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Body composition and cognition in preschool-age children with congenital gastrointestinal anomalies

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Abstract

Background: Children with congenital gastrointestinal anomalies (CGIAs) experience multiple stressors while hospitalized in neonatal intensive care units during an essential time of growth and development. Early stress and inadequate nutrition are linked to altered growth patterns and later neurodevelopmental delays. In other at-risk populations, improved fat-free mass (FFM) accretion is associated with improved cognitive outcomes.

Objective: To determine if body composition is associated with cognitive function in preschool-age children with CGIAs.

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Authorship Statement

Dr. Plummer conceptualized and designed the study, performed and coordinated data acquisition, coordinated statistical analysis and interpretation, drafted the initial manuscript, critically revised the manuscript, and approved the final manuscript as submitted. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ms. Wang conducted the final statistical analyses, drafted parts of the manuscript, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Larson-Nath conceptualized and designed the study with Dr. Plummer, advised on study protocol, and interpretation of data analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Scheurer conceptualized and designed the study with Dr. Plummer, advised on study protocol, and interpretation of data analysis, drafted parts of the manuscript, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Ramel conceptualized and designed the study with Dr. Plummer, advised on study protocol, and interpretation of data analysis, drafted parts of the manuscript, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest: The authors have no conflicts of interest to report.

Study design: An observational study examined body composition and cognition in 34 preschool-age children with CGIAs. Anthropometric measurements and body composition testing via air displacement plethysmography were obtained. Measurements were compared with a reference group of healthy, term-born children. Cognition was measured with the NIH Toolbox Early Childhood Cognition Battery. Linear regression was used to test the association of body composition with cognitive function.

Results: Compared with the reference group, children with CGIAs had similar anthropometric measurements (weight, height, and body mass index z-scores) and body composition at preschool-age. Processing speed scores were lower than standardized means (p=0.001). Increased FFM was associated with higher receptive vocabulary scores (p=0.001), cognitive flexibility scores (p=0.005), and general cognitive function scores (p=0.05).

Conclusions: At preschool-age, children with CGIAs have similar growth and body composition to their peers. In children with CGIAs, higher FFM was associated with higher cognitive scores. Closer tracking of body composition and interventions aimed at increasing FFM may improve long-term outcomes in this population.

Keywords

Body composition; Neonatal surgery; Neurodevelopment; Outcomes; Inflammation; Fat-free mass

1. Introduction

Children with congenital gastrointestinal anomalies (CGIAs) (e.g. gastroschisis, omphalocele, Hirschsprung’s disease, esophageal and bowel atresia, and diaphragmatic hernia) are often exposed to multiple stressors early in life during a vital time of growth and development. These stressors include hospitalization in the neonatal intensive care unit (NICU), anesthesia exposure, and major surgery. Additionally, these children are at significant risk for prolonged periods of inadequate nutrition related to enteral feeding intolerance and increased catabolic stress [1]. Exposure to physiologic stressors and inflammation during the neonatal period may have harmful effects on the developing infant, and they have been implicated as risk factors for future growth failure [2,3] and neurodevelopmental delays [4–7].

Like children with CGIAs, children born prematurely are often exposed to physiologic stressors (e.g. NICU hospitalization, inadequate nutrition, infection) early in life. It is well known that premature infants are at risk for growth failure [8,9] and future neurodevelopmental delays [10–12], potentially related to critically timed nutrient deficiencies [4,13,14]. Improved early growth is associated with improved neurodevelopmental outcomes amongst preterm infants [15–17]. Specifically, improved fat-free mass (FFM) gains in children born prematurely have been associated with improved neurodevelopment at 12 months of age and faster speed of processing at 4 months and 4 years of age [18–20]. To our knowledge, no published study has reported associations between body composition and neurodevelopmental outcomes in children with CGIAs.

In this study, we aimed to describe growth and neurodevelopment in this unique group of children and identify areas in which targeted interventions may be applied to promote optimal growth and development. We hypothesized that children with CGIAs demonstrating higher FFM accretion would show higher performance scores on cognitive tests. Conversely, those demonstrating higher fat-mass (FM) and higher percentage body fat (%BF) would show lower performance scores on cognitive tests.

2. Methods

2.1. Participants

Preschool-age children (4 to 5 years-old) born between September 2011 and December 2013 admitted to one of three, large, level 4 neonatal intensive care units in a metropolitan Midwest area with a surgical diagnosis affecting the gastrointestinal system (i.e. gastroschisis, omphalocele, esophageal and bowel atresia, imperforate anus, Hirschsprung's disease, and diaphragmatic hernia) were recruited to participate. Children born prior to 35 weeks gestation and those with chromosomal anomalies known to affect growth or cognition were excluded. Clinical data regarding the child's diagnosis, birth history, surgical history, and initial hospitalization were collected from the electronic medical record.

2.2. Study design

A prospective, observational study design was used to evaluate growth, body composition, inflammation, and cognition in preschool-aged children with CGIAs. Eligible children whose parents consented to be contacted for research studies were identified by ICD-9 and ICD-10 codes for the desired diagnoses and recruited via mail and/or phone calls. Each preschool-age child participated in one study visit. At time of the study visit, the parent gave informed written consent for their child's participation in the study. Ethical approval was acquired from both participating hospital systems through their respective Institutional Review Boards. The study was conducted from November 2016 to March 2018.

2.3. Growth assessment

Standard anthropometric measures (weight, height, and body mass index (BMI)) were obtained at the time of the study visit. Weight was measured with an electronic scale to the nearest 0.1 gram, and height was measured using a stadiometer (Seca; Hamburg, Germany). Body composition (total body FM and FFM) was determined using air displacement plethysmography (Bod Pod with Pediatric Option, Cosmed, Ltd.; Concord, CA) as described by Fields and Allison [21]. Body measurements were compared with de-identified measures obtained from a reference group of 51 appropriate for gestational age children born at term who were enrolled in a previous study [18].

2.4. Neurodevelopmental assessment

Cognitive function was evaluated using the National Institutes of Health (NIH) Toolbox. This assessment tool was chosen due to its ability to directly target multiple aspects of cognition, and its ease of use via an iPad application. For this study, the Early Childhood Cognition Battery was utilized, which has been validated in children ages 3–6 years [22]. This battery evaluates several subdomains of cognitive function including receptive language

(Picture Vocabulary test, PV), attention (Flanker Inhibitory Control and Attention test, FL), episodic memory (Picture Sequence Memory test, PSM), cognitive flexibility (Dimensional Change Card Sort test, DCCS), and processing speed (Pattern Comparison Processing Speed test, PS). In addition, it generates a Cognition Early Childhood Composite score (CECC), which is a measure of general cognitive function based on the successful completion of the first four tests within the battery (PV, FL, PSM, DCCS). For our analysis, fully corrected t-scores normed for age, gender, race, ethnicity, and parent's education were utilized [23].

2.5. Statistical analysis

Descriptive statistics were expressed as mean (standard deviation) or median (interquartile range) for continuous variables, or count (percentage) for categorical variables. Comparisons of demographics and body measurements between the group of children with CGIAs and the healthy reference group were performed using two-sample t-test or Fisher's exact test, as appropriate. Cognitive test scores (i.e. NIH toolbox fully corrected t-scores) were compared with their corresponding standardized population value normed for age, gender, race, ethnicity and parent's education value using a two-sample t-test.

Associations between body measurements and cognitive test scores were assessed by simple linear regression or multivariate linear regression for adjusted analysis. Pearson correlation was used to assess the associations between the initial hospital course characteristics (mechanical ventilator days, total parenteral nutrition (TPN) days, length of stay) and body composition/cognitive test scores. All analyses were performed using SAS (v9.4; SAS Institute, Cary, NC). Statistical significance was defined as $p \leq 0.05$.

3. Results

3.1. Patient characteristics

A total of 34 children were enrolled in this study. 186 eligible children were identified from a search within the electronic medical record. Successful contact was made with 105 families of eligible children, and 34 families consented to participation. Table 1 describes the characteristics of the participating children with CGIAs. The majority of participating children were diagnosed with gastroschisis (23%) or Hirschsprung's disease (21%). NICU hospital courses varied in severity. All children underwent at least one abdominal surgery, with 19 (55%) requiring additional surgeries. 11 (32%) children required mechanical ventilation beyond the perioperative period (>2 days). All children received TPN (range 3–116 days) with 12 children (35%) receiving TPN for less than 7 days, and 6 (18%) receiving TPN for more than 30 days. Four children (12%) had gastrostomy tubes placed prior to their discharge from the NICU, and all but one gastrostomy tube had been removed by the time of their study visit at preschool-age. Only one child had been diagnosed with short bowel syndrome.

3.2. Anthropometric measurements and body composition

All children completed anthropometric measurement and body composition testing. Table 2 describes these measurements as compared with a reference group. Children with CGIAs had lower gestational age (37.9 vs. 39.8 weeks, $p<0.001$), lower birth weight (3.2 vs. 3.5 kg, p=0.02), and were older at the time of their preschool visit (4.7 vs. 4.4 years, p=0.005) than children in the reference group. Despite these differences, anthropometric measurements (weight, height, and BMI z-scores) and body composition (FFM, FM, and %BF) were similar between the groups. After adjusting for age and sex, body composition measurements remained similar between the groups.

3.3. NIH Toolbox Early Childhood Cognition Scores

Figure 1 depicts the NIH Toolbox Early Childhood Cognition test scores for children with CGIAs in relation to standardized values (mean 50, SD 10). Cooperation with the testing was variable, as reflected in the varying n for each test. Overall, the children with CGIAs achieved scores similar to the standardized mean for receptive language (PV), attention (FL), cognitive flexibility (DCCS), and episodic memory (PSM). General cognitive function scores were higher than the standardized mean (CECC, p=0.04) while processing speed scores were lower (PS, p=0.001).

3.4. Cognition in relation to body composition

Table 3 shows the associations between body measurements and cognitive test scores in children with CGIAs. Increased FFM was associated with higher receptive language scores (PV, β=3.1, SE=0.9, p=0.002), higher cognitive flexibility scores (DCCS, β=1.7, SE=0.6, p=0.005), and higher general cognitive function scores (CECC, β=1.5, SE=0.7, p=0.05) on unadjusted analysis. When adjusted for age and sex, FFM was no longer significantly associated with receptive language scores or general cognitive function scores at the 0.05 level. However, these associations continued to reach significance at the 0.1 level.

Increased FM and %BF were both negatively associated with attention scores (FL) after adjusting for age and sex (FM, β=−3.7, SE=1.6, p=0.03; and %BF, β=−0.9, SE=0.3, p=0.009). Increased BMI was associated with higher cognitive flexibility scores (DCCS, β=4.2, SE=1.6, p=0.01) and higher general cognitive functioning scores (CECC, β=4.9, SE=2.1, p=0.03). Weight and height z-scores were not significantly associated with any cognitive test scores.

When evaluating associations between the initial hospital course and body measurements/ cognitive tests, increased length of stay and increased number of mechanical ventilator days were associated with lower FFM (r=−0.34, p=0.04 and r=−0.40, p=0.01 respectively). Both length of stay and ventilator days were not associated with cognitive test scores. The number of TPN days (a marker of overall nutritional status) was not significantly associated with body measurements or cognitive test scores.

4. Discussion

Children with CGIAs experience multiple stressors early in life during a time of rapid growth and brain development. These early exposures to suboptimal nutrition and growth as well as exposures to multiple surgeries and inflammation may impact future growth and neurodevelopmental potential. Reassuringly, this cohort of at-risk children with CGIAs were similar in size and body composition to a group of healthy, term-born children, and they generally performed well on cognitive testing. However, similar to other at-risk populations

[18], processing speed scores were significantly lower than standardized means. When analyzing the relationship between growth and neurodevelopmental outcomes, we found that increased FFM in children with CGIAs was associated with higher receptive language scores, higher cognitive flexibility scores, and higher composite cognitive function scores.

Growth failure has been described in children with CGIAs prior to preschool-age. Neonates requiring surgery for GI diagnoses have been described as shorter, lighter, and with lower FM than matched controls at 43–44 weeks corrected gestational age [2]. Children with gastroschisis have been described as having suboptimal weight gain at 1 year [24] with continued suboptimal weight and linear growth at 2 years [25], and children with Hirschsprung's disease have been described as having decreased length at 1 year [26]. In our cohort of preschool-age children with CGIAs, growth and body composition were similar to a reference group of healthy children. This suggests that any potential differences in growth are corrected, and that these children are able to catch-up to the growth of their peers by preschool-age. A similar phenomenon is seen in preterm infants whose growth and body composition differ early in life from healthy, term-born peers but largely catch-up and are similar by preschool-age [9,27,28].

Although the potential early differences in growth were no longer present at preschool-age, brain growth and resulting brain function may still be impacted by early stress, inflammation, and inadequate nutrition. Several studies have described lasting neurodevelopmental delays in children requiring neonatal surgery including deficits in cognition [29,30], receptive language/verbal intelligence [29–31] executive function [32], working memory [33], attention [31,34], gross motor skills [29,34], and fine motor skills [30,31]. Perhaps one of the most thorough longitudinal studies involving a patient population similar to our cohort was conducted by Ludman et al. [7,35,36]. This prospective observational study evaluated neurodevelopmental outcomes in children requiring major neonatal surgery. At 3 years of age, these children had cognitive abilities that were similar to matched controls [36]. At school-age (11–13 years), they were significantly behind in all measures of educational attainment (English, Math, Science, academic performance) [7]. The authors hypothesize that the increased presence of neurodevelopmental delays later in life may be related to early neural damage that only becomes apparent when cognitive tasks require more complex skills.

In our study, children with CGIAs completed a series of cognitive tests to closely examine several subdomains of cognition and potentially detect subtle differences in cognition that may be present at preschool-age and impact later school performance. Overall, children with CGIAs performed well on these tests and achieved the mean standardized scores in the cognitive subdomains of receptive language, attention, episodic memory, and cognitive flexibility. General cognitive function scores were in fact higher than the standardized mean, which potentially reflects the high motivation and educational status of the families participating in this study.

Although children with CGIAs generally performed well on cognitive testing, processing speed scores were significantly lower than standardized means. Deficits in speed of processing have also been described in children born prematurely [18–20]. Myelination and the structural integrity of white matter tracts are important factors in speed of processing [37,38]. The formation of these structures may be particularly vulnerable to the physiologic stressors and inflammation likely experienced by both preterm-born children and children with CGIAs during the newborn period. Early damage to these structures and subsequent deficits in speed of processing may not be noticed until school-age when children are required to work under pressure to complete more rigorous tasks.

Although the brain may be more vulnerable to physiologic stressors early in life, it is also a time when the brain is most plastic and amenable to interventions [4,39,40]. Optimizing nutrition with the goal of increasing FFM gains may be one intervention targeted to improve brain growth and cognitive function, specifically speed of processing. In preterm infants, increased growth during and following NICU hospitalization has been associated with improved neurodevelopmental outcomes [16,41–43]. Scheurer et al. showed that increased FFM was associated with faster speed of processing and higher IQ scores in preschool-age children born prematurely [18]. Similarly in our study, higher FFM was associated with higher receptive language, cognitive flexibility, and general cognitive function scores in preschool-age children with CGIAs. However, the associations between FFM and receptive language and general cognitive function scores lost some significance when adjusting for age and sex in this small cohort.

Similar to the associations seen with increased FFM, increased BMI was associated with increased cognitive flexibility scores and general cognitive function scores in children with CGIAs. BMI is a traditional measurement of body fat based on adult height and weight. In children, BMI does not reliably predict body fat percentage [44]. Furthermore in non-obese children, increased BMI may more closely reflect increased FFM [45], which potentially explains the similar associations seen with increasing FFM and increasing BMI in our cohort of non-obese children.

Conversely, increased FM and %BF were associated with decreased attention scores. Increased FM gains during toddlerhood have also been associated with lower full scale IQ and lower processing speed scores in healthy, term-born children [18]. Additional studies have likewise shown associations with obesity and poor academic performance [46,47]. Increased FM and obesity have been linked with increased inflammation [48,49], and the presence of chronic inflammation has been shown to adversely affect brain development [50,51].

This study has some limitations in addition to the small sample size. As with other studies, it is possible that we are over-estimating cognitive abilities in our cohort due to selection biases. Families that have the resources and the motivation to participate in research studies are also likely to have exposure to educational and nutritional resources that may improve their child’s growth and developmental outcomes [52]. Additionally, only those children willing to participate in the given tests could be scored making it difficult to distinguish between those who are unmotivated versus those who are cognitively unable to complete the tests. Therefore, this study may not be capturing the true extent of cognitive deficiencies present in the population of children with CGIAs.

5. Conclusion

This is the first study to examine body composition in relation to cognition in preschool-age children with CGIAs. Similar to preterm-born children, we found that children with CGIAs had slower processing speed and that increased FFM was associated with higher scores on cognitive testing. Increased FFM may be a marker of improved nutritional status, organogenesis, and brain growth, which ultimately results in improved cognitive function. Chronic inflammation and higher FM may also negatively impact later cognition. Results from this study suggest that early interventions aimed at optimizing FFM gains through improved nutrition may lead to more optimal long-term outcomes for this population.

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Abbreviations:

CGIA	congenital gastrointestinal anomaly
FFM	fat-free mass
FM	fat mass
%BF	percent body fat
BMI	body mass index
NICU	Neonatal Intensive Care Unit
TPN	total parenteral nutrition
NIH	National Institutes of Health
PV	Picture Vocabulary test
FL	Flanker Inhibitory Control and Attention test
DCCS	Dimensional Change Card Sort test
PSM	Picture Sequence Memory test
PS	Pattern Comparison Processing Speed test
CECC	Cognition Early Childhood Composite score

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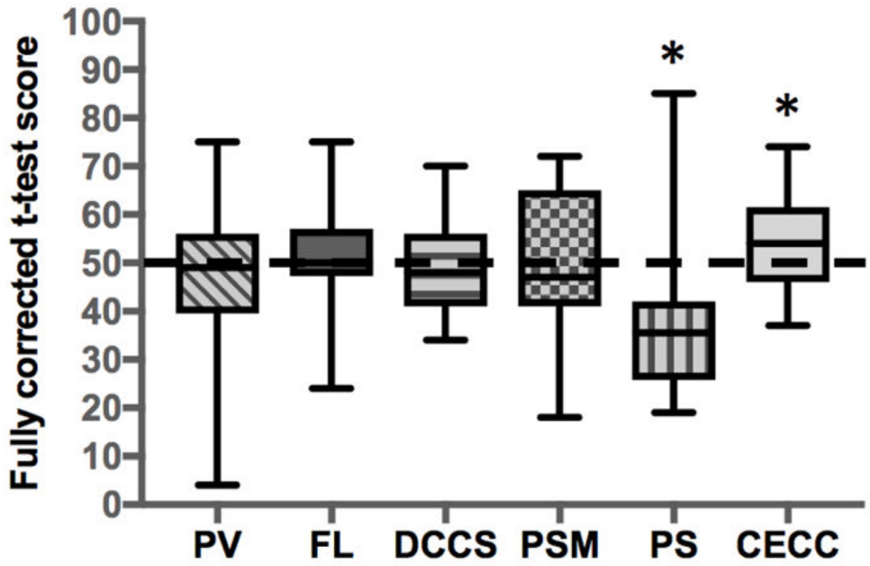
Highlights:

- Children with congenital gastrointestinal anomalies are at significant risk for growth failure and neurodevelopmental delays given their early exposures to physiologic stressors such as major surgery and inadequate nutrition.
- At preschool-age, children with congenital gastrointestinal anomalies had similar body composition to a reference group of peers, and they generally performed well on cognitive testing. However, speed of processing scores were significantly lower than standardized means.
- Like children born prematurely, higher fat-free mass was associated with higher cognitive test scores in children with congenital gastrointestinal anomalies.



Box and whisker plots represent mean, IQR, and max/min scores on cognitive tests, dashed line represents the standardized mean (50), *p-value <0.05, p-values calculated using t-test comparing cohort mean and standardized mean, PV=Picture Vocabulary test (n=34, mean 47.6), FL=Flanker Inhibitory Control and Attention test (n=28, mean 51.5), DCCS=Dimensional Change Card Sort test (n=30, mean 49.0), PSM=Picture Sequence Memory test (n=27, mean 51.4), PS=Pattern Comparison Processing Speed test (n=26, mean 37.9), CECC=Cognition Early Childhood Composite score (n=22, mean 55.2)

Figure 1.

NIH Toolbox Early Childhood Cognition test scores in children with CGIAs.

Table 1.

Characteristics of children with CGIAs

Variable	CGIA (n=34)
Primary diagnosis	
Gastroschisis	8(23)
Hirschsprung's disease	7(21)
Imperforate anus	4(12)
Tracheoesophageal fistula esophageal atresia	4(12)
MalrotationVolvulus	3(9)
Congenital diaphragmatic hernia	3(9)
Jejunal atresia	2(6)
Duodenal stenosis	2(6)
Omphalocele	1(2)
Delivery mode (n=33)	
C-section	17(52)
Vaginal	16 (49)
Maternal age at delivery (years)	31 (28. 32)
Birth weight category	
SGA	7(21)
LGA	5(15)
Apgar score. 5 minute (n=31)	9 (8. 9)
TPN days	14 (5. 26)
Gastrostomy tube placed	4(12)
Cholestasis present	7(21)
Ventilator days	2(1.10)
Number of operations	
One	15 (45)
Multiple	19(55)
Antibiotic days	2 (1.10)
Length of stay days	19.5 (10. 44)
Health problems following NICU discharge	
0: No problem	9(27)
1: Mild (eczema, asthma. UTL ear infection)	3(9)
2: Moderate (outpatient investigations. <2 admissions)	14(41)
3: Severe (>2 admissions, major surgery)	8(23)
Any preschool attendance	24 (76)

Data expressed as median (IQR) for continuous variables or n (%) for categorical variables, SGA=small for gestational age, LGA=large for gestational age, TPN=total parenteral nutrition, NICU=neonatal intensive care unit, UTI=urinary tract infection

Table 2.

Anthropometric measurements and body composition of children with CGIAs compared with a reference group of term-born, healthy children at preschool-age

Variable	CGIA (n=34)	Reference (n=51)	p-value
Demographics			
Male sex	22 (65)	26 (51)	0.27
White Race	31 (91)	38 (75)	0.09
Mother's education (college & above)	29 (85.3)	45 (88.3)	0.75
Gestational age (wks)	37.9 (1.71)	39.8 (1.03)	<0.001
Birth weight (kg)	3.22 (0.69)	3.53 (0.46)	0.02
Age at preschool visit (yrs)	4.7 (0.63)	4.37 (0.23)	0.005
Anthropometric measurements			
Weight z-score	−0.16 (1.05)	0.02 (1.03)	0.40
Height z-score	0.04 (1.00)	−0.08 (0.84)	0.56
BMI z-score	−0.18 (0.91)	0.16 (0.77)	0.07
Body composition			
Fat-free mass (kg)	14.0 (2.57)	13.72 (1.40)	0.56
Fat mass (kg)	3.59 (1.23)	3.46 (1.13)	0.62
Percent body fat	20.38 (6.38)	19.85 (5.00)	0.68

p-values calculated from two-sample t-test, data expressed as mean (standard deviation) for continuous variables or n (%) for categorical variables

Table 3.

Associations between body composition and NIH Toolbox Early Childhood Cognition Battery test scores in children with CGIAs

Test	Cognitive Subdomain	BMI z-score		Fat-Free Mass		Fat Mass		Percent Body Fat	
		β (SE)	p-value	β (SE)	p-value	β(SE)	p-value	β (SE)	p-value
PV	Receptive Language	3.5 (2.9)	0.23	**3.1 (0.9)**	**0.001**	−1.5 (2.2)	0.51	−0.8 (0.4)	0.06
				1.9 (1.0)[a]	0.08[a]	−0.6 (1.9)[a]	0.76[a]	−0.3 (0.4)[a]	0.41[a]
FL	Inhibitory Control and Attention	1.4 (2.3)	0.54	0.7 (0.8)	0.35	−2.7 (1.8)	0.14	−0.6 (0.3)	0.06
				0.7 (0.9)[a]	0.46[a]	**−3.7 (1.6)**[a]	**0.03**[a]	**−0.9 (0.3)**[a]	**0.009**[a]
DCCS	Cognitive Flexibility	**4.2 (1.6)**	**0.01**	**1.7 (0.6)**	**0.005**	0.7 (1.4)	0.63	−0.2 (0.3)	0.47
				1.8 (0.7)[a]	**0.01**[a]	0.9 (1.4)[a]	0.51[a]	−0.1 (0.3)[a]	0.77[a]
PSM	Episodic Memory	2.4 (3.0)	0.43	1.3 (1.0)	0.23	0.3 (2.2)	0.89	−0.1 (0.3)	0.76
				0.6 (1.1)[a]	0.58[a]	0.1 (2.0)[a]	0.97[a]	−0.04 (0.5)[a]	0.93[a]
PS	Processing Speed	3.3 (3.7)	0.38	−0.1 (1.3)	0.96	2.1 (2.7)	0.45	0.5 (0.6)	0.37
				−0.2 (1.4)[a]	0.89[a]	1.2 (2.5)[a]	0.62[a]	0.4 (0.5)[a]	0.47[a]
CECC	General Cognitive Function	**4.9 (2.1)**	**0.03**	**1.5 (0.7)**	**0.05**	1.9 (1.8)	0.33	0.04 (0.4)	0.92
				1.5 (0.8)[a]	0.08[a]	1.2 (1.8)[a]	0.49[a]	−0.01 (0.4)[a]	0.98[a]

Linear regression analysis utilizing NIH Toolbox fully corrected t-scores normed for age, gender, race, ethnicity, and parent’s education

[a]Adjusted for age and sex, PV=Picture Vocabulary test (n=34), FL=Flanker Inhibitory Control and Attention test (n=28), DCCS=Dimensional Change Card Sort test (n=30), PSM=Picture Sequence Memory test (n=27), PS=Pattern Comparison Processing Speed test (n=26), CECC=Cognition Early Childhood Composite score (n=22)