefit beyond infancy. Literature best supports growth in the first 4 months after discharge from the NICU is associated with improved neurodevelopment. However, Belfort found that higher BMI gains from 4 to 12 months CA were also associated with lower odds of IQ below 85 (4), and Ramel reported higher linear growth to 12 months CA was associated with improved 24 months CA cognitive performance (2). The relatively long time between Visits 2 and 3 limits more specific definition of the most beneficial time periods for FFM gain. While one period of growth may be influenced by growth in the prior period (28), we found that growth during each time period was associated with different cognitive changes, pointing to sensitive growth periods for each affected domain. Future studies with more frequent follow-up visits will be important to define these critical periods, particularly as excess growth during this timeframe may incur increased metabolic risk (4).

Our primary aim of the study was to explore the relationship of body composition changes with cognition in the preterm children, yet we also found that increased adiposity during early childhood was associated with poorer cognitive performance in the full-term children. Previous research suggests adequate early growth is important for preschool cognition in full-term AGA children (29), while rapid early growth does not incur additional neurodevelopmental benefit (30) and is, in fact, associated with lower cognitive scores (29). We suggest increasing adiposity during early childhood may be detrimental to long-term cognitive outcomes and should be monitored more closely.

Our study has some limitations. The preterm group was small and heterogeneous in regards to GA. Also, follow-up at Visit 3 was suboptimal for the full-term group, though those seen were similar to those who did not follow-up (11). We were unable, given the sample size, to adjust for additional covariates that may affect body composition or cognition (e.g. nutrition, physical versus sedentary activity, neonatal illness). Larger studies with additional follow-up visits are important to confirm these preliminary findings.

We report preliminary evidence in a heterogeneous preterm population that body composition changes following NICU discharge-- decreased early adiposity and increased later FFM-- are associated with enhanced preschool cognitive performance. Lower infancy to preschool adiposity gains may also incur neurodevelopmental benefit in the full-term population. Further research aimed to improve neurodevelopment and minimize metabolic risk will define optimal body composition growth patterns. Ultimately, intervention trials targeting these patterns will inform best practices from the NICU through childhood.

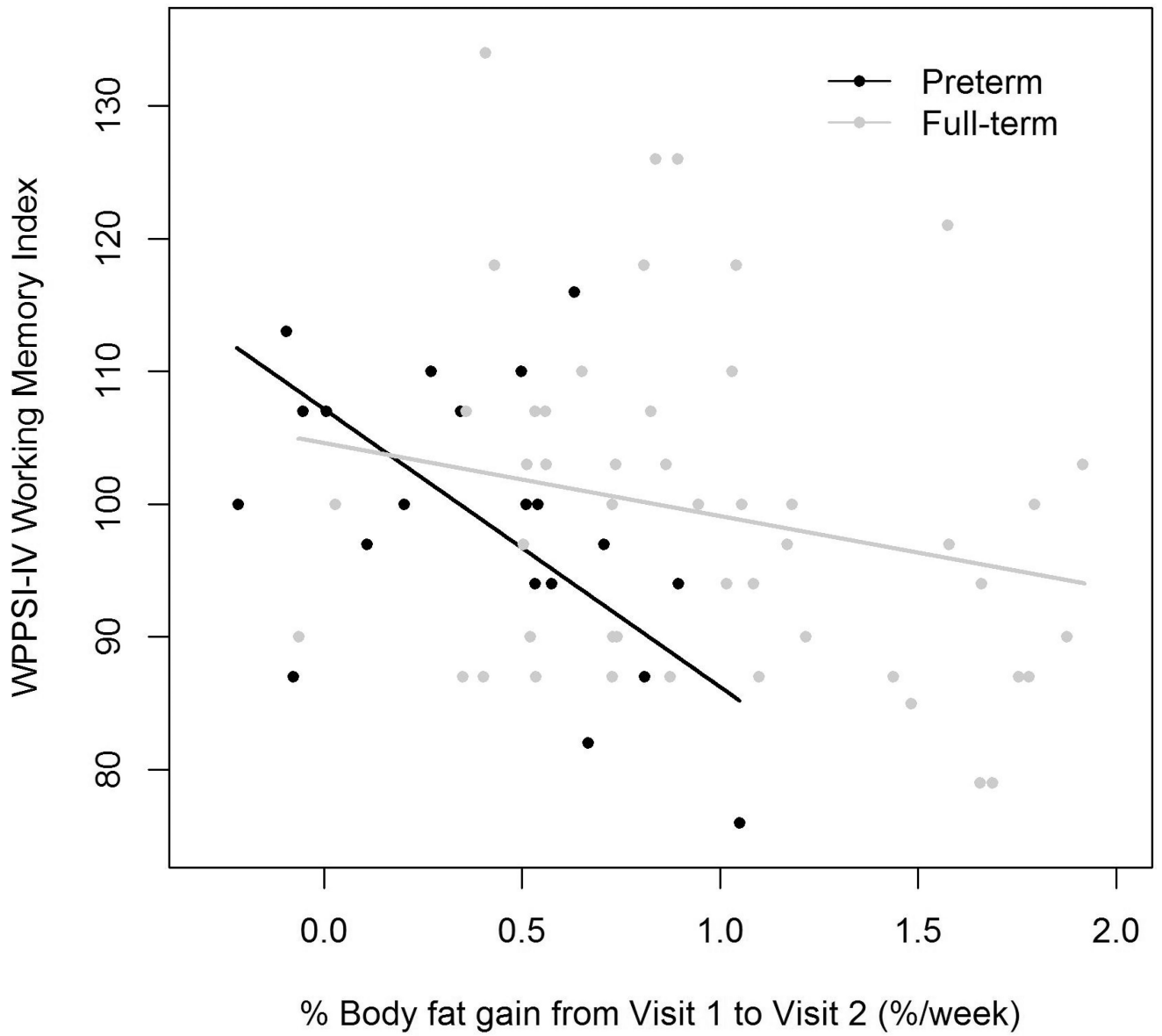
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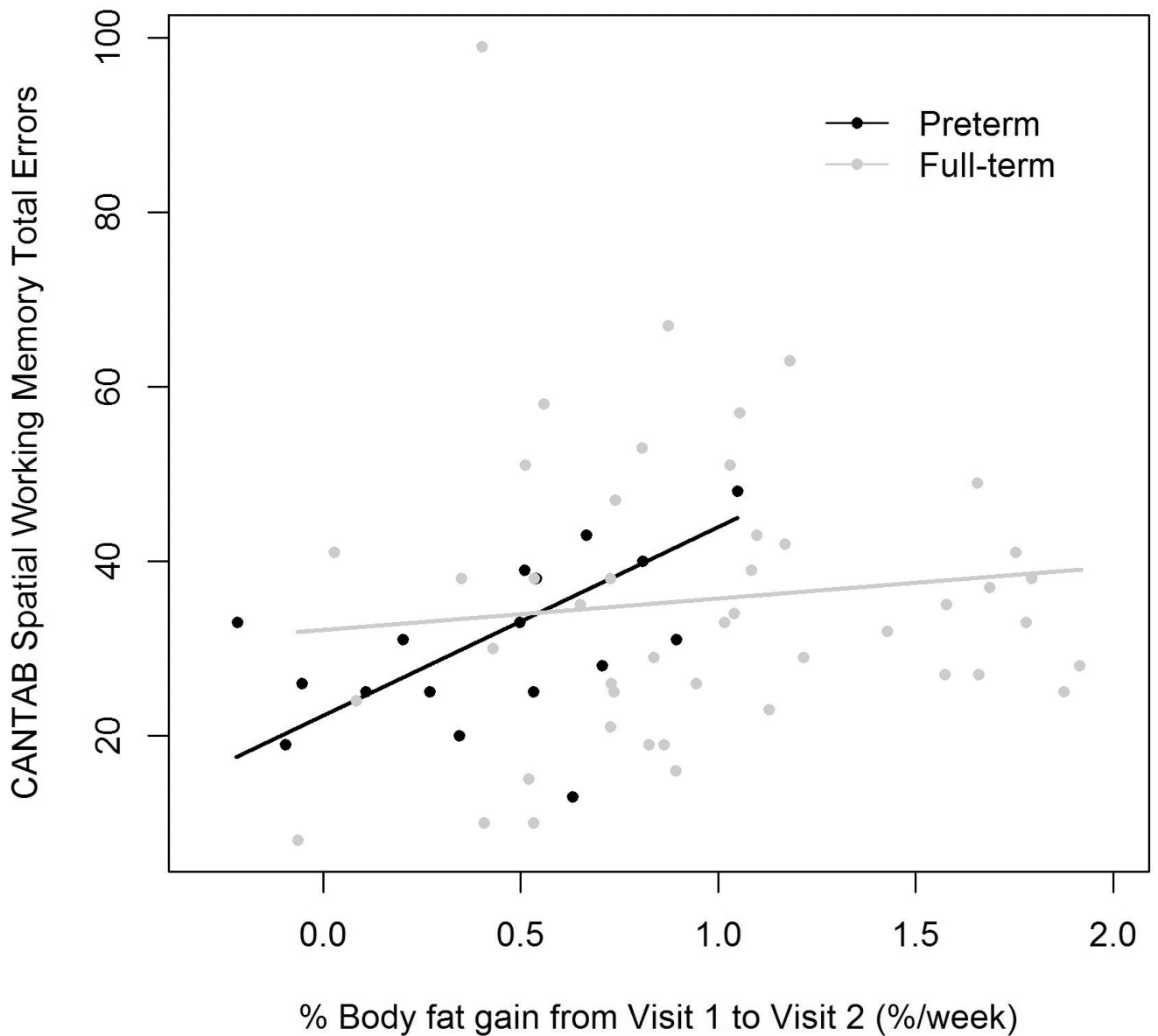


Figure 1. Rate of % Body Fat Gain from Visit 1 to Visit 2 Associations with Visit 3 Working Memory Testing

a.) WPPSI-IV Working Memory Index

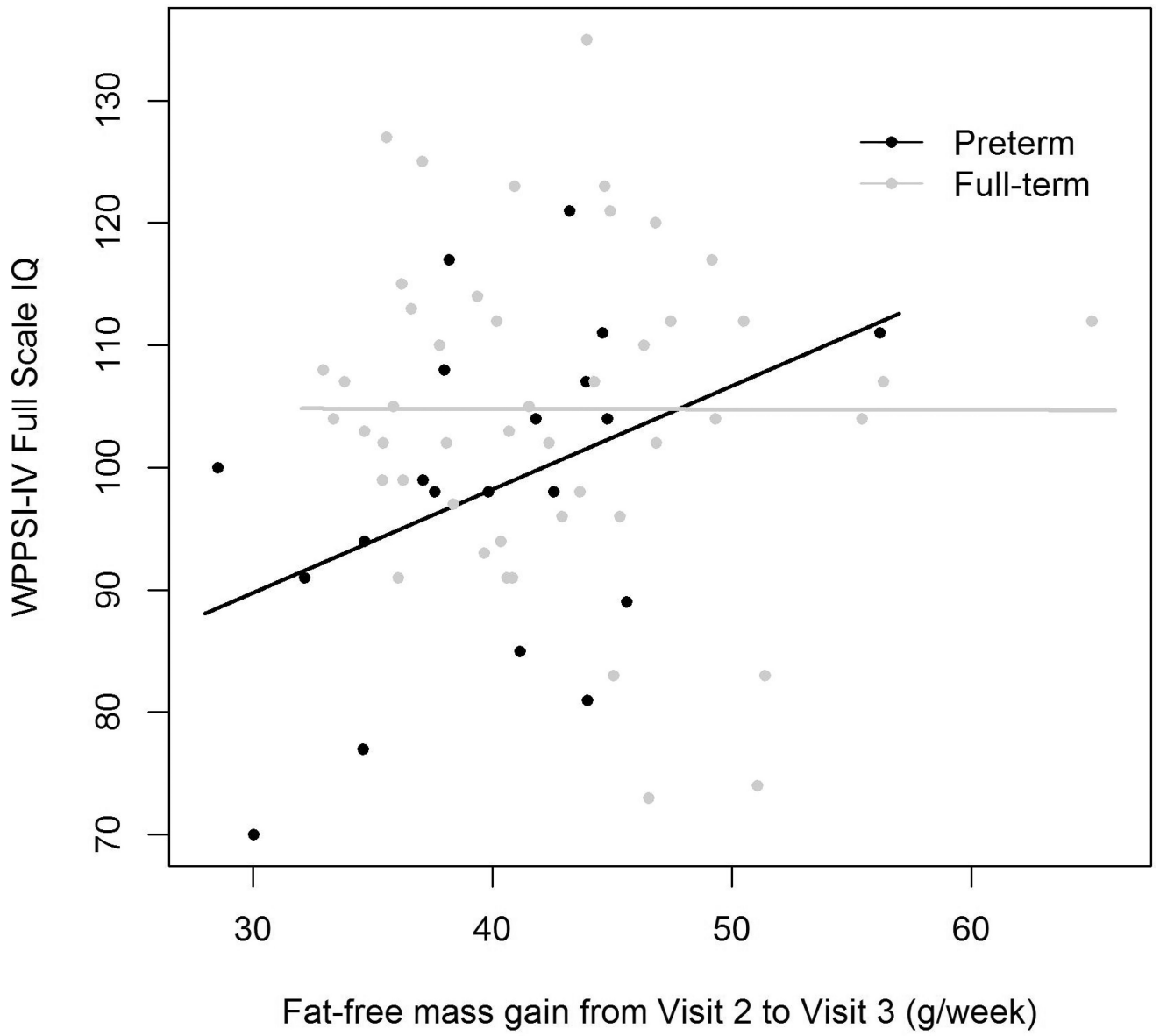
Preterm β (SE)=-20.9 (6.29), $p=0.005$, $R=0.51$

Full-term β (SE)=-5.50 (3.69), $p=0.14$, $R=0.15$

b.) CANTAB Spatial Working Memory Total Errors

Preterm β (SE)=21.6 (6.08), $p=0.005$, $R=0.63$

Full-term β (SE)=3.61 (5.00), $p=0.47$, $R=0.15$



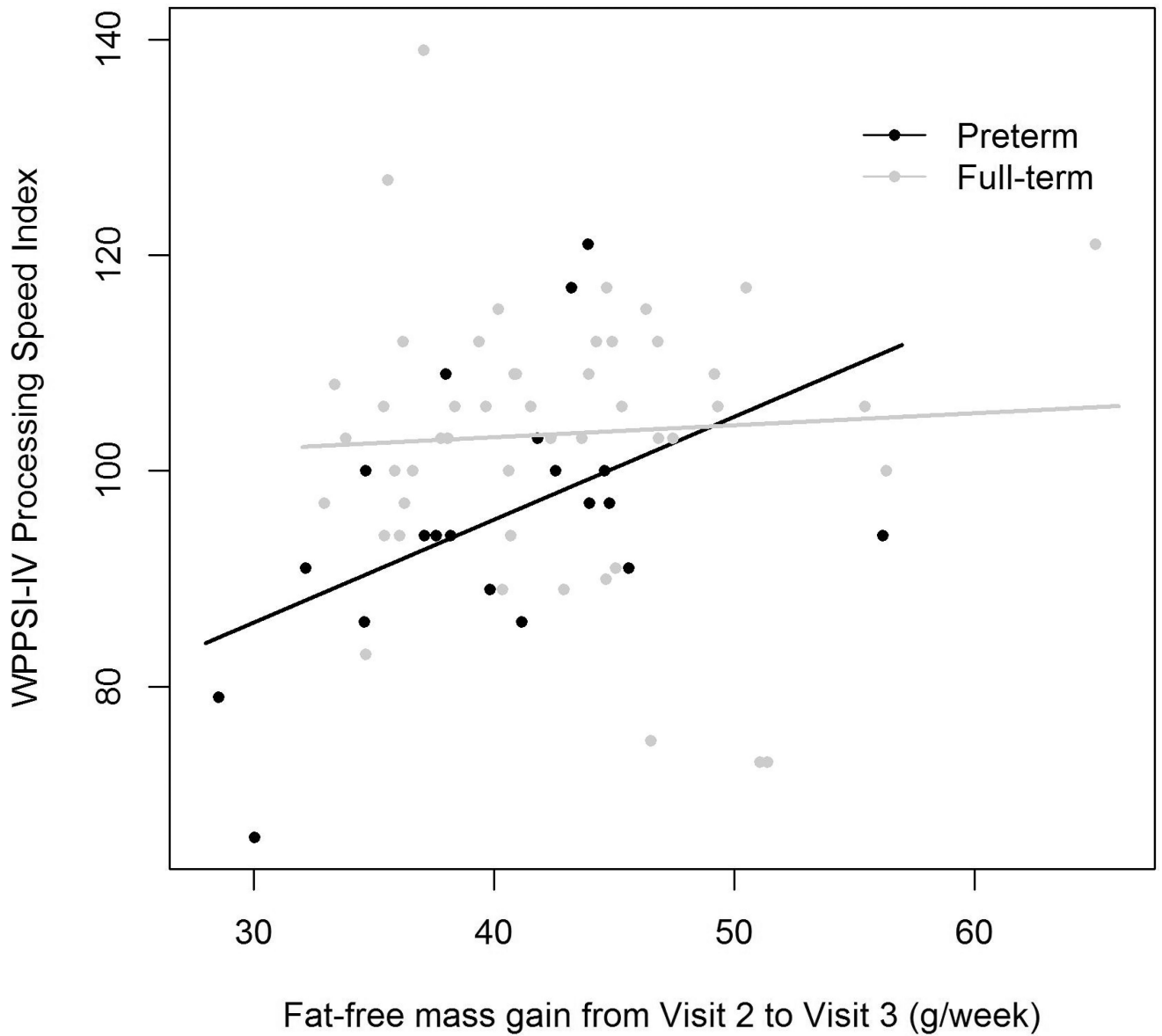


Figure 2. Rate of Fat-free Mass Gain from Visit 2 to Visit 3 Associations with Visit 3 Cognitive Testing

a.) WPPSI-IV Full Scale IQ

Preterm β (SE)=0.85 (0.36), $p=0.033$, $R=0.63$

Full-term β (SE)=-0.004 (0.33), $p=0.99$, $R=0.03$

b.) WPPSI-IV Processing Speed Index

Preterm β (SE)=0.95 (0.35), $p=0.015$, $R=0.59$

Full-term β (SE)=0.11 (0.32), $p=0.73$, $R=0.039$

Table 1

Participant characteristics and preschool cognitive testing

| Variable ^a | Preterm (n=20) | Full-term (n=51) | p-value ^b |
|---|-----------------|------------------|----------------------|
| Birth data | | | |
| Birth weight (g) | 1843 (586) | 3535 (459) | <0.01 |
| Birth weight z-score ^c | 0.04 (0.62) | 0.47 (0.89) | 0.051 |
| Gestational age (weeks) | 31.9 (2.57) | 39.8 (1.03) | <0.01 |
| Demographics | | | |
| Male sex | 13 (65) | 26 (51) | 0.31 |
| White race | 17 (85) | 38 (75) | 0.53 |
| Maternal education >High school | 14 (70) | 45 (88) | 0.084 |
| Preterm hospitalization data | | | |
| Antenatal steroids | 15 (75) | - | - |
| Day 1 Score for Neonatal Acute Physiology ^d | 5.5 (2–17) | - | - |
| Head ultrasound abnormal ^e | 1 (5) | - | - |
| Postnatal steroids | 0 | - | - |
| Energy deficit, kcal/kg ^f | 88.4 (17.8–230) | - | - |
| Protein deficit, g/kg ^g | 2.7 (–0.14–5.9) | - | - |
| Visit 1 (Near term, preterm corrected age) | | | |
| Weight z-score ^c | 0.00 (0.85) | 0.10 (0.74) | 0.61 |
| Length z-score ^c | –0.02 (1.2) | 0.27 (0.88) | 0.26 |
| Occipitofrontal head circumference z-score ^c | 0.92 (0.90) | 0.82 (0.90) | 0.67 |
| Breast milk, yes ^h | 17 (85) | 49 (96) | 0.13 |
| Visit 2 (3–4 months, preterm corrected age) | | | |
| Weight z-score ^c | –0.38 (1.2) | –0.055 (0.89) | 0.21 |
| Length z-score ^c | –0.19 (1.2) | 0.38 (0.89) | 0.029 |
| Occipitofrontal head circumference z-score ^c | 0.77 (0.96) | 0.75 (0.76) | 0.94 |
| Breast milk, yes ^h | 7 (35) | 32 (63) | 0.062 |
| Visit 3 (4 years) | | | |
| Weight z-score ^c | –0.41 (1.2) | 0.02 (0.84) | 0.088 |
| Height z-score ⁱ | –0.45 (0.97) | –0.08 (0.84) | 0.12 |
| WPPSI-IV^j | | | |
| Full scale IQ | 98.2 (13.2) | 105 (13.0) | 0.068 |
| Verbal Comprehension Index | 104 (14.3) | 108 (14.7) | 0.27 |
| Visual-Spatial Index | 97.7 (14.7) | 105 (15.3) | 0.067 |
| Fluid Reasoning Index | 97.2 (11.9) | 99.2 (12.0) | 0.53 |

| Variable ^a | Preterm (n=20) | Full-term (n=51) | p-value ^b |
|--|--------------------|-------------------|----------------------|
| Working Memory Index | 98.9 (10.5) | 99.2 (12.8) | 0.91 |
| Processing Speed Index | 95.4 (12.2) | 103 (12.7) | 0.022 |
| CANTAB^j | | | |
| Motor screen: average latency (msec) | 1553 (311) | 1532 (455) | 0.83 |
| Motor screen: error number | 1.32 (2.31) | 0.73 (1.67) | 0.33 |
| Spatial span longest span length | 1.68 (1.42) | 2.12 (1.47) | 0.27 |
| Spatial working memory, 4-box error | 6.61 (4.55) | 7.85 (6.19) | 0.38 |
| Spatial working memory, 6-box error | 24.0 (7.91) | 28.0 (13.72) | 0.15 |
| Spatial working memory, total errors | 30.4 (9.22) | 35.4 (16.8) | 0.14 |
| Delayed match to sample, % correct first try | 42 (12) | 41 (15) | 0.83 |
| Visual evoked potentials^k | | | |
| P100 latency (msec) | 131 (19.9) | 127 (21.4) | 0.39 |

^aContinuous data are reported as mean (SD) and categorical data as number yes (%) unless otherwise specified in the row.

^bThe p-value is calculated from two-sample t-test for continuous variables, and Fisher's exact test for categorical variables.

^cCalculated for weight, length (Visits 1 & 2) or height (Visit 3), and head circumference on Fenton or World Health Organization growth chart as appropriate for preterm/full-term status and post-menstrual age.

^dReported as mean (range).

^eOne infant had bilateral grade 2 intraventricular hemorrhage without hydrocephalus on serial images.

^fEnergy deficit calculated using a 120kcal/kg/day goal and subtracting or adding actual calories received each day of hospitalization and combined for entire hospitalization (kcal/kg); reported as mean (range).

^gProtein deficit calculated using a 3.5g/kg/day goal and subtracting or adding actual protein received each day of hospitalization and combined for entire hospitalization (g/kg); reported as mean (range).

^hNumber of infants feeding breast milk either exclusively or partially per maternal report.

ⁱExcluding full-term participants without (n=3) or with incomplete (n=1) data.

^jExcluding participants without data (preterm n=1, full-term n=2) or with incomplete data (preterm n=1, full-term n=3).

^kExcluding participants without data (preterm n=1, full-term n=1).

Table 2

Body composition changes between visits

| Variable | | Preterm ^a (n=20) | Full Term ^a (n=51) | p-value ^b |
|---------------------------|------------|--------------------------------|----------------------------------|----------------------|
| Fat Free Mass (g/week) | V1–V2 rate | 120 (24.2) | 120 (32.4) | 0.96 |
| | V2–V3 rate | 39.9 (6.33) | 42.6 (6.59) | 0.12 |
| Fat Mass (g/week) | V1–V2 rate | 59.8 (29.7) | 90.7 (41.7) | 0.001 |
| | V2–V3 rate | 7.56 (6.89) | 8.86 (4.84) | 0.45 |
| Percent Body Fat (%/week) | V1–V2 rate | 0.39 (0.36) | 0.96 (0.51) | <0.001 |
| | V2–V3 rate | –0.03 (0.04) | –0.02 (0.03) | 0.57 |

V1 = Visit 1 at term or term corrected age (preterm participants)

V2 = Visit 2 at 3–4 months (preterm corrected age)

V3 = Visit 3 at 4 years

^aData are reported as mean (SD).^bThe p-value is calculated from two-sample t-test.

Table 3

Cognitive factors associated with body composition changes in preterm infants at 4 years of age

| Variable | Test | % Body fat Rate (%/week) | | | Fat-free mass Rate (gram/week) | | | | |
|-------------------------|---------------------------------------|-------------------------------------|--------------|------------------------------------|--------------------------------|-------------------------------------|------------------------------------|--------------------|------------------|
| | | Visit 1-Visit 2 Estimate (SE) | p-value | Visit 2-Visit3 Estimate (SE) | p-value | Visit 1-Visit 2 Estimate (SE) | Visit 2-Visit3 Estimate (SE) | p-value | |
| Working Memory | WMI | -20.9 (6.29) | 0.005 | -18.6 (72.1) | 0.80 | -0.14 (0.18) | 0.47 | 0.28 (0.43) | 0.52 |
| | SWM Total errors ^a | 21.6 (6.08) | 0.005 | -58.8 (83.7) | 0.50 | 0.22 (0.17) | 0.21 | 0.45 (0.51) | 0.40 |
| IQ | Full Scale IQ | -5.63 (7.90) | 0.49 | -62.0 (68.2) | 0.38 | 0.03 (0.18) | 0.86 | 0.85 (0.36) | 0.033 |
| | PSI | 1.47 (8.15) | 0.86 | -41.0 (70.3) | 0.57 | 0.07 (0.18) | 0.69 | 0.95 (0.35) | 0.015 |
| Processing Speed | DMS Mean Correct Latency ^a | 431 (1530) | 0.78 | 7110 (1270) | 0.59 | -13.1 (29.7) | 0.67 | -244 (43.6) | <0.001 |
| | VEP p100 Latency | -12.5 (15.8) | 0.44 | 331 (94.8) | 0.004 | 0.27 (0.33) | 0.43 | 0.01 (0.78) | 0.99 |

Multivariable linear regression analysis with adjustment for sex, race (white versus non-white), and maternal education (high school versus >high school).

^aCANTAB analysis additionally adjusted for age at V3

- Visit 1 at term (preterm corrected age)
- Visit 2 at 3-4 months (preterm corrected age)
- Visit 3 at 4 years
- WMI= WPPSI-IV Working Memory Index
- SWM= CANTAB Spatial Working Memory
- Full Scale IQ = WPPSI-IV Full Scale Intelligence Quotient
- PSI= WPPSI-IV Processing Speed Index
- DMS= CANTAB Delayed Match to Sample
- VEP= Visual evoked potential