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Incidence of specific absolute neurocognitive impairment in globally intact children with histories of early severe deprivation

Michael E. Behen^{1,2}, Emily Helder¹, Robert Rothermel¹, Katherine Solomon¹, and Harry T. Chugani^{1,2,3}

¹ Department of Pediatrics, Children's Hospital of Michigan, Wayne State University, Detroit, USA.

² Department of Neurology, Children's Hospital of Michigan, Wayne State University, Detroit, USA.

³ Department of Radiology, Children's Hospital of Michigan, Wayne State University, Detroit, USA.

Abstract

Postnatal deprivation is associated with neurocognitive delay/dysfunction. Although “catch up” in global cognition following adoption has been reported, this study examined the incidence of specific absolute impairment in adopted children with intact global cognitive functioning. Eighty-five children (38 males, mean age=112.8, SD=30.3 months; range 61–209 months) raised from birth in orphanages underwent comprehensive neuropsychological evaluation. Fifty-four were deemed globally intact (IQ>85). Of those deemed globally intact, 46 percent evidenced absolute impairment in at least one domain of functioning. Duration of stay in the orphanage was directly associated with incidence of impairment and number of domains affected. A substantial proportion of participants evidenced persistent, absolute impairment in one or more domains of neurocognitive function despite integrity of basic intellectual functions.

Introduction

Studies in both animals and humans have demonstrated that early severe deprivation is associated with impaired development and behavioral abnormalities (Rosenblum & Harlow, 1963; Rutter, Kreppner & O'Connor, 2001). Much of the recent empirical work on early severe deprivation in humans has examined development in post-institutionalized children, particularly children adopted into the UK, US, or Canada from Eastern European orphanages. With regard to neurocognitive status, a number of such studies have found that 70% to 90% of such children have impaired global cognition and/or multi-faceted developmental delays at the time of adoption (Judge, 2003; Rutter, 1998). Longitudinal studies of these children, however, have reported an impressive degree of “catch-up” in global cognitive functioning, as well as decreased number of functional and behavioral impairments (Judge, 2003; Rutter, et al. 2001), in a majority of children. For instance, in the Rutter et al., (2001) sample, only 14% of Romanian adoptees continued to evidence global cognitive impairment at assessment several years post adoption. A recent meta-analysis examining cognitive functioning in internationally adopted children similarly concluded that these children did not differ from non-adopted controls in IQ; however, problems in learning and language delays were more prevalent in the former group (Juffer & van IJzendoorn, 2005).

Few published studies, however, have comprehensively examined the complete neurocognitive status of children post-adoption. Therefore, it is unclear whether the catch-up observed in the

above studies extends beyond global cognition to functioning within normal limits in specific domains as well (e.g., language, memory, executive functioning). Recent studies in our laboratory examining the neurobiological correlates of early severe deprivation have included comprehensive assessments of neurocognitive functioning and found specific impairment in various domains including language, memory, executive, achievement, and motor functions, even in children with intact global cognitive functioning (Chugani et al., 2001; Eluvathingal et al., 2006). In these studies, while group means for most domains tended to be measured well within normal limits, absolute impairments in one or more domains were observed in a substantial percentage of participants. The aim of the present study was to determine the incidence of *specific* absolute impairment in a group of children who have experienced early severe postnatal deprivation but who are globally intact either by virtue of recovery/catch-up or resilience of basic intellectual functioning. Additionally it was hypothesized that presence of impairment would be associated with duration of orphanage experience.

Method

Participants

Eighty five children (mean age at testing=112.8, SD=30.3 months, range = 61 to 209 months; 38 males/47 females) raised from birth in Eastern Europe (including Romania, Poland, Armenia, Ukraine), Northern Asia (including Russia, Kazakhstan), or South Asia (including China, Vietnam), and later adopted in the US, underwent comprehensive neuropsychological evaluation as part of a research program evaluating structural and functional imaging correlates of early severe deprivation. All children were recruited through advertisement presented to local and national parent-support groups as well as newsletters for various international adoption groups. All of the children were separated from their biological mothers at birth, and were placed into orphanages immediately upon release from the hospital. Mean duration of time spent in the orphanage was 29.4, SD=19.9 months; mean duration of time spent in the adoptive home was 82.0 ± 36.4 months. Fifty-five percent ($n=47$; mean duration of time in the orphanage = 35 months) of the sample had been in Eastern European orphanages, 22% ($n=19$; mean duration of time in the orphanage = 26 months) in Northern Asian orphanages, and 22% ($n=19$; mean duration of time in the orphanage = 16 months) in orphanages in Eastern Asia. Mean t-score for head circumference was 33.5, SD=19.4 at the time of study (Farkas 1994), placing the group mean at approximately the fifth percentile compared to same age peers. Sixty three (74%) of the participants were right-hand dominant, with twenty-two participants left or mixed-handed. All of the children in the study were English-speaking and attended school regularly. Adopted mother's mean education was 16.4 years, SD=1.86; and adopted father's education was 16.4 years, SD=2.9.

In order to minimize the occurrence of major confounding factors with known neurobiological effects, children with current and/or historical indication of any of the following were excluded from the study: prematurity, pre- or peri-natal difficulties, current or historical medical problems, epilepsy, documented suspicion of or known prenatal exposure to alcohol and/or other substances, and/or focal findings on neurologic examination. Alcohol exposure was directly assessed by a neurologist as part of the neurological examination using the Miller et al. (2006) criteria. Children with a "high" phenotypic suggestion of alcohol exposure (greater than 12) were not included in the study. Given the limited historical (e.g., pre-, perinatal histories) information available on many of the participants, as well as very limited data on all of the participants' experiences in the orphanage, it was not possible to fully control for these variables.

Procedure

Participants were initially screened by telephone for inclusion/exclusion criteria. Those participants that were thought to be likely to meet all inclusion and exclusion criteria were then scheduled for neuropsychological evaluations and neurological examinations. Written informed consent was obtained from all participants prior to enrollment in the study. The study involved two components over two visits: 1) a neurologic screening and neuropsychological evaluation 2) functional and structural MRI studies. On the first visit, all the children enrolled in the study underwent a neuropsychological evaluation and neurologic exam to ensure that they met all the criteria for further participation in the study. This visit took 4–6 hours to complete. All 85 participants included in the current study met all inclusion and exclusion criteria for participation. Five additional potential participants were excluded from further participation following neurological examination; four due to scores in the high range for alcohol exposure, and one for the presence of medical diagnoses. Results of the MRI components of the study are discussed elsewhere (Eluvathingal et al., 2006).

Neuropsychological Evaluation

The neuropsychological evaluation consisted of evaluation of global, verbal comprehension, perceptual-organizational, freedom from distractibility, and processing speed indices of intellectual functioning; expressive and receptive language processing; verbal and visual memory; academic achievement; executive functions (attention, impulsivity); manual dexterity; and behavioral functioning. The battery included the following measures: Wechsler Intelligence Scales for Children - Third Edition (WISC-III); Token Test for Children, Comprehensive Evaluation of Language Functions-Third Edition (CELF-3), Wide Range Assessment of Learning and Memory (WRAML), Wide Range Achievement Test-Third Edition (WRAT-3), Gordon Diagnostic System (GDS), Grooved Pegboard. In addition, the Behavioral Assessment Scales for Children (BASC) was administered to evaluate internalizing and externalizing behavioral problems. The psychometric properties of the above measures have been well established and the above measures are widely used with both clinical and research populations (Sattler, 2001a; Sattler, 2001b). The evaluation also included a social-historical interview with the child's adoptive parent(s). Summary scores for the following measures were used to quantify functioning in eight domains: Receptive Language (Token Test, Total score), Expressive Language (CELF-3, composite of Producing Word Associations and Rapid Automatic Naming), Verbal Memory (WRAML, Verbal Memory Index), Visual Memory (WRAML, Visual Memory Index), Sustained Attention (GDS, Vigilance Hits), Impulsivity (GDS, Vigilance false alarms), Manual dexterity (Grooved Pegs, dominant and non-dominant hand), Achievement (WRAT-3, Reading, Spelling, Arithmetic). Global intellectual functioning was defined as WISC-III, Full scale intelligence quotient (FSIQ).

Determination of Absolute Impairment

Scores for all above measures were converted to standard scores, with a mean of 100, and SD of 15. Areas of absolute impairment were defined as any domain score measured 2 or more SD below the mean of the normative sample for that measure. The neurocognitive profiles of children with measured global intellectual functioning below 85 were considered "globally impaired" and were not examined for absolute impairments.

Results

Overall Sample Neuropsychological Profile

Table 1 presents the neuropsychological profile for the entire sample of 85 participants. Global intellectual functioning was measured within normal limits, in the average range (FSIQ=92.5, SD=17.01; range=50–132). Further, group means for all domains were measured within

normal limits (average to low average range), with borderline range scores for a behavioral control (impulsivity) task. Internalizing (T-score = 53.4, SD=12.4) and externalizing (60.4; SD=14.3) behavioral problems for the sample were also measured within normal limits.

Three percent (n=3) of the overall group had measured global intellectual functioning below 70; and 14% (n=12) below 78 (greater than 1.5 SDs below the normative mean). However, for the present study, globally intact was defined as IQ within one SD of the normative mean (FSIQ $\geq$ 85). Thirty-six percent (n=31) of the sample had measured global intellectual functioning below SS=85 and were excluded from further analysis of individual neurocognitive domains (see Figure 1). Means for the *remaining* globally intact group (n=54) are presented in Table 2. As can be seen, means for all domains fell in the low average or average ranges. Internalizing (T-score = 52.2, SD=11.9) and externalizing (54.7; SD=11.4) behavioral problems for the sample were also measured within normal limits.

Incidence of Absolute Impairment

Of the 54 children measured to be globally intact, 54% (n=29) evidenced no area of absolute impairment, while 46% (n=25) of the sample showed at least one area with absolute impairment. Of the 25 globally intact children with area(s) of absolute impairment, 15 children had impairment limited to one domain; 10 had impairment in two or more domains (5 impairment in two domains; 3 impairment in three domains; and 2 children impairment in four domains) (see Figure 1). The incidence of absolute impairments in each of the domains for the “globally intact” group is presented in Table 3.

With regard to type of impairment, 18% (n=10) of the globally intact children showed language impairment (30% expressive, 50% receptive, 20% mixed), 17% (n=9) memory impairment (66% verbal, 22% visual; 11% both verbal and visual), 24% (n=13) executive function impairment (30% inattention; 23% impulsivity; 46% both inattention and impulsivity); 5% (n=3) impairment in at least one area of achievement; and 11% (n=6) of the sample had measured deficits in manual dexterity (see Figure 2).

With regard to behavioral impairment, 26% (n=14) of the globally intact sample had either externalizing and/or internalizing behavior problems rated in the at-risk range ($\geq$ 85th percentile) by their parent(s).

In order to evaluate whether any of the following subject variables - age, duration of orphanage stay, duration of time in adoptive home, region of adoption, adoptive parental education level, gender, head circumference, handedness, and behavioral functioning (internalizing and externalizing behavioral problems) - were predictive of incidence of specific impairment and/or number of impairments, the sample was divided into the following groups: No impairment (NI, n=29); specific impairment in one domain (SI, n=15), impairments in multiple domains (n=10) and globally impaired (GI, n=31). Between-group differences were tested via one-way ANOVAs for continuous variables and with Chi-square (gender) and Kruskal-Wallis tests for analyses with categorical variables (region of adoption). In order to control for multiple comparisons, Bonferroni correction for multiple comparisons was applied. Since there were 10 total comparisons, the adjusted alpha level for between-group analyses was $p=0.005$. The only significant findings was for duration of stay in the orphanage, $F(2,82)=7.88$; $p=.0001$. Tukey's B post-hoc tests revealed that the NI group spent less time in the orphanage than both the MI and GI groups (see Figure 3). There was also a trend for the children from Southern Asia to be less likely to be measured in the impaired range than either the Eastern Europe or Northern Asia groups ($p=0.018$), and for the MI group to have increased internalizing behavioral difficulties as compared to the NI group ($p=0.02$). In order to further examine the incidence of impairment at varying periods of duration, duration of time in the orphanage was categorized as follows: $\leq$ 6 months, 6–12 months, 13–20 months, 21–36 months, and >36

months - see Figure 4. As can be seen in the Figure, the incidence of impairment increases with duration of stay in the orphanage. The Kruskal-Wallis test for group differences was significant ($\chi^2_3=18.8$; $p=0.001$). The association between incidence of impairment and category of duration of stay was also tested without the globally impaired children (Figure 5); the group difference was significant ($\chi^2_2=13.7$; $p=0.001$).

The groups did not differ with regard to age, duration of time in adoptive home, adoptive parental education level, gender, head circumference, handedness or externalizing behavioral problems.

Discussion

It is important to note that the participants in this study were recruited from the community (i.e., from meetings and/or in response to advertising) rather than randomly selected from the population of international adoptees therefore the findings reported here may not be generalizable to the population of institutionally adopted children. In order to examine whether the data were biased in the direction of increased neurocognitive problems or behavioral difficulties, based on the notion that parents participated in the study because they had noticed the presence of cognitive or behavioral difficulties, we compared our findings with those reported by others including those employing random samples. These comparisons reveal a number of similarities between the sample in the present study and those presented in the literature. First, with regard to overall global cognitive functioning, the sample in the present study appears to be generally consistent with those of samples presented in other studies of internationally adopted children (Beckett et al., 2006; Ames, 1997). In the Beckett et al., (2006) study, which investigated global cognitive outcomes in a random sample of children adopted from Romanian orphanages that are being followed as part of the English and Romanian Adoptees (ERA) study, the global cognitive scores for the 6–24 and >24 months age of adoption groups were measured in the borderline to low average ranges at assessments at age 6 and 11 years. Global cognition in the Ames (1997) report on 157 children adopted after 8 months (mean duration=17 months) was measured at 90. Global cognition in the present sample was measured in the average range for both the full sample (FSIQ=92) and the globally intact (FSIQ=101) samples. Additionally, the incidence of global cognitive impairment in Rutter, Kreppner & O'Connor (2001) large n, randomly selected, sample using a cutoff of two standard deviations below the mean, was 14%. Although we report an incidence of 36% below one standard deviation below the normative mean, with a two standard deviation cutoff, only 3% were globally cognitively impaired. Thus, at least with regard to global cognition, the sample in the present study does not appear to be biased in a more pathological direction. With regard to behavioral problems, Colvert et al., (2008) followed up the ERA random sample and reported that approximately 25% of the institutionally raised Romanian adoptees at the 11 year old assessment were reported to have “marked emotional problems” (above 85th percentile cutoff); approximately 20% were above the 85th percentile cutoff for marked conduct problems. For the six year old assessments, approximately 15% of the sample were reported to be above the 85th percentile for emotional and conduct problems, respectively. Ames (1997) reported that 36% of her sample, assessed at 3.6 years post adoption, were measured above the clinical cutoff (T-score $\geq$ 70) for total behavior problems on the Child Behavior Checklist (CBCL). Gunnar & van Dulmen (2007) studied over 899 internationally adopted children who had spent at least 75% of their lives in institutions prior to adoption and found that 9 (internalizing) and 11% (externalizing) of children adopted at 0–24 months, and 18 (internalizing) and 33% (externalizing) of children adopted at >24 months were measured in the At-risk range for behavioral problems on the CBCL. In the present sample of children raised from birth in orphanages, with a mean duration of orphanage experience of 29.4 months, 26% of the globally intact group and 35% of the full group were measured above the At-risk level (86th percentile) for externalizing and/or internalizing behaviors. Thus, the present sample,

particularly the globally intact group, does not appear to be biased in the direction of increased global cognitive impairment or behavioral problems. Important to note is that few studies have assessed functioning in specific neurocognitive domains in school-aged children with histories of early deprivation and therefore there is little data in the literature with which to make comparisons outside of global cognition and behavior problems. Future research aimed at replicating the findings presented in this report and evaluating the incidence of specific impairment in random samples of globally intact internationally adopted children is warranted.

The major finding in this study was that a substantial proportion (46 percent) of globally intact children who have experienced severe deprivation exhibit persistent functionally relevant impairments in one or more specific cognitive domains. The domains most often affected were executive functioning, language, and memory with 41% of the globally intact children evidencing problems in at least one of these domains. Increased incidence of problems in language and in executive behavior (e.g., inattentive/overactive behavioral difficulties) in children with histories of early deprivation has been reported by others (Stevens et al., 2008; Croft et al., 2007). This is the first report of impairment in performance on a measure of sustained attention in children with such histories. Impairments in language, memory and executive functioning are likely to have important consequences for adjustment to academic and social environments, and may underlie the increased incidence in problems in learning that were noted in the meta-analysis of Juffer & van IJzendoorn (2005). Although the incidence of learning problems in the group of children in this study with specific impairments appears low (5%), especially in light of language and attentional impairments both of which have high comorbidity with learning disorders, this is likely due to the conservative definition of learning disorders employed in this study. For instance, in this study learning disorders were defined as absolute impairment (as achievement scores $>2SDs$ below the mean of the normative group), rather than as relative impairments determined by the discrepancy formula applied by formal (DSM-IV-TR, 2000) and academic classification systems.

Given that performance was measured for eight domains, across 59 “globally intact” participants, there is the possibility that some of the significant findings reported were due to chance. In fact, given that there were 8 comparisons per individual (with a .025 level of significance - 2 SDs below the normative mean), with no direct control for multiple comparisons, 20% of the findings ($.025 \times 8$) could be attributable to Type I error rather than indicative of actual impairment. While we did not directly control for multiple comparisons, we did employ a conservative approach to the data by, 1) excluding children with global IQs less than 85 rather than 70 (the standard index for impaired functioning), and 2) using a 2 SD threshold for identification of specific impairment (rather than a discrepancy formula). Thus, there was some conceptual control aimed at reducing the likelihood of chance findings. Further, while the possibility of Type I error cannot be ruled out, the magnitude of the impairments was impressive (e.g., approximately 50% of findings within the language domain were greater than 2.5 SDs below the normal mean), in the context of an overall globally intact profile. Thus, a false positive result would be highly unlikely for at least a preponderance of the cases. Also, we found that over 46% of the globally intact group had at least one area of neurocognitive impairment, a level beyond the 20% chance expectations. Finally, from a conceptual standpoint, while it is important to recognize the possibility of false positive findings (Type I error), it was deemed more important to reduce the likelihood of false negatives (Type II error) and therefore to not apply a more stringent direct control for multiple comparisons (e.g., Bonferroni correction) when evaluating each child's performance across neurocognitive measures.

The dose-response effect that is reported here, which involves increased incidence of impairment as duration of time in the orphanage increases, has been reported by others. O'Connor et al., (2000) found a linear relationship between duration of orphanage experience

and global cognitive functioning in children adopted from 0–42 months from Romanian orphanages. Additionally, Rutter, Kreppner & O'Connor (2001) found that greater than 70% of children adopted after the age of 24 months evidenced at least one area of behavioral impairment as compared to 30% of children adopted before six months. In another study, O'Connor & Rutter (2000) found that children with orphanage stays extending beyond 20 months were much more likely to express severe attachment disturbance as compared to children adopted at less than six months. However, more recently Beckett et al., (2006) reported that although greater than six months duration of orphanage experience was associated with poorer outcome, when the lowest functioning (bottom 15%) children were removed from dose-response analyses the linear effect for cognitive functioning in children with durations between 6 to 42 months (O'Connor et al., 2000) was no longer present. Croft et al. (2007) reported a similar absence of dose-response relationship for language functioning in the same sample. These authors report that being in an orphanage for 6 months represents the limit of safe exposure after which impairment is significantly more likely, but additional orphanage experience does not further increase the likelihood of impairment (Beckett et al., 2006; Croft et al., 2007). In the present study, global impairment and impairment in specific multiple domains were associated with longer orphanage stays (see Figure 3). Further, the dose response relationship present in the full sample (see Figure 4) remained even after the globally impaired children were removed, although the association was no longer linear but appeared nonlinear (i.e., sigmoidal) reflecting low likelihood of impairment up to a cutoff point (20 months) after which a majority of children evidence impairments (see Figure 5). The specific form of relationship identified in both the ERA and present samples demonstrates nonlinear (i.e., threshold) relationship between exposure and impairment. The differences in absolute threshold between these groups are likely attributable to differences in the sensitivity of measurement (i.e., global versus specific) and/or to differences in sample characteristics discussed previously. With these differences in mind, cross-validation of the findings (thresholds) presented here for specific impairment would be essential before any firm conclusions can be drawn regarding safe exposure or sensitive periods.

In considering dose-response it is important to note that we cannot completely rule out that this finding is driven, at least in part, by a parental selection bias, or the notion that prospective parents noted impairments in certain children and so did not adopt them. In this case, children with impairments would have been more likely to be adopted later than those without impairments. However, there are a number of arguments against this explanation. The most obvious indications of problems (to be perceived by potential adoptive parents) would be neurological, developmental or behavioral. With regard to neurological impairment, children underwent neurological screening in the present study and were excluded where problems were identified; which would remove this potential source of error. Further, *all* of the children in the present study evidenced developmental delays and “institutional” behaviors (i.e., stereotyped behaviors) at adoption. Thus, although it is plausible that parents were able to distinguish degrees of delays and/or behavioral difficulties, and chose those children with the least observable impairment, attributing the dose response finding completely to parental selection bias seems unconvincing. More importantly, Ames (1997) has pointed out that parents do not usually have choice as to which child they ultimately adopt. Also arguing against this notion, Stevens et al., 2006 has pointed out that, if parents did have choice, opposing forces would be at work, with some parents choosing children who were the most normally developing and others choosing the most impaired children out of a sense of charity present in many international adoptions. Finally, given the high mortality rates in orphanages, it would likely be the more resilient children that survive to be adopted at later ages rather than the most vulnerable group (Stevens et al., 2006). Thus, the likelihood that a parental choice selection bias completely underlies the dose-response reported here seems implausible.

Proposed mechanisms for the existence of such persistent functional deficits include early biological vulnerability, including genetic and/or pre- or perinatal insult, postnatal exposure to factors that affect physical development (e.g., malnutrition, illness, toxic substances, e.g., lead), chronic dysregulation/stress associated with inadequate caregiving, and the absence of experience-expectant stimulation associated with the deprivation experience.

With regard to the influence of biologic vulnerability, it was impossible to definitively rule out the presence of pre- and perinatal factors as contributors to outcome, despite efforts made to exclude children based on these factors (e.g., low birthweight, knowledge of prematurity, and/or identified suspicion of alcohol exposure prenatally). However, as with most studies of institutionally adopted children historical records were poor and it is likely that we had not completely excluded these confounds from the sample. Thus, pre- and perinatal factors likely contributed to outcomes in this study. In addition to pre and perinatal factors, some degree of malnutrition is known to have occurred in a majority (if not all) of the participants as is evidenced by small physical stature and head circumference. While exposure to factors such as malnutrition and/or prenatal substances often produce global rather than specific effects (Cone-Wesson, 2005; Laslo-Baker et al., 2004; Lucas, 2005; Nelson, Lerner, Needlman, Salvator, & Singer, 2004), a number of studies have shown that exposure in lower doses can produce specific effects (e.g., Morgan, et al., 2001). Therefore, it is likely that the findings in the present study were due to a mixture of the above mentioned pre- and postnatal factors. The higher incidence of problems in participants with longer duration of exposure would be due to a greater “dose” of these multiple factors. Whether these factors completely account for outcome beyond non-biological exposure factors is an important question. Ames (1997) addressed this issue in part by comparing children adopted out of orphanages with children adopted internationally at birth directly from the hospital setting. In essence this latter early adopted group served as a control for prenatal factors as both late adopted and early adopted children were assumed to have similar prenatal experiences. Her results indicated that early adopted children closely resembled normal controls across most cognitive and behavioral measures suggesting that orphanage experience is more important to outcome than prenatal factors. Additionally, in their random sample, Beckett et al., (2006) showed that weight at adoption, an index of subnutrition, had no relationship to cognitive functioning at age 11. Thus there is some empirical support for a role of orphanage specific deprivation as associated with outcome over and above biological factors (e.g., pre-, perinatal, nutrition) factors.

Dysregulation of stress-response as a result of social deprivation has been demonstrated in post-institutionalized children (Gunnar, Morison, Chisholm, & Schuder, 2001; Carlson & Earls, 1997). Further, prolonged stress is known to have adverse (typically focal) consequences for the developing central nervous system (Bremner & Vermetten, 2004). In a sample of children raised from birth in Romanian orphanages Chugani et al. (2001) found hypometabolic medial temporal and orbitofrontal brain regions; and Eluvathingal et al. (2006) found reduced integrity of the uncinate fasciculus, a limbic pathway. The most common neurocognitive impairments in the present study were executive dysfunction, language and memory impairment. These functions are thought to be subserved, at least partially, by limbic and infralimbic cortices and pathways; those regions that may be particularly susceptible to the physiological effects of stress (Bremner, 2007). Thus, it is suspected that prolonged stress may alter central biological systems and thus may play an important role in producing some of the persistent deficits observed in the present study. Several studies have demonstrated adverse effects of stress on episodic and spatial memory in animals and humans (de Quervain, Roozendaal, & McGaugh, 1998; Lupien & McEwen, 1997), as well as prolonged stress on cognitive dysfunction (McEwen & Sapolsky, 1995).

Findings of the present study may also be related to the lack of exposure to adequate domain-specific and experience-expectant stimuli during sensitive period(s) of development

(Greenough, Black & Wallace, 1987). For instance, presumed reduced language stimulation in the orphanage, particularly during the months and years during which language stimulation is expected to occur, may alter the neural pathways/structures that subserve language functions, and which presumably underlie impaired language function. In the absence of sufficient stimulation (which guides pruning or organization of the CNS, see Nelson, 2002), abnormal structural and/or functional organization of such substrates occurs, which may underlie such specific functional impairments as found in the present study. Research has shown that deprivation of sensory, motor, and social stimulation has profound effects on both function and structure of the developing nervous system and in domain-specific systems (e.g., Jeong Lee et al., 2005; Nakadate, Imamura, & Watanabe, 2001; Sharma, Dormin, & Kral, 2005; Vandermeeren, Bastings, Good, Rouiller, & Olivier, 2003).

Given that specific orphanage setting was not included as a variable in the study, it is not possible to exclude that variation across orphanages contributed to outcome. Bolstering this possibility is the finding of a trend in the present study that region of orphanage was associated with outcome, with Southern Asian children less likely to have impairments than children from Eastern European or Northern Asia. Important to note, was that region and duration of orphanage stay were confounded in the present study, with children from Southern Asia adopted earlier on average (mean age at adoption = 16 months) than children from the other regions (mean age at adoption = 30.5 months) evaluated in the study. Future work that examines regional differences is clearly warranted. However, previous research examining the role of variation across orphanage settings have reported that the majority of children institutionally adopted into the US or Canada from Eastern European or Asian orphanages have experienced severe deprivation (Johnson, 2000; Miller et al., 2006). Croft et al. (2007) used retrospective parent ratings of orphanage setting and found that, although degree of individualized caregiving was associated with language outcomes, setting was not related to outcome. Johnson (2000) estimated that children lose 1 month of linear growth for every three months they spend in an orphanage irrespective of specific orphanage or country of orphanage. Additionally, most of the institutionally adopted orphan children studied to date have experienced lack of proper nutrition, substandard medical care and very little social stimulation (Miller et al., 2006). In our study, interviews with parents indicated that *all* children were delayed in terms of motor and language milestones at the time of adoption. Mean head circumference of the children in the present study was measured at the 5th percentile suggesting deprivation and malnutrition were present at a severe level in the children included in our study. Thus although we cannot rule out this potential confound as a contributor to outcomes in the present study, research to date has not supported heterogeneity of orphanage setting as contributing significant variance outcomes.

Thus, it is suspected that both biological and non-biological orphanage-specific conditions contribute to whether or not a child develops global and/or specific impairment. Dose of deprivation, as measured by duration of the depriving experience, to a large extent determines magnitude of adverse outcomes (whether or not persistent impairment exists). Explaining the heterogeneity of response is more difficult, however. In other words, why does one child develop language disturbance (and abnormal language pathway), another executive dysfunction (and prefrontal abnormality), and yet another memory impairment (and medial temporal dysfunction)? While it is tempting to relate such differences to individual differences in the experience during the stay in the orphanage, there are little data at this point to support this view. Also, given the magnitude of deprivation, it is doubtful (although certainly possible) that the experience was that distinctive between children even across orphanages (O'Connor et al., 2000). However, one possible explanation is found in the work of Hofer (1994). This body of work has shown in rat pups that experience deprivation of different aspects of the mother results in distinct sets of neurophysiological and behavioral outcomes. Thus, different aspects of the deprivation experience may produce different quality of responses and

underlying neurophysiological abnormality. Alternatively, a diathesis-stress model that postulates some sort of weak organ hypothesis may also be useful in explaining the heterogeneity of response (Bleuler, 1963). In other words, specific phenotype is the result of both early biological vulnerability, genetic or otherwise, combined with the adverse developmental experience of early severe deprivation. The quality of poor outcome, then, is determined by whichever organ system is vulnerable. Differing vulnerabilities therefore determine the individual differences in response to the early severe social deprivation.

In summary, despite substantial catch-up in global cognitive functioning in children exposed to early severe deprivation, a substantial proportion may experience enduring effects in specific domains of functioning, which may have important consequences for academic and socio-emotional adaptation. The mechanisms for these impairments may involve biological factors including genetic and/or pre- and/or postnatal insult, adverse consequences of prolonged stress, and lack of expected environmental experience. Future investigations will examine the extent to which specific impairments are associated with behavioral adjustment, as well as specific structural and/or functional neuropathology. The implications of these findings are that, even in globally intact children who have experienced early deprivation, comprehensive neuropsychological evaluations may be indicated in order to rule out the existence of persistent specific functional impairments.

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Figure 1. Incidence of global impairment in the full sample (a), and incidence of specific impairment in the globally intact group (b)

Figure 2.
Duration of time spent in orphanage by impairment group

Figure 3.

Percentage of full sample (N=85) with impairment by duration of time in orphanage

Figure 4. Percentage of *globally intact* (n=54) sample with impairment by duration of time in orphanage

Table 1
Group neurocognitive profile for the overall sample (N=85)

	Mean	Std. Deviation
Full scale IQ (FSIQ)	92.49	17.01
Verbal Comprehension Index (VCI)	93.40	17.34
Percept. Organizational Index (POI)	94.80	18.62
Freedom from Distractibility Index (FDI)	86.29	18.12
Processing Speed Index (PSI)	99.05	19.05
Verbal Memory Index	81.95	17.02
Visual Memory Index	94.19	17.62
Expressive Language Processing	87.34	20.40
Receptive Language Processing	84.01	23.37
Sustained Attention	83.11	35.26
<i>Impulsivity*</i>	78.46	36.00
Reading	91.89	19.23
Spelling	89.69	17.72
Arithmetic	87.84	19.04
Manual Dexterity - Dominant Hand	86.39	43.45
Manual Dexterity - Nondominant Hand*	83.76	38.05

* Item in italics represents a score in the borderline range of functioning

Table 2

Group neurocognitive profile for the globally intact sample (n=54)

	Mean	Std. Deviation
Full scale IQ	101.88	11.56
Verbal Comprehension Index (VCI)	101.98	13.69
Perceptual Organizational Index (PCI)	104.44	13.64
Freedom from Distractibility (FDI)	94.31	15.39
Processing Speed Index (PSI)	106.81	13.98
Verbal Memory Index	88.08	16.07
Visual Memory Index	99.97	15.87
Expressive Language Processing	94.64	19.79
Receptive Language Processing	92.15	20.67
Sustained Attention	85.50	31.23
Impulsivity	80.44	37.67
Reading	99.41	16.02
Spelling	96.00	14.74
Arithmetic	95.33	15.90
Manual Dexterity-Dominant Hand	101.48	18.53
Manual Dexterity-Nondominant Hand	97.66	24.56

Table 3

Incidence of absolute impairment in the globally intact group for each domain (N=54)

Domain	Language			Memory			Executive Functions			Learning	Motor
n %	10 18%			9 17%			13 24%			3 5%	6 11%
Subdomain											
n %	Receptive	Expressive	Mixed	Verbal	Visual	Both	Attention	Impulsivity	Both		
	6 30%	3 50%	2 20%	6 66%	2 22%	1 11%	4 30%	3 23%	6 46%		