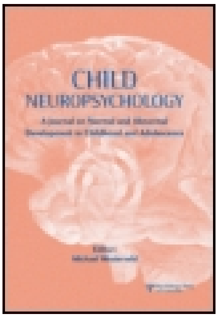

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Language difficulties in children adopted internationally: Neuropsychological and functional neural correlates

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Language difficulties in children adopted internationally: Neuropsychological and functional neural correlates

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Children who have experienced deprivation as a result of orphanage care during early development are at increased risk for a number of cognitive, emotional, and social difficulties (MacLean, 2003). This study examined the neuropsychological and behavioral profile of internationally adopted children with language difficulties, one of the most common cognitive challenges (Behen et al., 2008). In addition to neuropsychological testing, fMRI was utilized to examine activation patterns during expressive fluency and receptive language tasks. In comparison to internationally adopted children without language difficulties and nonadopted controls, participants with language difficulty had worse performance on tasks of verbal memory and reasoning, academic skills, and working memory. Behaviorally, all internationally adopted participants, regardless of language ability, had more parent-reported hyperactivity and impulsivity compared with controls. The fMRI tasks revealed reduced activation in traditional language areas in participants with language difficulty. The impact of early adverse experience on later development is discussed.

Keywords: International adoption; Early deprivation; Language, fMRI.

Language delays are commonly reported in studies examining children residing in orphanage settings. For example, Windsor, Glaze, and Koga (2007) compared 30-month-old children currently living in a Romanian orphanage with children in foster care and community children raised with their biological parents. Children currently residing in an orphanage setting were significantly delayed in their speech compared to both other groups. Some studies have also reported that these language difficulties can persist for a portion of children following adoption (i.e., Behen, 2008). Despite finding a great deal of variability in language performance, Scott, Roberts, and Glennen's (2011) meta-analysis of language outcomes reported an increased risk for language difficulties in international adoptees, though several moderators were important in predicting the type of difficulties and which children were most at risk.

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Factors Predicting Language Functioning in International Adoptees

A variety of factors have been investigated as possible predictors of language functioning following international adoption. One of the most consistently reported predictors is age at adoption. Croft et al. (2007) found that adoption after 6 months of age resulted in significantly worse language functioning compared to domestic adoptees and international adoptees adopted before 6 months of age. Additionally, a smaller percentage of children adopted after the age of 6 months experienced full language recovery after adoption, with only 56–76% of children having scores within one standard deviation of the mean across language tasks by school age. Although Croft et al. (2007) reported a lack of significant relationship between language outcomes and age at adoption beyond 6 months, other studies have reported a linear association between these variables with later ages of adoption. For example, Windsor et al. (2011) found a significant negative correlation between age of foster care placement and language performance in their study of Romanian children tested at 30 and 42 months in their birth language. However, they also reported significantly worse language outcomes in children placed in foster care after the age of 24 months, despite over a year of more normal language input. Their results revealed this later-placed group was often not significantly different from children who continued to be raised in institutional settings over the follow-up period. Loman, Wiik, Frenn, Pollak, and Gunnar (2009) also reported that receptive language functioning was negatively correlated with length of institutional care in their study of children adopted from a variety of countries. Summarizing results from multiple studies, Scott et al.'s (2011) meta-analysis found a slight trend for increasing difficulties with language as age at adoption increased beyond 12 months of age.

Recovery of normal language functioning following early deprivation has also been found to be associated with preverbal skills and birth language functioning at adoption. In a study of children adopted at 7.5–32 months of age, arrival preverbal skills such as initiating and responding joint attention predicted language performance 6 months later (Glatzhofer, 2010). Croft et al. (2007) also reported that children who had the ability to produce speech sounds in their native language at adoption (based on retrospective parent report) were found to have better language and higher IQ scores postadoption. It was suggested that having a few words at adoption reflected both a cognitive reserve present in those children as well as an indication that they were less severely affected by the orphanage experience.

Language functioning may also be related to the quality of the preadoption environment. For example, Windsor et al. (2007) found that children residing in orphanages who had a preferred caregiver had better language functioning compared with children in the same setting who did not have a favorite caregiver. Additionally, parent ratings of orphanage quality (level of individualized care, opportunity for motor development, and the psychological environment) have been found to be significant predictors of language outcomes at later ages (Croft et al., 2007).

Several study-specific factors have also been explored in relation to research on language outcomes in international adoptees. Scott et al. (2011) reported that age at the time of assessment, type of assessment tool utilized, and choice of comparison group were significant predictors of reported findings. Specifically, studies that assessed children at school age rather than during early childhood, those that utilized norm-referenced tests rather than survey instruments, and those that used a socioeconomically matched comparison group were more likely to find language difficulties in their samples of internationally adopted children. For example, Behen et al. (2008) reported that 18% of their sample of internationally adopted children with broadly average range IQs displayed impaired language performance on direct cognitive testing (>2 standard deviations below mean) when tested at a mean age of 9 years (with an average of 6 years postadoption).

In contrast, recovery of normal language functioning has been found to be unrelated to adoptive family characteristics such as parental education (Croft et al., 2007). Language functioning has also been found to be unrelated to the country of adoption, after controlling for length of time spent in the orphanage (Loman et al., 2009).

Neuroimaging Findings in International Adoptees

Imaging studies have been conducted with this population in order to examine neural correlates of orphanage experience. Several structural studies utilizing Magnetic Resonance Imaging (MRI) have reported significantly less grey and white matter in children who have been raised in orphanages in comparison to noninstitutionalized and foster care control groups (Mehta et al., 2009; Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012). Additionally, MRI studies with this population have also revealed an enlarged amygdala, especially on the right, with larger volumes associated with longer time in orphanage care (Mehta et al., 2009; Tottenham et al., 2010). Structural studies utilizing Diffusion Tensor Imaging (DTI) in internationally adopted children have revealed abnormalities in the organization of several white matter pathways, including the uncinate fasciculus (Eluvathingal et al., 2006; Govindan, Behen, Helder, Makki, & Chugani, 2010) and superior longitudinal fasiculus (Govindan et al., 2010). Recent studies have also connected white matter integrity in prefrontal and fronto-striatal areas with executive functioning test performance and parent-rated hyperactivity among international adoptees with orphanage experience (Behen et al., 2009; Hanson et al., 2013), suggesting that a more diffuse organization of these white matter pathways underlies frequently observed clinical difficulties in the domains of attention and executive functioning.

Functional neuroimaging studies utilizing Electroencephalography (EEG) and Event-Related Potentials (ERP) have found decreased high-frequency power at rest (Almas et al., 2012; Marshall & Fox, 2004) that moderates the relationship between attachment security and social skills. Additionally studies examining ERP response to faces (Slopen, McLaughlin, Fox, Zeanah, & Nelson, 2012), go/no-go tasks (McDermott, Westerlund, Zeanah, Nelson, & Fox, 2012), and memory tasks (Guler et al., 2012) have found abnormalities for several wave forms in children experiencing orphanage care, as compared with foster care and never institutionalized control groups. Functional MRI (fMRI) studies in this population have revealed hypoactivation of the nucleus accumbens (Goff et al., 2012) and ventral striatum (Mehta et al., 2010).

To summarize, both structural and functioning imaging studies often find abnormalities in the frontal lobes, limbic system, and basal ganglia in children who have spent time in orphanages. The abnormalities have been linked to many of the most commonly occurring clinical difficulties in this population, including attention, behavioral regulation, and social-emotional adjustment.

Largely missing from this literature is the examination of neuroimaging correlates of language difficulties in children who have been internationally adopted. Two structural imaging studies exist that examine the integrity of white matter tracts involved in language. Govindan et al. (2010) utilized diffusion tensor imaging (DTI) and tract-based spatial statistics to examine white matter integrity in a sample of internationally adopted children compared to a group of never-institutionalized, typically developing controls. The results revealed reduced integrity/strength (fractional anisotropy) of several components of the left superior longitudinal fasciculus in the children who had been internationally adopted.

Importantly, fractional anisotropy for the left superior longitudinal fasciculus was directly correlated with language functions measured through neuropsychological testing in the internationally adopted group. The authors suspected the arcuate fasciculus, a pathway known to be involved in language functions, may also have been affected, though the specific analysis method chosen for the study (tract-based spatial statistics) precluded firm conclusions about specific tracts. A more recent study utilizing deterministic tracking examined the integrity of the arcuate fasciculus specifically (Kumar et al., 2013). This study reported reduced fractional anisotropy and increased mean diffusivity in the arcuate fasciculus of internationally adopted children with orphanage experience as compared to nonadopted controls. Performance on language testing was positively related to fractional anisotropy of the left arcuate fasciculus. These studies provide evidence that orphanage experience is associated with structural abnormality of the arcuate fasciculus pathway, which underlies the language difficulties commonly observed in this population. Given these structural imaging studies finding evidence of abnormalities in language regions in internationally adopted children, functioning imaging studies examining these regions are needed.

Current Study

Although language difficulties have been commonly described in children adopted from orphanage settings, the overall neurocognitive profile and behavioral adjustment of children with language difficulties and orphanage experience have not been adequately described. Additionally, the functional neural correlates of language difficulties in this population have yet to be fully elucidated. This is especially the case with regard to in vivo functioning of traditional language regions during completion of language-based tasks.

The current study examined language functioning and fMRI activation in children who were adopted from orphanage settings. Within the internationally adopted group, participants with language difficulties were compared to participants without language difficulties and also to a normal control group with regard to neuropsychological and behavioral functioning and functional activation on language fMRI tasks.

With respect to the neuropsychological testing, it was hypothesized that internationally adopted children without language difficulties would closely resemble the normal control group while internationally adopted children with language difficulties would show worse performance, especially on verbally mediated tasks.

Additionally, it was hypothesized that the groups would significantly differ on fMRI activation patterns across both expressive fluency and receptive language tasks. It was hypothesized that those with language difficulties in the internationally adopted group would show decreased activation levels in classical language areas during the tasks as compared to internationally adopted participants without language difficulties and the normal control group. Also, it was hypothesized that the internationally adopted children with language difficulties would show more bilateral, diffuse activation on fMRI compared to both groups.

METHOD

Participants

Following approval from the Human Subjects Review Board, participants were recruited through community contacts previously established by several members of the

Children's Hospital of Michigan Positron Emission Tomography Center. These contacts included postadoptive service agencies serving families of children adopted internationally and newsletters for parents of internationally adopted children.

Inclusion criteria for the internationally adopted group were the following: aged 6–18 years and a history of being separated from biological mother at birth and placed into orphanage immediately upon release from the hospital. Additionally, only children who had been in their adoptive home for greater than 3 years were included in order to ensure that English-language cognitive testing could be reliably conducted (Glennen, 2009; Roberts & Scott, 2009). In order to minimize the occurrence of major confounding factors with known neurobiological effects, families expressing interest in participating underwent phone screening and were not included in the study if either of the following were present: (a) prematurity (<37 weeks), low birth weight (<2500 grams), or pre- or perinatal difficulties as indicated on medical records from the orphanage and/or adoptive parent report (Wolke & Meyer, 1999); (b) current or historical major medical problems (i.e., head injury, stroke, hearing loss, epilepsy) as indicated by parent report. It is important to note that many parents and adoption agencies did not have medical records providing information about their child's birth and perinatal history, thus it is possible that some children were included in the study who did not meet these exclusion criteria, due to limited records and reporting of these factors. Phone screening was also used to exclude potential participants with electronically, magnetically, or mechanically activated implants, pacemakers, tattoos, or braces due to normal MRI contraindications.

Forty-five children that satisfied the above criteria were evaluated for additional exclusionary criteria. A neurological exam was used to exclude participants who had evidence of focal neurological impairment on neurologic examination and/or evidence of exposure to alcohol and/or other substances during pregnancy. Evidence of alcohol exposure was assessed by a neurologist using the criteria outlined by Miller et al. (2006) with scores above 12 considered as high phenotypic suggestion of fetal alcohol syndrome. Neuropsychological testing was used to identify and exclude children with a full-scale IQ of more than two standard deviations below the normal mean (<70) on the Wechsler Intelligence Scale for Children-III (WISC-III; Wechsler, 1991). Nine children were excluded from further analysis on the basis of either the neurological exam ($n = 2$) or their performance on measures of intelligence ($n = 7$). Participants who were excluded at this point in the study did not differ from included participants with regard to age at testing, time in adoptive home, parental education, or gender. They were, however, more likely to be adopted from Northern Asian countries, $\chi^2 = 6.681$, $p = .035$, and had been older at the time of adoption, $t(45) = -2.121$, $p = .039$.

Internationally Adopted Group. The 38 remaining participants were included in the internationally adopted group. The mean age of this overall group at the time of testing was 120 ± 32 months, with an average length of stay in the orphanage of 23 ± 15 months. Participants had resided in their adoptive home for an average of 96 ± 34 months. There were 14 males/24 females and 28 right-handers/10 left-handers. Fourteen of the children had been adopted from South East Asia (China, Vietnam), 11 from Eastern Europe (Romania, Poland, Ukraine), and 13 from Northern Asia (Russia).

Eighteen of the internationally adopted participants scored more than 1.5 standard deviations below the normative mean on the Clinical Evaluation of Language Fundamentals – III Receptive and/or Expressive Language Indices (CELF-III; Semel, Wiig, & Secord, 1995) and were classified as having language difficulties for the purposes of the current study. Participants in this group had a mean age at testing of 129 ± 35 months. Their mean age at time of adoption was 27 ± 17 months and they had been residing in their adoptive home for an average 104 ± 39 months. They had been adopted from a variety of regions, including South East Asia ($n = 7$), Eastern Europe ($n = 8$), and Northern Asia ($n = 3$). This group included 6 males and 12 females as well as 15 right-handers and 3 left-handers.

The 20 participants without language difficulties (scoring within 1.5 standard deviations of the mean in the CELF-III) had an average age of 111 ± 28 months at time of testing. Their mean age at adoption was 21 ± 14 months and mean time in adoptive home was 90 ± 29 months. The regions of adoption included South East Asia ($n = 7$), Eastern Europe ($n = 3$), and Northern Asia ($n = 10$). This group included 8 males and 12 females and 13 right-handers and 7 left-handers.

Internationally adopted participants with language difficulties were significantly more likely to be adopted from Eastern Europe, $\chi^2 = 5.95$, $p = .05$, and were more likely to have an insecure attachment to their primary caregiver (based on semi-structured interview), $\chi^2 = 7.56$, $p = .006$, as compared with internationally adopted participants without language difficulties. The two groups did not significantly differ on age at testing, age at adoption, time in adoptive home, gender, handedness, maternal education (language difficulties: $M = 17 \pm 2$ years; no language difficulties: $M = 16 \pm 2$ years), body mass index (language difficulties: $M = 17 \pm 3$; no language difficulties: $M = 16 \pm 3$), or head circumference (language difficulties: $M = 39 \pm 20$ T-score; no language difficulties: $M = 37 \pm 20$ T-score).

Control Group. In order to provide a nonadopted comparison group that would aid in controlling for factors such as gender and socioeconomic status on the neuropsychological testing and fMRI results, a control group was recruited utilizing e-mail announcements within the Children's Hospital of Michigan and Wayne State University. Interested participants were screened to ensure that they were between the ages of 6–18 years, had been raised with their biological parents and had no current and/or historical neuropsychiatric diagnoses, medical conditions (including prematurity, low birth weight, pre-/perinatal difficulties, epilepsy, head injury, etc.), current prescriptions for any centrally activating medications, and MRI contraindications. Seventeen normal control participants were identified and received neuropsychological testing to ensure that intelligence and language scores were within normal limits (IQ and CELF-III > 85). Normal control participants had a mean age of 151 ± 31 months, included 12 males/5 females and included 16 right-handers/1 left-hander. Their maternal education ($M = 17 \pm 2$ years) did not differ significantly from either of the internationally adopted groups.

Normal control participants were significantly older than the internationally adopted children without language difficulties ($F(2, 52) = 7.73$, $p = .001$) and had a larger body mass index (control BMI: $M = 21 \pm 4$) than both internationally adopted groups, $F(2, 52) = 9.164$, $p < .001$.

Procedures

Neurologic Examination. All internationally adopted participants received a standard neurological examination to assess for exclusionary criteria such as phenotypic evidence of alcohol exposure (see specific cutoffs above) and focal neurologic impairment, as well as to ascertain head circumference measurements.

Neuropsychological Evaluation. All participants received a complete neuropsychological evaluation in English. Intelligence was assessed using the Wechsler Intelligence Scale for Children-III (WISC-III; Wechsler, 1991). The Verbal Comprehension Index, Perceptual Organizational Index, Freedom from Distractibility Index, and Processing Speed Index were used in the current study to assess verbal reasoning, visual reasoning, working memory, and processing speed, respectively. Language functioning was assessed using the Clinical Evaluation of Language Fundamentals – III (CELF-III; Semel, Wiig, & Secord, 1995). The Receptive Language Index, comprised of several subtests that require participants to complete tasks such as following verbal commands by pointing and categorizing words that are presented verbally, was used to assess receptive language. The Expressive Language Index, in which participants complete tasks such as generating sentences about pictures using a stimulus word or expressive fluency tasks, was used to assess expressive language. Memory was assessed utilizing the Wide Range Assessment of Memory and Learning (WRAML; Sheslow & Adams, 1990). The Verbal Memory Index (including list learning, story learning, and repetition of number and letter strings) was used to assess verbal memory. The Visual Memory Index (including memory for designs, pictures, and visual motor patterns) was used to assess visual memory. Sustained attention and impulsivity were assessed using the Gordon Diagnostic System (GDS; Gordon, 1983). This roughly 9-minute task requires participants to respond with a button press to target stimuli while withholding a response to nontarget stimuli. The participant's ability to correctly respond to target stimuli was used as a measure of sustained attention (Vigilance Hit Score) and their responses to nontarget stimuli was used as a measure of impulsivity (Vigilance False Alarms Score). Academic achievement domains (reading, spelling, and math) were measured using the Wide Range Achievement Test – 3 (WRAT-3; Wilkinson, 1983). Dominant and nondominant hand fine motor dexterity were assessed using the Grooved Pegboard (Matthews & Klove, 1964), a speeded task that requires participants to place key-shaped pegs into a pegboard with randomly positioned slots. Behavioral functioning was assessed by parent report, utilizing the Behavioral Assessment Scales for Children, parent report form (BASC; Reynolds & Kamphaus, 1992) and the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 1996). The Attachment Questionnaire for Children (AQC; Muris & Maas, 2004) was used to categorize internationally adopted participant's attachment.

Parent Interview. The evaluation for the internationally adopted group also included a social-historical interview with the child's adoptive parent(s) to gain information that they might have about the child's birth status and preadoption medical history. Additional information about behavioral and cognitive status since adoption was also collected.

fMRI. Functional MRI was performed on a Siemens 1.5 Tesla Sonata MR scanner (Erlangen, Germany) located in the Harper Hospital MRI facility. Along with a high-resolution T1-weighted MR scan for precise anatomical localization, functional data were acquired covering the whole brain across twenty-seven 5 mm thick slices using a single-shot spin echo-planar imaging pulse sequence: recovery time (TR) = 2.0 sec; echo time (TE) = 50; delay in TR = 0; 64 x 64 matrix (pixel size: 3.12 x 3.12mm^2); field of view (FOV) = 240 mm. The expressive fluency task was performed using 4-second frames whereas the Receptive language task was performed using 3-second frames. Parameters of acquisition optimized blood oxygen level-dependent (BOLD) signal contrast and minimized susceptibility artifacts at the pituitary area.

While in the MRI scanner, participants were required to complete several tasks designed to assess expressive fluency and receptive language functioning. The total time that children were required to be in the scanner was roughly 45 minutes.

fMRI Expressive Fluency Task. In order to assess expressive fluency, participants were asked to complete a verbal fluency task in which they generated words that fit into categories (animals, first names, foods, clothing, jobs/occupations). There were five activation blocks of 20 seconds each. Participants were asked to generate words covertly (silently) for each category and were shown a picture of a green traffic light during this time. Activation blocks were separated by five blocks of 28-second rest periods that consisted of a neutral task in which children are asked to stop thinking about words and to listen to white noise (Hertz-Pannier et al., 1997, 2002). Children were shown a red traffic light picture during the rest condition. Following the task, while still in the scanner, participants were asked to generate words overtly (out loud) for the same semantic categories. Overt-word-generation blocks were not used to assess activation patterns but were instead used to assess participation in the task. The control group was able to generate significantly more words during the overt trials than the internationally adopted (IA) participants with language difficulties (Normal control: $M = 43.4 \pm 7.90$; IA no language difficulties, $M = 33.6 \pm 10.73$; IA with language difficulties: $M = 31.60 \pm 12.04$), $F(2, 39) = 4.91$, $p = .013$.

fMRI Receptive Language Task. In order to assess receptive language, participants listened to five simple stories, recorded in a female voice, from the CELF-III "Listening to Paragraphs" subtest that varied with regard to length (Story 1: 27 seconds, Story 2: 39 seconds, Story 3: 39 seconds, Story 4: 39 seconds, Story 5: 48 seconds). None of the participants had completed this subtest of the CELF-III during their neuropsychological testing as it is a supplemental subtest. While stories were being played a headphone picture was shown to participants. Again, stories were interspersed with periods of rest. While resting, participants were shown a picture of headphones with a red "x" over top. The length of the rest periods varied with the length of the stories so that each story-plus-rest combination was 60 seconds (Rest 1: 33 seconds, Rest 2: 21 seconds, Rest 3: 21 seconds, Rest 4: 21 seconds, Rest 5: 12 seconds). Following the end of the fMRI scan, participants were asked a set of five questions about the stories in order to assess participation. There was no significant difference among the three groups with regard to number of questions answered correctly (Normal control: $M = 4.69 + .63$; IA no language difficulties: $M = 4.07 + 1.44$; IA with language difficulties: $M = 4.29 + .99$), $F(2, 39) = 1.109$, $p = .341$.

The above tasks have been used extensively in both adults and children and have been shown to activate classical language areas consistently (Hertz-Pannier et al., 1997). The decision was made to include visual stimuli to indicate beginning and stopping points in order to facilitate understanding in children with language difficulties who may have difficulty with reading.

Data Analysis

Demographic Factors and Neuropsychological and Behavioral Variables. All neuropsychological and behavioral tests from the battery were scored based on age-adjusted norms for performance. A one-way analysis of variance (ANOVA) was used to compare the groups on their age, body mass index, and parental education. The internationally adopted groups were compared using a *t*-test to examine differences for head circumference and lengths of time in orphanage and adoptive home. Chi-square tests were used to assess differences among groups for handedness, gender, and, for the internationally adopted groups, country of adoption and attachment category.

A multivariate analysis of variance (MANOVA) was used to compare the normal control and internationally adopted groups on neuropsychological variables. A second MANOVA was used to compare the groups on behavior ratings. Follow-up univariate ANOVAs were used to determine the nature of significant findings utilizing a Bonferroni adjustment for multiple comparisons.

fMRI Data Analysis. All images were processed and analyzed using the SPM2 software (Wellcome Institute of Cognitive Neurology, London, UK). For each subject, after discarding the first three images to account for T1 equilibration effects, the remaining images were realigned to correct for head movements, corrected for slice-timing, and spatially normalized to the Montreal Neurological Institute (MNI) template brain. Previous work by Muzik, Chugani, Juhasz, Shen, and Chugani (2000) examined the effects of normalizing to the adult MNI template in pediatric samples. Their findings indicated that in children above the age of 6 years, normalization to the adult template does not result in artifacts in statistical parametric mapping (SPM) analyses. The images were then smoothed spatially with a three-dimensional Gaussian kernel of 8 mm full-width at half-maximum and resampled, resulting in 2 x 2 x 2 mm voxels. Subsequently, the data were modeled voxelwise, applying a general linear model (GLM) that compared each condition of the language tasks against the respective neutral rest conditions across all presentations as well as between presentations. Moreover, the data were high-pass filtered (cutoff, 1/128 s) in order to remove low-frequency signal drifts. To assess regionally specific effects within each subject, T-statistics were calculated in multiple voxels across the whole brain (spmT). To correct for the number of false positives, the statistical threshold was set to $p < .05$ at the cluster level (with a standard voxel level cutoff of $p < .001$) and the whole brain was corrected for family-wise errors using Gaussian random field theory (Poline, Worsley, Evans, & Friston, 1997). While this is a somewhat liberal approach to correcting for multiple comparisons, it was used in order to balance the risk of Type I and II errors.

For an individual subject, the inference regarding the significance of an effect is based on the error variance within the same subject (within-subject variance). The first-level analysis in a single subject therefore involves a fixed-effect analysis because the subject effect is treated as fixed. However, to infer abnormal regional brain responses, the patient's activation has to be compared to a control group. This is a random effects analysis because subjects are assumed to be drawn randomly from a large population. The between-subjects variance is then assumed to correspond to the variance of the general population. Two-sample *t*-tests within SPM2 were conducted comparing each group's activation patterns for each separate task. Results were corrected for multiple comparisons ($p < .001$).

RESULTS

Group Differences on Neuropsychological Variables

An overall MANOVA comparing the normal control group and the two internationally adopted groups on the domains assessed with the neuropsychological assessment was significant, $F(2, 54) = 1.908$, $p = .018$. Follow-up ANOVAs were conducted, utilizing an adjusted significant p-value of less than .003 due to multiple comparisons (.05/15 tests, see Table 1).

In addition to the CELF-III tasks, which were used to classify participants with language difficulties, several other language-mediated tasks separated the internationally adopted participants with language difficulties from those without language difficulties and the normal control group. For example, the participants with language difficulties scored significantly lower on the verbal comprehension index from the WISC-III compared to both groups, $F(2, 54) = 8.6$, $p < .001$. However, they did not score significantly different from those groups on the perceptual organizational (nonverbal reasoning) index, $F(2, 54) = 1.8$, $p = .18$. Additionally, the internationally adopted participants with language difficulties also scored significantly lower than the participants without language difficulty and the normal control group on verbal memory, $F(2, 54)$, $p < .001$, the Freedom from Distractibility Index (WISC-III), $F(2, 54) = 10.2$, $p < .001$, and academic achievement in reading, $F(2, 54) = 9.3$, $p < .001$, in spelling, $F(2, 54) = 13.4$, $p < .001$, and in mathematics $F(2, 54) = 17.1$, $p < .001$, but did not differ on measures of fine motor dexterity dominant hand, $F(2, 54) = 1.8$, $p = .18$, nondominant hand, $F(2, 54) = 0.2$, $p = .83$, attention, $F(2, 54) = 2.1$, $p = .14$, or impulsivity, $F(2, 54) = 4.4$, $p = .02$.

Group Differences on Behavioral Ratings

An overall MANOVA compared normal controls and the internationally adopted groups on parent ratings of behavior and executive functioning. The overall MANOVA

Table 1 Neuropsychological Battery Results by Group (Standard Scores, $M = 100$, $SD = 15$).

	Normal control ($n = 17$)	IA no language difficulties ($n = 20$)	IA language difficulties ($n = 18$)	F (2, 54)	p[†]
WISC-III VCI	111 (15)$_a$	108 (14)$_a$	94 (12)$_b$	8.6	.001*
WISC-III POI	105 (16)	104 (13)	97 (14)	1.8	.18
CELF-III Expressive	111 (12)$_a$	105 (11)$_a$	84 (14)$_b$	22.3	<.001*
CELF-III Receptive	107 (13)$_a$	106 (11)$_a$	85 (19)$_b$	12.6	<.001*
WRAML Verbal Memory	96 (13)$_a$	94 (12)$_a$	78 (13)$_b$	11.1	<.001*
WRAML Visual Memory	111 (16)	105 (14)	94 (16)	5.4	.01
WISC-III FDI	106 (17)$_a$	101 (15)$_a$	84 (13)$_b$	10.2	.001*
Gordon Vigilance Hits	95 (15)	88 (25)	71 (52)	2.1	.14
Gordon Vigilance FA's	95 (21)	83 (23)	57 (58)	4.4	.02
WISC-III PSI	106 (16)	111 (15)	97 (18)	3.7	.03
WRAT-3 Reading	111 (8)$_a$	107 (11)$_a$	93 (18)$_b$	9.3	.001*
WRAT-3 Spelling	110 (7)$_a$	103 (11)$_a$	91 (14)$_b$	13.4	.001*
WRAT-3 Math	114 (14)$_a$	101 (12)$_a$	86 (16)$_b$	17.1	.001*
Dominant Hand Pegs	97 (21)	104 (17)	92 (21)	1.8	.18
nonDominant Hand Pegs	92 (22)	97 (29)	93 (19)	0.2	.83

Notes. Means sharing a common subscript are not statistically different at $\alpha < .05$ according to the Tukey HSD procedure; IA = Internationally adopted.

*Significant at Bonferroni corrected level.

[†]Bonferroni adjustment to $p < .003$.

Table 2 Behavior Ratings by Group (T-scores, Mean = 50, SD = 10).

		Normal Control (n = 17)	IA no language difficulties (n = 20)	IA language difficulties (n = 18)	F (2,54)	p†
BRIEF	Inhibition	49 $(8)_a$	61 $(12)_b$	64 $(16)_b$	7.19	.002
	Shift	47 $(9)_a$	56 $(10)_a$	68 $(15)_b$	13.24	<.001*
	Emotional Control	48 $(8)_a$	54 $(13)_a$	63 $(15)_b$	6.85	.002*
	Initiate	54 (10)	58 (14)	65 (10)	4.36	.02
	Working Memory	52 (10)	59 (13)	65 (10)	5.51	.007
	Plan/Organize	52 (9)	59 (12)	63 (8)	5.34	.008
	Organization of Materials	56 (10)	58 (8)	60 (10)	0.46	.64
	Self-Monitoring	50 $(11)_a$	61 $(10)_b$	63 $(10)_b$	8.1	.001*
	Behavioral Regulation Index	48 $(8)_a$	58 $(11)_b$	67 $(15)_b$	11.48	<.001*
	Meta-Cognition Index	53 (9)	60 (11)	64 (9)	5.9	.005
	Global Executive Composite	51 $(9)_a$	60 $(11)_b$	66 $(11)_b$	8.67	.001*
BASC	Hyperactivity	44 $(11)_a$	57 $(12)_b$	63 $(16)_b$	9.88	<.001*
	Aggression	51 (13)	54 (7)	61 (12)	4.27	.02
	Conduct Problems	48 (12)	53 (10)	63 (16)	6.43	.003
	Anxiety Problems	49 (9)	49 (13)	58 (11)	3.37	.042
	Depression	46 (9)	51 (13)	62 (19)	6.41	.003
	Somatization	44 (9)	42 (7)	49 (9)	3.02	.06
	Atypicality	44 $(5)_a$	53 $(11)_a$	66 $(16)_b$	16.25	<.001*
	Withdrawal	46 (7)	52 (16)	55 (18)	1.62	.21
	Attention Problems	51 (10)	60 (13)	63 (9)	6.59	.003
	Externalizing Problems	47 $(13)_a$	55 $(8)_a$	65 $(14)_b$	9.86	<.001*
	Internalizing Problems	46 $(8)_a$	47 $(11)_a$	58 $(12)_b$	7.25	.002*
	Behavioral Symptoms Index	46 $(10)_a$	56 $(10)_b$	67 $(13)_c$	15.21	<.001*
	Adaptive Skills	51 (10)	46 (8)	40 (9)	5.69	.006

Notes. Means sharing a common subscript are not statistically different at $\alpha < .05$ according to the Tukey HSD procedure; IA = Internationally adopted.

*Significant at Bonferroni corrected level.

†Bonferroni adjustment to $p \leq .002$.

was significant, F (2, 54) = 2.27, p = .002. Follow-up ANOVAs were conducted utilizing an adjusted p-value of less than or equal to .002 to determine statistical significance (.05/24 tests, see Table 2).

Normal controls had significantly fewer parent-rated difficulties with regard to inhibitory control, self-monitoring, and hyperactivity when compared with all internationally adopted children, $F(2, 54) = 7.19$, $p = .002$, $F(2, 54) = 8.1$, $p = .001$, $F(2, 54) = 9.88$, $p < .001$, respectively. Additionally, internationally adopted participants with language difficulties had significantly more parent-rated difficulties with regard to shifting between activities, $F(2, 54) = 13.24$, $p < .001$, emotional control, $F(2, 54) = 6.85$, $p = .002$, and with atypical behaviors, $F(2, 54) = 16.25$, $p < .001$, in comparison to normal controls.

Group Differences on fMRI

Forty-two participants completed fMRI scans whereas 13 were unable to be scanned (4 normal control, 6 IA without language difficulties, and 3 IA with language difficulties). An additional 2 participants (1 IA without language difficulties, 1 IA with language difficulties) who did complete scans were removed from analyses due to too much movement artifact. Also, only right-handed participants were included for the following fMRI analyses (thus further removing 1 normal control, 4 IA without language difficulties, and 1 IA with language difficulties) due to the increased incidence of anomalous language organization in left-handed individuals (Tzourio-Mazoyer, Josse, Crivello, & Mazoyer, 2004). There were no significant differences between children who were and were not scanned in terms of age, time spent in the adoptive home, age at adoption, gender, handedness, Body Mass Index, parental education levels, head circumference, attachment group, or Full-Scale IQ. Thus, the following fMRI results included 12 normal controls (7 males/5 females, mean age = 145 ± 29 months), 9 IA participants with no language difficulties (5 males/4 females, mean age = 108 ± 35.6 months), and 13 IA participants with language difficulties (5 males/8 females, mean age = 130 ± 31.5 months).

Receptive Language fMRI

Analyses of the fMRI results using SPM2 comparing activation patterns among groups were conducted:

- *NC vs. IA no language difficulties*: Results indicated that during the receptive language task the NC group had significantly more activation in motor areas compared to the IA no language difficulties group ($T = 4.41$, $p < .001$, Talairach −18, −10, 72). Also, the IA no language difficulties group had significantly more activation in the left superior temporal region compared to the NC group ($T = 4.79$, $p < .001$, −30, −14, 24; $T = 4.30$, $p < .001$, −56, −6, 0, see Figure 1).
- *NC vs. IA with language difficulties*: The IA with language difficulties group had significantly more activation in the midbrain ($T = 3.58$, $p < .001$, 12, −22, −14) and medial temporal areas ($T = 3.30$, $p < .002$, 20, −16, −12) than the controls.
- *IA no language difficulties vs. IA with language difficulties*: The IA no language difficulties group had more activation in the left superior temporal ($T = 4.56$, $p < .001$, −52, −12, 22) and left inferior parietal areas ($T = 4.55$, $p < .001$, −28, −16, 26) compared to the IA with language difficulties group (See Figure 2).

Age and number of questions answered correctly were examined as possible covariates. However, when analyses of covariance (ANCOVAs) were conducted including these covariates, they were found to be nonsignificant predictors in the model. Due to the fact that this resulted in a reduction in power without improving prediction, the covariates were not included.

Expressive Fluency fMRI

Groups were also compared on the expressive fluency task using SPM2:

- *NC vs. IA no language difficulties*: The NC group had significantly more activation in the right inferior parietal ($T = 4.0$, $p < .001$, 36, −26, 28) and right inferior frontal areas ($T = 3.99$, $p < .001$, −22, −78, 14) than the IA no language difficulties group. There were no areas that were significantly more activated in the IA no language difficulties group than the NC group.
- *NC vs. IA with language difficulties*: The NC group had more activation in the left inferior frontal region ($T = 4.81$, $p < .001$, −24, 8, 22, see Figure 3) than the IA with language

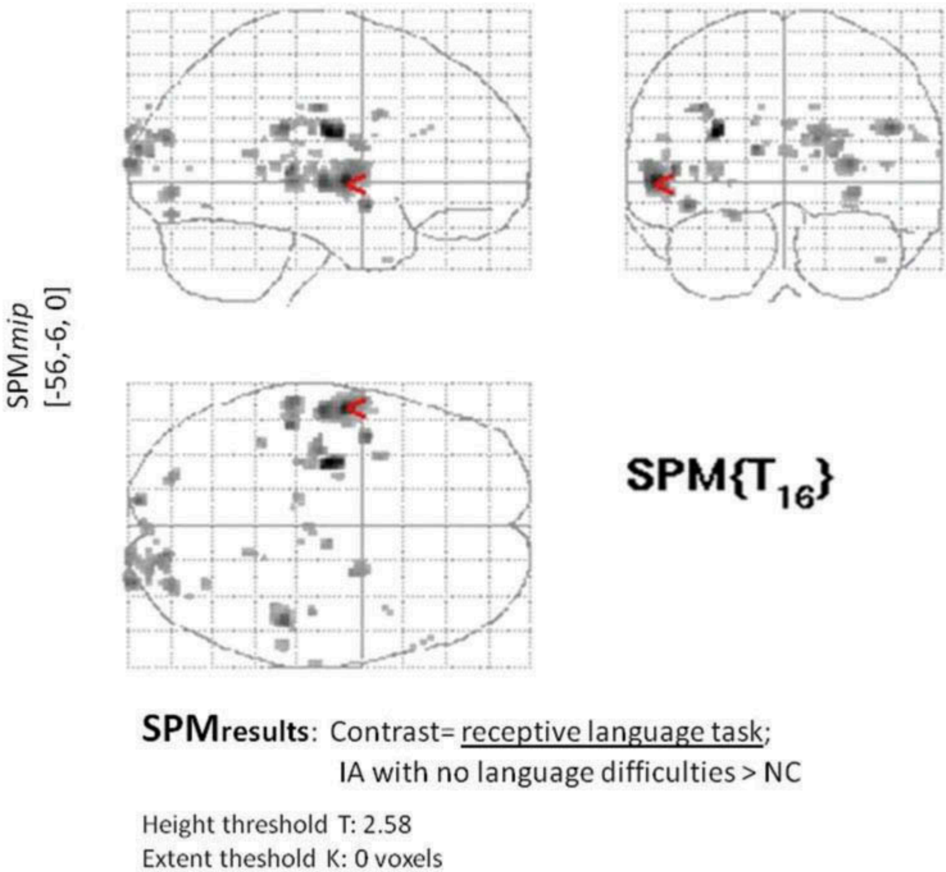

Figure 1 Glass brain showing the pattern of activation for *receptive language* contrast IA with no language difficulties group > normal controls. As can be seen, the IA with no language difficulties group had significantly increased activation in the left superior temporal region.

difficulties group. In turn, the IA with language difficulties group had more activation in the right motor strip ($T = 3.82$, $p < .001$, 46, −12, 58) than the NC group.

- *IA no language difficulties vs. IA with language difficulties*: The IA with language difficulties group had increased activation in the right motor strip ($T = 3.78$, $p < .001$, 16, −2, 46) and left superior temporal region ($T = 3.79$, $p < .001$, −34, −24, 28) compared to the IA no language difficulties group.

DISCUSSION

One of the main goals of the current study was to gain a better understanding of language difficulties in children who have been internationally adopted. To this end, the internationally adopted group was divided into two groups based on their performance on standardized testing of receptive and expressive language in order to assess whether there were any meaningful significant differences between these groups beyond receptive and expressive language test scores.

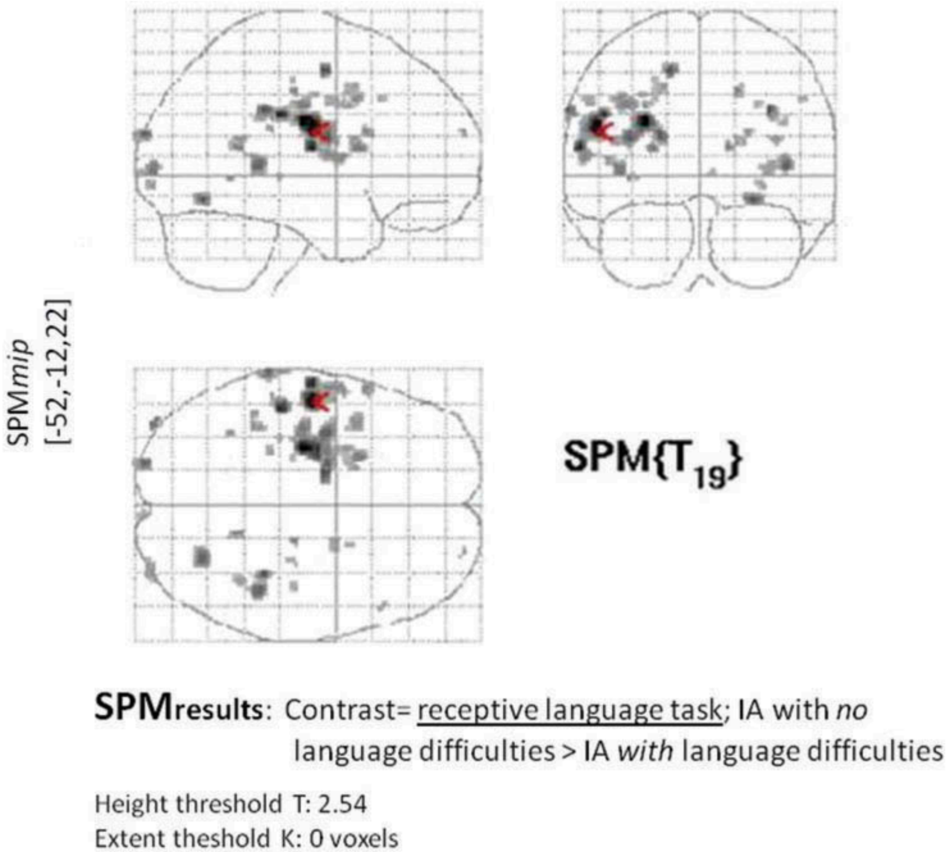

Figure 2 Glass brain showing the pattern of activation for *receptive language* contrast IA with no language difficulties group > IA with language difficulties group. As can be seen, the IA with no language difficulties group had significantly increased activation in the left superior temporal and inferior parietal regions.

Consistent with the hypotheses regarding neuropsychological performance, the internationally adopted participants with language difficulties performed worse on verbal reasoning, verbal memory, academic achievement, and working memory tasks in comparison to both the normal control group and a group of internationally adopted children without language difficulties. These findings correspond closely with several lines of research, including those that link language difficulties with academic skill deficits in nonadopted children (i.e., Snowling, Bishop, & Stothard, 2000) and Eigsti, Weitzman, Schuh, De Marchena, and Casey (2011), which found significant associations between language functioning in internationally adopted children and performance on domain-general cognitive processes such as explicit verbal memory and executive functioning tasks. Importantly, associated difficulties on the working memory tasks for the participants with language difficulties may also be related to the choice of task in the current study, rather than reflecting deficits in this domain specifically. The Freedom from Distractibility Index from the WISC-III is comprised of two subtests, Arithmetic and

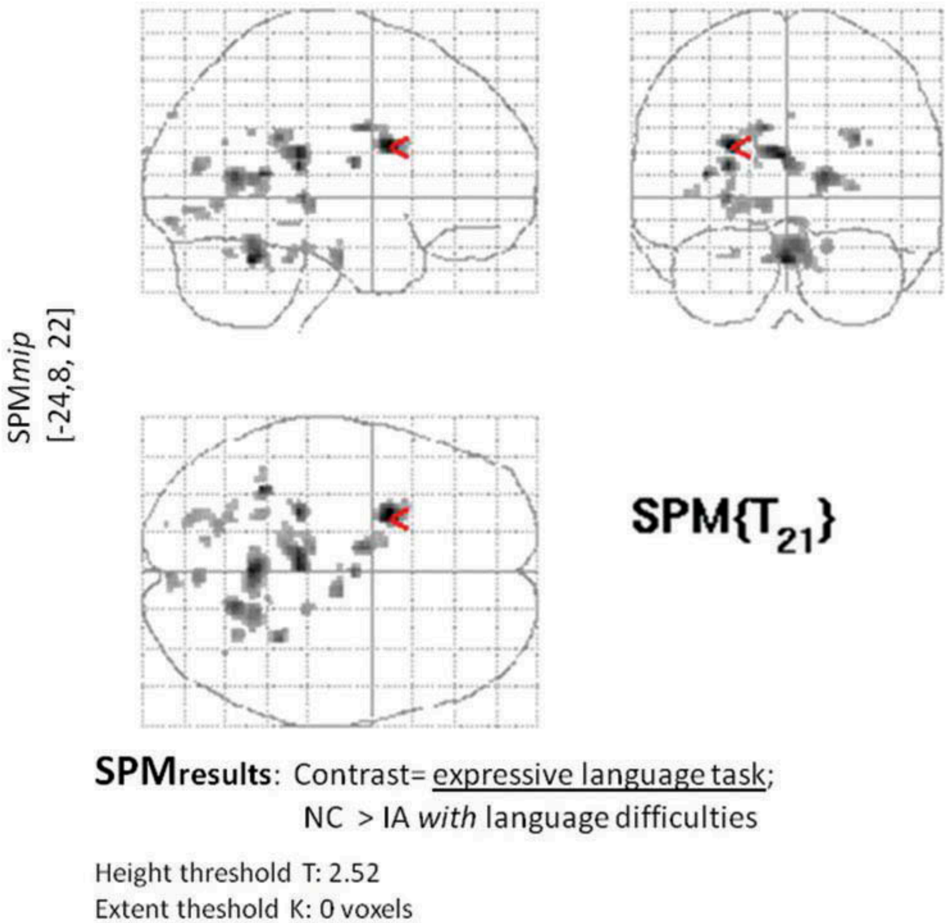

Figure 3 Glass brain showing the pattern of activation for *expressive language* contrast Normal controls > IA with language difficulties group. As can be seen, the IA with language difficulties group had significantly reduced activation in the left inferior frontal region than the normal controls.

Digit Span. Arithmetic, in particular, may be affected by difficulties with receptive language as it requires participants to listen and understand math story problems presented aurally.

In contrast to neuropsychological measures, behavioral ratings by parents less clearly distinguished between the two internationally adopted groups, with several differences observed when comparing normal controls to all internationally adopted groups regardless of language difficulties (hyperactivity, self-monitoring, and impulsivity). The areas of behavioral challenge for internationally adopted participants reported in this study are very consistent with what has been found by others with regard to an Inattentive/Overactive behavioral profile in children adopted from orphanage settings (i.e., Judge, 2003). Internationally adopted children with language difficulties did differ compared with normal controls and internationally adopted children without language difficulties for increased difficulty shifting between activities and in demonstrating more atypical behaviors.

The second hypothesis was also supported as fMRI results reliably distinguished among groups, with internationally adopted participants with language difficulty having less activation in typical language areas (i.e., Broca's area during expressive fluency task) and more diffuse activation while completing language tasks as compared to normal controls and to internationally adopted children without language difficulty. These results suggest that language networks in some internationally adopted children are poorly organized and this may underlie their functional difficulties with language. Functional difficulties on expressive fluency tasks have previously been reported in neuropsychological studies of international adoptees. For example, Callejón-Póo et al. (2012) reported below average performance on a phonemic verbal fluency task in children adopted from Russia. In the current study, increased activation during the fMRI tasks outside of traditional language areas may reflect a more diffusely organized and less efficient language system, similar to what Behen et al. (2009) suggested regarding attention networks. These findings lend further support to structural imaging studies (Govindan et al., 2010; Kumar et al., 2013) that found abnormalities in white matter tracts that support language functioning.

Previous theoretical work has discussed that the lack of exposure to adequate domain-specific and/or experience-expectant stimulation during sensitive period(s) of development is expected to be related to abnormal structural and functional neural development (Gunnar & van Dulmen, 2007; Nelson, 2002) seen in some internationally adopted children. For example, presumed reduced response-contingent care in the orphanage is hypothesized to be related to alterations of the attentional and self-regulation systems resulting in inattentive/overactive behaviors (Gunnar & van Dulmen, 2007). The same may be true with regard to language functioning. For example, lack of or reduced language stimulation, especially during periods in which language skills are emerging, could result in alterations in the pruning and development of language pathways/structures. These pathways, if altered, presumably underlie difficulties with language function over time (see Windsor et al., 2007, for a review). Imaging studies described earlier have supported the fact that certain pathways (uncinate and arcuate fasciculus) are altered in these children (Eluvanthingal et al., 2006; Govindan et al., 2010; Kumar et al., 2013). Domain-specific stimulation/experience guides selective pruning in infants and children, which supports the normal organization of neural substrates that subserve any particular function, serving to increase efficiency of processing (Nelson, 2002). In the absence of sufficient stimulation, abnormal structural and/or functional organization of such substrates occurs, which may in part underlie specific cognitive difficulties such as those found in children who have been adopted from international orphanages. For language in particular, abnormal development of classical language areas (perisylvian cortex) and/or pathways (e.g., arcuate fasciculus) would be expected. It is suspected that a component of the neurocognitive and behavioral deficits observed in children with language difficulties following orphanage stays is related to prolonged exposure to environments that failed to provide the adequate experience-expectant stimulation during specific sensitive periods, resulting in altered/abnormal neurodevelopment (Greenough, Black, & Wallace, 1987). In the current study, significant differences in fMRI activation patterns between groups on language tasks supports anomalous function of language regions in a portion of the children who were internationally adopted.

An alternative explanation for language difficulties following orphanage stays that does not rely on differences in domain-specific exposure is laid out by Eigsti et al. (2011). This model proposes that the experience of early stress from the orphanage experience alters regulation of glutocorticoids, which has a proportionately greater impact on the hippocampus, amygdala, and prefrontal lobe than on other areas of the brain. This physiological process affects domain-general cognitive skills, such as explicit memory and cognitive control that in turn impact children's ability to acquire normal language skills.

It is important to acknowledge, however, that drawing conclusions about the impact of *specific components* of deprivation (e.g., lack of language stimulation, specific types of stressors) on brain structure and function as well as other cognitive variables is limited by additional components of the orphanage experience that are difficult to quantify and/or measure reliably. These variables include malnutrition, prenatal and postnatal exposure to toxins, genetic predispositions, and individual experiences in the orphanages.

For instance, given the weight at time of adoption, body mass indices, and head circumferences, as well as physical examinations soon after adoption, some degree of malnutrition is suspected in a large proportion of children raised in orphanages (Johnson, 2000). Additionally, many studies have supported the fact that children in international orphanages have poor prenatal care and are often exposed to toxins (e.g., Miller et al., 2006). Ames (1997) addressed this issue by examining early adopted children and late adopted children. Early adopted children who were adopted immediately after birth from the hospital, served as a control for the late adopted children in that they likely had similar prenatal experiences and exposures as the late adopted children but had not experienced deprivation in an orphanage setting. She hypothesized that if differences between internationally adopted children were due to prenatal factors only, then the early and late adopted children would be similar and distinct from never adopted children. However, her results indicated that early adopted children were more like never adopted controls across a number of areas, suggesting that the depriving experience of an orphanage contributed to the deficits in the late adopted children.

The current study sought to reduce the impact of outside factors such as pre- and postnatal exposure to toxins as much as possible by developing specific exclusion criteria, such as not allowing children with a strong phenotypic suggestion of fetal alcohol syndrome to participate in the study. Additionally, the internationally adopted participants with language difficulties served as somewhat of a control for the internationally adopted children without language difficulties in that length of time in the orphanage and head circumference (rough estimates of malnutrition) did not differ between these two groups in the current study. It is important to note, however, that the current study does not seek to draw conclusions about the contribution of *specific* components of the orphanage experience (i.e., lack of social interaction) to language functioning; rather it sought to examine the orphanage experience as whole, including factors such as inadequate stimulation, malnutrition, and physical illness.

Given that the internationally adopted groups did not differ in terms of the usual measures of orphanage quality and severity (head circumference, length of stay, body mass index) or in postadoptive factors (time spent in adoptive home, parental education level), alternative explanations (i.e., beyond simple length of exposure to English) for their differences in language functioning and fMRI activation need to be considered. Most likely these factors are related to individual differences with the care received in the orphanage and/or individual differences within the child.

Castle et al. (1999) found that the degree and quality of individualized care in the orphanage (as rated by parents immediately postadoption) was the only orphanage factor that predicted cognitive outcome at later ages. Windsor et al. (2007) addressed this specifically in their study of language in 30-month-old children, some who were in orphanage care in Romania, others who had been in orphanage care but now lived with foster families, and a control group of children raised with their biological parents. Children currently in orphanage care had the worst language functioning of all three groups. However, when examining within-group differences, the children who were currently in orphanage care but had a preferred caregiver had significantly better language skills than children in orphanage care who did not have a preferred caregiver. It is possible that the internationally adopted children in the current study who had normal language skills received better individualized care during their orphanage stay and/or had a favorite caregiver that led to an increase in language stimulation.

Another possible explanation for the differences between the internationally adopted groups on language functioning despite equivalence on other factors could be individual differences specific to the children themselves. Nelson (1999) and Rutter (2007) have both theorized that the heterogeneity in outcome following orphanage stays may be related to an interaction between genes and environment. Results from several studies of internationally adopted children have indicated that certain polymorphisms of the serotonin transporter gene (Kumsta et al., 2010) and the brain-derived neurotrophic factor gene (Gunnar et al., 2012) moderate the impact of orphanage care on cognitive and emotional outcomes. Thus, it is also possible that internationally adopted children with language difficulties have individual characteristics that put them at a higher risk to develop these language problems following the stressful experience of orphanage care.

Within the internationally adopted group, attachment quality significantly differed between the two groups with participants with language difficulty having an increased likelihood to have insecure attachments. Other researchers have also identified a relationship between attachment quality and cognitive functioning. For example, Chisholm (1998) found that insecure attachment was related to worse intellectual functioning and more behavior problems in her sample of internationally adoptees (mean age approximately 6 years old). Additionally, Stevens et al. (2008) found that the presence of inattentive/overactive behaviors in internationally adopted children was linked with disinhibited attachment.

Most likely, the influence of attachment on cognitive functioning (such as language) is bidirectional, with attachment problems influencing cognitive development and cognitive delays/impairments impeding the formation of secure attachments with adoptive parents. Morison and Ellwood (2000) found that children who had been a favorite caregiver (i.e., established a secure attachment with an orphanage caregiver) had better cognitive outcome. Children who are caregiver favorites within orphanages likely receive more stimulation and thus develop better cognitive skills. When these children are adopted into families, they are likely better prepared to establish a secure relationship with their adoptive parent. This secure attachment could result in more positive interactions between adoptive parent and child, thus increasing stimulation and exposure to enriching environments. However, there are numerous longitudinal studies suggesting that children with behavior problems (i.e., Lyons-Ruth, 1996) or cognitive difficulties (van Ijzendoorn, Dijkstra, & Bus, 1995) may have more difficulties establishing a secure attachment. Children who come into the adoptive home with behavior problems or cognitive difficulties likely have a harder time adjusting and may have fewer positive interactions with their adoptive parents, perhaps resulting in insecure attachments with their adoptive parents.

The current study is limited by several factors. First, participants were recruited through contacts including parental support groups, physicians and therapists specializing in international adoption, and parent newsletters. Rather than randomly selecting internationally adopted children from the total population of those adopted into the region, this may have resulted in a self-referral bias in which parents of children with difficulties were more likely to seek to participate. Thus, the percentage of children with language difficulties may be higher in the current study than in the general population of international adoptees. A second limitation is that the group sizes were small. This may impact the fMRI results the most due to the fact that only right-handed participants were examined for these analyses. Future studies with larger samples would be helpful to replicate these findings. A third limitation that is present in the current study, as well as many other studies examining this population, is the choice of control groups. Previous research has utilized control groups of nonadopted peers (i.e., Ames, 1997; Eigsti et al., 2011) as in the current study. This has the potential to provide an important control for socioeconomic status, given that internationally adopted children are more often adopted into families with high socioeconomic status. Other studies have also included a domestic adoption control group that did not spend time in orphanage settings (Rutter & the English and Romanian Adoptees Study Team, 1998). MacLean (2003) discusses the relative benefits of various control groups as each provides a unique and important piece of information. In the current study, only a nonadopted control group was used in order to provide a gender, age, and socioeconomic comparison. This was seen as especially important for the fMRI results, given that the hypothesis was that internationally adopted participants without language difficulty would closely resemble nonadopted children. However, the use of a nonadopted control group with language difficulties would have provided additional evidence about the activation patterns of the internationally adopted participants with language difficulties. Future research utilizing various comparison groups would be helpful in teasing apart and interpreting results in studies of children adopted from international orphanages.

The findings from the current study suggest that a portion of children who have been adopted internationally continue to struggle with language skills even years after entering more enriched family environments. Additionally, language difficulties are often accompanied by worse performance in related cognitive domains, such as verbal reasoning and memory, verbal working memory, and academic skills. Our results also suggest that behavioral and emotional functioning is fairly similar in international adoptees whether or not they have difficulties with language as the more prominent differences in hyperactivity and impulsivity were seen in comparing the nonadopted controls to the entire internationally adopted group. Alterations in the functioning of language regions, as observed on fMRI, appear to underlie some of the language difficulties observed in this population. In addition to assisting treatment professionals and adoptive families by contributing to a more detailed understanding of language in internationally adoptees, the current study also addresses some theoretical issues regarding the importance of experience-expectant stimulation and the detrimental effects of stress on development during sensitive periods. Future studies with larger samples utilizing longitudinal designs that begin shortly after adoption and include comprehensive cognitive assessments as well as imaging techniques would contribute significantly to this growing body of research.

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