Published in final edited form as:

Arch Pediatr Adolesc Med. 2010 June ; 164(6): 507–516. doi:10.1001/archpediatrics.2010.56.

Growth and relations between auxology, caregiving environment and cognition in socially deprived Romanian children randomized to foster vs. ongoing institutional care

Dr. Dana E. Johnson, M.D., Ph.D., Dr. Donald Guthrie, Ph.D., Dr. Anna T. Smyke, Ph.D., Dr. Sebastian F. Koga, M.D., Dr. Nathan A. Fox, Ph.D., Dr. Charles H. Zeanah, M.D., and Dr. Charles A. Nelson III, Ph.D.

Department of Pediatrics, University of Minnesota, Minneapolis (Dr. Johnson); Semel Institute, University of California, Los Angeles, California (Dr. Guthrie); Department of Psychiatry and Neurology, Tulane University, New Orleans, Louisiana (Drs Smyke and Zeanah); Department of Neurosurgery, University of Virginia, Charlottesville, Virginia (Dr. Koga); Department of Human Development, University of Maryland, College Park, Maryland (Dr. Fox); and Department of Medicine, Children's Hospital Boston/Harvard Medical School, Boston, Massachusetts and formerly Institute of Child Development, University of Minnesota, Minneapolis, Minnesota (Dr. Nelson)

Abstract

Objective—To determine the effects of improved nurture compared with institutional care on physical growth and the relations between growth and cognitive development.

Design—A randomized controlled trial beginning at baseline (mean 21.0, range 5.4–32 months) with follow-up at 30, 42 and 54 months of age.

Setting—Institutionalized and community children in Bucharest, Romania

Participants—136 institutionalized though otherwise healthy children from six orphanages and 72 typically developing, never-institutionalized children.

Corresponding Author: Dana E. Johnson, M.D., Ph.D. Department of Pediatrics, Division of Neonatology, MMC 211, 420 Delaware St. SE, Minneapolis, MN 55455, USA <johns008@umn.edu>, office (612) 624-1989, fax (612) 624-8176.

Financial Disclosures: None.

Additional Contributions: We thank Hermi R. Woodward and the MacArthur Foundation Research Network on Early Experience and Brain Development for input regarding the conceptualization, design, and implementation of this project; Gwen Gordon for assistance in data management; Elizabeth Furtado for ongoing project coordination and the caregivers and children who participated in this project.

Author Contributions: Dr Johnson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Nelson, Fox, Zeanah

Acquisition of data: Johnson, Koga, Smyke, Nelson, Fox, Zeanah

Analysis and interpretation of data: Guthrie, Johnson.

Drafting of the manuscript: Johnson.

Critical revision of the manuscript for important intellectual content: Johnson, Guthrie, Smyke, Koga, Fox, Zeanah, Nelson.

Statistical analysis: Guthrie, Johnson.

Obtained funding: Nelson, Fox, Zeanah.

Study supervision: Smyke, Koga, Nelson, Fox, Zeanah.

Intervention—Institutionalized children were randomly assigned to foster care or to receive institutional care as usual.

Outcome Measures—Auxology and measures of intelligence over time.

Results—Growth in institutionalized children was compromised, particularly in infants <2,500 grams. Mean height and weight, though not head size, increased to near normal within 12 months in foster care. Significant independent predictors for greater catch-up in height and weight included age <12 months at randomization and higher caregiving quality, particularly caregiver sensitivity and positive regard. At 54 months, birth weight < 2500 grams was associated with a 11.0 ± 3.7 (standard error) point lower IQ and each incremental increase of one in standardized height scores between baseline and 42 months was associated with a 6.2 ± 3.0 point increase in IQ ($p < .05$).

Conclusions—Foster care had a significant effect on growth particularly with early placement and high quality care. Growth and IQ in low birth weight children are particularly vulnerable to social deprivation. Catch-up growth in height under more nurturing conditions is a useful correlate of caregiving quality and cognitive abilities.

Trial Registration—clinicaltrials.gov Identifier: NCT00747396

Introduction

A syndrome of poor growth in socially deprived children has been recognized since the eponymous Kasper Hauser was discovered stunted and developmentally delayed outside the gates of Nuremberg in 1828.¹ Several sub-types have been described,^{2–5} though all share two characteristics: otherwise unexplained growth failure occurring in association with socially stressful conditions and significant catch-up when a child's caregiving environment improves.³ Understandably, studies to date have relied on convenience samples of children referred to specialists for evaluation of short stature,^{2, 3, 5, 6} entering the child protection system^{7–9} or placed for adoption from institutional care settings.^{4, 10–12} Under these circumstances basic social and medical information is lacking and it has been virtually impossible to ascertain the type, severity or duration of adversity experienced by the child. This absence of randomized, controlled studies examining environment and growth may account for reported variations in the response of children to deprivation and social intervention, as well as the variety of growth failure subtypes described.

The Bucharest Early Intervention Project (BEIP), the first randomized controlled study of foster vs. institutional care, offered a unique opportunity to study growth within otherwise healthy institutionalized and never institutionalized Romanian children. These subjects had measures of growth, caregiving environment, behavior, brain and cognitive development assessed before and at intervals following randomization of those institutionalized to foster vs. institutional care as usual.^{13–32} Contrasting these children with matched, never institutionalized controls, we explored biologic and environmental factors contributing to growth failure and recovery and investigated the relations between growth and cognitive outcome.

Methods

Study Design

Subject selection has been discussed in detail in past publications but will be summarized briefly.^{18, 22, 27} Enrollment, group assignments and follow-up of subjects through 54 months have been published previously (Fig. 1).¹⁸

Children in Institutions (IG)—All children < 32 months of age living in institutions for infants in all six sectors of Bucharest, other than those scheduled for adoption, were included (n=187). Children (n=51) with serious handicapping conditions were excluded e.g., genetic syndromes, facial features (3 or 4) indicative of high risk of prenatal alcohol exposure,^{33, 34} severe microcephaly, cerebral palsy or a high suspicion of bilateral hearing loss. Subjects were recruited from February through June 2001.

Care as Usual (CAU) and Foster Care Groups (FCG)—Following identification and baseline assessment of the institutionalized cohort (IG) (n=136), equal numbers were randomly assigned to remain within institutional care and receive care as usual (CAU), or to foster care (FCG). Eleven of the children originally cleared for participation in the study were later determined to have conditions that met exclusion criteria and were eliminated from analyses.²² Because government sponsored foster care was unavailable when our study commenced, we created our own foster care program.^{23, 27} Irrespective of changes in caregiving environment over the duration of the study, an intent-to-treat approach was followed, whereby all analyses we report are based on children's original group assignments. Thus, our findings represent a conservative estimate of the response to intervention

Never-Institutionalized Group (NIG)—Children (n=72) were recruited from community pediatric clinics and were born at the same hospitals as the institutional children. They were living with their birth family, had no history of institutional care and were approximately matched on age and gender to CAU and FCG.

Ethical Considerations

The rationale behind the study, justification and critique of the randomized controlled design, and the approval process and procedures put in place to safeguard these children have been discussed in depth in previous publications.^{18, 27, 35–37} Approval was obtained from the Institutional Review Boards of the home institutions of the principal investigators (Charles Nelson, Charles Zeanah, and Nathan Fox).

Data Collection

Assessments of cognitive level and caregiving environment were obtained at three time points, baseline [21.0±7.4(s.d.), range 5–32 months], 30 and 42 months as previously described.^{18, 22} Birthweight was obtained from record review (IG) or from parent report (NIG) and was available for 90% of the children from IG and 94% of the children from NIG. Information on gestational age at birth for IG was either not available or deemed unreliable so it was impossible to determine whether low birth weight (LBW) infants

(<2,500 grams) were appropriate or small for gestational age (SGA). In addition to baseline, 30 and 42 month auxology, measurements were scheduled monthly in CAU and FCG. Cognitive testing was also obtained at 54 months. All reported p-values are two sided. Data were analyzed using SPSS (Version 11.0 for Macintosh) and SAS (version 9.1) software.

Physical growth—Length/height, weight and weight-for-height were converted to age-standardized scores (z-scores) based on CDC 2000 data³⁸ using the formula

$$z = (x - \mu) / \sigma,$$

where x is the raw measurement, μ is the age-specific mean, and σ is the age-specific standard deviation. Using z-score measures standardized sizes, thus making them comparable across age ranges. Occipital frontal circumference (OFC) z-scores were calculated using the standardized data (0–18 years of age) of Roche and colleagues³⁹

Cognitive development and caregiving environment—Developmental quotients (DQ) at baseline, 30 and 42 months were based on the Bayley Scales of Infant Development II Mental Developmental Index.^{22, 40} The Wechsler Preschool Primary Scale of Intelligence-II (WPPSI) was used at 54 months.⁴¹ The Observational Record of the Caregiving Environment (ORCE)⁴² was adapted and used to assess a child's caregiving experience in either the institution or family settings as previously described.²² The Caregiving Quality Score (CQS) was obtained by averaging five qualitative ORCE scales [i.e. detachment (reversed) flat affect (reversed), positive regard for child, sensitivity and stimulation of development], each of which received a rating from 1 (not at all characteristic) to 4 (highly characteristic). CQS ranged from 1 (lowest possible score) to 4.

Results

Control Analyses

Children in NIG were primarily ethnic Romanians (Table I). Birthweight was lower for IG children and the incidence of LBW (<2,500 grams) was higher than in NIG. At baseline, children randomized into CAU and FCG groups did not differ from one another in any of these parameters.

Auxology at Baseline

At baseline, all physical measurements were significantly smaller and z-scores < -2 more frequent in IG vs. NIG. The CQS was significantly lower in IG vs. NIG (Table I) and increased with age [$y = 1.8 + .02$ (age in months) $F(1,114) = 6.00$, $p = .016$, $R^2 = .05$]. The prevalence of wasting (weight-for-height z-scores < -2) in IG was high (16%)⁴³ and was especially common in younger children [25% <12 mo vs. 6% 24 mo, $\chi^2(1) = 7.14$, $p < .01$].

Multiple regression models accounted for significant variance in baseline z-scores for height, weight, OFC and weight-for-height (Table II). Significant unique predictors of lower z-scores at baseline included lower birth weight (height, weight, OFC and weight-for-

height), older age (height), non-Romanian ethnicity (OFC) and younger age (weight-for-height). Within IG, LBW children were significantly more growth impaired than children with birth weights ≥ 2.5 kg in all parameters other than OFC ($p = .08$) (Table III). Both birth weight groups were significantly different vs. NIG. Institutionalized children of Roma/other/unknown ethnicity had smaller OFC z -scores at baseline than children who were of Romanian ethnicity [$-1.43 \pm .83$ (s.d.) vs $-.83(1.03)$, $t(118)=3.43$, $p=.001$]. However, birth weight, baseline CQS and baseline DQ did not differ between these two ethnic groups making it more likely that this difference was an inherent auxologic characteristic rather than the result of pre- or post-natal factors.

Post-Randomization Growth

CQS at 30 and 42 months improved for FCG and did not differ significantly from NIG (Table I). Children randomized to CAU were deinstitutionalized at the discretion of child protection officials and only 48% remained institutionalized at 42 and 35% at 54 months of age. Consequently, caregiving scores improved over time for CAU as well.

Growth was first examined from baseline to 42 months of age, $19 \text{ mo} \pm 6.7$ (s.d.) months (range 9.1–31.2 mo, 93% ≥ 12 mo) after randomization. Random effects linear growth models (SAS PROC MIXED) with monthly measurements between baseline and 42 months of age in raw, non-standardized form indicated that children in FCG grew significantly faster in height and weight than CAU (Fig. 2a). Growth in head circumference did not differ between FCG and CAU. We also conducted a one-way within-subjects ANOVA within each group with the factor being time (baseline, 30 months, 42 months) and the dependent variables being measurements (Fig. 2b,c). When corrected for regression to the mean,⁴⁴ only height ($+.50z$) and weight z -scores ($+.46z$) in FCG and weight z -scores ($+.08z$) in CAU showed improvement.

To study the effect of intervention duration, we plotted growth at six-month intervals over the 18 months following randomization (Fig. 3). Measurements were included in the analyses if they were obtained within a ± 1 -month window of the target intervals (6, 12, 18 months). FCG showed rapid increases in height and weight z -scores during the first 12 months while CAU showed no improvement. When corrected for regression to the mean, height ($+.30z$) and weight z -scores ($+.48z$) changed significantly. By 12 months 100% of FCG were in the normal range (≥ -2) for height, 90% for weight and 94% for weight-for-height. No significant change in any parameter occurred between 12 and 18 months post-placement.

Factors Associated with Growth Recovery

We next examined factors influencing z -score changes (Δz) in FCG. To determine whether there were sensitive periods for catch-up growth, as previously reported for cognitive outcomes,¹⁸ attachment²⁴ and certain measures of electroencephalogram power and coherence¹⁵ in BEIP, five dichotomized ages of entry into foster care (12, 15, 18, 21, 24 months) were tested. Multiple regression models accounted for significant variance in Δz for all four measures (Table IV). Significant unique predictors of greater Δz included lower baseline z -scores (height, weight, OFC) and age of randomization <12 months (height,

weight, OFC, weight-for-height). Higher post-placement CQS were also significant unique predictors of catch-up in height and weight, Individual components of the CQS quantifying caregiver detachment (height only) were negatively correlated while those quantifying positive regard for the child and sensitivity were positively correlated with z 's for height and weight (Table V).

There were no significant gender differences in z -scores at 42 months or z 's baseline to 42 months and there were no significant differences between low (<2.5 kg) and normal (≥ 2.5 kg) birth weight infants in z 's baseline to 42 months (Table VI). While low birth weight infants tended to be smaller at 42 months of age, the difference was significant for head size alone.

Growth and Cognitive Improvement in the Foster Care Group

Reestablishment of normal kinetics in the growth hormone-IGF-1 axis (GH-GF-1 axis) has been shown to be a factor in growth recovery in neglected children placed in more nurturing environments. Based on this fact and on reports of improved stature correlating with cognitive gains in stunted, cognitively impaired children treated with growth hormone^{45–47}, we investigated whether catch-up growth in FCG could predict cognitive abilities at 42 months, and if so, whether the effects would persist at 54 months. Included were child characteristics, CQS in foster care, baseline OFC, z -scores between baseline and 42 months in height, weight and OFC and the binary age variable (24 months) previously reported to define a sensitive period for cognitive development in this cohort.¹⁸ Multiple regression models accounted for significant variance in both cognitive measures (Table VII). Baseline DQ and z -height were both significant unique predictors positively related to DQ-42 and Full IQ-54. Birth weight and female gender were significant unique predictors positively related to Full IQ-54. As predicted by the risk factors of low birth weight and delayed placement into foster care,¹⁸ children with birth weights ≥ 2.5 kg placed in foster care prior to 24 months of age had a mean IQ score 25 points higher than LBW infants placed after 24 months of age (Fig. 4).

Discussion

Children raised in institutions had globally suppressed growth followed by recovery of height and weight but not OFC within those removed and placed in foster care. These observations mirror the report of suppressed growth within institutional care settings and recovery within adoptive families reported in a meta-analysis by Van Ijzendoorn and colleagues.¹¹ Both the current data and the meta-analysis showed that height catch-up improved if placement occurred prior to 12 months of age. Data from BEIP confirmed the same sensitive period for weight, OFC and weight-for-height. In FCG, catch-up growth for height and weight were robust and essentially complete by 12 month after randomization when both height and weight z -scores were close to 0.

Though growth has shown improvement within cohorts of neglected and or abused children once removed from an adverse environment,^{9, 11, 48, 49} the contribution of individual child-caregiver interaction to catch-up growth has never been directly explored. The BEIP is the first to evaluate growth in children living under adverse social circumstances in relation to

standardized measures of individual caregiving environments. The data indicate that caregiving quality was a significant independent predictor of catch-up growth in height and weight. Components of the CQS that were positively correlated with catch-up included sensitivity (child-centered, contingent responses) and positive regard for the child (acceptance, respect and warmth including expressions of physical affection).

Following the initial report of Talbot and colleagues⁵⁰ investigators have described four syndromes of impaired growth associated with adversity based on several factors including: age, nutrition, behavioral or emotional co-morbidities and status of the GH-IGF-1 axis.²⁻⁶ All share the diagnostic features of suppressed growth within the context of adversity followed by catchup growth after improvement in caregiving environment; a central finding observed in children in FCG. Caloric deprivation has been reported to play a central role in growth failure during infancy (Type I), while changes in the GH-IGF-1 axis (Types IIA, IIB and III) becomes more important in growth suppression and recovery in children beyond the first 18–24 months of life.²⁻⁶ Both nutrition and production of endogenous growth factors are likely to be affected by an institutional environment.

Nutritional requirements in children vary depending on growth rates and whether preexisting deficits exist. During the rapid growth phase between birth and 18 months the effects of even modest nutritional deficits become magnified. Both low birthweight infants and children with orofacial malformations or neuromotor problems are overrepresented within institutional care settings and may have difficulty obtaining and/or consuming sufficient calories to grow.^{10, 12, 22, 51} With the time and fiscal constraints experienced by virtually all orphanages worldwide, it is highly unlikely that the nutritional needs of individual children can be accommodated within an environment where dietary plans and feeding protocols are strictly regimented and caregiver actions are based on efficiency and expediency rather than being responsive to child-based cues.⁵²

Considering that neglected infants are highly susceptible to insufficient intake, it is not surprising that malnutrition is felt to be the principal cause of deprivation-associated growth failure within this age group.^{2, 53} Two observations in BEIP including, lower CQS during infancy, and that wasting was significantly more common in younger children underscore the importance of malnutrition as a major determinant in psychosocial growth failure during infancy. Outside of the first years of life, there is less evidence that caloric deprivation is a primary factor in the etiology of growth failure in neglected and/or abused children as weight-for-height has been reported to be essentially normal.^{2, 3, 6} Consistent with past studies, weight-for-height in the IG at baseline was greater in older children and only 6% of children > 24 months were wasted vs. 25% in those < 12 months.

In older children, alterations in the GH-IGF-1 axis have been documented to play a key role in growth failure and catch-up.^{2-6, 48} In a cohort of post-institutionalized Eastern European children of similar age to those in BEIP (mean 20.4 months, range 7.3–59.9), levels of IGF Binding Protein-3 shortly after placement was an independent predictor of height z-score.¹² As would be expected with abnormal GH-IGF-1 axis function, height but not weight, head circumference or weight-for-height at baseline in BEIP was lower in older institutionalized children (IG).

It was impossible for us to directly measure serum growth factors given constraints imposed on us by local authorities and IRBs and the labor intensive process of nutritional evaluation could not be conducted with resources available. However, auxology in BEIP is consistent with previous work in this area and implicates both nutrition and alterations in the GH-IGF-1 axis in growth suppression. The relative importance of these two factors and the consequent clinical presentations almost certainly relate to a child's age with malnutrition contributing more during periods of rapid growth and utter dependency and depression of the GH-IGF-1 axis becoming more important as growth rates slow, children are more able to regulate their own dietary intake and linear growth becomes more dependent on growth hormone.^{54, 55}

The observation that catch-up growth in height was the only significant independent auxologic predictor of cognitive abilities at 42 and 54 months suggests that the GH-IGF-1 axis may also play a role in cognitive recovery. The role of this complex system in cognitive development is supported by substantial experimental,^{56, 57} and clinical evidence. In normal 8- to 9-year-old children IGF-1 levels were shown to be positively related to IQ.⁵⁸ Children with 18q deletions,⁴⁵ Prader-Willi Syndrome⁴⁶, or born SGA,⁴⁷ conditions characterized by both short stature and cognitive delays, have shown significant improvement in height, IQ and brain structure following treatment with GH. Finally, children with defects in the GH receptor, have IQs and brain structural abnormalities that differ depending on which exon contains the point mutation or deletion.⁵⁹

Irrespective of whether there are direct causative relations, improvement in stature proves not only to be a useful biologic measure of caregiving environment but an informative indicator of cognitive improvement in at-risk children. As countries heed the call to eliminate institutions by developing kinship and foster care, post-placement growth could be used as a cost-effective marker of caregiving quality and child well being pending sufficient staffing and funding of more comprehensive social services programs.

From this study, several significant themes emerge with relevance to policies for care of institutionalized children. Infants who are LBW are particularly vulnerable to the effects of social deprivation and should be the first triaged to family care. The unique nutritional needs of LBW infants are unlikely to be appreciated and even if they are, dependence on conformity in orphanages makes it unlikely that specific nutritional interventions needed to optimize growth would be offered for growth retarded or premature infants. Growth at baseline in our institutionalized LBW infants was particularly impaired, consistent with the global growth failure described in LBW infants who experienced social deprivation in early life.^{12, 60-62} They were also at higher risk for cognitive compromise and smaller head size at 42 months, findings that have also been observed in LBW infants exposed to social deprivation.⁶¹⁻⁶³ Second, the sensitive period for growth recovery (< 12 months) is even earlier than the sensitive period (< 24 months) described in BEIP for cognitive recovery,¹⁸ attachment behavior²⁴ and improvement in the electroencephalogram¹⁵ strengthening the argument for placement within family care as early as possible. Not only will delayed placement affect growth in LBW as it does for all infants but the combination of LBW plus prolonged duration of institutional care > 24 months¹⁸ resulted in severe cognitive compromise. Finally, though family is clearly preferable to institutional care, establishing

higher quality child-caregiver interactions with appropriate screening, training in emotional engagement and contingent caregiving and monitoring insures the best outcomes in terms of growth.

The significance of these findings extends beyond the millions of institutionalized children worldwide to hundreds of millions of impoverished children who are stunted and/or do not meet their developmental potential. The interdependence of nutrition and social environment on child outcomes has recently received attention in regards to achieving UN Millennium Development Goals.⁶⁴ This study of growth in institutionalized children adds strong experimental support to the conclusion of Black and colleagues, that strategies that fail to address nurture along with health and nutrition will likely fail to achieve significant improvements in overall child well-being.⁶⁴ Psychosocial deprivation within any caregiving environment during early life is as detrimental as malnutrition and must be viewed with as much concern as any severely debilitating childhood disease.

Acknowledgments

Funding/Support: The work reported in this manuscript was supported by funds from the John D. and Catherine T. MacArthur Foundation. C.A.N. also acknowledges the generous support of the Richard David Scott endowment and the Binder Family Foundation.

Role of the Sponsor: The study sponsors had no role in the design and conduct of the study; in the collection, analysis, management, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Abbreviations

BEIP	The Bucharest Early Intervention Project
CAU	Care as Usual Group
CQS	Caregiving Quality Score
DQ	Bayley II Developmental Quotient
z	Change in z-scores
FCG	Foster Care Group
GH	Growth Hormone
IG	Institutionalized Group at Baseline
IGF-1	Insulin-Like Growth Factor 1
LBW	Low Birth Weight
NIG	Never Institutionalized Group
OFC	Occipital-frontal circumference
ORCE	Observational Record of the Caregiving Environment
SGA	Small for Gestational Age
WPPSI	Wechsler Preschool Primary Scale of Intelligence

References

1. Money, J. The Kaspar Hauser syndrome of “psychosocial dwarfism”. 1. Amherst, NY: Prometheus Books; 1992.
2. Blizzard, RM.; Bulatovic, A. Syndromes of psychosocial short stature. In: Lifshitz, F., editor. Pediatric Endocrinology. 3. New York: Marcel Dekker; 1996. p. 83-93.
3. Gohlke BC, Frazer FL, Stanhope R. Body mass index and segmental proportion in children with different subtypes of psychosocial short stature. *Eur J Pediatr*. 2002; 161(5):250–254. [PubMed: 12012218]
4. Mason P, Narad C. Long-term growth and puberty concerns in international adoptees. *Pediatr Clin North Am*. 2005; 52(5):1351–1368. vii. [PubMed: 16154467]
5. Skuse D, Albanese A, Stanhope R, Gilmour J, Voss L. A new stress-related syndrome of growth failure and hyperphagia in children, associated with reversibility of growth-hormone insufficiency. *Lancet*. 1996; 348(9024):353–358. [PubMed: 8709732]
6. Gohlke BC, Khadilkar VV, Skuse D, Stanhope R. Recognition of children with psychosocial short stature: a spectrum of presentation. *J Pediatr Endocrinol Metab*. 1998; 11(4):509–517. [PubMed: 9777571]
7. Oliván G. Catch-up growth assessment in long-term physically neglected and emotionally abused preschool age male children. *Child Abuse Negl*. 2003; 27(1):103–108. [PubMed: 12510033]
8. Taitz LS, King JM. Growth patterns in child abuse. *Acta Paediatr Scand Suppl*. 1988; 343:62–72. [PubMed: 3195334]
9. Wyatt DT, Simms MD, Horwitz SM. Widespread growth retardation and variable growth recovery in foster children in the first year after initial placement. *Arch Pediatr Adolesc Med*. 1997; 151(8): 813–816. [PubMed: 9265884]
10. Johnson, DE. Medical and developmental sequelae of early childhood institutionalization in Eastern European adoptees. In: Nelson, CA., editor. The effects of early adversity on neurobehavioral development: The Minnesota Symposia on Child Psychology. Mahwah, NJ: Lawrence Erlbaum Associates; 2000. p. 113-162.
11. Van Ijzendoorn MH, Bakermans-Kranenburg MJ, Juffer F. Plasticity of growth in height, weight, and head circumference: meta-analytic evidence of massive catch-up after international adoption. *J Dev Behav Pediatr*. 2007; 28(4):334–343. [PubMed: 17700087]
12. Miller BS, Kroupina MG, Iverson SL, et al. Auxological evaluation and determinants of growth failure at the time of adoption in Eastern European adoptees. *J Pediatr Endocrinol Metab*. 2009; 22(1):31–39. [PubMed: 19344072]
13. Ghera MM, Marshall PJ, Fox NA, et al. The effects of foster care intervention on socially deprived institutionalized children’s attention and positive affect: results from the BEIP study. *J Child Psychol Psychiatry*. 2009; 50(3):246–253. [PubMed: 19309327]
14. Marshall PJ, Fox NA. A comparison of the electroencephalogram between institutionalized and community children in Romania. *J Cogn Neurosci*. 2004; 16(8):1327–1338. [PubMed: 15532128]
15. Marshall PJ, Reeb BC, Fox NA, Nelson CA 3rd, Zeanah CH. Effects of early intervention on EEG power and coherence in previously institutionalized children in Romania. *Dev Psychopathol*. 2008; 20(3):861–880. [PubMed: 18606035]
16. Nelson CA, Furtado EA, Fox NA, Zeanah CH. The deprived human brain. *American Scientist*. 2009; 97:222–229.
17. Nelson CA, Parker SW, Guthrie D. The discrimination of facial expressions by typically developing infants and toddlers and those experiencing early institutional care. *Infant Behav Dev*. 2006; 29(2):210–219. [PubMed: 17138276]
18. Nelson CA 3rd, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, Guthrie D. Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. *Science*. 2007; 318(5858):1937–1940. [PubMed: 18096809]
19. Parker SW, Nelson CA. An event-related potential study of the impact of institutional rearing on face recognition. *Dev Psychopathol*. 2005; 17(3):621–639. [PubMed: 16262985]

20. Parker SW, Nelson CA. The impact of early institutional rearing on the ability to discriminate facial expressions of emotion: an event-related potential study. *Child Dev.* 2005; 76(1):54–72. [PubMed: 15693757]
21. Smyke AT, Dumitrescu A, Zeanah CH. Attachment disturbances in young children. I: The continuum of caretaking casualty. *J Am Acad Child Adolesc Psychiatry.* 2002; 41(8):972–982. [PubMed: 12162633]
22. Smyke AT, Koga SF, Johnson DE, et al. The caregiving context in institution-reared and family-reared infants and toddlers in Romania. *J Child Psychol Psychiatry.* 2007; 48(2):210–218. [PubMed: 17300560]
23. Smyke AT, Zeanah CH Jr, Fox NA, Nelson CA 3rd. A new model of foster care for young children: the Bucharest early intervention project. *Child Adolesc Psychiatr Clin N Am.* 2009; 18(3):721–734. [PubMed: 19486847]
24. Smyke AT, Zeanah CH, Fox NA, Nelson CA, Guthrie D. Placement in foster care enhances quality of attachment among young institutionalized children. *Child Dev.* in press.
25. Windsor J, Glaze LE, Koga SF. Language acquisition with limited input: Romanian institution and foster care. *J Speech Lang Hear Res.* 2007; 50(5):1365–1381. [PubMed: 17905917]
26. Zeanah CH, Egger HL, Smyke AT, et al. Institutional Rearing and Psychiatric Disorders in Romanian Preschool Children. *Am J Psychiatry.* 2009
27. Zeanah CH, Nelson CA, Fox NA, et al. Designing research to study the effects of institutionalization on brain and behavioral development: the Bucharest Early Intervention Project. *Dev Psychopathol.* 2003; 15(4):885–907. [PubMed: 14984131]
28. Zeanah CH, Smyke AT, Dumitrescu A. Attachment disturbances in young children. II: Indiscriminate behavior and institutional care. *J Am Acad Child Adolesc Psychiatry.* 2002; 41(8): 983–989. [PubMed: 12162634]
29. Zeanah CH, Smyke AT, Koga SF, Carlson E. Attachment in institutionalized and community children in Romania. *Child Dev.* 2005; 76(5):1015–1028. [PubMed: 16149999]
30. Moulson MC, Fox NA, Zeanah CH, Nelson CA. Early adverse experiences and the neurobiology of facial emotion processing. *Dev Psychol.* 2009; 45(1):17–30. [PubMed: 19209987]
31. Moulson MC, Westerlund A, Fox NA, Zeanah CH, Nelson CA. The effects of early experience on face recognition: an event-related potential study of institutionalized children in Romania. *Child Dev.* 2009; 80(4):1039–1056. [PubMed: 19630892]
32. Zeanah CH, Egger HL, Smyke AT, et al. Institutional rearing and psychiatric disorders in Romanian preschool children. *Am J Psychiatry.* 2009; 166(7):777–785. [PubMed: 19487394]
33. Astley SJ, Clarren SK. A fetal alcohol syndrome screening tool. *Alcohol Clin Exp Res.* 1995; 19(6):1565–1571. [PubMed: 8749828]
34. Astley SJ, Clarren SK. Measuring the facial phenotype of individuals with prenatal alcohol exposure: correlations with brain dysfunction. *Alcohol.* 2001; 36(2):147–159.
35. Miller FG. The randomized controlled trial as a demonstration project: an ethical perspective. *Am J Psychiatry.* 2009; 166(7):743–745. [PubMed: 19570933]
36. Millum J, Emanuel EJ. Ethics. The ethics of international research with abandoned children. *Science.* 2007; 318(5858):1874–1875. [PubMed: 18096792]
37. Zeanah CH, Koga SF, Simion B, et al. Response to commentary: Ethical dimensions of the BEIP. *Infant Mental Health Journal.* 2006; 27(6):581–583.
38. Kuczarski, RJ.; Ogden, CL.; Grummer-Strawn, LM., et al. Advance data from vital and health statistics. No. 314. Hyattsville, MD: National Center for Health Statistics; 2000. CDC growth charts: United States. DHHS publication no. (PHS) 2000-1250 2000-0431
39. Roche AF, Mukherjee D, Guo SM, Moore WM. Head circumference reference data: birth to 18 years. *Pediatrics.* 1987; 79(5):706–712. [PubMed: 3575026]
40. Bayley, N. Bayley scales of infant development. 2. New York: Psychological Corporation; 1993.
41. Wechsler Preschool and Primary Scale of Intelligence. San Antonio, TX: Harcourt Assessment; 2000.
42. NICHD Early Child Care Research Network. Characteristics of infant child care: Factors contributing to positive caregiving. *Early Child Res Q.* 1996; 11:269–306.

43. Fernandez ID, Himes JH, de Onis M. Prevalence of nutritional wasting in populations: building explanatory models using secondary data. *Bull World Health Organ.* 2002; 80(4):282–291. [PubMed: 12075364]
44. Cameron N, Preece MA, Cole TJ. Catch-up growth or regression to the mean? Recovery from stunting revisited. *Am J Hum Biol.* 2005; 17(4):412–417. [PubMed: 15981181]
45. Cody JD, Semrud-Clikeman M, Hardies LJ, et al. Growth hormone benefits children with 18q deletions. *Am J Med Genet A.* 2005; 137(1):9–15. [PubMed: 16007630]
46. Myers SE, Whitman BY, Carrel AL, Moerchen V, Bekx MT, Allen DB. Two years of growth hormone therapy in young children with Prader-Willi syndrome: physical and neurodevelopmental benefits. *Am J Med Genet A.* 2007; 143(5):443–448. [PubMed: 17103437]
47. van Pareren YK, Duivenvoorden HJ, Slijper FS, Koot HM, Hokken-Koelega AC. Intelligence and psychosocial functioning during long-term growth hormone therapy in children born small for gestational age. *J Clin Endocrinol Metab.* 2004; 89(11):5295–5302. [PubMed: 15531473]
48. Gohlke BC, Frazer FL, Stanhope R. Growth hormone secretion and long-term growth data in children with psychosocial short stature treated by different changes in environment. *J Pediatr Endocrinol Metab.* 2004; 17(4):637–643. [PubMed: 15198295]
49. King JM, Taitz LS. Catch up growth following abuse. *Arch Dis Child.* 1985; 60(12):1152–1154. [PubMed: 4091579]
50. Talbot NB, Sobel EH, Burk BS, Lindemann E, Kaufman SB. Dwarfism in healthy children: it's possible relation to emotional, nutritional and endocrine disturbances. *N Engl J Med.* 1947; 236:783–789. [PubMed: 20239242]
51. Landgren M, Andersson Gronlund M, Elfstrand PO, Simonsson JE, Svensson L, Stromland K. Health before and after adoption from Eastern Europe. *Acta Paediatr.* 2006; 95(6):720–725. [PubMed: 16754554]
52. Muhamedrahimov, RJ. New attitudes: Infant care facilities in St. Petersburg, Russia. In: Osofsky, JD.; Fitzgerald, HE., editors. *WAIMH handbook of infant mental health.* Vol. 1. New York, NY: Wiley; 1999. p. 245-294.
53. Whitten CF, Pettit MG, Fischhoff J. Evidence that growth failure from maternal deprivation is secondary to undernourishment. *JAMA.* 1969; 209(11):1675–1682. [PubMed: 5820163]
54. Hochberg Z, Albertsson-Wikland K. Evo-devo of infantile and childhood growth. *Pediatr Res.* 2008; 64(1):2–7. [PubMed: 18652011]
55. Rosenfeld RG. Insulin-like growth factors and the basis of growth. *N Engl J Med.* 2003; 349(23):2184–2186. [PubMed: 14657423]
56. Rodriguez S, Gaunt TR, Day IN. Molecular genetics of human growth hormone, insulin-like growth factors and their pathways in common disease. *Hum Genet.* 2007; 122(1):1–21. [PubMed: 17534663]
57. Scheepens A, Modersheim TA, Gluckman PD. The role of growth hormone in neural development. *Horm Res.* 2005; 64 (Suppl 3):66–72. [PubMed: 16439847]
58. Gunnell D, Miller LL, Rogers I, Holly JM. Association of insulin-like growth factor I and insulin-like growth factor-binding protein-3 with intelligence quotient among 8- to 9-year-old children in the Avon Longitudinal Study of Parents and Children. *Pediatrics.* 2005; 116(5):e681–686. [PubMed: 16263982]
59. Shevah O, Kornreich L, Galatzer A, Laron Z. The intellectual capacity of patients with Laron syndrome (LS) differs with various molecular defects of the growth hormone receptor gene. Correlation with CNS abnormalities. *Horm Metab Res.* 2005; 37(12):757–760. [PubMed: 16372230]
60. Elgen I, Johansson KA, Markestad T, Sommerfelt K. A non-handicapped cohort of low-birthweight children: growth and general health status at 11 years of age. *Acta Paediatr.* 2005; 94(9):1203–1207. [PubMed: 16278985]
61. Emond AM, Lira PI, Lima MC, Grantham-McGregor SM, Ashworth A. Development and behaviour of low-birthweight term infants at 8 years in northeast Brazil: a longitudinal study. *Acta Paediatr.* 2006; 95(10):1249–1257. [PubMed: 16982498]
62. Kelleher KJ, Casey PH, Bradley RH, et al. Risk factors and outcomes for failure to thrive in low birth weight preterm infants. *Pediatrics.* 1993; 91(5):941–948. [PubMed: 8474814]

63. Escalona SK. Babies at double hazard: early development of infants at biologic and social risk. *Pediatrics*. 1982; 70(5):670–676. [PubMed: 7133816]
64. Black MM, Walker SP, Wachs TD, et al. Policies to reduce undernutrition include child development. *Lancet*. 2008; 371(9611):454–455. [PubMed: 18262026]

Figure 1.

Group status at age 54 months for children living in Romanian institutions who were assigned to usual care or foster care.

Figure 2.

Growth in the foster care group (FCG) vs care as usual group (CAU) at baseline, 30 and 42 months of age.

a) Mean growth rates (s.e.) from random effects linear growth models for height (cm/mo), weight (kg/month) and OFC (cm/month) * $p < .001$. FCG 0.81 ± 0.02 cm.(s.e.), 0.26 ± 0.01 kg. per month, vs. CAU 0.71 ± 0.02 cm., $0.17 \pm .01$ kg.

b) Comparison of ν height and λ weight z-scores (s.e.) from baseline to 42 months of age. ANOVA FCG height [$F(1, 50) = 100.6$, $p < .001$, partial $\eta^2 = .67$] and weight z-scores [$F(1, 50) = 94.0$, $p < .001$, partial $\eta^2 = .65$]. CAU weight z-scores [$F(1, 50) = 10.3$, $p < .01$, partial $\eta^2 = .17$]

At 42 months, height-z in FCG vs. CAU $0.06 \pm .97$ (s.d.) vs -0.62 ± 0.99 , $t(1,108) = -3.65$, * $p < .001$ and weight-z -0.31 ± 1.05 vs -0.75 ± 1.17 , $t(1,108) = -1.98$, † $p = .05$

c) Comparison of ν weight-for-height σ and ofc z-scores (s.e.).

Figure 3.

Growth in the foster care group (FCG) vs care as usual group (CAU) at baseline, 6, 12 and 18 months post-randomization.

a) Comparison of ν height and λ weight z-scores (s.e.m.) in CAU and FCG from baseline ($n=51, 54$) 6 ($n=46, 57$), 12 (42, 51) and 18 (21, 50) months post-randomization. ANOVA FCG height [$F(1, 43) = 57.32, p < .001$, partial $\eta^2 = .57$] and weight z-scores [$F(1, 43) = 63.65, p < .001$, partial $\eta^2 = .60$].

* $p < .001$, † $p < 0.05$ FCG vs. CAU at 12 and 18 months.

b) Comparison of ν weight-for-height and σ ofc z-scores (s.e.m.) from baseline to 18 post-randomization.

Figure 4.

Full Scale IQ $\pm$ SE at 54 months vs. age of randomization and birthweight.

v 2.5 kg, λ < 2.5 kg, * $p < 0.001$ vs. children 2.5 kg randomized at < 24 months [66.6 ± 6.2 (s.e.), vs. 91.1 ± 3.9 ($t(21) = 3.84$)]

Table I

Demographic, growth, caregiving quality and cognitive scores ($\pm$ s.d.) for the institutionalized and community groups pre- and post-randomization.

Child Characteristics	Institutionalized (N=125)	Never Institutionalized (N = 72)
Age (months) (SD)	21.0 (7.4)	19.3 (7.1)
Ethnicity		
Romanian	55% *	91%
Roma (Gypsy) Other/Unknown	45%	9%
Female	50%	57%
Birthweight (grams)	2,834 (596) *	3,333 (459)
< 2500 grams	24% *	3%
Percent of life Institutionalized	62.9% (25.1) *	0
Baseline height z-score	-.84 (.86) ‡	.13 (.91)
% < -2	9% *	2%
Baseline weight z-score	-1.23 (1.08) *	-.05 (1.00)
% < -2	25% *	0%
Baseline head circumference z-score	-1.10 (.99) *	-.15 (.86)
% < -2	17% †	2%
Baseline weight-for-height z-score	-.67 (1.14) *	.16 (.96)
% < -2	16% †	2%
Post Randomization Group	CAU (62)	FCG (63)
Baseline Caretaking Quality Score	2.06 // (.62)	2.29 // (.57)
30 Month Caretaking Quality Score	2.46 \$, //, ¶ (.63)	2.75 \$ (.52)
42 Month Caretaking Quality Score	2.53 \$ (.58)	2.79 \$ (.57)
Mean 30/42 Month Caretaking Quality Score	2.49 \$, //, ¶ (.48)	2.76 \$ (.48)
Cognitive Measures		
Baseline DQ	72.5 // (13.2)	76.1 // (13.1)
DQ 42 months	77.1 \$, //, ¶ (13.3)	85.7 \$, // (14.2)
WPPSI Full Scale IQ -54 Months	73.3 // ¶ (13.1)	81.0 \$, // (18.5)

t- or χ^2 tests

* *p* < .001 vs. NIG

† *p* < .01 vs. NIG

‡ *p* < .05 vs NIG

\$ *p* < .05 vs baseline scores

One-way ANOVA post-hoc tests

// *p* < .05 vs. NIG

¶ *p* < .05 vs. FCG

Table II

a) Multiple regression of baseline measures on gender, ethnicity, birth weight, age and caregiving quality in the institutional group (IG) at baseline.

	Baseline Height z-score	Baseline Weight z-score	Baseline OFC z-score	Baseline Wt/Ht z-score
	β (SE β)	β (SE β)	β (SE β)	β (SE β)
Intercept	-1.53 (.46) *	-3.64 (.62) *	-2.17 (.57) *	-3.04 (.70) *
Gender (f = 0, m = 1)	-.17 (.15)	-.04 (.20)	.04 (.18)	.08 (.22)
Ethnicity (Romanian = 0, other = 1)	-.07 (.15)	-.15 (.20)	-.50 (.18) †	-.09 (.23)
Birth Weight (kg.)	.67 (.13) *	.79 (.17) *	.36 (.16) †	.47 (.20) †
Caregiving Quality Score	-.24 (.13)	-.09 (.17)	.05 (.15)	.15 (.19)
Age (months)	-.03 (.01) †	.02 (.01)	.01 (.01)	.03 (.02)
Adjusted R ²	.233 *	.189 *	.084 †	.083 †

* p .001,

† p .01,

‡ p < .05

Table IIIEffect of low birth weight (< 2.5 kg) on baseline growth in IG vs NIG ($\pm$ s.e.).

Measures	IG < 2.5 kg (N =27)	IG 2.5 kg (N =85)	NIG 2.5 kg (N =65)
Baseline Height z-score (SD)	-1.19 (.15) [‡] , *	-.70 (.10) *	.13 (.12)
Baseline Weight z-score	-1.80 (.20) [‡] , *	-1.04(.12) *	-.09 (.13)
Baseline OFC z-score	-1.35 (.17) *	-.97 (.11) *	-.15 (.11)
Baseline Wt-for-Ht z-score	-1.12 (.23) [‡] , *	-.56 (.13) *	.11 (.13)

[‡] p .05 vs. IG 2.5 kg,

* p < .001 vs NIG 2.5 kg

Equal variance was assumed unless Levine's test for equality of variance was significant (< .05).

Table IV

a) Multiple regression of z-scores on gender, ethnicity, birth weight, caregiving quality, age and baseline z-scores in FCG after randomization.

	Height z-score	Weight z-score	OFC z-score	Wt/Ht z-score
	β (SE β)	β (SE β)	β (SE β)	β (SE β)
Intercept	.04 (1.18)	.44 (1.39)	1.09 (1.12)	1.47 (1.70)
Gender (f = 0, m = 1)	-.01 (.20)	.39 (.23)	.24 (.18)	.55 (.28)
Ethnicity (Romanian = 0, other = 1)	-.32 (.20)	-.17 (.24)	-.15 (.19)	-.09 (.29)
Birth Weight (kg.)	.10 (.19)	.08 (.21)	.11 (.17)	-.20 (.24)
Post-Placement Caregiving (mean CQS at 30 & 42 months)	.62 (.19) [†]	.76 (.24) [†]	.05 (.18)	.56 (.30)
Duration of Intervention (age at 42 month testing – placement age)	-.01 (.02)	-.01 (.03)	-.02 (.02)	-.03 (.03)
Age (< 12 mo = 0, 12 mo = 1)	-1.13 (.49) [‡]	-1.79 (.57) [†]	-1.16 (.46) [*]	-2.29 (.71) [†]
Baseline z-score	-.36 (.14) [‡]	-.37 (.12) [†]	-.29 (.09) [†]	-.26 (.14)
Adjusted R ²	.271 [†]	.391 [*]	.359 [*]	.295 [†]

* p .001,

[†] p .01,

[‡] p < .05,

Table V

Pearson correlations between mean (30 and 42 mo) ORCE caregiver interaction scale ratings and z-scores post-randomization in FCG.

ORCE Qualitative Ratings of Caregiver Interactions ^I	z-scores Baseline to 42 Months (N = 53)			
	Ht-z	Wt-z	OFC	Wt/Ht
Detachment ² Caregiver is emotionally uninvolved, disengaged, and unaware of infant's needs.	-.410 [†]	-.149	-.016	-.009
Flat affect ² Caregiver expresses no emotion or animation.	-.124	-.188	.05	-.123
Positive regard for the child Caregiver expresses positive feelings in interactions with the child.	.453 [*]	.329 [‡]	.125	.208
Sensitivity Caregiver responds to the infant's social gestures and is attuned to the infant's needs and moods.	.412 [†]	.291 [‡]	.054	.163
Stimulation of cognitive development Caregiver engages in activities that can facilitate the infant's learning.	.201	.236	-.062	.175
Total Caregiving Quality Score CQS	.398 [†]	.289 [‡]	.016	.160

* p .001,

† p .01,

‡ p < .05

^I Scores range from 0 (not at all characteristic) to 4 (highly characteristic)

² Items that were reverse scored when calculating the total ORCE score

Table VI

Effect of low birth weight (<2.5 kg) and gender on catch-up growth and cognitive measures following randomization to FCG, mean z-scores ($\pm$ s.e.).

Measures	Male (N = 31)	Female (N = 32)	< 2.5 kg (N = 17)	2.5 kg (N = 40)
42 month Height z-score	-.10 (.16)	.22 (.20)	-.26 (.22)	.19 (.17)
42 Month Weight z-score	-.35 (.20)	-.28 (.24)	-.59 (.21)	-.25 (.22)
42 Month OFC z-score	-1.28 (.21)	-1.12 (.21)	-1.67 (.25)	-.93 (.17) *
42 Month Wt-for-Ht z-score	-.54 (.22)	-.63 (.29)	-.70 (.27)	-.61 (.26)
ht-z bl-42 mo	.92 (.16)	.94 (.13)	.87 (.18)	.99 (.14)
wt-z bl-42 mo	1.15 (.23)	1.04 (.15)	1.06 (.18)	1.10 (.19)
ofc-z bl-42 mo	.06 (.14)	-.13 (.15)	-.11 (.15)	.02 (.14)
w/ht-z bl-42 mo	.41 (.23)	.23 (.21)	.30 (.21)	.29 (.21)
Baseline ORCE	2.23 (.11)	2.35 (.10)	2.34 (.15)	2.23 (.10)
Mean ORCE at 30 and 42 mo.	2.70 (.07)	2.81 (.10)	2.82 (.12)	2.73 (.08)

*
p < .05

Equal variance was assumed unless Levine's test for equality of variance was significant (< .05).

Table VII

Multiple regression of cognitive variables on gender, ethnicity, birth weight (kg.), baseline developmental quotient (DQ), post-placement caregiving, age, and catch-up growth in institutionalized children randomized to foster care (FCG).

Variable	DQ-42 mo n = 47	-DQ BI-42 mo n = 47	Full Scale IQ-54 mo n = 45	-DQ/IQ BI-54 mo n = 45	Performance IQ-54 mo n = 45	Verbal IQ-54 mo n = 45
Intercept						
	β (SE β)	β (SE β)	β (SE β)	β (SE β)	β (SE β)	β (SE β)
Gender (f = 0, m = 1)	41.25 (17.31)	41.25 (17.31)	15.38 (27.18)	15.38 (27.18)	29.49 (25.67)	19.11 (27.00)
Ethnicity (Romanian = 0, other = 1)	-4.60 (3.24)	-4.60 (3.24)	-8.09 (5.09)	-8.09 (5.09)	-8.61 (4.81)	-6.06 (5.05)
Birth Weight (kg.)	-5.00 (3.26)	-5.00 (3.26)	-2.04 (5.07)	-2.04 (5.07)	-7.45 (4.79)	2.80 (5.04)
	-2.25 (2.70)	-2.25 (2.70)	9.22 [‡] (4.33)	9.22 [‡] (4.33)	9.49 [‡] (4.09)	7.04 (4.30)
Baseline DQ	.45 [†] (.13)	-.55 [*] (.13)	.46 [‡] (.20)	-.54 [*] (.20)	.38 [§] (.19)	.45 [‡] (.20)
Post-Placement Caregiving (mean ORCE at 30 & 42 months)	5.49 (3.47)	5.49 (3.47)	2.48 (5.49)	2.48 (5.49)	.28 (5.18)	4.47 (5.45)
Age < 24 mo. = 0, 24 mo. = 1	-3.85 (3.89)	-3.85 (3.89)	-2.73 (5.96)	-2.73 (5.96)	1.68 (5.64)	-5.14 (5.92)
ht-z bl-42 mo	8.14 [‡] (3.61)	8.14 [‡] (3.61)	9.28 [§] (4.71)	9.28 [§] (4.71)	3.31 (4.45)	12.36 [‡] (4.68)
wt-z bl-42 mo	-4.19 (2.44)	-4.19 (2.44)	-3.35 (3.83)	-3.35 (3.83)	1.78 (3.62)	-7.32 (3.80)
ofc-z bl-42 mo	-.78 (2.27)	-.78 (2.27)	-2.50 (3.40)	-2.50 (3.40)	-4.32 (3.21)	-1.61 (3.34)
Adjusted R ²	.545 [*]	.566 [*]	.404 [‡]	.418 [‡]	.379 [‡]	.403 [‡]

* P .001,

[†] P < .01,

[‡] P < .05,

[§] P < .06

Developmental quotient (DQ) at 42 months, DQ at 42 months of age [DQ at 42 months – baseline (BL) DQ], WPPSI full scale, performance and verbal IQ scores at 55 months and the DQ/IQ between baseline and 55 months of age. SE = standard error of estimate