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Growth failure associated with early neglect: pilot comparison of neglected US children and international adoptees

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Abstract

The long-lasting impact of different neglectful environments on growth in children is not well studied. Three groups of children, 3–10 years old, were recruited ($n = 60$): previously institutionalized international adoptees living in stable home environments for at least 2 years (IA; $n = 15$), children with a history of neglect born in the USA (USN; $n = 17$), and controls ($n = 28$). Children underwent physical examination, anthropometry, and collection of serum for growth parameters. Mean height standard deviation scores (SDS) were different ($p < 0.05$). Age-adjusted head circumference (HC) was significantly smaller ($p < 0.05$) in IAs. Insulin growth factor (IGF-1), a marker of growth hormone action, was higher in US neglected children. IGF-1 adjusted for age and weight SDS were different ($p < 0.05$) between control and US neglect groups. The degree of growth failure in height and HC in IAs was more severe than neglected US children. These findings may reflect differences between the impact of chronic and intermittent deprivation on the growth hormone system.

Keywords

child neglect; growth; international adoption; obesity

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Introduction

Inadequate nurturing during the early years of a child's life has been shown to lead to stunted growth. Multiple studies have reported a high prevalence of underweight, short stature, and reduced head circumference (HC) in children adopted from orphanages in Eastern Europe (1–3). The longer the period of institutionalization, the more profoundly the growth process appears to be affected, with children adopted from Eastern Europe and Asia having an estimated 1-month height delay for every 2.6–2.9 months of institutionalization (2, 4, 5).

The etiology of growth delay in institutionalized children is thought to be multifaceted. Children living in an institution often experience emotional and nutritional deprivation that precludes adequate environmental stimulation and nutrition for normal growth. Growth delay in the setting of emotional deprivation or abuse has been termed psychosocial dwarfism or psychosocial short stature and can occur even when adequate caloric intake is provided (6). Stress from psychological harassment has been shown to lead to abnormal circadian rhythms and suppression of growth hormone release (7).

Although growth failure from early neglect has been well researched in international adoptees, less is known about the impact of neglect on growth in US children at least partially due to the challenges of the chronicity and duration of this type of maltreatment. Comparing these two populations of neglected children may help identify crucial timing or environmental circumstances that influence the response to early adversity. Identification of similarities and differences between these populations could guide clinical screening for health issues related to early adversity.

In the current pilot study, we recruited children with a history of international adoption and children with a history of neglect or deprivation from their biologic parents to test the hypothesis that both groups would reveal effects on growth but that the growth characteristics of children who have experienced the more chronic early adversity due to living in an orphanage (international adoptees from Russia) will have a more severe impact on growth than those with a history of intermittent but significant neglect (US neglect). These groups were compared to a control group of US children without a history of abuse, neglect, or international adoption.

Methods

In this Institutional Review Board-approved study, three groups of children ages 3–10 years ($n = 60$) were actively recruited through flier advertisement, from primary care clinics, or by word of mouth as they were identified: [1] children adopted from Russia with a history of institutionalized care, who had lived in a stable home for at least 2 years (international adoptees, IA, $n = 15$); [2] children with a history of neglect, defined as having a history that met the threshold for a report to Child Protective Services but now in a stable home with non-offending parent or kinship guardian (US neglect, USN, $n = 17$). There was no child protection agency involvement as children were in a stable kinship guardian or a stable adult parent environment at the time of enrollment. A control group of children from two-parent

homes with no known history of abuse, neglect, or adoption were recruited from the general population (CTL, $n = 28$). After informed consent was obtained from adoptive parent (IA), parent/kinship guardian (USN), or biologic parent (CTL), the parent/guardian was interviewed in the home for home environment and history of neglect or abuse.

Children were seen in the Clinical and Translational Research Center at the Medical University of South Carolina. Physical examinations including vital signs, height, weight, HC, and standardized anthropometric measures using skin fold calipers were performed. In order to control for age, all standard deviation scores (SDS) (Z scores) for height, weight, weight for height, and body mass index (BMI) were calculated based upon Centers for Disease Control and Prevention normative growth data (8). Fat mass and percent fat were estimated using the Dezenberg equation that incorporates weight, triceps skinfold, gender, and ethnicity (9). Serum was collected for analysis of growth factors. Insulin growth factor (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) measurements were performed by standard chemiluminescent assay (Nichols Institute Diagnostics, CA, USA).

Statistical analysis

In order to determine statistical differences between groups, univariate analysis of variance was performed for each variable after controlling for age and sex with significance $p < 0.05$. In order to control for the impact of nutrition on the relationships between growth factors and auxology, the variable lean mass was created as the residual of the relationship between the sum of skin folds (fatness) and the weight for age Z score. SPSS (SPSS, Inc., Chicago IL, USA) was used for analysis.

Results

Of 76 children recruited to the study, 60 met criteria for enrollment, and parental consent was obtained from the adoptive parent, legal guardian, or biological parent. Physical and biologic measures of growth are outlined in Table 1. There were no significant differences between groups on race, age, or gender. However, USN had significantly lower median current income (\$30,000) than IA (\$100,000; $p = 0.000$) and CTL (\$75,000; $p = 0.007$). Prior to placement, the USN spent significantly more time in a neglectful environment (35.1 ± 3.8 months) than IA (20.7 ± 3.4 , $p = 0.008$) resulting in a larger proportion of lifetime spent in a neglectful environment for USN ($55.8\% \pm 6.0\%$) compared to IA ($30.8\% \pm 5.1\%$, $p = 0.004$). The institutional setting was felt to represent more severe social deprivation overall. Due to the important relationships of height and age with HC (10, 11), HC data were analyzed when controlling for these variables resulting in adjusted means for HC that were significantly different among groups (IA 50.1, USN 51.1, CTL 51.7; $p = 0.001$). Adoptive parents reported that the orphanages where the children were adopted were reported to have a poor adult-to-child ratio.

Height SDS showed significant differences between groups ($p < 0.05$). However, despite the use of Z scores to control for age (67.3 months), when the means for height SDS were further adjusted for age (IA -0.45 , USN $+0.00$, CTL $+0.29$), there was no longer any statistically significant difference ($p = 0.07$). There was almost statistical significance toward heavier weight SDS in USN ($+0.10$) than in IA (-0.59 , $p = 0.06$).

Mean IGF-1 and IGFBP-3 levels were highest in the USN group. However, the difference was only statistically significant for IGF-1. This was also true when IGF-1 (IA -0.10 , USN $+0.76$, CTL -0.01) and IGFBP-3 (IA $+0.56$, USN $+1.35$, CTL $+0.75$) were expressed as age-related standard deviation scores. When mean IGF-1 was adjusted for age and weight, there was a significant difference ($p = 0.019$) between CTL and neglected groups (IA 130.7 , USN 155.8 ng/dL, CTL 124.3).

Due to the known regulation of serum IGF-1 by nutrition (12), we explored the relationship of weight SDS and fatness with IGF-1 values. When controlling for the impact of fatness on IGF-1, all trends toward relationships were lost (adjusted IGF-1 means: IA 123.8 , USN 153.4 , CTL 127.5 ; $p > 0.1$). This suggests that the relationship of higher IGF-1 in USN than in adopted children was related to their difference in fatness. However, when controlling for the impact of weight SDS on IGF-1, we found a significant relationship (adjusted IGF-1 means: IA 129.4 , USN 157.8 , CTL 124.3 ; $p = 0.001$). The control and neglected groups were significantly different ($p = 0.029$), showing that weight SDS and IGF-1 were related but fatness and IGF-1 were not.

Discussion

In this study, we compared growth impairment in US children who experienced early neglect to international adoptees that spent the first months of their life in an orphanage and a control group of children with no history of abuse or neglect. By adoptive parents' report, all the institutions where the children were adopted were reported to have a poor adult-to-child ratio. The IA group had impairment of height and head size similar to that seen in previous studies (13, 14). Interestingly, we found that USN children did not demonstrate impairment of height or HC. This finding was unexpected as the amount of time spent in the neglectful environment was, on average, longer in USN than IA children. As the IA children are typically in institutionalized settings with sparse and varied caretakers, they are vulnerable to have difficulty with bonding and attachment, which can lead to relative growth hormone deficiency, poor linear growth, and poor head growth. This may be reflected in differences in growth factors between USN and IA children that persist after improvement of their circumstances. The relative impairment in height and HC in IA children could also suggest that IA children experience more severe postnatal neglect/deprivation, a prenatal insult, or a combination of prenatal and postnatal insults that impact growth. In contrast to the USN and IA subjects in our study, children with nutritional impairment alone would be expected to have low weight, low weight for height, low height, low growth factors, and relative sparing of the HC (15).

Of note, USN children had significantly higher weight and BMI than IA and CTL children. This is supported by a recent report of an increased risk of obesity in US adolescents following childhood neglect (16). In addition, USN children have higher levels of growth factors that may be related to increased weight in this group. We found this difference related to normalized weight but not fatness represented by a sum of skinfold measurements. This was surprising as IGF-1 is regulated by nutrition, though this relationship is most visible at extremes of nutrition (12). These differences in growth factor values between these

groups may reflect different mechanisms by which the interplay between nutrition and stress affects regulation of the growth hormone axis.

Stress-suppressed growth hormone release has been suggested to occur through the hypothalamic neuropeptide-Y-immunoreactive system (17). As neuropeptide Y is involved in the regulation of appetite, it is possible that the differences between growth and weight gain in USN and IA children reflect how these stressful environments differentially impact the hypothalamic stress response systems. It is also possible that the increased weight and BMI seen in the USN children compared to IAs is due to differences in the relative access to nutrition in USN compared to IA children that could result in excessive weight gain. Alternatively, the difference may be explained by the clinical finding of more common sensory issues in IA children that can lead to poor intake, picky eating, and poor weight gain (18). Finally, this may be a reflection of the general trend toward obesity in children in the USA that may be exacerbated by the economic differences among these populations (19).

Limitations

Our pilot study has a number of limitations including small sample size, potential bias related to study personnel recruiting subjects also responsible for determining if subjects qualified for the study, lack of ability to reliably determine prenatal exposures in our cohorts, and lack of ability to determine if degree and type of neglect was similar in both neglect environments. An additional limitation could be that we did not control for the amount of time the subject was in the stable environment. We are not certain of the exact time that the neglect started and ended for all the children in this study. In an ideal research setting, we would account for that in the results. However, since our neglected cohorts had been in stable environments for more than 2 years at the time of enrollment in our study and significant catch-up growth in height and weight would have been expected to occur within 6 months, this would reduce this likelihood (20). In general, the IA families had more financial resources. In comparison, the neglected children were in kinship relationships that had limited financial resources and still qualified for Medicaid.

In conclusion, our study has identified subtle differences in the growth of USN and IA children that may help elucidate the mechanisms through which early adversity impacts long-term health (growth, development, and obesity). Our clinical work has often revealed more significant short stature in youth adopted from institutional care than those from foster care settings. However, to our knowledge these observations have not been previously reported. The findings of this and other studies support close monitoring of growth and weight gain in children following early neglect (16). Further studies are necessary to better understand the relationship of the psychosocial environments related to early neglect in US children and how this may influence later growth problems and obesity. Studies that compare growth patterns in international adoptees in foster care versus institutionalized settings may provide additional evidence that poor caretaker-to-child ratio is the primary determinant of growth delay and especially short stature in this population.

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Table 1

Demographics and growth parameters.

Variable	IA (n = 15, 9 male)	US neglect (n = 17, 8 male)	Control (n = 28, 15 male)	Between groups ^a
Age, months	73 ± 3	64 ± 7	67 ± 4	
Height Z	-0.50 ± 0.21 ^b	0.03 ± 0.32	0.29 ± 0.23	p = 0.157
Weight Z	-0.59 ± 0.22	0.10 ± 0.28	0.01 ± 0.26	p = 0.275
Weight for height Z	-0.31 ± 0.28	0.19 ± 0.22	-0.24 ± 0.21	p = 0.267
BMI Z	-0.32 ± 0.23	0.21 ± 0.23	-0.11 ± 0.21	p = 0.341
HC, cm	50.1 ± 0.5 ^c	50.9 ± 0.4	51.9 ± 0.4 ^d	p = 0.002 [*]
IGF-1, ng/mL	124 ± 11 ^b	153 ± 11	126 ± 11 ^b	p = 0.085
IGFBP-3, µg/mL	3.25 ± 0.24	3.83 ± 0.23	3.28 ± 0.19	p = 0.154
Lean mass	16.9 ± 1.1	16.1 ± 0.6	17.4 ± 1.3	p = 0.302
Percent Fat	13.7 ± 0.9 ^a	17.1 ± 1.2 ^c	15.7 ± 0.8	p = 0.074

*
p < 0.05,

^a Univariate analysis of variance between the three categories.

^b Significant difference compared to USN in pairwise comparison, p < 0.05.

^c Significant difference compared to CTL in pairwise comparison, p < 0.05.

^d Significant difference compared to IA in pairwise comparison, p < 0.05.