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A Functional MRI Study of Language Function in International Adoptees

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Abstract

Objective—To test the hypothesis that international adoption of Chinese and Eastern European girls after 9 months of age results in long term changes in the neural circuitry supporting monolingual English in later childhood.

Study design—Functional MRI (fMRI) was used to test this hypothesis by comparison with a control group of American-born English speakers (n=13). Girls now age 6–10 years adopted from China (n = 13) and Eastern Europe (n = 12) by English-speaking families were recruited through a pediatric hospital-based international adoption center after spending more than 6 months in an orphanage or other institution, a measure of early environmental deprivation. FMRI scans were performed on a 3 Tesla MRI scanner using a verb generation language fluency task. Composite activation maps were computed for each group using a general linear model with random effects analysis.

Results—Chinese born adoptees demonstrate atypical lateralization of language function with an apparent shift of Temporal-Parietal and Frontal areas of brain activity toward the right hemisphere. Eastern European adoptees exhibited a rightward shift relative to controls in both Frontal and Temporal-Parietal brain regions.

Conclusions—Significant differences in lateralization between the Chinese and American-born groups in Temporal-Parietal language areas highlight the possible impact of early tonal Asian language exposure on neural circuitry. Findings suggest that exposure to an Asian language during

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infancy can leave a long-term imprint on the neural circuitry supporting English language development.

Keywords

international adoption; functional MRI; neural circuitry; language; lateralization indices; Chinese; Eastern European

Children adopted from other countries are at elevated risk for long-term language delays due to a lack of verbal interaction and stimulation during the early weeks and months of life, particularly among those institutionalized prior to adoption.

Infants develop the ability to categorize and discriminate speech sounds as well as an awareness of the rhythm and allowable combinations of sounds within their native language long before they utter their first word [3, 4]. Children adopted from other countries face the unique situation of losing their initial language due to lack of interaction with other speakers [2], while learning a new language. The lack of these linguistic skills in their adoptive language places children adopted internationally at additional risk for subsequent language delays [2, 5]. Studies of adoptees from China and Eastern Europe indicate rapid language development following adoption, with older children exhibiting both more rapid learning and greater deficits relative to same-age peers [5, 6]. Although English language production begins later than same-age peers initially, gradually adoptee's language skills catch-up with or exceed their native speaking peers [7]. Differences in prosody, syntax, and phonology between the birth and adoptive language may contribute to interference between the two languages and delays in second language development [6]. Longitudinal investigations of language development in adoptees from Eastern Europe provide limited evidence of interference on emerging language skills [2, 8, 9]. Children adopted from China and Eastern Europe are more likely to have experienced institutionalization prior to adoption [10, 11]. Duration of institutional care prior to adoption has been shown to contribute to long-term cognitive/academic, behavioral, and social difficulties [10, 12].

Functional neuroimaging provides a unique opportunity to understand differences in neural activation and processing that contribute to observed differences in linguistic development. Functional magnetic resonance imaging (fMRI) studies of language processing in native born versus internationally adopted adults indicate persistent neural alterations in processing the second language characterized by less extensive regions of activation relative to the native speakers [13]. Although fMRI studies of children are lacking, these findings point to potential differences in neural substrates of language following international adoption. In this study, we sought to test the hypothesis that international adoption after 9 months of age produces long-term changes in the neural circuitry supporting monolingual English in later childhood. To examine this hypothesis we used fMRI to measure lateralization of language activity in the brains of children adopted from China and Eastern Europe. Lateralization patterns in these groups were compared with those found in an age-matched control group born in the United States.

Methods

The study protocol was approved by local IRB committee and written informed consent was obtained from parents of the participants. Participants included 15 children adopted from China and 14 children adopted from Eastern Europe. Participants recruited for the study were 6–10 years of age at the time of the study and were adopted by English speaking families between 9 months and 3 years of age. To ensure that all children experienced comparable early environments, participants also had to have spent 5 months in an

orphanage or other institution (ie, hospital). China and Russia/Eastern Europe were selected because they are currently among the two largest sources of internationally adopted children in the USA and have been the focus of previous research [3–6, 14]. To equate the groups on sex, only girls were selected because nearly all children adopted from China were female. Two Chinese and two Eastern European children were excluded due to motion during the scan that rendered data unusable for further analysis. The total number of participants included 13 female children adopted from China (mean age: 8.35 ± 1.15) and 12 female children adopted from Russia or Eastern Europe (Eastern European, mean age: 8.26 ± 0.91). Of the Eastern European group 10 of the girls were adopted from Russia ($n=10$) and two were from Bulgaria ($n=2$). Age- and sex-matched American-born controls (AB) ($n = 13$, mean age: 8 ± 0.99) were selected from a normative database [15]. Inclusion and exclusion criteria for subjects in this database were normal hearing, no neurological disorders, normal neurocognitive function as indicated by age appropriate Wechsler Intelligence Scales, normal language ability as measured by Oral and Written Language Scales (OWLS) [16], no history of special education or psychotherapy. The groups were well matched with respect to age and socioeconomic status with no significant differences, and individual subjects were only loosely matched (not one to one matching). This allowed us to align the mean values of key descriptive statistics while keeping the sample size of each group consistent.

Full scale IQ (FSIQ) scores for all three groups were in the average to high-average range and within one standard deviation of the mean as follows: Chinese group Weschler Abbreviated Scale of Intelligence (WASI) [17] Full Scale IQ Score: mean = 107, SD = 13; Eastern European group WASI Full Scale IQ Score: mean = 99, SD = 14; AB group Weschler Intelligence Scale for Children-III (WISC-III) [18] Full Scale IQ Score: mean 110, SD = 11).

The Verb Generation task involves the auditory presentation of a series of concrete nouns every five seconds, to which the participant responds by covertly thinking of as many verbs as possible associated with that noun during the remainder of the 5-second interval [19]. A bilateral finger tapping task cued by a tone every 5 seconds, to mimic the auditory stimulation during the noun presentation, is used as the control task. In addition to minimizing non speech-related activation in auditory cortex due to the auditory stimulation by single noun prompts in the Verb Generation task, the motor control phase also distracts the child from continuing to generate verbs during the control period and provides a reference area of activation within the motor strip as a means of validating task compliance. This task has been used successfully with children > 5 years of age and the supporting neural circuitry has been well documented [20, 21].

MRI scanning was performed on a 3 Tesla Bruker Biospec MRI scanner (Ettlingen, Germany). The entire MRI series, including anatomical imaging, phase reference scans, and fMRI scans was completed in less than one hour. T1-weighted 3D anatomical images were acquired in 9 mins with $1 \times 1.5 \times 1.5$ mm resolution [19]. A T2* weighted gradient echo EPI sequence was used to acquire functional scans. The image parameters used for the scan are as follows: TR/TE = 2000/38 msec, FOV/Matrix = 25.6 cm/64×64, Slice thickness = 5mm. 24–32 transverse slices were acquired in 5.5 minutes.

Data collected from the scanner were then processed using in-house software. Several pre-processing steps including geometric distortion correction and motion correction were performed to enhance homogeneity and reduce artifacts in the images as described elsewhere [19]. The images were then transformed to Talairach space for composite analysis. The fMRI data were post-processed using a general linear model (GLM) implemented in IDL (Interactive Data Language, ITT, Boulder, CO) on a pixel-by-pixel

basis to identify the activated brain regions in a given experiment. Statistical parameter maps generated by this analysis were used for subsequent calculations.

To estimate differences in the distribution of brain activity between groups in a quantitative manner, the fMRI data were further reduced to an index of laterality that parameterizes the degree of left-right asymmetry in language function. Lateralization Index (LI) is a widely accepted measure of hemispheric or regional lateralization of brain function and is thought to represent hemispheric specialization of brain function [19]. In this study language-based regions of interest (ROI) were defined in the Frontal lobe and the Temporal-Parietal junction. Following the method outlined in Karunanayaka et al, [21] group independent component analysis was applied to the concatenated data from all participants and a component corresponding to the left lateralized semantic language network was selected and reflected to the right hemisphere. This component includes both a Frontal and a Temporal-Parietal region, which were separated and used as the ROIs for computation of the LI. Segregation of this left lateralized independent component network into anterior and posterior ROIs is consistent with the widely accepted model for the speech processing network and correspond to the elements identified in the dorsal stream for language processing, responsible for auditory perception of speech and conceptual access mechanisms[22–24]. The LI was calculated for each subject in both ROIs as follows. Within each ROI we counted the number of voxels with z-scores exceeding a threshold value computed as the median z-score for the ROI. The LI was then defined as the difference between the number of voxels in the left (L) and right (R) ROI divided by the total number of the activated voxels [25]: $LI = (L - R) / (L + R)$. Positive LI values indicate left hemisphere lateralization and negative values indicate right hemisphere lateralization. LI values close to zero ($-0.1 \leq LI \leq 0.1$) indicate a bilateral language distribution.

Statistical Analyses

LIs for individuals and mean LIs for each group were computed. Because the matching of subjects was not one to one, we wanted to be conservative and used a oneway Analysis of Variance (ANOVA) to examine the difference in mean LI among the three groups. If the resulting F-test was significant then this test was followed by a post-hoc test to identify groups that are significantly different from each other, accounting for multiple comparisons using a conservative Bonferroni test. To preserve statistical power in our relatively small sample, we did not include handedness as a covariate in the current analysis. This decision is justified based on a previous study that found handedness did not significantly influence language lateralization in normally developing, American born, girls [26].

Results

Thirteen Chinese (13/15 – 86.67%) and 12 (12/14 – 85.7%) Eastern European children successfully completed the imaging protocol and yielded usable data. Table I includes a summary of relevant data from all adopted participants by country of origin, age at adoption, length of institutionalization, IQ, handedness and other potentially relevant variables for language development. Children were institutionalized an average of 16.64 months (range 5 – 29 months) and this did not differ by country of origin. Eight children were identified as having chronic medical conditions including four with allergies and asthma. However, none had known hearing impairments. The composite activation maps generated for each group show the composite t-maps generated for Chinese (n = 13), American-born Control (n = 13) and Eastern European (n = 12) participants using a cluster size = 30; post-processing smoothing filter = 3 mm and threshold t-value = 5 – 10; corresponding to a corrected significance value of $p < 0.05$ (Figure 1).

Mean LI for each group and each ROI are represented in Table II, along with the standard deviations. Histograms showing the frequency of participants in each cohort with a given LI value for both Frontal and Temporal-Parietal ROIs (Figure 2). The difference in mean LIs between groups and the significance of the differences is listed in Table III. The ANOVA test on the LI in Temporal-Parietal area ($F = 7.15$, $p = 0.003$) and Frontal area ($F = 5.03$, $p = 0.012$) were statistically significant, indicating that there are significant differences among the groups. The post-hoc Bonferroni analyses indicated that there was a significant difference in the mean LI between the Chinese group and the AB group for both Temporal-Parietal area ($p=0.002$) and Frontal ROI ($p=0.013$), but the differences between the Eastern European and AB or Chinese and Eastern European groups were not significant. Chinese born adoptees tended to have atypical lateralization of semantic language function with a shift of Temporal-Parietal activation toward the right hemisphere and bilateral language activation in the Frontal ROI (mean $LI_{\text{Frontal}} = 0.03 \pm 0.24$; mean $LI_{\text{Temporal-Parietal}} = -0.05 \pm 0.24$). American-born control subjects, indicated by the solid line in the outline of the histogram plots of Figure 2, tended to be left hemisphere dominant in both ROIs as shown (mean $LI_{\text{Frontal}} = 0.303 \pm 0.23$; mean $LI_{\text{Temporal-Parietal}} = 0.298 \pm 0.28$). This is consistent with previously published findings for monolingual English speaking children performing this task [15, 19, 20]. Eastern European adoptees demonstrate bilateral language activity in both the Frontal area and Temporal-Parietal areas (mean $LI_{\text{Frontal}} = 0.096 \pm 0.21$; mean $LI_{\text{Temporal-Parietal}} = 0.096 \pm 0.17$).

There is some variation in the age at adoption, continued exposure to native language, chronic medical conditions and history of speech therapy among the participants in both adoptions groups. We tested the influence of each of these variables (Table 1) on the LI values calculated for the groups and entering into the group comparisons. First we excluded all participants who had a history of continued exposure to the native language ($n=2$, Chinese group) from the group comparison. LI comparisons in Table III remained significant without these two participants. We repeated this process, excluding participant who received speech therapy and again for those with a chronic medical condition. The LI differences between the groups remained statistically significant in each of these secondary analyses, despite the reduced statistical power. We examined the relationship between age at adoption and LI measures for both Chinese and Eastern European adoptees using Spearman correlation analysis and found no significant association.

Discussion

The present study examined the neural substrates of language in internationally adopted children relative to an American-born comparison cohort. The results provide evidence of persistent differences in lateralization among Chinese adoptees. The children adopted from China displayed a broader and more bilateral distribution of activation in the Temporal-Parietal area and Frontal area. The finding of differences in Temporal-Parietal area only among the children adopted from China may relate to the early exposure of the Chinese adoptees to their native languages; even though none of the children were fluent in their birth language at the time of the study. Prior studies have indicated that native Chinese speakers tend to process tonal aspects of Chinese language utilizing stronger contributions from right hemisphere language areas than is typical of native English speakers [27, 28]. It is possible therefore, that early exposure to Chinese languages, prior to adoption, may have influenced the development of language networks in the brains of the Chinese adoptees, creating a more bilateral representation in the posterior Temporal-Parietal areas. In Chinese-English bilingual adults for example it has been shown that English as the second language is represented by a more bilateral network than the first language (Chinese) during a semantic classification task [29]. The bilateral tendencies for Temporal-Parietal activation in the Chinese born adoptees may relate to maintenance of accurate speech prosody of English

as these children established right hemisphere capabilities to support this aspect of speech during early development. Within this context, early influences from exposure to Chinese may affect the perception and processing of single words and fluency of the noun-verb association processes such that Chinese adoptees rely more heavily on right hemisphere areas than non-Chinese exposed children.

Eastern European adoptees did not exhibit significant lateralization to differences in either ROI compared with the AB control group while the Chinese adoptees exhibited significant differences from the controls for both ROIs examined. This lateralization of differences does not correspond to neurocognitive deficits in the Chinese girls. Weitzman & Albers found deficits in academic abilities and achievement to be more pronounced in children adopted from Eastern Europe than in children adopted from Asia [12]. In our sample the Full Scale IQ in the Chinese group was in the high-average range and surpassed that of the Eastern European but did not differ significantly from the AB group. Although left lateralization of language abilities has been well documented for semantic and expressive tasks, its implications for general intelligence are less clear. Researchers [30] found no differences in measures of academic achievement, foreign languages, and verbal fluency among healthy adults with left, bilateral, or right language lateralization. Similarly, another study of healthy adults [31] found that individuals with more symmetrical (ie, bilateral) distribution of neural connections performed better on verbal recall tasks than those with left lateralization. Consequently it is unclear whether a more bilateral distribution of language function has any implication for neurocognitive ability or function in other domains. Findings from an imaging study in adults adopted from Korea as children by French parents, failed to reveal differences in patterns of activation compared with native French speakers, in response to French, Korean and unknown language stimuli [13]. These findings suggest that the effects of early exposure to Korean on the neural circuitry of language may have fully dissipated by adulthood. In that study all adoptees had reported forgetting Korean.

Participants in our study were adopted to monolingual English speaking, native born American parents. Additional exposure to the birth language occurred following adoption in two Chinese adoptees. Recalculating LI values for the Chinese group without including these two participants did not change the significance of the findings in Table III. On the contrary, without these two participants, lateralization differences between the Chinese and AB groups becomes slightly stronger in both ROIs, providing evidence that early exposure to Chinese may still influence the neural circuitry of language during childhood; even though the language itself appears to be forgotten.

Children adopted from other countries are at risk for delays in language development as a consequence of both environmental deprivation and possible interference from their original language. In the present study, it was not possible to distinguish the consequences of lack of early language stimulation and other environmental factors from leaving one's initial language for a second language. While all of the adoptive children enrolled spent at least 6 months in an institution prior to adoption and subsequently immigrated to the United States with their adoptive parents, the American-born control group did not experience such transitions or environmental deprivation during early childhood. Thus, it is possible that differences between the groups could arise from early environmental differences rather than from early language exposure

Because the verb generation fMRI paradigm used in the current study requires a covert response with no explicit measure of performance during the scan, it is possible that differences in performance between groups accounted for the differences in lateralization of brain activity between the cohorts. When this task has been used extensively in studies of child language development during the past decade [19], developmental trends [20], as well

as group differences [32], have withstood corrections for performance differences on a post-hoc quiz assessing recall of verbs generated during the fMRI paradigm: a surrogate marker of performance during the task. Although brain activation has been found to correlate with performance on an event-related version of the verb generation task in which responses were recorded during the fMRI procedure [33], there is no evidence suggesting that performance on this task had a significant impact on the lateralization of activation in the regions of interest analyzed in this report. Because the study did not include a complete language assessment, we cannot preclude the possibility that differences in lateralization may reflect differences in language abilities. However, given that IQ scores were comparable in the Chinese and AB groups, we do not believe that the current findings can be attributed to differences in overall cognitive ability.

Subtle differences between the Chinese and Eastern European born groups highlight a possible differential influence of early exposure to tonal Asian languages on later brain organization. Further research is needed to disentangle the effects of early language exposure from those of institutionalization and social deprivation. Additionally, research examining the associations between neural activation and performance on language tasks will be necessary to more fully understand the implications of the current findings for child language development.

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Abbreviations

ANOVA	analysis of variance
fMRI	functional magnetic resonance imaging
GLM	general linear model
IQ	intelligence quotient
LI	lateralization index
L	left
ROI	region of interest
R	right
WASI	Weschler Abbreviated Scale of Intelligence
WISC-III	Weschler Intelligence Scale for Children
TR	Repetition Time
TI	Inversion Time
TE	Echo Time
T1	Longitudinal relaxation time contrast MRI
T2*	Apparent Transverse relaxation time and susceptibility contrast MRI
EPI	Echo Planar Imaging

FOV Field of View
FSIQ Full Scale IQ

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Figure 1. Composite fMRI activation maps (z-scores) for the verb generation task in Chinese (left), Eastern European (right) and American-born control (center) groups. Cluster size = 30; smoothing filter = 3 mm, significance threshold $p < 0.05$, corrected for multiple comparisons. Maps are displayed in radiological orientation.

Figure 2.

Distribution of Lateralization Index (LI) values for Frontal and Temporal-Parietal regions of interests (ROIs) for Chinese, Eastern European and American-born control groups. See Table 2B for LI descriptive statistics. ANOVA test between the three groups yielded significant differences in LI for both the Frontal ($F = 5.03$, $p = 0.012$) and Temporal-Parietal ROIs ($F = 7.15$, $p = 0.003$) as described in Table 2B.

Table 1

Participant data with information about the age at adoption in months, FSIQ (Full Scale IQ), handedness, months in institution, speech delays at adoption, speech therapy, exposure to native language and chronic medical condition. Note: IDs in the 1000's indicate Chinese born participants and IDs in the 2000's indicate Eastern European born participants.

Subject ID	Age @ adoption in months	FSIQ	Handedness	Months in Institution	Speech Delays @ adoption	Speech Therapy	Exposure to Native Language	Chronic Medical Condition
1001	23	97	Left	21	Yes	Yes	No	Yes
1002	30	110	Right	14	Yes	No	No	No
1003	23	107	Right	23	Yes	Yes	No	Yes
1004	17	126	Left	17	No	No	No	No
1006	9	107	Right	9	No	No	No	No
1007	13	100	Left	13	Yes	Yes	No	No
1008	12	85	Right	12	No	Yes	No	No
1009	9	99	Right	9	No	No	No	Yes
1010	9	107	Right	8	No	No	No	No
1012	14	110	Right	14	Yes	Yes	Yes	No
1013	22	115	Right	22	Yes	Yes	No	No
1015	24	96	Left	24	No	No	No	No
1017	29	133	Right	28	No	No	Yes	Yes
2001	23	103	Right	21	No	No	No	No
2002	14	128	Left	14	No	No	No	No
2003	15	88	Right	15	Yes	Yes	No	No
2004	42	90	Right	27	Yes	No	No	No
2006	29	98	Right	29	Yes	Yes	No	Yes
2007	28	81	Right	22	No	No	No	No
2008	24	107	Right	9	No	No	No	No
2009	35	90	Right	5	Yes	Yes	No	No
2010	20	90	Left	20	No	No	No	No
2011	16	111	Right	16	Yes	Yes	No	No
2012	42	118	Right	16	No	No	No	Yes

Subject ID	Age @ adoption in months	FSIQ	Handedness	Months in Institution	Speech Delays @ adoption	Speech Therapy	Exposure to Native Language	Chronic Medical Condition
2014	8	86	Right	8	No	Yes	No	Yes

Mean Lateralization Indices (LI) for frontal and Temporal-Parietal regions of interests (ROI) for Chinese, Eastern European, and American-born control groups.

Table II

Groups	Frontal ROI				Temporal-Parietal ROI			
	N	Mean LI	SD	Lateralization	N	Mean LI	SD	Lateralization
Chinese	13	0.03	0.24	Bilateral	13	-0.05	0.24	Bilateral
Eastern European	12	0.096	0.21	Bilateral	12	0.096	0.17	Bilateral
American-born Controls	13	0.303	0.23	Left Lateralized	13	0.298	0.28	Left Lateralized

Table III

Comparisons of LI means between study groups using Bonferroni method for the Frontal and Temporal-Parietal regions of interest (ROI).

Group Comparison	Frontal ROI			Temporal-Parietal ROI		
	Between Group LI Means	95% Confidence Intervals		Between Group LI Means	95% Confidence Intervals	
		Lower	Higher		Lower	Higher
American-born vs Chinese	0.272	0.047	0.497	0.348	0.116	0.580
American-born vs Eastern European	0.207	-0.023	0.436	0.202	-0.035	0.438
Eastern European vs Chinese	0.065	-0.164	0.295	0.146	-0.091	0.383
						0.002*
						0.118
						0.392

Difference in LI means, 95% confidence intervals. Significance between the groups are tabulated for the Frontal and Temporal-Parietal area ROIs.

* p-values are significant.